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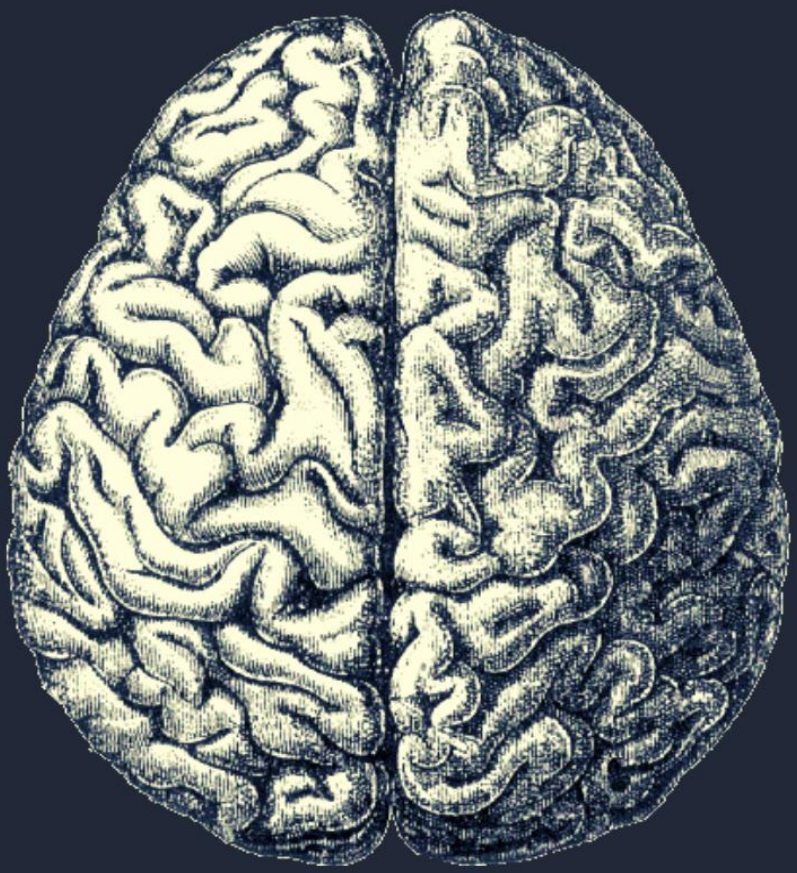

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A neurosurgical challenge: awake mapping in "critical" language area tumours

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Keywords
awake craniotomy, language area tumours, intraoperative neurophysiological monitoring, glioma, neurocognitive evaluation

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ABSTRACT

Introduction. Despite the technological development lesion located in or near language area still represent a challenge for every neurosurgeon. Awake craniotomy and intraoperative neurophysiological monitoring come to our help. Different techniques variation exists among specialized centres. We present our experience and the set up for this procedure.

Materials and methods. We conducted a retrospective analysis of collected data from 10 patients with brain tumours located in or near language area to which we performed awake craniotomy and intraoperative neurophysiological monitoring. They were admitted in Third Department of Neurosurgery," Prof. Dr. N. Oblu" Emergency Clinical Hospital, Yassi, Romania, between January 2014 and July 2018.

Results. Presenting symptoms had a duration more than a month in 60 % of patients. In 80% of them were represented by epileptic seizures and the rest of 20 % had transient aphasia elements. The median age of presentation was 28 years old with a male dominance. The histological reports indicated: fibrillary astrocytoma – 40%, anaplastic astrocytoma – 30%, oligodendroglioma – 20% and metastases – 10%. Gross total resection was performed in half of the cases and subtotal in just one case, in which the spontaneous speech and object naming showed repeated impairment in time of tumour debulking. The surgical intervention was well tolerated by all the patients. The intensity of cortical stimulation used was between 4 – 10 mA. Postoperatively two patients had neurological aggravation, with full recovery at 3 months follow up period, two were stationary and six had symptoms remission.

Conclusion. A young age of presentation, a paucity of symptoms, the chance for an increase in overall survival and progression free survival impose the need for direct

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communication and feedback with the patient in time of tumour resection. Thus, awake craniotomy and intraoperative neurophysiological monitoring is the golden standard for selected cases of language area tumours.

Introduction

The role of surgery in the management of brain tumors is nowadays more and more prominent. This results from the fact that the extent of resection, e.g. in glioma cases is linked to increased survival rate and progression free survival [30]. The most challenging cases of them all are those located in and near eloquent areas, because of the high risk of producing new neurological deficit or worsen the previous ones, after surgery. For this reason, traditionally, the approach of those lesion was less invasive and with great caution [2, 11, 25].

To obtain the goal of a higher degree of resection with minimal neurological impairment, in language area surgery it is used the technique of awake craniotomy (AC) and intraoperative neurophysiological monitoring (IOM) [7, 17]. This is helpful especially for those with preserved speech function like for example those manifested through epileptic seizures. For a proper selection of the cases, suitable for this technique, preoperative neurocognitive assessment is crucial and special battery of tests must be applied. [5, 15].

Despite the fact that the principals of those intraoperative techniques are the same worldwide there are some difference in implementing them. In this study we present our experience and method from surgical, anesthetic, neurocognitive and intraoperative brain mapping point of view.

Materials and methods

We conducted a retrospective analysis of collected data from 10 patients with brain tumors who underwent awake craniotomy and were admitted in the Third Department of Neurosurgery," Prof. Dr. N. Oblu" Emergency Clinical Hospital, Yassi, Romania, between January 2014 and July 2018. Inclusion criteria were: (1) patients diagnosed by contrast enhancement MRI with tumors located in or near language areas, (2) age > 18 years old, (3) preserved preoperative language function or slightly affected, (4) presented at 1 and respectively 6 months postoperative evaluation.

Every patient proposed for this surgical technique, from the neurosurgical point of view was evaluated by the psychologist and the anesthesiologist to confirm that it's completely eligible. Before the intervention they were prepared for 3 days, repeating and working with the psychologist on the items used intraoperatively. The initial assessment consisted in a battery of tests with an accent on reviling even the slit language dysfunction (spontaneous and automatic speech, word repetition, objects/images/forms naming and reading special texts from speech exercises). Other function tested include: executive function, praxis, memory, calculus and the writing.

The neuroanesthesia consisted in asleep-awake-asleep variant. After the induction step, the patient was positioned in a manner that allowed an easy access to the airway, comfortable for him and for the surgeon and also permitted communication with the psychologist. After the patient's head fixation, the skin incision was infiltrate with a mixt of lindocaine and epinephrine. When the craniotomy was finished and we started to open the dura mater the procedure of awakening the patient begun and throughout the tumor resection it was used total intravenous anesthesia (TIVA, Propofol -50 – 150 μg /kgc/min, the opioid used was Fentanyl 0, 5 - 1μg/kgc/h).

The neurocognitive intraoperative assessment was made by the same psychologist who evaluated the language function, testing patient's spontaneous speech, counting, object / images naming and depending on the case, limb muscle strength.

In all cases we performed direct cortical and subcortical brain stimulation with a bipolar probe (ball tips ends 5 mm apart, NimEclipse system, Medtronic) and we chose the high frequency technique. The start stimulation intensity was increased gradually with 0,5mA. We preferred to stimulate all the expose brain with the same intensity and after that to rise it. A site was considered positive if 2 of 3 stimulation lead to language tests dysfunction. The stimulation was repeated in time of resection, the subcortical pathways were tested more often at the end of debulking. The quantification of resection was made using intraoperative echography (Esaote system).

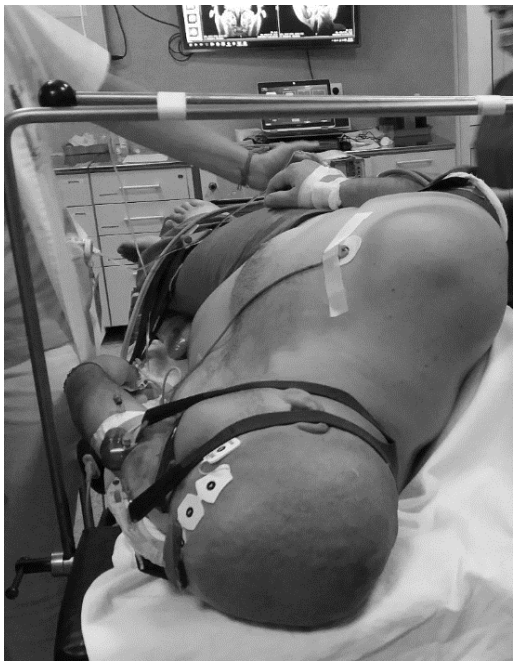
Results

At the beginning of our study we identified a total of 58 cases of tumors located in or near language area,

but only 10 of them have met all the criteria, the vast majority had important speech dysfunction (45 cases with motor or sensitive aphasia, in 2 cases we performed only biopsy and one patient was under 18 years old). The gander ratio showed male dominance; the median age distribution of the group was 28 years old. The clinical manifestation was represented by transient language disturbance with aphasia elements (2 patients) and epileptic seizures (8 patients). The symptoms duration was more than a month in 60% of cases. Other patient's characteristic are presented in Table 1.

No.	Age	Gender	Location	Histology	Degree of resection	Postop evolution	6mo Postop MRI + C	RCTX
1.	66	F	Left T	MTS	Total	Fav	no c.e.	+
2.	46	M	Left T	ODG III	NTR	Fav	no c.e.	+
3.	37	F	Left T	FA	STR	Stat	stat	-
4.	27	M	Left T	AA	GTR	Stat	no c.e.	+
5.	37	M	Left F	FA	NTR	Fav	stat,no rec	-
6.	38	M	Left T	ODG III	NTR	Fav	p.c.e.	+
7.	20	M	Left F	AA	GTR	Agg	p.c.e.	+
8.	22	F	Left T	AA	NTR	Fav	p.c.e.	+
9.	28	M	Right T	FA	GTR	Agg	no rec.	-
10.	28	M	Left F	FA	GTR	Fav	no rec	-

TABLE 1. Some characteristic of patients from the study: F- female, M-male, T-temporal lobe near/in Wernicke area, F-frontal lobe near/in Broca area, MTS- metastasis, ODG-oligodendroglioma, FA- fibrillary astrocytoma, AA- anaplastic astrocytoma, fav- favorable, stat- stationary, agg- aggravation , no c.e. – no contrast enhancement, p.c.e- peripheral contrast enhancement, no rec- no recurrence. RCTX- radio-chemotherapy.

a.   b.

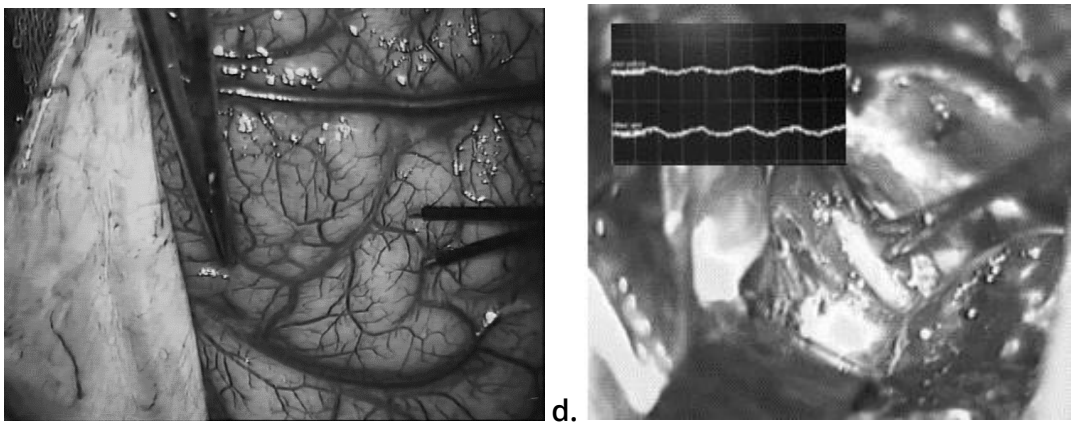


FIGURE 1. a. anesthesia and patient's positioning; b. awake stage, psychologist showing images/cards for naming test; c. brain mapping - direct cortical stimulation with bipolar probe, choosing the site for cerebrotomy; d. deep tumor resection and subcortical stimulation of white matter tracts, no motor respons (upper left) on electomyographic registration of abductor policis and tibialis anterior muscle (NimEclipse, Medtronic).

All patient tolerated well the surgery. The stimulation intensity used was between 4-10mA. In one case, in time of tumor resection we registered language dysfunction with tests performance decreasing. No intraoperative seizures were found. The interval from starting the process of awakening and proper communication was between 20 and 40 minutes. In Figure 1 are presented the intraoperative steps of the intervention, from anesthesia to cortical mapping and tumor debulking.

In two cases we registered postoperative neurologic aggravation as follow: one patient had transient sensitive aphasia elements which remitted completely until discharge, under anti-edematous drugs administration and another case manifested with motor aphasia which needed logopedic therapy. At 6 moths' evaluation the resolution of symptoms was completed.

All patients were monitored al list one year postoperatively (clinical and imagistic). Two of our cases first enrolled in the study presented neurologic deterioration associated with imagistic sign of recurrence and needed reoperation, at 4 and respectively 5 years after the first intervention. The histological reports reveal tumor progression from anaplastic astrocytoma to glioblastoma. Recurrence with no surgical solution was found in one case of grade III ODG, at three and a half years evaluation.

DISCUSSION

Maximizing the extent of resection and minimizing the postoperative neurological and neurocognitive disturbance becomes nowadays mandatory in the surgical treatment of brain tumors [6, 27]. Due to oncological impact on overall survival and progression free survival in low-grade glioma (LGG) cases some suggested an early surgical approach or resection when those lesions are discovered incidentally [21]. To support this statement Duffau presented the idea of supratotal cytoreduction in diffuse gliomas. Even though the study included only 15 patient and the follow up period was short it was registered a reduction in the malignant transformation rate compared with the group of only complete resection [40]. Another proposal from Kamp et al. consisted in the supramarginal resection of metastases. The cases in which it was practiced this technique had a one-year local recurrence rate of 29,1% compared with 58,6% for those with only gross total resection [22].

Although there are some controversies about the modern treatment of high-grade-glioma (HGG) cytoreductive surgery still represents a key element in their management [1, 3, 16]. This is shown by Lacroix et al. how observed on a study of 416 glioblastoma (GB) that the reduction of tumor volume more than 98% is associated with a significant survival advantage [24]. Other study on 500 glioblastomas from 2011 published Sanai et al. noticed a significant increase in survival rate ($p<0,0001$) even when the degree of resection was 78% [32].

It's well known that oligodendroglial tumors have an increase sensitivity to chemotherapy and there is

a development of the oncological treatment with introduction of radiotherapy and immunotherapy in their protocols, however the first step in the management of those lesion is still represented by surgical resection. Studies shows that more than 90% of tumor volume reduction is associated with increase in the overall survival and progression free survival. Having a relatively good prognostic, the quality of life and the neurological status must be one of the neurosurgeon priorities [35, 38, 39].

To achieve such a goal, we need improvement and development of techniques designed to help use us in evaluating and detecting in real time the functional brain tissue and to set the relationship with the lesion. Another reason to implement those methods lays in the fact that brain tumors with a high incidence are usually located in or near eloquent areas. One example is represented by LGGs which are usually found in those locations, because of chemoarchitectonic and cytoarchitectonic similarities [13, 28]. The third most common gliomas – oligodendroglioma are located with predilection in those regions as well (frontal lobe 50-65%, temporal lobe 45%, parietal lobe 7-20%) [35]. Although our number of patients is small, there is a dominance from the histological point of view of LGGs (i.e., fibrillary astrocytoma, 40%) followed by high-grade-glioma (HGG i.e. anaplastic astrocytoma, 30%) and oligodendroglioma (20%), matching the literature data.

There is a shift from imagine - guided surgery (intraoperative functional MRI and neuronavigation) towards functional - guided interventions (awake craniotomy and intraoperative neuropsychological monitoring). This is because neuroimaging concept is based on reduction only not taking into account the functional feedback. Preserving the classical anatomical landmarks for eloquent cortex, which have a wide variability interindividual is not enough. Also, it is hard to differentiate primary critical region from secondary or compensatory ones whose resection wont produces permanent neurological or neurocognitive deficits, thus reducing the degree of resection and the chance of prolonged free survival [12]. Hence the utility of combining the neurocognitive assessment during awake craniotomy and the result form direct cortical/subcortical mapping (DCM).

The history and the development of awake craniotomy starts in 1886 and was done by Victor Horsley, first being used in epileptic surgery. Special anesthetic protocol are needed for this type of surgery and different variants are available by now. The improvement and introduction to asleep-awake-asleep (AAA) method was performed by Penfield, Ingvar and Hall in 1950, later Hansen described and used the awake-awake-awake anesthesia. The third option is represented by asleep-awake variant [36, 41]. Our anesthetic team chose and utilized the AAA variant.

Even though the number of patient with lesion located near/in language area was initially 58 only 10 meet all the inclusion criteria. Because of the complexity and potential risks of this procedure the contraindication must be evaluate wisely. Of the relative ones we enumerate: neurological causes: aphasia, confusion, agitation and cognitive disorders; psychiatric diseases; highly vascular tumors; airway problems; history of difficult intubation, obstructive sleep apnea; morbid obesity [23, 41]. For these reasons in our practice, before deciding to perform this procedure, the psychologist and the anesthetist evaluate the case too and together discuss the eligibility for this type of intervention.

While awake craniotomy provides a close communication and an accurate evaluation, there is still room for other functional intraoperative tools. In a study published in 2010 de Benedictis et al. it is shown that the association between awake craniotomy and DCM increases the extent of resection and secondary the overall survival in patients with LGGs. This is achieved by resecting all the affected tissue up to critical individual limits with no need for safety margin around the eloquent area [10, 11]. Kelm et al. evaluated 61 gliomas located in language area in which it was performed awake craniotomy and observed that GTR was higher in the patient operated and with IOM (61, 7% vs. 28, 6%). Beside the maintaining the integrity of the eloquent cortex, conservation of the subcortical pathways and tracts it's even more important because in this part of the brain the potential for neuroplasticity and reshaping is much smaller comparing to the cortical surface. Damaging the white matter tracts increases the risk for permanent neurological deficits. Although the preoperative imaging modalities have developed and we have many information about de language function localization and about the cortical and subcortical network involvement in this process,

mapping remains an essential step along with awake craniotomy in the surgical management of language area tumors [7, 18, 20, 23].

The advantage of using both methods was reflected in the degree of resection of our cases too. So, because we had a real time assessment of neurologic and neurocognitive performances, we could achieve gross total resection in half of the patients, with more confidence in the postoperative functional and imagistic status. This had a favorable impact especially for fibrillary astrocytoma cases because: first of all, the patients were young (28 yo) whose quality of life was an extremely important outcome factor and secondly the risk of malignant transformation was reduced. Those cases were followed up 2 years with no signs of recurrence.

Still in the light of quality of life preservation and because the admission symptoms were epileptic seizure in 90% of cases, the maintenance of language integrity was essential. Therefore, in one case were decided to perform only subtotal resection. It's about a 37 years old female, with the histological report of fibrillary astrocytoma, in which we had intraoperative language disturbance manifested by speech blockage and even sensitive aphasia when the tumor margins were stimulated and further resect was attempted.

Until now we talked about the role and advantages of an extensive resection, but this dogma should not be obtained by sacrificing the functional status. In 2015 Duffau published an article where is presented the multistage surgical resection. The idea is based on the action of neuroplasticity process. A functional reorganization and the chance for a new intervention without postoperative permanent deficits, in individual cases may be obtain. The reshaping may be induced by the surgery itself and other contributing factor may be represented by the rehabilitation therapy and tumor growth [8, 14].

It's important to know when is the proper time for the patient to stat the testing. Meskelevicius et al. published in 2019 a study in which it's shown the strong correlation between the speed of reaction and the patient's age and the fact that the speed of reaction it's at list two times slower than in the preoperative period, being the slowest in the first 10-20 minute after the awaking. Although we had a small number of cases none of them failed and we could perform the awake surgery in all. Our patients started to react better after minimum of 20 minutes after awakening. During resection the psychologist communicated and evaluated continuously the language and motor function. We didn't find the positive cortical sites for language in all the cases. One possible reason must be the fact that the size of the craniotomy wasn't very big and so the exposed surface of the brain was limited. Another plausible reason is represented by the neural reshaping induced by the neuroplasticity process and so the imagistic landmarks for the eloquent area didn't match with the cortical ones. Some surgeon prefers a larger exposer to find the eloquent cortical sites not basing on these negative language sites [26, 29].

The stimulation technique and the value of stimulus parameters varies between different studies. The discrepancy comes from the fact that there are an inter- and intra-individual factor which determine this, for instance: tumor histological type and symptoms duration [9]. Usually a biphasic current it is used, the intensity it's raised gradually with 0,5 or 1 mA at a maximum of 10 mA. To find the threshold which generates the response and not to generate the after-discharge byproducts it's a matter of perseverance, skill and a challenge [19, 31, 37]. We used the same parameters and in situation were no response was found we didn't raise the intensity higher than 10 mA, because of the increased risk for seizure induction, especially in the patients with these symptoms

In meta-analysis published by Satoer et al in which he evaluated the studies about the possibility of cognitive preservation in eloquent area glioma surgery, in the postoperative period, language function was found altered in seven out of nine studies. At 3 months follow up period five out of six studies have revealed improvement in language deficit to a preoperative level [4, 34]. The percentage of postoperative deficit reposts varies: Sanai found a rate of 14% - new speech deficit, and 8, 4% aggravation; Duffau noticed a high degree of impairment 33%-100%, but with no severe permanent disability [11, 33]. In our cases postoperative speech deterioration were observed in two patients but full recovery was obtained after logopedic therapy. One of them remitted the symptoms even before discharge and the other one at 6 months evaluation returned to the initial stat.

Conclusions

There is a diversity of histological types of tumors located in eloquent areas of the brain, some of them have a relatively slow growth pattern allowing the neuroplasticity process to act. For this reason, the patients presenting symptoms are just mild dysfunction instead of severe problems as in the cases of rapid growth rate tumors. With this in mind and with the chance for a prolonged overall survival, the importance of quality of life impose the necessity for a balanced decision between the degree of resection and the possibility of new postoperative neurologic deficits.

Despite the obvious development of preoperative functional evaluation only a direct approach and communication with the patient through tumor removal may increase the chances for a good postoperative functional status outcome and a higher degree of resection. Awake craniotomy and intraoperative neurophysiological monitoring meet those criteria and are the golden standard for selected cases of 'critical' language area tumors.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Cardiac dysfunction evoked by ECG and echocardiography changes and release of cardiac biomarkers in patients with aneurysmal subarachnoid haemorrhage. Case presentation and literature review

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Keywords
subarachnoid haemorrhage – SAH,
cardiac dysfunction,
electrocardiogram – ECG,
cardiac enzymes,
troponin,
NT-proBNP,
echocardiography

ABSTRACT
The invisible brain-heart link has been observed and described for centuries now, although a greater interest in the matter has been manifested over the past several decades, especially in patients with aneurysmal subarachnoid haemorrhage (aSAH). We present the case of a patient with aSAH and signs of cardiac injury evoked by ECG changes and elevated cardiac enzymes. Furthermore, we reviewed current medical literature by searching the international database PubMed for recent articles on the subject of cardiac biomarkers, ECG and echocardiography changes in the setting of SAH. Our analysis of the selected articles, published between 2012 and 2018, revealed that 22 are patient population studies, 16 are case studies and 6 are reviews of the literature. The most common ECG changes were prolonged QTc andnonspecific ST/T-wave changes. Echocardiography changes included regional wall-motion abnormalities, typically involving the base of the heart (neurogenic stunned myocardium), yet there was also the scenario of Takotsubo cardiomyopathy (stress cardiomyopathy), which affects the apex of the heart. There is a significant statistical association of elevated levels of troponin and NT-proBNP with a bad outcome after SAH, and we should always keep in mind the dramatic scenario of misdiagnosing the cerebral haemorrhage and treating for a coronary syndrome instead. Therefore, the management of aSAH requires a close cooperation between neurosurgeons, intensivists, cardiologists and radiologists in high volume centres.

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INTRODUCTION

Cardiac dysfunction in patients with an intracranial pathology represents a well-known complication and a pressing problem for both neurosurgeons and intensivists treating such a patient. The matter is

probably best described for cases of subarachnoid hemorrhage (SAH), which account for approximately 10% of all strokes. Most SAHs are caused by ruptured saccular (berry) aneurysms.

This is a devastating clinical event, with a high mortality rate - average case fatality of 51%, as well as substantial neurologic morbidity in survivors (1-7).

The complex interactions between the affected brain and the heart are responsible for unique cardiovascular morbidity and mortality - up to 23% of deaths caused by cardiovascular and pulmonary complications (1)(8)(9). A number of cardiac changes occur in the acute phase of SAH, including ECG changes, structural changes on echocardiography, and acute troponin and NT-proBNP elevations (3)(10-16).

Case presentation

A 47-year-old man, with a medical history of hypertension, was brought to the emergency department in Pitesti for repetitive generalized seizures. Upon presentation, he had a Glasgow Coma Scale of 5 (E1, V1, M3), therefore he was sedated and intubated. His wife told the doctors that a few hours earlier he had complained of a severe headache, followed by a reduction in visual acuity for the left eye. Moreover, 2 weeks back, he had presented another severe headache and vomiting. The head CT revealed an interhemispheric hemorrhage and a right-sided fronto-temporo-parietal subdural hematoma. The patient was then transferred to the University Emergency Hospital in Bucharest. Upon admission, he was sedated, with a GCS of 3, anisocoria (mydriasis of the right eye) and left hemiplegia; he was intubated and mechanically ventilated and cardiovascularly stable, with a normal ECG (Fig. 1). An emergency angiography revealed a ruptured aneurysm on the anterior communicating artery, which was embolized. The subdural hematoma was also evacuated.

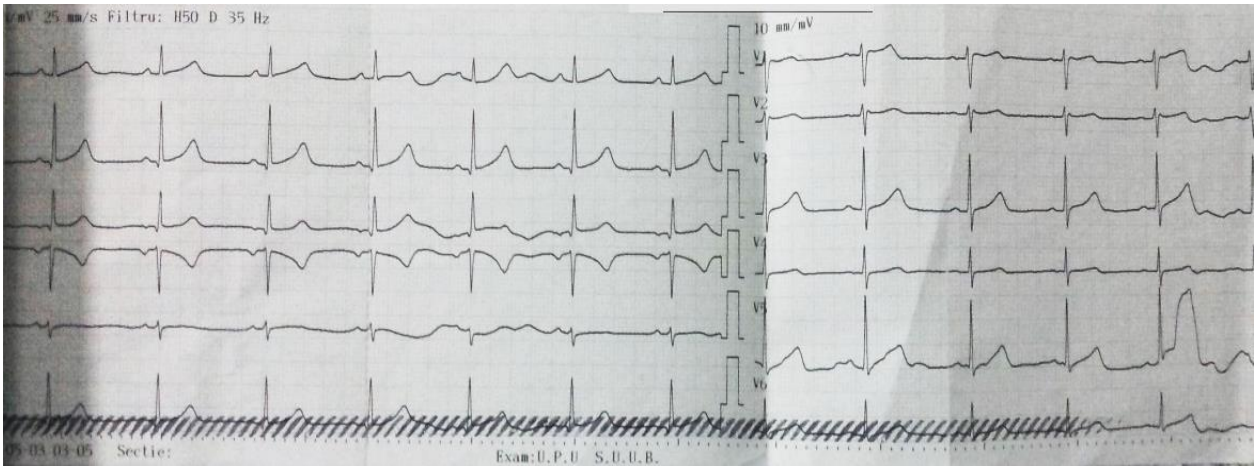

Figure 1. Normal ECG upon admission

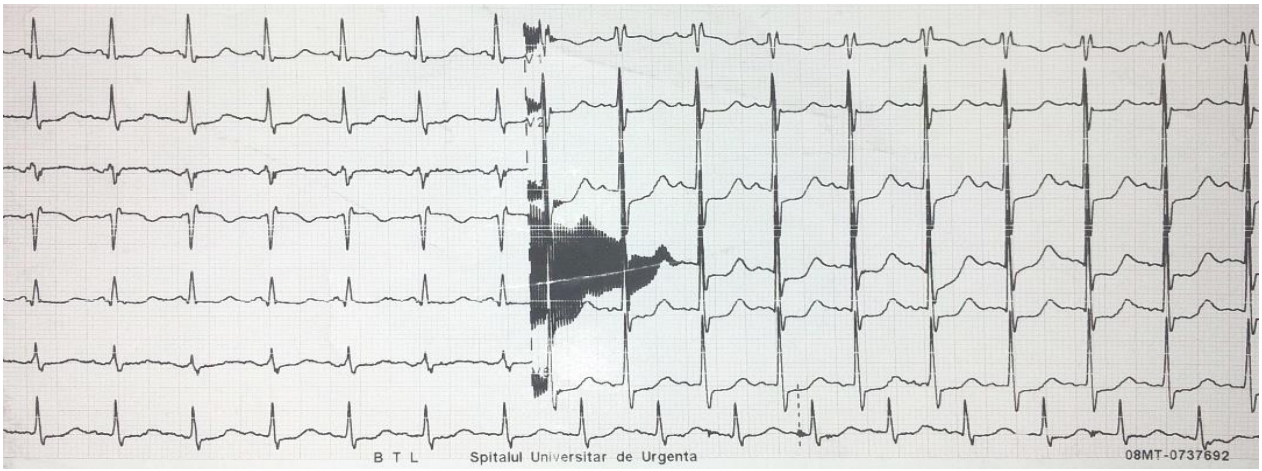

Figure 2. ST segment depression in the anterolateral territory (V2-V6)

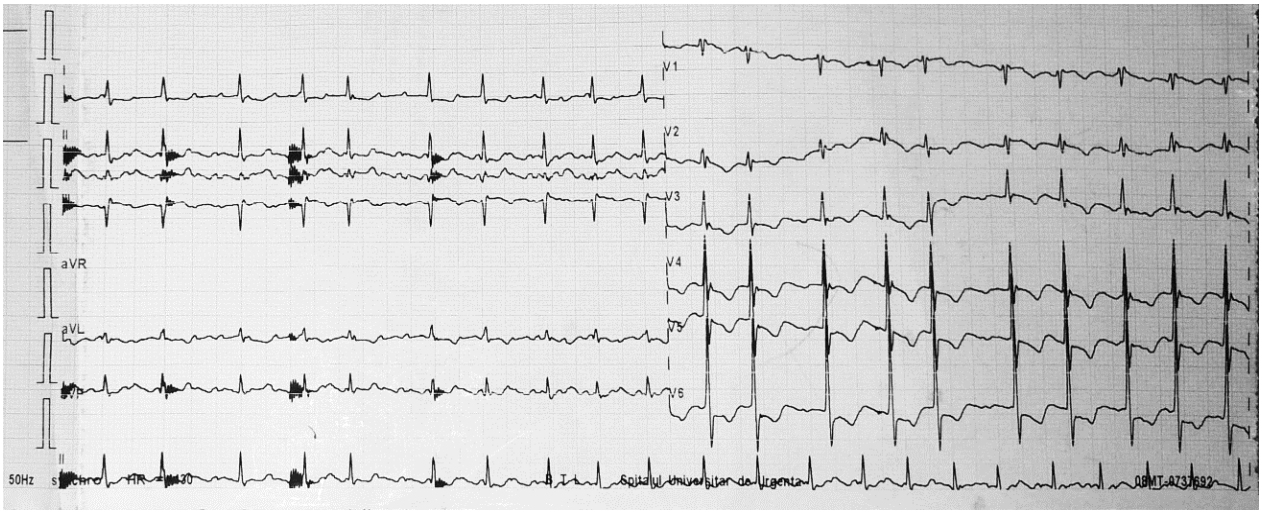

FIGURE 3. Atrial flutter, with variable atrio-ventricular block, and antero-lateral ST depression

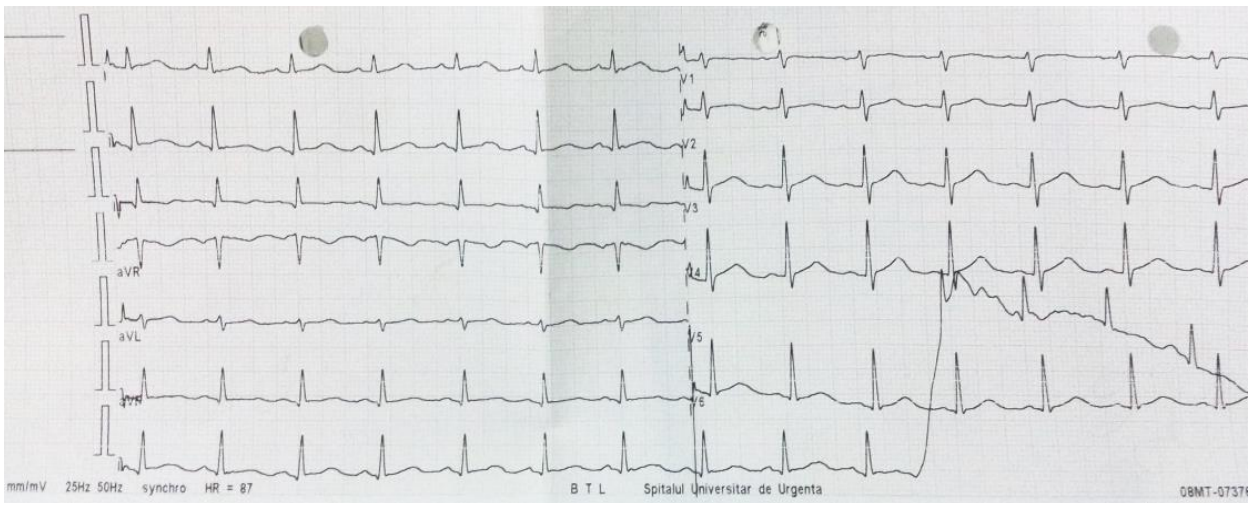

FIGURE 4. T wave flattening in DII, DIII, aVF, V1-V2 and V6

On the third day, the patient was neurologically better – a CGS of 8 (E2, V1, M5), maintaining left hemiplegia, yet still intubated and mechanically ventilated, with an arterial pressure of 105/65 mmHg, tachycardic 108 bpm. His ECG started changing, at first with ST segment depression in V2-V6 (antero-lateral territory), followed by atrial flutter, with variable atrioventricular block, and anterolateral ST depression (Fig. 2,3). Cardiac enzymes were also high – CK 807 U/L, CKMB 105 U/L, troponin I 1,5 ng/ml and NT-proBNP 173 pg/ml, with normal creatinine clearance and electrolytes. On echocardiography, there was a normal left ventricular ejection fraction and no wall-motion anomaly, thus the scenario was interpreted by the cardiologist as neurologically mediated. CK (1262 U/L) and CKMB (203 U/L) reached their peak value 8 hours later, while troponin had a maximum value of 8,26 ng/ml approximately 20 hours later.

A repeated head CT on day 5 revealed a frontal intraparenchymal hemorrhage of 55/14 mm in axial plane and 27 mm cranio-caudal and a bilateral frontal cortico-subcortical ischemic area in the vascularisation territory of the anterior cerebral artery. The vasospasm was confirmed by 2 subsequent angiographies performed on day 5 and 7, when Nimotop (nimodipine) was also locally injected.

CK and CKMB normalized on day 5, while troponin I normalized on day 7. On day 36, the patient was conscious, with a CGS of 13-14 (E 4 V 3-4, M 6) and a residual left hemiparesis, spontaneously

breathing, cardiovascularly stable and a relatively normal ECG (T wave flattening in DII, DIII, aVF, V1-V2 and V6) (Fig. 4).

Material ad method for the literature review

We queried the international database PubMed for recent articles using the syntax: subarachnoid [title/abstract], hemorrhage [title/abstract], cardiac [title/abstract], restricted with filters: publication date from 2012/01/01 to 2018/04/01; humans. Afterwards we selected 44 articles tackling the aspects of raised levels of troponin and NT-proBNP and ECG and echocardiography changes in patients with SAH.

Results

Our analysis of the selected articles revealed that 22 are patient population studies, 16 are case series and 6 are reviews of the medical literature.

ECG abnormalities

Jeong et al., in a study of 122 patients with SAH and no previous heart disease (62% women) [17] aimed to determine the frequency, influencing factors and impact on outcome of cardiac arrhythmias after aSAH. 50% of their population had a clinically significant ECG change, the most common type being nonspecific ST-T changes. A multivariate analysis showed no significant association of various factors (age, sex, Hunt-Hess grade, Fisher grade, hypertension, symptomatic vasospasm and ICU length of stay) with clinically significant arrhythmia. Yet, the presence of ECG changes wasindependently predictive of death and poor outcome. On the other hand, July et al. (18) managed to demonstrate that ECG abnormalities were significantly associated with total cortisol an day 4 and free cortisol on day 2, while Amin et al. (19) observed a statistically significant association between SAH and QTc prolongation.

Prolonged QT was the most prevalent ECG change in 413 patients from CONSCIOUS-1, a prospective randomized trial of clazosentran for the prevention of angiographic vasospasm (10). In this group of patients, the authors tried to identify ECG changes associated with angiographic vasospasm following SAH and concluded that, on multivariate analysis, QT prolongation and tachycardia are both associated with this complication. Moreover, tachycardia and ST changes were associated with worse clinical outcome.

In another large prospective study - 447 SAH patients, Schmidt et al. (20) confirmed that uncontrolled prolonged heart rate elevation (PEHR) is associated with an increased risk of major cardiopulmonary events: hypertension and hypotension requiring vasoactive therapy, pulmonary edema, myocardial injury evidenced by troponin I elevation and poor outcome. 39% of their patients developed PEHR (heart rate of at least 95 beats/minute, for more than 12 hours), with 68% of them having late-onset PEHR (more than 72 hours after SAH onset), which was correlated with an increased risk of delayed cerebral ischemia from cerebral vasospasm. Multifactorial logistic regression revealed the factors associated with PEHR: nonwhite race, Hunt-Hess score of at least 4 at admission, high admission APACHE-2 score and modified Fisher score. In this study, pre-hospital beta-blocker use was protective against PEHR.

By contrast, in a retrospective review of 254 patients with SAH, Crago et al. found (21) no relationship between the pre-hospital use of ACE inhibitors and/or beta-blockers and the development of pulmonary congestion, elevation in troponin or CKMB, heart rate, ECG changes or echocardiography findings. Moreover, a relationship was described between the use of these drugs and arrhythmias (ventricular or supraventricular) recorded by Holter monitoring, with patients taking beta-blockers.

A study from Japan (22) draws attention on the clinical scenario of comatose patients resuscitated from SAH-associated out-of-hospital cardiac arrest (OHCA) (SAH-OHCA) who often have clinical signs that mimic acute coronary syndrome-associated OHCA (ACS-OHCA) patients. As the management of SAH is totally different from that for ACS, doctors should be able to differentiate between the two as quickly as possible. Yamashina et al. analysed the retrospective data of 1259 consecutive OHCA and included in their study 23 resuscitated comatose ACS-OHCA patients and 20 resuscitated comatose SAH-OHCA patients. ST-T abnormalities on the ECG suggesting myocardial damage were noted in most patients in both groups (95% in the ACS-OHCA and 85% in SAH-OHCA), yet reciprocal ST depression was significantly more often absent in the SAH-OHCA group. Moreover, pulseless electrical activity (PEA) or asystole as the initial cardiac rhythm, female gender, and preserved left ventricular ejection fraction were

significantly more common in the SAH-OHCA group. In their group, initial PEA/asystole and presence of 1 other factor was sufficient to differentiate between SAH and ACS-OHCA patients (100% sensitivity, 91% specificity, 95% accuracy).

Almost all the 16 case reports also point to the possibility of SAH masquerading as an ACS (23-36). One of them presents the scenario of SAH with the pattern of sinus node dysfunction on the ECG (37), while Elsharkawy et al., on a cohort of 20 SAH patients observed that patients with fluctuating ECG changes had a poor outcome compared with patients with fixed abnormalities (38).

Troponin and NT-proBNP elevation

In a retrospective review of 617 patients with aSAH conducted by Ahmadian et al. (13), 14.1% (87 patients) required a cardiac evaluation: 63% had arrhythmia, 47% suffered a myocardial infarction and 31% developed heart failure. The majority of cases with a myocardial infarction (90.2%) were non-ST elevation MI, while atrial fibrillation was the most common form of tachyarrhythmia described. Among the patients who had a cardiac event at the time of a SAH, those with myocardial infarction, and in particular those with a troponin level greater than 1 mcg/L had a 10 times higher risk of death.

Oras et al. (11), in a single-centre prospective observational study including 126 SAH patients, managed to conclude that both peak levels of troponin (hsTnT in their study) and NT-proBNP are independently associated with cerebral infarction due to delayed cerebral ischemia. hsTnT had its peak level at admission followed by a daily decline; by contrast, NT-proBNP had lowest levels on day 1 after SAH and increased on days 2 to 4. Moreover, age, poor neurological status upon admission, cerebral infarction and peak hsTnT were independently associated with poor late outcome.

The area under the curve (AUC) for the first 4 days was used by Nyberg et al. (39) to quantitatively measure the BNP load during the first critical part of the disease in 138 patients with a SAH. A more severe SAH defined by a higher Fisher and World of Neurosurgical Societies grade, neurological deficits, an aneurysm, infections or higher levels of troponin I at admission had a larger AUC for NT-proBNP. Women, older people and those with poor outcomes also had larger AUC for NT-proBNP.

Terao et al. (40) investigated the relationship between urinary albumin/creatinine ratio (ACR), NT-proBNP level and neurological outcome after SAH in 61 patients. NT-proBNP highest levels were above normal limits in 93% patients, while 85% of them developed microalbuminuria. The study demonstrated on the one hand that the peak value of NT-proBNP was significantly associated with peak troponinI value and highest ACR. On the other hand, peak ACR and Hunt-Hess grade were independent predictors of poor neurological outcome.

Neurogenic myocardial stunning

Prunet et al (3)(41) evaluated cardiac glucose metabolism and myocardial perfusion and assessed the duration and reversibility of cardiac sympathetic impairment after SAH in 30 hemodynamically stable acute phase SAH patients, by using F-fluorodesoxyglucose positron emission tomography (^{18}F-FDGPET), ^{99m}Tc-tetrofosmin and ^{123}I-meta-iodobenzylguanidine (^{123}I-mIBG). 83% revealed initial impairment of cardiac glucose metabolism and the defect pattern could not be explained by a single coronary artery distribution, while 90% exhibited initial impairment of cardiac sympathetic innervation. All patients had normal myocardial perfusion and normal left ventricular systolic function. There was a concordance of ^{123}I-mIBG and ^{18}F-FDG uptake abnormalities, as well as a common temporal evolution, which suggests the close relationship between myocardial sympathetic function and glucose metabolism; yet neither of them produced left ventricular systolic or diastolic dysfunction in this group of patients (41).

In a group of 300 ash patients, Malik et al. (42) tried to determine the risk factors for the occurrence of neurogenic stress cardiomyopathy (NSC), which they defined as having at least one of the following: ECG changes (long OQ, T wave inversions), troponin level higher than 0.1 or decreased ejection fraction and wall motion abnormalities on the echocardiogram. After a multivariate analysis, they concluded that higher Hunt-Hess grade on admission, smoking, older age and lack of hypertension were the strongest predictors of NSC.

In a larger group of 715 SAH patients, Bihorac et al. (43), aimed to compare short- and long-term outcomes in patients with different patterns of regional left ventricular dysfunction (RLVD) as a manifestation of stress-induced cardiomyopathy

after SAH. 28% (200 patients) of these patients had an echocardiogram for clinical evidence of cardiac dysfunction, 30% of whom (59 patients) had RLVD. The observation was that the risk of death was significantly higher in patients who need an echocardiogram in the first place, regardless of the presence or absence of RLVD on that echocardiogram.

Conclusion

SAH should probably be the most feared type of stroke event among clinicians. On the one hand, it affects younger adults and individuals in their prime, therefore the individual disability burden and consequential social impact is devastating. On the other hand, SAH is a multisystem disease, and medical complications have been identified as factors that can contribute to worse outcomes, thereby awareness of this fact is warranted.

Cardiac abnormalities are common after SAH, even in non coronary-disease patients. Clinically significant arrhythmias after SAH are associated with a high mortality rate, as well as serious cardiac and neurological comorbidities [17]. These patients should be submitted to a close cardiac monitoring.

Some patients (20-30%) present with acute cardiac enzyme elevation, and an increase in troponin I, which occurs in more severe patients, correlates with poor long-term outcome. Increased levels of troponin, but also NT-proBNP, upon admission are both independently associated with delayed cerebral ischemia (11)(12). Troponin I and NT-proBNP elevation should therefore be early detected and closely monitored and those patients timely managed by a multidisciplinary team of doctors (44).

We should also bear in mind the fact that cardiac alterations associated with SAH include both systolic and diastolic dysfunction of the left ventricle, and that, in order to prevent pulmonary and other organ congestion due to heart dysfunction, it is strongly advised to perform echocardiography on admission of a SAH patient, and to repeatedly monitor this way a patient with SAH and RLVD during the triple H therapy (2)(14)(34)(36).

For comatose OHCA resuscitated patients, initial ED evaluation might be sufficient to differentiate between an ACS or a SAH as the cause of the cardiac arrest, prior to further, time consuming tests (22).

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Finite element method to study cervical postoperative stability

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ABSTRACT

A cervical spine model built by means of the finite element method was used to determine the risk of postoperative cervical instability in relation to the type of discectomy, in cervical disc herniation. Furthermore, this model was employed to check whether, at the adjacent levels of the fusion discectomy, the intervertebral translation during cervical movements will maintain the normal amplitude [normal ROM] or its amplitude will decrease.

The intervertebral displacement and the tension arising from motion and weight in the cervical vertebral structure were thus determined through computer modelling using the above-mentioned method and the software Abaqus. It resulted in a cervical spine model consisting of 739666 finite elements interacting through 210530 nodes, with biomechanical properties following the vertebral anatomical structures modelled.

Two movement situations were studied to determine the behaviour of this model. Firstly, the moment of force for flexion and extension of 1 Nm. Secondly, we aimed to establish the maximum flexion and extension for a normal cervical spine model in order to determine the momentum value of moving forces for each of them.

It was showed that both anterior cervical microdiscectomy without fusion and cervical discectomy with cage fusion (used for the surgical treatment of cervical disc herniation at one level), ensure postoperative vertebral stability when performed properly. Both types of surgery reduce the mobility of the cervical spine, although more in the case of fusion discectomy. The intradiscal tension increases in movement in both models, with a higher intensification in the fusion discectomy model.

The practical conclusion is that microdiscectomy without fusion is preferable in the case of a single-level cervical disc herniation occurred to a cervical spine without instability.

Keywords
cervical discectomy,
cervical postoperative stability,
finite element method,
microdiscectomy without fusion

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INTRODUCTION

Cervical spine stability after discectomy is evaluated biomechanically by determining the intervertebral displacement, tensions and stresses in the cervical spine. The finite element method is based on dividing complex structures into smaller ones, called finite elements, with simple geometric forms and easily to be included within the simulation of the process to be studied while tracking their parameters in situations close

to real conditions. These finite elements are interconnected with each other at points called nodes, which define the requests as unknown parameters, respectively the movement or displacement and the load or stresses. We used a cervical spine model built through this method to determine the risk of postoperative cervical instability in relation to the type of discectomy.

MATERIALS AND METHODS

We worked with computer programs for image processing, for modelling finite elements of the cervical spine and simulating cervical motion and load. More precisely, we used the MIMICS software, which creates 3D models from 2D DICOM images. Thus, the images in DICOM format obtained from the CT scan of a normal cervical spine were introduced in MIMICS, transformed into points with 3D spatial coordinates, then exported to a special format (.stl). MIMICS software transposes images scanned by CT into a point cloud with spatial coordinates, creating a 3D model. Moreover, it can recreate the model of bone structures. The vertebrae model was obtained this way, whilst the other tissues, the intervertebral disc and ligaments were added manually.

The cervical vertebral model made in MIMICS in the form of coarse discretization was further processed to be used through the finite element analysis model. The vertebrae were imported into Abaqus CAE and the cervical spine model was recreated.

To build a model of the cervical spine with finite elements as closest to the real one, we assigned to each modelled structure the specific biomechanical properties of the column (elasticity, rigidity /deformability, resistance to deformation represented by Young's module, and Poisson's coefficient) for each finite element corresponding to the modelled anatomical structures (Table 1).

TABLE 1. Characteristics in terms of elasticity and strength attributed to the corresponding finite element of the modelled anatomical structures.

Anatomical structure	Finite element type	Modulus of elasticity (MPa)	Coefficient of Poisson
Vertebra - the bony cortex	First-order tetrahedral element:4 nodes	10.000	0.29
Vertebra - cancellous bone	First-order tetrahedral element:4 nodes	100	0.29
Anterior longitudinal ligament	Bar with 2 nodes	30	0.3
Posterior longitudinal ligament	Bar with 2 nodes	20	0.3
C1-C2 joint capsule	2nd order tetrahedral element:10 nodes	7.7	0.39
C1-C2 supraspinous ligament	Bar with 2 nodes	10	0.3
Yellow ligament C1-C2	Bar with 2 nodes	10	0.3
C2-C3 joint capsule	2nd order tetrahedral element, hybrid:10 nodes	10	0.3
C3-C7 levels joint capsule	2nd order tetrahedral element, hybrid:10 nodes	20	0.3
Yellow ligament levels C2-C7	Bar with 2 nodes	1.5	0.3
Interspinous, supraspinous ligament, levels C2-C7	Bar with 2 nodes	1.5	0.3

Thus, a cervical spine model consisting of 739666 finite elements that interact through 210,530 nodes resulted, with biomechanical properties according to the modelled vertebral anatomical structures (Figure 1).

Once this model with finite elements was settled, we were able to determine its behaviour at load and movement. In this purpose, we appreciated that the head weighs approximately 4.5 - 5.5 Kg and exerts an average force of 50 N applied to the vertebra C1, in the vertical direction lower oriented. Movements in the cervical spine are complex, but instability is evident especially in those of flexion and extension.

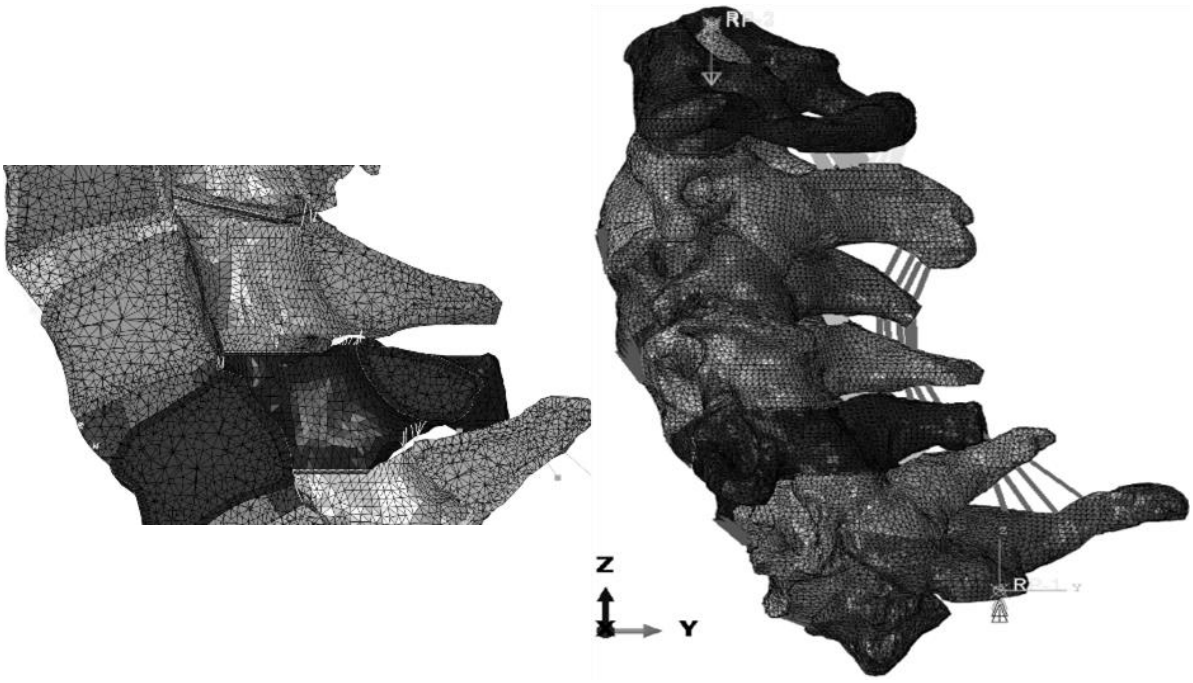


FIGURE 1. Cervical spine model obtained using the finite element method.

To study cervical instability during the flexion-extension movement, we considered the C7 vertebra as a fixed point. Then, we applied a force of displacement to the upper extremity of the cervical spine, respectively at the level of the C1 vertebra.

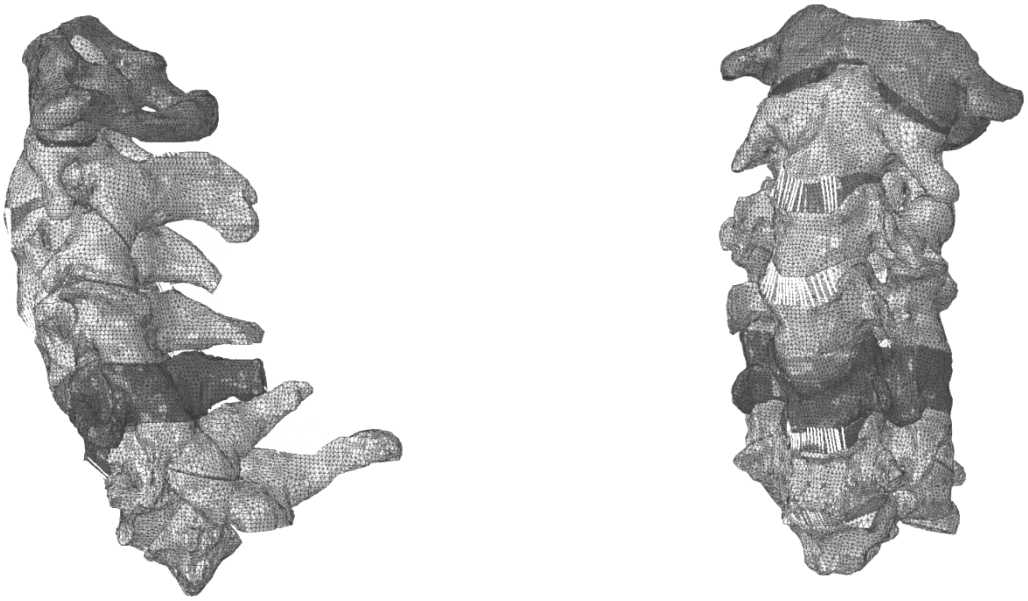
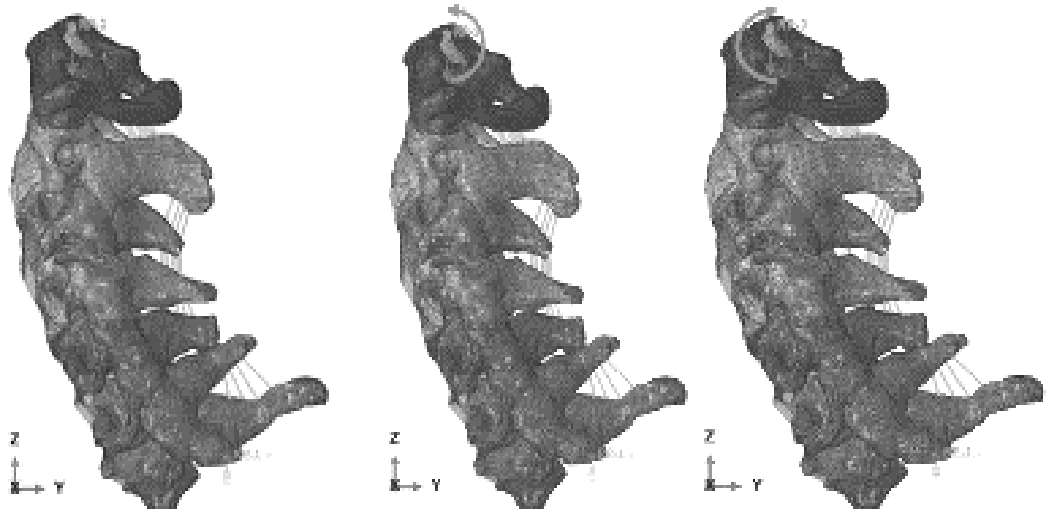


FIGURE 2. Cervical spine model obtained using the finite element method

Three models of the cervical spine were studied using this method:

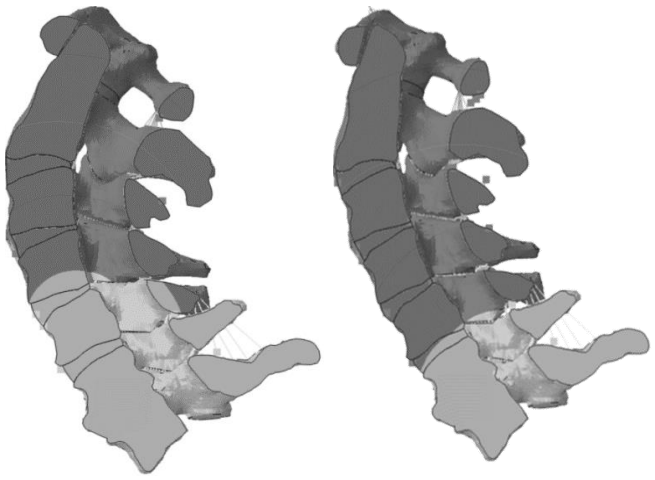
- a normal cervical spine,
- a cervical spine with microdiscectomy without fusionat the level C6-C7
- a cervical spine with discectomy and cage stabilization at the level C6-C7



A. B. C.

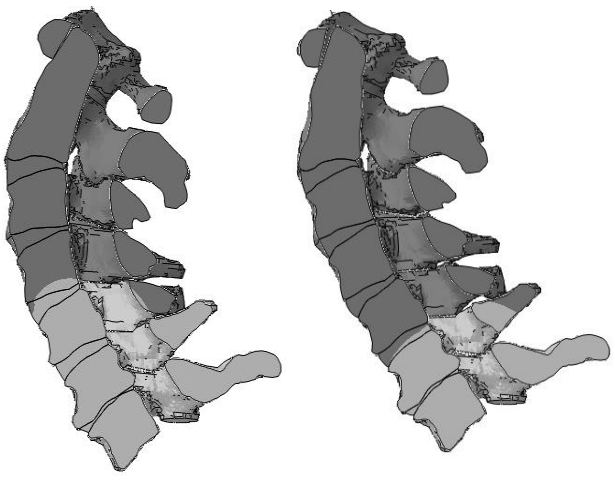
Figure 3. Cervical spine model built by using the finite elements method (a), with the moment of the displacement force for the flexion (b) and extension movements (c).

For each model, movements of flexion and extension were simulated starting from the cervical intermediate position by applying a displacement force for flexion and extension, respectively by considering a moment of force applied to the movement.



A. B.

Figure 4. Flexion movement by applying the force of 1 Nm
a. the model with microdiscectomy C6-C7
b. the model with discectomy and cage C6-C7



A. B.

Figure 5. Extension movement by applying the force of 1 Nm
a. the model with C6-C7 microdiscectomy
b. the model with discectomy and C6-C7 cage

Two movement situations were studied to determine the behaviour of these three models, as follows:
- the moment of force for flexion and extension of 1 Nm,
- establishing the maximum flexion and extension for the normal cervical spine model and determining the

value of the momentum of the movement force for these movements.

These values are: the moment of force for maximum flexion is 7.3 Nm and the moment of force for the maximum extension is 2 Nm.

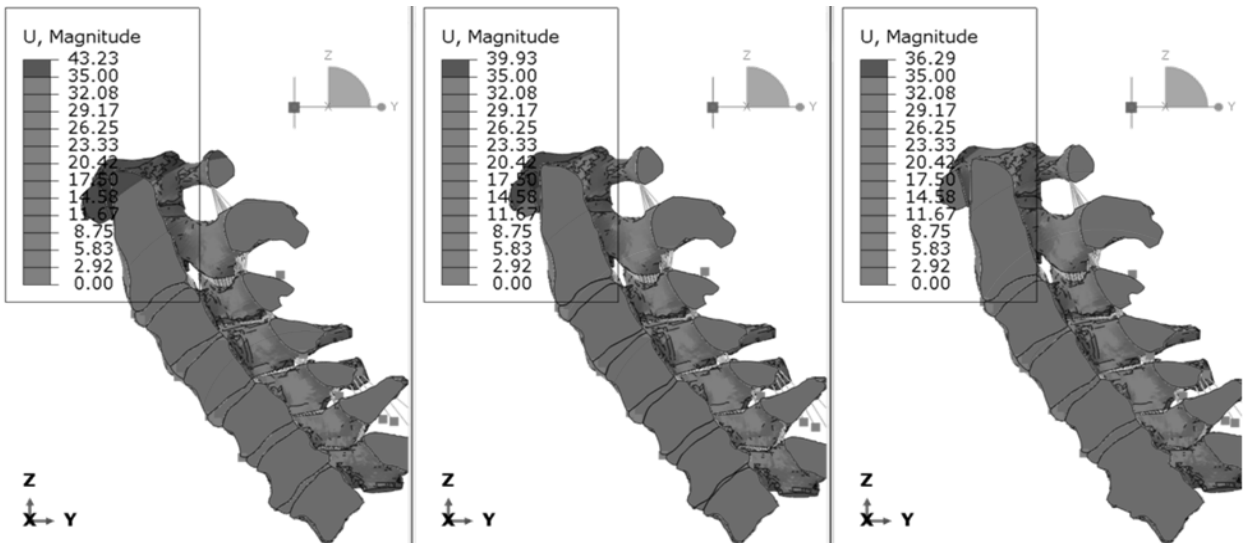


Figure 6. Flexion movement for the moment of force of 7.3 Nm, with cervical displacement at a. normal column, b. C6-C7 microdiscectomy and c. C6-C7 discectomy and cage model.

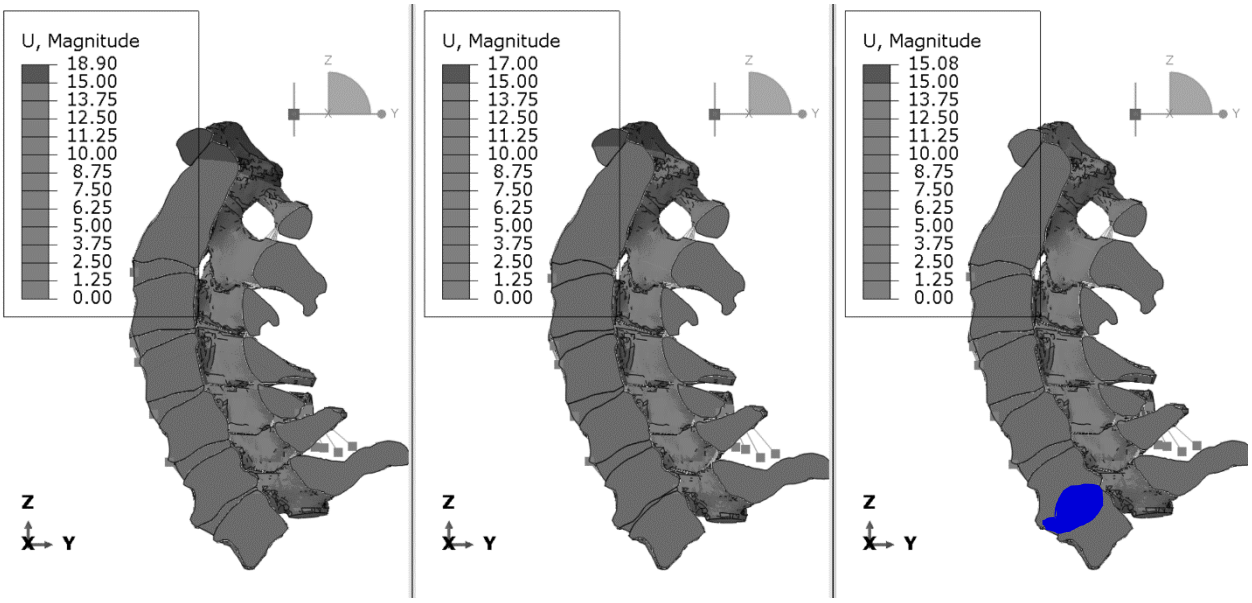
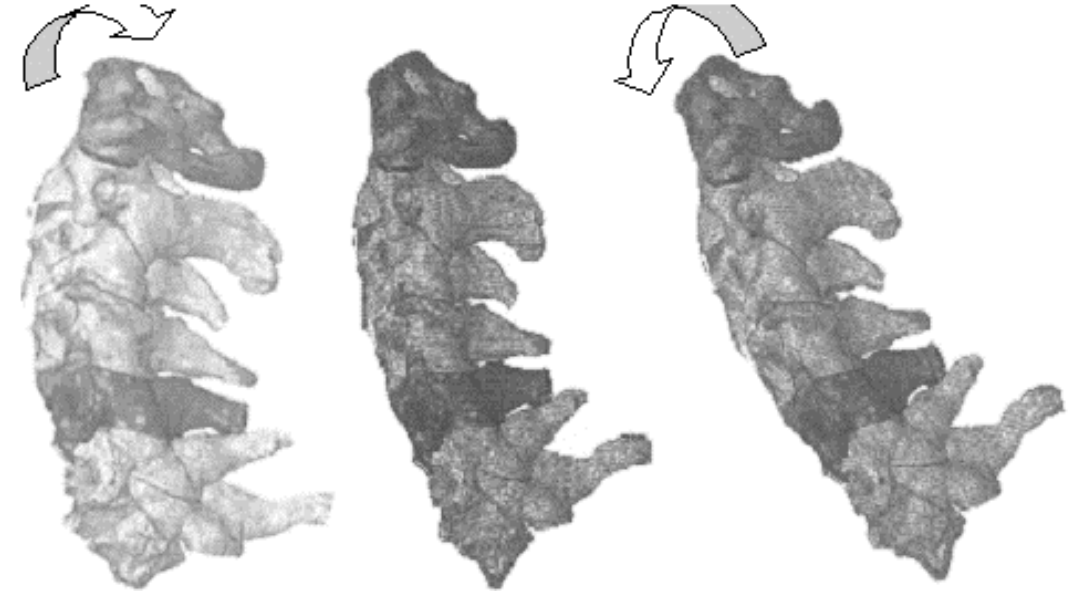


Figure 7. Extension movement by applying the force of 2 Nm, in the three models:
a- normal column, b- model with microdiscectomy C6-C7 and c- model with discectomy and cage C6-C7.



A. B. C.

FIGURE 8. Cervical models with discectomy and cage fixation at the C6-C7 level, at which mobility is studied: a. extension, compared with b. intermediate position and c. flexion

Movement	Model 1	Model 2		Model 3	
	mm	mm	% of Model 1	mm	% of Model 1
Extension	12.37	11.91	3.72%	11.12	10.11%
Flexion	11.65	10.63	8.76%	8.57	26.44%

TABLE 2. Cervical mobility in the sagittal plane when applying a moment of force of 1 Nm

RESULTS

We obtained the following results based on the finite element model with movement in flexion and extension by applying a moment of force of 1 Nm (Table 2).

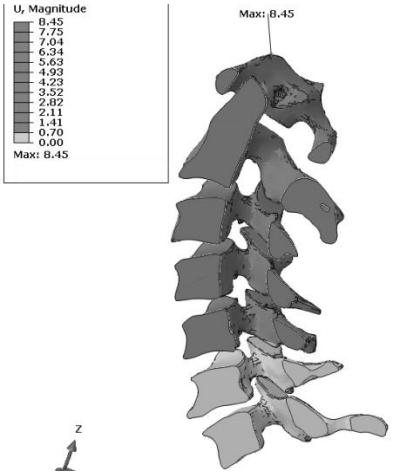
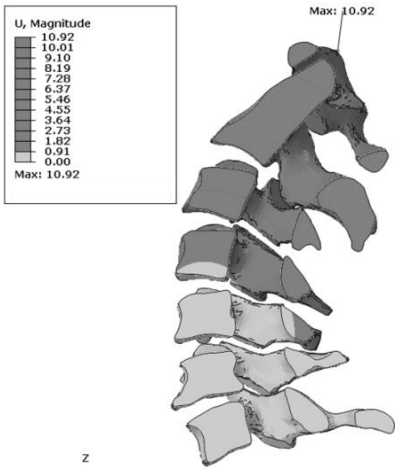


FIGURE 9. Cervical spine model with the extension of vertebrae

In the cervical spine model operated for C6-C7 disc herniation by microdiscectomy without fusion, it was found that the height of the C6-C7 disc space decreased to 50% off the initial disc height although it still allows a degree of intervertebral mobility without the occurrence of vertebral instability.



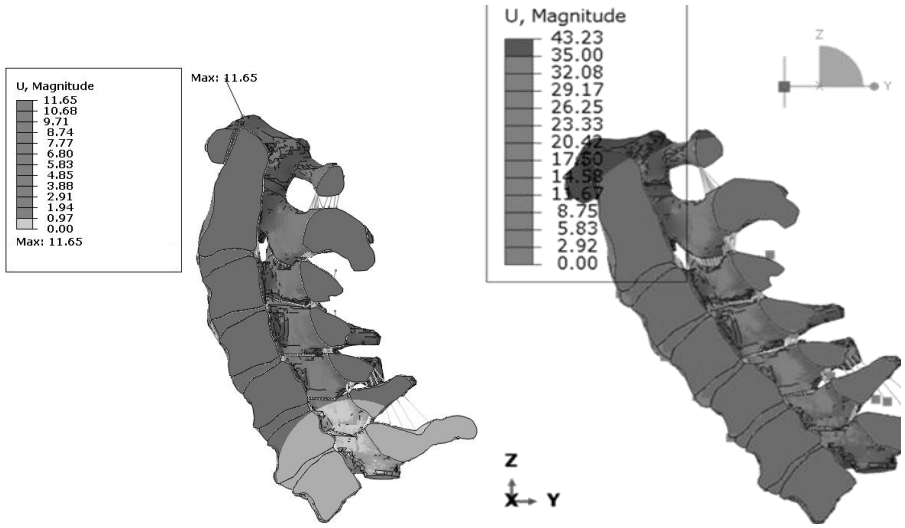
In the cervical spine model operated by discectomy and fusion using C6-C7 intervertebral cage, the operated disc space is blocked, there is no instability and the cervical movements of flexion and extension are performed by moving the upper vertebrae of the C6 vertebra. The C6 and C7 vertebrae form a fixed block and vertebral mobility is missing. It was found that surgery reduces the mobility of the flexion movement and blocks the C6-C7 disc space with a cage that reduces mobility with 26% in flexion. In the case of microdiscectomy without fusion, the overall cervical mobility decreases by 8.76% compared to the unoperated model.

When applying the moment of force corresponding to the maximum movement to the model of not operated cervical spine, respectively the moment of the force for flexion of 7.3 Nm and the moment of the force for extension of 2 Nm on the other two models, we obtained the results presented in Table 3.

The flexion and extension movement for all three models is much wider and the differences of mobility per the ensemble movement are 7.63% for microdiscectomy without fusion and 16.05% for discectomy with fusion.

TABLE 3. Cervical mobility at the moment of application of 7.3 Nm in flexion and 2 Nm in extension

Movement	Model 1	Model 2		Model 3		
	mm	mm	% of Model 1	mm	% of Model 1	% of Model 2
Extension	18.9	17	10.05%	15.08	20.21%	11.29%
Flexion	43.23	39.93	7.63%	36.29	16.05%	9.12%



A B

FIGURE 10. Flexion movement for the same model of the cervical spine with finite elements under the action of different moments of force: a. moderate flexion at the moment of force of 1 Nm and b. maximum flexion at the moment of force of 7.3 Nm.

DISCUSSIONS

Cervical disc herniation is a common degenerative pathology of the cervical spine and surgical treatment is the optimal solution in cases with surgery indication. A cervical discectomy removes from the anterior column an important component for resistance and the axial transmission of movement and weight and, consequently, may affect the stability of the cervical spine. The prospect of postoperative cervical instability has led us to this study, aiming to bring improvements to the operative techniques used so far or replace some of them in order to prevent or correct it.

We intended to determine the conditions in which post cervical discectomy instability may occur in relation to the surgical procedure used and to

show which technique is appropriate to prevent it.

After microdiscectomy without fusion, postoperative healing is based on the formation of an intradiscal fibrous scar to ensures the stability of the cervical spine at the level operated. The postoperative intradiscal scar allows a minimum degree of mobility without overloading the adjacent levels.

In the case of discectomy with fusion, a block is formed between the vertebrae adjacent to the operated disc, with the advantage of keeping the normal foramina, but with the loss of the intervertebral mobility at the level operated.

We used the normal cervical spine model, not operate, to apply a moment of force of 1 Nm in flexion, respectively extension, from the middle position. It determined a small amplitude displacement, namely of 11.65 mm in flexion and 12.37 mm in extension compared to the initial position. The simulation of maximum flexion and extension on this model allowed us to determine the maximum value of the moment of force of displacement for the maximum amplitude of these movements, respectively for 7.3 Nm - maximum flexion and 2 Nm - maximum extension. The maximum values of displacement in flexion and extension for the normal model were 43.23 mm - flexion, and 18.9 mm - extension, starting from the initial intermediate position.

The cervical model of microdiscectomy without fusion at the level C6 - C7 had the following values of amplitude for the moment of force of 1 Nm applied on flexion and extension in movement: 10.63 mm in flexion and 11.91 mm in extension. This means a decrease in the amplitude of the cervical movement of 8.76% in flexion and 3.72% in extension. These values are not significantly lower compared to the amplitude of the normal movement in ordinary situations.

A moment of force of maximum amplitude resulted in 39.93 mm in flexion and 17 mm in extension. In this case, the decrease with respect to the amplitude of the normal maximum movement was of 7.63% in flexion and 10.05% in extension. It was found that the decrease in flexion in the patient operated for disc herniation at the C6 - C7 level by fusion without microdiscectomy is between 7.63% and 8.76% for maximum flexion, respectively for current flexion. In contrast to flexion, the extension movement decreased slightly, only with 3.72% for the current extension, but the amplitude of the extension decreases by 10%, determined by the moment of maximum force compared to these movements in the case of the cervical spine.

In the third model, discectomy with fusion performed at the level C6 - C7, 1 Nm force produced a stronger decrease in the amplitude of movement: 8.57 mm in flexion, which means a decrease of 26.44% off the value of normal flexion, and 11.12 mm in extension, so with 10.11% less than the normal value. This decrease in amplitude of both movements of flexion and extension is significant and it is explained by the obstruction of the C6 - C7 disc space due to the fusion. Practically, the movement is produced by having as a fixed point the C6 vertebra. When a moment of force of maximum amplitude is applied on this model, it produces a flexion movement with the amplitude of 36.29 mm (meaning a decrease of 16.05% off the normal movement) and an extension of 15.08 mm, *i.e.* a decrease of 20.21% off the normal extension.

The simulation of flexion-extension movements on this third model established the marked decrease in cervical mobility as a whole, both for the current movement performed at a moderate request (moment of force = 1 Nm) and for the maximum movement, namely for a moment of force of 7.3 Nm in flexion and 2 Nm in extension. This decrease in amplitude in both flexion and extension is explained by the diminished length of the vertebral segment that executes the movement.

The study thus showed that limiting the moderate amplitude of the cervical movements is more important in the case of cage fusion discectomy compared to non-fusion microdiscectomy. The ration of amplitude decrease in movement between these two models is 3:1.

For a maximum movement, respectively for applying a moment of force of 7.3 Nm in flexion and 2 Nm in extension, the comparison between the biomechanical behaviour of the two cervical models showed that the decrease in the amplitude of movement is double in the case of discectomy with fusion than in the non-fusion model, both related to the normal, unoperated, cervical model.

Conclusions

The cervical spine model obtained through the finite element method (739666 finite elements and 210530 nodes), in which the vertebral mobility was simulated

for usual and maximum movements, showed that both models of cervical spine operated ensure postoperative stability at the level of the operated intervertebral disc. Both types of surgery reduce the mobility of the cervical spine, most notably the model with fusion discectomy.

The practical conclusion is that microdiscectomy without fusion is preferable in the case of a single-level cervical disc herniation in a cervical spine without instability because, by comparing the two operative models, it appeared that microdiscectomy without fusion at one level does not significantly decrease the mobility of the cervical spine, nor does it tensile the overload intervertebral discs adjacent to the operated disc level.

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Extradural autologous temporal muscle graft mimicking a meningioma. Case report

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Keywords
temporal muscle graft, dural lesions, meningioma, computed-tomography

ABSTRACT
Meningiomas are the most common dural tumour, but there are also many other dural masses which mimic their appearances, such as neoplastic and non-neoplastic lesions. In this paper we report another mass which may mimic a dural lesion, namely a muscle graft harvested from the temporal site and left in situ, used to achieve haemostasis in a posttraumatic temporal extradural hematoma in a young male patient. Solid knowledge of differentiating neuroimaging characteristics of dural masses, as well as its corroboration with the patient's medical history are extremely helpful in establishing an accurate diagnostic.

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INTRODUCTION

Meningiomas are intracranial tumours and make up about one third of all primary central nervous system tumours, with an incidence rate that has increased in recent years (1, 2, 3, 4, 5), at the same time being the most common dural tumours. However, there may be a variety of other dural lesions (neoplastic and non-neoplastic lesions) mimicking their imagining appearance (6) (Table 1). Unfortunately, the information about the prevalence of these dural lesions is limited, and most of the examples in literature are small case series and case reports.

Many of these dural lesions share similar computed tomographic, magnetic resonance imaging and angiographic characteristics with meningiomas such as increased vascularity, avid enhancement, a dural tail and similar signal characteristics (7). In addition to these multiple dural lesions mimicking meningiomas, we report in this paper the existence of a muscle graft harvested from the temporal site and left *in situ*, used to achieve haemostasis in a case of left temporal extradural hematoma (Figure 1).

CASE REPORT

We report the case of a 40-year-old male patient, victim of a road accident (bicyclist knocked over by a car), who was brought to the emergency room of our hospital with a GCS of 3 and anisocoria (pupil in the left eye > right eye). The cranial CT scan carried out on his admission revealed a left temporal extradural hematoma with left temporal fracture (Figure 1). A surgical procedure was performed immediately to remove the hematoma and the patient's subsequent evolution was excellent, with no post-operative neurological deficiencies. During surgery, the source of bleeding was identified as being the middle meningeal artery and in order to achieve better haemostasis, a piece of the temporal muscle was left in situ, which was later revealed by the cranial post-operative follow-up CT scan (Figure 1. D, white arrow). Also, during surgery, in order to reach the skull base and stop the bleeding, the bone flap was complemented by temporal craniectomy, for which a cranioplasty with titanium mesh was later performed (Figure 2). During periodic imaging follow-up, we noticed that the piece of temporal muscle left *in situ* for haemostasis purposes had become vascularized and a native cranial CT scan revealed its homogeneous appearance (Figure 3). Also, the electroencephalogram did not reveal any pathological changes.

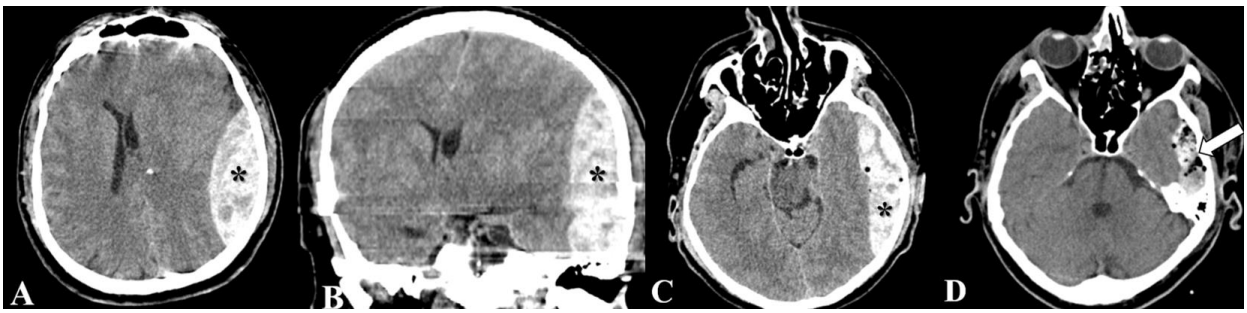

FIGURE 1. Preoperative cranial CT scan with left temporal extradural hematoma (*) (A, B, C). Postoperative cranial CT scan showing temporal muscle left *in situ* (white arrow) (D)

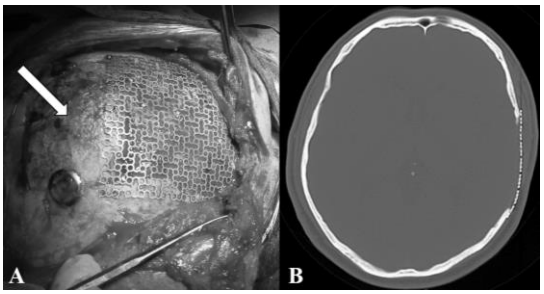

FIGURE 2. Intraoperative photo showing the bone flap (white arrow) and cranioplasty with titanium mesh (A). Postoperative CT scan showing the cranioplasty (B)

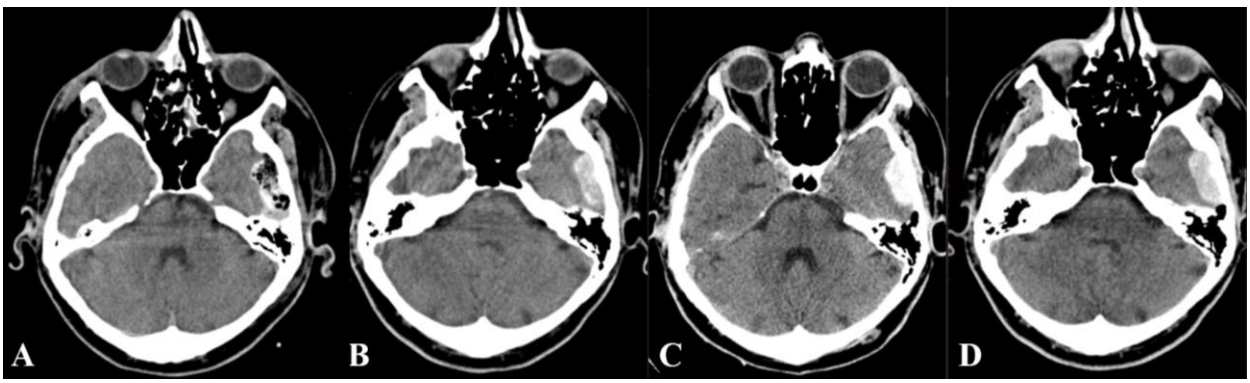

FIGURE 3. The follow-up cranial CT scan performed after 1, 2 and 3 years (B, C, D) revealed the hypervascular muscle graft mimicking a meningioma or other hypervascular lesions

Discussions

In neurosurgery, just like in all the other surgical fields, proper haemostasis is a *sine qua non* requirement when it comes to preventing dramatic postoperative bleedings the consequences of which are not negligible. Among the various local haemostatic agents used in neurosurgery (8, 9, 10), fresh muscle harvested from the temporal muscle or thigh is still commonly used to achieve haemostasis (8).

Before the 1950's, neurosurgeons used fresh chicken breast as topical haemostatic agents, which were delivered before the surgical procedure. The muscle grafts were applied on the brain during ten minutes, while washing the surgical field with warm serum, and they were removed before closing the dura (8). The first reports on the use of muscle grafts in haemostasis belong to Cushing and Horsley (11, 12). Later, Clute also reported the efficient use of both free and viable muscle grafts in achieving haemostasis in different organs (13). The idea of fresh muscle harvested from the temporal site or thigh, which may be left *in situ*, appeared later. The technique is still used sometimes. In addition to muscle grafts, neurosurgeons have also used other autologous human tissues for haemostasis, such as clots, fascia, dura or fat, yet these have not proven better (12, 14). Moreover, autologous human muscle grafts have proven their efficiency and superiority in the management of significant haemorrhage not only in brain surgery, but also in all the other surgical fields which they were used in (15, 16, 17, 18, 19, 20).

The use of muscle grafts for haemostasis during neurosurgery has reemerged these last few years (21), and fresh muscle graft is also used in neurosurgery in case of cerebrospinal fluid leak (20) or to repair the internal carotid artery during endoscopic surgery (22). Thus, extensive research has proven muscle tissue efficiency in controlling carotid artery bleeding, both in animal and in human models (16, 18, 23, 24). Moreover, research on animal and patients undergoing endoscopic sinus surgery has shown that muscle tissue may efficiently control high-flow and high-pressure carotid artery bleeding (16, 18, 23).

In a study on human muscle extracts, in which Rajiv *et al*. investigated the haemostatic potential of muscle tissue through various coagulation and platelet aggregation tests, the authors concluded that platelet aggregation plays an important role in the haemostatic efficiency of muscle grafts and the muscle grafts adhere well to blood vessels (21). Jukes *et al.* also showed in a study conducted on autologous but crushed muscle, that this caused a consistently increased ratio of platelet activation when compared with uncrushed muscle (25).

In order to understand the imaging appearance of muscle graft left in situ better, the knowledge about dura mater vascularization and about the encephalo-duro-myo-synangiosis mechanism is the key (26, 27). The dura mater is a thick non-elastic membrane made up of fibrous and elastic connective tissue, which surrounds the brain and spinal cord. The cranial dura mater consists of two layers: an external periosteal layer and an inner meningeal layer which are generally fused except when they separate to allow the passage of the dural venous sinuses. Of the two layers, the external periosteal layer adheres closely to the skull bone and is highly vascular and innervated and contains blood vessels that supply the bone, exhibits greater angiogenic activity and is like an internal periosteum for the cranium (7, 28, 29). The inner meningeal layer of the dura is smooth and avascular and is lined on its inner surface by mesothelium (7, 28). The neovascularization in the outer layer cannot extend to the inner layer to the cortical surface, so that it is safe to say that the meningeal layer is a natural barrier between the circulation of the external and internal carotid arteries (30, 31).

Practically, in the case of our patient, the existing vessels in the scalp tissue and temporal muscle passed through the titanium mesh and recruited the vessels in the muscle graft. This vascularization of the external periosteal layer of dura mater has also contributed to the repermeabilization and neovascularization of the muscle graft left *in situ* to achieve haemostasis. The various vascularized tissues communicate through the titanium mesh (32) and this was also considered by Badie *et al*. who used a reconstruction technique involving the placing of a titanium mesh between two layers of continuous vascularized pericranium in patients with large anterior skull defects. The technique has been proven safe and effective (33).

This revascularization mechanism is essential for the effectiveness of burr holes for indirect revascularization in patients with moyamoya disease (34). It seems that new vessels are formed by two distinct phenomena: angiogenesis and

arteriogenesis (34, 35). Angiogenesis is the formation of new vascular segments altering the preexistent vascular network, whereas arteriogenesis is the formation of blood vessels from endothelial precursors (35). Whether these processes occur simultaneously or sequentially is still to be determined (36, 37). In our patient, the muscle graft became hypervascularized by the double contribution of the meningeal arteries irrigating the dura and the superficial temporal artery vascularizing the scalp tissue, a model which was also taken into consideration by other authors (38).

The follow-up CT scan performed after 1, 2 and 3 years, respectively (Figure 3) revealed that the muscle graft became hypervascular and had higher perfusion values, mimicking a meningioma or other hypervascular lesions (e. g. renal tumour metastases), compared with most other extra-axial lesions (6). For the treatment of moyamoya disease, Houkin *et al.* showed that collateral circulation develops within 3-4 months after surgery (39) and is directly related to the size of the bone flap (40, 41). This explains the good vascularization of the muscle graft revealed by the periodic cranial CT scans (Figure 3). The medical imaging examination of the muscle graft perfectly mimics a dural lesion, therefore the differential diagnosis with the other dural lesions is required (Table 1). Also, the patient's clinical examination and personal medical history may be extremely helpful in guiding the diagnosis setting process.

TABLE 1. Dural lesions (after 6 and 42 ref)

Neoplastic: • Meningioma • Metastasis (colon, breast, lung, prostate, leiomyosarcoma) • Glioblastoma • Lymphoma • Hemangiopericytoma • Solitary fibrous tumor • Hodgkin's Disease • Carcinomatosis • Plasmocytoma • Ewing sarcoma • Epstein-Barr virus-associated smooth muscle tumors
Granulomatous: • Tuberculosis • Neurosarcoidosis • Granulomatosis with polyangiitis • Plasma cell granulomas
Lymphoproliferative: • Rosai-Dorfman disease • Erdheim-Chester disease
Autoimmune: • IgG4-related disease
Other: • Extramedullary hematopoiesis

CONCLUSION

In neurosurgery, there are many pathologies affecting the dura and mimicking meningiomas. They include primary and secondary neoplastic lesions, inflammatory and infectious lesions, which may be mistaken for one another because of their similar imaging characteristics. In addition to all these dural lesions, in this case report we mention the existence of autologous muscle graft left *in situ* mimicking a dural lesion. Solid knowledge of differentiating neuroimaging characteristics, as well as its corroboration with the patient's medical history may help set the right diagnosis and find new optimal therapeutic approaches.

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Secondary giant cell glioblastoma in a multiple drug abuser - simple association or ethiopathogenic correlation? Case presentation and literature review

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ABSTRACT

Experimental investigations have shown that drug abuse initiates a cascade of pathophysiological events including toxic and hypoxic-ischemic injury on neurons, microglia and astrocytes, which finally lead to widespread disturbances in the brain. There are many reports about the psychiatric and neurologic effects of multiple drug abuse, but only a few clinical studies reporting possible correlation between recreational illicit drugs and gliomas.

In this paper we present the case of a 40 years-old male patient, with a long history (almost ten years) of multiple drug abuse, including cocaine, heroin, marijuana, ethnobotanical drugs and nicotine, who was diagnosed and surgically treated for a supratentorial secondary giant cell glioblastoma (sgcGB) developed in a diffuse astrocytoma NOS. Depending on the type of the illicit drug used by the patient and the moment of life he used them, the morphological features identified in the histological samples of our patient confirmed the gliomagenesis effect of chronic multiple drug abuse, but also its inhibitory effects on tumour cells growth. This was due to the fact that although the tumour was large in size and caused brain sub-falcine herniation, the patient reported the onset of seizures only late in the evolution.

In conclusion, the diagnosis of a brain tumour should take into consideration not only patient's clinical and imaging data, but also his lifestyle, especially his addiction to recreational drugs.

INTRODUCTION

The Psychostimulants (cocaine, methamphetamine, etc.), opiates and opioids (heroin, methadone, etc.), sedatives (benzodiazepines), and

some other drugs such as cannabis (marijuana) and nicotine are the most widely consumed recreational drugs in order to obtain a sense of well-being. Unfortunately, in the same time, these drugs of abuse have a significant negative impact on public health as they can induce pulmonary (1-4), cardiovascular (5, 6), renal diseases (7), gastrointestinal and endocrine diseases or infections (8).

However, psychiatric and neurologic symptoms are the most common manifestations of drug abuse toxicity. Along with the psychotic effects of recreational psychostimulants (9, 10), there are also reports of their neurological side effects, such as vasogenic edema formation (11), cerebral and spinal cord infarction, cerebral vasculitis associated with intraparenchymal or subarachnoid haemorrhage (12), hypoxic-ischemic leukoencephalopathy (13), ischemic optic neuropathy as well as partial and generalized seizures (14, 15).

Some researchers have made systematic histological, immunohistochemical and morphometric investigations in order to identify the morphological alterations in the brains of multiple abusers. There are reports of intramyelinic edema and mitochondrial dysfunction due to cocaine abuse, but also of neurovascular toxicity due to heroin (16). Other studies reported a toxic spongiform leukoencephalopathy after intravenous heroin injection or after inhaling heroin vapors (17-19). The morphological substrate of this disease is a spongiform demyelination that develops due to a dysfunction of the oligodendrocyte mitochondria (20, 21).

Neuropathological features encountered included neuronal loss, neurodegenerative alterations with significant widespread axonal damage (22), specific astroglial reaction patterns (23, 24), with a reduction of glial fibrillary acidic protein-immunopositive astrocytes, concomitant microglial activation as well as reactive and degenerative changes of the cerebral microvasculature (due to alterations of the endothelial cell and the basal lamina) (25). Fredericks et al. reported nonnecrotizing, nonleukocytoclastic small-vessel arteritis associated with cocaine use (26). On the molecular level, alterations in the expression of transcription factors and changes of brain neurotransmitter systems have been reported, too (27).

All these results have provided evidence that drugs of abuse initiate a cascade of pathophysiological events including toxic, hypoxic-ischemic injury, microglial and astrocytic - associated cytokine releases, which finally lead to widespread disturbances within the complex network of central nervous system cell-to-cell interactions (25, 28).

However, as far as we know, there is a scarcity of literature concerning the correlation of drug abuse with the development of a cerebral glioma. There is only one epidemiological study published in 2004 by Efird et al. that found a 2.8-fold increased risk for malignant primary adult-onset glioma for people who had smoked cannabis once or more per month (29).

In this paper we present the case of a 40 years male patient, a chronic multiple abuser for ten years, who was diagnosed and treated for a supratentorial secondary giant cell glioblastoma (sgcGB) developed in a diffuse astrocytoma NOS. We discuss the possible role of drug of abuse effects on tumour initiation, development and progression taken into consideration patient's history of multiple abuse.

CASE PRESENTATION

A male patient, 40 years old, heavy smoker (about 20 cigarettes per day for 30 years), was brought by his family to the "Socola" Institute of Psychiatry, Iași, Romania, for strong headache and altered mental status over the last 24 hours. They considered that patient's status was the effect of his dependence on psychoactive substances as he had a long history (almost ten years) of multiple abuse, including cocaine, heroin, marijuana, and ethnobotanical drugs. Firstly, he used cocaine for five years, then he continued with heroin and marijuana for another two years and finally he only consumed ethnobotanical drugs over the most recent three years. The patient's relatives also declared that he had symptoms of anger or euphoria and changes in behaviour over the last twelve months, but also a state of sleepiness in the last month.

The patient complained of intermittent diffuse headaches, which developed during the preceding months and improved with the use of ethnobotanical drugs.

On physical examination the patient was apparently conscious, cooperative, and partially communicative. He had temporo-spatial orientation

and only presented a slight attention deficit. He denied any hallucinations and alcohol consumption, referring only to the chronic consumption of psychoactive substances.

The general medical examination was unremarkable. His blood pressure was 136/96 mmHg, pulse = 90 beats/minute, temperature = 36.3^0C, and glycemia = 113 mg/dl. There were no relevant family risk factors for neoplastic disease.

One day after his admission in the psychiatric unit, the patient's condition progressively worsened. The vomiting was triggered with a continuous frequency, even from the sitting position. Brain computer tomography (CT) scans, carried out in emergency, highlighted a large, irregularly shaped fronto-temporo-parietal expansive mass lesion, being hypo- and isointense on native examination, and with evidence of post-contrast heterogeneous enhancement; it was surrounded by an edema and induced an important mass effect. He was transferred to the 2nd Neurosurgery Clinic, "Prof. dr. N. Oblu" Emergency Clinical Hospital, Iasi, Romania, and a surgical intervention was performed the same day after admission with partial tumour resection.

The histopathological examination identified an astrocytic tumour of low cellularity, moderate nuclear atypia and focal microcystic degeneration (Figure 1, A and B). Some tumoural cells demonstrated apoptotic changes (smaller size, dark eosinophilic cytoplasm, condensed and hyperchromatic chromatin) (Figure 2, C and D). There were only few thin-wall vessels with near normal morphology (Figure 2,E and F). The diagnosis of a secondary anaplastic astrocytoma, WHO grade III (30), developed into a diffuse astrocytoma was established.

Approximately two weeks after his brain tumour surgery, the patient once again presented himself to our neurosurgical department with nausea, vomiting, diffuse headache, vertigo, and an episode of convulsive crisis. Blood pressure was 130/70 mmHg, pulse = 88 beats/minute, and temperature = $36,8^O$C. Neurological examination showed left facial paresis, muscular weakness and a slightly loss of sensibility of his left part of the body. Some minimal changes of the preoperative laboratory investigation due to previous surgery were identified. There were a slightly increased absolute number of WBC ($13.03x10^3$ /mm^3) and slightly elevated polymorphonuclear neutrophils (71.3%) on a differential count. In addition, a slightly fibrinogenemia (465 mg/dl) and slight hyperglycemia (120mg/dl) were recorded.

Brain CT scans revealed a right fronto-temporo-parietal enhancing tumour with a digitiform perilesional edema, with larger dimensions than the first tumour and with compression and dislocation of medial cerebral structures to the left (approximately 13.1 mm).

The patient underwent surgical therapy with partial resection of the tumour. The microscopical exam of hematoxylin-eosin (H&E) stained histological specimens revealed a highly malignant glial tumour made up of large, grotesque looking multinucleated giant cells, some containing up to 7 nuclei with abnormal shapes (Figure 4, A-D). Some of the nuclei contained prominent nucleoli and atypical mitotic figures. There were numerous blood vessels of various sizes and shapes, many of them presenting marked endothelial proliferation (Figure 4, E and F). Both large and small areas of ischemic necrosis were also observed. Histological reevaluation of all the available specimens highlighted the fact that the tumour was in fact a secondary giant cell glioblastoma (sgcGB), WHO grade IV (30), developed in a diffuse astrocytoma NOS.

One week after surgery the patient had a first check-up brain IRM scan that revealed an increase in the size of the lesion. The patient was referred to the Regional Institute of Oncology in order to be treated with adjuvant chemotherapy (with temozolomide) and radiotherapy. It should be mention that the patient didn't use any psychostimulants in all during this period.

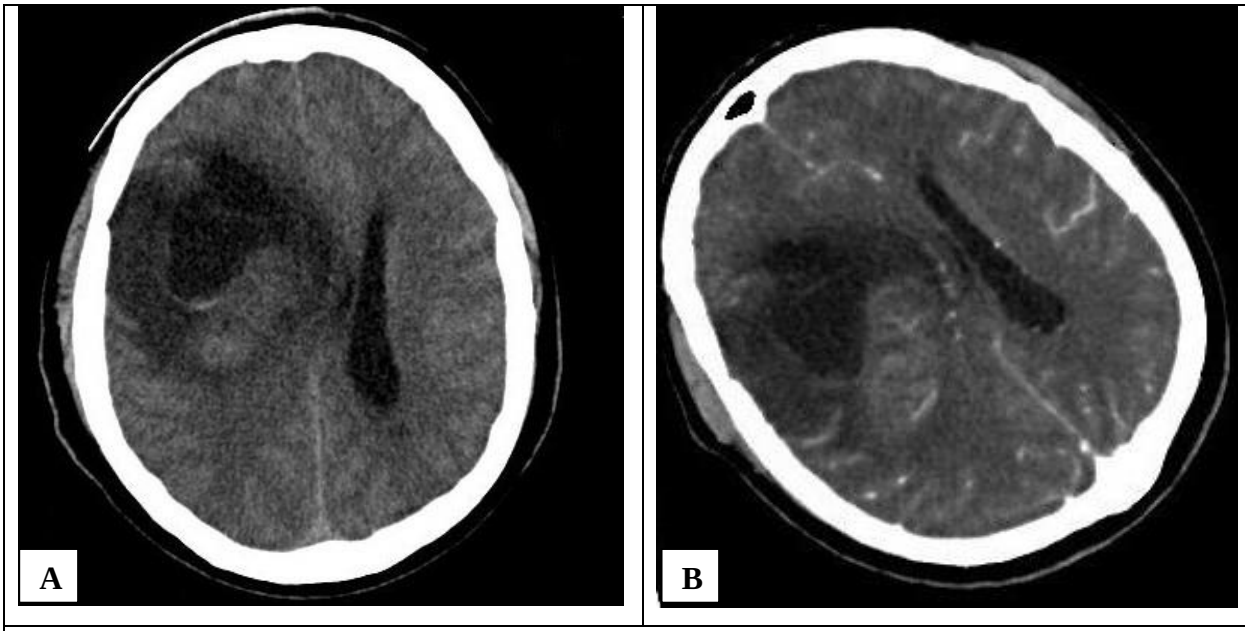
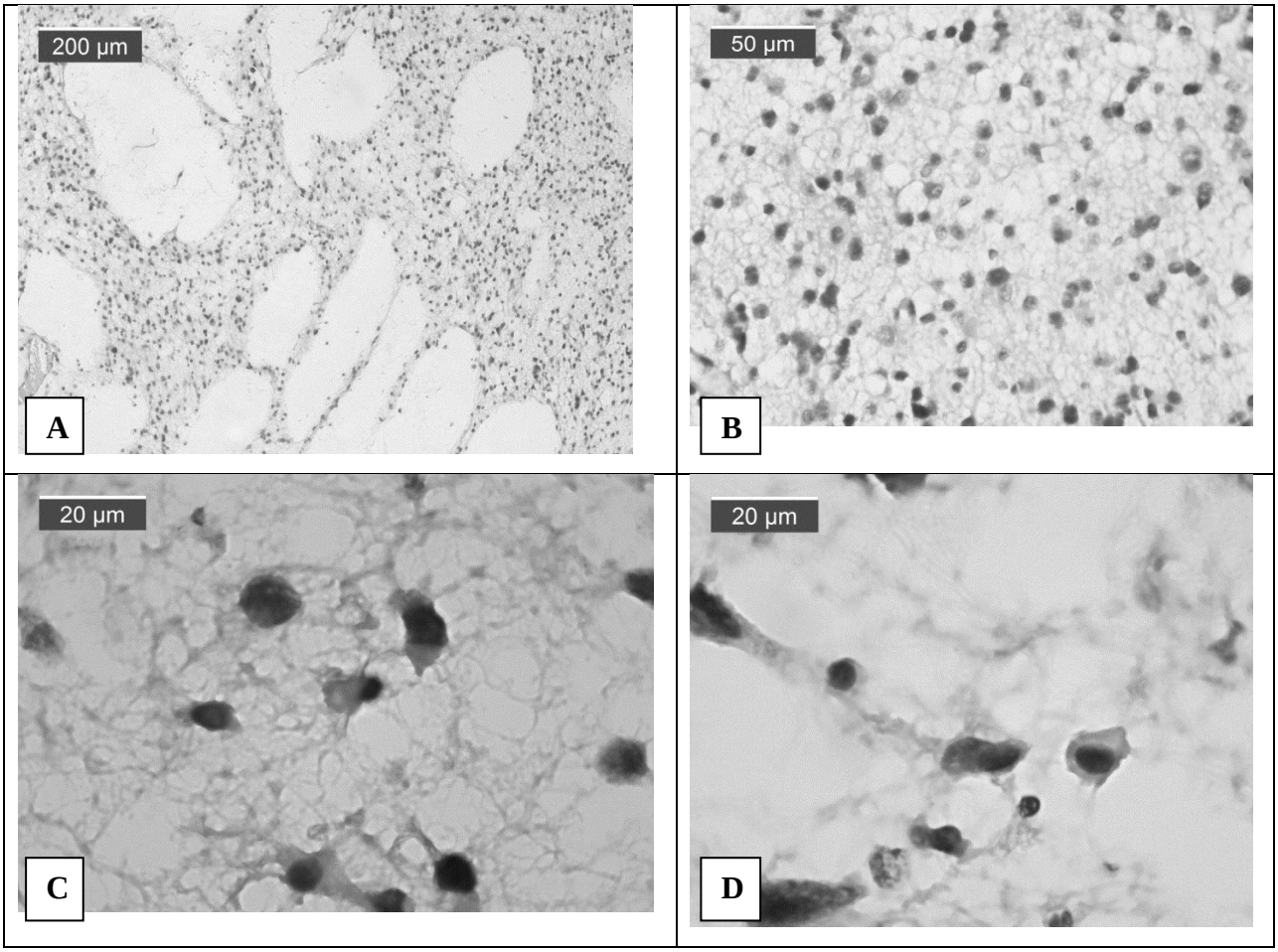


FIGURE 1. Preoperative axial head computed tomography scan (A. native; B. after contrast administration) performed on patient's first admission showed a large irregularly outlined cerebral lesion with central necrosis, peripheral contrast uptake, compression and dislocation of medial cerebral structures to the left.



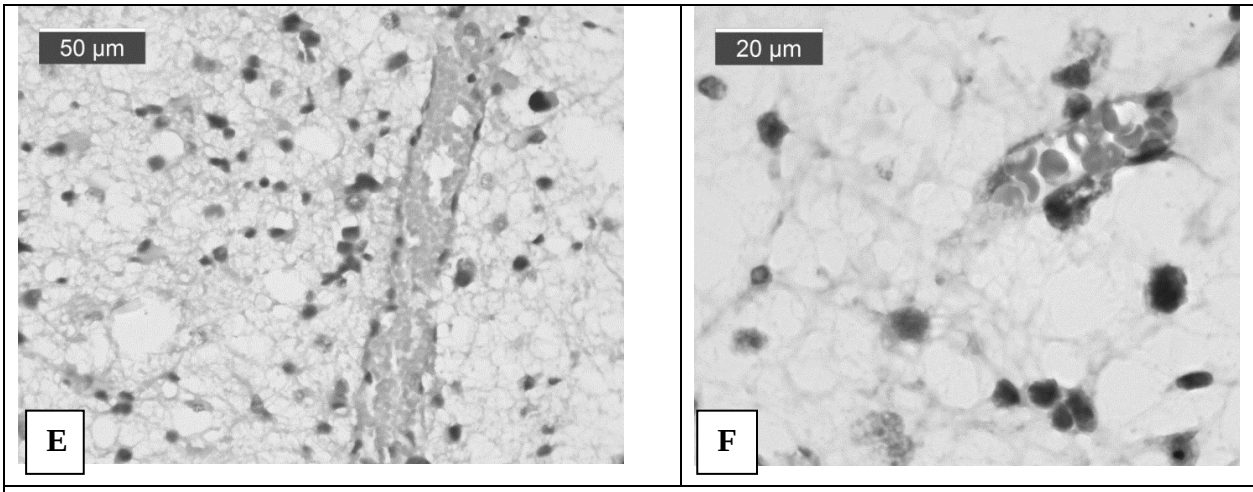


FIGURE 2. Histological sections of the first excised sample identified a glial tumor with focal microcystic degeneration and moderate cell density, made up of uniform cells resembling mature astrocytes, accompanied by dispersed anaplastic cells [A. (H&E, x10); B. (H&E, x40)]; at higher magnification, some tumoral cells revealed apoptotic changes (smaller size, dark eosinophilic cytoplasm, condensed and hyperchromatic chromatin) [C. (H&E, x40); D. (H&E, x100)]; there were also thin-wall vessels with near normal morphology, but surrounded by anaplastic astrocytic cells [E. (H&E, x100); F. (H&E, x100)].

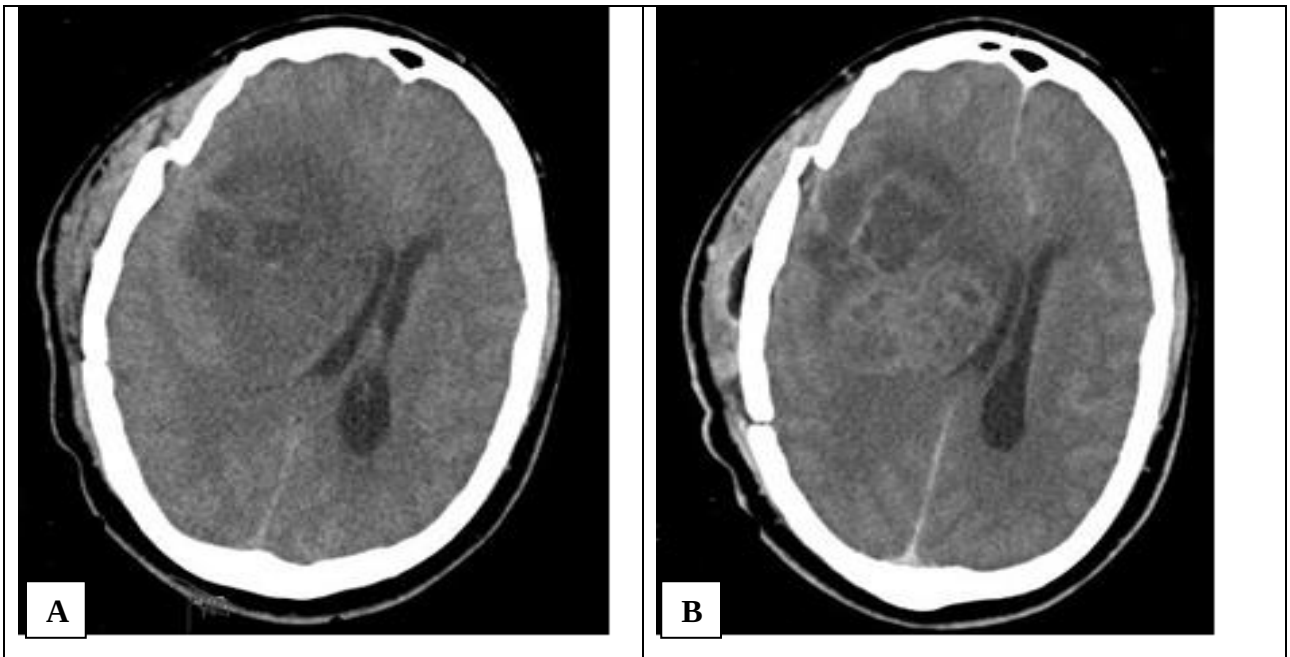


FIGURE 3. Axial head computed tomography scans (A. native, B. after contrast administration) performed on patient's second admission (at two weeks after first tumor resection) identified temporal scalp swelling, temporal craniotomy and increased lesion size with compression and dislocation of medial cerebral structures to the left.

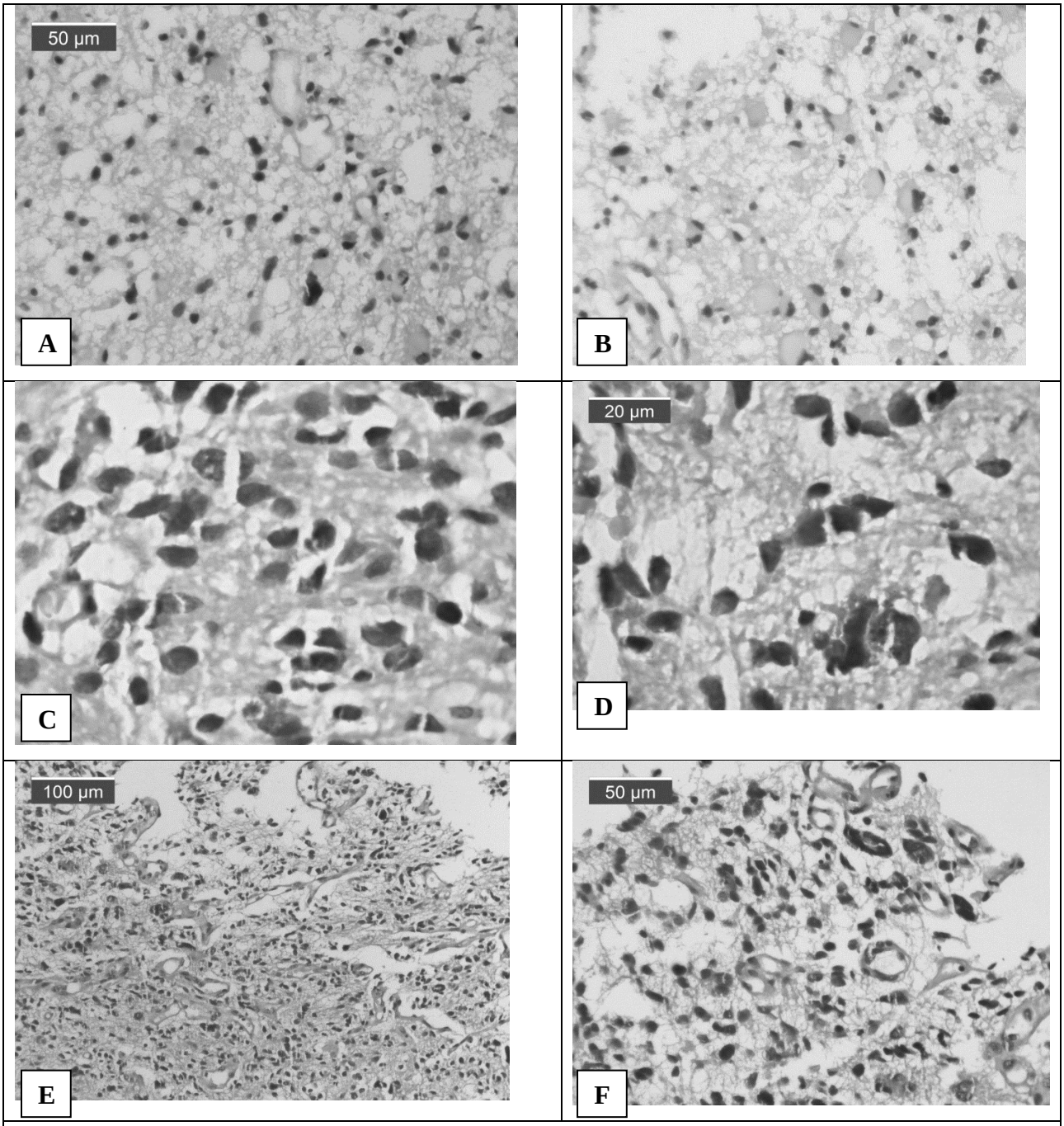


FIGURE. 4. Histological section of the second excised sample pointed out a glial tumor with moderate cell density, and cellular and nuclear pleomorphism [A. (H&E, x40); B. (H&E, x40); a higher magnification revealed in some other areas a highly cellular tumor tissue made up of bizarre looking, giant glial cells, with rich eosinophilic cytoplasm and one or many hyperchromatic irregular shaped nuclei [C. (H&E, x100); D. (H&E, x100)]; in areas close to the central part of the tumor there were many thick-wall vessels with disordered arrangement and moderate endothelial and pericytic proliferation [E. (H&E, x20); F. (H&E, x40)].

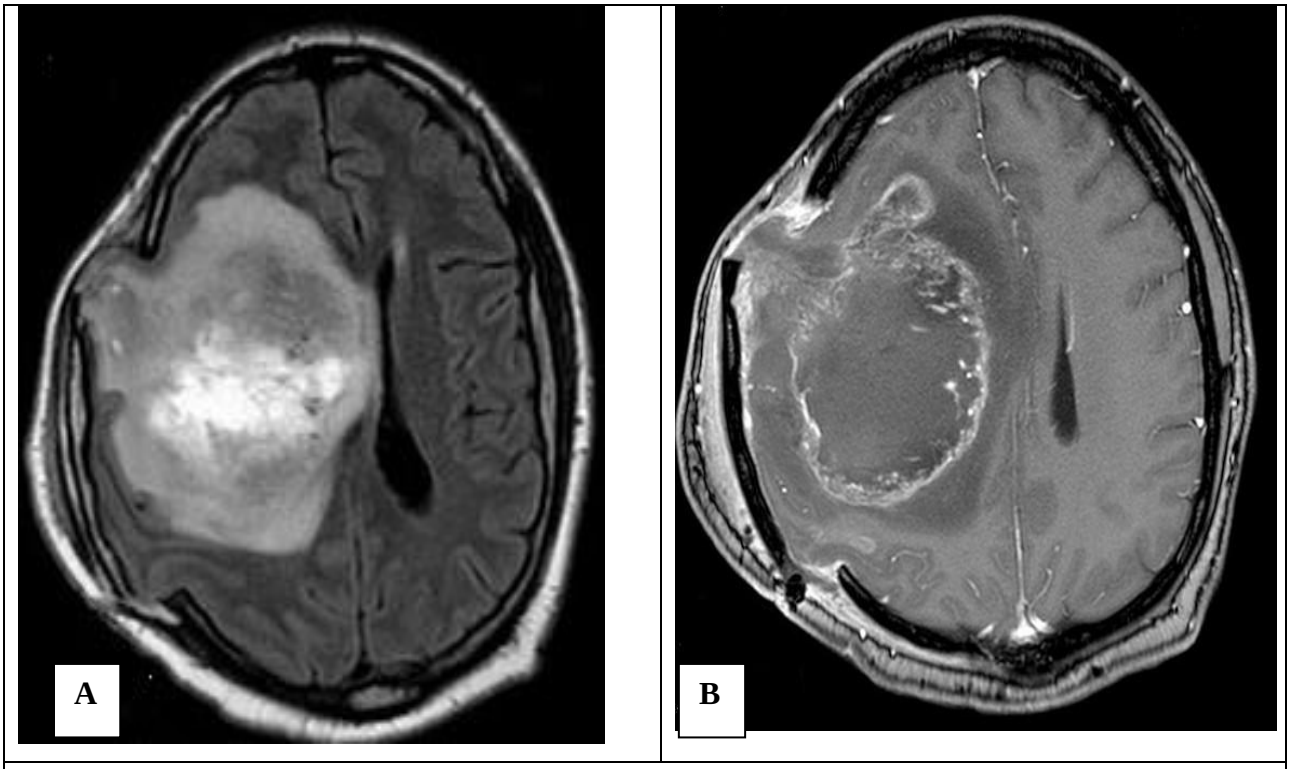


FIGURE 5. Axial MR images (A. FLAIR; B. T1 gadolinium-weighted) performed at one week after the second surgery highlighted a huge heterogeneous infiltrating mass that filled frontal, temporal and parietal lobes, with extensive peripheral edema and midline shift, all these features being indicative of rapid tumor progression.

DISCUSSION

The World Health Organization (WHO) defines multiple drug use "as the use of more than one drug or type of drug by an individual, often at the same time or sequentially, and usually with the intention of enhancing, potentiating, or counteracting the effects of another drug" (31). The most common association is with caffeine, nicotine and alcohol. However, the most important is the association of cocaine, with various combinations of heroin, barbiturates, and marijuana.

Our patient, a multiple drug abuser, who used at least four types of drugs (cocaine, heroin, marijuana, and nicotine) during a period of at least 10 years, presented a glioblastoma that developed in his right fronto-temporo-parietal area, which is known to be affected by alterations due to drug abuse (32).

Major neuropathological mechanisms underlying chronic abuse of recreational psychostimulants (such as cocaine) or nicotine consist of pronounced levels of oxidative stress and mitochondrial dysfunction in the blood-brain-barrier (BBB) endothelium and perivascular cells, i.e. astrocytes, due to an uncontrolled increase in cellular reactive oxygen and nitrogen species (33, 34). The abuse of drugs also induces neuroinflammatory signals and disrupts glutamate homeostasis through their interaction with microglia and astrocytes (35).

The German legist Andreas Büttner, who extensively investigated the neuropathological changes induced by chronic drug abuse, considered that the alterations of the intracellular messenger pathways, transcription factors and immediate early genes within the brain reward system are the most important factors for the development of addiction (25).

In 2016, some American researchers concluded that cocaine determines the proliferation of human astrocytes as this drug increased cyclin A2 (an essential regulator of the cell cycle) expression in human astrocytes. Lee et al. used cocaine with various concentrations and applied them to human astrocyte culture. They found that cocaine with increasing concentrations significantly increased human astrocyte proliferation using the JNK MAP kinase pathway as a driver of cell proliferation (36).

In the same year, certain other American researchers (37) reported the potential of the psychostimulant drugs such as cocaine in inducing astrogliosis through the sequential activation of endoplasmic reticulum stress and autophagy in human astrocytes.

It was possible to demonstrate that cocaine could also induce microglial activation via both the endoplasmic reticulum stress and autophagy pathways (38, 39). Cocaine potentially modulates the immune response in the CNS leading to an neuroinflammatory state that is characterized by enhanced activation of glial cells in the brains of addicts (40) as it seems that cocaine-mediated-increased upregulation of GFAP correlated with increased expression of proinflammatory mediators such as TNF, IL1B, and IL6 (37).

Reactive astrocytosis and microgliosis are classical features underlying neuroinflammation observed in drug abusers and in various neurodegenerative diseases. Astrogliosis is accompanied by the release of a wide range of neurotoxic mediators consisting of chemokines, complementary factors, cytokines, growth factors and reactive oxygen species (41), which remodel the cellular homeostasis in the CNS.

Recently, it has been reported that reactive astrocytes are prone to develop gliomas. Taken into consideration, the older Hansemann concept that tumours were derived by dedifferentiation of mature cells, it is possible to consider that astrocytes are able to dedifferentiate into a pluripotent precursor as a critical step in gliomagenesis (42, 43). In 2002, Bachoo et al. showed that combined loss of p16(INK4a) and p19(ARF), but not of p53, p16(INK4a), or p19(ARF), enables astrocyte dedifferentiation in response to EGFR activation (44) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3033226/ - R61) thus suggesting a possibility that an astrocyte, due to some extrinsic factors in its environment, could acquire some mutations necessary for its oncogenic transformation.

Based on all these scientific facts and the histopathological features of our patient's tumour that revealed a sgcGB developed in a diffuse astrocytoma, we can presume that during those five years of cocaine use, astrogliosis and then gliomagenesis have been triggered. Firstly, a low grade astrocytoma developed as we were able to see in the peripheral areas of the tumour. As he began to use heroin and marijuana, it is more likely that these substances had beneficial effects by reducing edemas, intra tumoural inflammation and the progression of the disease due to tumour cells apoptosis as some other reports have shown (45-46).

Because our patient wasn't able to buy cocaine, heroin or marijuana over the last three years (however only ethnobotanical drugs containing at least benzodiazepine) the tumour slowly progressed to an anaplastic astrocytoma and ultimately to secondary glioblastoma as the histopathological features of these two tumours can be seen in the middle portion and in the center of the tumour, respectively. Also, the absence of the symptoms induces by glioblastoma could correlate with the inhibitory role of benzodiazepine on glioblastoma proliferation (47). However, when the tumour had grown to considerable size, the patient presented periods of apathy alternating with periods of nervousness and ultimately somnolence, nausea and vomiting, that led him to the psychiatrist.

Many scientific studies have indicated the potential use of cannabinoids in the fight against cancer. Experiments carried out on cell lines *in vitro* and on animal models *in vivo* have shown that phytocannabinoids, endocannabinoids, synthetic cannabinoids and their analogues can lead to inhibition of the growth of many tumour types, exerting cytostatic and cytotoxic neoplastic effects on cells thereby negatively influencing neo-angiogenesis (48). Our patient's glioblastoma showed extensive necrotic areas, however intra tumoural microvasculature was reduced and there was only mild proliferation of the pericytes, demonstrating neoangiogenesis inhibition probably due to the toxic effect of multiple drugs abuse.

Pokrywka et al. have shown that the main molecular mechanism leading to inhibition of glioma cell by cannabinoids is apoptosis, being a consequence of induction of endoplasmic reticulum stress and autophagy (49). Indeed, a detailed examination of our patient's histological samples revealed many apoptotic tumour cells with cell shrinkage, dark eosinophilic cytoplasm, and condensed chromatin.

Forty years ago, White et al. (50) demonstrated the fact that cannabinoids inhibited tumour growth because delta9-tetrahydrocannabinol (delta9-THC) decreased DNA synthesis in transformed cell cultures. More recently, other studies have

investigated the molecular mechanism of anti-cancer effect of cannabinoids and have found that these substances inhibited tumour cell growth and induced apoptosis by modulating different cell signaling pathways e.g. via the upregulation of the endoplasmic reticulum stress-related genes ATF-4, CHOP, and TRB3 (51). Delta (9)-tetrahydrocannabinol (THC), the main active component of marijuana, induces human glioma cell death through stimulation of autophagy, a precursor event of apoptosis (52, 53).

The first clinical study with the aim to evaluate cannabinoid anti tumoural action was a pilot study conducted in 2006 in a cohort of terminal patients harbouring recurrent glioblastomas (54). All these patients were administered Δ^9-Tetrahydrocannabinol intra tumouraly. Inhibition of tumour-cell proliferation *in vitro* and decreased tumour-cell Ki67 immunostaining were observed.

Literature has shown that giant cell glioblastoma represented a distinct pattern of cytogenetic alterations when compared with small cell glioblastoma and suggested that multinuclear giant cells evolved from a non-giant tumour cell at an early tumour stage (51). Routine histological preparations of our patient's surgical specimens showed a variety of characteristic changes in tumour cell and nuclear morphology (prominent formation of giant monstrous cells, with bizarre, irregular, and hyperchromatic nuclei, a decrease in the number of mitoses, and severe cytoplasmic degeneration) indicating inhibition of tumour cell division. These morphological changes, quite similar with those induced by chemotherapy on glioma cells (56, 57), probably represent the effects of drug abuse on glial tumour cells.

Johnson and Weissman also reported an interference of cocaine with cell replication as it produced fine structural nuclear alterations in cultured neuroglioblastoma cells. (58). In 1993, Garg et al. exposed C6 glioma cells to cocaine and observed a reduced thymidine and uridine incorporation in these cells after four days of exposure (59). After almost ten years, other experimental studies have shown that various concentrations of cocaine caused a significant down-regulation of CYP2C8 and CYP2C9 genes and a decrease in the level of cellular protein in human U373 MG astrocytoma cells (60). More recently, Badisa et al. have demonstrated that the dual inhibition of cell cycle phases at G0/G1 and G2/M could appear in C6 glioma cells exposed to cocaine (61).

All these articles represent the evidence that cocaine exposure may be the cause for the appearance of monstrous, bizarre looking nuclei identified in our patient's tumoural astrocytes as their cell cycle was affected. The main molecular mechanism leading to inhibition of proliferation of cancer cells by cannabinoids is apoptosis (49) which was also identified in great number in our patient's histological sections.

Conclusion

The effects of illicit psychostimulant drugs exposure are not fully known. The morphological features identified in the histological samples of our patient revealed a sgcGB developed in a diffuse astrocytoma and in this respect, the case we presented in this paper was able to confirm the gliomagenesis effect of chronic multiple drug abuse. On the other hand, the drugs could have had inhibitory effects on tumour cells growth because, although the tumour was large in size and caused brain sub-falcine herniation, the patient only reported the onset of seizures late in the evolution.

Alongside the toxic effects on healthy organs and systems, these illicit drugs also have the effects of both inducing and inhibiting cancerogenesis, depending on the type of the drug. Therefore, the diagnosis of a brain tumour should take into consideration not only patient's clinical and imaging data, but also his lifestyle, especially his addiction to recreational drugs.

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Pitfalls and problems encountered in rat model sciatic nerve surgery

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ABSTRACT

When learning the basics of microsurgery, a trainee must be equipped with patience and perseverance in order to evolve. One must have the ground knowledge when it comes to peripheral nerve injury and nerve regeneration process in order to fully understand that the technique is vital for the outcome and final results. Furthermore, a trainee must practice on non-living tissue before performing successful in vivo operations and even in this case, one may be confronted with problems regarding the surgical technique. [1] The following article aims to reveal the main problems/mistakes when performing sciatic nerve surgery in an in vivo experimental model and the solutions for these problems.

Keywords
sciatic nerve,
rat model,
experimental surgery,
microsurgical technique

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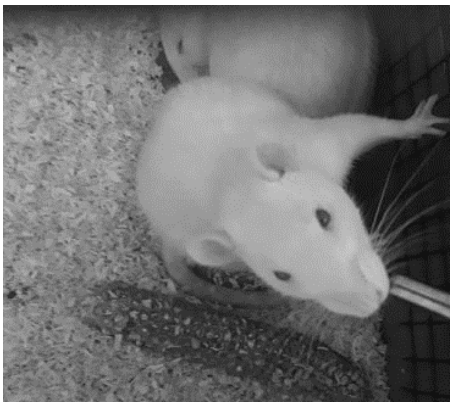
INTRODUCTION

There are many experimental surgical projects performed on the sciatic nerve of the rat. [2] There are many reasons why researchers choose this model: high similitude in nerve regeneration between the rat and the human; the lab rat (most commonly used the Wistar rat) is more available compared to other species and easier to manipulate; the anatomy of the sciatic nerve of the rat offers easy access, without significant comorbidity; the diameter and the length of the nerve permits different types of experiments (direct suture, reconstruction of different gaps with nerve conducts). [3] The sciatic nerve has a length of ~ 2,5-3cm before it divides into 3 terminal branches - common peroneal nerve, tibial nerve and sural nerve.

Although rat's sciatic nerve is one of the most used models for nerve regeneration it still may cause difficulties for an inexperienced surgeon. The problems one may encounter are related to anesthesia, [4] rat anatomy knowledge or microsurgical technique and each one of these issues may cause an enormous impact on the final outcome. Understanding the theoretical aspects of nerve regeneration [5],[6],[7] may help improve the surgical technique, especially when it comes to atraumatic manipulation.

Material and method

For this review there were used Wistar rats in different microsurgery training laboratories. The rats varied in age and weight (between 250-350g or 7-9 weeks). The anesthesia protocol consisted of a mixture of ketamine (75mg/kg) and xylazine (10mg/kg) administered intraperitoneally. A precise scale was used to weigh every animal before administrating the anesthesia. There were used proper microsurgical instruments as well as a microscope and appropriate sutures (8-0,9-0,10-0).



Wistar rat

Scale

Microsurgical instruments

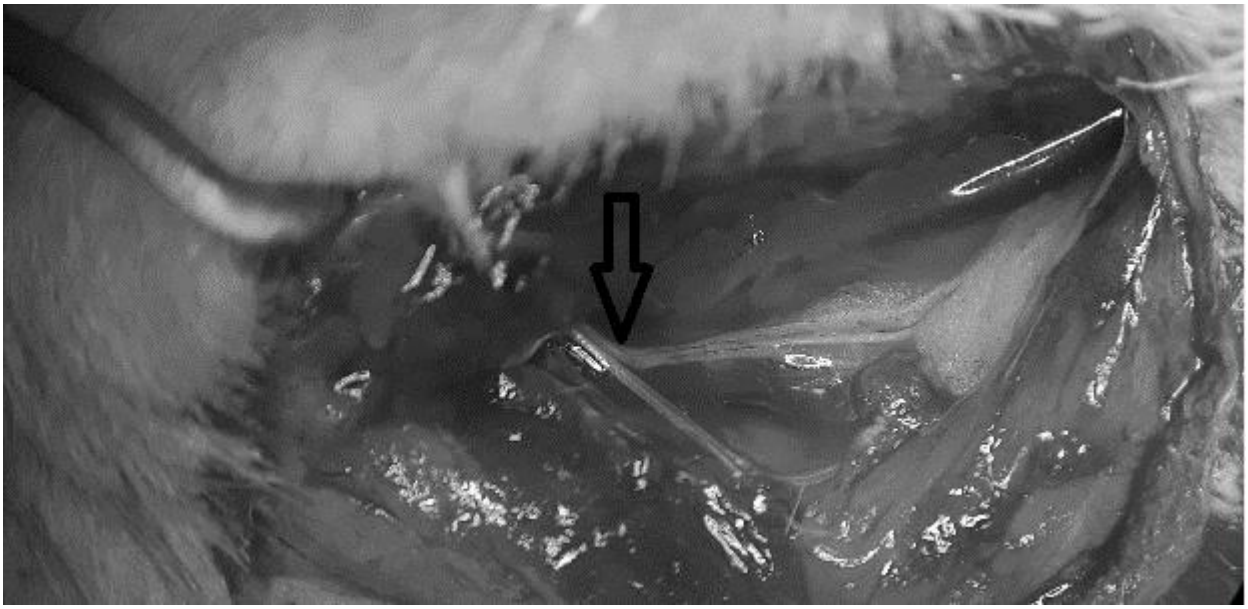
Sciatic nerve exposure

After shaving the dorsal aspect of the gluteal and thigh region, the rat is placed in prone position. An oblique-transverse skin incision is made and dissection along the biceps muscle fibers is performed in order to expose the underlying sciatic nerve. Mehedintu et al described different types of incisions to access the sciatic nerve. [7],[8] After nerve exposure, the rest of the operation is done under the microscope. This involves nerve dissection, nerve section and subsequent nerve repair. Proximal to the its division, the sciatic nerve can be used for various operations (direct suture after section, autografting, using different nerve conducts for iatrogenic nerve defects).

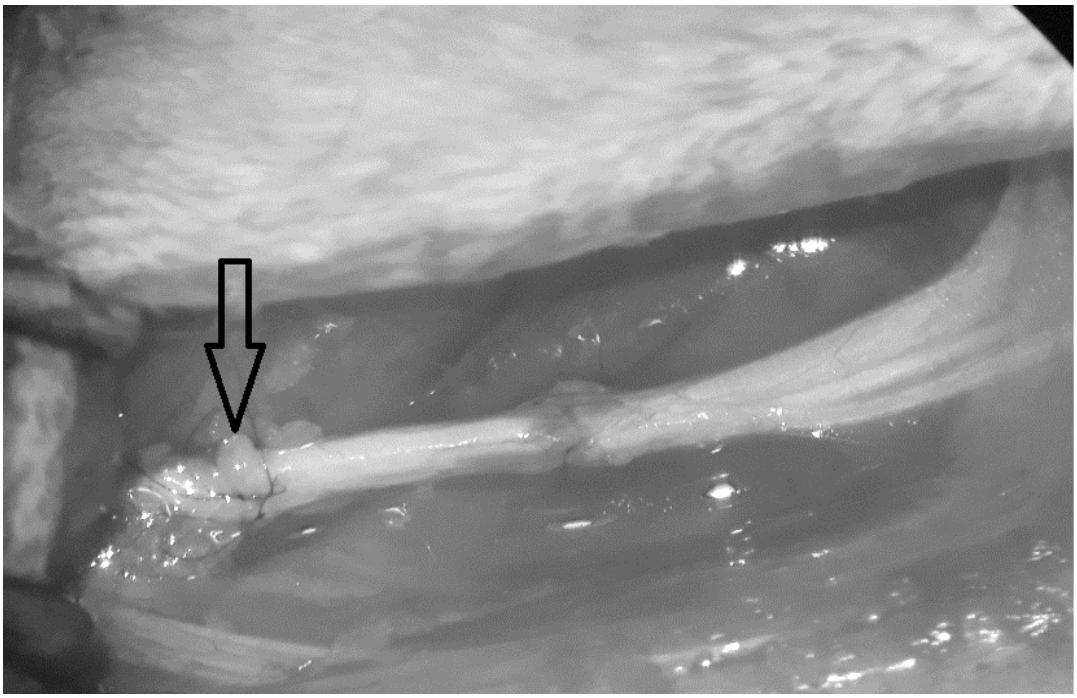
Results

A frequent mistake of the in vivo experiment is the incorrect administration of the anesthesia, which must be very well dosed and not lead to to overdosing and rat death.

Aside from the anesthetic issues, the most frequent problems when repairing a nerve defect with autograft arise from lack of experience. [9] These are: identifying the sciatic nerve correctly, improper incision site, excessive nerve dissection for a better exposure, choosing an unsuitable location to create the nerve gap, as well as microsurgical technique errors (inappropriate cooptation, high suture tension). Inadequate sutures for the nerve size also influence the recovery results.



Distal incision beyond the division of the sciatic nerve (marked with arrow)



Axoplasmatic protrusion (arrow) in the proximal nerve suture due to insufficient proximal dissection

Identifying the sciatic nerve correctly poses no problem if the skin incision site and the muscle dissection is performed in the right area and in a proper plane. A distal incision (too lateral and caudal), however, may create confusion in case not all branches are visible, thus mistaking the sciatic nerve to one of its branches. A contributing factor to this problem is represented by the placing of the rat in a slight prone-lateral position (instead of the custom prone position). These branches are half or even 1/3 of the sciatic nerve diameter (~1mm). To prevent this situation, the skin incision should be placed more cranial and medial, parallel and 1cm inferior to the femur, with the rat in prone position. When suspecting that the first incision is inappropriate, with exposure of just one branch of the sciatic nerve, extending the incision more proximal can solve the problem by identifying the correct nerve.

Another technical error is creating the nerve gap

too proximal (or not dissecting enough of the sciatic nerve from the muscle tissue in the proximal part). After nerve sectioning, the elastic fibers in the structure of the nerve determine retraction of the proximal stump in a plane which is hard to access, thus making the nerve suture difficult to perform. In order to prevent this problem, a proper dissection and the selection of the central area of the sciatic nerve to create the gap is recommended. The consequences of suturing a retracted stump are: inappropriate traction of the nerve (which risks injuring the nerve fascicles), unmatched fascicles in the suture (the surgeon is no longer able to observe the epineural vessels to guide a correct cooptation), axoplasmatic protrusion due to excessive traction and uneven suture. In all cases, inappropriate dissection results in prolonged operating times.

Creating the nerve gap too distal (close to the division of the sciatic nerve) poses a problem for nerve suturing because an epineural suture tends to shred the common sheath of the branches, dividing them into 3 separate nerves (which require individual repair). The ideal distal sectioning site is ~0,7cm proximal to the visible division of the sciatic nerve in order to have enough connective tissue for a strong nerve suture.

Discussion

It is recommended not to operate on rats lighter than 250g and younger than 7 weeks of age. Otherwise the nerve diameter might be smaller than 2mm, requiring adequate microsurgery equipment as well as a greater experience in nerve surgery. Above 350g or 9 weeks of age, the animals require more substance to induce anesthesia, without any extra benefits.

Multiple administration of anesthesia might lead to overdose, causing respiratory distress and in the end exitus. For this reason, if the anesthesia doesn't work accordingly from the beginning with the calculated dose, the operation should be postponed and the anesthetic options should be revised.

The iatrogenic nerve gap should be placed centrally, after exposing the sciatic nerve from its origin to its division.

Conclusions

Microsurgery requires adequate instruments and special training. Calculating the exact quantity of anesthetic reduces the death risk. Experience and attention are key factors in avoiding different complications related to nerve surgery. The microsurgical technique involves an atraumatic manipulation of the tissue, correct cooptation without suture tension and right alignment of the nerve fascicles. Respecting these rules results in a good nerve regeneration, with positive clinical outcomes.

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Gamma Knife radiosurgery: effect on corticotropin-secreting pituitary adenoma

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ABSTRACT

Introduction: Cushing's disease (CD) is a complex endocrine disorder characterized by an increased risk of recurrence and persistence of hypercortisolism after initial transsphenoidal adenomectomy, a situation requiring alternative therapeutic measures.

Case presentation: A 21-year-old female patient was admitted for weight gain with centripetal fat distribution, transient headache, hair thinning and psycho-emotional lability. Clinical examination revealed round facies, acne, purple-red striae, hirsutism with a Ferriman-Gallwey score of 20. The hormonal profile revealed high serum cortisol (of 283.1 ng/mL, normal:70-225 ng/mL) and high ACTH (Adrenocorticotropic Hormone) levels (of 260.6 pg/mL, normal: 7.2-63.3 pg/mL). The pituitary MRI (Magnetic Resonance Imaging) examination found a 4.3/4.4/6.2mm left paramedian microadenoma. The persistence of hypercortisolism after adenomectomy required GKRS (Gamma Knife radiosurgery). Four months after radiosurgery, complete remission of the disease was achieved and it was maintained at the last evaluation. At present, the patient is 20 weeks pregnant.

Conclusions: Gamma Knife radiosurgery offers a high control rate of pituitary adenomas and a reasonable rate of remission of residual hypercortisolism after neurosurgical treatment. After surgery or GKRS, periodic monitoring is necessary for patients with CD due to the risk of pituitary insufficiency or relapse.

Keywords
Cushing's disease, radiosurgery, Gamma Knife

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Introduction

Cushing's disease is a complex disorder, characterized by a series of symptoms such as central obesity, hypertension, diabetes, as well as psychiatric and neurocognitive changes, caused by an ACTH–secreting pituitary adenoma leading to cortisol hypersecretion [1].

The gold standard treatment for CD is transsphenoidal surgical excision of the tumour, which is often curative.

However, there is a failure rate of 10 to 35% in reaching complete remission, while a proportion of patients also experience disease recurrence in time [2-6].

A second-line treatment used to achieve control of hypercortisolism is represented by targeted radiation of the sellar adenomatous tissue, the most reliable therapy being GKRS [7,8].

Case presentation

A 21-year-old female smoker, without significant past medical history, was admitted for weight gain of 20 kg in the past two months with centripetal distribution, transient headache, hair thinning, sleeping disorders and psycho-emotional lability. Clinical examination revealed height of 160 cm, weight of 76 kg, BMI (Body Mass Index) of 29.68 kg/m^2, blood pressure of 125/85 mmHg, heart rate of 64bpm, round facies, acne, purple-red striae and hirsutism with a Ferriman-Gallwey score of 20. The hormonal profile showed high serum cortisol levels of 283.1 ng/mL (normal: 70-225 ng/mL) with maintained circadian rhythm, high 24-hour urine free cortisol (UFC) of 456.61μg/24h (normal: 50-190 μg/24h), non-suppression of cortisol after the 1 mg DXM (dexamethasone) suppression test (of 145.9 ng/mL, normal <18 ng/mL), adequate suppression after the two-day, 8 mg DXM test, high ACTH level of 260.6 pg/mL (normal: 7.2-63.3 pg/mL), high levels of DHEAS (Dehydroepiandrosterone-sulfate) and testosterone (Table 1). Pituitary function tests showed normal plasma gonadotropin levels, normal PRL (prolactin) and TSH (Thyroid Stimulating Hormone) of 0.51μUI/mL with low FT4 (Free Thyroxine) of 0.86 ng/dL (normal: 0.89-1.76 ng/dL). There were no changes in biochemical parameters. Pituitary MRI (Magnetic Resonance Imaging) examination described a left paramedian microadenoma of 4.3/4.4/6.2 mm in diameter. Treatment with 25 μg tyroxine daily was initiated. Transsphenoidal adenomectomy was performed one month later. A massive intraoperative haemorrhage did not allow the removal of the tumour, therefore GKRS at a dose of 25 Gy was performed three weeks later. Four months after radiosurgery, complete remission of the disease was achieved, which was maintained at the one-year post-radiosurgery evaluation (Tabel 1). MRI revealed the cystic transformation of the pituitary microadenoma. At present, the patient is 20 weeks pregnant.

Parameter	Before surgery	After radiosurgery	Normal limits	Units
Morning plasma cortisol	283.1	176.2	70-225	ng/mL
Plasma cortisol 11pm	148.9	74.9	50-165	ng/mL
24-h urinary cortisol	456.61	52.8	50-190	μg/24h
ACTH	260.6	43.14	7.2-63.3	pg/mL
Morning plasma cortisol*	145.9	9.1	< 18	ng/mL
Morning plasma cortisol**	94.7		<50***	ng/mL
DHEA-S	8.19	2.79	0.9-3.6	μg/mL
Testosterone	1.22	0.66	0.3-1	ng/dL
TSH	0.51	0.297****	0.4-4	μUI/mL
FT4	0.86	0.96****	0.89-1.76	ng/dL

Table 1: The endocrine parameters of a 21-year-old female patient diagnosed with Cushing's disease: before surgery and post-Gamma Knife radiosurgery. *after the 1mg overnight Dexamethasone suppression test; **after the two-day, 8 mg Dexamethasone suppression test; ***more than50% reduction; 24-h= 24-hours; ACTH= Adrenocorticotropic Hormone; DHEA-S= dehydroepiandrosterone-sulfate; TSH=Thyroid Stimulating Hormone; FT4=Free Thyroxine; ****25 μg/day Thyroxine therapy.

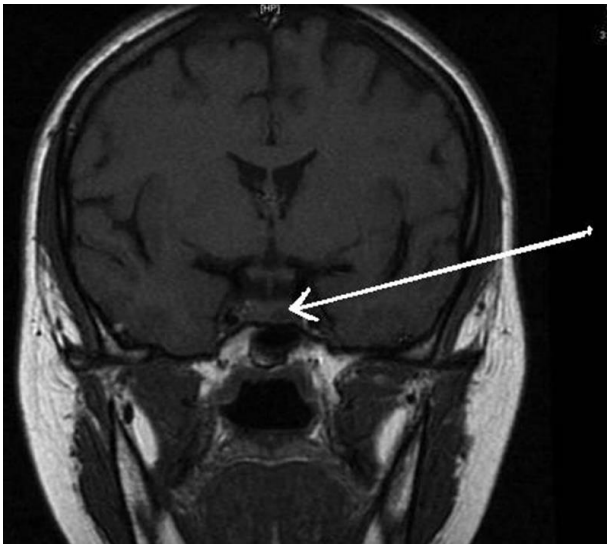

Figure 1: Preoperative contrast-enhanced pituitary MRI of a 21-year-old woman diagnosed with Cushing's disease: microadenoma measuring 4/6.5mm. Coronal plane.

Discussions

Cushing's disease remains a challenge in clinical practice, both in terms of diagnosis and treatment, especially for young patients [9-12]. Transsphenoidal adenomectomy, the first-line therapeutic option, is not always curative. Consequently, all patients should be informed that recurrence can occur in a delayed fashion and that annual endocrine testing should be done to track and confirm disease status [11-13]. In our patient's case, the failure of transsphenoidal adenomectomy was due to an intraoperative complication consisting of massive haemorrhage in the nasal mucosa. Considering the age of the patient and the desire to obtain a pregnancy, GKRS was recommended. The low risk of pituitary insufficiency and the relatively rapid remission of hypercortisolism are the main arguments for GKRS in persistent postoperative CD [14]. In this case, after GKRS, the secondary hypothyroidism persisted and was adequately controlled by thyroxine replacement therapy.

Generally, the secretor pituitary tumours are approached by neurosurgery, medical therapy in cases like acromegaly, prolactinoma (in this particular situation medical therapy is usually the first line), and Cushing's disease while radiotherapy remains a final option due to slow rate of response and the risk of associated hypopituitarism [16,17,18]. In this particular case the effect was rapidly observed. The non-secretor pituitary tumours are referred to surgery only if mass effect is positive [19,20]. As final option in Cushing's disease one time or two times bilateral adrenalectomy is done knowing the risk of lifelong adrenal insufficiency [21,22].

Menstrual disorders and infertility are common in CD patients [15]. In our patient's case there were no changes in ovarian function before GKRS, except for a higher level of testosterone. The normalization of cortisol, testosterone and DEAS levels in less than 6 months after GKRS allowed spontaneous pregnancy. Considering the therapy used in this case, it is advisable to carefully monitor pituitary function throughout pregnancy.

Conclusions

Gamma Knife radiosurgery offers a high control rate of pituitary adenomas and a reasonable rate of remission of residual hypercortisolism after neurosurgical treatment. Close follow-up is necessary for patients with CD due to the risk of possible relapse and pituitary insufficiency after surgery or GNRS.

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Preliminary study of thrombogenicity induced by the nanoparticle surface coating of intracranial stents

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ABSTRACT

Endovascular treatment of intracranial aneurysms with intracranial stents was proven to be clinically safe and effective, but is still associated with a risk of thromboembolic complications. Stent thrombosis could be a sever complication associated with specific stent surface coatings and designs. Standardized in vitro tests for investigation of thrombogenicity induced by different nanomaterials were used as the basic method in carrying out the present study. Therefore, the aim of this study was to evaluate the thrombogenicity of three different nanomaterials (ZnO, TiO2 si Fe3O4) possible used as surface coating for intracranial stents. This study is based on a procedure for in vitro analyses of plasma coagulation time. To measure the plasma coagulation time, platelet-poor plasma from human whole blood was in vitro exposed to nanoparticles and analysed in prothrombin (PT) and activated partial thromboplastin (APTT).

Keywords
intracranial stents, thrombogenicity, nanomaterials, surface coating

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INTRODUCTION

A variety of intracranial stents are used in permanent blood contact. Thrombogenicity is the property of a material to induce a thrombus formation, which may result in partial or complete blood vessel occlusion. Thus, thrombogenicity of intracranial stent may have important implication in the long-term outcome of neurosurgical patients that may lead to a life-threatening condition such as stroke. Stent / blood contact surface activity has been a widely subject discussed and reported and, notwithstanding the clinical significance of this phenomenon is still controversial.

Moreover, the surface coatings of these implants that are in permanent contact with blood are often subjected to tests on coagulation in order to use the least thrombogenic materials. Activated partial thromboplastin time (aPTT), prothrombin time (PT) and the international normalized ratio (INR) are indicated as the techniques of choice used to help detect and diagnose a bleeding disorder or excessive clotting disorder. In our study, an in vitro model was established, which allows investigation of neurovascular stents with

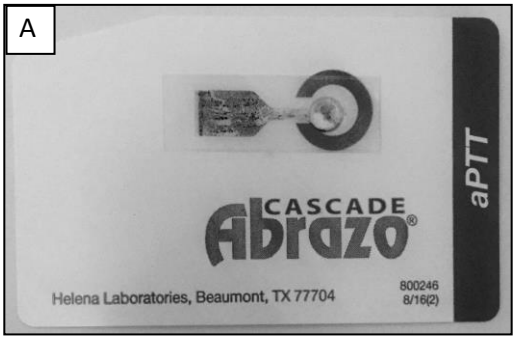
regard to thrombogenicity and coagulation activation. The preliminary study was designed to compare these 3 methods to address the coagulation property of three biomaterials (ZnO, TiO2 si Fe3O4) with emphasis on the sensitivity and reproducibility of the test. These three biomaterials prepared in the form of nanoparticles were evaluated for their coagulation profile during incubation in human plasma. The study presents a revised version of these methods to include updated details on sample preparation of nanoparticles, selection of nanoparticle concentration for in vitro study, and updated details on test controls [4,5,6].

MATERIALS AND METHODS

Platelet rich plasma (PRP) is obtained from fresh human blood derivative incubated with nanoparticles for 15 minutes at 37 ° C. This probe is subsequently analysed by evaluating the plasma coagulation time and how the nanoparticles affect this part of the haemostasis control system.

The materials listed below are required for coagulation tests for the study of nanoparticles (Fig. 1):

1. Vacuum test tubes for coagulation testing;
2. 12% sodium citrate.
3. Thermostat bath;
4. Special centrifuge with tubes test stand;
5. Fresh human blood completely anti-coagulated with sodium citrate and obtained from at least three healthy donors known to be out of any anti-inflammatory and antihistamine drug, blood thinning agents and birth control pills;
6. APTT and PT / INR test cards for Abrazo Cascade equipment;
7. Coagulation tester analyzer Abrazo Cascade System from Helena Laboratories;
8. Nanoparticle sample for analysis.



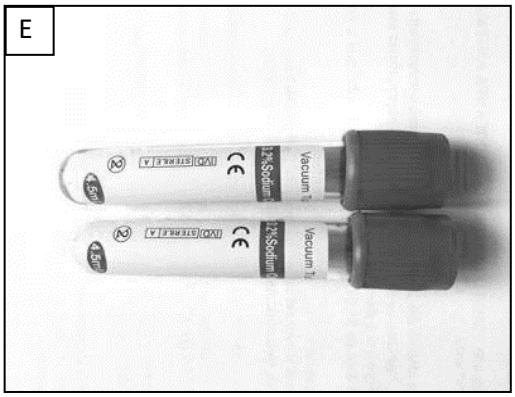


Figure 1: **A**- aPTT tester card; **B**- PT / INR tester card; **C**- Abrazo Cascade Coagulation Test Equipment; **D**- Centrifuge; **E**- Vacuum test tubes with citrate; **F**- Thermostatic bath.

PREPARATION OF THE STUDY SAMPLES

The concentrations used in these assays are based on an estimated plasma concentration in a medium-sized human patient at the desired therapeutic dose. In our study, we refer to this concentration as the theoretical concentration of plasma. The hypotheses and considerations for estimating theoretical plasma concentration have been reviewed in the literature [4] and are summarized below.

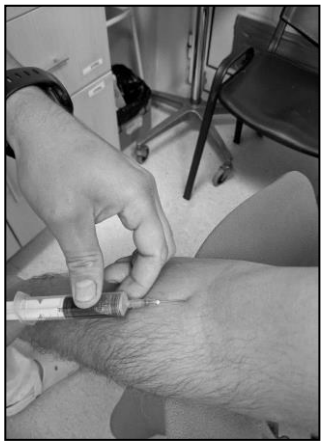
For the calculation of nanoparticle concentration, we used in vitro test reports in mice.
If the mouse dose used is approximately 123 mg / Kg in this example the human dose can be calculated as follows:

$$\text{human dose} = \frac{mouse\ dose}{12.3} = \frac{123\frac{mg}{kg}}{12.3} = 10\ \text{mg/kg}$$

It is known that blood volume accounts for about 8% of body weight (for example, an adult of 70 kg has about 5.6 L (8% of 70) blood. This allows an extremely crude estimate of maximum blood concentration.

$$\text{in vitro concentration}_{human\ matrix} = \frac{human\ dose}{human\ blood\ volume} = \frac{70\ kg\ x\ 10\frac{mg}{kg}}{5.6\ L} = \frac{700\ mg}{5.6\ L} = 0.125\ \text{mg/mL}$$

Each test evaluates a nanoparticle formulation of three different materials at preset concentrations. When the predicted therapeutic concentration is not known, the highest final concentration is 1 mg per ml.



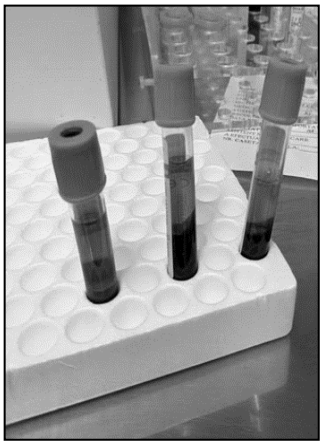


Figure 2: **A**- Blood collection; **B**- Centrifuge with multiple cartridges; **C**- Vacutainer tubes with centrifuged plasma.

PLASMA PREPARATION

When the blood collection procedure is started the first 10 ml of blood must be discarded [fig.2] due to necessity to prevent the activation of cells and plasma biochemical cascades by the venous puncture procedure. Exposure and storage of blood or plasma at extreme temperatures (<20 C or> 37 C) can affect the quality of test results and should be avoided. Two types of plasma can be obtained to perform this experiment: platelet rich plasma (PRP), platelet poor plasma (PPP). Plasma from individual donors can be analyzed separately or collected together. The combined plasma is prepared by mixing plasma from at least two individual donors.

NORMAL TEST PLASMA PREPARATION

Fresh whole blood must be used within 1 hour after collection. The blood is then centrifuged for 10 min at 3000 g at 20–22 C and plasma is collected from at least two donors. The combined plasma is stable for 8 hours at room temperature. The assay can also be performed in plasma from individual donors, when needed for mechanical tracking experiments. Two duplicates (four total samples) of plasma test are analyzed in each of the coagulation tests. A duplicate is performed prior to analyzing the nanoparticle samples and the second duplicate at the end of each run to verify that plasma functionality is not affected throughout the experiment.

NANOPARTICLE-TREATED TEST PLASMA PREPARATION

In a micro-tube, 0.125 mg of nanoparticles and 1 ml of plasma are combined. Mix well on a shaker and incubate for 30 min at 37 ° C. Three test tubes are prepared for each test sample (ie, when each nanoparticle is tested at four concentrations, one needs three test tubes for each concentration for a total of 12 test tubes per nanoparticle test).

PLASMA COAGULATION TESTS (Fig. 3)

1. Prepare the Cascade Abrazo equipment as described in the manufacturer's manual.
2. Preheat all tubes to 37 C.
3. Configure the instrument test parameters for each of the two tests (aPTT and PT / INR).
4. Add to the micro-tubes with pre-loaded nanoparticles 1 ml of plasma.
5. Stir micro-tubes for 5 minutes.
6. Scan each specific tester card (aPTT and INR / PT) before testing;
7. Insert the test card into the Cascade Abrazo device;
8. Allow the instrument to warm up before use.
9. Extract the test solution with the micropipette.
10. When the test timer starts, transfer the solution to the test card's geode by pressing the PIP button to activate the pipette.
11. When the time is up, the device will beep and the recording of coagulation time will remain displayed on the screen until further testing begins.
12. The average of the three values must be calculated for each control or test.
13. The average for each control and test sample should be between 25%.
14. If two duplicates of the same study sample showed different results more than 5%, this sample was reanalysed.

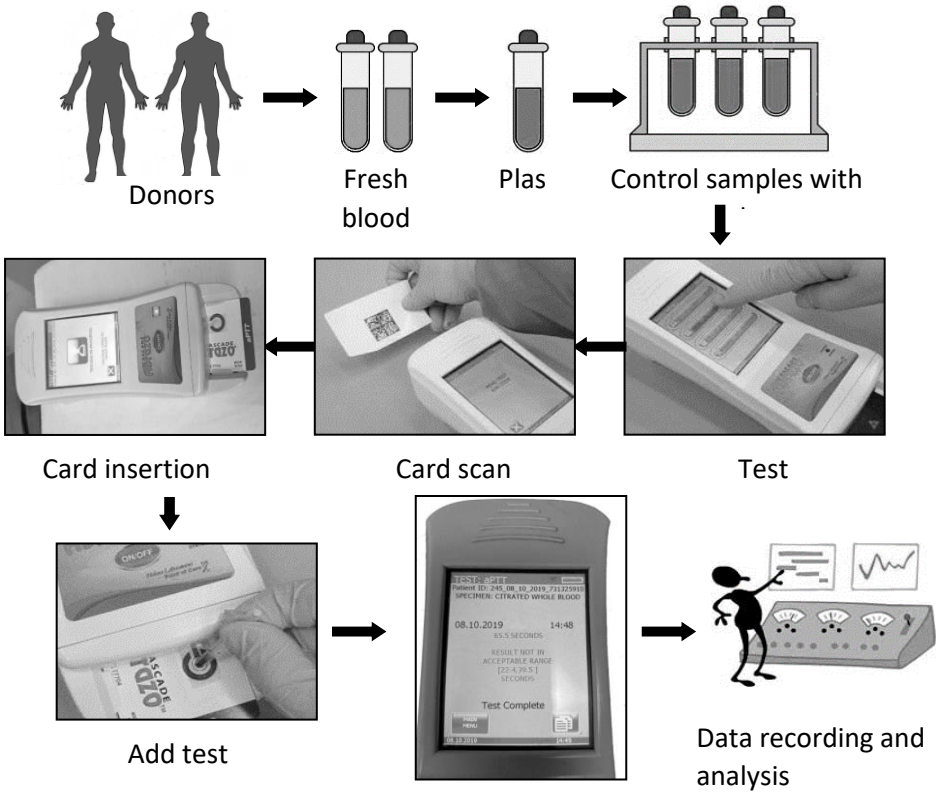
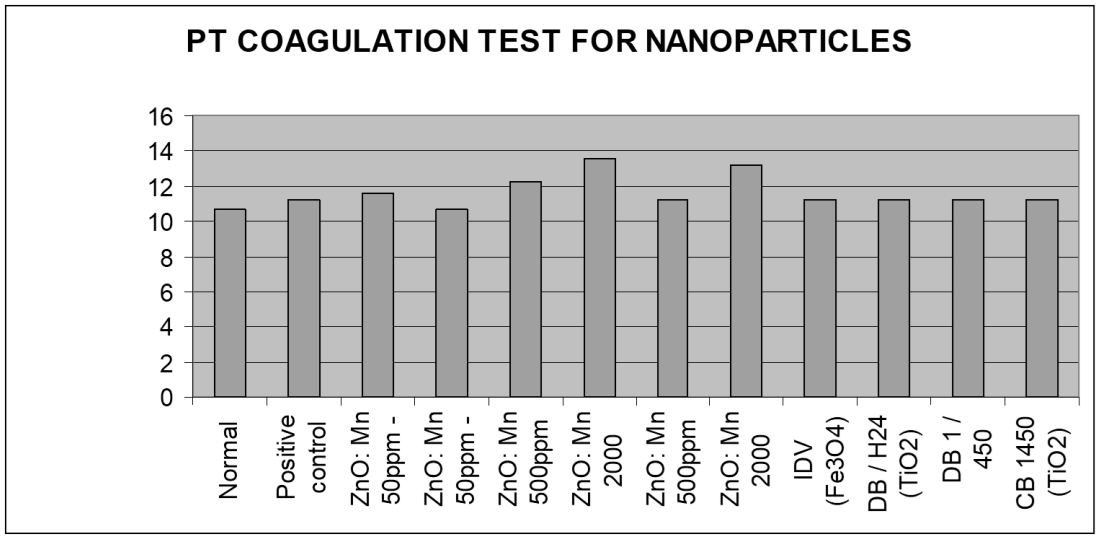
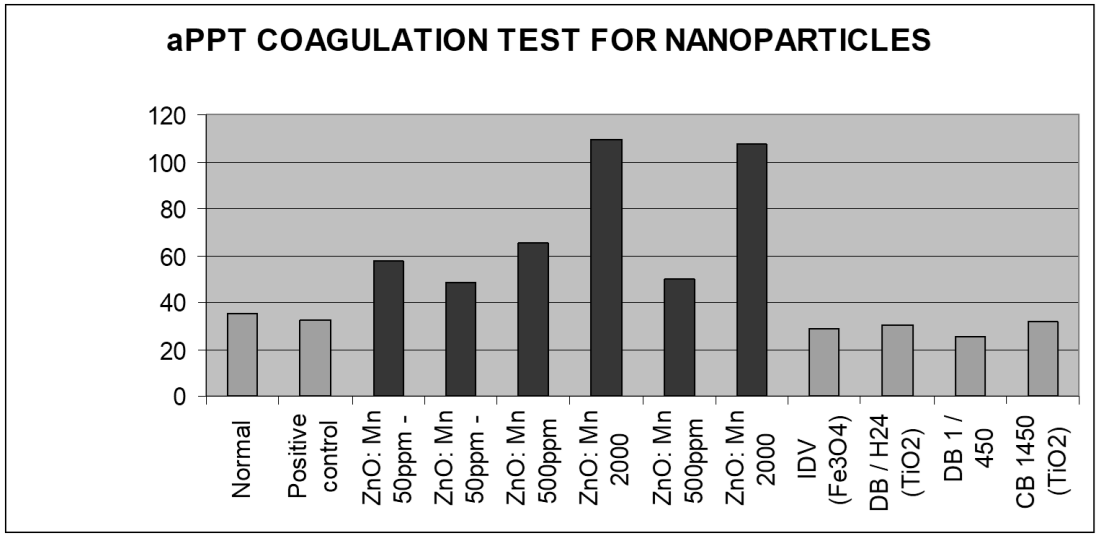


Figure 3: Schematic diagram of coagulation time measurement.

Results

The results shown in this study indicate that ZnO nanoparticles administered in the blood vessels can adsorb the coagulation factors in a specific form to the surface functional group, without activating these factors and that the adsorbed coagulation factors are not functional. Also, ZnO nanoparticles delayed the coagulation time with the size or surface functional group specificity, because all types of ZnO nanoparticles adsorbed the coagulation factors of the common pathway, some types of nanoparticles adsorbing more factors than others. The thrombogenicity study of TiO2 and Fe3O4 nanoparticles suggests that nanoparticles should be an effective agent in prolonging the blood clotting time, thus exerting an anti-coagulant effect, thus improving the hemocompatibility of the coating. The ability of TiO2 and Fe3O4 nanoparticles to regulate platelet adhesion and plasma coagulation was thus demonstrated in vitro.





Discussions

Treatment of neurosurgical patients with functionalized coating surfaces stents continues to evolve with the current emergence of nanoparticle functionalization technology that offers a combination of pharmacological and mechanical approaches to prevent thrombosis and arterial restenosis. Despite the promising short term and mid-term outcomes of surface coated stents, there are serious concerns about adverse clinical effects of late stent thrombosis. Certain nanoparticles intended for drug delivery application are designed

to reduce the effect of thrombogenicity of an intracranial stent in the bloodstream for a prolonged coagulation time in the circulatory system. Thus, a larger therapeutic window is offered until systemic anti-aggregation is administered. Studies evaluating nanoparticles effects on plasma coagulation time and their tendency to initiate vascular thrombosis are useful to assess nanoparticle thrombogenicity [1,2,3].

A number of nanotechnology approaches have been borrowed and applied in stent technology. Stents with biofunctionalized surfaces with nanoparticles with high stability and carrier capacity, able to reduce the interaction with blood components and to incorporate substances as carriers for bioactive factors and drugs have been manufactured. There are already implants in the form of drug-eluting or biodegradable stents that induce healing reactions by triggering the body's natural processes [2,3].

At present, there is not much data on the thrombogenicity of stent materials dictated by nano-scale observations. Because thrombogenicity is a multiparametric process, our study tests the hypothesis of the influence of surface nanotopography on platelet activation, in order to produce nano-coatings with less thrombogenic stent by adapting their surface properties. It is in fact intended to implement a real-time study of platelet response to biomaterials to improve hemocompatibility.

The primary phenomenon of blood-material interaction was the rapid and selective adsorption of proteins through a three-step process represented by the transport to the interface, the adsorption reaction and the conformational rearrangement. Thus, the engineering of the surface properties (physical and chemical characteristics) of the implants aims to reduce the adsorption of proteins and cellular interactions resulting in the improvement of implant biocompatibility.

Platelets are the main cells present in the blood that play the most important role in blood-material interactions. The adhesion of platelets to a surface is conditioned by two independent mechanisms. These are the transport of platelets to the surface, which depends on the flow conditions and the reaction of platelets with the surface, which depends on the nature of the surface and the adsorbed proteins.

In this paper, we want to verify the influence of nanotopography and surface characteristics on the thrombogenicity of different possible types of nano-coatings (ZnO, TiO2 and Fe3O4). Thus, the results obtained by us are in line with previous hemocompatibility studies in the literature regarding the influence of these nanoparticles on coagulation. These lead us to the conclusion that nanotopography and surface roughness of biomaterials influence their biological behaviour. The studies within our project will be continued by thrombogenicity analyses on nanoparticle-coated metal bands.

This study about thrombogenicity induced by the nanoparticle is the subject of the grant: "New diagnostic and treatment methodologies: current challenges and technological solutions based on nanoparticles and biomaterials", that won the 2017 complex projects completed in consortia CDI, grant number: PN-III-P1-1.2-PCCDI-2017-0062, funded by CNCS – UEFISCDI Romania.

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Nonsteroidal anti-inflammatory drugs-induced hypersensitivity reactions: algorithm for the diagnostic and management

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Keywords
Nonsteroidal Anti-Inflammatory Drugs (NSAID), drug hypersensitivity reaction, perioperative, diagnostic, management

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ABSTRACT

The role of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) in neurosurgical practice is a secondary one, however they are still constantly involved in perioperative management of pain or in nonoperative management of acute radiculopathy. Beside the well-known adverse reactions (ADRs), the neurosurgeon practitioner should also take in account the drug hypersensitivity reactions (DHRs) of NSAIDs and be able to deal with it. The aim of this paper was to review the diagnostic and management steps for NSAIDs-induced Hypersensitivity Reactions. The actual stratification of NSAIDs-induced Hypersensitivity Reactions is based on understanding of the heterogeneity of immunological/non-immunological mechanisms of reactions and complexity of clinical manifestations. Practically, this stratification allows the physician to assess suspicion of DHR, based on anamnesis and clinical analysis, and to consider further practical steps to manage and eventually confirm the diagnosis. Drug allergies are considered only the DHRs for which a definite immunological mechanism (either drug-specific antibody or T cell) is demonstrated. In conclusion, clinical analysis and anamnesis of patient with NSAIDs-induced Hypersensitivity Reactions can be realized by any physician and could be enough to diagnose, but it is not sufficient to confirm the diagnosis. In vitro tests and oral provocation challenges may be necessary to be undertaken by an allergy specialist.

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INTRODUCTION

Post-operative pain management in neurosurgery is very complex because the administration of some drugs might interfere with postoperative outcomes or with the neurological evaluation[22]. Although the use of nonsteroidal anti-inflammatory drugs (NSAIDs) in neurosurgery has been restricted due to their platelet dysfunction and risk of intracerebral bleeding, the postoperative pain is a nociceptive type pain which responds well to NSAIDs[17]. Furthermore, NSAIDs are

effective to reduce morphine requirements by 25%–50% in a broad spectrum of postoperative (consequently decreasing adverse effects secondary to opioids administration) and for rescue analgesia in post-craniotomy pain management (may have even greater benefit when administered preemptively)[8,22]. The use of NSAIDs has been proved to be efficient also for the pain management after spine surgery[19,21]. Besides perioperatory involvement, NSAIDs are often prescribed (for short term) in addition to muscle relaxants and oral corticosteroids for nonoperative management of acute cervical radiculopathy[4,10].

A recent study from the UK, conducted by Marinho et al., in 2016, reported the use of mainly opioids (82%) by anesthesists, followed by paracetamol (56%) and NSAIDs (28%). Diclofenac was the most commonly used NSAID for perioperative pain, followed by parecoxib and ibuprofen[15]. In a survey study of 31 neurosurgical units in Great Britain, 42% of these reported prescribing NSAIDs, with 19 % prescribing NSAIDs on a regular basis for post-craniotomy analgesia[13].

Drug Hypersensitivity Reactions (DHRs) after NSAIDs administration are less taken into account by practitioners, because gastrointestinal bleeding, platelet dysfunction, increased bleeding times and cardiovascular risk are the most known and severe adverse drug reactions induced by NSAIDs[6]. Depending on the method of assessment, the analyzed population and type of reaction, the general prevalence of NSAIDs hypersensitivity ranges from 0.6 to 6% and according to the Online Latin American Survey on Anaphylaxis (OLASA), NSAIDs were the culprit agents in 73% of the drug-induced anaphylaxis[18].

NSAIDs are frequently involved in DHRs because they are frequently prescribed at all ages. Every practitioner should be aware that any drug can induce a DHR and the NSAIDs (especially Ibuprofen) beside some antibiotics are more likely to be the culprit for immediate reactions such urticaria and anaphylaxis[6]. We propose a model of clinical approach for the neurosurgical patient with suspected NSAID hypersensitivity reaction.

I. NSAIDs-induced hypersensitivity reactions - Diagnostic steps

According to WHO (World Health Organization), **Adverse Drug Reactions induced by drugs** are classified as:

- **A-type reactions:** predictable and dose dependent, with a frequency of approximately 75%;
- **B-type reactions or DHR:** unpredictable and dose-independent, with a frequency of approximately 25%; based on their mechanisms these are classified as:
  - ***immunologically mediated (allergic reactions)*:** due to a specific IgE or due to a T cell response
  - ***non-immunologically mediated* (*non-allergic reactions*** or ***cross-reactive*):** due to an increased release of cystenyl leukotrienes by inflammatory cells, secondary to the inhibition of COX-1 enzyme[16]; these are caused by changes of pharmacological pathways (e.g. inhibition of cyclooxygenase)[14].

In the general medical practice, when a drug allergic reaction is suspected, DHR is the used term, according to international consensus on drug allergy[5]. Drug allergies are considered only the DHRs for which a definite immunological mechanism (either drug-specific antibody or T cell) is demonstrated.

Cross hypersensitivity represents the majority of DHRs induced by NSAIDs compared to specific immunological mediated-reactions (76 vs. 24%)[14].

Based on the time-lapse between the last drug administration and the onset of the reaction, the DHRs of NSAIDs are classified as[5]:

- **immediate reactions** (usually immediate to several hours after the drug exposure):
  - **IgE-mediated (immunological):**
    - **single-NSAID-induced urticarial / angioedema / anaphylaxis (SNIUAA)** manifested as urticaria, angioedema and/or anaphylaxis induced by a single NSAID or by several NSAIDs belonging to the same chemical group in subjects that tolerate other chemically nonrelated NSAIDs and usually do not have a history of chronic urticaria or asthma → labeled as;
  - **Non IgE-mediated (non-immunological or cross-reactive):**
    - **NSAIDs-exacerbated respiratory disease (NERD)** manifested as bronchial obstruction, dyspnea, and nasal congestion/rhinorrhea induced by aspirin or other NSAIDs in patients with an

underlying chronic airway respiratory disease (asthma/rhinosinusitis/nasal polyps);
    - **NSAIDs-exacerbated cutaneous disease (NECD)** manifested as wheals and/or angioedema – induced by aspirin or other NSAIDs in patients with a history of chronic spontaneous urticaria;
    - **NSAIDs-induced urticaria/angioedema (NIUA)** manifested as wheals and/or angioedema – induced by aspirin or other NSAIDs (at least two NSAIDs with different chemical structure - not belonging to the same chemical group) in healthy subjects (without history of chronic spontaneous urticaria);
- **non-immediate reactions** (usually more than 24 h after exposure):
    - **Single-NSAID-induced delayed hypersensitivity reactions (SNIDR)** are T cell – mediated, manifested as cutaneous symptoms (exanthema), fixed drug eruption, Drug Reaction with Eosinophilia and Systemic Symptoms, acute generalized exanthematous pustulosis, Stevens-Johnson Syndrome/toxic epidermal necrolysis, severe organ-specific or systemic symptom – induced by a single NSAID.

Immediate to several hours after the drug exposure, as a chronological stratification, has limitations:

- the exact onset of initial symptoms might be hard to pinpoint;
- the route of administration can influence the time interval in which the reaction occurs.
- cofactors such as co-medications, food intake, alcohol and exercise, can speed up or slow down the onset or progression of a reaction[2].

	NSAIDs-induced hypersensitivity				
	NSAIDs-Exacerbated Respiratory Disease (NERD)	**NSAIDs-Exacerbated Cutaneous Disease (NECD)**	**NSAIDs-Induced Urticaria/ Angioedema (NIUA)**	**Single-NSAID-Induced Urticaria/ Angioedema or Anaphylaxis (SNIUAA)**	**Single-NSAID-Induced Delayed Hypersensitivity Reactions (SNIDR)**
Clinical manifestations?					
	respiratory symptoms (bronchial obstruction, cough, wheezing dyspnea, and nasal congestion/rhinorrhea)	wheals and/or angioedema		urticaria, angioedema and/or anaphylaxis	very diverse symptoms – from cutaneous symptoms (with different degree of severity) to severe organ-specific or systemic symptoms
Onset time of the reaction?					
	1-2 hours after drug intake, up to 24 hours (when reaction occurs within minutes or during the 1st hour there is highly susceptible for SNIUAA or NERD/NECD)				more than 24 hours after drug intake
History/relapse of symptoms?					
	history of similar symptoms caused by other strong COX-1 inhibitor and/or history of good tolerance of selective COX-2	history of reaction to more than one chemically unrelated COX-1 inhibitor		history of cutaneous (urticaria and/or angioedema) and/or anaphylactic reactions to a single NSAID	usually no typical history
Underlying chronic diseases?					
	asthma and/or rhinosinusitis with nasal polyps	episodes of spontaneous chronic urticaria / angioedema, unrelated to NSAIDs	typical no underlying diseases		

Table 1. Diagnosis steps for NSAIDs-induced hypersensitivity

After the physician has gone through previous anamnesis and corroborates the obtained clinical data with DHRs classification represented in Table 1, there is a high probability to clinically diagnose a DHR as follows:

- the typical form of **SNIDR** can be clinically diagnosed (heterogenic reactions, mainly cutaneous symptoms, 24 h or more after last drug administration), but in clinical practice, in time-lapse between the intake of culprit drug and onset of delayed reactions other drugs are administrated, which can make the diagnosis assessment difficult;
- **NERD** can be suspected when a patient with asthma and/or rhinosinusitis with nasal polyps accuses respiratory symptoms (cough, wheezing, dyspnea, nasal congestion, nasal discharge). The diagnosis of NERD is confirmed if he reports a history of similar symptoms after other strong COX-1 inhibitors and/or history of good tolerance of selective COX-2;
- in the case of acute cutaneous symptoms (urticaria/angioedema) and/or anaphylactic symptoms after intake of NSAIDs, we have to distinguish between three subtypes of hypersensitivity: NECD, NIUA or SNIUAA. The detailed history of previous reactions establishes whether the patient is sensitized to a single drug or is the case of a cross-reactive type of NSAIDs hypersensitivity:
  - allergic type I reaction (SNIUAA) is based on a history of cutaneous (urticaria and/or angioedema) and/or anaphylactic reactions to a single NSAID.
  - nonallergic type reaction (cross-reactive) is suspected in a patient with history of more than one chemically unrelated COX-1 inhibitor. The diagnosis of NECD is based on history of episodes of spontaneous chronic urticaria/angioedema to several chemically unrelated NSAIDs. The diagnosis of NIUA is based on history of hypersensitivity cutaneous reactions to several chemically unrelated NSAIDs concomitant and a negative history of spontaneous urticaria/angioedema.

The clinical reality may not always look like in the above description – 10% of patients with NECD have respiratory symptoms (bronchoconstriction) that resembles the NERD23. Moreover than this, concomitant rhino-conjunctivitis in patients with NSAID-induced cutaneous reactions are reported3.

II. NSAIDs-induced hypersensitivity reactions - management

The main indication in case of an already diagnosed NSAID DHR is the avoidance of drugs from the same family. However, the neurosurgeon has the possibility of an alternative NSAID related on type of DHR:

- in the case of SNIUAA, when the specific NSAID has been identified, it can be replaced by another NSAID with similar anti-inflammatory potency but an unrelated chemical structure;
- in the case of NERD/NECD, preferential COX-2 inhibitors (around 91 to 99% of patients with hypersensitivity NSAIDs tolerate meloxicam - doses higher than 15 mg daily should be avoided) and highly selective COX-2 inhibitors (celecoxib with a rate of only 4% positive reactions and etoricoxib with a rate of reactions ranging from 2,9% to 4%) are generally well tolerated9,11,12; leukotriene-modifying drugs may bring benefits in correlation with standard chronic urticaria management1;
- NIUA – avoidance of NSAIDs (desensitization done by allergolog).

In case of patients who have taken multiple drugs (in addition to an NSAID), the administration of alternative drugs has to be suspended firstly; drugs continuously taken for months are not suspected (exception is angiotensin-converting-enzyme which can develop angioedema after months or even years of intake).

Particularly when a patient, with known DHR to a COX-1 inhibitor, needs urgently analgesic medication, the opioids should be recommended due to the differences in structure. Also the selective COX-2 might be an alternative, but a benefit – risk analysis is imperative.

III. NSAIDs-induced hypersensitivity reactions with potential of severe progression

In the case of a suspected DHR, a severe progression should always be taken into account. According to Scherer K et. al and to the more recently task force report of European Academy of Allergy and Clinical Immunology, the severe progression could be

indicated by the presence of some clinical signs [20,7] (Table 2).

Immediate reaction (anaphylaxis)	Non-Immediate reaction (delayed reaction)
• Severe urticaria • Rapid onset of extensive pruritus (especially scalp and palmo-plantar) • Angioedema of the oral mucosa (especially pharynx and larynx) • Hypotension • Conjunctivitis and rhinitis with flush on face and neck • Dyspnea with bronchospasm (particularly in asthmatics)	Cutaneous symptoms: • Hemorrhagic necrotizing lesions • Centrofacial edema (diffuse erythematous swelling) • Purpura • Involvement of large body surfaces or erythroderma • Painful skin • Atypical target lesions • Nikolsky sign positive • Erosive stomatitis • Mucositis (involving more than one mucosal area)
	Symptoms suggesting internal organ involvement: • Unexplained rapid onset of high fever (> 39 °C) • Arthritis and arthralgias • Disseminated lymphadenopathy

Table 2. Clinical signs for a potential severe progression of NSAIDs-induced hypersensitivity reactions.

IV. Criteria to refer a patient with DHS to allergist

First steps that include a clinical analysis and anamnesis of patient can be realized by a non-specialist and could be enough to diagnose in some cases, but frequently NSAID hypersensitivity, is not sufficient to confirm the diagnosis (Fig. 1). In vitro tests and oral provocation challenges may be necessary to be undertaken by an allergy specialist.

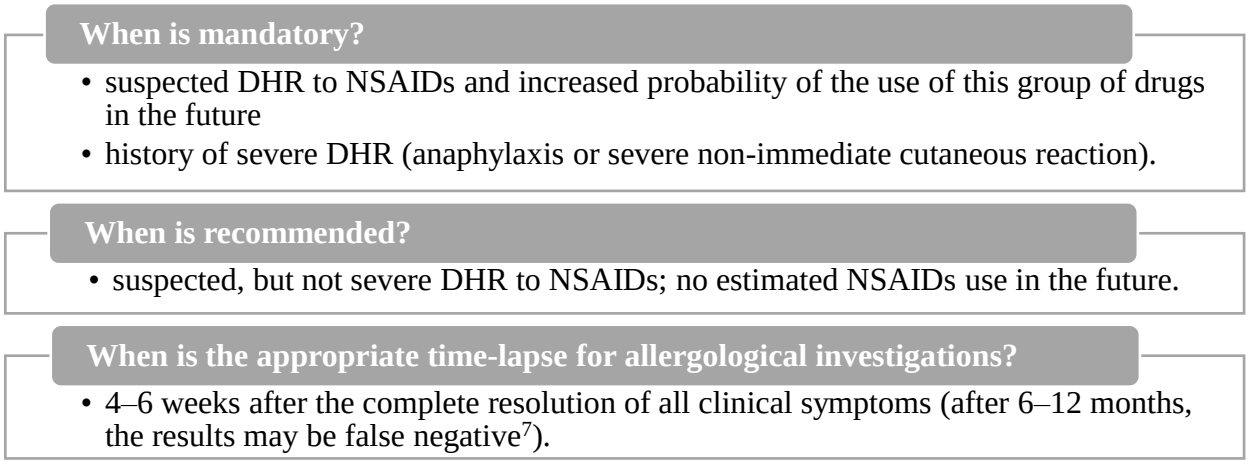

Figure 1. Criteria to refer a patient with DHS to allergist

Up to 1/3 of patients with chronic spontaneous urticarial report exacerbations of cutaneous symptoms upon ingestion of NSAIDs. The level of sensitivity could temporary variate in relation to coexisting chronic spontaneous urticaria and consequently, sensitivity may decrease and even disappear – therefore reassessing the tolerance to NSAIDs is appropriate14.

Conclusions

The neurosurgical practice implies often moderate-to-severe postoperative pain in a multitude of procedures such as craniotomies for aneurysm clipping, craniotomies for tumor resections and epilepsy surgery, neuroradiological procedures and penetrating traumatic brain injury. Post-operative pain management is very complex due to interference of drugs with postoperative outcomes or with the neurological evaluation22. Nociceptive type pain responds well to NSAIDs, even their use in neurosurgery has been restricted due to the platelet dysfunction and risk of intracerebral bleeding17.

Diagnosing DHRs is a complex issue. Clinical analysis and diagnostic of a DHR can be realized by any physician, but the confirmation of the diagnosis needs in vitro tests and oral provocation challenges which should be undertaken by an allergy specialist. If the NSAID-induced hypersensitivity is confirmed,

recommendations based on the current classification for drug avoidance, use of alternative NSAIDs, and other management modalities, including aspirin desensitization, can be implemented.

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Current applications of 3d printing in neurosurgery

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ABSTRACT
Medical implications of 3-dimensional (3D) printing technology have progressed with increasingly used especially in surgical fields. 3D printing techniques are practical and anatomically accurate methods of producing patient specific models for medical education, surgical planning, training and simulation, and implants production for the assessment and treatment of neurosurgical diseases. This article presents the main directions of 3D printing models application in neurosurgery.

Keywords
3D printing, neurosurgery, 3D models

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INTRODUCTION

Since its initial appearance in the 1980s, three-dimensional (3D) printing has revolutionized the practice of rapid prototyping in many areas, such as design, engineering and medicine. This technique consists in the manufacture of 3D physical models, based on computer models, by depositing successive layers of material in the underlying structure to build 3D objects. [1,3,5] Modelling by 3D printing uses either a thermoplastic material that hardens after it has been heated during extrusion, or uses a low power ultraviolet (UV) laser to solidify a liquid photosensitive polymer in the case of stereolithography. The development of this technique has allowed the elimination of intermediate stages of product development allowing a cheap and rapid transition of concepts into prototypes or finished products.

The numerous innovations in the field of technology and materials of the last decade have allowed improving the precision level of the printed objects and have increased the range of printable materials. Thus, the applications of 3D printing technology have expanded greatly in the medical and biomedical fields. Applications in clinical medicine appear especially in maxillofacial reconstructions, neurosurgery and spinal surgery. The ability of 3D printing to produce individualized models, devices and implants has greatly contributed to the development of so-called "personalized medicine". In addition, the proven utility in surgical planning and simulation, assisting in the consent process and use as an educational tool have significantly marked the role of 3D printing in medicine [2,4,6].

3D PRINTING EVOLUTION IN NEUROSURGERY

In the field of neurosurgery, the 3D printing technique has made substantial progress since 2007 as a result of the development of cranioplasty techniques that required the implementation of implants with increasingly complex anatomical configurations. Initially, the evolution of this technique was limited as the commercially available printers were still in the beginning and allowed printing only in one material and density. Subsequently, 3D printing has progressed, following the success of making models with as accurate spatial representations of the patient's anatomy. Thus, with the development in 2012 of printers with the possibility of printing in several materials and densities (Shore value), the technique of 3D printing in neurosurgery has developed in several main directions: - development of anatomical models specific to the patient for surgical planning; - vocational training and education; - design of neurosurgical devices for the evaluation and treatment of neurosurgical diseases; - and not least, the development of biological tissue implants. In this article, we will review the achievements of 3D printing in every direction in the neurosurgery field to evaluate the usefulness of final products, the challenges encountered and the progress of the field [1,5,7].

CRANIOPLASTY (RECONSTRUCTION OF SKULL DEFECTS)

Cranioplasty is one of the oldest neurosurgical procedures, practiced since 3000 BC. The most common defects of the skull can appear after trauma, neurosurgical procedures such as decompressive craniotomy, tumor resections with bone invasion, infections and congenital defects. The purpose of the cranial repair is to protect the underlying brain tissue, to reduce the local pain, to restore the patient's psychological balance by improving the cranial aesthetics.

The materials used initially in the cranioplasty procedure were pieces of autologous bone, polymeric, ceramic and metallic biomaterials. These autologous bones represented by the autologous calvarial bone removed from the patient during the initial operation had long-term problems, including subsidence, disintegration and infection. Thus, in a large number of patients, these plates disintegrated following their re-implantation, creating large defects, often accompanied by pain at the edges of the disintegrated defect. Subsequently, autologous bones were excluded and various acrylic or metal-based materials became increasingly used in cranial reconstructions. One of the disadvantages of these materials is the need to model them in situ during the operation, usually manually or with minimal equipment. These had to be cut and bent to fit, often reaching with sharp edges that represented a risk to both the surgeon and the patient's overlapping skin. All of these resulted in an extension of the intervention time and also created a number of problems, including poor match and unsatisfactory cosmetic result.

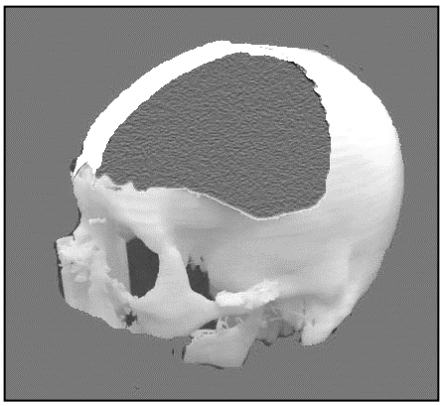


Figure 1: PMMA reconstruction on 3D printed model

With the advent of 3D printing, most of the problems mentioned above have managed to be overcome. Initially the 3D printing method was used to create a mould model on which the reconstruction joints are prefabricated. Also, another approach consisted in the initial creation of some models in the corrected form, and the titanium plates were subsequently modelled to suit the defect based on reconstruction. Implants thus reconstructed were then tested on the 3D printed model of the defect before sterilization and surgery. In addition to titanium, other materials such as acrylic (PMMA) and PEEK (polyether ether ketone) have also been used to create implants using similar techniques (figure 1). The use of these materials allowed the creation of a personalized prosthesis using 3D printing moulds characterized by an excellent cranial contour. Using the standard printing method described above, it was possible to avoid the possibility of deterioration of adjacent tissues due to the exothermic reaction during the polymerization process. Thus, intraoperative

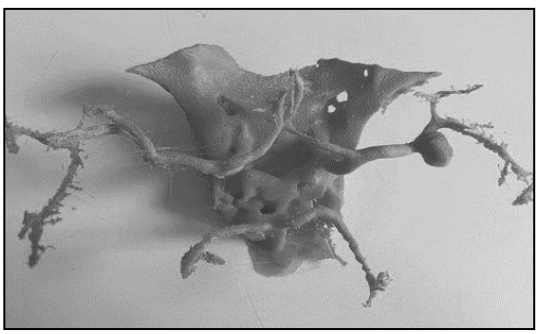
modelling of the final implant can be performed in just a few minutes [1,6,7,8,9].

The introduction of the 3D printing technique by the continuos multilayer deposition method in obtaining the cranioplasty implants determined the elimination of the intraoperative manipulation through cutting and modeling.

As the geometry of the facial bones and skull is extremely complex and most of these defects primarily involve underlying bone structures, the application of this more advanced 3D printing technology has proven ideal.

Neurosurgical training

Surgical training is usually a multi-step process by which the trainee acquires knowledge and skills of practicing surgical procedures. Thus, as the trainee gains skills, he will be able to progress to more complex steps and be given more autonomy. The effectiveness of this learning model can be influenced by the existence of the teaching material (most often represented by the availability of corpses), the number of cases and the interval of pathology related to a certain surgical unit. 3D printing offers solutions to bypass some of these problems and improve the internship experience. The trainees can practice and master the individual operative steps on the models before practicing with a real patient. This can improve learner confidence (especially in cases involving a difficult or unusual anatomy) and can help speed up the training timeline, as skill acquisition is achieved concomitantly with the actual operating experience of the patient. Also, the use of 3D printed models in vocational training helps surgical educators standardize the acquisition of operator skills among trainees. 3D printing thus offers a number of advantages, which allow it to be a useful adjunct to existing surgical simulation methods, such as cadaveric dissection and virtual reality techniques [1,2,4,7,9].



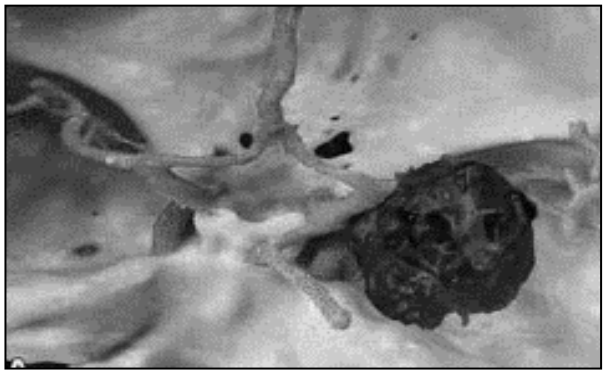


Figure 2: 3D printed models for vascular aneurysm and sphenoid wigs tumour intervention training.

The main directions of neurosurgical pathology that have benefited from the advantages of 3D printing have been the provocative anatomy lesions, such as cerebral vascular malformations of the aneurysm or MAV, brain tumors, and techniques such as ventricular or transnational endoscopy, which involve visualization constraints. One area where learning has generally been limited in the operating room is aneurysmal blinking. With the large-scale introduction of the treatment of aneurysms by coil embolization and the lack of cadaveric tissue, simulation-based training has become an absolute must in the strategy of vascular neurosurgery training. Mashiko et al. using hollow elastic replicas of the different aneurysms from their vascular networks in a 3D printed model, they offered young neurosurgeons the opportunity to gain experience in selecting the appropriate clip, understanding the shape of the aneurysm and the direction of the clip [1,3,10].

Similar to the field of vascular neurosurgery, the surgical training for excision of brain tumors has included the use of simulators based on anatomical models obtained by 3D printing (Figure 2). Thus, the use of 3D printers has allowed the development of simulators created from a multitude of materials with different consistencies and densities. This achievement contributed to the improvement of the simulation by replicating the handling characteristics of the different types of tissues [1,2,3,4].

It is very well known the absolute necessity of the surgical training in the case of spinal pathology, especially due to the multitude of types of implants proposed at present by the specialized companies. The continuous evolution of the spinal implants correlated with the development of the

instrumentation specific to each type made the introduction of 3D printed models inevitable in this area. Thus, the need for training for specialists in spinal neurosurgery aimed at acquiring the skills of use for various types of implants and instrumentation has greatly increased the use of these 3D printed models and due to the impossibility of access to such a large number of anatomical biological structures.

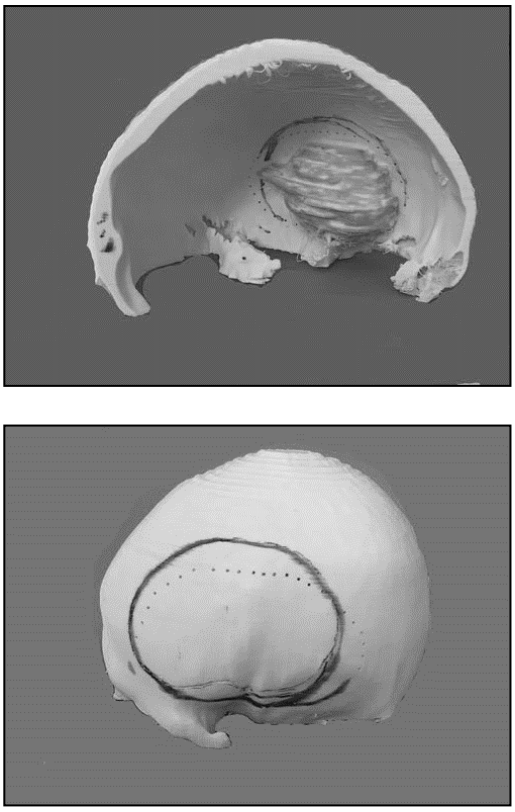


Figure 3: 3D printed models for a meningioma approach training.

PLANNING IN NEUROSURGICAL PATHOLOGY

Surgical intervention for intracranial aneurysm requires a complete and clear understanding of the complex 3D structure of the aneurysms and individual relationships with the carrier vessels and adjacent branches, in addition to accurate knowledge of the surrounding anatomical structures. Despite the evolution of 3D imaging acquisitions and processing (3D-CTA or 3D-DSA), the visualization and analysis of aneurysmal and MAV lesions by neurosurgeons are paradoxically deprived of a flat-screen 2D computer, making depth interpretations difficult. With the advent of 3D printing, this approach has become a feasible option, which has allowed faithful 3D physical reproduction of the vascular networks of an individual patient [Figure 1]. Thus, these physical models that can be viewed from any angle and correctly appreciated dimensionally represent a potentially more advantageous method. Studies in the literature comprising both qualitative and quantitative evaluations did not show significant dimensional differences between the imaging acquisitions and the printed model, proving the usefulness of using this printing technique. Most of the discrepancies reported were the result of the residual support material from the lumen of the vessels. Namba et al. reported for the first time the possibility of using these 3D printed models for endovascular planning (choosing the shape of the microcatheter and the coils occlusion).

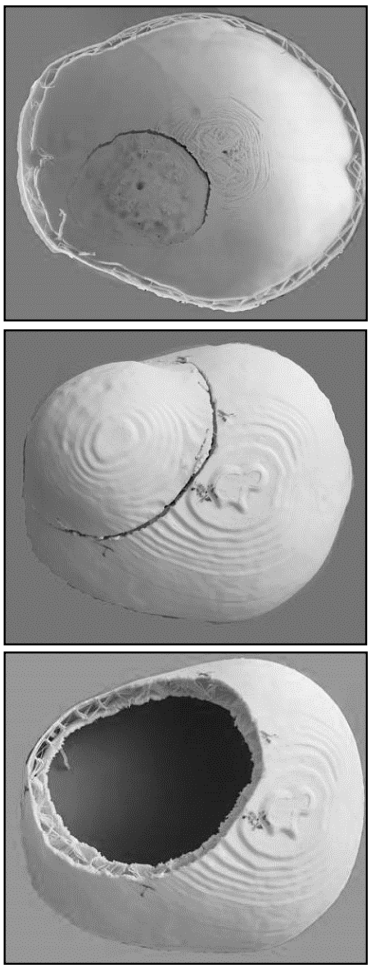


Figure 4: 3D printed models for a calvarial tumour planning approach.

Surgical planning in the resection of brain tumours mainly involves the use of MRI imaging. Even with the advantages offered by this imaging technique, the relationships between the tumour formation and the

adjacent anatomical elements are difficult to appreciate especially in the case of infiltrative ones. 3D printing technology has allowed the translation of MRI imaging data into patient-specific models that show the associations between tumour, skull, vascularisation and non-pathologic brain tissue [Figure 4]. [5] Moreover, the use of functional MRI imaging allowed a much more precise surgical planning through a clear demarcation of the areas of eloquent cortex that needed to be avoided in microsurgical resection manoeuvres. Large complex models of skull and brain tissue based on MRI could also be used for surgical planning in the case of transnational or transventricular endoscopic approaches. In addition, these models can be used in the planning and development of new treatments for brain tumours such as noninvasive thermocoagulation [1,10].

The identification and understanding of the anatomy in the case of spinal fractures is a fundamental component for the surgical treatment. CT and MRI imaging techniques, although, allow a good visualization of the anatomical elements or proved insufficient as regards the spinal interventional planning. This is reinforced by the development of intraoperative referral procedures used in spinal neurosurgery. Numerous specialized studies have shown that 3D printed representations of these pathological situations at the spine level are extremely efficient in choosing fixation and prosthesis systems, but also in exercise in implanting them especially in the case of minimally invasive percutaneous interventions. Thus, the detailed visual analysis of these 3D printed models allows a much clearer and more accurate dimensional and conformational assessment of the anatomical situation. This technique will allow neurosurgeons to establish some more precise dimensional parameters of the surgical implant insertion trajectory that can be transferred to the intraoperative guidance systems (Figure 5).

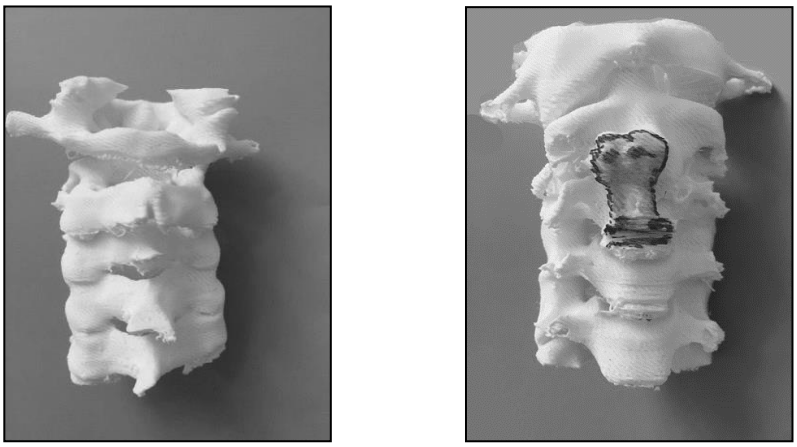


Figure 5: 3D printed models for cervical spine planning approach.

Assisting in the consent process

Any medical procedure requires informed consent that involves a direct communication between the doctor, the patient and his family regarding the patient's condition, the treatment possibilities, along with its advantages and disadvantages, the consequences of the non-treatment, as well as the risks and complications of each form of therapy. [1,7]. Statistical studies have shown that each step of informed consent can be better explained and understood through the use of a tangible object, in other words by materializing an abstract concept.

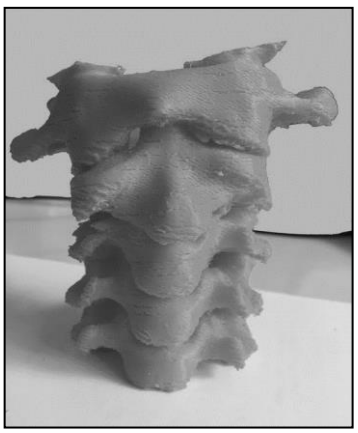
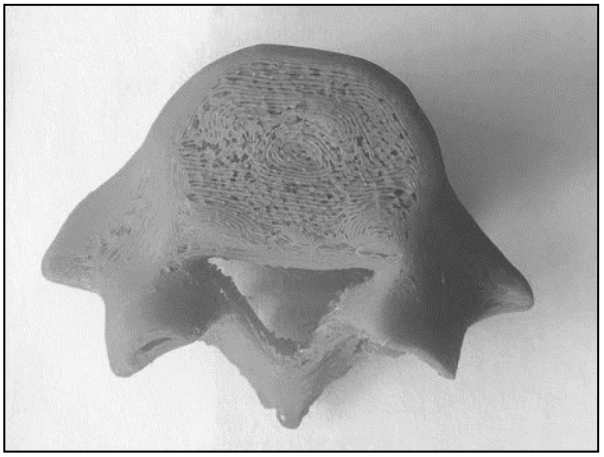


Figure 6: Spine 3D printed model for assisting in the consent process.

The use of 3D printed models proved to be very useful in the patient's consent procedure by considerably improving the discussions with them, due to the much clearer explanations of the proposed pathology and interventions. Thus, physicians can use customized physical models with in situ pathology for each individual patient. The stages of the surgery as well as the possible specific complications are much better explained to the nonmedical staff through physical models. Also, these 3D printed models help to better understand the disease and the results of the treatment, thus reducing the patient's uncertainty about the medical act, preventing complaints, discontents and accusations of malpractice (Figure 6) [7,8].

Medical education

The use of 3D printed models has proven to be an extremely useful teaching tool for both students in the anatomy discipline, and surgical disciplines as well as for residents in the neurosurgery specialty. 3D printing techniques offer significant advantages in the process of medical education within the university and postgraduate programs, compared to the existing methods of anatomical modelling, which include cadaveric dissection, plastic models and plastinated corpus specimens. Although traditionally medical education in the field of anatomy and surgery was provided primarily by cadaveric dissection, this learning mode was associated with difficulties related to the costs of setting up and maintaining an anatomical dissection laboratory, the existence of a sufficient number of bodies for educational programs, safety issues for students and staff, and last but not least ethical issues with the use of cadaveric material.



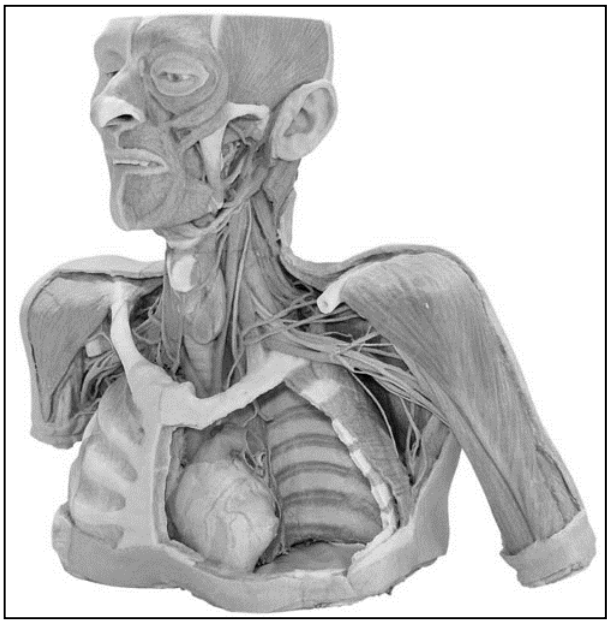


Figure 7: 3D printed models for student medical education [10].

The use of plastic models as an adjunct to cadaveric dissection to demonstrate certain organs or skeletal anatomy is limited by their lack of anatomical realism and the lack of representation of the variation or pathology specific to the patient. In contrast, 3D printing techniques allow the production of precise models characterized by a great variability and particular anatomical normality, but also pathological. Unlike plastination, which presents the major disadvantage of the resources required to create anatomical models, 3D printing does not limit the amount of 3D printed models produced, depending on the number of original copies (Figure 7).

Studies published in the literature have already shown improvements in the scores of anatomy tests of medical students after using 3D printing in the learning process. Thus, 3D printed models offer viable solutions for the vast majority of the difficulties faced by educators using more traditional training methods [1,5,10].

Conclusions

The technique of 3D printing has undergone a remarkable development and use in the field of neurosurgery in the last decade. The possibility offered by this rapid prototyping technology provides a practical and anatomically precise means of producing patient-specific and disease-specific

models. Besides applications already known in the fields of education and anatomical modelling, surgical planning, simulation and training, the creation of personalized implants for the treatment of various neurosurgical pathologies represents the real challenge of these technologies. Thus, extending this technology in neurosurgery will serve both medical students and interventionist, but especially to patients.

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The supraorbital keyhole approach for clipping of anterior circulation ruptured aneurysms

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Abstract

Introduction. The supraorbital approach has been demonstrated to be useful, particularly in minimization of brain retraction and exposure to air, decreases blood loss, surgical trauma, operative time and infection rates. While its shortcomings include difficult control of frontal air sinus, narrower surgical view and limited exposure of sylvian fissure.

Patients and methods. We retrospectively reviewed the files of patients who underwent clipping of anterior circulation aneurysms through the supraorbital keyhole approach at Neurosurgery Department, Mansoura University between Jan 2014 and May 2016.

Results. Twenty-five consecutive patients harbouring aneurysm at anterior circulation underwent clipping through the supraorbital keyhole approach, sixteen A-com artery aneurysms and nine cases of ICA aneurysms Table 1 show the location of aneurysms. Eleven patients were males, and 14 were females. The ages ranged from 44 to 69 with a mean age of 61.9 years. All patients were presented with subarachnoid haemorrhage due to rupture of aneurysms in anterior circulation The Hunt and Hess grade was (1.50 ± 0.65) and Fisher grade was (1.67 ± 0.45). The average operative time was 3.32 ± 1.14 hours. Follow-up ranged from 1 to 16 months with a mean of 7 months

Conclusion. Surgical clipping of some selected aneurysms of anterior circulation can be operated through minimally invasive supraorbital approach which minimize the dissection and retraction of the brain, reduce operative time and blood loss with small incision and good cosmetic results.

Keywords
supraorbital approach,
ruptured aneurysm,
keyhole concept

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Introduction

Conventional approaches to anterior skull base lesions including anterior circulation aneurysms highly developed since the large skin incision and fronto-temporal craniotomy described by Dandy to the less invasive pterional approach suggested by Yasargil [25] till the minimally invasive eye brow incision with supraorbital keyhole craniotomy [15, 20, 21, 24].

The pterional approach is popular and widely accepted among neurosurgeon; it provides wide central exposure, direct access to whole length of sylvian fissure, adequate visualization of anterior and

posterior circulation. However, pterional approach has disadvantages like longer operative time, blood loss, brain exposure, damage to frontal branch of facial nerve with subsequent facial asymmetry, temporalis wasting and interference with mandibular function [2, 9, 10, 11].

The supraorbital approach was early described and applied to a pituitary tumor by Frazier in 1913[12], then it has been described for multiple types of intracranial pathologies including Tumors excision, infection drainage, Fractures and Aneurysms clipping [4, 6, 20, 21].

Jane et al, described the supraorbital approach for clipping of anterior circulation aneurysms for the first time in 1982[15]. The approach was refined and popularized by Axel Perneczky, the pioneer in the development of keyhole concept [24,21].

The supraorbital approach has been demonstrated to be useful, particularly in minimization of brain retraction and exposure to air, decreases blood loss, surgical trauma, operative time and infection rates. While its shortcomings include difficult control of frontal air sinus, narrower surgical view and limited exposure of sylvian fissure [14, 16, 19, 22].

Complications related to the supraorbital approach may include cosmetic problems like visible scar or bone defects, damage to supraorbital nerve with frontal hypoesthesia, lost eyebrow elevation and CSF rhinorrhea [3, 5, 6].

Materials and methods

In this report, we represent our experience in clipping of anterior circulation ruptured aneurysms through the supraorbital keyhole approach.

We retrospectively reviewed the files of patients who underwent clipping of anterior circulation aneurysms through the supraorbital keyhole approach at Neurosurgery Department, Mansoura University between Jan 2014 and May 2016.

Only patients presented by subarachnoid hemorrhage due to ruptured aneurysm of anterior circulation and their aneurysms have clipped through supra orbital approach were included in this study. Demographic data, Hunt and Hess grades, Fisher grade, consciousness, aneurysm location, size, craniotomy size, operative time, blood loss, operative details, early post-operative follow up CT and CTA before discharge, clinical and surgical complications and data from follow up visits were reviewed.

Operative technique

A lumbar drain was used in all cases. The patients were placed in a supine position with the head fixed in a Mayfield head holder, the neck extended and turned about 20º to the contralateral side .The skin incision placed in forehead crease extended from lateral edge of the supraorbital notch to the superior temporal line .Then fascia and frontalis muscle were incised in the line of the skin incision and retracted up .A free 3×2 cm bone flap using a fine craniotome as basal as we can. In case the sinus was opened we extended the incision laterally to expose temporalis fascia which used with a pericranial graft to control frontal air sinus after cauterization and stripping of mucosa and adequate disinfection, and packing with gelfoam soaked with bovodin. After adequate exposure, the dura was opened in transverse fashion, the lumbar drain opened, the frontal lobe falls backward aided by the effect of gravity and with minimal retraction the circle of Willis was identified, proximal control then clipping of the aneurysm. The incision above the eyebrow was sewn with a subcutaneous dissolving stitch. Figure (1 a-d)

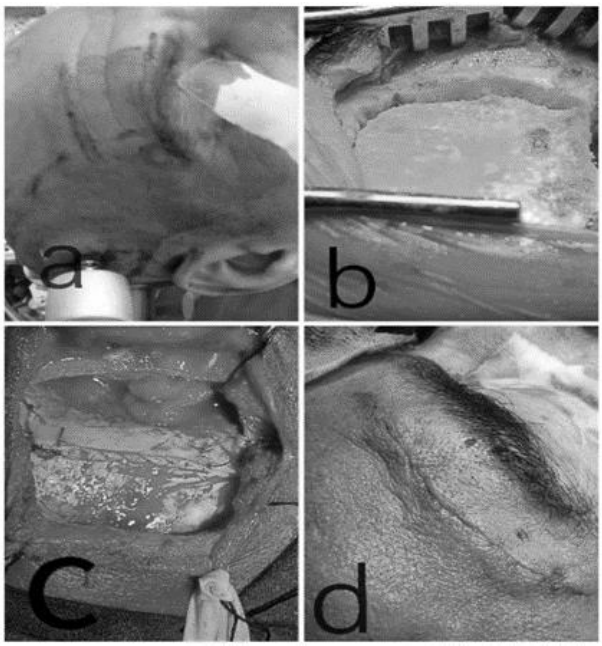

Figure 1. Operative technique - a) patient's head fixed to mayfiled fixator marking of skin incision and bone flap; b) minicraniotomy; c) closure of dura; d) closure of skin incision.

Results

Twenty-five consecutive patients harboring

aneurysm at anterior circulation underwent clipping through the supraorbital keyhole approach, sixteen A-com artery aneurysms and nine cases of ICA aneurysms Table 1 show the location of aneurysms. Eleven patients were males, and 14 were females. The ages ranged from 44 to 69 with a mean age of 61.9 years. All patients were presented with subarachnoid hemorrhage due to rupture of aneurysms in anterior circulation The Hunt and Hess grade was (1.50 ± 0.65) and Fisher grade was (1.67 ± 0.45). The average operative time was 3.32 ± 1.14 hours. Follow-up ranged from 1 to 16 months with a mean of 7 months

Table 1. Location of Treated Aneurysms

Location	Number
Anterior communicating	16
Anterior cerebral	4
Posterior communicating	3
Ophthalmic	1
Bifurcation	1

Visualization and orientation of aneurysm neck was feasible through mini craniotomy in 24 cases (96%) in whom successful aneurysm clipping was possible. (Figure 2, 3 and 4) In one patient, early aneurysm rupture obscures the field and procedure aborted after bleeding control then the patient was re-operated later through inter-hemispheric approach. Table 2 summarizes the operative findings.

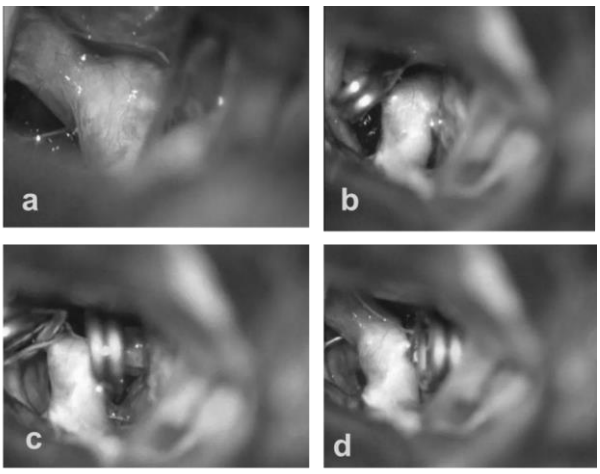

Figure 2. Case of Posterior communicating segment aneurysm a- aneurysm identification b- temporary clip application C- application of permanent clip d- removal of temporary clip and dissection of dome.

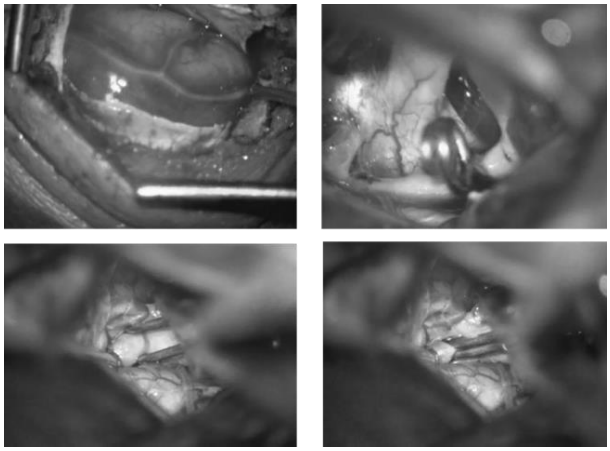

Figure 3. Case of anterior communicating artery aneurysm a- opening of dura and SAH and brain selling is identified b- temporary clip application c&d- application of permanent clip.

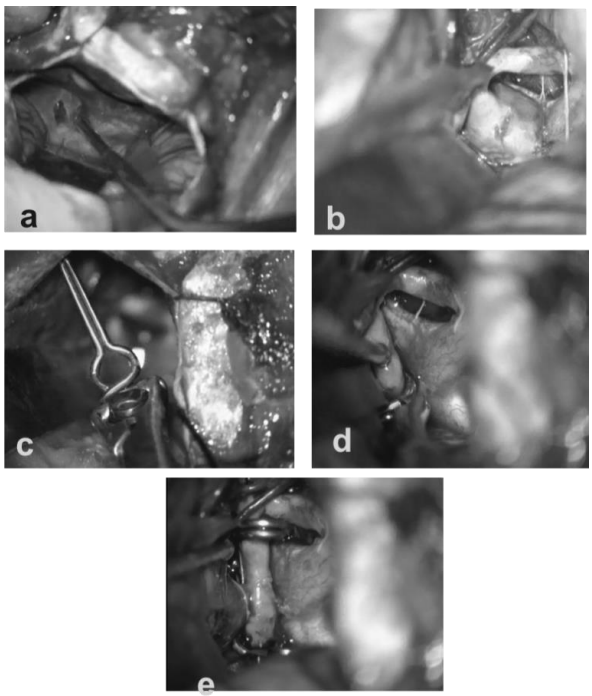

Figure 4. Case of large anterior communicating artery aneurysm: a) opening of dura and SAH and brain selling is identified; b) identification of aneurysm with wide neck; c) Right angle fenestrated clip for reconstruction of anterior communicating artery; d) application of the first permanent clip; e) application of another fenestrated clip to reconstruct A.com artery.

Intra operative rupture Occurred in two cases (8%); one carotid bifurcation aneurysm controlled by a temporary clip over proximal internal carotid artery. Another one ugly large multi lobulated A.com aneurysm ruptured very early during frontal retraction. The dominant Left anterior cerebral

couldn't be controlled from the right supraorbital approach. This patient was planned for clipping through this approach according CT angiogram only while DSA revealed the complicated configuration of aneurysm. Patient planned later for inter-hemispheric approach the aneurysm was clipped after the A1 segment of Left anterior cerebral artery was proximally controlled before dissection of the aneurysm neck.

TABLE 2. Operative findings

Total number	25
Number clipped	24
Mean operation time	190 minutes
Estimated Blood loss	50-300 (100ml)
Size of aneurysm	7±3 mm
Size of craniotomy	3±1.7 × 2±1.2 mm
Lumbar drain	25
Gyrus rectus subpial resection	4
Post-operative hospitalization stay	2-18 (7) days

TABLE 3. Post-operative CT and CTA findings

CTA residual neck radiological vasospasm	 0 6/25(24%)
CT brain Hemorrhage Br contusion Oedema Infarction	 1/25(4%) 2/25(8%) 3/25(12%) 3/25(12%)

Frontal air sinus was breached in 2 cases (8%) securing of sinus was done in both cases, one of those two cases was 60 years old patient developed CSF rhinorrhea which needed reoperation the basal dura was successfully repaired with fascia lata graft.

CT brain and CTA routinely have done for all patients, table 3 summarize the of post-operative radiological findings.

9 patients (36%) suffered transient periorbital ecchymosis and oedema that resolved few days later. Three patients (12%) showed post-operative transient deficit which improved later. Two patients died in this study one patient died due to symptomatic vasospasm and another patient died before discharge from hospital after postoperative pneumonia.

23 patients were Clinically followed-up for duration ranged from 3 to 30 months, 82.3% (19/23) of patients attained a favorable outcome (Glasgow Outcome Scale IV or V), no re-bleeding was noted.

As regard cosmetic outcome, the survived 23 patients were questioned for their subjective satisfaction about the esthetic outcome of their surgical incision on 3 months follow up visit. Figure 5. Nineteen patients (82.6%) were happy and satisfied about cosmetic outcome, while 4 patients were not satisfied; one female patient complained frontal hypothesia with denervation pain and itching lead to hyperpigmentation of forehead and alopecia behind hair line, Figure 6. another patient complained depression of forehead with loss of forehead elevation and 2 patients were worry about hyper pigmented scar.

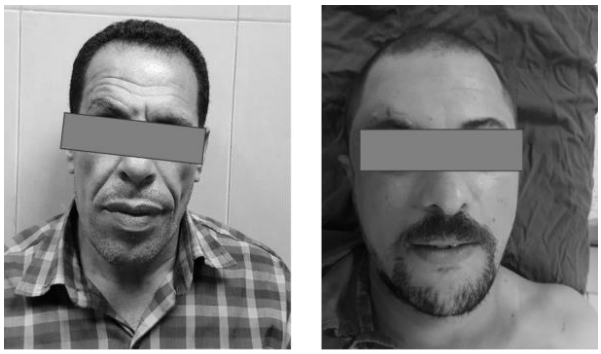

FIGURE 5. Early and late cosmetic outcome

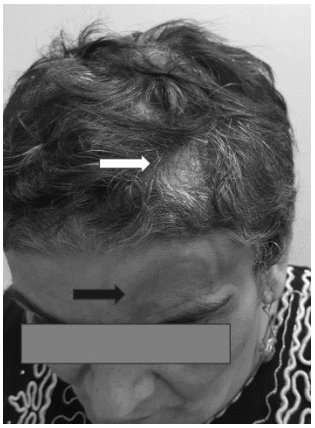

FIGURE 6. Hyperpigmentation (blue arrow) and alopecia (white arrow) after injury of supraorbital nerve and denervation pain and itching.

DISCUSSION

The endovascular coiling for management of ruptured intracranial aneurysms are less invasive than surgical clipping and this made a challenge for surgical approaches to be less traumatizing,

otherwise, it won't be accepted by many patients as alternative option [1, 8, 13, 18].

Surgical clipping of aneurysm provides visualization of vasculature and perforators, permanent secure of aneurysm, cleaning blood from subarachnoid spaces which decreases incidence of vasospasm and hydrocephalus, however, the International Subarachnoid Aneurysm Trial (ISAT) study comparing both modalities showed marginal superiority for endovascular techniques for management of ruptured aneurysm [18]. One explanation for these results is the application of standard approaches so the approach related morbidity down the outcome of surgical cases [18].

Supraorbital approach uses a smaller bone flap than others standard microsurgical approaches and minimize brain exposure, retraction, and traumatization, and possibly improve cosmetic results due to small incision, avoiding the injury of the frontal branches of facial nerve or the temporalis muscle and not interfere with mandibular function [7, 12, 17].

In this study we reported feasibility of clipping of ruptured anterior circulation aneurysms using the keyhole supraorbital craniotomy which proved by good results.

Our results of clipping 96% of aneurysms and 82.3% of patients attained favorable outcome support others conclusions [3, 5, 7, 16] that the supraorbital approach can be performed reliably and safely to clip ruptured anterior circulation aneurysms. However, the fact that we spare the approach for certain selected aneurysms doesn't support its use for all anterior circulation aneurysms. The minimally invasive nature of this approache with less trauma, operative time and blood loss is suitable for relatively small aneurysms with simple configuration, and should be on the armamentarium of vascular neurosurgeon to be provided as option for some patients.

Narrower surgical view and limited exposure, un-familiar view of anatomy especially of sylvian fissure which appeared laterally in the operative field. This make this approach not universe for all cases and not standard approach like pterional, but should be served for cases when the size and extent of exposure is enough for safe proximal control of parent vessel, appropriate dissection of the aneurysm neck and secure clip application [14, 16]

We faced intraoperative early rupture of aneurysm in 2 cases (8%) in one patient we couldn't clip the aneurysm a situation realized later and after doing DSA to be related to planning and selection of the aneurysm. Madhugiri et al [17] in a systematic review of Intraoperative Rupture Rates in suprabrow and pterional approaches, they analyzed a total number of 3039 ruptured aneurysms, 2848 aneurysms in the pterional group and 191 in the suprabrow group and they found the rate of intraoperative rupture is higher in suprabrow patients than pterional group 19.37% and 13.8% respectively.

Chalhouni et al [5] reported higher rate of intraoperative aneurysm rupture in the supraorbital group compared to pterional (10.6% vs 2.5%) they explained it as the lesser degrees of proximal control and the narrow available space for dissection and maneuverability of instruments, and advocated the supraorbital keyhole approach to be performed by neurosurgeons who have gained sufficient experience with the technique.

Exposure of frontal air sinus in 2 cases with persistent post-operative CSF rhinorrhea in spite that we have planed the craniotomy on preoperative CT bone window for assessment of the penumatization of the frontal air sinus. We didn't consider the supraorbital approach if there is large sinus that extends beyond the expected line of supraorbital nerve. The incidence of CSF rhinorrhea after supra orbital approach in the literature is ranged between 0% and 9.1%. Thaher et al. studied 350 patients of supraorbital keyhole craniotomy and reported 25.1% radiographic breaching of the frontal sinus and 2.3% developed CSF rhinorrhea postoperatively [23].

In their report of 139 patients Van Lindert et al performed a supraorbital craniotomy for aneurysm clipping, craniotomy size was 2-3.5 cm in width and 1.5-2 cm in height. They reported no frontal sinus exposure and emphasized the importance of measurement of the frontal sinus on pre-operative images [24]. Kim et al made wider craniotomy (4.5cm) and report one sinus exposure in their 10 approaches [16].

The two cases of mortality were of high Hunt–Hess and Fisher grads, and we think their checkered post-operative course was related to their clinical condition and ICU stay rather than to be related to the approach used for clipping.

We routinely used lumbar drain inserted before

positioning of patient which opened after opening of dura for CSF drainage which facilitate relaxation of the frontal lobe, we think it is of extremely important step because all of our patients presented by aneurysm rupture and brain swelling is expected and blood in subarachnoid spaces made opening of cisterns and drainage of CSF of limited value However some report operating on ruptured aneurysm as early as 2 days through keyhole approach and found slow CSF drainage from cistern is feasible [20]. Others drain cerebrospinal fluid by intraoperative ventriculostomy at Paine's point [6, 14, 16].

The small sample size, retrospective design of this study and selection of certain aneurysm size type and location are limitations of this report but we reported our experience of clipping the ruptured anterior circulation aneurys through this approach. Despite few comparative studies comparing the approach to conventional ones still we need large size randomized blind trial to compare minimally invasive approaches to conventional open approach and to endovascular technique.

Conclusions

Surgical clipping of some selected aneurysms of anterior circulation can be operated through minimally invasive supraorbital approach which minimize the dissection and retraction of the brain, reduce operative time and blood loss with small incision and good cosmetic results.

Authors contributions

This work was carried out in collaboration between the two authors. Authors, designed the study, Author, Mostafa M. Nabeeh wrote the protocol, managed the literature research, Author Ashraf Ezz ElDin revised the final manuscript. All surgical procedures were carried out by the same surgical team including the two authors. All authors read and approved the final manuscript.

Abbreviations

CT: Computerized Tomography.
CTA: Computerized Tomography angiogram.
DSA: Digital Subtraction Angiogram.
CSF: Cerebrospinal Fluid.
A. com: Anterior communicating artery
P. com: Posterior communicating artery

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Adeloye-Odeku Disease in Irrua, South-South Nigeria. The experience so far in a rural neurosurgical setting

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Keywords
Adeloye-Odeku, congenital, inclusion dermoid, Cyst, anterior fontanelle

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ABSTRACT

First described in a publication by two Nigerian Neurosurgeons, Adeloye A and Odeku EL, in 1971, Adeloye-Odeku disease is a solitary congenital subgaleal inclusion dermoid cyst of the anterior fontanelle. This rare lesion, which makes up about 0.1-0.5% of all cranial tumours and 0.2% of all inclusion cysts, was initially thought to be found only in Africans. However, further reports have shown it to have a universal occurrence, as it has been reported in Caucasians, Chinese, Indians, and other part of the world. This lesion is also known as Congenital inclusion dermoid cyst (CIDS), is a benign slow-growing lesion, and if untreated, may persist to adult life.

This article gives a highlight of the disease and its management and goes further to report 3 cases of this rare benign lesion seen in Irrua, South-South Nigeria, a rural, low-resource tertiary health institution.

Incidentally and interestingly, all three cases presented within three consecutive months (January-March, 2019) at the neurosurgery outpatient clinic. Being uncomplicated cases, private and group counselling was done. The parents of the patients were much more reassured and relieved from their anxieties seeing others with similar problem. They were all worked up for surgery at different dates, had excision of the cysts with no complication and are currently being followed at the outpatient clinic.

INTRODUCTION

Adeloye-Odeku disease, also known as congenital inclusion dermoid cyst (CIDC), is a solitary congenital subgaleal inclusion dermoid cyst of the anterior fontanelle. It is named after Adeloye A and Odeku EL, who first reported it in 1971, presenting series of 18 patients seen at the University College Hospital, Ibadan. They also published a full description of the cyst and its management.[1]

CIDC is an inclusion dermoid, a developmental anomaly in which displaced dermal elements are included in the neuroaxis along the embryonic fusion line. In this case, it occurs under the epicranial aponeurosis over the anterior fontanelle. Surgical excision, preferably enucleation, is curative for this disease, and no recurrence has been reported so far.

Epidemiology

Following its first report from patients in Nigeria in 1971, it was initially thought to be an African disease.[2] However, subsequent publications from various parts of the world have shown the cyst to be multiracial and to have a universal occurrence.[3,4,5,6] The cyst accounts for 0.1 -0.5% of all cranial tumours6 and 0.2% of all inclusion cysts.[7]

Although present at birth, its initial small size draws little or no attention. Hence, most cases are seen after the age of 3 months. If left untreated, it may persist till adult life as already reported.[8,9]

Aetiopathogenesis

The disease is caused by a developmental anomaly in which displaced dermal elements are included in the neuroaxis along the embryonic fusion line around the epicranial aponeurosis over the anterior fontanelle. This forms a slow-growing inclusion dermoid with no intracranial connection.

The cyst has a fibrous tissue wall lined by stratified squamous epithelium and it contains mainly a clear and colourless fluid with striking resemblance with cerebrospinal fluid (CSF) but with much smaller quantity of sugar and protein. The fluid may be mixed with cholesterol crystal, sebaceous materials and desquamated epithelial cells. These may form clumps or floccules floating over the surface of the fluid or line the inner wall, giving it a rather rough and shaggy appearance.[10]

Clinical features

The history is usually that of a slow-growing swelling over the anterior fontanelle present since birth.

The swelling is oval, spherical, non-tender, fluctuant, with intact overlying skin. It transilluminates brilliantly but does not show transmitted cough impulse due to no intracranial communication.

The size of the cyst varies with the age of the patient at the time of the diagnosis.[4] However, a range of 1-7cm have been recorded.[6] The lesion is loosely attached to the overlying aponeurosis and underlying pericranium and the absence of cough impulse differentiates it from a meningocoele or encephalocoele.

Differential diagnoses

The differential diagnoses of this condition include encephalocoele, meningocoele, sebaceous cyst, lipoma, haemangioma, cephalohaematoma. However, CIDC is differentiated from the above by its clinical features and this is corroborated by the findings of appropriate radiological and laboratory investigations employed.

Management

Usually, the patient is stable with an uncomplicated lesion, presenting at the clinic. A good history is taken and clinical examination done and all findings documented. Necessary radiological and laboratory investigations are carried out.

Counseling is done and this should cover the pathology, its cause and course, investigations required, treatment options and possible complications. Informed consent is obtained appropriately and the patient is worked up for excision thereafter. The cyst is excised completely and sent for histology so as to get a confirmatory tissue diagnosis. Patient is the followed up appropriately.

Investigations

Radiological investigations

To identify the location, size, nature and possible contents of the cyst and find out if there is any intracranial communication. They also serve as a guide for the surgeon intra-operatively. They include:

Transfontanelle Ultrasound Scan /Ultrasound Scan of the mass

This is much used for this condition in low economic regions where there is no Computed Tomography (CT)/ Magnetic Resonance Imaging (MRI) scan or, even if present, patient cannot afford them as seen Irrua. The scan usually reveals a cystic mass with homogenous or heterogenous echogenicity, well circumscribed, and lying over the anterior fontanelle with no intracranial extension.

Computed Tomography (CT)/ Magnetic Resonance Imaging (MRI) scan

These outline the lesion and confirm the cyst. Usually, a well-defined extracranial, subcutaneous fluid-density cyst over the anterior fontanelle is seen. It also gives the opportunity to visualize intracranial contents and usually there is no intracranial extension.

Body fluid investigations

Necessary for preoperative work up to assess patient's fitness for surgery include: Full blood count, Serum electrolyte, urea, creatinine, and random blood glucose/ fasting blood glucose (especially for diabetics).

Histology and Cyst fluid analysis

This is done post excision of the cyst. It confirms the diagnosis and rules out malignancy. The usual finding is that of cyst wall connective tissue lined by stratified squamous epithelium while the cyst fluid is clear with varying amount of glucose, protein, potassium, sodium, urea and LDH. Some cysts will contain sebaceous glands, hair follicles, etc, in the adnexial layer.

TREATMENT

Surgery is the mainstay of treatment. This involve enucleation of the lesion through a transverse scalp incision, usually under general anaesthesia, is curative for the disease. Care is taken to avoid injury to the underlying dura if fontanelle is still patent, and the cyst is delivered without capsular rupture. Redundant scalp may be excised and the wound closed appropriately, bearing in mind the need to achieve satisfactory aesthetic outcome.

COMPLICATIONS

These are usually rare. However, some of the possible complications include:

Cyst rupture and secondary infection if left untreated. Dura breach with resultant CSF leak as a complication of surgery. There is however no report of such in the literatures reviewed. Surgical site infections may be seen.

THE IRRUA EXPERIENCE SO FAR (CASE SERIES)

CASE I

A 4-month old male infant who was brought to the outpatient clinic with a painless, progressive scalp swelling over the anterior fontanelle which has been present since birth. No associated skin changes or discharge. No neurological symptoms or deficits. No swellings in other parts of the body. Developmental milestones were achieved at the appropriate time for age and patient was up to date with the immunization schedule. No family history of such swellings. Pregnancy, birth and neonatal history were uneventful and mother was delivered via a spontaneous vaginal delivery. Birth weight is 2.8kg.

Examination revealed a 6cm diameter hemispherical mass over the anterior fontanelle which was cystic, non-tender, smooth, and non-pulsatile. There was no differential warmth and no cough impulse. It was loosely attached to the overlying skin and underlying pericranium and transilluminates well.

Other examinations revealed normal findings.

Transfontanelle ultrasound done revealed a well circumscribed cystic mass overlying the anterior fontanelle, containing dependent echogenic debris. It measures 8.76cm3. Underlying brain is normal and there is no intracranial extension of the mass.

A diagnosis of Adeloye–Odeku disease was made and the parents of the patient were counseled for surgery. Informed consent was obtained and preopereative work up done. Routine blood investigations were normal.

He had enucleation of the cyst via a transverse scalp incision under general anaesthesia. Intra-operative finding was a 6cm diameter oval cystic mass underneath the aponeurotic layer of the scalp over the anterior fontanelle. The tissue was sent for histology. Wound was closed with absorbable vicryl and patient did well postoperatively. He was discharged on the 2nd day post -operative and followed up in the outpatient clinic.

Histology report revealed an ovoid cystic mass with shining grey-brown capsule measuring 3x2x2cm on macroscopy. Cut surface revealed a cystic cavity containing clear-white jelly substance. Microscopically, the sections showed a benign cystic lesion, containing keratinous debris and lined by keratinized stratified squamous epithelium with focal areas of attenuation. The wall is composed of fibrocollageneous stromal element with several skin adnexial structures. A histologic diagnosis of Scalp mass: Dermoid cyst, was made.

The patient is currently being followed up on outpatient basis and is doing fine with no complication or recurrence so far.

CASE II

A 22-month old female child with progressive painless scalp swelling over the anterior fontanelle present since birth. No associated neurological deficits. No skin changes or discharge for the swelling. No other swelling in any other part of the body. Pregnancy, birth and neonatal history were uneventful. Developmental milestone was attained at appropriate time and the child will be properly immunized for age.

Examination reveals a 4cm diameter spherical swelling over the anterior fontanelle which was non-tender, cystic, with no differential warmth. It was loosely attached to the underlying structure and overlying skin and transilluminates. Other examinations were normal. A clinical diagnosis of sub galeal dermoid cyst was made.

Transfontanelle USS done revealed a cystic sub periosteal lesion measuring 19.9 X 19.2 X 78mm located in the midline between the outer and inner table of the frontal bone. There is no demonstrable communication with the CSF or brain meninges. Both lateral, third and fourth ventricle are normal in size and outline. No sonographic evidence of intraventricular hemorrhage, mass or hydrocephalus. The brain parenchyma appears normal sonographically with normal grey and white matter differentiation. The parents were counseled for surgery and informed consent was obtained. Pre-operative investigation was normal. She subsequently had excision biopsy done under general anesthesia via a transverse scalp incision.

The intra-operative finding was that of 3cm diameter ovoid cyst in the subgaleal layer of the scalp. The sample sent for histology and the wound closed with absorbable vicryl, both deep and subcuticular layer. Post-operative condition was satisfactory and patient was discharged on the second day post-op.

Histology report revealed: macroscopically, an encapsulated cystic mass that is grayish-white, weighing less than 50g, measuring 1.9 X 1.5 X 1.0cm. Sections showed a cystic lesion lined by stratified squamous epithelium with lamellated keratin in the cavity. The lining epithelium is in connection with a pilosebaceous unit in some areas while in the other area by sebaceous gland. The wall is extensively fibrocollagenous with collagenization in some areas and fibrosis and hemorrhage in other areas. Histological diagnosis of scalp mass-epithelial inclusion cyst was made. No evidence of neoplasm.

The patient is currently being followed up on outpatient basis with no complication or recurrence so far.

CASE III

A 7-month old female infant with a small painless scalp swelling on the anterior fontanelle noticed since birth. The swelling was progressively increasing in the size, though slowly. No associated overlying ulcer or discharge. No swelling in other parts of the body and no family history of such swelling. No neurological deficit. The pregnancy, birth and neonatal history were normal. No delayed developmental milestones and she was up to date with the immunization schedule.

Examination revealed a localized spherical swelling on the anterior fontanelle of about 5cm diameter. It was non-tender, well defined, and cystic, with no differential warmth. Not attached to the overlying skin and transilluminates. Other findings were grossly normal. A clinical diagnosis of Adeloye-Odeku disease was made.

Transfontanelle USS requested revealed a thick-walled echogenic collection with amorphous intra lesional solid components that appear villiform, overlying the anterior fontanelle. The collection measures about 23.0cm3. There is no communication between the collection and the intracranial structures. Intracranial structures appear grossly normal.

The parents were counseled for surgery (excision biopsy) and with informed consent obtained, she was worked up for surgery. Preoperative investigations were normal. She had enucleation of the cyst via a transverse scalp incision under general anaesthesia and the inra-operative findings was a 4cm diameter cystic mass underlying the aponeurosis over the anterior fontanelle and overlying the dura. The tissue was sent for histology and wound closed with absorbable vicryl and dressed appropriately. The post-operative condition of the patient was satisfactory and she was discharged on the second day post op.

The histology report revealed: macroscopically, a spherical grayish-white cystic tissue measuring 3x2x2cm. Cut surface revealed a colourless fluid, a cystic wall coated with whitish friable material with interspersed shaft. Microscopically, histologic

sections showed a benign cystic lesion which contains keratin debris and surrounded by a wall made up of fibrocollagenous with collagenization in some areas and fibrosis and hemorrhage in other areas.

A histological diagnosis of anterior fontanelle swelling: Benign inclusion cystic was made.

The patient is currently being followed up on outpatient basis and is doing well with no complications or recurrence so far.

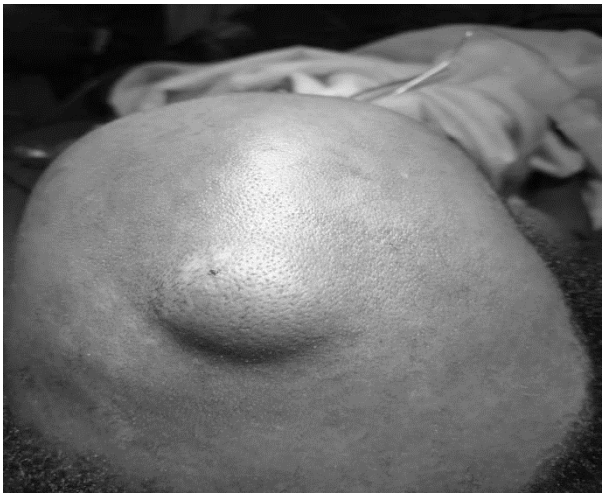

Figure 1. Preoperative photograph of Case II

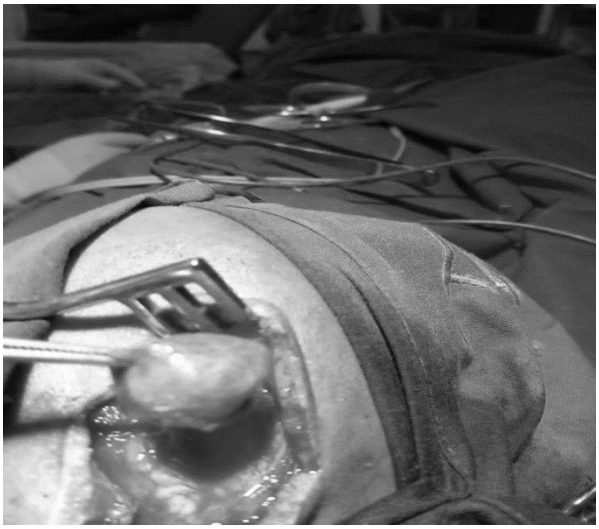

Figure 2. Intraoperative, showing lesion being excised

Figure 3. Post excision

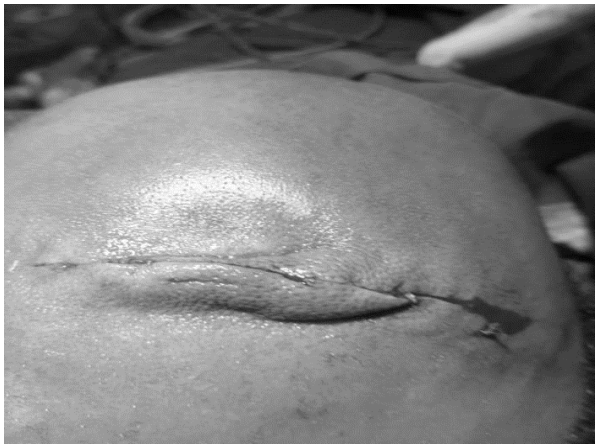

Figure 4. Just after wound closure

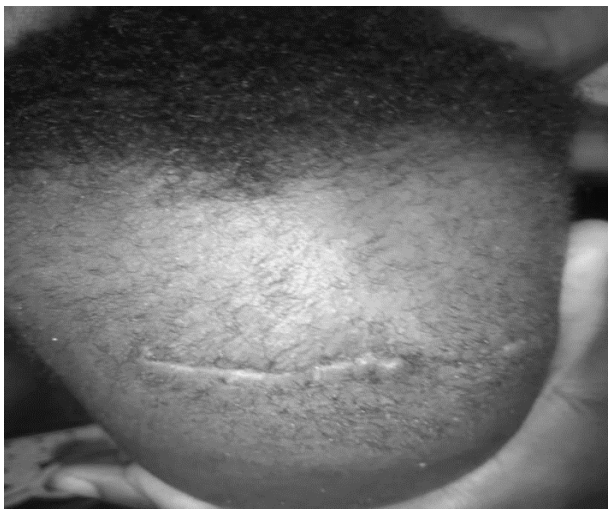

Figure 5. At first follow up visit post op

Summary of cases

Three cases of this rare lesion were seen within three consecutive months and they involved two females and a male child, all within the age range of 4-22months.

The scalp swellings, which had been present since birth in all cases, were of sizes ranging between 4-6cm diameters, located over the anterior fontanelle, non-tender, cystic, smooth, transilluminate, loosely attached to the underlying structure and overlying skin, with no positive cough impulse. None of them was ulcerated and there was no discharge from any. Clinical diagnoses of Adeloye-Odeku disease was made in all three cases and they had radiological investigations done to properly further define the lesions, especially their location, size, content, and if they communicate with the intracranial structures.

With no intracranial communications confirmed, the parents were counseled and informed consent obtained. Thereafter, all three patients had enucleation of the lesions via a transverse scalp incision under general anaesthesia. There were no intra or post-operative complications.

Histology reports of these lesions gave confirmatory tissue diagnosis of dermoid cyst, epithelial inclusion cyst, and benign cystic teratoma respectively. All were in keeping with Adeloye-Odeku disaease-congenital inclusion dermoid cyst over the anterior fontanelle. All three patients are currently being followed up with no complications or recurrence recorded so far.

Discussion

Adeloye-Odeku disease still remains a rare lesion though reports have shown its universality in occurrence and its multiracial prevalence[1,2,3,4,5,6,7,8,9,11,12,13,14] as against the initial thought of it being an African disease[1,2,3,4,5,6,7,8,9,]. So far, over 229 cases of this condition has been reported in literature until 2003.[4]

Nevertheless, a report by Dadlani et al suggest that its occurrence may be underreported and under-calculated due to observed non-uniformity in the nomenclature of the disease in various medical literatures and its management, in some cases, by other specialties (Paediatric surgeons, general and plastic surgeons).[11] Our report may give some credibility to the above as the 3 cases were seen within 3 months in a nascent neurological unit, just in less than 2 years of its existence.

Currently, the lesion accounts for 0.1-0.5% of all cranial tumours and 0.2% of all inclusion cysts.[6,7]

Aesthetic appearance and anxiety over the cause of the swelling are the main reasons for seeking surgical intervention by parents12. This was clearly evident in the response given by the parents of the children in this index report during consultation. All three couples saw the lesion as a form of deformity and were worried about what could be therein.

All three lesions in our report were present since birth, slow growing and with sizes ranging from 4-6cm, in keeping with the range reported in other studies.[7]

Our report involved 2 females and a male child, though no sex predilection has been established in this disease. While some reports have male preponderance[2,3,6,7] others reveal the disease to be more in females.[3,14]

The three cases in this report have the classical clinical features of the disease in keeping with other reported cases. There was, however, a major challenge in the radiological investigations to confirm the nature and extent of the lesion. In our report, transfontanelle ultrasound scan was used in place of CT and MRI scan due to financial constraints on the part of the parents of the patients who unfortunately have no health insurance. Nevertheless, we were able to establish the location, size and nature of the cyst and non-communication with intracranial structures via the USS done.

All three patients had excision of the cysts (enucleation) under general anaesthesia with no complications. The histology of the cysts in all 3 cases in our report showed benign cystic lesions lined by stratified squamous epithelium and containing skin appendages like hair follicles, sweat and sebaceous glands in the adnexial layers. This is in keeping with other reported cases.[5,6,9]

Two of our reported cases (1st and 3rd) revealed the content of the cyst to be clear, colourless fluid consistent with published cases[5,15,16,17]. However, further biochemical evaluation of its contents could not be carried out due to the technical limitations of our facility.

Nonetheless, the histology reports confirm all three cases to be dermoid cysts and ruled out any malignancy. All three patients are currently being followed up with no complications or recurrence so far and with satisfactory aesthetic outcome.

Conclusion

Adeloye-Odeku disease, first reported in Nigeria, and currently shown to be universal, remains a rare benign lesion of interest to the neurosurgeon. Total surgical excision is curative of the disease as shown in all reports.These case series have added credence to the above and has shown its successful management in a rural, low-resource setting.

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Extremely rare complication of granulomatosis with polyangiitis. Aneurysmal subarachnoid haemorrhage

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Keywords
granulomatosis with polyangiitis, complication, subarachnoid haemorrhage, aneurysm

ABSTRACT

The systemic vasculitis of the small-medium arteries, arterioles, venules and rarely large arteries that involves respiratory system and kidneys was defined as Granulomatosis with Polyangiitis (GPA) disease by Wegener in 1936. Intracranial aneurysms and subarachnoid haemorrhage (SAH) are extremely rare complications of GPA and our case will be the 2nd case treated with clipping aneurysm and the 11th case with subarachnoid haemorrhage in the literature.

A 43-year-old man presented to the emergency room with a severe headache and was admitted for further evaluation. He had GPA diagnosis 14 years ago with cytoplasmic anti-neutrophil cytoplasmic antibody (C-ANCA) and PR3-ANCA positive laboratory tests and kidney biopsy. SAH was seen on cranial computed tomography (CT) images. Then cerebral digital substraction angiography (DSA) performed and right middle cerebral artery aneurysm exposed. Aneurysm was clipped without any complication.

Intracranial aneurysms and SAH are extremely rare complications of GPA. GPA related aneurysmal SAH is an exceptional condition in neurovascular pathology. Monitoring patients with GPA for SAH must be remembered and kept in mind as a diagnosis.

✉
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INTRODUCTION

The systemic vasculitis of the small-medium arteries, arterioles, venules and rarely large arteries that involves respiratory system and kidneys was defined as Granulomatosis with Polyangiitis (GPA) disease by Wegener in 1936 (1). Wegener defined the disease with the findings that includes focal necrotizing glomerulonephritis, respiratory tracts'

necrotizing granulomatous vasculitis and systemic vasculitis as a diagnostic triad (1).

Inflammatory and autoimmune mechanisms are discussed for the pathogenesis of GPA but it still remains controversial. The involvement of central nervous system (CNS) has been reported in 7-11% whereas the cases with aneurysmal subarachnoid hemorrhage (SAH) are excepted (2). Clinical symptoms with positive proteinase 3 (PR-3) anti-neutrophil cytoplasmic antibody (ANCA) laboratory test shows both high sensitivity and specificity in diagnosis of GPA.

Intracranial aneurysms and subarachnoid hemorrhage are extremely rare complications of GPA. Previously, only 10 cases of SAH related to GPA have been reported in the literature. Only 1 of them was treated with surgical aneurysm clipping.

Case report

A 43 year old man presented to the emergency room with a severe headache. No pathological findings were detected in the neurological examination. He had no history of hypertension or a cardiac disease. Cranial computed tomography (CT) was performed and the patient was diagnosed with subarachnoid hemorrhage **(Figure 1A)**. While the patient was preparing for cerebral digital substraction angiography (DSA), his neurological examination suddenly worsened. The patient was intubated and cranial CT performed again **(Figure 1B)**. Cerebral DSA was performed to the patient who had bleeding again and right middle cerebral artery aneurysm exposed **(Figure 1C, D)**.

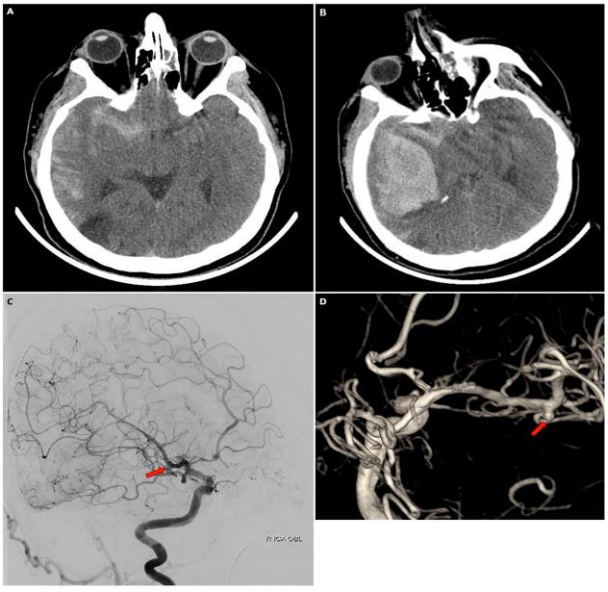

Figure 1 - A. Preoperative cranial CT image showing SAH; B. Intracerebral hemorrhage is seen after re-bleeding; C-D. Preoperative DSA images showing right middle cerebral artery aneurysm.

It was learned that the patient was followed up with the diagnosis of GPA. He applied to hospital with the symptoms of fever, coughing and hemopthisia in 2003. In his examination, bilateral arthritis on lower extremities, palpable purpura, episcleritis in the eyes were present. In thorax CT, consolidation areas and 10 cm cavitation were detected in the right lung. Urine test showed proteinuria and kidney biopsy reported as GPA. Laboratory tests revealed cytoplasmic anti-neutrophil cytoplasmic antibody (c-ANCA) and PR3-ANCA positivity. As a result of all tests, steroid and cyclophosphamide treatment was given to the patient.

In 2015, the patient had a tonic-clonic seizure in the bathroom and was found unconscious. He had homonim hemianopsia, left facial paralysis and hemiparesia. There was no hemorrhage on cranial CT. The diffusion weighted magnetic resonance imaging (DW-MRI) showed an acute ischemia in the right temporal-occipital and frontobasal areas. MRI-Angiography had been found normal.

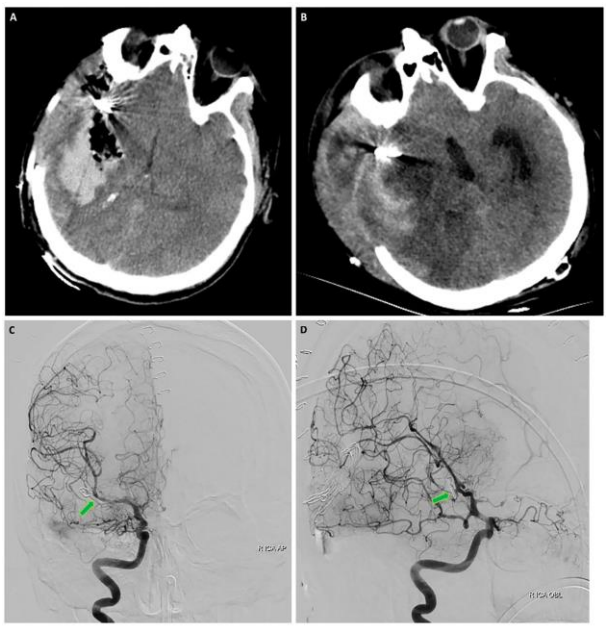

Figure 2 - A-B. Cranial CT axial sections in the early and late postoperative periods; C-D. Postoperative DSA images showing severe vasospasm and right middle cerebral artery aneurysm clipped without remnant.

Decompressive craniectomy was performed and right middle cerebral artery aneurysm was clipped without any complication. External ventricular drainage was placed due to hydrocephalus. Cranial CT was performed in the early and late postoperative periods **(Figure 2A, B)**. Postoperative DSA was performed to the patient. The aneurysm was clipped without remnant, but serious vasospasm was observed **(Figure 2C, D)**. Chest X-ray and thorax CT showed noduler infiltrations **(Figure 3A, B)**. The patient died on the 26th postoperative day due to respiratory tract infection and severe vasospasm.

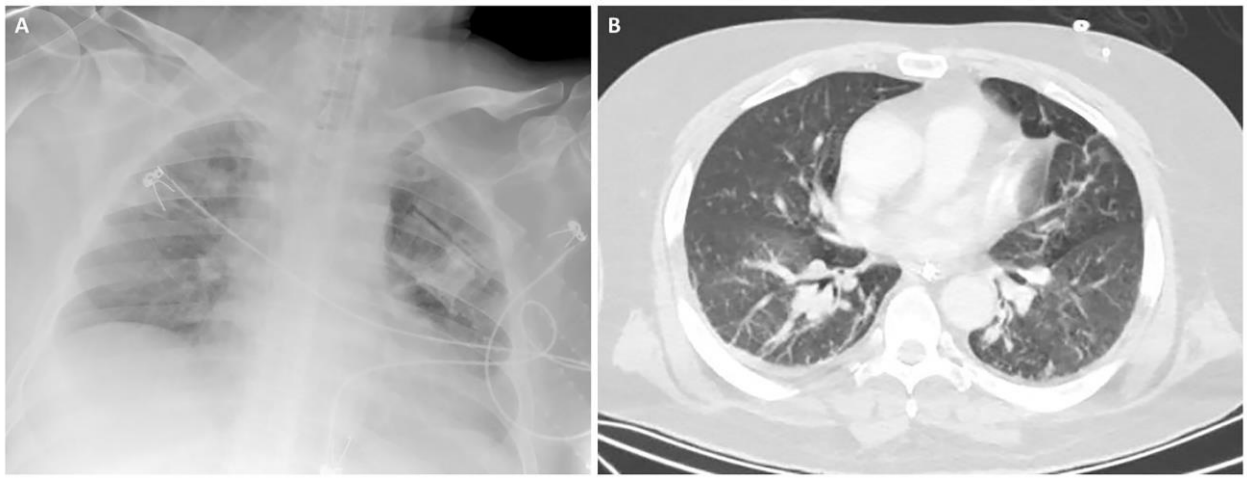

FIGURE 3 - A. X-ray chest graphy and; B. Thorax CT axial section showing noduler infiltrations in medial region.

DISCUSSION

GPA is typically diagnosed with by activated neutrophils accumulations, vasculitis, formation of microabscess, granulomas, glomerulonephritis and necrosis in pathological examination (3). Wegener defined the disease with the findings that includes focal necrotizing glomerulonephritis, respiratory tracts' necrotizing granulomatous vasculitis and systemic vasculitis as a diagnostic triad (1).

In 1990, The American College of Rheumatology announced diagnostic criterias to classify GPA (4). Classical diagnostic criterias were an abnormal sediment of urine, abnormal findings like cavities, nodules and infiltrations on a chest radiograph, oral or nasal mucosal ulcers; and biopsy concluded with granulomatous inflammation. Minimum two of the four criterias requested for the diagnosis of GPA and hemoptysis is added to the traditional format so classification tree was defined (4). Classification tree was reported more specific and sensitive than the traditional format (4).

Neurologic involvement is rarely seen in GPA and reported as ranging from 22% to 54% in the literatüre (5). Drachman et al. have discussed three major mechanisms which could be summarized as vasculitis of CNS, intracranial granuloma and extracranial granuloma invasions on causes of CNS involvement in GPA (6). Seror et al. reported CNS involvement of GPA with six patients that three of them with pituitary involvement, two patients with pachymeningitis, and last patient with cerebral vasculitis (7). The CNS involvements were attributed to GPA because they were diagnosed at disease onset or flare and also extracranial involvements, other CNS disease etiologies had been excluded, and/or they had attributed to sustained immunosuppressive therapy.

CNS vasculitis was reported as the cause of intracranial hemorrhages, transient ischemic strokes, cerebral infarctions, venous or arterial thrombosis, encephalopathy, ischemic myelopathy, seizures, dementia, altered consciousness, cortical blindness, visual loss and cognitive impairment (3, 8-11). Because of the rarity of CNS involvements in GPA, no specific treatment suggestions exist for management of them except combining cyclophosphamide and corticosteroids as systemic GPA therapy (12, 13).

Subarachnoid hemorrhage in GPA has been rarely reported in the literature **(Table 1)** (2, 6, 8, 14-19). Only two cases presented with subarachnoid hemorrhage and exposed the aneurysms with cerebral angiography. Takei et al. confirmed an anterior choroid artery aneurysm and Marnet et al.

reported an anterior communicating artery aneurysm (2, 16). Our case is 3rd as the middle cerebral artery aneurysm. Takei et al. had clipped the aneurysm as a first case, but Marnet et al. could not have clipped the aneurysm because of a vasculitis flare-up of disease (2, 16). So our case is the 2nd case of subarachnoid hemorrhage treated by clipping the aneurysm. Onodera et al. reported an incidentally found carotis aneurysm without subarachnoid hemorrhage in GPA but they made baloon occlusion with endovascular procedure for treatment (5). Survival rate is very low for the aneurysms of GPA but we can not evaluate the reason of it because the information about patients is limited due to fast deterioration **(Table 1)**.

Author	Age	Gender	Clinical Presentation	Diagnosis	Treatment	Result
Tuhy et al. (14)	39	M	Fatigue, cough, arthralgias, weight loss	Lumbar puncture and autopsy: SAH	Medical	Death
Drachman et al. (6)	30	M	Chronic rhinitis, persistent skin ulcers	Autopsy: SAH	N/A	Death
Venning et al. (15)	50	M	Epistaxis, nasal discharge, nasal polyp	CT: SAH	Medical	Recovery
Venning et al. (15)	36	M	Weight loss, hemoptysis, night sweats	Lumbar puncture: SAH	Medical	Recovery
Cruz et al. (8)	71	M	Subarachnoid hemorrhage	Lumbar puncture and CT: SAH	Medical	Recovery
Takei et al. (16)	34	M	Recurrent nasal obstruction	CT and cerebral angiography: Aneurysm	Clipping	Recovery
Nardone et al. (17)	78	F	Dyspnea, fever, hemoptysis	CT: Intracerebral hemorrhage and SAH	Medical	Death
Fomin et al. (18)	17	M	Cough, fever	CT&MRI: SAH and intravent. hemorrhage	Medical	Death
Miles et al. (19)	74	F	Paresthesias, diplopia, diz-ziness	CT: SAH and intraventricula r hemorrhage	Medical	Death
Marnet et al. (2)	63	F	Subarachnoid hemorrhage	Cerebral angiography: Aneurysm	Medical	Follow-up

TABLE 1. Cases of subarachnoid hemorrhage with GPA in the literature

Takei et al. reported the possible mechanism for the aneurysmal bleeding with GPA may have involved the ANCA-cytokine sequence, with activated polymorphonuclear neutrophils adhering to the endothel of the aneurysm origin, and with polymorphonuclear neutrophils degranulation liberating PR-3 and human leukocyte elastase (HLE) (16). Then PR-3 caused apoptosis of arterial smooth muscle cells. The destruction of the internal elastic lamina may also attributed to aneurysm formation and rupture (16).

Conclusion

Intracranial aneurysms and subarachnoid hemorrhage are extremely rare complications of GPA. GPA related aneurysmal SAH is an exceptional condition in neurovascular pathology. As inflammatory mechanisms are involved in the pathogenesis of aneurysm, the vasculitis flare-up could account for this SAH. Surgical clipping of aneurysm could be done for the treatment of aneurysmal subarachnoid hemorrhage in GPA patients. Finally, monitoring patients with GPA for SAH must be remembered and kept in mind as a diagnosis.

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Paediatric traumatic brain injury. Study of analysis of outcome predictors

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ABSTRACT

Introduction. Traumatic brain injury is a leading cause of death and disability among children, adolescents. Therefore, analysing outcome predictors and initiating preventive policies may contribute to decreased incidence and better prognosis.

Aim. Aim to describe the epidemiologic characteristics, mechanism of injury, radiological findings and also to analyse the determinants of outcome that could help to provide better critical care and also to establish effective preventive policies.

Material and Methods. We conducted a prospective study including patients ≤18 years admitted to our Neuro-intensive care unit at R.N.T. Medical College ,Udaipur, Rajasthan, India from September 2016 to June 2018.Factors including age, gender ,mode of injury, Glasgow coma score(GCS) at admission ,pupillary size-reaction, radiological findings and their relation to outcome was assessed .Patients were divided into mild, moderate and severe head injury according to GCS. Outcome of patients was assessed by Glasgow outcome scale. For statical Analysis used Chisquare test. Statistical Analysis was carried out using Stata 11.0(College station, Texas, USA)

Results. The study comprised of 84 paediatric patients. 44.4%of patients were within 1–5-year age group. The most common cause for trauma was falls and traffic accidents. Patients with mild, moderate and severe head injury were 38.1%, 47.6%and 14.3% respectively. Poor outcome predictors included severity of head injury, pupil size and reaction, midline shift on CT.

Conclusion. This study emphasizes increased burden of paediatric brain injury with assessment of predicting factors for more effective critical care of patients and emerging need for effective fall and traffic accidents prevention strategies.

Keywords
traumatic brain injury,
paediatric,
outcome predictors.

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INTRODUCTION

Traumatic brain injury(TBI) is a main cause of functional disability and death in children and adolescents worldwide.[1,2,3] Falls and Road traffic accidents have emerged as the major causes of pediatric head injuries and their prognosis in children differ from adults due to the different mechanisms of head injury and the structures of the skull.[4,5] Infants and young children are more vulnerable to abuse because of their dependency on adults.[6] Pediatric head injuries are critically important because of the risk of high mortality and potential for lifelong neurological disability which could mean dependence on others for

activities of daily living and years of compromised quality of life.

The study aims to describe various factors and determinants of outcome that could help to improve care and make better preventive policies.

MATERIAL AND METHODS

This study includes 84 patients of ≤18 years of age who presented with head injury and admitted in Neuro-intensive care unit at R.N.T. Medical College, Udaipur, and Rajasthan, India from September 2016 to June 2018. We further analyzed those 84 patients on the basis of various factors including clinical factors(age, gender), mode of injury, Glasgow coma score (GCS)at admission and Glasgow outcome scale (GOS).Patients were subjected to detailed general physical examination, systemic examination, and central nervous system(CNS) examination including GCS, pupil size and reaction. Based on GCS, the patients were divided into mild head injury (GCS 13–15), moderate head injury (GCS 9–12), and severe head injury (GCS ≤ 8) categories. All the patients were subjected to plain CT scan head, and CT findings were noted.

After prior stabilization and workup, the patients were managed conservatively or surgically as and when needed. The outcomes of all these patients were assessed by Glasgow Outcome Scale and divided into good (GOS-4,5) and poor (GOS-1,2,3) outcome. Outcome was assessed in relation to age, sex, GCS, pupil size and reaction, Noncontrast computed tomography scan (NCCT Head) features and other associated bodily injuries. For statical Analysis used Chisquare test. Statistical Analysis was carried out using Stata 11.0(College station, Texas, USA).

RESULTS

Mean age was 8.4 years. 44.4% of patients were within 1–5year age group. The male to female ratio was 2.1 to1. It was evident from our series that age and sex had no statistical significance in outcome (p>0.05). For statical Analysis used Chisquare test. [Table 1]

	Number of patients	**Good outcome**	**Poor outcome**
Gender			
Male	57(67.9 %)	51 (89.5%)	6 (10.5%)
Female	27(32.1 %)	24 (88.9%)	3 (11.1%)
Age (yr)			
<=5	37(44.1%)	34(91.9%)	3(8.1%)
6-12	19(22.6 %)	17(89.5%)	2(10.5%)
13-18	28(33.3 %)	24(85.7%)	4(14.3%)
Total	84(100%)	75(89.3%)	9(10.7%)

TABLE 1. Correlation of age, gender with the outcome analysis

The most common cause for trauma were falls(51.1%) followed by road traffic accidents(RTAs) (40.5%), assault (2.4%), sports injury (2.4%)and others (3.6%) which include injury by some object on head .RTA had a poor outcome in 14.7%while patients with fall had a poor outcome of 7% . [Table 2]

TABLE 2. Correlation of mode of injury, GCS score, pupil size with outcome analysis

	Number of patients	**Good outcome**	**Poor outcome**
Mode of injury			
Falls	43(51.1%)	40(93.0%)	3(7.0%)
Traffic accidents	34(40.5%)	29(85.3%)	5(14.7%)
Assault	2(2.4%)	2(100%)	0(0%)
Sports injury	2(2.4%)	2(100%)	0(0%)
Others (e.g.-fall of heavy objects)	3(3.6%)	2(66.7%)	1(33.3%)
GCS score			
13-15	32(38.1%)	31(96.9%)	1(3.1%)
9-12	40(47.6%)	39(97.5%)	1(2.5%)
<=8	12(14.3%)	5(41.7%)	7(58.3%)
Pupil size			
Normal	74(88.1%)	71(96%)	3(4%)
Fixed and dilated	3(3.6%)	0(0%)	3(100%)
Anisocoria	7(8.3%)	4(57.1%)	3(42.9%)
Total	84(100%)	75(89.3%)	9(10.7%)

The percentage of patients with mild head injury (GCS of 13–15), moderate (GCS of 9-12, and severe (GCS <=8) were 38.1%, 47.6%, and 14.3% respectively. Poor outcome was seen in the category of GCS ≤8 at 58.3%, followed by patients in group GCS 9–12 at 2.5% and group of patients with GCS 13–15 at 3.1%, which was statistically significant (p< 0.05) For statical Analysis used Chisquare test, Statistical Analysis was carried out using Stata 11.0(College station, Texas, USA). [Table 2]

Out of the 84 patients, 74(88.1%) patients had normal pupils, 7(8.3%) had anisocoria, and 3(3.6%) patients had fixed dilated pupils. Fixed dilated pupil had poor outcome (100%) followed by anisocoria (42.9%) and normal pupils (4%), which was statistically significant (p< 0.05) For statical Analysis used Chisquare test. [Table 2]

CT scan findings were noted as normal in 12 patients(14.3%), isolated skull fracture in 20(23.8%), contusion or hematoma in 20(23.8%), extradural hemorrhage(EDH) in 13 (15.5%),subdural hemorrhage(SDH)in 7(8.3%), brain edema in 7(8.3%), and subarachnoid hemorrhage in2(2.4%), pneumocephalus in 3(3.6%).Among the mode of injury, it is evident that diffuse brain edema had poor outcome in 28.6%, SDH in 28.6%, contusion in 5%, while in EDH it was7.7%. [Table 3] From our series, we also concluded that poor outcome was most strongly associated with midline shift (MLS) >3 mm (66.7%) and it was 20% with MLS of<3 mm and it was 7.9% in patients with no MLS (p< 0.05) For statical Analysis used Chisquare test. [Table 3]

TABLE 3. Correlation of Radiological findings on CT and assessment of midline shift with outcome analysis

	Number of patients	**Good outcome**	**Poor outcome**
Radiological-CT findings			
Fracture	20(23.8%)	19(95%)	1(5%)
EDH	13(15.5%)	12(92.3%)	1(7.7%)
SDH	7(8.3%)	5(71.4%)	2(28.6%)
SAH	2(2.4%)	2(100%)	0(0)
Contusion/hematoma	20(23.8%)	19(95%)	1(5%)
Edema	7(8.3%)	5(71.4%)	2(28.6%)
Pneumocephalus	3(3.6%)	2(66.7%)	1(33.3%)
Normal	12(14.3%)	11(91.7)	1(8.3%)
Midline shift(MLS)			
No	76(90.5%)	70(92.1%)	6(7.9%)
Yes<3mm	5(5.9%)	4(80%)	1(20%)
Yes >3mm	3(3.6%)	1(33.3%)	2(66.7%)
Total	84(100%)	75(89.3%)	9(10.7%)

On analysis for associated injuries, fractures of face were noted in 10(10.7%), limb fractures in 6(7.1%), abdominal trauma in 4(4.8%), spinal trauma in 2(2.4%), chest trauma in 2(2.4%), multiple traumas in 2(2.4%), and isolated head trauma in 59(70.2%). It was noticed that chest, spinal, and multiple injuries were associated with a poor outcome (p< 0.05). [Table 4]. Outcome of patients was assessed by Glasgow outcome scale [Table 5].

TABLE 4. Correlation of associated other bodily injuries with outcome analysis

	No of patients	**Good outcome**	**Poor outcome**
Associated injury			
No injury (head trauma only)	59(70.2%)	57(96.6%)	2(3.4%)
Fracture-facial bones	9(10.7%)	7(77.8%)	2(22.2%)
Abdominal organ injury	4(4.8%)	3(75%)	1(25%)
Fracture – limbs	6(7.1%)	5(83.3%)	1(16.7%)
Injury to chest	2(2.4%)	1(50%)	1(50%)
spinal injury	2(2.4%)	1(50%)	1(50%)
Multiple injuries	2(2.4%)	1(50%)	1(50%)
Total	84(100%)	75(89.3%)	9(10.7%)

TABLE 5. Glasgow Outcome Scale in the study group

Glasgow outcome scale	Functional status	No. of patients	Outcome
5	Resumption of normal life, there may be minor neurological and or psychological deficit	5 (6%)	Poor
4	Able to work in a shattered environment and travel by public transportation	2 (2.4%)	Poor
3	Dependent for daily support by reason of mental or physical disability or both	2 (2.4%)	Poor
2	Unresponsive for weeks or months or until death	6 (7.1%)	Good
1	Death	69 (82.1%)	Good

Out of the 84 patients, 58(69.1%) were managed conservatively and 26 (30.9%) patients were managed surgically. The various surgical procedures performed in patients include fracture debridement and elevation in 12 (46.2%), hematoma removal with fracture debridement in 3 (11.5%), and hematoma (EDH, Acute SDH, Hematoma removal with Decompressive craniotomy in 8 (30.8%)) Decompressive craniotomy alone (for cerebral edema with midline shift of more than 5 mm)) in 3 (3.57%), We followed up our patients for a week to maximum of 12 months.

DISCUSSION

Pediatric TBI remains an important public health concern worldwide, but with the advent of state of art - Intensive Care Unit and incorporation of multidisciplinary approach in developed countries, the outcome of the TBI patients has improved. Yet, it still continues to be a major challenge in our part of the world, which further necessitates the adoption and implementation of strict prevention strategies. Rivara et al. reported that boys have double the rate of brain injuries when compared with female counterparts. [7] In our study, 67.9% of the patients were boys. Although gender differences were important in the rate of injury, they did not appear to adversely affect neurological outcome.

In literature, there has been discrepancy regarding outcome in the pediatric age group. In our study, 37 (44.1%) were less than 5 year of age. One group of reports has indicated that outcome tends to be better in children under10 years of age[8,9]while others report that children under five have a higher mortality rate.[10]Although in our series there was no difference in poor outcome in children below5 years or above 5 years as was reported by Suresh et al.[11]

Falls and traffic accidents account for the majority of injuries in pediatric head trauma.[11,12]Fall from height is the most common cause of injury in our study(51.1%) similar to study by Garget al.[12]Motor vehicle accidents accounted for nearly 40.5% of cases. In 2.4%of patients, assault was the cause of trauma. As age increased, the incidence of falls decreased but that of traffic accidents increased greatly. This is in contrast to the reports in which high-velocity trauma is the most common mode. [13]

Many studies show that the initial GCS is an excellent predictor of mortality [12,14] However, we observed that the classification of head injury into mild, moderate, and severe on the basis of initial GCS is a good prognostic factor for predicting chances of mortality.[12,15]Suresh et al. reported poor outcome in the group of GCS 3–5 as 58.5%, GCS 6–8 had 35.2%, GCS 9–12 had 11.4%, and GCS 13–15 had1.3%.[11] Beca et al. Found that the initial GCS score was the single most important factor affecting outcome.[16]

In our study, we found abnormal pupillary response being the strongest predictor of outcome. Poor outcome in patients with normal pupils was 4%, patients with anisocoric pupils were 42.9%, and with fixed dilated pupils was 100%. Astrand et al. reported 100% poor outcome in dilated pupils unresponsive to light. [17]

We found isolated skull fracture in 20 (23.8%) patients with good outcome in 95% and poor outcome in 5%. Suresh etal.had17% patients with isolated skull fracture with good outcome in 94.1% and poor outcome in 5.9%.[11]Astrand et al.reported 48% of patients of EDH with good outcome in 98% and poor outcome in 2%.[17]Extradural hematoma is significantly less common in children than in adults and is even more rare in infants.[18]

The outcome of patients with SDH is significantly

worse than that of patients with EDH, mainly because of the underlying brain damage accompanying SDH and the resultant increased intracranial pressure. In our series, SDH was seen in 7 (8.3%) patients and out of those poor outcomes was noted in 2(28.6%) patients.

In our study, diffuse brain edema was observed in 7(8.3%) with poor outcome in 2 (28.6%) patients. Suresh et al. reported the incidence of diffuse brain edema as 30% with poor outcome in 25%. [11]

Quattrocchi et al. found prognostic significance of the presence or absence of Midline shift (MLS)on the basis of CT findings.[19] In our study, we found major prognostic significance of Midline shift and strong predictor of poor outcome. Athiappan et al. found the prognostic value of MLS to be more important in patients with single contusions or Intracerebral hematoma than for those with multiple lesions and extra axial or subdural hematoma. [20]

In our study, we found that 70.2% of patients had only head trauma, 10.7% had facial trauma, 7.1% had limb fractures, 4.8% had abdominal solid organ injury, 2.4% had spinal injuries, 2.4% had chest trauma, and 2.4% had multiple injuries. Paret et al. reported chest trauma in 62%, limb fracture in 32%, facial fractures in 29%, abdominal solid organ lesions in 20%, spinal cord injuries in 5% and multiple in 67%.[21]This difference is because we included all patients irrespective of severity of injury.

The overall outcome of our series of patients revealed a mortality of 6% and good outcome of 82.1% with 7.1% patients have moderate disability and 4.8% patients being completely dependent for their day-to-day activities. [Table5]

Conclusion

RTAs are more common in school children and adolescents, and falls are commoner in toddlers and preschool children. Poor outcome was seen in the category of GCS ≤8 patients had fixed dilated pupils had poor outcome followed by anisocoria. From our series, we also concluded that poor outcome was most strongly associated with midline shift (MLS) >3, there is an emerging need for effective fall and traffic accidents prevention strategies for children which includes educating about traffic rules and enforcement of road safety. Prompt and accurate assessment of the severity of injury may lead to early initiation with better critical care which may prevent mortality in these patients.

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Burden of traumatic brain injury in refugee population: unmet need of care and gaps in knowledge

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Keywords
traumatic brain injury, refugee population, prevalence, management options, asylum seekers

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ABSTRACT

Background and objectives. Due to marked increase in violence, the world is facing problem of refugee population either as a source of refugee population or shelter provider. These refugee population is exposed to prolonged physical and emotional distress over years, may result into spectrum of neuropsychiatric disease conditions including traumatic brain injury (TBI). Although trauma is one of the major events faced by refugee population, the exact details of the injuries still not documented and there is paucity of published literature; further these injuries may be recorded as unspecified.

Methods. The present article is intended to provide a theoretical overview of existing knowledge and gaps on trauma and injuries in refugee population. Authors analysed all relevant articles available on PubMed and Medline using the key words: "Refugee", "Traumatic Brian Injury", "Head Injury".

Results. There is a gap in knowledge for this particular demographic population. They suffer a wide range of physical and emotional to social traumatic events. The most common cause of head injury was assault; however, motor vehicle accidents were less prevalent, and there is an ongoing struggle for resources to fulfil basic needs

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leading to health care taking a backseat. There is high prevalence of post-traumatic stress disorder. Many of the refugees are settled in relative economically poorer countries which further add to the burden of a nation already besotted with internal requirements. There is a need for an international collaboration to tackle unique problem.

Conclusion. Authors recommends urgent need to handle the root causes responsible for the generation of refugee population and at the same time it is necessary to identify the epidemiology, patterns, management challenges and consequences of injuries and barriers to seek and provide care in refugee population.

Introduction

Increased prevalence of violence across the globe, forced a large population to leave their homes which started since the World War II. [1] According to an estimate approximately 60 million people are displaced globally and of which about 22 million have crossed an international border (i.e. refugees). [1] Authors observed most of the world is facing problem of refugee population either as a source or as a shelter provider to refugee population. [2-10] These refugee population is exposed to prolonged physical and emotional distress [11] which can result in spectrum of neuropsychiatric disease conditions [12] including traumatic brain injury (TBI). [13] It is being reported that approximately 2.1 million or 8.8% of refugees and asylum seekers has been given shelter in five wealthiest nations [10] still they do struggle to access health care. [14] In spite of the importance of these issues there is not much literature address many of the disease condition in refugee (or displaced) population[13, 15-17] which include injuries and TBI as well. [18, 19] The present is intended to provide a theoretical overview of existing knowledge and gaps on trauma and injuries in refugee population.

Injury distribution

Although trauma constitute one of the major events faced by refugee population, however the smaller number of published studies and inadequate data collection largely restricts the detail information regarding injury patterns. [20, 21] The trauma can range from physical and emotional to social traumatic events resulting in impairment in physical or emotional functions. [22-24] The exact details of the injuries may not be available and additionally the injuries may be recorded as unspecified. [21]In one study the patients presented with the complaint suggestive of head injury, fractures, skin injuries and burn injuries. [20, 25] The common cause of head injury was assault however, the motor vehicle accidents were less prevalent (probably due to limited access in refugee camps). [20] Although studies have tried to identify the causes of traumatic brain injury and recognized TBI as a significant cause of morbidity but the details are restricted by paucity of published data and further most of these studies are restricted to single center studies. [26] Many studies have highlighted that TBI is related to long- term neuro-psychiatric sequel [27-30] however exact burden and spectrum is lacking and also the need of the patients in refugee population is not assessed. Studies have further highlighted, refugee patients population usually prefer to use emergency services instead of regular outpatient's services, as these are easily available, affordable and accessible. [20,25]

Challenges in providing health care

Identifying the injured and injuries and providing care to them in refugee camps and refugee population is a big challenge as there is ongoing struggle for resources to fulfill basic needs (adequate food, clean water, shelter, and security) and at the same time no extra support the finances. [31] This can be easily understood by taking the example of refugee population who is settled in United States for years but still barriers to access healthcare. [32] This is not because of the limited resources alone; this may be due to the non-awareness the people to adequately utilize the services as well. [32-34]

How to approach?

Approach to the patients who seek care shall need a good understanding and trust between the victim and health care provider, safe environment, several interviews and overcoming the barriers (language and cultural). [35,36, 37] It has been shown that in the presence of culturally competent people [36-38] and professional interpreter [39-41] the chance of getting details information are more than when there is no interpreter or there was a non-professional interpreter [42]

The current situation

Amnesty International defines a refugee "as a person who has fled their country and is unable or unwilling to return because of a well-founded fear of being persecuted due to their race, religion, nationality, membership of a particular social group, or political

opinion". An asylum seeker is defined as an individual who is seeking international protection and whose claim has not been decided by the country to which they have submitted it. Ultimately, not all asylum seekers will be recognized as refugees. Traumatic Brain Injury is an injury resulting in abnormal brain function arising from the application of an external force to the cranium. It carries immense significance in this population as can be deciphered from our discussion. This significance can be viewed in terms of the difficulty in adapting to a new system and the spectrum of injuries experienced by this population.

Spectrum of injuries [1]

In a retrospective study of refugees of the ongoing civil war in Syria a major portion of the referrals were due to trauma cases when compared to the local population. The most common types of trauma were (in order of prevalence) head injury, fracture, skin injuries, and burns. Compared to the local population motor vehicle accidents were not the common cause of head injuries rather assaults was the most common cause. This was especially prevalent in young males and as expected included larger number of contusions and extra-dural hematoma. Still the amount of reported cases of assaults was less as compared to local population as access to the police department was limited. The lower prevalence of motor vehicle accidents likely reflects the limited presence of motor vehicles in camps and the greater number of people with a driving license and cars in the local population.

Another critical aspect of the refugee population is the prevalence of post-traumatic stress disorder among these cases. These problems of Syrian refugees arise due to further cofounding problems such as low living standards lack of adequate child care and hygiene, somatization of psychological disorders, and also the possible underlying relationship between posttraumatic stress disorder and physical violence which needs further evaluation. Trauma can be a direct cause of this as contusion or injury to the prefrontal cortex may lead to loss of executive function and cause difficulty in adjustment and adaptation. Depression can affect the cognitive functions and delay the return to daily activities. Prefrontal cortex damage leads to higher rates of substance abuse but most studies on psychiatric evaluation of these cases place current use of alcohol or any banned substance as an exclusion criterion and hence this aspect may be missed totally.

Any discussion on the status of refuge and asylum seekers is incomplete without discussing of the aspect of pediatric head injuries. Minors are a substantial portion of the refugee population around the world and trauma, in general, was more common among refugee children than in the locally residing population. Interestingly, minor closed head injury was much more common in local children as compared to refugee children who were more prone to open head injuries. This may be due to the fact that while local population children with concussions and emesis after closed head injury are primarily admitted and observed in a population to avoid a computed tomography of the head and the associated radiation exposure, refugee children are often given step-motherly treatment and discharged. Also, minor head trauma may not be perceived as a compelling reason to come to the hospital for evaluation by refugee families to the same extent as it is for resident parents, explaining the discrepancy observed.

Burden on state health resources and adoption by refugees [2]

One of the most critical aspects of treating a refugee population is the burden it places on the local health care system. While trauma admissions are actually a relatively small fraction of overall emergency admissions (a little over 2% for both refugees and local population), but their possible outcomes such as surgical procedures, extensive operations, longer hospital stays, repeated radiological and laboratory studies, control examinations as outpatients can cripple the existing health care system which may not be adequately geared up for the same. There is a risk of leaving permanent physical and more importantly mental damage in patients, which will increase health costs and thus emphasizes their importance to look at them more than just numerical values among other admissions. Refugees usually tend to admit to emergency clinic for various reasons such as relatively easier accessibility of the emergency clinic and abuse of health system to leave the camps more easily. This can potentially harm the local population emergency and thus lead to unintentional consequences.

Then there is the difficult aspect of adoption of

the local health care system. Entering and navigating a largely westernized healthcare system can be intimidating to someone with no knowledge of the procedures and mental trauma to boot. These individuals may place their own medical needs behind more dominant concerns of safety, securing food and clothing for their family, housing, utilities, or finding legal representation if seeking asylum. Again, opening to their past trauma is a painful aspect which many may not be willing to undergo. Two-thirds of refugees and asylum-seeking patients report not initiating discussion related to war injuries with their physicians. Reasons reported by refugees for withholding this information about a history of injury or trauma included feeling like they should be asked first before bringing anything up and "not wanting to think about it again". Even when medical encounters are successful, adherence to necessary care can prove inconsistent in refugees and asylum seekers. This problem is further magnified when they are finally granted asylum and the follow up has to be at a different hospital.

Eighty-six percent of the world's refugees and asylum seekers populations are resettled in poorer developing nations that may already be struggling to provide adequate resources for their own citizens. Even if some of these refugees make it to a developed nation healthcare costs become the prohibitive factor. Almost all the cases are uninsured and thus may have difficulty affording necessary care. In a focus group, one individual expressed frustration stating, "Doctors always tell us, 'don't worry about money, your health is more important.' But they do not understand our situation". Even after years of struggle and work health care costs at these places prevent from seeking treatment even for their progeny.

Table 1: Prospective problems and solutions for refugee head injury and health care[20, 43]

Problems	Possible solutions
Larger patient load and burden to local resources	Possible health centres near refugee camps set exclusively for the same Mobilization of international funds and international health agencies Possible incentives to health care personnel
Higher rates of open head injuries and emergency admissions	Better availability of minimum barebones setup Emergency services and imaging to be the focus of health care
Poor follow up and adherence	Improved local touch points and integrated health records
Mental health issues	Possible digital solutions to psychiatric care and assessment Increase training of health care personnel for psychiatric counselling
Paediatric head injuries	Specialized resources and specialists for the same Resuscitation fluids, medicines catered for the same.
Health care costs	Subsidized health care, universal funding

Conclusions

There is an urgent need to have a strong will to handle the root causes responsible for the generation of refugee population and at the same time it is necessary to identify the epidemiology, patterns, management challenges and consequences of injuries and barriers to seek and provide care in refugee population. The future not only focuses on the physical nature and its consequences but it should also address neuropsychological, financial and social sequel of the injuries. While taking care of the refugee population that we should be compromising care to local or hosting population as it may result in social imbalance and can create insecurity in the local population. There is a need to further confirm these findings and ascertain that these should be able to access regular services rather than emergency department visits and thus reducing the burden on emergency care services.

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Improved pain and quality of life outcomes after percutaneous vertebroplasty for thoraco-lumbar non-osteoprotic compression fractures

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ABSTRACT

Introduction: Vertebroplasty is a minimally invasive technique in which percutaneous injection of bone cement under fluoroscopic guidance Percutaneous vertebroplasty (PVP) has been widely and successfully accepted in the treatment of osteoporotic and neoplastic vertebral compression fractures to control pain refractory to medical treatment. However, using of vertebroplasty as primary line treatment for traumatic, non-osteoporotic compression fractures still not widely accepted and considered a debatable issue.

Patients and methods: This prospective comparative study was conducted at Neurosurgery department, Mansoura university hospital and Mansoura emergency hospital through the period between January 2015 and March 2016. 20 patients complaining of back pain due to single level thoracolumbar vertebral compression non-osteoprotic fractures were admitted to the study. Patients were divided into two groups 10 patients each, PVP group and conservative group. Outcome were assessed as regard pain improvement using Visual analogue scale VAS and quality of life using short form 36 scale (SF36).

Results: Ten patients in the PVP group received Vertebroplasty, eight males (80%) and two females (20%) the age ranged from 29 to 62 years with mean age of 44.2+8.3 (mean+SD) years. The conservative group included ten patients seven males (70%) and three females (30%) the age ranged from 31 to 64 years with mean age of 45.1+9.2 (mean+SD) years. The level of injury ranged from D6 to L4. VAS and SF36 results showed significant improvement in post injection results compared to preinjection and to the conservative group

Conclusion: Percutaneous vertebroplasty is safe and effective procedure to improve pain and quality of life in non osteoprotic patients complaining of traumatic compression fractures of thoraco-lumar region it decreases pain, and provide early ambulation of patients which improve their quality of life without significant morbidity.

Keywords
vertebroplasty,
vertebral compression fractures,
quality of life,
non-osteoporotic

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INTRODUCTION

Vertebral compression fractures (VCFs) represent a significant health care problem due to high incidence and their direct and indirect negative impact on quality of life, physical function, mental health and missed work hours as well as the burden on health care system [114,21,25].

Vertebroplasty is a minimally invasive technique in which percutaneous injection of bone cement under fluoroscopic guidance into the cancellous bone of a vertebral body with the objective of bone augmentation [19]. Galibert et al. in 1987 were the first to describe and introduced Vertebroplasty, they used the technique for management of vertebral angiomas in seven patients [10]. Percutaneous vertebroplasty is a relatively safe, simple and commonly performed interventional procedure for the management of vertebral compression fractures [11].

Percutaneous vertebroplasty (PVP) has been widely and successfully accepted in the treatment of osteoporotic and neoplastic vertebral compression fractures to control pain refractory to medical treatment [2,12, 15 18, 20,24, 25]. Taylor et al 2007 published a systematic review and found that There is Level III evidence to support balloon kyphoplasty and vertebroplasty as effective therapies in the management of patients with symptomatic osteoporotic vertebral compression fractures refractory to conventional medical therapy.[23]. However, using of vertebroplasty as primary line treatment for traumatic, non-osteoporotic compression fractures still not widely accepted and considered a debatable issue.

Decrease fracture healing, risk of infection and effectiveness of alternative conservative and surgical options are raised as rejection points, while minimally invasiveness than surgery and improvement of pain and quality of life than medical treatment are assumed as advantages of the technique [5,6,7,8, 22].

In this study, we compare the percutaneous vertebroplasty PVP and conservative medical treatment in the treatment of traumatic single level non-osteoprotic compression fractures. The 2 groups were compared with respect to baseline pain, quality of life, hospital stay and follow up at 1 and 3 months.

PATIENTS AND METHODS

This prospective comparative study was conducted at Neurosurgery department, Mansoura university hospital and Mansoura emergency hospital through the period between January 2015 and March 2016. 20 patients complaining of back pain due to single level thoracolumbar vertebral compression fractures were admitted to the study. Patients were divided into two groups 10 patients each, PVP group and conservative group. The choice between the 2 options was based primarily on patient's preferences and, to some extent, on counseling by the neurosurgeon on charge, the first and second authors who did the PVP procedure were called for performing the procedure by the neurosurgeons on duty and didn't involve in the process of decision making.

Pre-operative evaluation

Patients were assessed clinically by neurological and local examination. This aimed to exclude neurological deficit and identification of painful vertebra by local tenderness at the fracture site and detection of associated medical or surgical co-morbidities. It aimed also at defining the degree of pain by Visual analogue scale (VAS) for pain assessment with 0 as no pain and 10 as the worst pain ever experienced. Short form 36 test (SF 36) for quality of life assessment [4].

Imaging studies included Plain X-ray radiography to detect the level, type and number of fractures, degree of collapse (relative vertebral body height) and the degree of kyphosis (vertebral wedge or local kyphotic angle).

The relative vertebral height (RVH) was measured as the sum of the distance along the vertebral borders at the anterior, middle, and posterior locations of the fractured vertebral body in relation to the adjacent intact vertebral body as a reference. The kyphotic angle was determined by using the Cobb method as the angle between the superior and inferior endplates of the collapsed vertebral body. The relative heights of the fractured vertebrae and angle were assessed before and after vertebroplasty on a standard lateral radiograph, and assessed in the conservative group on admission then on discharge and during 1and 3 months follow up. CT scan with sagittal reconstruction was done for all patients to assess the type of fracture and the integrity of posterior wall of the vertebral body.

Patients included to this study had traumatic fracture with intolerable pain who had a normal BMD t-score (-1 or higher) and their age above 18 years old, compression fracture less than 50% of vertebral height, intact motor power, no or very small retropulsed segment. While pediatric patients, those having neurological deficit, fracture more than 50% , unstable fracture with posterior or middle column

disruption and compromise the canal, potential infection, bleeding tendency, oral anticoagulant, had previous spine surgery at same level, those have another painful disease of spine or pathological fractures either osteoporotic or neoplastic were excluded from our study.

Procedure

Patient was placed in prone position with translucent padding of the regions caudally and cranially from the fractured vertebra(e). oxygen mask was applied Oxygen saturation, blood pressure and heart rate are continuously monitored. sterile drapes were put after adequate sterilization of patient's back. Procedure is performed under local anaesthesia. Identification of the fractured level with the aid of fluoroscopy. (Figure 1).

Figure 1: Vertebroplasty procedure: a- two injection needles at place b- during injection c- the needle and injector d- C-arm device at neurosurgery department operative room, Mansoura University hospital.

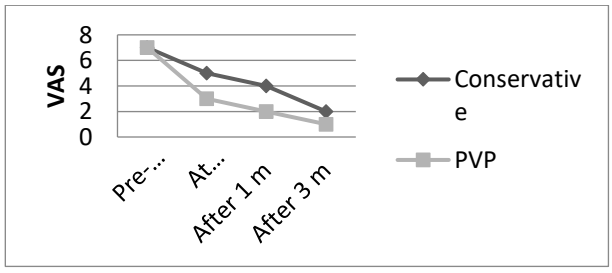

Figure 2: Graph of median pain based on VAS score, on admission, on discharge 1 month and 3 months following vertebroplasty. VAS, visual analogue scale.

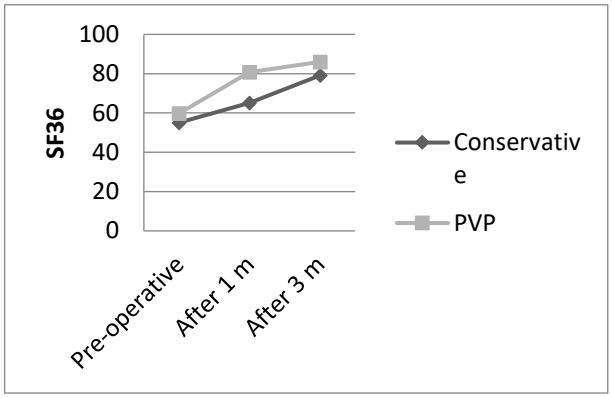

Figure 3: Graph of mean quality of life based on SF36 scores on admission, 1 month and 3 months of both groups.

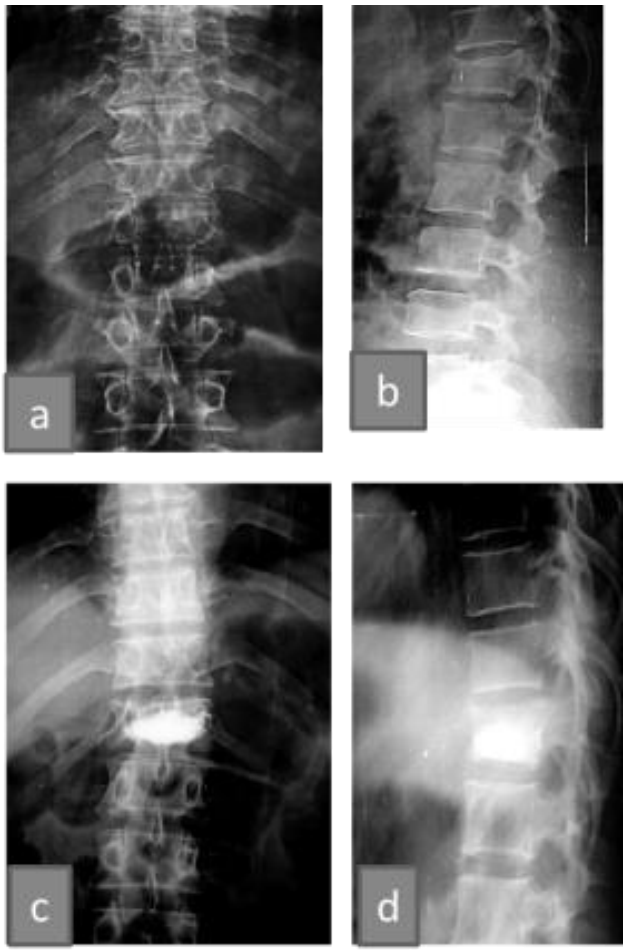

Figure 4: Pre- and post-operative x-ray AP & lat view

The fluoryscopy was manipulated till the fracture level centralized and both pedicle arches were identified on the antero-posterior (AP) image. Local anaesthesia was achieved by injection of Lidocaine 1% solution using thin spinal needle by which we infiltrated the whole pathway from facet joint till

subcutaneous tissue. The position of the thin needle used for lidocaine injection determines the direction of the vertebroplasty needle tract during fluoroscopy. Under fluoroscopic guidance one (preferred) or two needles were introduced to pedicle then under guidance of lateral fluoroscopy image the needle was advanced till half of vertebra near midline which confirmed again by AP image.

During insertion of the needle, the bevelled tip was pointed laterally to gain easy access to the pedicle. After pedicle penetration, the bevelled side was rotated medially to avoid breaching of the medial pedicle wall.

The PMMA cement (*Exolent spine, ® Italy)* was prepared and transferred to an injector. The air was eliminated from the system. After 2-4 minutes of cement mixing (depending on the viscosity of the cement and on the room temperature), the cement reached its proper viscosity (toothpaste-like), and is ready to be injected. The cement was then injected slowly and carefully under constant fluoroscopic imaging in order to achieve good filling of the intertrabecular space of the vertebral body. The injector is disconnected from the needle. the needle(s) was (were) removed with twist to separate the tip from the cement.

Post procedure care:

A post-procedural CT scan was performed to all cases to assess extent of bone cement and detection of any cement leak. Then the patient was placed in bed for transport to the ward Figure (5).

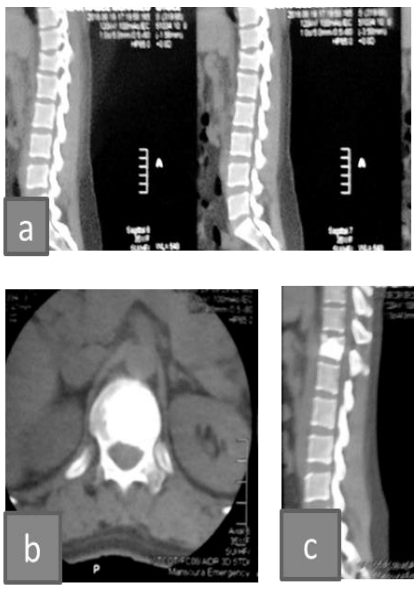

Figure 5: Pre and post operative CT a- preoperative sagittal view b- postoperative axial view showed filling of the fractured vertebra with bone cement with no leakage c- post operative sagittal view show restoration of vertebral height and angles.

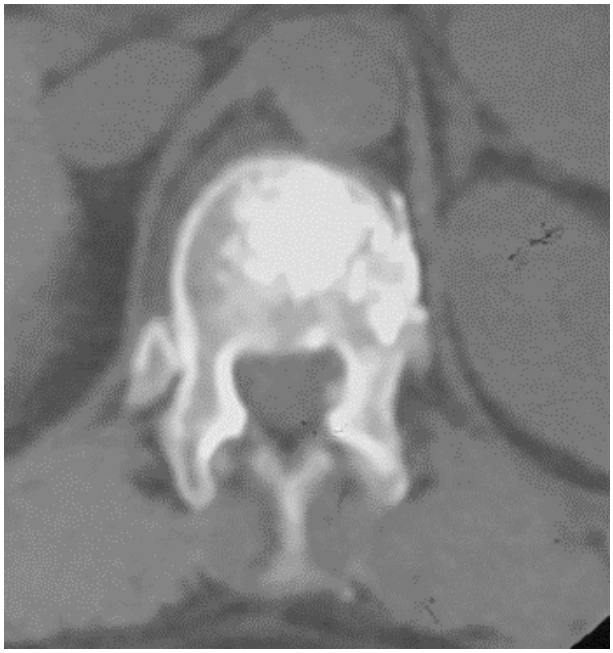

Figure 6: Unipedicular injection, cement cross the midline and small part of cement start to leak on the left side of vertebra.

Follow up

It was carried out at regular intervals; 2 weeks, 1months and 3 months. In each time the patient were evaluated clinically for Neurological examination, pain by visual analogue scale, evaluation of quality of life by short form 36 test [3]. And radiographically by Plain X-ray.

Statistical analysis:

Data were analysed using the Statistical Package of Social Science (SPSS) program for Windows (Standard version 21). The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Continuous variables were presented as mean ± SD (standard deviation) for parametric data and Median for non-parametric data. The two groups were compared with Student t test (parametric data) and Mann–Whitney test (non parametric data).

Level of significance

For all above mentioned statistical tests done, the threshold of significance is fixed at 5% level (p-value). The results were considered:

- Non-significant when the probability of error is more than 5% ($p > 0.05$).
- Significant when the probability of error is less than 5% ($p \leq 0.05$).

The smaller the p-value obtained, the more significant are the result.

Results

Twenty patients complaining of intractable back pain due to thoracolumbar vertebral compression fractures, and not responding to initial conservative measures and not associated with neurological affection. Ten patients in the PVP group received Vertebroplasty. Eight males (80%) and two females (20%) the age ranged from 29 to 62 years with mean age of 44.2±8.3 (mean±SD) years. six patients injured during fall from height while four sustained road traffic accidents. Unipedicular injection was performed for six vertebrae (60%), while bipedicular injection performed for four vertebrae (40%). The level of injected vertebra ranged from D8 to L4. The interval between trauma and injection ranged 3 to 12 days mean was 4.6±1.8 the mean post injection hospital stay was 1.7 days ranged from 6 hours to 3 days. The relative kyphotic angle was 10.42±3.8. The relative vertebral height was 77±7mm

The conservative group included ten patients seven males (70%) and three females (30%) the age ranged from 31 to 64 years with mean age of 45.1±9.2 (mean±SD) years. 5 patients injured during fall from height while 5 sustained road traffic accidents. The level of fractured vertebra ranged from D6 to L3. The relative kyphotic angle was 10.17±3.5. The relative vertebral height was 78±2mm.

Table 1: Comparison between both group regarding data on admission.

	Vertebral height	Kyphotic angle	age	Gender M F	p- value
Conservative	78±2.7	10.17±3.5	45.1±9.2	7 3	>0.05
PVP	78±2.7	10.42±3.8	44.2±8.3	8 2	

Table 2: Comparison between Conservative and PVP groups regarding VAS preoperative and at different follow up periods.

VAS	Conservative (n=10)	PVP (n=10)	Mann Whitney test	p- value
Admission Median (Min-Max)	7 (4-9)	7 (4-9)	0.194	0.846
VAS at discharge Median (Min-Max)	5 (4-7)	3 (1-6)	2.778	0.005*
VAS after 1m Median (Min-Max)	4 (2-5)	2 (0-4)	2.625	0.009*
VAS after 3m Median (Min-Max)	2 (0-2)	1 (0-1)	2.109	0.035*

*significant p <0.05

Table 2 showed the results of VAS on admission the differences between both group was statistically insignificant (P=0.846) The pain showed statically significant improvement in PVP group patients from preoperative VAS and compared to conservative group the level of significance was highest on time of discharge(p=0.005) and gradually decreased till 3 months (p=0.035).

In the PVP group Preoperative VAS ranged from 4 to 9(0% no pain, 0% mild, 10% uncomfortable, 40% distressing, 45% horrible & 5%worst). on discharge VAS ranged between 1 to 6(0% no pain, 40% mild, 45% uncomfortable, 10% distressing, 5% horrible & 0% worst). Table 1

Comparing unipedicular versus bipedicular techniques results, it is found that no significant difference between improvement of VAS between both techniques Table 3. showed results of VAS in unipedicular and bipedicular techniques.

TABLE 3: Comparison between unipedicular and bipedicular PVP regarding VAS preoperative and at different follow up periods.

VAS	Unilateral PVP (n=6)	Bilateral PVP (n=4)	Mann Whitney test	p- value
Pre-injection Median (Min-Max)	7 (5-8)	7 (4-9)	0.441	0.659
VAS at discharge Median (Min-Max)	3 (1-3)	4 (2-6)	1.453	0.146
VAS after 1m Median (Min-Max)	2 (0-3)	2 (1-4)	0.775	0.438
VAS after 3m Median (Min-Max)	1 (0-1)	1 (0-1)	0.267	0.789

The mean preoperative SF 36 test score was 55.10±12.57 pointsin conservative group versus 59.80±12.16 in PVP group (p=0.407). While the 1 month after discharge mean SF 36 test score was 65.1±10.37 points for conservative group while was 80.70±4.13 (p<0.001). on three months follow up SF36 score was 79.10 ± 6.84 and 86.00 ± 6.16 respectively. The improvement outcome of postoperative values compared with preoperative SF 36 test score was found to be statistically significant (P<0.001). table 4. As the results of VAS the difference between unipedicular and bipedicular injection in improving quality of on S36 score were insignificant Table 5 Comparing unipedicular versus bipedicular techniques results, the difference was found to be statistically insignificant. Table 5.

There was no mortality in both groups. We had only two cases of cement leakages one case of asymptomatic vascular extravasation of cement and another patient in whom cement leaked into upper disc space.

TABLE 4: Comparison between Conservative and PVP groups regarding SF36 pre injection and at different follow up periods.

SF36	Conservative (n=10)	PVP (n=10)	Student t-test	p- value
Pre-injection Mean ± SD	55.10±12.57	59.80±12.16	0.850	0.407
SF36 after 1m Mean ± SD	65.1±10.37	80.70±4.13	4.29	<0.001*
SF 36 after 3m Mean ± SD	79.10±6.84	86.00±6.16	2.370	0.029*

TABLE 5: Comparison between unilateral and bilateral PVP regarding SF36 preoperative and at different follow up periods.

SF36	Unilateral PVP (n=6)	Bilateral PVP (n=4)	Student t-test	p- value
Pre-injection Mean ± SD	55.67±11.39	66.00±11.91	1.381	0.205
SF36 after 1m Mean ± SD	80.00±4.09	81.75±4.57	0.633	0.544
SF 36 after 3m Mean ± SD	83.50±5.36	89.75±5.91	1.738	0.120

Table 5 studies addressed non ostoprotic traumatic fractures

Author	Study design	Type of fracture	Number of patients	Year
Chen and Lee	Case report	Burst	1	2004
Chen and Lee	Case series	Burst	6 patients	2004
Amoretti et al	Case series	Burst	5 patients	2005
Huet et al	Case series	Burst	12	2005
Szekely et al	Case report	Burst	1	2009
Knavel et al	Retrospective review	compression	15 patients	2009
Szekely Gy	Case series	Compression	15 patients	2012
Elnoamany	Case series	compression	23 patients	2015

Discussion

Conservative management, surgical fixation and vertebroplasty are available treatments options for traumatic VCFs. Medical treatment includes rest, thoraco-lumar orthosis and analgesic is indicated in case no neurological deficit, no any signs of instability and kyphotic angle less than 20 degrees and less than 50% vertebral height loss, which are the same indications for percutenous vertebroplasty. For vertebroplasty there is another relative indication which is the integrity of posterior wall of vertebral body [14,17].

Surgical intervention is not usually the first line of therapy and mostly is necessary if the kyphosis is above 20 degrees to prevent corporeal collapse and prevent subsequent neurological disorders or low back pain. The signs of instability like involvement of the posterior wall, disruption of the spinal arch or interpedicular olisthesis are indication for surgical intervention [1].

Nowadays vertebroplasty become a popular procedure for management of refractory pain in osteoprotic compression fractures and pathological fractures. However, there is a debat about its efficacy in pain relief, quality of life improvement, using it in traumatic cases and its complications. Few reports in litreture were addressed the implication of vertebroplasty in management of the non-osteoprotic traumatic VCFs [3, 6, 7, 9, 14, 21, 22], two of them are case reports and the others are limited sample cohort studies. Table (5) Up to our knowlage, no published comparative study compared the outcome of vertebroplasty to that of conservative management in patients suffering traumatic non osteoprotic thoraco-lumbar VCFs. This study is unique in comparing both treatment modalities in control of pain early mobilization and improving quality of life.

Our results showed that vertebroplasty was effective in reducing pain in all of the vertebroplasty group's patients within a very short period of time. VAS scores obtained on time of patient discharge, 1 month and 3 months after vertebroplasty from our 10 patients of the PVP group showed significant pain relief. And when compared to the VAS scores of the conservative group patients, there were statistically significant superiority to the vertebroplasty group. Pain relief was rapid and marked. This improvement was maintained and continued to improve through the whole follow up period and didn't decline by time.

Our results of pain improvement are supporting the result of Szekely et al in their 15 patients' report; all of them showed more than 5 points improvement of VAS [22]. El noamany reported injection of 29 vertebrae in 23 patients of non-osteoporotic VCFs, all of them showed improved pain scores both on rest and movement, the improvement started 2 hours post injection and continue during follow up, he advocated PVP as first line treatment of VCFs [9]. Chen and Lee performed PVP for management of traumatic Thoracolumbar spine bursting fractures with statistically significant improvement of pain their six patients [6]. Amoretti et al reported 5 patients of stable burst fracture percutaneous vertebroplasty was done under both fluoroscopy and CT guidance, pain improved in 4 out of their 5 patients [3].

The difference between both groups was statistically significant in the time of discharge and one month follow up visit and decline in the 3 months follow up visit. There were no significant differences in these Improvements due to the etiology of the fracture or due to the approach used wither unipedicular or bipedicular or the amount of cement used.

Kallmes et al and Buchbinder et al [5,16] published two randomized trials in 2009, they

reported that there is no beneficial effect of vertebroplasty compared with a sham procedure (placebo surgery) in patients with painful osteoporotic vertebral fractures, at 1 week or 1 or 3 months after treatment. No significant differences between groups were seen in the primary outcome of overall pain at 3 months. Despite their population were osteoprotic, we have many concerns about this result, as in our study pain improvement was significant which match with most of studies talking about pain improvement following PVP with a variable degree of pain improvement but in this study noting that there is no difference between PVP and sham procedure is questionable.

Despite small sample size, we found no statistical significance between the six patients received unipedicular injection and the 4 patients received bipedicular injection as regard improving VAS scores and quality of life on SF36. The same conclusion was announced by two studies, Knavel et al. [17] concluded from their retrospective study that, hemivertebroplasty in which cement is instilled in only one half of the vertebral body was as efficacious as bilateral cement infusion [17]. The results of ELnoamany study on non-osteoprotic VCFs confirmed Knavel's study results, since it showed no statistically significant differences in pain or quality of life scores, between hemivertebroplasty and bilateral vertebral filling [9,l7] which may be partially explained by increase the hardness of non osteoprotic bone. In our opinion, This piece of information is significant because it support the minimally invasive nature of the procedure which could be performed optimally through on side injection, and it facilitate performing vertebroplasty by local anesthetic infiltration rather than sedative anesthesia and this will encourage patients for taking their decisions and lastly it will decrease cost especially in poor countries.

Pain relief was obviously reflected on the quality of life of the patient and his/her resumption of social activities which were obvious in short form 36 test score improvements. as the short form 36 test SF36 take a survey for last month we found it difficult to be applied on time of discharge and that is why we applied it in one and three months follow up visit. The significant improve in SF36 score results in the vertebroplasty group between pre injection and follow up and between the vertebroplasty group and conservative group support the results accumulated from many previous studies that concluded improvement of quality of life after cement injection for compression fractures either in osteoporotic patients[4, 12,13,18] or in traumatic non osteoprotic VCFs[3,6,9, 14, 22] but may be our results is the first to compare the conservative treatment to vertebroplasty in head to head prospective randomized study that showed statistical significant improvement in quality of life in the vertebroplasy group.

A comparison of the pre and post vertebroplasty scores in the various SF-36 domains has shown a significant and clinically relevant increase in summary scores, thereby indicating a significant overall increase in the quality of life. During the two weeks after vertebroplasty significant improvement was seen only in the domains of physical function, which is known to have the highest correlation with physical faculties and pain, reflecting the results of the numerical pain score. The role physical and role emotional domains showed an obvious, non-significant decrease in the first month, probably due to general post-treatment role-inhibiting behavior. There was a significant improvement in summary scores of SF-36 domains at follow-up at one and three months in our series.

It has great potential to avoid various problems associated with prolonged bed-rest, including high medical expense used for analgesics and other medications, deterioration in bone density and function of the musculoskeletal system and progression of dementia in elderly patients. Persistent back pain may also cause psychological and sleep disorders.

Conclusion

Percutenous vertebroplasty is safe and effective procedure to improve pain and quality of life in non osteoprotic patients complaining of traumatic compression fractures of thoraco-lumar region it decreases pain, and provide early ambulation of patients which improve their quality of life without significant morbidity.

Disclosures

All The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article

Authors contributions

This work was carried out in collaboration between all authors.

Author Mostafa M. Nabeeh, designed the study, Author Hanee A. Awad wrote the protocol and collect clinical data, Author Nabil M. Ali managed the literature research, Author Mostafa M. Nabeeh performed the statistical analysis and revised the final manuscript. All vertebroplasty procedures were carried out by the first two authors. All authors read and approved the final manuscript.

ABBREVIATIONS

BMD: Bone Mineral Density.
CT: Computerized Tomography.
PVP: Percutaneous Vertebroplasty
PMMA: Poly Methyl Methacrylate .
RVH: Relative Vertebral Height
SF 36: Short Form 36
VAS: Visual Analog scale
VCF1: Vertebral Compression Fracture.

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Rapid spontaneous resolution of traumatic acute subdural hematoma: A case series and review of literature

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ABSTRACT

Introduction: Acute subdural hematoma (ASDH) is the most common type of traumatic intra -cranial hematoma accounting for 24% cases of severe head injuries and caries highest mortality. The mortality rates are seen to be ranging from 40% to 90%, diagnosed on computed tomography (CT) as extra axial, hyperdense, crescent lesion between the Dura and brain parenchyma1. Acute SDH is an acute space occupying lesion to increase intracranial pressure (ICP), and is often complicated by co-existing intracranial lesions, including a variety of diffuse injuries, contusional hematomas, and edema. Acute subdural post-traumatic hematoma's (SDH) continue to have a distressingly high morbidity and mortality.2 Clinical factors like presenting GCS, Pupils, time to operative interval, Hemodynamics and co-morbidities, plays a critical role in overall outcome from acute subdural hematoma.3Careful monitoring of the neurological status is mandatory even for selected acute SDH patients with intact consciousness and no brain shift because of the possibility of the unexpected worsening. Spontaneous resolution of an acute SDH has been reported in rare cases. We report a case series of spontaneous rapid reduction of acute SDH, also we discuss the prognosis of each patient according to a Clinicoradiological Prognostic Score developed by Gautam and Sharma3 as well as mechanisms related to the rapid resolution of acute SDH.

Keywords
traumatic,
acute,
subdural hematoma

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CASE SERIES

Case 1

40-year-old male presented with history of RTA followed by loss of consciousness for 30 min and one episode of vomiting, on admission in emergency department Glasgow coma score (GCS) was E3V3M5, both pupils were reactive to light, computed tomography (CT) scan shows acute SDH in right temporoparietal lobe (Fig 1: A). We assess this patient according to Gautam and Sharma score as score is 8 and this patient was managed conservatively. Repeat NCCT head done after 24 hrs showed acute SDH was completely resolved (Fig 1: B) Patient improved and discharge on GCS of E4V5M6.

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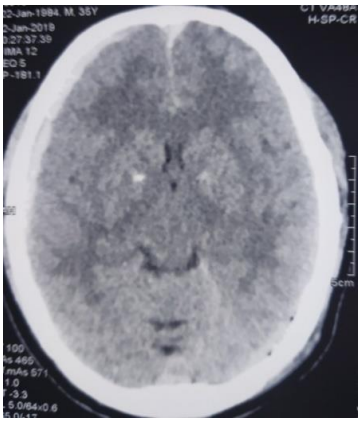


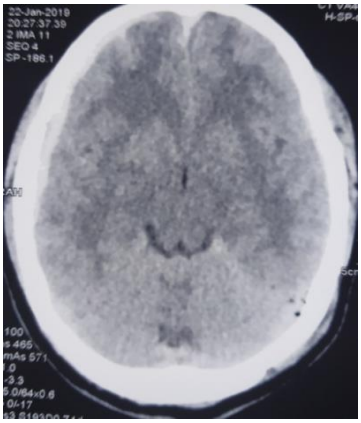
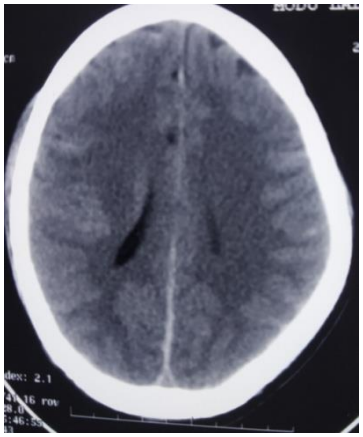


Figure 1 (A): CT scan at admission-shows right temporoparietal SDH.



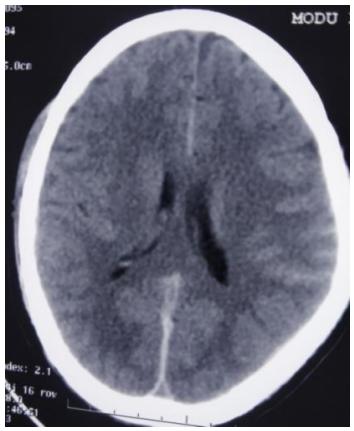
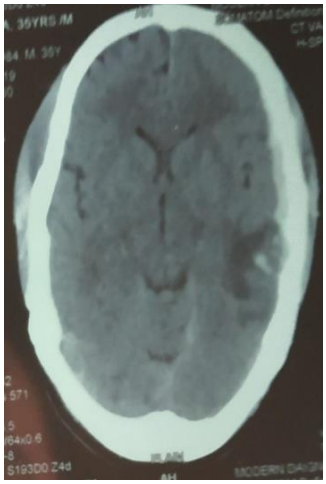


Figure 1 (B): (CT scan after 24 hrs shows rapid resolution of SDH.

Case 2

38 year old male admitted in emergency department with history of RTA with 2-3 episode of vomiting but without any history of loss of consciousness, GCS was E4V5M6.On admission NCCT head shows acute left temporoparietal SDH(Fig 2), his score was 8 on Gautam and Sharma score and we managed this patient conservatively.NCCT head done after 24 hrs which showed significant reduction/resolution in left temporoparietal SDH. He was discharge asymptomatically.



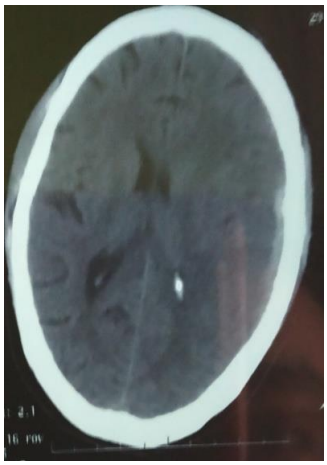


Figure 2: CT scan **(A)** shows left temporoparietal SDH; **(B)** shows repeat CT head reduction of left temporoparietal SDH.

Case 3

17-year-old male presented with history of RTA followed by loss of consciousness, on admission in emergency department patient was intubated, Glasgow coma score (GCS) was E1VtM5, both pupils were reactive to light computed tomography (CT) scan shows acute SDH in right fronto-temporoparietal lobe **(**Fig3). We assess this patient according to Gautam and Sharma score that was 7 and we also managed this patient conservatively.

Repeat CT head was done after 24 hrs which showed complete resolution of acute SDH. After 8 hrs of admission this patient was extubated and within 2 days he was oriented and following all commands, discharge on GCS of E4V5M6.

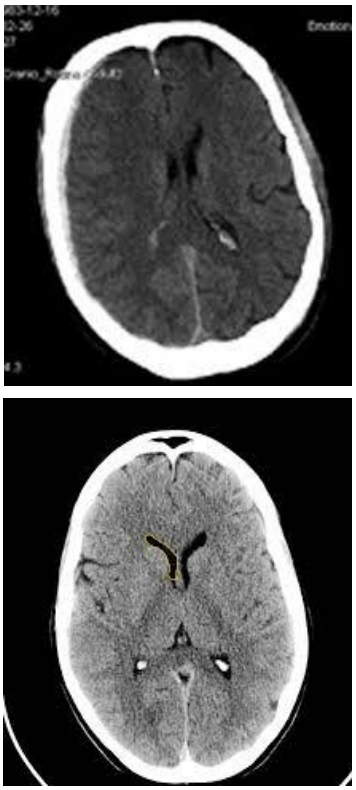


Figure 3: **(A)** NCCT head shows right frontotemporal SDH; **(B)** NCCT head after 24 hrs shows complete resolution of hematoma.

Case 4

25-year-old male presented after a road traffic accident with a brief loss of consciousness and minor facial injury. His condition declined in the emergency room necessitating a head computed tomogram (CT). At that point the patient was conscious but disoriented, his pupils were reacting and symmetric, was following commands, was able to say some words and he had movements in all extremities on verbal commands, Glasgow Coma Scale of 14 (E4V4M6). The scan demonstrated a large (1.1cm) right sided ASDH with significant mass effect and midline shift towards left side (Fig.4A). Past medical history is not significant for chronic illness. But his Gautam and Sharma score was 8 so we managed this patient conservatively; Patient was started on manitol and was admitted for observation in neurosurgical ICU. Overnight the patient was remained in same neurological status and no deterioration in consciousness. Repeat head CT (Fig.4B) performed approximately 24 hrs post admission revealed resolution of hematoma with no midline shift. The patient remained stable and was discharged home without operative intervention with advice of close follow up.

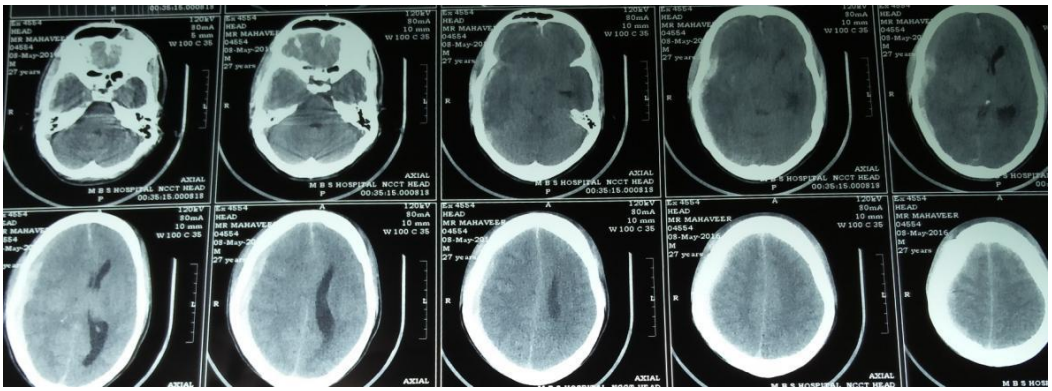


Figure 4 (A): Head CT Scan shows large right temporoparietal SDH with midline shift.

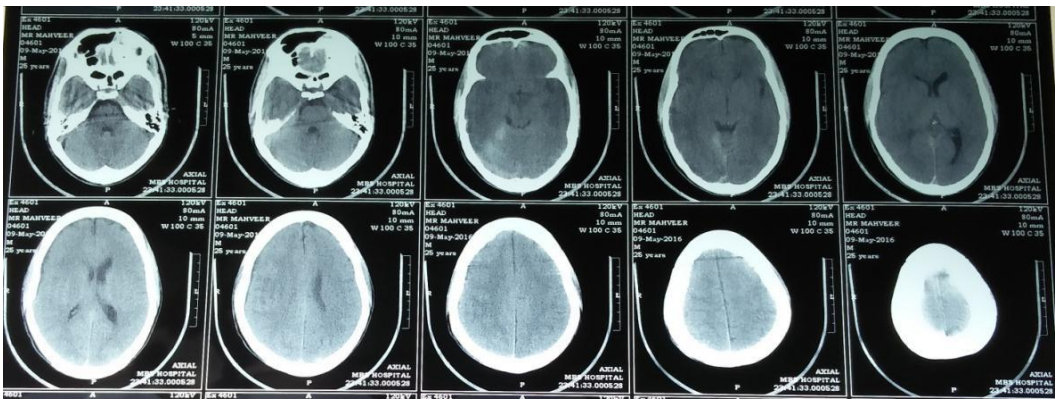


Figure 4 (B): Repeat CT Scan of head resolution of hematoma.

Case 5

14-year-old female presented in emergency room in state of unconsciousness due to road traffic accident with history of ear and nose bleed and history of vomiting, urgently NCCT head was done which showed left temporoparietal acute SDH with midline shift less then 5mm (Fig 5A). On examination her GCS was E1V1M3, her breathing was irregular, both pupils were symmetrical and reactive to light. She was shifted in critical care unit, intubated and put on ventilator her Gautam and Sharma score was calculated that was 6. Managed this patient conservatively, treated with manitol, higher antibiotics like meropenam and amikacin for associated injuries and aspiration pneumonitis. Repeat NCCT head after 48 hours which showed complete resolution of hematoma, continue treated patient conservatively, patient wean off from ventilator on day 4 of admission and following verbal commands on day 5, subsequent repeated CT head were also normal (Fig 5B). She was discharged after 8 days of hospitalization with GCS of 15.

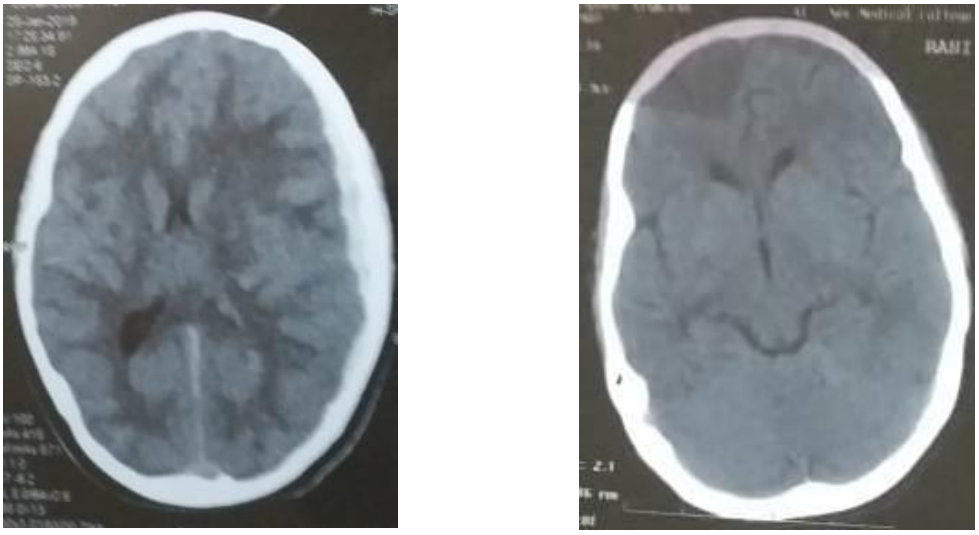


Figure 5 (A): shows left temporoparietal subdural hematoma with midline shift
(5B): shows complete resolution of hematoma.

Case 6

22 year old male presented in emergency department with history of loss of consciousness followed by road traffic accident ,there was also history of vomiting and right ear bleed present .On admission his GCS was E2V1M5 ,irritable , both pupils were symmetrical in size and reactive to light .Urgent NCCT head was done which shows right fronto-temporoparietal acute subdural hematoma(Fig 6A). Gautam and Sharma score was calculated after CT scan which was 8 and we decided to manage this patient conservatively started on manitol and supportive treatment. CT head was repeated after 24 hrs which shows complete resolution of acute SDH(Fig 6B). After 6 days of treatment patient improved significantly and discharged on GCS of E4V5M6.

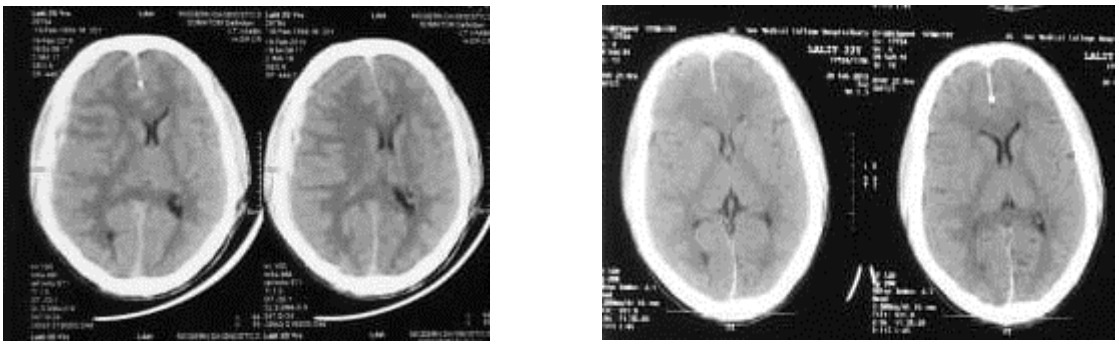


Figure 6 (A): NCCT head shows right frontotemporoparietal acuteSDH with midline shift; **6 (B)** repeat NCCT shows complete resolution of SDH

Prognostic factors	Score 0	Score 1
GCS On Arrival in Hospital	<8	>9
Hematoma Thickness (In mm) in NCCT head on arrival	>5	<5
Presence And/ Or Degree Of Midline Brain Shift (In mm) in NCCT head on arrival	>5	<5
Increase in midline shift and thickness of hematoma in repeatNCCT head after 6 hrs	Yes	No
Pupil Abnormality	Yes	No
Age	>60	<60
Availability Of OT, Neurointensive Care,CT and Other Facilities	No	Yes
Co-Morbidity And Associated Trauma	Yes	No
Time To Arrival In Tertiary Centre (In Hours)	<6 hr	>6hr
Drop Of GCS In Subsequent Examination	>2	<2

Gautam and Sharma Clinic-Radiological Prognostic Score (0 to 10)

Low Score – favours poor prognosis

High score – favours good prognosis, operative intervention not required

Discussion

Acute subdural hematomas are usually neurosurgical emergencies. Small sized hematoma in good neurological grade patients can be managed conservatively. Rapid spontaneous resolution of an acute subdural hematoma is seldom reported. Diagnosis of patients with acute SDH likely to resolve rapidly can avoid unnecessary surgery in some cases[4].

Large ASDH 10 mm or midline shift greater than 5mm on a computed tomography (CT) scan are considered neurosurgical emergencies[5]. There are reports of spontaneous resolution of the ASDH with various theories as to why this phenomenon occurs, Radiologic characteristics can be helpful in determining which ASDH is mostly likely to spontaneously resolve. As clearly illustrated in this case series that utilizing a neurological score which is based upon patient clinical profile at the time of arrival to hospital and radiological assessment of consecutive CT scan of head i.e. Clinicoradiological Prognostic Score in making that determination is critical in avoiding an unnecessary craniotomy. Wen et al.[6,7] reviewed the literature and identified 19 cases of spontaneous rapid resolution of ASDH. Based on their review, most patients who developed rapid resolution shared 5 characteristics: (1) transitory coma lasting no longer than 12 h, (2) exclusion of cerebral contusion, (3) band of low density between the skull and the hematoma on (CT) imaging, (4) thin width which is widely distributed, and (5) Glasgow Coma Scale >8 on admission. Two possible mechanisms have been proposed, First, the hematoma may be diluted by flow of cerebrospinal fluid (CSF) through the arachnoid tear, followed by retrograde flow into the subarachnoid space. This is supported by the presence of a low-density band between the ASDH and the inner table of the skull on CT scan. Transient neurological deterioration with subsequent dramatic improvement may be related to CSF influx and efflux within the subdural space. The prominent subarachnoid space with cerebral atrophy may facilitate dilution of ASDH. Second, the compression and redistribution of the hematoma can be induced by cerebral swelling and increased ICP. According Matsuyama et al Spontaneous resolution of the ASDH depends on both dilution due to CSF participation and redistribution of the blood[8].

Conclusion

It is well noted that a large ASDH and a deteriorated neurological examination should lead to emergent craniotomy. Spontaneous resolution of ASDH is a rare phenomenon with only a few reported cases in the literature. By using a Clinicoradiological Prognostic Score one can make a decision of conservative management to avoid an unnecessary craniotomy on patients having high scores. Simple anti edematous drugs, close monitoring of the neurological examination and observation with repeat imaging can result in avoidance of emergency craniotomy in young patients with good neurological status.

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Induced epidural haematoma

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ABSTRACT

Background: A novel case of epidural haematoma caused by general surgery

Case presentation: Fifty-four years male patient was admitted at Mansoura Emergency Hospital with Glasgow coma scale 4 on ventilator. rapid evacuation of EDH was done and the GCS became 9

Conclusion: rapid accumulation of epidural haematoma is fatal and may lead to death.

Keywords
epidural haematoma,
induced,
iatrogenic,
hepatocellular carcinoma,
disturbed conscious level

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BACKGROUND

An epidural hematoma (EDH) is an extra-axial collection of blood within the potential space between the outer layer of the dura mater and the inner table of the skull. It is confined by the lateral sutures (especially the coronal sutures) where the dura inserts. It is a life-threatening condition, which may require immediate intervention and can be associated with significant morbidity and mortality if left untreated. Rapid diagnosis and evacuation are important for a good outcome. It occurs in approximately 10% of traumatic brain injuries (TBI) requiring hospitalization. Both by traumatic and non-traumatic mechanisms can cause an epidural hematoma. The majority of cases related to a traumatic mechanism are a result of head injury due to motor vehicle collisions, physical assaults, or accidental falls (1). Non-traumatic mechanisms include the following:

- Infection/Abscess
- Coagulopathy
- Haemorrhagic Tumours
- Vascular Malformation

Most epidural hematomas result from arterial bleeding from a branch of the middle meningeal artery. The anterior meningeal artery or dural arteriovenous (AV) fistula at the vertex may be involved. Up to 10% of EDHs are due to venous bleeding following the laceration of a dural venous sinus. (1)

A novel and rare case in our practice had been developed showing induced epidural haematoma from left temporal soft mass, eroding

bone metastasis in skull, extending to subgalea and compressing the dura. The aim of this case can be used as a guidance for every practitioner to be cautious when dealing with any head swelling.

Case presentation

Fifty-four years male patient admitted at Mansoura Emergency Hospital with GCS 4 on ventilator. Urgent CT brain was done and showed large epidural hematoma with extra bony lesion (figure.1). Before that incident with three hours, the patient was fully conscious and he visited outpatient clinic where a general surgeon tried to aspirate left temporal soft lesion, causing skin swelling, doughted that it was subgaleal haematoma.

Operation

A left pteriyonal approach was done then a craniotomy with four burr holes. The soft lesion was excised completely with evacuation of EDH (figure.2) and the bone was repositionned with closure of skin. the lesion was sent to histopathological analysis and showed hepatocellular carcinoma. The patient remained in ICU with GCS 9 postoperative one week then died.

Conclusion

Epidural hematoma is a relatively common presentation to the emergency department, and if not diagnosed is associated with a high mortality. The condition is best managed by a multidisciplinary team that includes the emergency room physician, the trauma team, radiologist, neurologist, neurosurgeon, intensivist and the ICU nurses. The condition has been associated with mortality rates in excess of 15%. Every practitioner not related to neurosurgery should be careful when dealing with any case with head swelling and refer the case to a specialist avoiding iatrogenic death of patient.

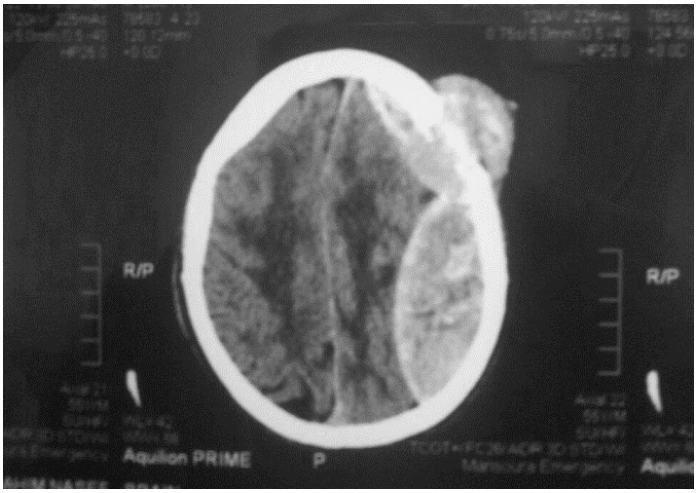

Figure 1: Pre-operative CT brain explaining large EDH with bony erosion and extra dural lesion

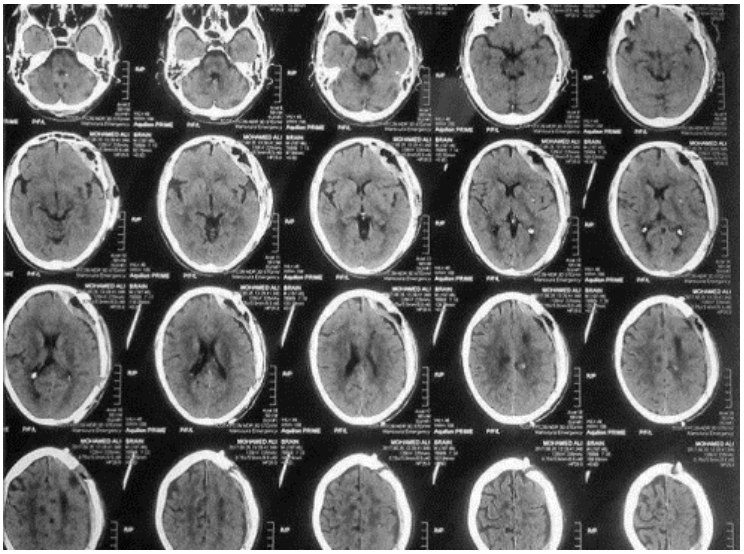

Figure 2: Post-operative CT brain explaining large EDH with bony erosion and extra dural lesion totally removed

List of abbreviation

GCS : Glasgow coma scale
ICU : intensive care unit
EDH : epidural haematoma
TBI : traumatic brain injuries
CT : computerized tomography
AV : arterio venous

Declarations

Acknowledgement
No other person contributed to this article
Funding
Nothing to disclose
Authors' contribution
The corresponding author and co-authors performed all of the procedures, clinical assessment, follow-up of patients, collection of results and are responsible for the study conception and design.
Consent for publication
This study reported no personal data for any patients; informed consents were obtained for all patients included in this study for the publishing of results.
None of the patient involved in this study had declined the publication of study results.
Competing interests
no conflict of interests.
Availability of data materials Raw data are available

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Quality and reliability of the information on YouTube Videos about Botox injection on spasticity

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ABSTRACT

Background: This study analyzes the botox injection on spastisite videos that have the highest views and likes on YouTube, and attempts to reveal the video qualities in order to contribute to the literature.

Methods: For review, "botox injection on spastisite" was written to the standard YouTube search bar, and the videos with the highest views were ranked using advanced search preferences. The 69 most widely viewed videos were watched and scored by one physician.

Results: The mean Modified DISCERN Score of the videos was 2,66+/-1,032 (the lowest: 1; the highest: 4) while the mean GQS score was 2,876+/-1,06 (the lowest: 1; the highest:4). In addition, the mean DISCERN score and the mean GQS value were 3,51 and 3,82, respectively, for the informational videos that were uploaded by health professionals but did not contain actual surgery.

Conclusion: We think that medical associations and state authorities in medicine should check the validity and accuracy of the information on the internet and should support the society in access to the most correct information.

Keywords
spasticity,
Botox,
YouTube

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INTRODUCTION

In recent years, the rate of receiving information from the internet has increased in almost every subject in daily practice due to the developing and increasing frequency of internet usage. Patients and health professionals apply to the Internet for information on many health-related issues. Among these sources of application, YouTube is the biggest video archive website in the world and attracts 95% of internet users with 30 million active users every day(1). There are also many health-related videos in the archive. Generally, patients apply to a physician and get detailed information about recommended treatments but they are also inclined to watch on YouTube the operation to be carried out. Therefore; the quality of a video, the persons who shot it and whether such video contains correct information are matters of great importance.

Spasticity is characterized by an increase in muscletone resulting from upper motor neuron lesions. It is a common condition in the upper

and lower extremity muscles after stroke in general cerebrovascular events (2). It is observed in 16% of patients after stroke (3). The increase in muscletone is a condition that makes mobilization and positioning difficult, delaying recovery to function that makes patients' daily life difficult. Spasticity is tried to be treated by various methods. Botulinium toxin is the most common invasive treatment method.

This study analyzes the botox injection on spastisite videos that have the highest views and likes on YouTube, and attempts to reveal the video qualities in order to contribute to the literature.

MATERIAL AND METHOD

Search Strategy and Data Collection

For review, "botox injection spastisite" was written to the standard YouTube search bar, and the videos with the highest views were ranked using advanced search preferences. The 69 most widely viewed videos were watched and scored by 1 physician.

Inclusion and Exclusion Criteria

The videos that were not in English language or did not have subtitles or speech or that did not explain the operation were eliminated.

Variables Extracted

Views, upload dates, like rates, uploaders, video lengths, comment numbers, like numbers and dislike numbers were identified as well as whether they were actual or animated videos.

Inaddition, video powerindex (VPI) values [(number of likes/number of likes þ number of dislikes) 100] were calculated to evaluate thepopularity of the videos.

Assessment of Usefulness

All videos were independentlye valuated by one physician for usefulness and categorized into the following mutuall exclusive categories.

1. Useful information : Videos designated as useful information were mainly focused on information delivery. They contained accurate information and were useful for learning how to do botox.

2. Misleading information :The videos contained incorrect information or did not contain usefull information.

3. Useful patient opinion: The videos in this group have the DISCERN and GQS scores as 3 or above and clearly explain the patient experiences, the performance of operations, and preoperational and postoperational pain scores.

4. Misleading patient opinion: The videos in this group have the DISCERN and GQS scores as 2 or lower and do not clearly explain patient experiences (Table 1).

Scoring System

Video reliability was scored using a modified five-point DISCERN tool (4), which was adapted from the original DISCERN toolforthe assessment of written healthin formation by Charnock et al. (5).

The overall quality of each video was rate dusing the five-point Global QualityScale (GQS). The GQS was developed as an evaluation tool for websiteresourcesand it assesses the flowandease of use of the information presented online, and the quality of video (Table 2) [4].

Table 1: Analyses of video characteristics by usefulness category

	Usefull information (Gr1)	Misleading information (Gr2)	Usefull Patient Opinion (Gr3)	Misleading Patient Opinion (Gr4)
Video Number	n:11(15,9%)	n:33(47,8%)	n:1(2%)	n:24(34,7%)
Viewspeerday	2,21 +/-0,31	1,257+/-0,12	4,32 +/-1,55	3,4+/-1,3
Video Lenght	24,562min (2,04-32,01 min)	6,50 min (0,20-7,17 min)	12,31 min	7,25 min (4,01-12,08 min)
Like	22+/-14	18,14+/-12,1	29,08+/-2,01	33,4+/-3,33
Dislike	1,32+/-0,45	2,74+/-1,1	1,02+/-0,32	1,47+/-1,21
Comments	26,8+/-2,33	27,2+/-1,33	92,1+/-7,41	113,4+/-11,2
DiscernScore	3,4	2,2	3,3	0,5
GQS Score	3,9	2,3	3,8	1,6

Statistical analysis

The results were statistically analysed using a nonparametric Kruskal–Wallis test. A p value of 0.05 or less was considered significant. The Statistical Package for theSocial Sciences version 23 software (SPSS, Chicago, IL, USA) was used for all statistical analyses (Table 2).

	Gr1-Gr2	Gr1-3	Gr1-4	Gr2-3	Gr2-4	Gr3-4
DiscernScore p value	0,518	0,708	0,001	0,652	0,332	**0,0018**
GQS Score p value	0,125	1,00	**0,001**	0,069	0,852	**0,001**

* Values of p 0,05 was accepted

Table 2: Pairwise comparisons of video groups according to usefulness

RESULTS

69 videos with the highest views were analyzed while 31 videos were later excluded from the analysis for they were neither in English language nor contained subtitles. There were 36 technically-narrated and actual videos by professionals, 25 patient view and 8 videos were botox processing. The oldest video was uploaded in 2010 while the newest one was added to the system in 2019. The videos were uploaded by hospitals (25 videos), health professionals and physicians (20 videos), and personal accounts (21 videos) (Figure 1).

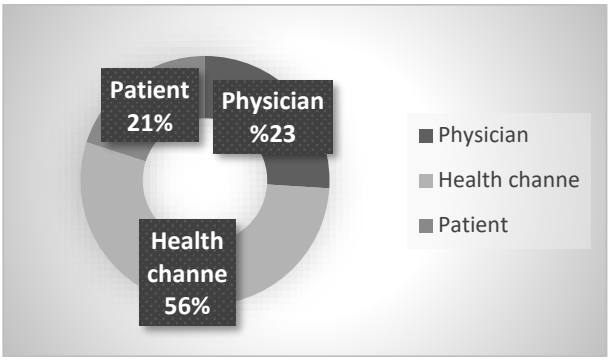

Figure 1: Uploaded videos by YouTube

The mean time of the video lengths was 41,623 sec (the shortest: 19 sec; the longest: 54.16 sec) , and the mean view was 88,293+/-9,75 (the least viewed: 4075; the most viewed: 825.731). The daily mean view of the videos was 42.444+/-72,77 (the least viewed: 5; the most viewed: 37405). The mean like rate was 23.27+/-,52 (the most liked:360 the least liked: 0), and the mean dislike rate was 1,34+/-0,21 (the most disliked: 15; the least disliked: 0).As for the comments, the mean number was 4,54+/-1,23 (the least commented: 0; the most commented: 65).Similarly, video power index (VPI) analyses showed that the mean VPI value of the 69 videos was 0,71+/-0,14 .

The mean Modified DISCERN Score of the videos was 2,88+/-0,318 (the lowest: 1; the highest: 4) while the mean GQS score was 3,56+/-1,206 (the lowest: 1; the highest:4) . In addition, the mean DISCERN score and the mean GQS value were 2,13 and 3,25, respectively, for the informational videos that were uploaded by health professionals. Similarly, the mean DISCERN score and the mean GQS value were 1,33 and 1,71, respectively, for the patient videos in which personal experiences were shared. No statistically significant correlation was found between the GQS and DISCERN scores according to both researchers and VPI values (P > 0.05).

DISCUSSION

Youtube is a video hosting site headquartered in San Bruno / California, USA. The site was founded in 2005 and started to be operated by Google in 2006. The primary purpose of the site is to download and share videos on any subject. Many health professionals, hospitals and patients share more intensive videos on medical issues. While using these videos to make inferences from the experience of the patients, the method and possible risks of the treatment to be performed by patients and their relatives; health professionals try to learn the interventional procedure live. However, there may also be incorrect, low-quality and prejudiced videos on this platform where everyone can upload videos free-of-charge without being subject to any inspection. Pubmed reviews reveal 1089 studies that measure the quality of YouTube videos on health issues (8,9).

The first of these is a study from 2007 that evaluate the training of health professionals (7).

Botulinium toxin-related treatment applications started in 1980. It has been used in the treatment of spasticity for the last 15 years. Botulinum A is a successful method used to increase theeffectiveness of pain, restlessness and physical therapy in spasticity(10,11). Botulinium A toxin is the most common market name in the world as Botox © and Dysport ©. Botox application is performed in spasticity in our country. When theliterature is screened, there are 3 controlled randomized studies on Botox(12,13,14).

In our study, it was to question whether a patient with spasticity who is planned to use botox is able to get reliable information when watching the youtube video in order to obtain information and ideas before the procedure. Apart from this, it is aimed to evaluate the quality of the information that the health professionals who want to make the initiative can learn theoretically and visually from the videos. The literature review we made did not produce any study concerning the subject in question. There are various scales and measures to evaluate the quality of the information in videos and on the internet. In this study, one researcher assesses the videos using modified DISCERN scoring system, Global Quality Index and Video Power Index (VPI). According to the analysis of the 69 videos with the highest views and VPIs, it was found out that the videos presented weak and poor-quality information to patients, patient relatives and professionals who desire to learn the narrated operation. However, it was also observed that 60.9% of the videos were uploaded by health professionals and institutions. In 8 (11.5%) videos with actual surgeries, it was seen that the average time was 15,24 seconds, the operators did not satisfactorily explain the methods before and after the operations, they did not clearly specify alternative treatments and effects and possible complications, and the videos were not supported with subtitles. It was observed that the videos did not explain the operations in simple language to convey the processes to patients and patient relatives but only the course was expressed, and that there were dialogs with patients during operations.

Furthermore, it was revealed that 11 (15.9%) videos with the highest results of evaluation were animated or notional surgery videos, made theoretical PowerPoint presentations and were supported with anatomic cross-sections.

When the 5 most watched videos were examined, it was seen that there were 3.73 impressions per day on average and these videos belonged to hospitals installing botox application.

The videos with the highest VPI values but had 2 or below in DISCERN and GQS scoring were found to convey inadequate information. In contrast with the foregoing, the videos with the highest scores had 2,21 views every day, on average, and did not appear on the first page when searched on YouTube. However, the videos that had the highest views but contained insufficient information appeared on top in YouTube searches. Apart from these, the video comment analyses demonstrated that the highest number of comments were entered to the uploads with patient experiences. In the content of the comments, it was seen that the regression rate of complaints and the duration of the complaint-free period were examined.

Accordingly, the videos with the highest like numbers were those that contained patient remarks.

The videos were divided into 4 groups in terms of usefulness, and only 11 videos were found to contain useful and valid information. All these were uploaded by health professionals and were generally about physician remarks. The mean time of these videos was 24,562 seconds. Useful patient remarks were identified only in 1 video, and their mean view time was 12,31 seconds.

The limitations of this study include the cross-sectional design (popularity based on number of views changes constantly), and the inclusion of only the 69 most widely viewed videos (an arbitrary cut point).

Conclusion

As a result, it may not always be accurate to believe that the medical videos with high view, comment and like numbers on YouTube contain reliable, comprehensible and correct information. Although the access to information and videos on medical subjects is very easy in today's world, it is more appropriate to apply to experienced health professionals in order to get information. We think that medical associations and state authorities in medicine should check the validity and accuracy of the information on the internet and should support the society in access to the most correct information.

Compliance with ethical standards

This study does not include any human participants or animals. Videos that were available to every one were evaluated for this study. Therefore, ethics committee approval was not required.

Table 3: Discern and GQS

Modifiy Discern (1 point per question answered yes)

1. Is the video clear, concise, and understandable?
2. Are valid sources cited? (from valid studies, physiatrists or rheumatologists)
3. Is the information provided balanced and unbiased?
4. Are additional sources of information listed for patient reference?
5. Does the video address areas of controversy /uncertainty?

Global quality scale

1. Poor quality, poor flow, most information missing, not helpful for patients;
2. Generally poor, some information given but of limited use to patients;
3. Moderate quality, some important information is adequately discussed;
4. Good quality good flow, most relevant information is covered, useful for patients;
5. Excellent quality and excellent flow, very useful for patients;

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Skull metastasis of hepatocellular carcinoma in normal liver. Case report

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Abstract

Background: So far hepatocellular carcinoma (HCC) is the most common liver malignant tumour; it is rarely encountered on a healthy liver (9). The metastasis from HCC cancer are seen in lymph nodes (16%–40%) and lungs (34%–70%), (1,3,4,5,7,8), bone metastasis is unusual and some locations stay rare among them the skull (2,4,5). We report here a case of a patient operated in our department for skull metastasis. That patient was followed for hepatocellular carcinoma in digestive surgery department.

Case presentation: The patient is a 57 years old male presenting HCC on healthy liver, the patient was referred to our department by digestive surgery colleagues to manage a parietal subcutaneous mass; brain CT scans were performed objectified a calvarial osteolytic process. We remove the tumour and we put a cranioplasty using surgical cement, later the histological studies were in favour of secondary location of hepatocellular carcinoma.

Conclusion: Skull metastasis from hepatocellular carcinoma is rare, reporting such cases strengthen the idea of evoking HCC metastasis in the differential diagnosis of cranial subcutaneous mass.

Keywords
hepatocellular carcinoma,
metastasis,
skull tumour

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Introduction

The development of hepatocellular carcinoma on a healthy liver is unusual and skull metastasis from this type of cancer is rare; this make evoking the diagnostic of a metastatic hepatocellular carcinoma for a skull lesion difficult, we report a case of skull metastatic lesion from a hepatocellular carcinoma on patient with a healthy liver.

Case presentation

The patient is a male of 57 years old who presented weeks before he consulted an epigastric pain, then one month later a cranial left parietal subcutaneous mass. First an abdominal CT was performed objectified a tissue mass of 57 mm on the segment II of the liver extended to the gastro-hepatic omentum reaching the lesser curvature of the stomach,

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the surrounding hepatic tissue appeared to be normal; and all laboratory tests was initially normal. The patient was scheduled to a surgical resection meanwhile he was referred to our department to manage the cranial mass. The clinical exam at the admission found a conscious patient without neurological deficit presenting a left parietal mass with a diameter of 5 cm, soft, painless, fixed, pulsing, and without cutaneous defect. The brain CT objectified a tumor interesting the left parietal bone without cerebral invasion intensely enhanced after injection of the contrast product, on bony window the lesion is an irregular erosion measuring 48 x 53 mm, (Figure 1). On the brain MRI the tumor was hypointense on T1 weighted images intensely enhanced by Gadolinium, the T2 weighted images have a heterogeneous signal, the angio-MRI images objectify a multiple thin vessels inside the tumor, there was a shift effect on the dura but there was no invasion to either dura or cutaneous tissues (Figure 2). Bone scan with TC99m objectified a calvarial left parietal lake of fixation without any other skeleton locations. We operated the patient and we remove the lesion with the surrounding normal bone, it was a soft brown cauliflower-like mass highly vascularized, easily dissected from the cutaneous tissue pushing the dura witch was eroded at some spots, so we performed a dura plasty using a galea and a bone plasty using surgical cement to repair the bone defect. The histological study of the specimen found a predominance of pseudo glandular trabecular tissue and in the immunohistochemical examination there was a high expression of the hepatocyte antigen, so the diagnosis was in fact a secondary location of a fibro lamellar HCC. There was a full postoperative recovery. The patient was discharged from our department 7 days after the operation without any neurological deficits. We referred him back to general surgery where the liver tumor was resected with 2 cm of security marge and a portion of the stomach lesser curvature; the postoperative recovery was optimal. The patient is still followed in our external consultation since 24 months and there is no tumor recurrence on brain CT scans.

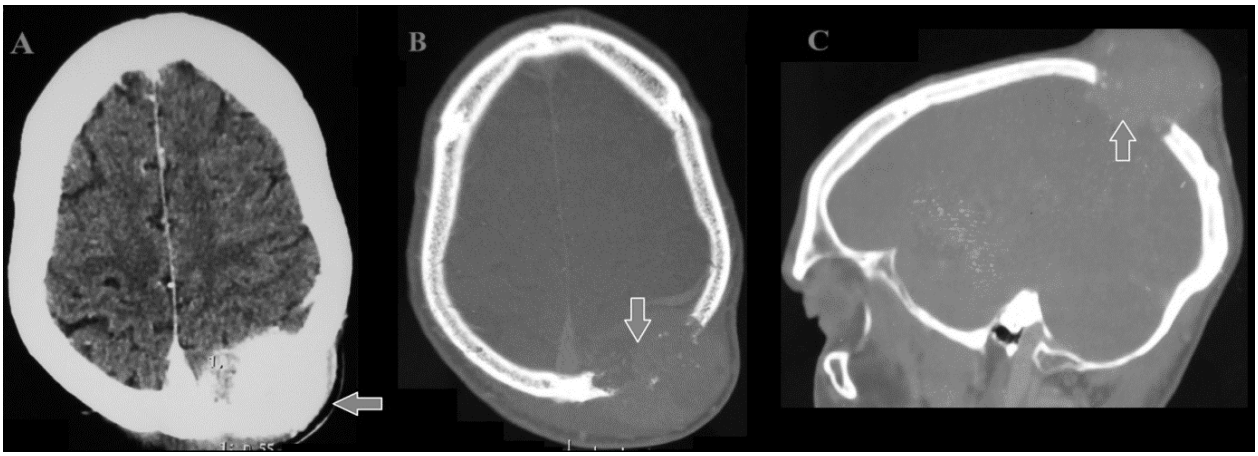

Figure 1: Preoperative brain CT scan. A: injected axial slide; B: bony window axial slide; C: sagittal bony window, showing an osteolytic left parietal lesion intensely enhanced after injection of the contrast product (red arrow).

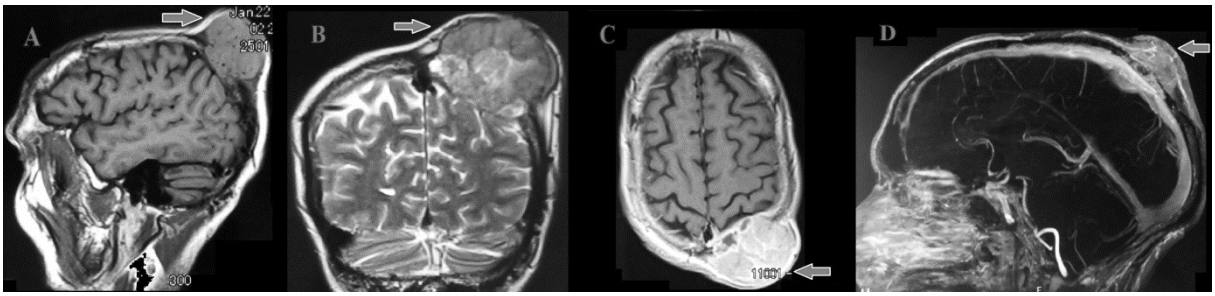

Figure 2: Preoperative brain MRI. A: T1 weighted imaging sagittal; B: T2 weighted imaging coronal; C: T1 enhanced; D: Angio MR, showing that the tumor is limited at skull plan without brain invasion and its hyper vasculazation nature

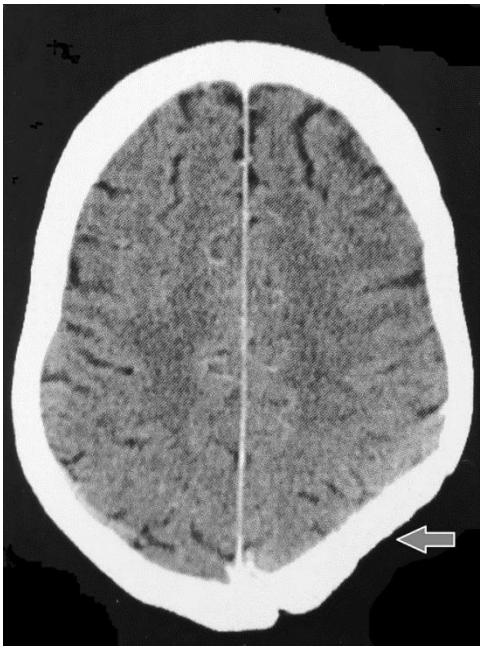

Figure 3: Preoperative brain CT. Bone plasty (red arrow), there is no tumor recurrence

Discussion

So far hepatocellular carcinoma is the most frequent malignant liver tumor; the incidence in a healthy non cirrhotic liver is rare, according to different series it is between 1.7% and 14% (9). Skull metastasis are most commonly seen from breast, lung, prostate, and thyroid cancers (2, 4), metastasis from hepatic cancer is rare (5,2,4) it was reported in 0.5 to 1.6% of patients with HCC in most studies (3,4,1), in a review performed in 2014, a total of 59 patients with solitary skull metastasis from HCC were published (1).Males are largely more exposed to this affection than females (1,4).Metastases occurring in the calvarial site were more frequent than those occurring in the skull base and facial skeleton (1).The most common clinical presentation is a subcutaneous mass with occasional painful sensation (57%), followed by neurological deficits(51%), headache (15%) and seizure (3%) (1). The subcutaneous mass is usually firm solitary painless or occasionally painful rapidly evolving neglected by the patient (1,6,4,3). The tumor size and location are related to the neurologic deficit which is rather present in the skull base tumors (visual disturbance, dysphagia, deafness and facial numbness), than in the volt tumors where the weakness of the limbs is more frequent (4,5,7). Although rare cases of tumor bleeding were reported, the per operative hemorrhage risk should be kept in mind and preventive measures should not be neglect (2,3,4,6). In plane X rays the lesion appears to be osteolytic in all reported patients (1,2,3,4,5,6,7,8). The brain CT shows the bone defect, and a significant homogenous enhancement in all cases (1,4,5). In MRI the lesion appears as iso or hypo intense in T1 and T2 weighted images. The treatment for skull metastasis, includes radiotherapy, chemotherapy, surgery and palliative care. A single calvarial metastasis can be treated surgically (4)**.** Although many reports suggest that the life expectancy is related to the liver failure and the presence of HCC skull metastasis don't change it significantly (7); all studies suggest that the surgical treatment for HCC metastasis may relief the patient, esthetic, reduce the risks of neurological sequelae, and thus improve the quality of life (1,2,3,4,5). Pre-operative embolisation is preferred (4).

Conclusion

Hepatocellular carcinoma (HCC) is responsible in rare reported cases of cranial metastasis, which clinical presentation is a subcutaneous mass and appears as an osteolytic lesion on radiological investigations. Although the vital prognostic is depending on the initial lesion, early diagnostic and surgical removal of the metastasis may improve the life quality.

Declarations of interest

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Surgical consideration in posterior C1-2 instrumentation in case of vertebral artery anomaly

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ABSTRACT

Anatomical variations in the course of the vertebral artery have been previously described in the literature. Generally, these predictable patterns of variations commonly observed in lower cervical vertebral artery anatomy and less commonly described for upper cervical vertebral artery anatomy. Due to presence of these variations, treatment options for upper cervical spine pathology may be influenced and sometimes prevent commonly performed stabilization procedures. Herein author presented a case of vertebral artery anatomic variation at the craniovertebral junction and management option for such variations.

Keywords
vertebral artery anomaly, cervico-vertebral junction, cervical stabilization

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INTRODUCTION

Steady advances have been made in fixation of an unstable atlantoaxial complex over the last century. There are many options for fixation of the atlantoaxial complex like posterior clamps or wiring techniques, C1-C2 transarticular screw fixation, posterior C1 lateral mass screw with C2 pars or pedicle screw fixation, and anterior transoral C1 lateral mass to C2 vertebral body fixation[1].

Advantage of the C1-2 screw technique is that it can completely obliterate rotational, flexion or extension motion of the atlantoaxial joint. However, the disadvantages of this technique are the steep learning curve and risk of serious complications like injury to spinal cord, hypoglossal nerve or vertebral artery laceration. To avoid these complications, pre-operative computerized tomography (CT) scanning of the cervical spine is necessary. This is mainly to identify an anomalous vertebral artery course, bony status of the intended site of screw fixation, or unacceptably small C2 pars[1].

To minimize the risk of vertebral artery injury, screw placement should be done only if the preoperative CT scan confirms the normal anatomic position of the vessel. If aberrant vessel present on unilateral side then screw placement should be done on normal side. If vertebral artery injury occurred during screw placement, then screw placement

should be done to tamponade the bleeding and contralateral screw placement should be avoided in order to prevent the risk of bilateral vertebral artery injury[1,2].

Herein we presented a case of type 2 vertebral artery anomaly which was managed by placing C1 lateral mass and C2 translaminar screw on normal side and sublaminar wiring on abnormal side.

CASE REPORT

16 years old male admitted in Neurosurgery department with chief complaints of heaviness in neck and weakness in all four limbs for 4 months. On examination, his power was 4/5 in all four limbs as per MRC (Medical Research Council) grading. Tone was increased in all four limbs and hyperreflexia was present. Bladder- bowel was normal. Magnetic resonance imaging (MRI) cervical spine showed compression over cervicomedullary junction with hyperintense signals in cord (Image 1). Dynamic CT of craniovertebral (CV) junction showed reducible atlantoaxial dislocation (AAD) with os odontoidum (Image 2). MRI angiogram neck showed anomalous origin of left posterior inferior cerebellar artery (PICA) at C1-C2 level and intradural entry from left side at C1-2 interlaminal space (Image 3). Thus, preventing safe placement of C1 and C2 screw from left side. To minimize the risk of vertebral artery injury, we placed C1 lateral mass screw (40x34mm) and C2 translaminar screw (35x28 mm) (C2C system) on right side and sublaminar wiring with iliac crest graft on left side (Image 4). Patient tolerated the procedure well and showed improvement.

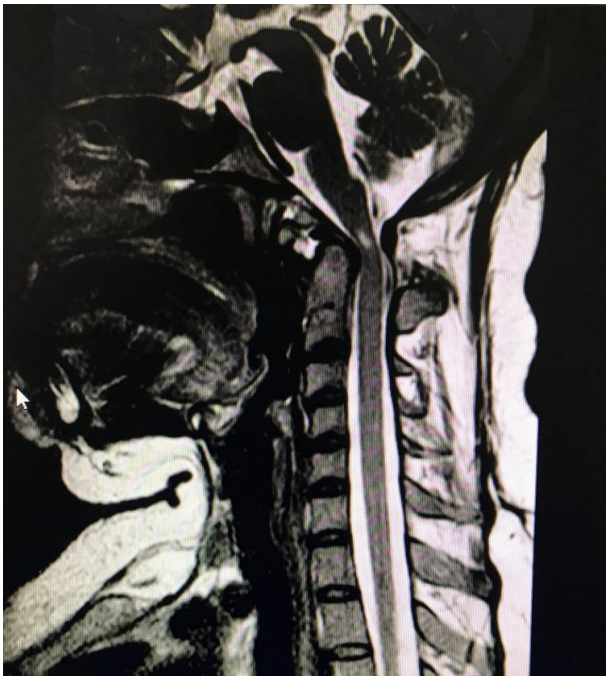
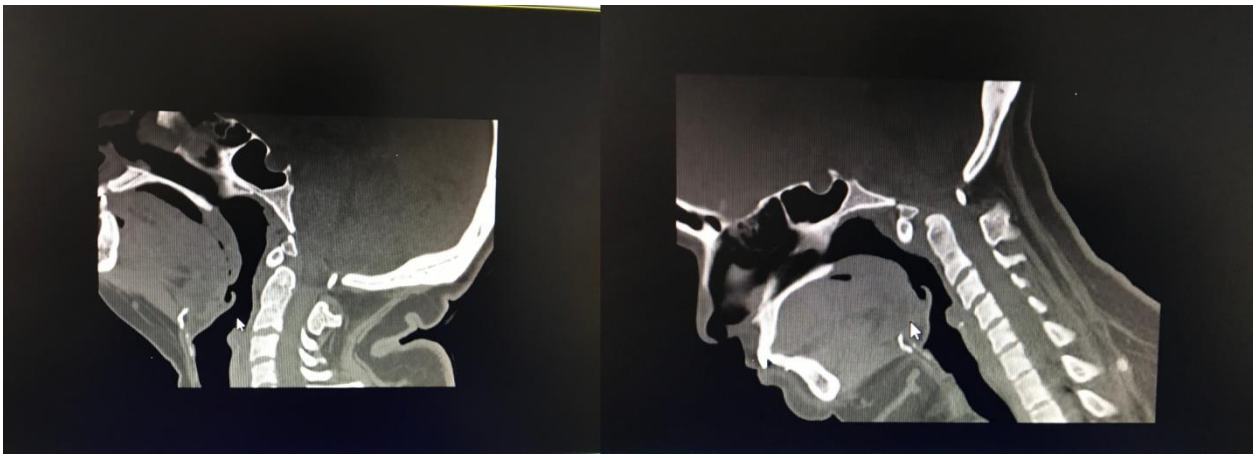


Image 1: Preoperative MRI cervical spine showed compression over cervicomedullary junction with hyperintense signals in cord.

Image 2: Dynamic CT of craniovertebral junction showed reducible atlantoaxial dislocation (AAD) with os odontoidum.



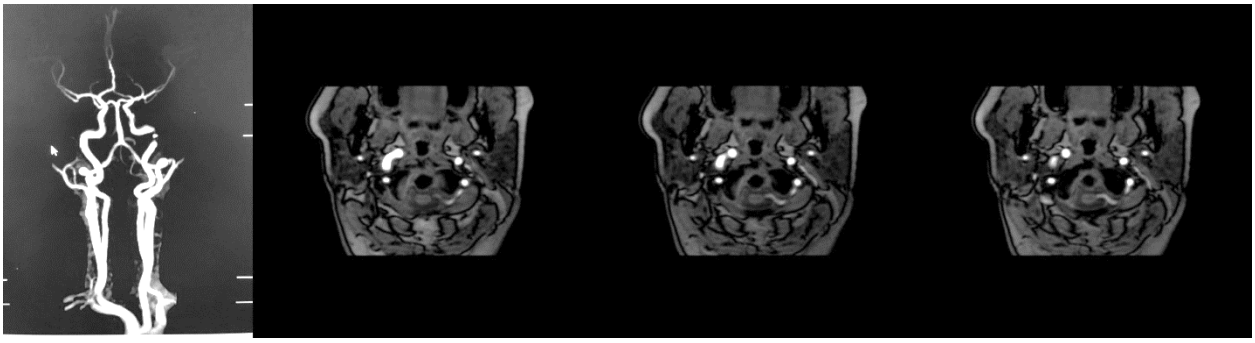


Image 3: MRI angiogram neck showed anomalous origin of left posterior inferior cerebellar artery (PICA) at C1-C2 level and intradural entry from left side at C1-2 interlaminal space.

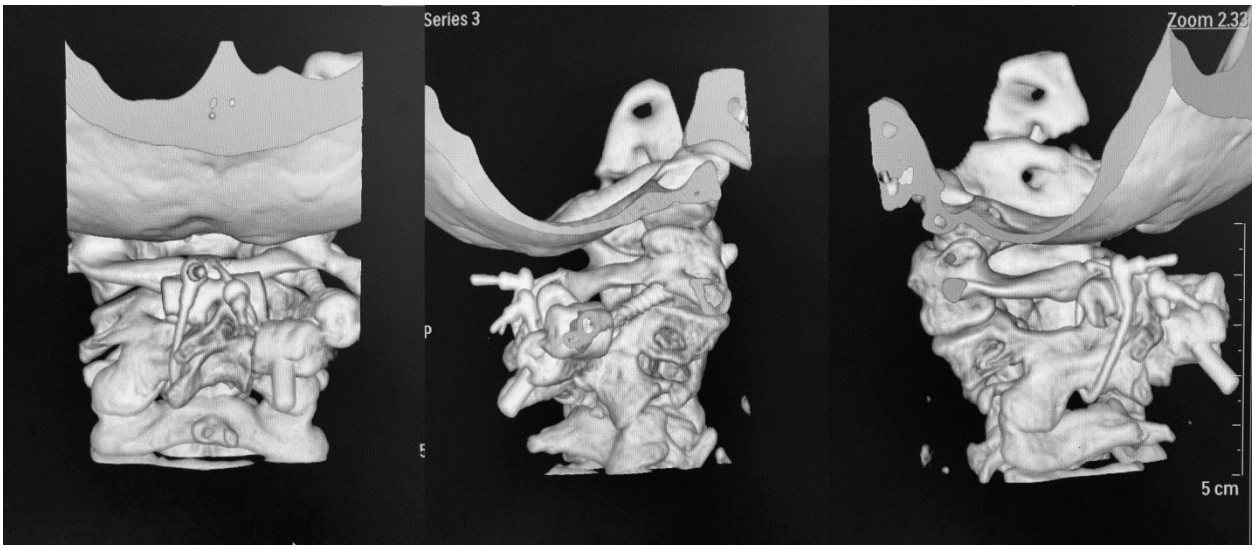


Image 4: C1 lateral mass & C2 translaminar screw on right side and sublaminar wiring with iliac crest graft on left side.

Discussion

The presence of vertebral artery variation at the craniovertebral junction may influence treatment options so it should be identified preoperatively. This helps the surgeons for planning of surgery and minimizes the risk to the vertebral artery injury[3].

Three types of vertebral artery variation at the craniovertebral junction have been described in the literature. The most common variant is a persistent first intersegmental artery (FIA), in this the aberrant vertebral artery have taken an anomalous course and enter the spinal canal between C1 and C2 and the normal vertebral artery branch is absent. It found in 3.2% of patients. The second most common variation is an extracranial C1/2 origin of the posterior inferior cerebellar artery (PICA). It present in 1.1% of patients. In this variant, the FIA continues to the PICA without reuniting with the vertebral artery. The third variant is fenestration of the vertebral artery and it is also the least common variant. It presents in 0.9% of patients. All 3 of those variants could have an effect on screw placement because the abnormal vertebral artery passes directly dorsal to the C1 lateral mass. Other less common variants have been described but are beyond the scope of this article [3,4,5].

There is no algorithm for surgical consideration in posterior C1-2 instrumentation in case of vertebral artery anomaly. Only few case reports are available in the literature. Hong JT et al used as C1 superior lateral mass as an entry point in case of type 1 vertebral artery anomaly [5]. Abtahi AM et al performed occiput-C3 fusion in case of type 1 vertebral artery anomaly [6]. Yamazaki M performed

occiput - C2 fusion in case of type 3 (fenestration of vertebra artery) vertebral artery anomaly [7]. Song et al in his case series conclude that unilateral C1-2 facet screw fixation with interspinous bone graft wiring is an excellent alternative in the treatment of atlantoaxial instability when bilateral screw fixation is contraindicated. But in his case series there was no vertebral artery anomaly presents [8]. In our case there was type 2 vertebral artery anomaly on left side so C1 lateral mass and C2 translaminar screw insertion was done from right side and sublaminar wiring with iliac crest graft from left side.

There are multiple reports of injury to the vertebral artery during anterior cervical decompression surgery exist in the literature. Five studies reported rates of 0.10 to 1.96%, depending on the type of anterior cervical spine procedure. There is paucity of literature with respect to vertebral artery injury associated with a posterior cervical surgical exposure. Molinari et al recently reported vertebral artery injury in two cases involving a persistent first intersegmental artery in the region of C1–C2. Both injuries were occurred with routine posterior exposure of the C1–C2 anatomy [8,9,10].

Conclusion

This particular vertebral artery anomaly produces great risk to the conventional placement of C1 lateral mass screws through previously described techniques. These anomalies can be identified preoperatively by computed tomography angiography.

To minimize the risk of complications, thorough assessment of the vascular anatomy is recommended before operative intervention in the upper cervical spine pathology.

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Management of spinal dural arterio venous fistula with peri-medullar drainage. Experience of a north-African centre

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ABSTRACT

Introduction: Spinal Dural Arterio Venous Fistula (SDAVF) is an arteriovenous communication on the spinal dura with peri-medullar venous drainage. It is a curable cause of myelopathy and the most common form of spinal arterio venous malformation (AVM). The average age of revelation is the fifth decade; it is a diagnostic and therapeutic emergency.

Materials and methods: This is a retrospective study conducted in the neuro surgical department of CHU Bab El Oued in Algiers during a five years time from November 2013 to September 2018. We assessed the clinical status of patients according to the Aminoff-Logue disability score before and after surgery. All patients did a total spine MRI followed by a Medullar angiography which facilitated the pin-pointing of the exact location of the dural fistula. The mean follow-up is 30 months.

Results: There were five males and two females, all of them older than 45 years of age. At the admission, patients presented with signs of neurological deficits. After the diagnosis of SDAVF the surgical intervention consisted of a disconnection of the arteriovenous communication by coagulation and section of the fistula at the foot of the vein after a laminectomy. Functional rehabilitation was prescribed for all patients and they were regularly followed-up.

Conclusion: Treatment of AVF is surgical or endovascular. Results depend largely on preoperative neurological status.

Keywords
arteriovenous fistula, arteriovenous malformation, myelopathy

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INTRODUCTION

The spinal dural Arterio Venous Fistula (SDAVF) with peri-medullar venous drainage is an abnormal communication within an afferent artery and an adjacent vein without interposition of capillary bed. This communication occurs at the spinal dura and is followed by a peri medullar venous drainage. Individualize by Kendall and Merland in the 1980s, it is a rare pathology even if it represente the most frequent spinal arteriovenous malformation accounting about 60–80% of all spinal vascular malformations [1,2,3,4].

Arterial blood flow is shunted directly into the venous plexus, under arterial pressure. The venous plexus subsequently becomes "arterialized," and obstruction of venous outflow leads to venous congestion, venous hypertension, and progressive ascending myelopathy [5]

The average age of revelation is the fifth decade. Clinical signs are not specific, that is the reason of the diagnosis delay causing sometimes severe disability; for that reason, SDAVF constitute a diagnostic and therapeutique emergency. Treatment of AVF is usually surgical or endovascular. The objective of our study is to assesses the surgical treatment of SDAVF and the clinical outcome of patients operated for SDAVF in the neurosurgical department in CHU BEO Algiers.

Materials and methods

This is a retrospective study conducted in the neuro surgical department of CHU Bab El Oued in Algiers during a five years time from November 2013 to September 2018. We analyze clinical data of patients operated for SDAVF.

We assessed the clinical status of patients according to the Aminoff-Logue disability score before and after surgery (Table 1).

Function & Score	Definition
gait	
0	normal
1	leg weakness, abnormal gait or stance but no restriction of activity
2	restricted activity but not requiring support
3	requiring 1 stick for walking
4	requiring 2 sticks, crutches, or walker
5	confined to wheelchair
urination	
0	normal
1	hesitancy, urgency, frequency, altered sensation, but continent
2	occasional urinary incontinence or retention
3	total incontinence or persistent retention
defecation	
0	normal
1	moderate constipation
2	severe constipation or occasional incontinence
3	total incontinence

Table 1: Aminoff-Logue disability score

This score has 4 grades: grade 1: 0-2; grade 2: 3-5; grade 3: 6-8; grade 4: 9-11

We performed a total spinal MRI which suspect the SDAVF and spinal digital subtraction angiography (DSA) that facilitated the pin-pointing of the exact location of the dural fistula.

All patients underwent microsurgical approach; the day before surgery we perform a plan x ray on a metallic landmark to guide the skin incision. The microsurgical approach consisted of a disconnection of the arteriovenous communication by coagulation and section of the fistula at the foot of the vein after a laminectomy.

Patients presenting disabilities were send for functional rehabilitation.

Results

During the time of our study we registered 7 patients suffering of SDAVF, there is predominance of male with a sex ratio of 5/2; The mean age of our patients is 56 years with extreme from 49 to 68 years. The time before consultation is fifty one month's with extreme from 6 to 60 months.

All patients suffered for motor disturbance (100%), a leg weakness is found in 5 patients representing 71, 42%, one patient require a stick for walking and another one require walker to move. Urination disturbance is present in all patients (100%) as occasional incontinence is found in 3patients (42, 85%), frequency urination is found in 2 patients (28, 57%) and occasional retention in 2 patients (28, 57%). Six patients presented defecation disorders representing 85, 75 % of patients, like moderate constipation for 4 patients (57, 14%), severe constipation for one patient, another one presented occasional incontinence. Three (3) patients present Sensibility disorder which represent 42, 85% of patients. The pre-operative disability scale of Aminoff-logue is III for 2 patients (28, 57%) and II for 4 patients (57, 14%), and I for one patient.

All patients did a total spine MRI, this investigation objectified serpiginous images and flow void sign of peri medullar vessels dilation; also, an intra medullar hyper intensity (figure 1).

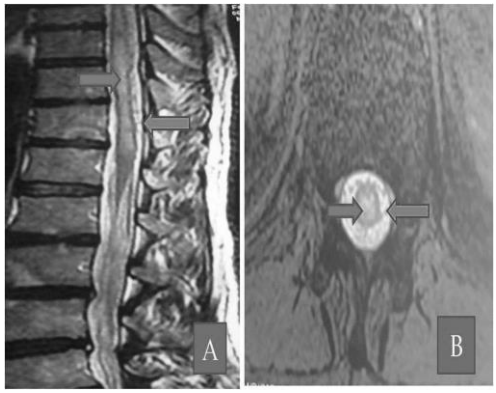

Figure 1: A: MRI sagittale T2 weithed showing flow void sign (yellow arrow) and intramedullar hyper intensity (red arrow).

To locate the communication, we performed medullar angiography for all patients; angiography has facilitated the pin-pointing of the exact location of the dural fistula. The investigation permits us to see the afferent pedicles, the peri medullar drainage vein which is dilated and serpiginous, also the dural fistula (figure 2). All our patients presented thoracic single fistula.

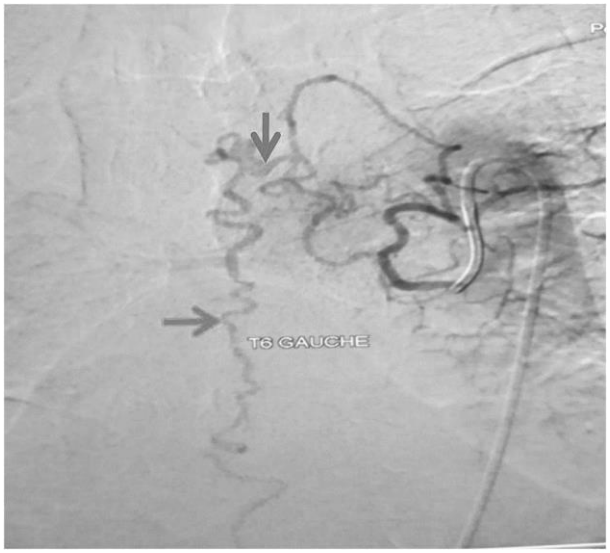

Figure 2: DSA: after catheterisation of Left T6 showing a fistula (red arrow) and an arterialized vein (yellow arrow)**.**

Figure 3: Per operative image, after durotomy showing the fistula (yellow arrow) and the tortuous varterialized veins (red arrow)**.**

For all our patients we performed microsurgical approach; under general anesthesia, on prone position, a median skin incision is made at the level of the fistula; we perform a laminectomy one level above and one below the fistula to expose the work field before a median durotomy and suspension of the dural edges. Under microscope the arterialized veins are found tortuous and colored in red and the fistula is found communicating aradicular artery (figure 3). We performed the coagulation of the fistula and section of it at the foot of the vein. At the end of the procedure we spent about 30 minutes after the section of the fistula to make sure that the arterialized vein become progressively blue, which is the vein normal color. The dural closure is assured with continuous running suture.

Patients presenting disabilities were send for functional rehabilitation. The post-operative outcome 7 days and 6 months after surgery is summarized in the following table.

	Initial Aminoff-Logue Grade	Day 7 after surgery	6 Months later
Patient 1	III	IV	III
Patient 2	III	IV	II
Patient 3	II	III	I
Patient 4	II	II	II
Patient 5	II	II	I
Patient 6	I	I	I
Patient 7	II	II	I

Table 2: Post-operative outcome of patients at Day 7 and 6 months later.

The mean follow-up is 30 months; patients are seen in the clinic weekly for the first month and every month for three months and every trimester until one year.

Discussion

In our study there is predominance of male with the Average age of revelation the fifth decade as reported by many authors [6, 7]. The time before consultation is long about 51 months in our series; it is comparable to the time reported in the literature [8, 9,]. This is due to the difficulty to diagnose the SDAVF because of lack specific signs. The diagnosis delay reduces the chance of recuperation even after the treatment.

The most frequent signs in our series is motor and sphincter disturbance representing 100% of patients followed by sensibility disturbance which represent 42, 85% of patients. Many authors

reported the predominance of motor disturbance follow by sensory disturbance and sphincter disturbance [2, 10, 26].

We performed MRI for all our patients, in case of SDAVF suspicion a DSA is performed to confirm and locate the level and number of fistula, the feeders as well. Yamaguchi [11] reported that Spinal CT angiography could be used to demonstrate the fistula localization. In practice it is not safe because of the radiation quantity, before getting the exact location of the fistula. MRI images signs On T1-weighted scans, the swollen cord is slightly hypointense and enlarged. Following contrast administration, diffuse enhancement may be seen within the cord as a sign of chronic venous congestion with a breakdown of the blood spinal cord barrier [13, 14]. On T2-weighted sequences, the cord edema is depicted as a centromedullary not well-delineated hyperintensity over multiple segments that is often accompanied by a hypointense rim, most likely representing deoxygenated blood within the dilated capillary vessels surrounding the congestive edema spin echo [3D-TSE]) compared with standard T2 TSE sequences [12].

The help of MR angiography in the positive diagnostic was emphasized by some authors. For Efrat Saraf-Lavi [15] the principal advantage of MR angiography is the improved detection of the fistula level, with the correct level ± one level identified in 73% of true positive cases. They supported that Overall, the combination of MR imaging and MR angiography provides improved screening for dural AVF and benefits the subsequent radiographic DSA study by helping target the level of the fistula.

We performed for all our patients a total spine MRI, this investigation objectified suspicion signs of SDAVF but to confirm the diagnostic the DSA was used, this investigation allow us to locate the fistula, the number of afferent arteries. Many authors recognize the Digital angiography as a helpful tool that can give a map of the vascularisation and help to plan the endovascular treatment. It is the gold standard for the diagnostic of SDAVF [16, 17, 18, 19].

All our patients presented thoracic single fistula, many authors reported that the thoracic level is the most frequently affected [2,26,34] and most of patients present a single fistula, the multiple are rarely reported [2,9].

All patients underwent microsurgical approach; the surgical technique consisted of a disconnection of the arteriovenous communication by coagulation and section of the fistula at the foot of the vein after a laminectomy. Permanent vascular clips could be used [22].Authors reported the use of microsurgery or endovascular to be effective [7, 20, 21].Many authors reported a rate of recanalization after embolization with polyvinyl alcohol, in up to 83% of cases [27,28].but with the evolution of material use Endovascular embolization with liquid adhesive material is reported to have a very low rate of recanalization [29,30]. The success rates of endovascular therapy have been reported to vary between 25% and 75% [31, 32] but For J. Marc et al the Advantages of the endovascular technique are its noninvasiveness and the possibility of an immediate angiographic control of the treatment [10]. Steinmetz MP et al in a recent meta-analysis suggested complete occlusion of the fistula following surgery in 98% [33].

The outcome was marqued by a worsening of the Aminoff–Logue disability scale in three patients in the first week after the surgery. But after six months of occupational therapy five patients (71.42%) improved their Aminoff–Logue disability scale while two patients remain stable. They did not improve their disability after two years. Approximately 75% of patients get a degree of satisfaction as report in the literature [22].

In their series of 17 patients treated by microsurgery Jakub w et al reported that functional improvement or good stable condition was achieved in 65% of the patients at discharge and in 76% in long-term follow-up [34]. Chibbaro S et al advocated multidisciplinary approach based on direct cooperation between endovascular specialists and neurosurgeons before the choice of the treatment option. They obtained the excellent result of 100% cure rate with no procedural complications after patient's selection for microsurgical treatment [21]

The most complications of the microsurgical treatment are CSF leak, infection, haematoma, and neurological sequelae [23, 24, 25]. In our study we did not experiment such complications.

Conclusion

SDAVF is a rare pathology, with unspecific clinical signs leading to diagnostic difficulties. To avoid misdiagnosis a multidisciplinary collaboration is required. The neuroradiologist help is very

important using MRI and DSA to get the exact location of the fistula and guide the treatment, either surgical or endovascular. After our series we conclude that microsurgery is a good option for the treatment but the post-operative outcomes depend largely on preoperative neurological status.

Conflict of interest: none

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Transzygomatic anterior infratemporal fossa approach and high cervical approach for resection of infra temporal fossa and parapharyngeal space solitary fibrous tumours.
Report of 2 cases and review of literature

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Keywords
transzygomatic,
anterior infratemporal fossa,
resection,
parapharyngeal space,
solitary fibrous tumours

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ABSTRACT

The infratemporal fossa (ITF) is the region under the floor of the middle fossa giving passage to most major cerebral vessels and cranial nerves.(1) It is closely related to important adjacent regions such as the middle fossa, pterygopalatine fossa, orbit, and nasopharynx.(2) Due to the anatomical complexity in the ITF, surgical removal of the lesions in or around it is still challenging.(3) Since the 1960s, many surgeons have reported various surgical approaches. the preauricular transzygomatic approach via a transcranial route was reported to be used for exposure of the antero-superior portion of the ITF (2,3). Solitary fibrous tumours (SFTs) were first described by Klempere and Rabin in 1931 as spindle-cell tumours originating from the pleura.(4) With the exception of myopericytoma, infantile myofibromatosis and HPC-like lesions of the sinonasal tract showing myoid differentiation, all other HPC like lesions are best considered as subtypes of SFT.(5) Only a few cases of SFT have been described in the literature involving the skull base and parapharyngeal space.(6–8) The purpose of this article is to show anatomical dissections involving this surgical approach and to evaluate our surgical experience using it.

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FIRST CASE

45 yr old female presented with swelling over left cheek without any neurological deficit. MRI revealed left middle cranial fossa base lesion extending into infratemporal fossa. Patient underwent surgery by left anterior infratemporal fossa approach and gross total excision of lesion. Postoperatively patient developed left V3 dysesthesia, which improved over a period of one month. Biopsy- solitary fibrous tumor

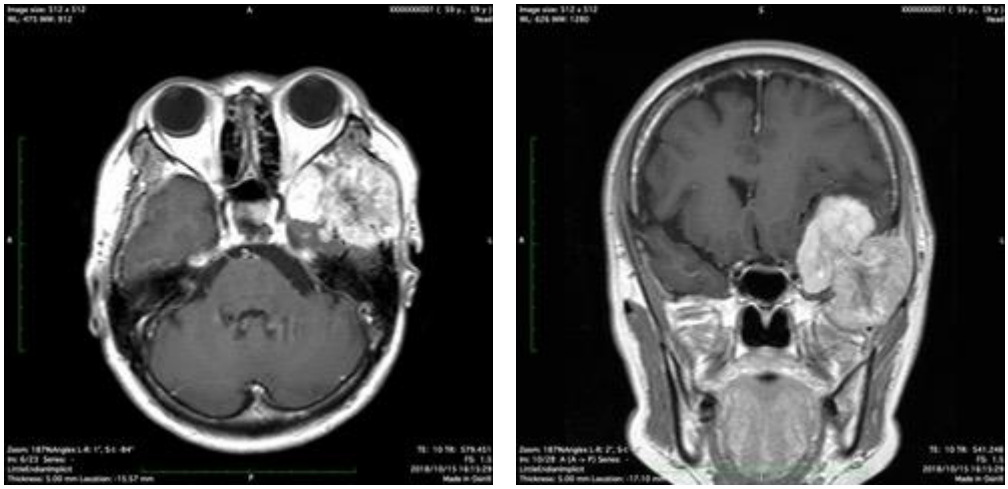
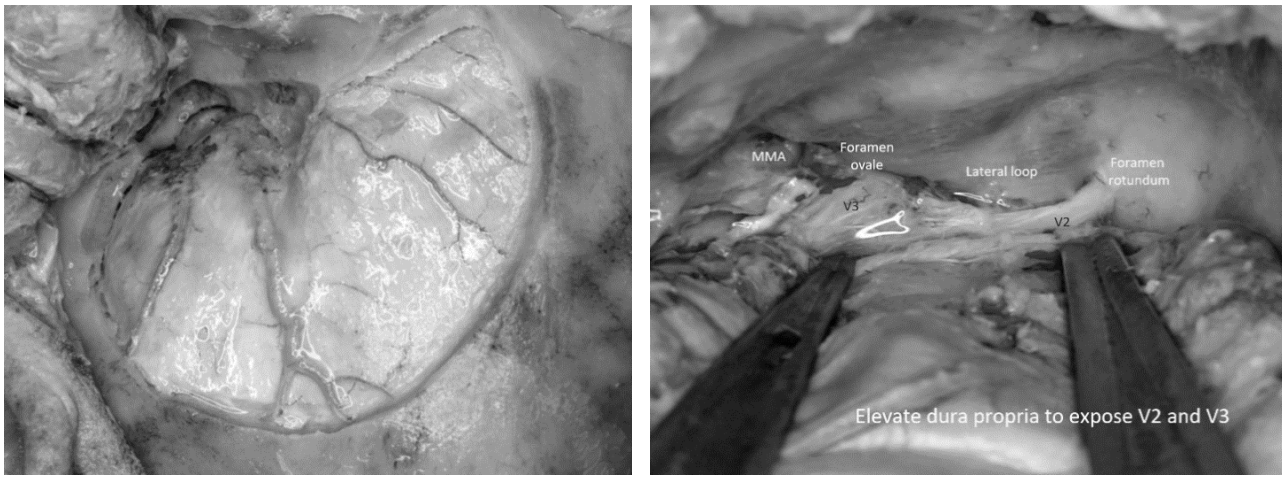
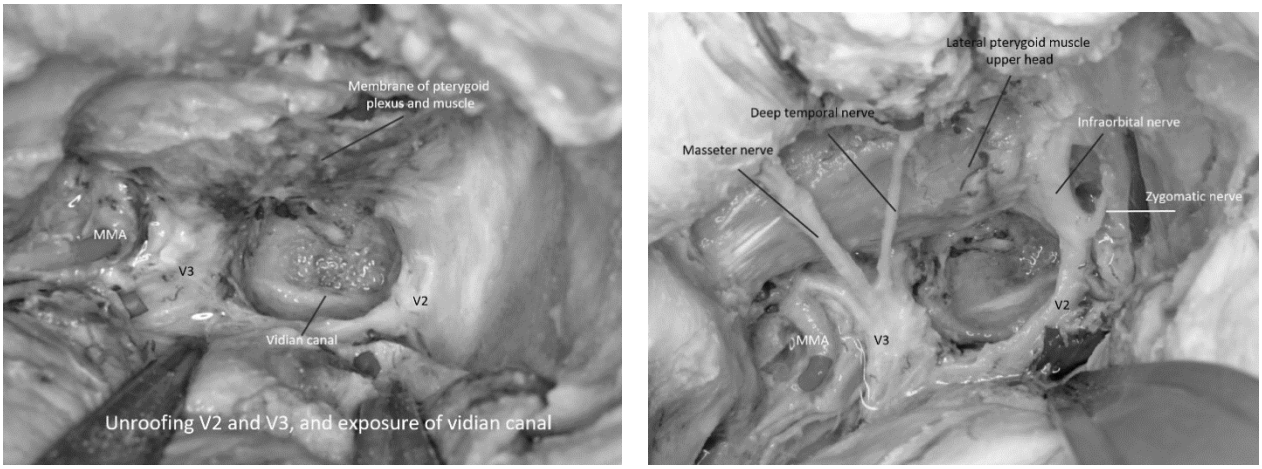


Figure 1: MRI images showing infratemporal fossa tumor with extension into middle cranial fossa.





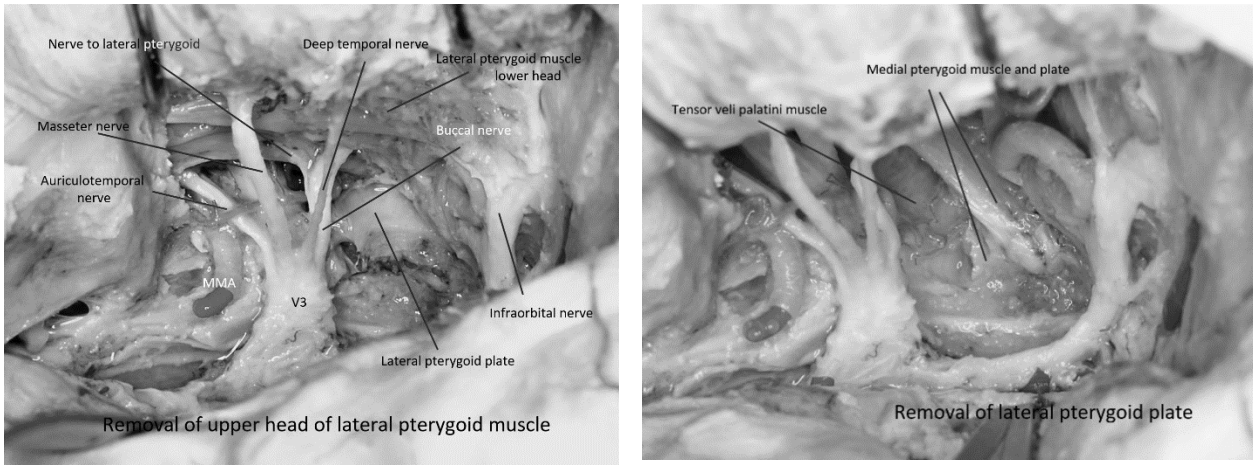
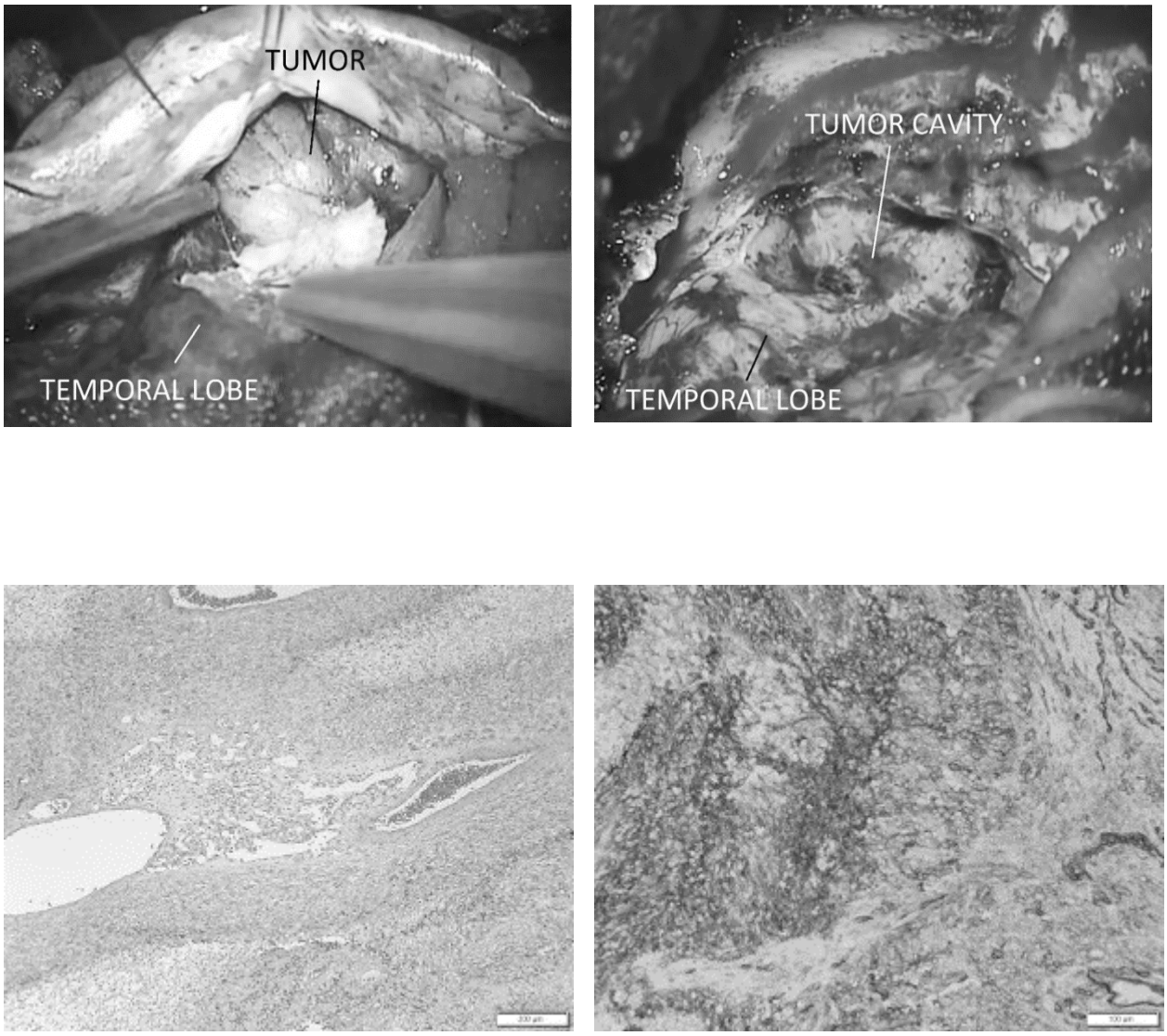
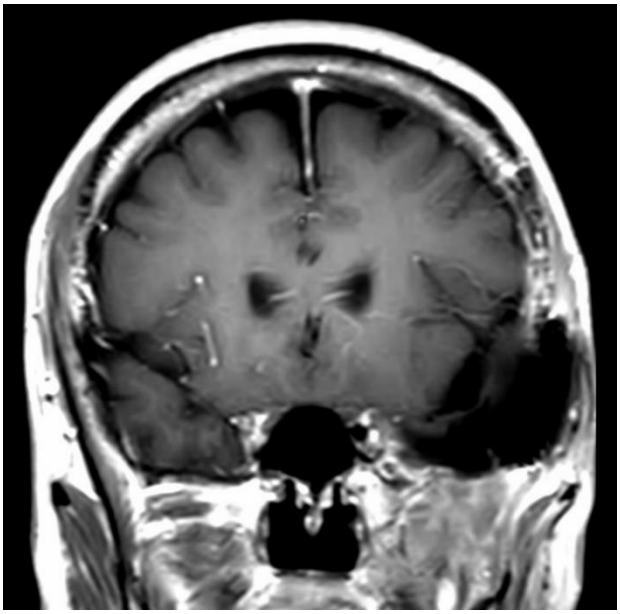


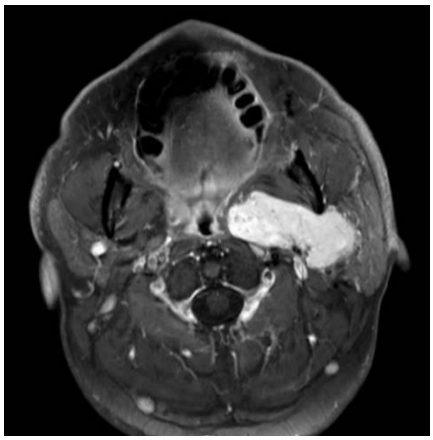
Figure 2: (A-F). A) Frontotemporal craniotomy with elevation of zygomatic arch.

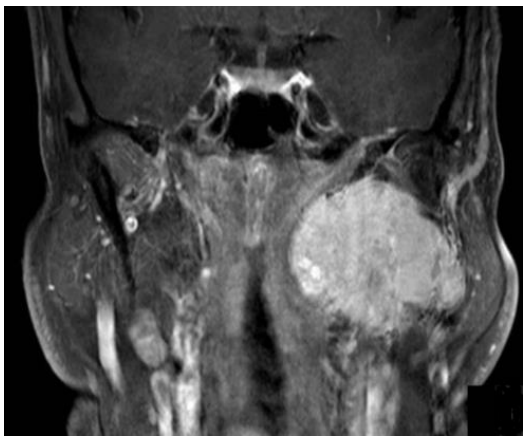


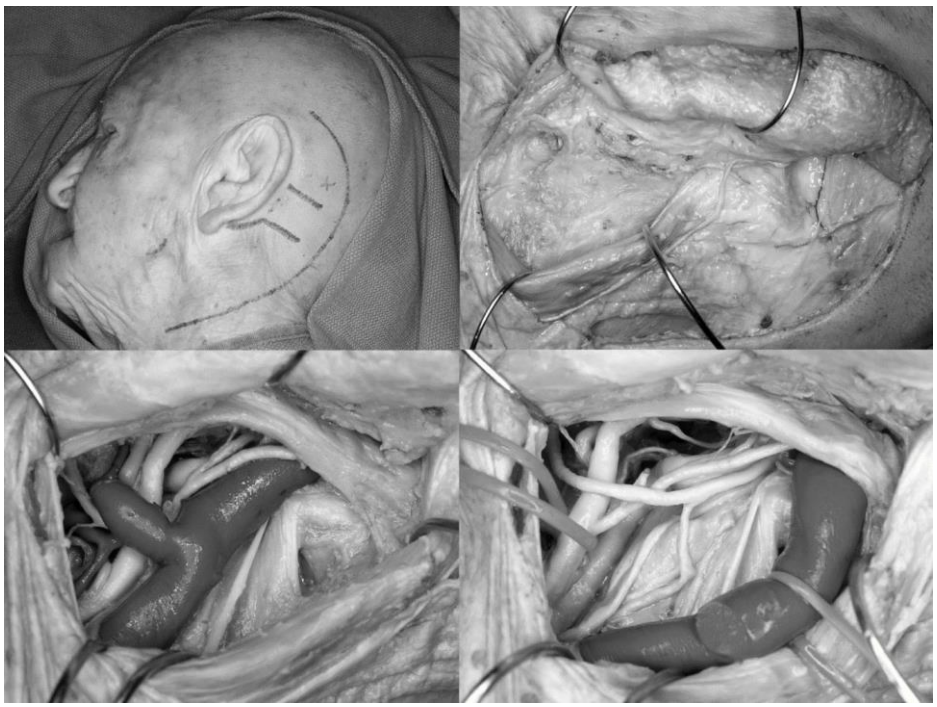


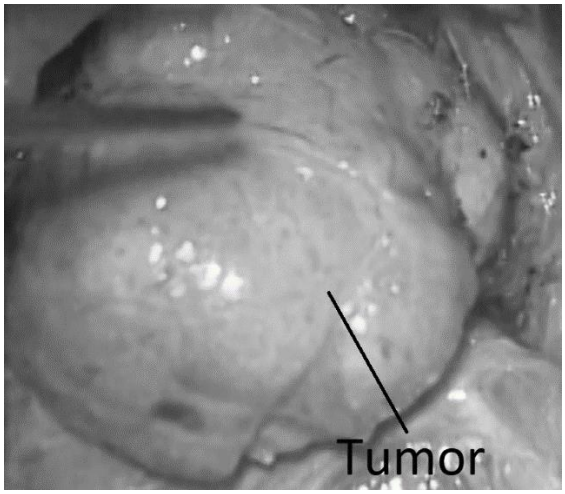
SECOND CASE

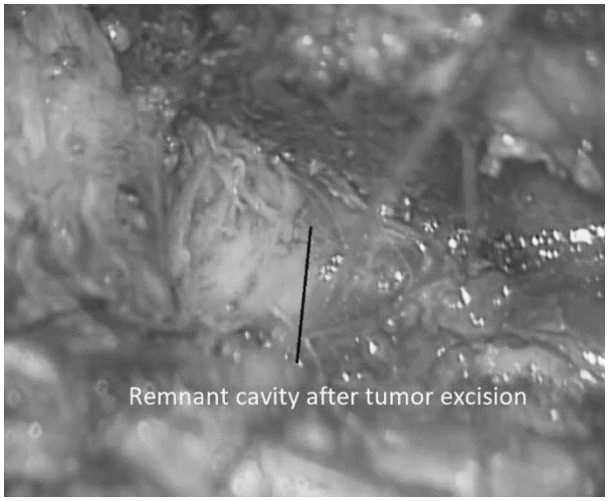
38-year-old male presented with left infra auricular swelling without any neurological deficit. MRI revealed left parapharyngeal space tumor. Patient underwent surgery by high cervical approach and gross total excision of tumor. Biopsy – solitary fibrous tumor.

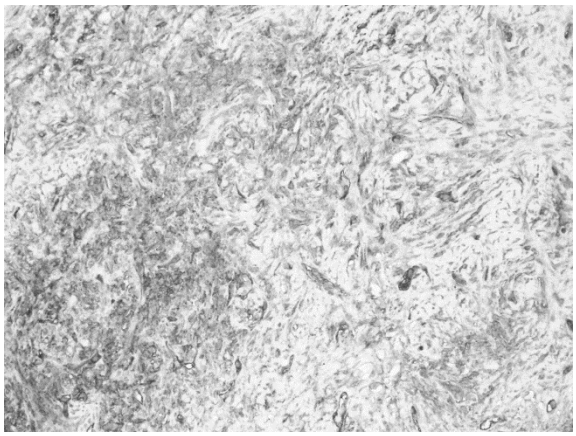


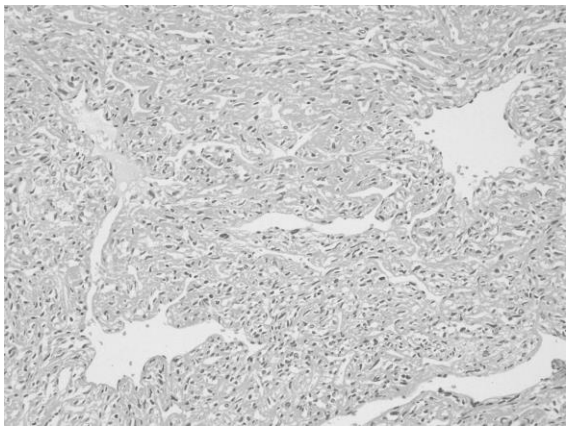


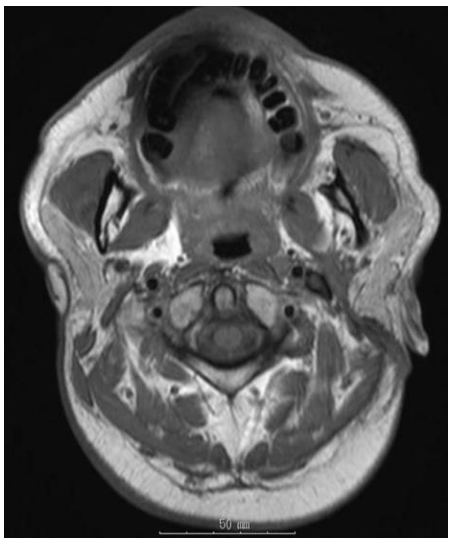


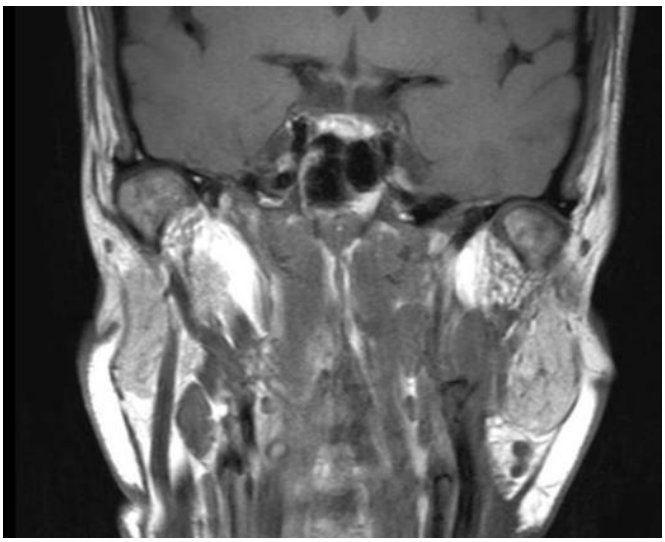












Discussion

Most cases of soft tissue SFTs occur in the early fifth decade of life.(9). Its occurrence is less than 2% of all soft tissue tumours.(9)

A study conducted by Demicco et al of 110 cases found about 32% to be in the abdomen/pelvis, 32% to be pleural, 16% in the extremities, 12% in the trunk, and 12% in the head and neck.(10)

Skull base SFTs may include a wide variety of symptoms, although they are usually asymptomatic

on presentation.(11)

The symptoms manifest most frequently as a slowly expanding painless mass. SFTs from any site are usually benign and surgical resection alone is Curative.(12,13)

The presence of infiltrative margins with surrounding tissues, high mitotic count (≥4 mitoses per 10 high-power high fields) of cellular pleomorphism and tumour necrosis also suggests malignancy.(9,12)

The main treatment is surgical for benign and malignant SFTs. But when histopathology suggests malignancy or when there are positive surgical resection margins, radiotherapy must be discussed, as for other sarcomas.(9,14)

Parapharyngeal space tumours are a rare neoplasm, comprising less than 0.5–1% of tumours of the head and neck. SFT is very uncommon but should be part of the differential diagnosis in patients with a skull base lesion. Diagnosis is difficult but pathologists should be aware of the classical finding of this disease consisting of spindled cells in a disorganized pattern, with alternating hypocellular and hypercellular areas separated by hyalinized collagen. Immunophenotyping staining positive for the presence of CD34 and Bcl-2 can be useful.

Most important prognostic factor in patients with solitary fibrous tumour is completeness of resection. The pioneers of the ITF were Conley [6] and Barbosa [3].

A variety of surgical approaches to the ITF have been developed. variations include anterior (transfacial, transmaxillary, transoral, and transpalatal), lateral (transzygomatic and lateral infratemporal), or inferior (transmandibular and transcervical) approaches.

Fukushima et al. developed a classification of ITF approaches into three types: anterior, middle, and posterior ITF approaches.

Transcervical approach for parapharyngeal space is the easiest approach for resection of these tumors.(15).

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Radiological, biomechanical and histopathological characteristics of rat brain in Kaolin-induced hydrocephalus

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Keywords
brain, hydrocephalus, kaolin, mechanical properties, viscoelasticity

ABSTRACT

Objective: A better understanding of the pathophysiology and underlying mechanisms of brain damage in hydrocephalus is vital in developing diagnostic, observational and treatment tools that will have an impact on hydrocephalus outcomes. In this study, we aimed to demonstrate the radiological, biomechanical and histopathological characteristics of rat brain tissue in an experimental hydrocephalus model.

Materials and Methods: Thirty-six male Sprague-Dawley rats (21 days old, weighing between 150 and 200 grams) were used in this study. Animals were randomly assigned to control (n = 6), 1-week hydrocephalus (n = 10), 2-week hydrocephalus (n = 10) and 3-week hydrocephalus (n = 10) groups. Hydrocephalus was induced with cisternal kaolin injection and controls received sham injection. Magnetic resonance imaging was used to measure ventricle size and cortical thickness. Vital signs, cerebral blood flow (CBF), mechanical tests and brain histology were assessed.

Results: Three rats in the hydrocephalus group died during the follow-up, yielding an overall mortality of 10% among animals from hydrocephalus groups. Ventricular width, cross-sectional area of the lateral ventricles, ventricular index and ventricle / brain area ratio progressively increased and cortical thickness progressively decreased following kaolin injection. CBF was significantly lower at baseline than at 1st, 2nd and 3rd week ($p < 0.05$, for all). ICP was significantly elevated in all hydrocephalic groups in comparison with controls. EIT that was calculated from the first load-unload indentation test showed a significant increase at 2nd week post-injection ($p=0.0001$), indicating increased intracranial stiffness. However, this significant difference disappeared at 3rd week ($p=0.956$). Quantitative immunohistochemistry showed that hydrocephalic brains demonstrated significantly less NeuN-positive cells and significantly higher IBA-1-positive microglia and glial fibrillary acidic protein positive astrocytes cells in the cortex.

Discussion and Conclusion: Cisternal kaolin injection causes varying degrees of

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ventricular enlargement in a rat model and hydrocephalus might contribute to neuronal and axonal damage and alter brain stiffness through axonal stretching or local hypoperfusion progressively over a period of days to months. As shown in this study, irreversible changes in viscoelastic behaviour and cellular structure develop in the late stages of hydrocephalus, suggesting the importance of early intervention in the treatment of hydrocephalus.

Introduction

The basic definition of hydrocephalus is "an abnormal accumulation of cerebrospinal fluid (CSF) within the ventricles of the brain" [13]. The estimated prevalence is 1–1.5% and the incidence of congenital hydrocephalus is approximately 0.9–1.8/1000 births [17,23]. Early onset hydrocephalus often results in the poorest neurological outcomes, with approximately 80% of patients suffering with residual neurological deficits [21].

Experimental animal models have been developed using various methods and agents to induce hydrocephalus or through genetic mutations in rodents. Although none of these models can fully mimic human condition, they can provide basic information that contributes to better understanding the pathogenesis of hydrocephalus and underlying causes. Although ventriculomegaly occurs naturally in congenital rat models, they are not ideal for long-term studies unless hydrocephalus is surgically intervened. Thus, the most common method of inducing experimental hydrocephalus without genetic mutation is the cisternal kaolin injection model that was introduced in the 1930s [19]. Kaolin is injected into the cisterna magna and spreads in the subarachnoid space, where it induces an inflammatory reaction and leads to an obstruction in the CSF pathways [8]. It is a simple, inexpensive and consistent way of inducing hydrocephalus in experimental animals [15].

Both clinical hydrocephalus and experimental hydrocephalus are often associated with symptoms of increased intracranial pressure (ICP) with ventricular dilatation. Understanding the biomechanical properties of the hydrocephalic brain can help in predicting mechanisms, simulating the disease and creating a treatment protocol. However, due to the complexity of the brain and the surrounding structures, data on the mechanical properties of living neural tissue is limited and variable [10,22].

In this study, it was aimed to demonstrate the radiological, biomechanical and histopathological features of rat brain tissue in kaolin-induced hydrocephalus model.

Materials and methods

All animal experiments were conducted in accordance with the Institutional Animal Care and Use Committee of Istanbul University guide for the care and use of laboratory animals in consultation with institutional veterinarians. Specific protocols used in this study were approved by Istanbul University Laboratory Animals Local Ethics Committee (2013/47). Anaesthesia, preoperative animal preparation, anaesthesia delivery, perioperative analgesia practices, and surgical protocols were optimized to minimize trauma to the animals.

Thirty-six male pathogen-free Sprague-Dawley rats (age, 21 days; weight, 150-200 g) were maintained on a 12-hour light/dark cycle and had free access to water and pellet food. Animals were randomly assigned to control group (n=6), one-week hydrocephalus group (n=10), two-week hydrocephalus group (n=10) and three-week hydrocephalus group (n=10). All hydrocephalus groups underwent cisternal 0.02 mL sterile kaolin (200 mg / mL kaolin in 0.9% saline solution) injections, whereas controls received sham injection. All groups underwent magnetic resonance imaging (MRI), mechanical tests and histopathological examination.

Induction of Experimental Hydrocephalus

Rats were anesthetized with ketamine HCl (Ketalar, Parke Davis-Eczacıbaşı, Istanbul) and Xylazine (Rompun, Bayer, Istanbul) before surgical procedures. The head was secured in a stereotactic frame and a small vertical incision was made over the back of the neck from the top of the occiput to C1. The nuchal muscle layers were divided in the midline and retracted laterally to expose the atlanto-occipital membrane (Figure 1). In all rats in the hydrocephalus groups, 0.02 ml kaolin suspension was injected slowly into the cisterna magna through a 27-gauge needle. Control rats were subjected to sterile saline injection. The muscle layers and skin were sutured and rats were allowed to recover. After recovery from anaesthesia, rats were kept at room temperature and provided with standard chow and water ad libitum. They were examined daily for clinical signs of illness. Rats were weighed daily and monitored for neurological deficits.

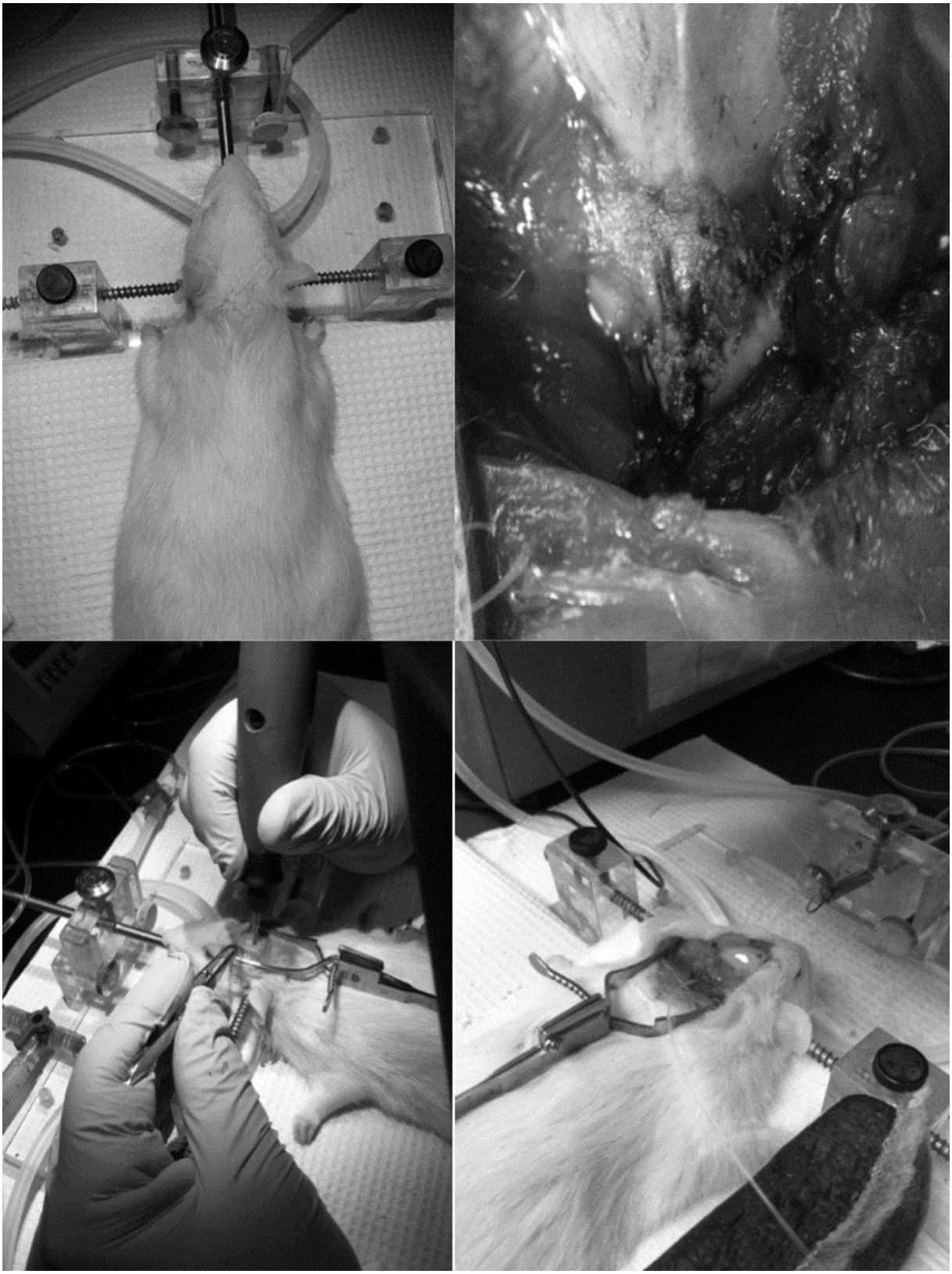

Figure 1. Basic demonstration of animal preparation. Custom custom-made stereotactic frame (upper left), atlanto-occipital membrane (upper right), preparation of cranial windows (lower left), and cerebral blood flow measurement with laser speckle microcirculation imager and pressure transmitter probe in the cisterna magna for monitoring intracranial pressure (lower right) can be seen.

Magnetic Resonance Imaging

MRI studies were performed under general anaesthesia by the use of a human MR scanner equipped with a 48-cm bore magnet operating at a field of 1.5 T (Brivo MR355, GE Healthcare, Waukesha, US) with a custom coil to obtain T2-weighted images of the brain in the coronal plane. The total area of the lateral ventricles and the brain area were evaluated by a radiologist using the PACS workstation (Neorad®, Teleradiology & 3D, Serman Medical Information, Istanbul, Turkey) on the coronal brain section that includes the anterior wall of the third ventricle. The frontal ventricle-to-brain area ratio, ventricle width index and cortical thickness measurements were performed as described by Shulyakov et al. [26].

Animal Preparation

After MRI, spontaneously breathing rats were induced with 4% isoflurane gas delivered by 100% oxygen. The rats were placed in the supine position on a homoeothermic blanket system and instrumented with a rectal temperature probe and foot pulse oximeter to continuously monitor body temperature, blood oxygen saturation, and heart rate. Under the operating microscope, the trachea was intubated with a 16G tube through a tracheostomy. The rats were then maintained with mechanical ventilation at fixed tidal volume (7 mL/kg) and inspired oxygen (40%). The left common carotid artery was dissected and cannulated for continuous blood pressure monitoring, serial blood gas analysis and fluid replacement. Isoflurane was titrated to maintain a mean arterial pressure of 80-120 mm Hg and oxygen saturation >90%. The rats were then positioned prone, fixed in a custom-made stereotactic frame and previous midline incision was used to expose the skull. The periosteum was incised and dissected. The skull was bilaterally thinned using a high-speed drill equipped with a 1.8-mm diamond burr bit to create bilateral penetrating cranial windows, leaving the dura-arachnoid membranes intact. A pressure transmitter probe was inserted into the cisterna magna for monitoring ICP. For cerebral blood flow (CBF) measurement, Laser Speckle Microcirculation Imager was positioned over the rat with the desired cranial window aligned in the camera field of view. Speckle images within a 1.2-cm x 1.6-cm region were acquired at a frequency of 50 Hz with a resolution of 100 mm/pixel, with 18.526K points/perfusion unit value. Baseline images were recorded and CBF in arbitrary perfusion units was obtained throughout the procedure. Physiological data were recorded continuously during the procedure. Baseline and hourly blood gas levels were analysed in all animals. The core temperature was measured via rectal probes and used as a reference for brain temperature.

Mechanical tests

A custom-made indentation instrument with a half-spherical indenter was used. The indenter was fastened to the custom-made stereotactic frame and it was positioned over the centre of craniectomy to achieve a planar initial contact. With the use of previously described mechanical force parameters [27,31], a standard sequence of indentation tests including loading-unloading test, load and hold test, and multicycle loading-unloading test was performed. Indentation modulus (EIT), viscous deformation and viscous nature of the material were assessed. Recovery periods of approximately 15 minutes were allowed between tests.

Histological Examination

Animals were overdosed with pentobarbital after mechanical testing, and transcardially perfused with saline and then 4% paraformaldehyde. Brains were post-fixed and subsequently immersed in the same fixative solution overnight at 4 °C and then washed in phosphate-buffered saline and stored in ethanol until processing. Coronal slices were sectioned and embedded in paraffin. The paraffinized tissue slices were sectioned at 5 mm thickness. To assess neuronal integrity, activated microglia, and activated astrocytes, the following primary antibodies were used: anti-FOX3 (NeuN) 1:2000, anti-Iba-1 1:1000, and anti-glial fibrillary acidic protein (GFAP) 1:500. Images from the cortex were taken at 200x magnification. Using Image J, NeuN, Iba-1, and GFAP stained cells were counted.

Statistical analysis

Statistical analysis was performed using SPSS 18 (IBM Corp., Armonk, NY, USA). All data are expressed as mean ± standard error of the mean. Comparison across the groups was made by using analysis of variance. Statistical significance was accepted at $p < 0.05$.

Results

In total, thirty rats underwent induction of hydrocephalus. None of the rats in the hydrocephalus groups experienced major neurological deficits. Three rats in the 3-week hydrocephalus group died during the study, yielding an overall mortality of 10% among animals from hydrocephalus groups. Two rats died during the 3rd week of hydrocephalus and no cause could be identified. One rat died during indentation testing, probably due to anesthesia overdose. Therefore, the assessments were performed with a total of 33 rats.

During the study, all animals, regardless of group, showed an increase in body weight ($p < 0.0001$). Hydrocephalic rats lost weight after kaolin injection, typically for 2–3 days. By 1-week post-injection, the rats started gaining weight. Nonetheless, rats in the hydrocephalus groups weighed less than controls regardless of hydrocephalus week ($p=0.0014$ for one-week hydrocephalus; $p<0.0001$ for two-week hydrocephalus and $p<0.0001$ for three-week hydrocephalus).

MRI imaging showed that the ventricular width, cross-sectional area of the lateral ventricles, ventricular index and ventricle / brain area ratio progressively increased and cortical thickness progressively decreased following kaolin injection (Table 1) (Figure 2)

	MRI parameters	Ventricular width	Cross-sectional area of the lateral ventricles	Ventricular index	Ventricle / brain area ratio	Cortical thickness
Hydrocephalic rats	1st week vs. 2nd week	<0.0001	<0.0001	<0.0001	0.0005	0.0142
	1st week vs. 3rd week	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Control rats	1st week vs. 2nd week	0.99	0.99	0.96	0.86	0.87
	1st week vs. 3rd week	0.79	0.72	0.68	0.61	0.50

Table 1. Statistical evaluation of MRI parameters in hydrocephalic and control rats.

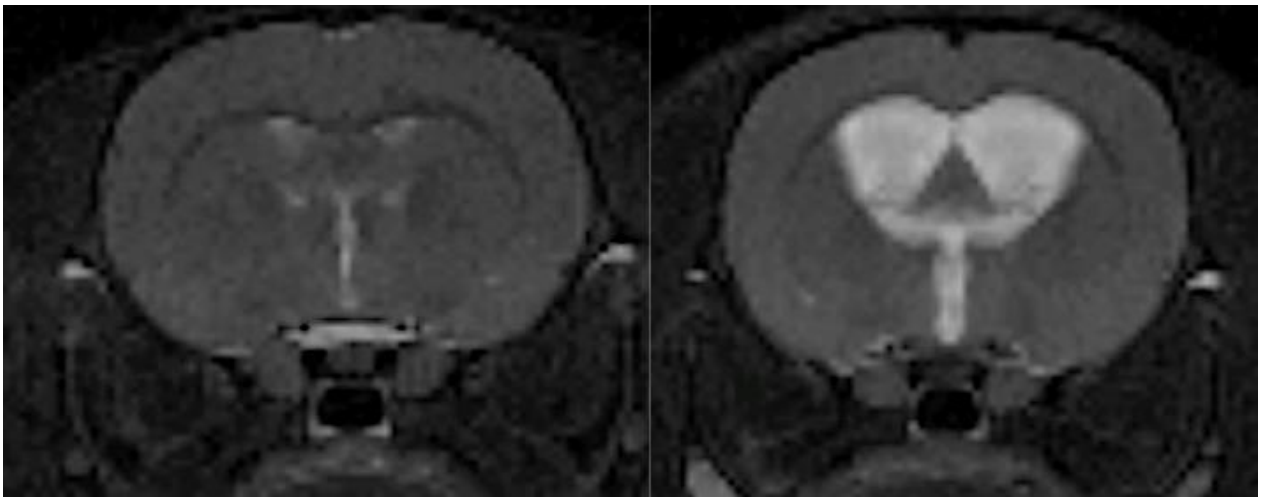

Figure 2. Magnetic resonance image demonstrating increase in ventricular size in a hydrocephalic rat at 3rd week (right) compared to a control rat (left).

In control rats, CBF was significantly lower at baseline than at 1st, 2nd and 3rd week ($p < 0.05$, for all). Hydrocephalic rats also showed an increase in CBF with time, but this was not significant ($p=0.2429$). Hydrocephalic rats at 1st week had a lower CBF than controls; however, the difference was not significant

(p=0.3134). At 2nd and 3rd weeks, hydrocephalic rats had a significantly lower CBF than controls with a highest percentage reduction of 59% (p<0.0001) (TABLE 2).

	Mechanical parameters	CBF	ICP	Heart rate	E_{IT}	Strain during load-hold	Strain during multi-cycle
Hydrocephalic rats	1st week vs. 2nd week	0.48	<0.0001	<0.0001	<0.0001	<0.0001	0.0214
	1st week vs. 3rd week	0.1865	0.4255	0.0145	0.9443	<0.0001	0.1340
Control rats vs. Hydrocephalic rats	Control vs. 1st week	0.0004	<0.0001	<0.0001	0.8842	0.0002	0.0555
	Control vs. 2nd week	<0.0001	<0.0001	<0.0001	<0.0001	0.0001	0.0176
	Control vs. 3rd week	<0.0001	<0.0001	<0.0001	0.956	<0.0001	0.0082

TABLE 2. Statistical evaluation of physiological and mechanical parameters in hydrocephalic and control rats
CBF: cerebral blood flow; ICP: intracranial pressure; EIT: indentation modulus

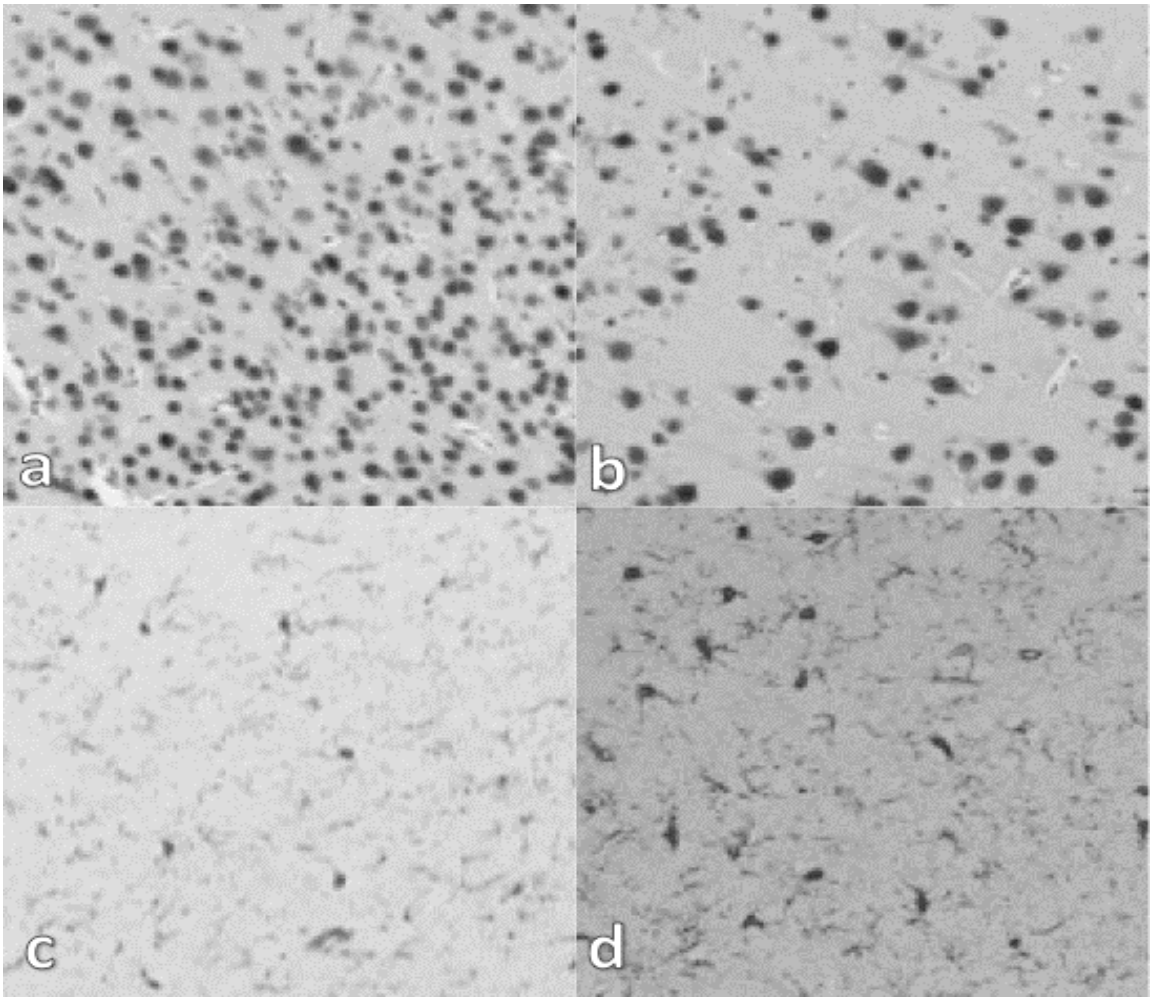

FIGURE 3. Representative histomicrographs showing significantly decreased NeuN-positive cells in the cortex of rats in the hydrocephalus group at 3rd week (b) compared to controls (a), and significantly increased Iba-1-positive microglia (red) and GFAP-positive astrocyte cells (gray) in the cortex of rats in the hydrocephalus group at 3rd week (d) compared to controls (c).

For the control and hydrocephalic groups, the indentation tests were associated with an ICP increase up to 20%. EIT that was calculated from the first load-unload indentation test showed a significant increase at 2nd week post-injection (148 kPa vs. 278 kPa, p=0.0001), indicating increased intracranial stiffness. However, this significant difference disappeared at 3rd week (p=0.956). In the load-hold indentation test, control and hydrocephalic brains exhibited gradual deformation and the associated intracranial strain was significantly greater at each time points in the hydrocephalus groups (p=0.0002 at 1st week, p=0.0001 at 2nd week and p<0.0001 at 3rd week). The multi-cycle indentation test also caused gradual deformation of the intracranial contents in all groups, but there was no significant difference between groups (p=0.0555 at 1st week, p=0.082 at 2nd week and p=0.176 at 3rd week) (TABLE 2).

Systemic blood pressure and mean arterial pressure were stable during mechanical tests; however, due to increased ICP, cerebral perfusion pressure and CBF decreased. After withdrawal of the indenter, blood flow returned immediately to baseline values I all groups. Baseline core temperatures were not statistically different between all groups and changes were not significant during indentation (TABLE 2).

ICP in controls was 6.5 ± 0.86 mmHg. Compared to controls, ICP was significantly elevated in all hydrocephalic groups, with the pressure being highest at 2nd week (p<0.0001 at all-time points). ICP showed a rapid pressure rise during indentation and returned immediately to baseline values after withdrawal in all groups. During indentation, bradycardia was identified at the point of maximal ICP (TABLE 2).

Quantitative analyses of NeuN-positive, IBA-1-positive, and GFAP-positive cells in the cortex of animals with hydrocephalus demonstrated significantly less NeuN-positive cells that reflects altered neuronal integrity, and significantly more Iba-1-positive microglia and GFAP-positive astrocyte cells that indicate higher inflammatory signals (FIGURE 3).

DISCUSSION

To investigate the radiological, biomechanical and histopathological changes in experimental hydrocephalus, we analyzed the impact of kaolin-induced hydrocephalus in rats. The present data indicate that kaolin-induced hydrocephalus created a reproducible hydrocephalus model with altered brain morphology along with disturbed mechanical properties and neuronal integrity.

Besides genetic mutations, experimental animal models have been developed using numerous agents to induce hydrocephalus [8,15]. All of these models provide important information to understand the causes and potential treatments of hydrocephalus. The most commonly used method is the injection of kaolin into the cisterna magna [9] and it is an inexpensive, simple and reliable method that has been previously studied in rats [6,7,11,12,18]. In our study, the experimental rats were particularly 21-day old rats, as it corresponds to the first 6-month period of human brain development in which cerebral myelination is rapid [24,30]. The rats in our study tolerated the kaolin injection fairly well with acceptable levels of mortality (10% died during 3 weeks, one possibly due to anesthesia overdose) and no evidence of hemorrhage was observed following removal of the brain. Compared to higher rates of mortality in the literature, it was thought that the difference might be due to post-operative animal care, animal breed used and the chemical properties of kaolin [5,20]. However, it should be noted that none of these models, including kaolin-induction method, is perfect in imitating human conditions.

Although kaolin-induced hydrocephalus model offers dose-dependent responses to some extent, there is variable dispersion of kaolin in the subarachnoid space, and this may account for the relatively unpredictable rate and magnitude of ventricular dilatation [8]. Consistent with the literature, in our study, kaolin presumably caused a moderate to severe hydrocephalus with a ventricle/brain area ratio of 0.105 ± 0.02 at 3 weeks, compared to 0.018 ± 0.002 at baseline. Kaolin causes an inflammatory response, thus causing blockage of the fourth ventricle and mimicking hydrocephalus caused by meningitis. Although this model has been criticized for its inflammatory effects such as evident macrophages, CD4- and CD8- lymphocytes in the subarachnoid space and in surrounding brain parenchyma, and reactive microglia in the white matter surrounding the ventricles [7,16,25], it was reported that kaolin had clearly been ingested by macrophages and there were minimal neutrophils and eosinophils at 10th day post-injection with histologically unaltered brainstem and cerebellum

adjacent to kaolin collections [29]. Brain injury in hydrocephalus is a multifactorial process marked by ventricular enlargement leading to stretching of axons with concomitant cortical compression. However, these histologically evident progressive destructive changes can be difficult to quantify due to profound tissue distortions [16]. In our study, quantitative analyses of NeuN-positive, IBA-1-positive, and GFAP-positive cells in the cortex of animals with hydrocephalus demonstrated significantly less NeuN-positive cells and significantly more Iba-1-positive microglia and GFAP-positive astrocyte cells.

Due to the complexity of the brain and the surrounding meningeal structure, information about the mechanical properties of living neural tissue is insufficient [10,22]. To learn about the mechanical changes and to better understand the physical mechanisms involved in hydrocephalus, it is necessary to learn about the mechanical properties of the brain in vivo [1]. The main advantage of in vivo testing is that the tissue structure remains largely intact, as close to its natural state as possible [4]. It is widely known that the mechanical properties of neural tissues are associated with their microstructure [2]. Thus, changes in tissue microstructure can be reflected as an altered stiffness. In our study, the live brain mechanical properties reflected a combination of several different anatomical and physiological systems including the dura mater, the intact CSF system, and the brain itself. The stiffness of cortical gray matter increased despite the differences in tissue microstructure at 2nd week, similar to the study by Shulyakov et al. [26]. However, Juge et al. [14] did not find such an increase in the same hydrocephalus rat model. The main difference of their study was that they used MR elastography to measure brain stiffness and the contribution of hydrostatic pressure to mechanical properties was eliminated by elastography analysis method [28]. Despite the increase at 2nd week, the difference between controls and hydrocephalic group disappeared at 3rd week. Regarding this, it can be suggested that microstructural rearrangement occurs in brain during chronic phase of hydrocephalus possibly through neuronal damage. This damage was also demonstrated in our study by significantly less NeuN-positive cells in the hydrocephalic group at 3rd week. The absence of permanent change in viscoelastic behaviour in the brain in the early stages of hydrocephalus in our study shows the importance of early intervention in the treatment of hydrocephalus.

The main limitation of our study was that we could not use an animal MRI equipped with a higher magnetic field strength. However, in a previous study, 1.0T MRI was shown to be a reliable equipment to assess MRI features in experimental hydrocephalus [3].

Conclusion

Cisternal kaolin injection causes varying degrees of ventricular enlargement in a rat model and reflects the hydrocephalus pathology seen in foetuses and premature infants in some aspects. Hydrocephalus might contribute to neuronal and axonal damage and alter brain stiffness through axonal stretching or local hypoperfusion progressively over a period of days to months. The absence of permanent change in viscoelastic behaviour in the brain in the early stages of hydrocephalus necessitates early intervention.

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Treatment of chronic pain by spinal cord stimulation

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Keywords
neuromodulation,
pain,
failed back syndrome,
spinal cord stimulation,
epidural stimulation

Abstract
Failed back surgery syndrome (FBSS) is often used to describe the condition of patients who have experienced continued pain after surgery. It is of multifactorial genesis and may be the consequence of various lumbar spinal diseases; lumbar disc herniation surgery or spinal canal stenosis laminectomy. The presented series included 13 patients affected with chronic pain related to FBSS who underwent implantation of spinal cord stimulation. The mean percentage of pain relief was 90 % for all patients. 60% of the patients were in a better psychological status and the intake of analgesic medications has been reduced of more than 70%. More than 50% of the patients could resume professional activities. Analysis of the risks and benefits comes in favour of spinal cord stimulation.

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Introduction

Chronic pain can be seen in 12 to 40% of patients that underwent a spine surgery according to the series (13,14). This persistent pain is known as Failed Back Surgery Syndrome (FBSS) (8). Clinically it appears in the form of lumbar and / or radicular pain. This Pain syndrome often appears after multiple surgical procedures for disc herniation or stenotic spinal canal. It can usually be explained by the contribution of several factors including arachnoiditis or periradicular fibrosis (15). The patients have mixed pain syndrome of neuropathic and nociceptive character; the neuropathic component is found in 80 to 96% for lumbosciatic and 8 to 16% for lumbago (5). The FBSS is one of the indications of the spinal cord stimulation after failure of conservative treatment (13). This neurostimulation performed for the first time by Shealy et al in 1967, consists of placing electrodes in the epidural space in contact with the spinal cord. According to the series, this technique can improve this pain syndrome in 55 to 88% of cases (2).

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Materials and methods

Patient's selection

We performed a prospective a study of 13 patients with a spinal cord stimulator for persistent chronic pain after spinal surgery. This work was held from May 2013 to December 2017. Our serie includes 6 women and 7 men with an average age of 42 years with extreme ages of 21 and 66 years. All patients had a detailed clinical evaluation including their pain characteristics, the intensity of the pain using the Visual Analogue Scale (VAS), the drugs intake using MQS (Medication Quantification Scale), and an assessment of the psychological impact of the pain (Table 1). Imaging investigations and electrophysiology were performed before spinal cord stimulation. Imaging, represented by CT and / or spinal MRI, eliminated the presence of disc herniations or stenotic spinal canal. Implantation concerned patients with severe pain (VAS> 5/10), chronic pain (> 6 months) and resistant pain to usual treatment.

Etiologies

The chronic pain that affected our patients was due to herniated disk surgery in 11 cases (84.6%), of narrow lumbar canal surgery in one case (7.7%) of scoliosis surgery also in one case (7.7%). Patients who had been implanted for post-traumatic spine pain or for any other condition were excluded from the study (Table 1).

Characteristics of the pain

Patients suffered from radiculalgia of the lower limbs with or without chronic low back pain. They were of neuropathic type (> 4 at the DN4 score), evolving for more than six months, resisting to several categories of treatments including opioids, anticonvulsants, and tricyclic antidepressants. Four patients had previously benefited from transcutaneous stimulation that did not cover the entire pain territory. The delay between the onset of pain and implantation of the spinal cord stimulator was average of 8 years with an interval between 2 and 24 years.

Implant procedure

We use wide and flat electrodes with 16 contacts (PENTA, Saint Jude®). Their plate configuration allows them to be in contact with the dura over a large area and to generate a 180° stimulation field in the direction of the spinal cord. These types of electrodes are designed to reduce energy consummation by minimizing losses. The wide conformation of the electrode requires an open surgical approach for better visual control of the epidural space. The procedure is performed under general anesthesia in the prone or right lateral position. After minimal skin incision and dissection of the musculo-fascial planes, the electrode is introduced through an inter-spinous approach to have a bilateral effect, at the T9-T10 space (Figure.1). A radiological check is performed to confirm the correct positioning (Figure.2). Then, the wires of this electrode are tunneled to the left subcostal or left subclavian level. A short incision is made at this point to implant the generator after having connected it to the wires of the electrode.

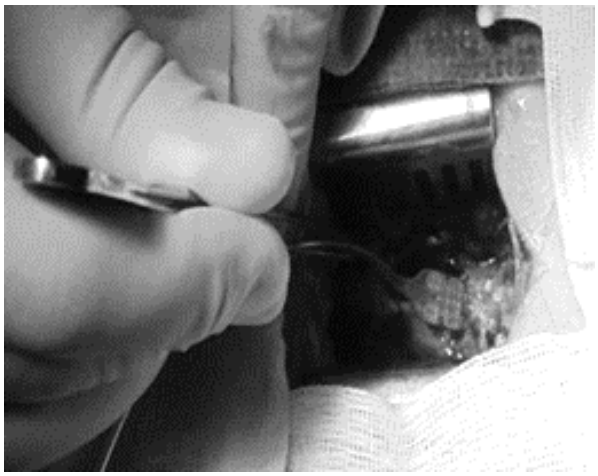
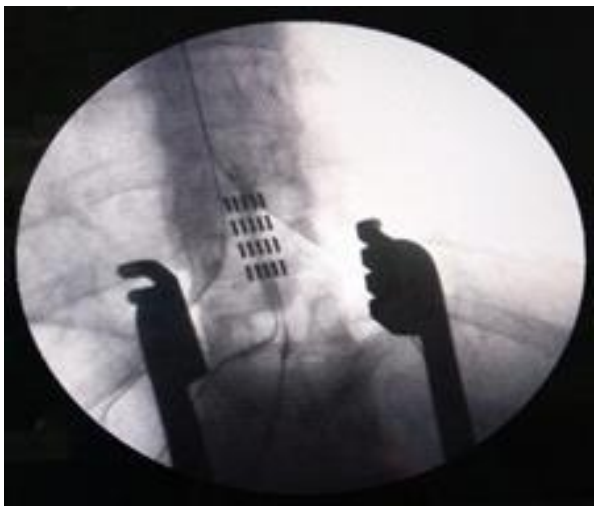


Figure 1: The electrode is introduced into the Epidural space in contact with the spinal cord.

Figure 2: Control X-ray for the good position of the electrode.



Results

The stimulator is started the day after surgery. The parameters used are variable according to the patients with 200 microseconds on average (between 50 and 500 µsec), a frequency of 30 Hz (between 30 and 400 Hz) and amplitude of 6 mA (between 2 and 20 mA). The settings are refined between 1 and 3 months. The long-term evaluation was performed at 6 months for five patients, at one year for three patients and beyond two years for five patients. The average duration of follow-up is 20 months. All patients reported a relief of more than 50% of the pain intensity at the end of the first settings of the stimulation. Statistical analysis showed a significant improvement. The improvement is estimated at 90% with a VAS that went from 8.8 to 0.8. The consumption of analgesics has been reduced by 71.8%. This reduction goes hand in hand with improving the quality of life of patients in more than 60% of cases. The professional reintegration concerned more than half of the patients in activity with an arranged post in 60% of the cases. The surgical technique was not accompanied by serious complications. We noted a pain of the surgical site resolving under analgesic, a case of dura tear repaired in per operative and a case of hematoma development around the generator requiring drainage.

Patients	Sex	Age	Surgery	Locations	Initial VAS	Initial MQS	Lower opioids	Higher opioids	Follow-up (months)
1	M	21	Dis	Dif, LL, Bil	8.5	32	YES	NO	54
2	F	37	Dis	Dif, LL, Bil	9.5	32	NO	YES	34
3	F	40	Dis	LS, Uni	9.5	32	YES	NO	31
4	M	47	Dis+Lam	Dif, LL, Bil	8.5	32	YES	NO	26
5	M	52	Lam	Dif, LL, Bil	8	32	YES	NO	26
6	M	66	Dis+Lam	Dif, LL, Bil	9.5	32	YES	NO	20
7	F	34	Dis+Lam	LS, Uni	10	32	YES	NO	19
8	M	41	Scol	Dif, LL, Uni	10	27	NO	NO	14
9	F	49	Dis+Lam	LS, Uni	7	18	YES	NO	9
10	M	47	Dis+Lam	GU	8.5	30	YES	NO	8
11	M	47	Dis+Lam	LS, Bil	8.5	23	NO	NO	8
12	F	63	Dis+Lam	Dif, LL, Bil	8.5	24	NO	NO	8
13	F	48	Dis+Lam	Dif, LL, Bil	8.5	7	NO	NO	6

Table 1: summery of the preoperative data and the follow up duration for each patient. Dif : diffuse, LS : lombosciatalgia, GU : Genitourinary, LL : lower limb, Bil : bilateral, Uni : unilateral, Dis : discectomy, Lam : laminectomy, Scol : scoliosis correction rods removal, VAS (Visual Analogue Scale), MQS (Medication Quantification Scale).

Discussion

Persistent pain after spinal surgery or "FBSS" is the result of several factors including major and / or prolonged compression of the nerve root during the preoperative period, the occurrence of a surgical complication or nerve damage in peroperative (14,23). The occurrence of arachnoiditis or periradicular fibrosis is a major contributor to pain (10,14), and infection can lead to chronic pain after the appearance of a epidural compressive fibril tissue (23). All our patients presented, prior to implantation of the spinal cord stimulator, a radicular pain at the electromyogram (EMG) with scar tissue on the operative site on imaging but without recurrence of herniated disk or residual stenotic spinal canal. The patients suffered from pains of the two lower limbs mainly in lombosciatalgia often extended without precise territory. These pains had a neuropathic character with a DN4 score greater than 4, it is in this context that the indication of spinal cord stimulation was retained. The indication of spinal cord stimulation in neuropathic pain, especially in the "FBSS", is widely accepted (4). The control of pain by spinal cord stimulation is based on gate control theory developed by Melzack and Wall in 1965 (16), in fact, reinforcing the large diameter Aβ fibers, increases the inhibitory system of interneurons in lamina II of the dorsal horn of the spinal cord on the transmission of ascending pain. We implanted our patients with 16 contact electrodes (PENTA, Saint Jude®) surgically. The open-air implantation allows a

better visual control of the epidural space. The wide configuration of the electrodes makes it possible a large contact with the convexity of the dura (19). The use of 16-contact electrodes allows a multitude of programming combinations (11). This is interesting in cases of pain with a territory that is very extensive or difficult to recruit (12). The collection of the different evaluation criteria highlights a significant gain on the MQS (Medication Quantification Scale) and VAS (Visual Analogue Scale) (16). Drug use is reduced by 42.7% at 3 months and by 71.8% at more than 6 months with suppression of opioids. In fact, the mean value of the initial MQS (preoperative) was 27.15 ± 7.58 (95% CI: 22.57-31.74); passed to 15.54 ± 8.08 (95% CI: 10.66-20.42) at 3-month, and to 8 ± 8.90 (95% CI: 2.62-13.38) at more than 6 months (Figure 3). The drug reduction has been planned and progressive. It was accompanied by fewer side effects and an improvement in the quality of life. The effectiveness of spinal cord stimulation is defined as obtaining a relief of at least 50% of the intensity of neuropathic pain (14). In the literature, the results of spinal cord stimulation vary, depending on the series, between 47% and 88% (3,6,14). For our part, we obtained a regression of 90% of the pain. The average preoperative VAS was 8.81 ± 0.85 (95% CI: 8.29-9.32). Average postoperative VAS at 3 months increased from 3 ± 1.08 (95% CI: 2.35-3.65) to 0.88 ± 1.04 (95% CI: 0.25-1.52) at more than 6 months (Figure. 3). The average duration of follow-up is 20 months with an interval between 6 and 54 months. The gradual improvement of VAS beyond the first three months is linked to the optimization of stimulation parameters during successive consultations. Patients reported walking facilitation due to improved proprioceptive conduction (1). All this has allowed half of the patients in working age to return to work with an arranged post in 60% of them. These results of spinal cord stimulation in the FBSS show a significant gain on both the pain and its repercussions. Moreover, the lack of response to the transcutaneous stimulation in the preoperative phase in our patients is not a negative value of spinal cord stimulation. The delay between the onset of pain and implantation of the pacemaker is 8 years on average. This delay is considered relatively long, but it has not acted negatively on the outcome of the results. In the literature, the factors predicting the efficacy of spinal cord stimulation are dependent on several elements, in particular, the neuropathic pain that evolves in uni or bilateral radicular mode (6), and the delay exceeding 3 years after the first surgical intervention. (13,14). The low rate of complications encountered in this series corroborates the results of the literature (11). The phenomenon of tolerance or habituation, synonymous with exacerbation of pain over time, has not been observed in our patients. This phenomenon is not frequently cited by the authors (9). However, it can be overcome by an adaptation of the stimulation parameters. The long-term socio-economic impact is in favor of spinal cord stimulation if we take into account the relief of pain, the reduction or even the stopping of medications and the possibility of reintegration in work (7).

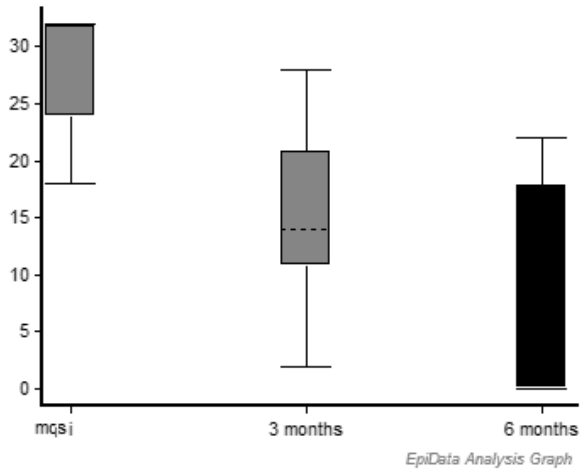


Figure 3: Evolution of the MQS (Medication Quantification Scale): preoperative (mqsi) and postoperative (at 3months and> 6months).

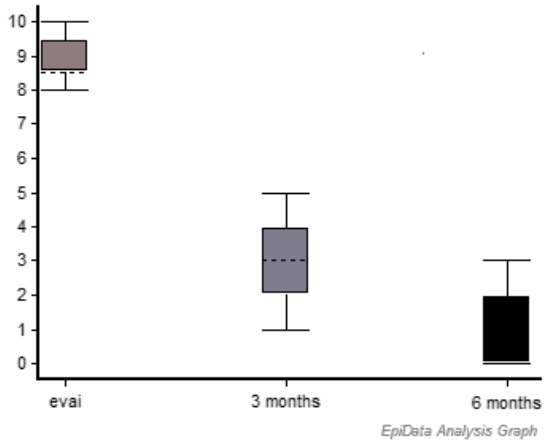


Figure 4: Evolution of the VAS (Visual Analogue Scale): preoperative (VASi) and postoperative (at 3months and> 6months).

Conclusion

The benefit / risk ratio is largely in favor of spinal cord stimulation in the management of patients with FBSS. The indication is dependent on a good selection of patients. Finally, spinal cord stimulation must be part of the therapeutic arsenal of the FBSS.

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None.
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Microscopic trans-cerebellar approach for infratentorial cavernous malformation near the lateral recess associated with developmental venous anomaly. Case report

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Keywords
cavernous malformation, developmental venous anomaly, trans-cerebellar approach

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ABSTRACT

Background: Reports showed the intimate association of the developmental venous anomaly with infra-tentorial cavernous malformation. This association has several clinical and surgical implications, sometimes this association will be a surgical challenge and affect the selection of the safest approach to the lesion. Surgery for infratentorial cavernoma is indicated for accessible symptomatic lesion only.

Case scenario: we present a case of deep cerebello-pontine CM adjacent to the lateral recess, presented with acute clinical deterioration to the emergency department of the Neurosurgery Teaching Hospital in Baghdad, Iraq, with the only possible approach was Trans-cerebellar approach because of the medial location of the associated DVA.

Conclusion: The association of developmental venous anomaly with infratentorial cavernous malformation has a pivotal role in selection the most appropriate and safe surgical approach which should be based upon the individualized patient anatomy and the location of the target lesion.

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INTRODUCTION

Developmental venous anomaly is also called venous angiomas, although the latter is abandoned at time being (1). DVA drains normal brain tissue, and its formation is still controversial, with most studies suggest that DVA represent an arrested development of primitive

medullary venous system (1). Other emerging studies suggesting the acquired nature of this vascular lesion with possible causation of the associated CM by alteration of the local hemodynamics (2,3).

Before the introduction of brain CT scan and brain MRI, the association between developmental venous anomaly (DVA) and cavernous malformation (CM) was not well established. The initial report was at 1984 after introduction of CT scan then followed by frequent reports supporting and confirm this association especially when the brain MRI included as a common investigating tool for intracranial vascular lesions (4-6). Recent reports showed that up to 30% of DVA are associated with CM, and up to 100% of CM are intimately associated with DVA (7-10).

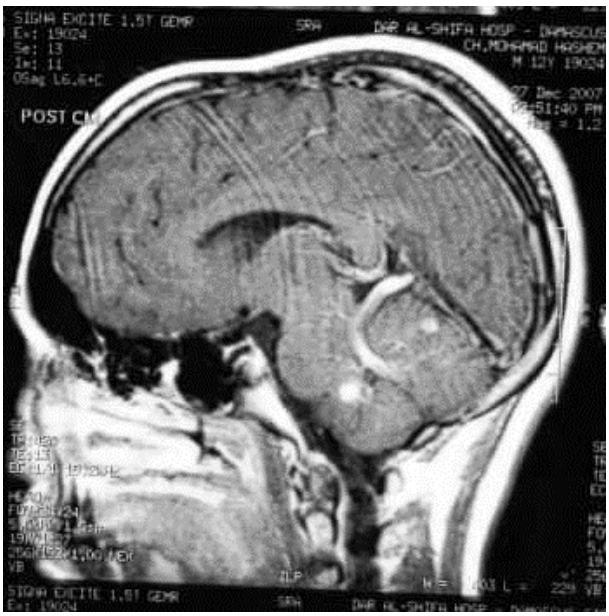
The MRI features of the CM include the classic "popcorn appearance" due to the presence of hemorrhages at different ages. The DVA are usually angiographically evident in the form of the classic caput medusa and may be very clear on MRI also especially when being large in size. Developmental venous anomalies may be visible only after excision of the associated CM (10).

Surgery for infratentorial cavernoma is indicated for accessible symptomatic lesion only.

We present a case of deep cerebello-pontine CM adjacent to the lateral recess with the only possible approach was Trans-cerebellar approach because of the medial location of the associated DVA.

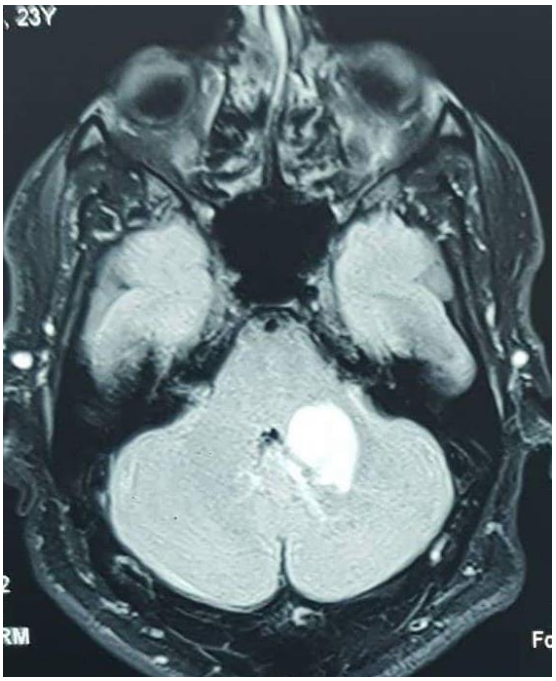
Case scenario

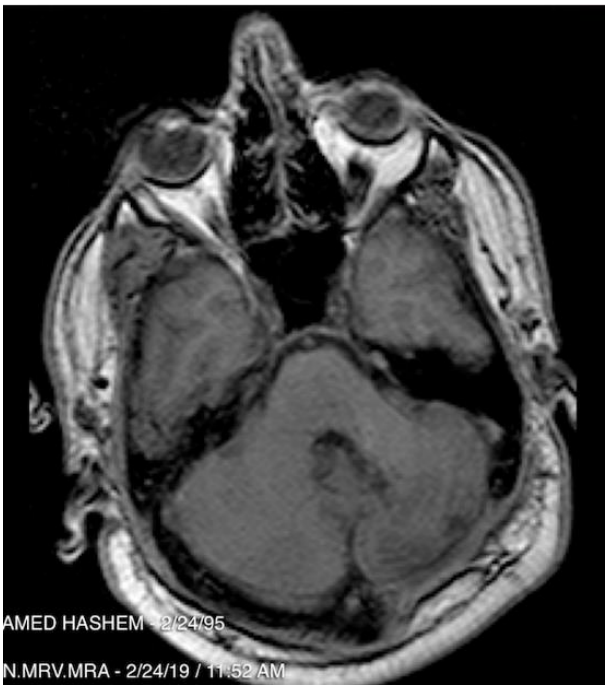
A twenty-nine years old male, a known case of CM, presented to the emergency department of the neurosurgery teaching hospital, Baghdad, Iraq, with acute onset of drowsiness, left side ataxia and cerebellar signs, nystagmus with previous two mild attacks. Imaging revealed a new and larger deep cerebello-pontine hemorrhage as compared with previous imaging, the MRI suggest confirmation of the previous diagnosis as hemorrhagic cavernoma, associated with very large DVA that runs medial then superior to the CM to be drained into the Galenic venous system, with no hydrocephalus (Figure 1A,1B). Based on the acute presentation, the location and size of the hematoma, the history of recurrent hemorrhages, we decide to evacuate the hematoma urgently. With the patient in prone position, left trans-cerebellar approach was done through left suboccipital craniectomy, the hematoma and the CM are totally removed using microsurgical technique. The associated DVA is preserved to avoid any unwanted events. The patient improved gradually over the first 5 days' post operatively and discharged home 10 days after the admission with significant improvement. Three months follow up MRI show the complete evacuation of the CM with preservation of the adjacent DVA. The patient was conscious, neurologically intact apart from very mild ataxia of the left side on follow up visits (Figure 1C).



A

B





C

Figure 1: Deep cerebello-pontine hemorrhagic CM associated with very large DVA that runs medial then superior to the CM to be drained into the Galenic venous system, with no hydrocephalus. pre-operative sagittal (A) and axial (B) MRI with contrast, showed both the CM and the large DVA. (C): post-operative axial T1 MRI, showed the resection cavity.

Discussion

The usual surgical approaches for infratentorial CM near the lateral recess include trans-lateral recess telovellar approach, transcerebellomedullary fissure approach, presigmoid approach, or rarely the anterior endoscopic approach (11,12). The presence of a DVA associated with the CM may render the common approaches not feasible. Our case of cerebello-medullary CM adjacent to the lateral recess with the only possible approach was Trans-cerebellar approach because of the medial location of the associated DVA.

The surgical strategy for infratentorial CM involves two critical goals:

1. CM should be totally excised to prevent the risk of recurrent hemorrhages without affecting the surrounding normal parenchyma.
2. Extreme care should be taken to preserve the associated DVA to prevent venous disasters to the normal brain tissue.

Thus, the usual approach that should be preferred according the accessibility of the CM, will be greatly affected by the location of the associated DVA. the usual entry zones may be disturbed by the overlying vascular tissue. Although there are frequent reports showed that coagulating some parts of the DVA when mandatory during surgery of CM, may pass peacefully especially if the DVA is already detected in the preoperative imaging and considered during presurgical planning (10,13). To note that till now there is no approved research comparing DVA resection against DVA preservation during CM resection surgery (10,14,15).

Although the trans-cerebellar approach is not always a preferable approach as it involves transgression of important anatomical structure especially deep cerebellar nuclei, but in this case, the advantage of hematoma evacuation outweighs other disadvantages. Also, the use of meticulous microsurgical technique with good planning that take in consideration the anatomical landmarks and the possible obstacles, this approach remain a viable option particularly when other approaches are not possible or not safe.

Conclusion

The association of developmental venous anomaly with infratentorial cavernous malformation has a pivotal role in selection the most appropriate and safe surgical approach which should be based upon the individualized patient anatomy and the location of the target lesion.

Abbreviations list:
CM: Cavernous Malformation
DVA: Developmental Venous Anomaly
CT: Computerized Tomography
MRI: Magnetic Resonance Imaging

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Communicating spinal epidural thoracic arachnoid cyst en-bloc resection. A case report

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ABSTRACT

Background: Spinal extradural arachnoid cyst is an uncommon, expanding lesion which may communicate with the subarachnoid space, The etiology still remains unclear, but the most accepted explanation is the existence of areas of weakness in the spinal dura , Spinal arachnoid cysts are usually in the thoracic spine, and they may cause symptoms due to spinal cord compression.

Case Presentation: Patient is a 54-years-old female who presented with progressive back pain and motor deficit, Magnetic resonance imaging (MRI) study revealed an extradural cyst extending from T2 to T4 isointense with the cerebrospinal fluid (CSF) on all sequences and did not enhance on T1-weighted post-contrast MRI. Patient underwent T2-T4 laminectomy, en-bloc resection of the lesion was achieved and the histopathological examination objectified an arachnoid cyst.

Conclusion: Spinal extradural arachnoid cyst can cause neurologic deficit and the mainstay of treatment in patients with neurological symptoms is surgical removal of the cyst together with ligation of the communicating pedicle and closure of the dural defect.

Keywords
spinal cord, arachnoid cyst, laminectomy, resection

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INTRODUCTION

Arachnoid cysts are benign lesions located in the brain or spinal cord; usually found incidentally during radiological exploration (1), Spinal arachnoid cysts result in a collection of cerebrospinal fluid that can occur in a perineural, extradural, intradural, or intra-extradural site (2). Spinal arachnoid cysts are a rare cause of spinal cord compression. spinal arachnoid cysts may be associated with other neural tube defects such as spina bifida occulta and diastematomyelia (2).

MRI is the diagnostic procedure of choice as it is noninvasive and can demonstrate the nature of cyst, size, and the anatomic relationship with the spinal cord. Surgical treatment is required when neurological symptoms develop due to cyst induced spinal cord or nerve root compression (4). Here we reported our experience on the management of a 54 years old female who presented a communicating spinal epidural thoracic arachnoid Cyst.

Case report

We reported here a case of a 54 years old female without past medical or surgical history complaining with progressive back pain, and paresthesia in lower limbs which has been initiated from9 years worsening in the last 3months with weakness of lower extremities. Clinical examination at admission revealed a paraparesia 4/5. There was no history of recent traumatism.

The spinal MRI showed a thoracic extradural arachnoid cyst from lower edge of T2 to lower edge of T4 and cervical spinal canal stenosis, the cyst is hyper intense signal in T2-weighted, hypo intense signal in T1-weighted and did not enhance on T1-weighted post-contrast (Figure 1 and Figure 2).

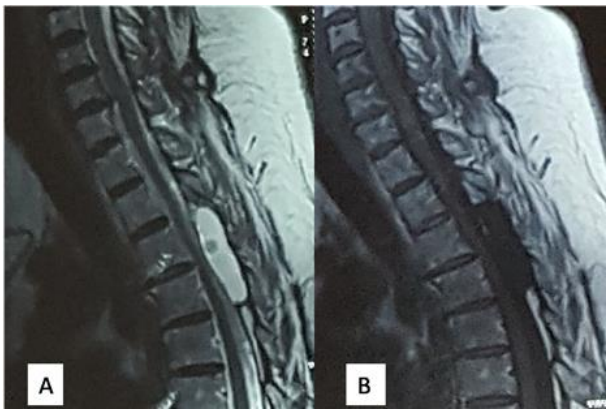

Figure 1. Pre-operative spinal MRI shows a cystic lesion extending from lower edge of T2 to lower edge of T4 with hyper intense signal on T2-weighted MRI accompanied by a central hypo intense signal (A), hypo intense signal on T1-weighted MRI(B).

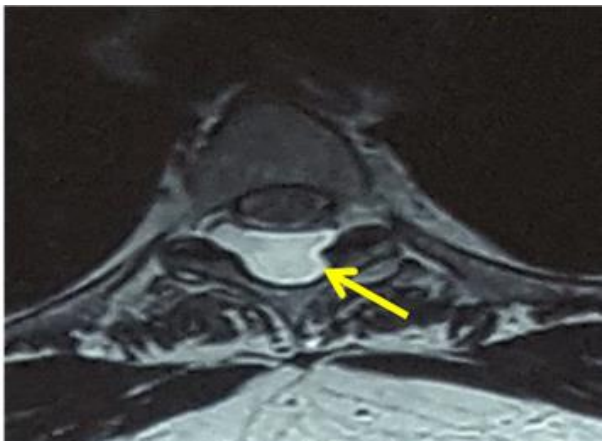

Figure 2. T2-weighted MR imaging sequences showing arachnoid cyst with high signal intensity at T2 to T4 level.

We operated the patient under general anesthesia in prone position. We performed a midline incision followed by laminectomy (T2-T3-T4), after exposure of the lesion and identification of its superior and inferior poles, we began the soft dissection of the lower pole lesion towards the superior pole, then we identified the communication between the cyst and the subarachnoid spaces through a dural defect, after total excision en bloc we close the dural defect with a muscular patche (Figure 3).

Postoperative histologic findings were compatible with the presence of an arachnoid cyst with fibrous cyst wall-like tissue. back pain in the patient and paraparesis were gradually improved.

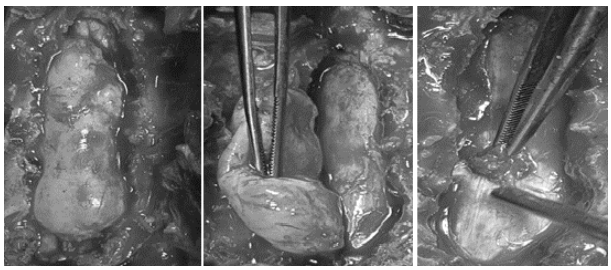

Figure 3. Intra-operative view. (a): Following laminectomy and visualization of the cyst (yellow star); (b): En-bloc resection of the lesion and visualization of the dura (blue star); (c) Ligation of the communicating pedicle and closure of the dural defect (yellow arrow).

Discussion

Arachnoid cysts are benign developmental cysts that occur in the craniospinal axis in relation to the arachnoid membrane. We report a case of extra dural arachnoid cyst, for many authors the spinal arachnoid cysts may be intradural or extradural and are composed of normal or slightly thickened arachnoid (6)

A spinal extradural arachnoid cyst is a rare disease, accounting for approximately 1% to 3% of spinal tumors (5, 8). They can be idiopathic or acquired, usually intradural, but can also rarely be extradural, primary spinal arachnoid cysts present in the thoracic spine in 80%, Secondary arachnoid cysts are usually due to trauma, hemorrhage, inflammation, surgery, or lumbar puncture (8).

Spinal extradural arachnoid cysts are most commonly found in the middle or lower thoracic spine, and less frequently found in the lumbar region, although they can be detected at any lesion of the spine (1, 3, 4, and 5). The case we report is in the most frequent site. These lesions are more common in men (sex ratio 2/1) and occurs in the

second decade of life. These lesions may be associated with vertebral anomalies, neural tube defects and syringomyelia (1, 2, 3, 5, and 6).

Various hypotheses have been proposed to explain why spinal arachnoid cysts form: 1- proliferation or loculation of arachnoid trabeculae in the septum posticum; 2- a fault in the expansion of the arachnoid trabecula and 3- the formation of arachnoid diverticuli in weak areas of the spinal dura mater (5).

Spinal extradural arachnoid cysts are usually asymptomatic; they can compress the spinal cord and give a neurological deficit; the medullary compression mechanism is still unclear but many authors have speculated that these cysts act as a unidirectional valve that let fluid in but not out (1,3). The most common presenting symptoms are pain, paresthesia, intermittent claudication, and variable degrees of spastic weakness (3,4,6) like our patient who experiment back pain, paresthesia and paraparesia.

The differential diagnoses include: tarlov or perineural cyst, ganglion cyst, synovial cyst, epidermoid cysts, cystic neoplasms, parasitic cysts meningeal diverticula next to the nerve roots, meningocele, dermoid cyst, cysticercosis and hydatid cysts (1,5).

We use the spinal MRI to get the diagnosis , this investigation showed a thoracic extradural arachnoid cyst from lower edge of T2 to lower edge of T4 and cervical spinal canal stenosis, the cyst is hyper intense signal in T2-weighted, hypo intense signal in T1-weighted and did not enhance on T1-weighted post-contrast. Many authors reported signs of that lesion on other investigations tools. Radiographs of the spine usually show bone erosion with widening of the canal, erosion ofpedicles, foraminal enlargement, and scalloping ofthe vertebral bodies or the sacrum (3).

CT can be helpful to identify a cyst complicated by internal hemorrhage as the quickest and most readily available neuroimaging test. However, an MRI is the most useful tool to diagnose a Spinal extradural arachnoid cyst. Radiological studies report that a Spinal extradural arachnoid cyst appears with low signal intensity on a T1-weighted image and with high signal intensity on a T2-WI, similar to cerebro-spinal fluid. Fluid attenuated inversion recovery sequences (FLAIR) sequences are also useful to confirm the similarity of the cyst fluid to CSF. Diffusion weighted imaging is essential to differentiate arachnoid cysts, inparticular from epidermoid cysts which can sometimes have a similar appearance (7). The management of these cysts can vary according to the patient's symptoms. There are many surgical options reported in the literature: bone decompression, subtotal or total resection of the cyst, drainage and marsupialisation of the cyst. In asymptomatic patients, conservative management with subsequentclinical observation is recommended(4, 5).The goal of surgical treatment is not only neural decompression but also the prevention of cyst refilling.For symptomatic extradural spinal arachnoid cysts the preferred treatment is surgical removal of the cyst together with ligation of the communicating pedicle and closure of the dual defect (3, 4). In the reported case we achieved the identification of the communication between the cyst and the subarachnoid spaces through a dural defect and after total excision en bloc we close the dural defect with a muscular patch.

Conclusion

Spinal extradural arachnoid cyst is rare lesion, it is typically asymptomatic but sometimes can cause spinal cord or nerve root compression and may present with myelopathy. The etiology, pathogenesis and treatment of the spinal extradural arachnoid cysts have not been well established. To treat a spinal extradural arachnoid cyst, diverse surgical techniques have been introduced. However, there is no consensus regarding the most reasonable treatment.

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Romanian neurosurgery at European standards. The 45th Congress of the "Romanian Society of Neurosurgery"

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Keywords
Romanian neurosurgery, The 45th Congress of the "Romanian Society of Neurosurgery"

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In Romania, neurosurgery has started to develop as a separate speciality since 1935, when Prof. Al. Moruzi set up the first neurosurgery service, at the "Socola" Hospital in Iassy. Then Prof. D. Bagdasar set up the Neurosurgery Service at the Central Hospital in Bucharest in 1936.

The years have passed and the Bucharest clinic of neurosurgery in „Gh.Marinescu" Hospital was developing under the leadership of Acad. Prof. Constantin Arseni, and later under the leadership of Prof. Alexandru Constantinovici.

Contemporary Romanian Neurosurgery benefiting from the technological explosion and the openness to European neurosurgery , has evolved toward performance.

The Romanian Society of Neurosurgery was founded in 1982, the first president being Acad. Prof. Constantin Arseni until 1991. The first Congress of RSN was held in the same year, and after that the RSN activity raised year by year.

Today (2019), the committee of Romanian Society of Neurosurgery is formed by: President (Assoc. Prof. Horia Ples,MD, PhD) , Honorary President (Prof. A.V. Ciurea, MD,PhD, MSC, Dr.H.C.Mult.) three vice-presidents (Prof.R.M. Gorgan,MD,PhD ; Prof.I. Poeata ,MD,PhD ; Lecturer V. Saceleanu, MD, PhD), ex-president (Prof. Dr. I.S. Florian) ,secretary , treasurer,residents representative and three other members. The comitee of RSN is chosen at a period of 2 years (2018-2020).

The RSN Congress is held anually, in the autumn season, in the city chosen by vote at the last Congress In 2018, the 44th Congress of R.S.N. was organized in Timisoara between 5 and 8 of September, and was chaired by Asocc. Assoc. Prof. Horia Ples, MD, PhD; There, was took the decision that the next annual congress will take place in Sibiu.

The 45th Congress of the Romanian Society of Neurosurgery ((RSN) was held in Sibiu, (a historical framework recognized as German burg – Hermannstadt - founded in 1191), at Ramada Hotel between 16 and 19 of October, including the 4th Francophone Medical Course and the 3rd Symposion of Nurses. The 45th Congress of the RSN had the full support of "Lucian Blaga" University of Sibiu and the Sibiu City Hall.

The congress works were opened on the 17th of October, at 9.00, by the Congress President, Lecturer Vicentiu Mircea Saceleanu, who addressed a welcome word to all participants and stressed the importance of this event to the Sibiu neurosurgery center and to Romania. (**Picture 1**).

Picture 1. The Welcome words at the 45th Congress of Romanian Society of Neurosurgery

The whole participation at the RSN Congress was impressive - **420** participants starting from students in medicine **(21%),** young residents **(18%)** to university professors **(49%)** from both the country and abroad. **(Picture 2)**. The entire pathology of tumor neurosurgery, vascular, pediatric, spinal pathology, etc. were addressed.

During the scientific event, the whole neurosurgical pathology was adressed: tumoral, vascular,pediatric, spinal, etc- through 18 scientific sessions, 112 oral presentations (aprox. 20 minute each) and 30 E-posters.

Among the presentations that have recorded an increased interest there are: Abdessamad El Ouahabi (Maroc)– Multimodal treatment of pituitary adenomas, Alexandru Vlad Ciurea (Romania) – Craniopharingyomas in children / Overview of pediatric intracranial arachnoid cysts , Stefano Ferraresi (Italia) – Accessory nerve injuries/ Lumbosacral plexus injuries, Ioan-Stefan Florian (Romania) – Posterior fossa tumors at the pediatric age/ Neurovascular malformation at the pediatric age, Radu Mircea Gorgan (Romania) – Prognostic factors associated with survival for brain metastases,

Lukas Rasulic (Serbia) – New horizons in brachial plexus surgery , Keki Turel (India)- Complications in skull base surgery, Victor Volovici (Olanda) - Microvascular education from the lab to the OR, from basics to bypass, Peter A. Winkler (Austria) – Epilepsy surgery - seven steps to improve the results ,Grigore Zapuhlih (Moldova) – Hunterian proximal arterial occlusion for giant unclippable intracranial aneurysms, etc.

Picture 2. An impressive number of participants at the Congress of "Romanian Society of Neurosurgery", 45th edition, Sibiu

Picture 3. Special speech transmitted from the President of Romania, Klaus Werner Iohannis

In the evening, after the first day of congress, the participants were invited to a Cocktail reception at the Sibiu City Hall. Lecturer Vicentiu Saceleanu, as the host of the event, has held a welcome speech. The Mayor of Sibiu, Madame Astrid Fodor, invited as a

special guest, has pointed out the importance of the 45th RSN Congress for Romania and especially for Sibiu. To the astonishment of everyone, counselor Prof.dr.Diana Paun came with an encouraging message for the congress events, **message especially sent from the President Of Romania Klaus Werner Iohannis.** The organizers were honoured to recieve such a praise. **(PICTURE 3).**

The congress events took place in three halls simultaneously , diverse papers being presented at a time. Besides the classical neurosurgical elements that took place during the three days of congress, there were also a Young Neurosurgeons Corner (**PICTURE 4**) and sessions of the Medical Assistants (**12 %** of the congress participants were nurses).

Picture 4. Young Neurosurgeons Corner – Session I

In the period of preparations of the congress Prof. Dr. Ioan-Stefan Florian (**PICTURE 5**) and Prof. Dr. Alexandru Vlad Ciurea (**PICTURE 6**) continuously collaborated to coagulate all the factors that followed the good scientific and organizational development of this event.

Picure 5. Ex-President of RSN - Prof. Ioan Ștefan Florian, MD, PhD, Head of Neurosurgery Clinic Cluj-Napoca

Picure 6. Honorary President of RSN - Prof. Alexandru Vlad Ciurea, MD, PhD, Head of Neurosurgery Department at Clinical Hospital Sanador, Bucharest

The Congress President, Lecturer Vicentiu Saceleanu, MD, PhD (**Picture 7**), the President of Romanian Neurosurgery Society – Assoc. Prof. Horia Ples, MD, PhD (**Picture 8**) and the organizing firm **Medevents** have created an appropriate scientific and social framework for such a valuable event. Furthermore, a truly remarkable organizational involvement had the Sibiu Students Circle of Neurosurgery coordinated by Dr. Vicentiu Saceleanu.

Such congress should be an example of scientific elevation, organization and social-touristic presentation for the next scientific neurosurgical manifestations.

Picure 7. Vice-President of RSN - S.L. Dr. Vicențiu Săceleanu, Lecturer at ULB Sibiu, Head of the Neurosurgery Department at Sibiu County Hospital

Picure 8. President of RSN - Conf. Dr. Horia Pleș

In the last day of the Congress, a session with two special presentations was held : Prof. Amir Samii, MD,PhD **(Picture 9)** (Germania) – "Current concepts in the treatment of vestibular schwannomas /Auditory midbrain implant: a new approach for hearing restoration in neural deafness"; and Prof. Saleem Abdulrauf, MD, Phd (**Picture 10**) (SUA) – „Future directions in microneurosurgery" - Prof. Abdulrauf, using his speaker talent, has fascinated the audience with interactive case presentations, and also created a special and strong bond between him and the young students who attended his lecture.

A special praise for Akio Morita (**Picture 11**) (Japan) who presented the top neurosurgical equipment and new elements of Science Fiction robotics in Japanese neuroscience, a dream difficult to accomplish, but not impossible.

Picture 9. Prof. Amir Samii, MD,PhD, Vice-president of the Neuroscience Institute Hanovra, Germany 'head of the program' Intraoperative Mapping and Visualization of the Human Brain" , professor of Neurosurgery in Hanover; next to Lecturer Vicențiu Săceleanu, MD,PhD, The RSN Congress President 2019

Picture 10. Prof. Saleem Abdulrauf, MD,PhD , Chairman of the Department of Neurological Surgery at Saint Louis University School of Medicine

Picture 11. Prof. Akio Morita, MD,PhD , Nippon Medical School · Department of Neurosurgery Japan · Tokyo

All of these astonishing presentations were carefully assembled in a very useful Book of Abstracts that was included in the October edition of The Official Journal of "Romanian Society of Neurosurgery".

The congress works ended on the 19th of October, where, at the closing ceremony,a surprisingly large number of participants took part, and where the closing remarks offered by Prof. Al. Vlad Ciurea ,Prof. Horia Ples and by the Congress President, Lecturer Vicentiu Saceleanu underlined once more the high quality of all scientific and social manifestations and the excellent organization, thus making the 45th Congress of RSN one of the most successful scientific events organized by far.

Next year , in the autumn of 2020 we invite you in Bucharest, the capital city of Romania, to participate at the works of the **46th Congress of Romanian Society of Neurosurgery – In memoriam of the Founder Prof.Dr.Constantin Arseni**, organised by Prof.dr.R.M.Gorgan – the head of the "Bagdasar-Arseni" Neurosurgical Clinic.

Ultimately , we go back to the first statements and we consider the remark of Dr. Madjid Samii (INI Center, Hanovra) presented at **43RD Congress of Romanian Society of Neurosurgery held in Cluj-Napoca (2017): "Romanian Neurosurgery is situated at European level**".

Corrigendum

Long term prognosis of ventriculoatrial shunt for idiopathic normal pressure hydrocephalus in the elderly

Kiyoshi Takagi (1,2), Yoko Kato (2)

1. Centre of Normal Pressure Hydrocephalus, Nagareyama Central Hospital, Japan.
2. Fujita Health University Banbuntane Hotokukai Hospital, Japan.

Romanian Neurosurgery (2017) **XXXI 4**: 490 - 494; doi: 10.1515/romneu-2017-0076

Correction to: Romanian Neurosurgery (2017) **XXXI 4**: 490 - 494; doi: 10.1515/romneu-2017-0076; published 15 December 2017

Since the publication of the article, the journal was notified that the authors were incorrectly presented. The authors are after correction:

Long term prognosis of ventriculoatrial shunt for idiopathic normal pressure hydrocephalus in the elderly

Kiyoshi Takagi (1,2), Yoko Kato (2)
1. Centre of Normal Pressure Hydrocephalus, Nagareyama Central Hospital, Japan.
2. Fujita Health University Banbuntane Hotokukai Hospital, Japan.

The authors apologise for any inconvenience caused.

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