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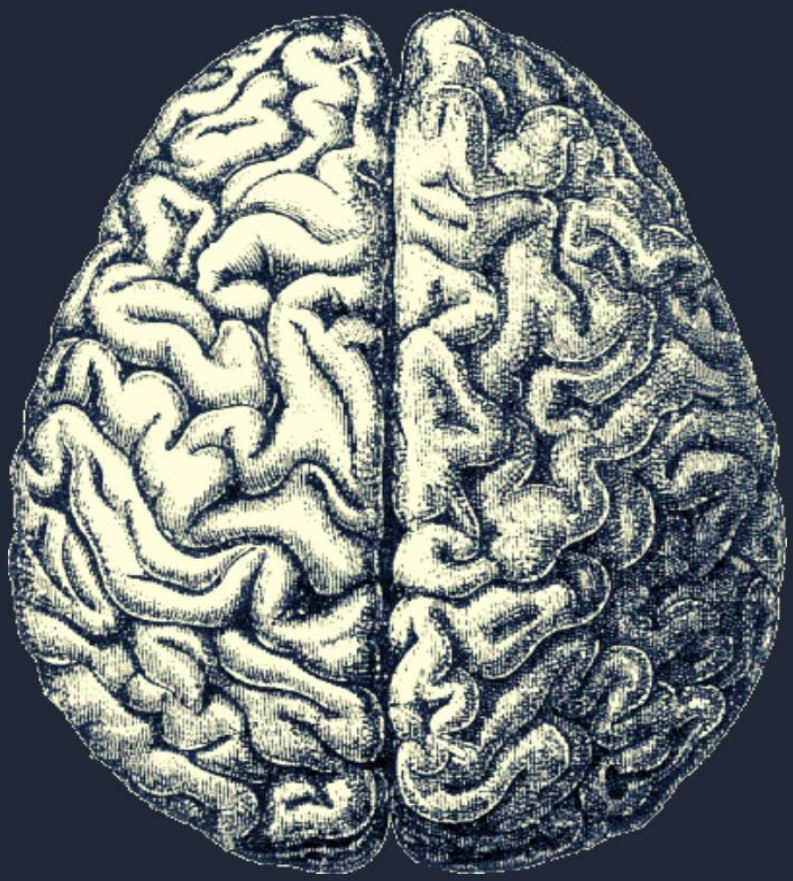

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Subarachnoid haemorrhage. A critical neurosurgical emergency

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Keywords
risk factors, neurosurgical emergency, CT, angiography, subarachnoid haemorrhage scales, cerebral vasospasm

ABSTRACT
Subarachnoid haemorrhage (SAH) accounts for 3% of all strokes and is the cause of 5% of stroke mortality. SAH by rupture of cerebral aneurysm or arterial-venous malformation (AVM) remains the most devastating cerebrovascular disease. During admission for SAH, about 30-70% of patients suffer a rebleed, and from all rebleeds, about 90% lead to death no matter the treatment. Available current scales help predict the prognosis and guide the therapy. Considering that the lifestyle risk factors for SAH are of increasing prevalence, it is expected that it will affect even more people in the future. SAH should not be regarded as a disease but rather a set of events with devastating complications requiring adequate management from debut extending long after patient discharge.

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EPIDEMIOLOGY

Subarachnoid haemorrhage stands for 3% of all cerebral vascular strokes and is responsible for the 5% mortality coming from CVAs. Incidence peak for SAH is 55-60 age group. During hospital admission for this pathology 30-70% of patients suffer a rebleed and approximately 90% of all rebleeds will end in death whatever the treatment.

PHYSIOPATHOLOGY AND AETIOLOGY

Subarachnoid haemorrhage occurs as a consequence of a blood vessel rupture in the subarachnoid space or near it. Following this rupture, blood will invade the space between the pia mater and the arachnoid,

the subarachnoid space, which normally contains just cerebrospinal fluid.

Etiologically, which is considering the reason that led to the event, following types of SAH stand out – traumatic SAH or spontaneous.

The spontaneous form of SAH occurs in cases of high arterial blood pressure (hypertensive SAH) or is the direct consequence of an aneurysmal rupture, a cerebral or spinal arterial-venous malformation rupture or secondary to cervical-cerebral arteries dissection. [3,12] Actually about 85% of all SAH forms are due to the rupture of a cerebral aneurysm. Brain aneurysm typically occurs during spring and autumn and is considered directly linked to temperature changes, similar to CVAs. [2,12]

A rare form of spontaneous SAH is the idiopathic subarachnoid hemorrhage, in the presence of risk factors considered non-traditional and *modifiable* – alcoholism, smoking, cocaine or amphetamine abuse. Besides these forms, literature provides a series of traditional risk factors, which are not subject to medical or lifestyle intervention and thus called *non-modifiable*, frequently linked to SAH occurrence: family history of SAH, soft tissue disease (polycystic kidney disease, neurofibromatosis type I, Ehlers-Danlos syndrome mainly type IV and other collagen abnormalities), female sex (1.5 times the risk), African descent (2 times the risk), Japanese or Finnish descent, vasculitis, even more rare factors – parasitosis, Moya-Moya disease, eclampsia, blood disorders, coagulation disorders. [1,2,11,12] It is important to point out that as prevalence of the non-modifiable risk factors gets higher, it is expected that SAH incidence will increase in the following decades.

Clinic of subarachnoid haemorrhage

Clinically the first symptom and nonetheless the most constant is severe headache with sudden onset – approximately 97% of cases, describes as a *thunderclap headache* and acknowledged by the patient as "the most intense headache I ever had". [12]

A more particular situation is the *sentinel headache* – a sudden and severe pain that goes away, allowing for a symptom-free period with neglection of said episode, followed shortly by severe mental status alteration, paroxysmal phenomena known by neurosurgeons as "walk, talk and die patients." [1,3]

Photophobia as an accompanying symptom is frequent, together with ocular symptoms such as subhialoid hemorrhage, retinal or vitreous hemorrhage. In medical literature vitreous hemorrhage associated with SAH is known as Terson's syndrome. [8]

Eye fundus examination may reveal papillary edema secondary to increased intracranial hypertension secondary to bleeding into the subarachnoid space. Vegetative phenomena such as emesis or syncope are common.

Sometimes, although not rarely the patient seeks medical attention after a loss of consciousness episode or for altered mental status, as neurological status on admission might vary from slight confusion to deep coma. Epileptic seizures occur frequently as about 20% of patients develop such symptoms in the first 24 hours since debut. They are considered to be a straight effect of increased intracranial pressure, associated hyponatremia or aneurysm site, especially when it involves sylvian arteries territory. [3,9]

Neurological examination reveals early meningeal signs: neck stiffness, headache, photophobia, ocular pain, emesis. Neck stiffness usually develops within 6 to 24 h from the debut of SAH. Within a few hours from debut signs such as Kernig, Brudzinki or bilateral Lassegue can appear or focal neurological signs. *Psychiatric acute onset* is more common and sometimes even specific among elderly patients. Some other accompanying signs or symptoms are acute urinary retention, diminished or abolished osteo-tendinous reflexes (usually after 4 to 6 h from the debut of the hemorrhage) and eventually focal neurological signs. Elderly patients, most commonly after 70 years old very often present with a far worse neurological status on admission. [9,12]

Diagnosis

The elective diagnostic tool in SAH is the plain cerebral CT examination on arrival in the emergency room, which shows blood in the subarachnoid space. The Fisher grade is thus immediately established. This diagnostic imaging tool is nonetheless the actual gold standard in diagnosing the subarachnoid hemorrhage, its limitation being that when not enough time since the debut of the hemorrhage has passed, the first examination might turn out negative

and will become positive a few tens of minutes later. The Fisher grading system is based upon the results of the plain cerebral CT examination and it appreciates the risk of developing cerebral vasospasm. It is summarized in the table below. [14]

Fischer Grade	Presence of blood in the SA space	Other aspects	Vasospasm risk
Grade 1	No blood in the cisterns	No clots	21%
Grade 2	Blood <1 mm thickness	No clots	25%
Grade 3	Blood >1 mm thickness	+/- clots	37%
Grade 4	Rare blood, diffusely in the basal cisterns	Intraventricular hemorrhage or parenchymal	21-37%

Table 1. Fisher Scale (1982).

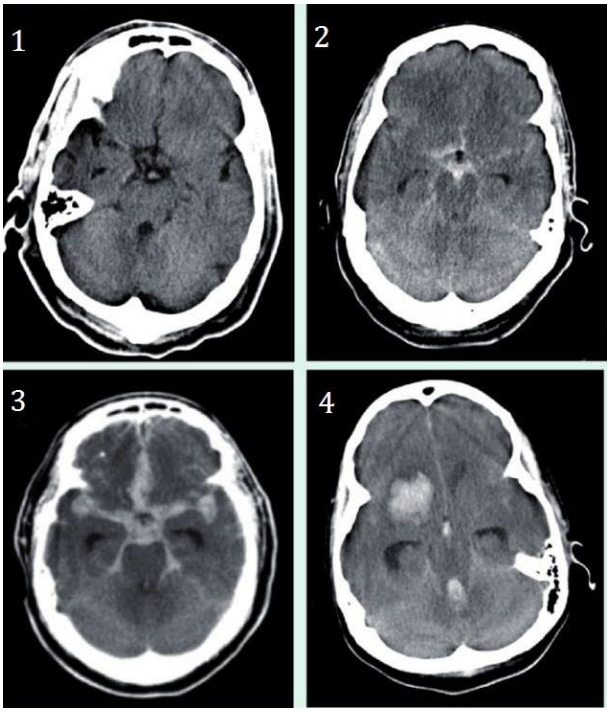

Figure 1. Cranio-cerebral CT axial sequences showing the 4 Fisher grades (1 – grade 1, 2 – grade 2, 3 – grade 3, 4 – grade 4). Source Future Neurol @ 2013 Future Medicine Ltd.

If the CT examination is negative but the clinical suspicion of SAH is still high, a lumbar puncture may be helpful for diagnostic purpose, but it is to be performed with every precaution and only after eye fundus examination excludes intracranial hypertension, in order to avoid cerebral herniation. This procedure can induce a rebleed if intracranial pressure is too abruptly decreased, which is why a minimal amount of a CSF sample is to be drawn. [3,5] Lumbar puncture is according to available date the most sensitive diagnostic tool for SAH. A positive result consists of increased CSF pressure, xanthochromic CSF, more than 100 000 thousand erythrocytes per mm3, increased proteinorrhachia (>50 mg/dl) and normal or slightly decreased glycorrhachia (<50-70 mg/dl) [3,4,5].

Cerebral MRI imaging with FLAIR sequencing, CT angiography or MRI angiography do not add very much relevance to the SAH diagnosis in the first 24-48 hours following debut, but they prove to be excellent between day 3 and 7, with good premises for identifying a cerebral aneurysm and its anatomical features. [7]

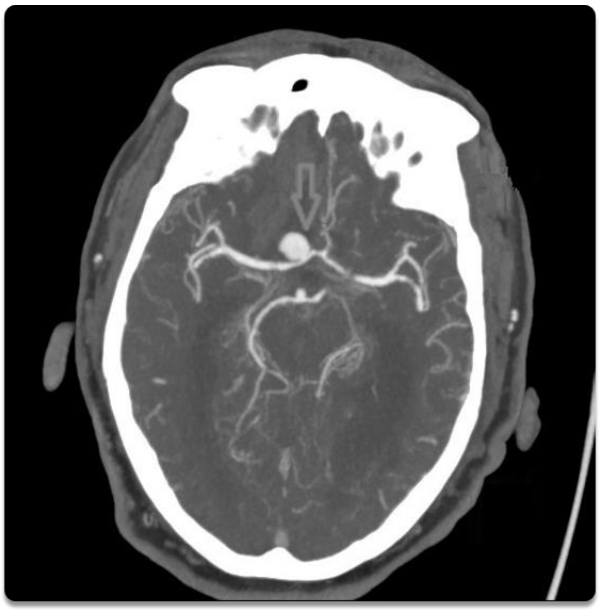

Figure 2. Axial enhancement cerebral CT sequence – red arrow points to an anterior communicating artery aneurysm – Collection of Neurosurgery I Clinic, Emergency University Hospital of Bucharest.

Digital subtraction angiography (DSA) - now a tool of capital importance in the management of subarachnoid hemorrhage – consists of selectively injecting contrast material using a catheter inserted into a large artery under radiologic screen. It is an extremely useful resource in the evaluation of cerebral aneurysms and it can also come in as a both diagnostic and therapeutic tool, providing the possibility of simultaneously embolizing the incriminated aneurysm or AVM.

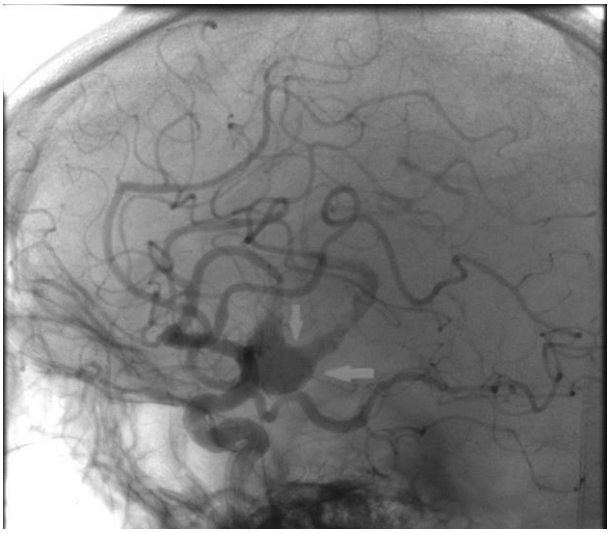

Figure 3. Right sylvian artery giant dissecting aneurysm near M1 and M2 segments junction. Right internal carotid angiography clichee. Collection of Neurosurgery I Clinic, Emergency University Hospital of Bucharest.

Aneurysm with sacs smaller than 5 mm are ideal for endovascular coiling, while for the rest of them the risk of recanalization or incomplete occlusion are considered too high, thus needing stent or balloon assisted coiling.

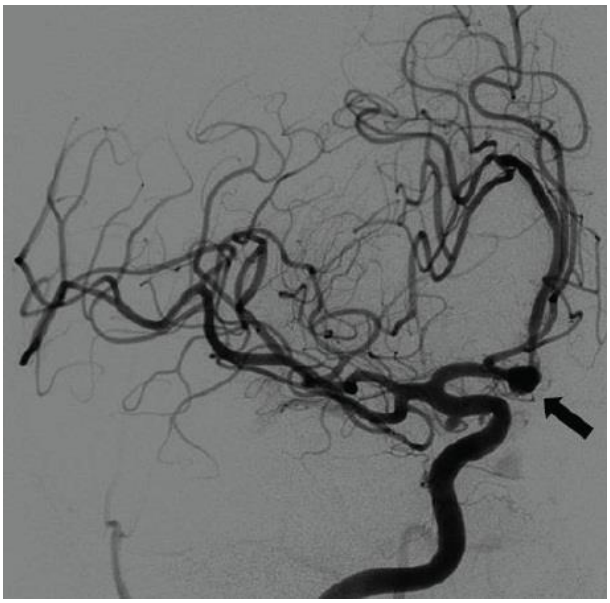

Figure 4. Digital subtraction angiography sequence – black arrows points to a anterior communication artery aneurysm – Open Source image.

Management

Once the diagnosis has been confirmed therapeutic measures are immediately started based on patient's clinical and neurological status and in closed connections with SAH etiology. Diagnosis is further completed with other needed tests. The patient should be admitted into a neurosurgical service with dedicated intensive care unit in case of need of advanced vital function support.

Drug treatment consists of maintaining an optimal blood pressure of systolic BP < 160 mmHg, considering that high blood pressure values are associated with worsening SAH and rebleed risk. Vasospasm prevention is to be addressed by administering Nimodipine. Cerebral edema prevention, maintaining normal volemia and preventing hyponatremia are the next medical considerations, as even with maximal therapy they are extremely difficult to correct if they occur. Anti-seizure prophylaxis is mandatory because of the irritation of cerebral cortex by blood in the subarachnoid space. [6,9]

The neurological status of the patient suffering from SAH is to be appreciated with the help of Hunt & Hess scale and WNFS scale (World Neurosurgical Federation Society scale - 1988) and it is extremely important in the surgical indication. Classification into a Hunt & Hess (1968) grade is determined after clinical and neurological assessment as follows: [15]

Grade I: absent or mild headache, absent or minimal neck stiffness
Grade II: severe headache, franc neck stiffness, possible cranial nerves paresis
Grade III: confusion or lethargy, mild focal deficits
Grade IV: stuporous, hemiparesis forte, decerebrate
Grade V: comatose, decerebrate.
WFNS Scale is based upon Glasgow Comma Scale and the presence or absence of neurological deficits as such:
Grade I: GCS 15 points, no neurological deficits
Grade II: GCS 13-14 points, no neurological deficits
Grade III: GCS 13-14 points, present neurological deficits
Grade IV: GCS 7-12 points, whatever the neurological deficits
Grade V: GCS 3-6 points, whatever the neurological deficits.

Another scale of great clinical and therapeutical significance is the Fisher scale previously presented, with four degrees of severity, based upon computed-tomography aspects such as the presence of blood

in the ventricular system or parenchymal hematoma and thickness of subarachnoid blood.

The right moment to perform surgery in aneurysmal SAH is nowadays considered to be at 24-72 hours from debut in patients with Hunt & Hess grades 1 or 2 and consists of aneurysm securement through classical surgical clipping or endovascular coiling. Patients with a higher Hunt & Hess grade (altered mental status or neurological deficits) are to be admitted and monitored in the intensive care unit for vital functions support with the goal of obtaining a better neurological status in order for the aneurysm securement to be achievable with a more favorable risk/benefit balance.

Exception to this rule occurs when SAH of any etiology is accompanied by large parenchymal hematoma (Fisher grade IV) that come with vital risk to the patient and it requires emergency intervention whatever the Hunt & Hess grade. A similar situation occurs when patient's life is endangered on the sort-term due to intracranial hypertension (secondary to acute obstructive hydrocephalus following SAH) - a external ventricular drainage is placed together with an *intracranial pressure monitoring device* – in order to obtain clinical and neurological amelioration until definitive treatment of the cause that led to SAH is possible. [9, 10]

Following surgery, after securing the aneurysm whose rupture produced the subarachnoid hemorrhage, together with general medical measures and complications prevention, a transcranial Doppler ultrasound is needed in order to appreciate the blood flow through the main cerebral arteries and possible vasospasm, as well as control cerebral CT examination for the verifying of occlusion devices used and for the visualizing the aspect of the ongoing SAH. In cases of drug resistant vasospasm *intraarterial endovascular vasodilator therapy* may be used – vasodilator agents are selectively injected directly into the cerebral arteries under angiographical control.

Complications

In the postoperative period medical treatment measures must be continued. Considering the risk of rebleed, which stand at 30-70% despite adequate treatment and knowing that 90% of rebleed lead to death, postsurgical patients must be monitored in the intensive care unit.

Despite these therapeutic resources, the major risk of devastating complications particularly difficult to treat persists – cerebral vasospasm and late cerebral ischemia, vegetative phenomena of central origin, parenchymal hematoma, rebleed, electrolytes imbalance, normal pressure hydrocephalus. [10]

The risk of developing cerebral vasospasm stands present since the debut of SAH but is considered to be at its highest between days 3-7 and extending up to 3 weeks. It is very accurately appreciated with the help of the Fisher grading system, risk correlation being proportionate with a higher grade.

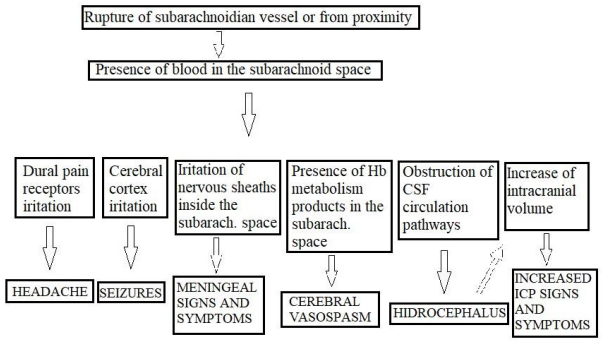

Figure 5. Résumé of SAH complications and their mechanism. Personal illustration.

Neurological rehabilitation

The treatment of subarachnoid hemorrhage is a multidisciplinary one, step-by-step and one which address simultaneously the etiological factor, the worsening factor and at the same time the prevention of complications. [2,12] For a favorable outcome and prognosis, and also for survivors' rehabilitation a quick and adequate diagnosis is required. It should happen in a primary neurosurgery center with radiology and intensive care optimal facilities available at all times. The prognosis of these patients and their neurological rehabilitation require the right cooperation between the medical team consisting of emergency room physician – radiologist – interventionist – neurosurgeon – intensivist – neurologist and rehabilitation physician.

Conclusions

A curative *treatment* of subarachnoid hemorrhage is out of the question at the moment, with it being not actually a disease but rather a course of pathological events that develop in a chain like manner and that

imply a series of serious consequences over cerebral structures, both short term and long term.

Methods of treatment of SAH complications are currently under development, and even though they are based on hypotheses decades old, some of them are highly debatable according to some authors, such as subarachnoid space washout-out with drugs designed to prevent vasospasm. [13]

Considering that about 15-20% of patients that suffer from SAH decease before getting to medical attention of any kind according to WHO data, and that 40% of survivors from SAH of any kind will have permanent neurological deficits, two things stand out: early identification of high suspicion SAH cases is critical and referral to an *emergency neurosurgical service* is of paramount need.

Abbreviations

AVM – arterial-venous malformation;
BP – blood pressure;
CSF – cerebrospinal fluid;
CVA – cerebrovascular accident;
ICP – increased intracranial pressure;
WHO – World Health Organization.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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Meningioma in shape. Can the appearance of tumour margins be considered as a prognostic factor?

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Keywords
atypical meningioma, tumour shape, tumour margins, recurrence, prognostic factors

ABSTRACT

Objective: The aim of this study was to evaluate the possible relationship between the appearance of tumour margins of atypical meningiomas and the risk of tumour recurrence, as well as progression-free survival. We also evaluated the correlations between the tumour margins and the neuroimaging characteristics (e.g. brain oedema and contrast enhancement) along with pathological features (e.g. brain invasion and mean value of Ki-67 LI).

Material and methods: In our study, we included 81 patients diagnosed with atypical meningioma (grade II meningioma), who have undergone surgery at the "Prof. Dr N. Oblu" Emergency Clinical Hospital Iasi, between January 1, 2010, and December 31, 2019. We followed the MRI imaging characteristics (e.g. tumour margins patterns, contrast enhancement, oedema grading and tumour volume), but also the pathological characteristics such as brain invasion and the mean value of the Ki-67 labelling index. The assessment of tumour recurrence was made using MRI imaging (T1+ contrast), over a follow-up period of 5 years after the surgery.

Results: In our study, we observed that 59.3% (*n=48*) of meningiomas had an irregular appearance. The irregular margins predominated in the male population (65.1%) and were statistically significantly correlated with brain oedema ($p<0.001$), contrast enhancement ($p<0.01$), anatomical location ($p<0.014$) and the mean value of the Ki-67 labelling index ($p<0.01$). The tumour margins were not correlated with brain invasion or volume of meningiomas.

Conclusion: In our series of patients we found that the irregular margin was not a prognostic factor for tumour recurrence over a period of 5 years or for progression-free survival.

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Introduction

Meningiomas are the most frequent primary tumors of the central nervous system and represent about one third of all primary brain tumors (1). A preliminary study of ours has shown that in our region, the incidence of these tumors has increased in recent years (2, 3).

The World Health Organization (WHO) classification of central nervous system tumors, divides meningiomas into three major groups: WHO grade I meningiomas are typical or benign (88-94%), grade II meningiomas are atypical (5-7%), and grade III meningiomas that are anaplastic or malignant (1-2%) (4, 5). Although the vast majority of meningiomas are benign, these tumors are still a challenge for neurosurgeons and radiologists, especially in terms of neuroimaging features and the orientation of preoperative diagnosis. Regading this, various authors have reported certain "malignant" neuroimaging characteristics, such as: bony destruction, hyperostosis of the adjacent skull, extracranial tumor extension through the skull base, marked peritumoral brain edema, arterial encasement, absence of calcifications, presence of irregular margins or "mushrooming" (6–8). However, many of these studies have limitations, and no one can specify a clear predictive value for these characteristics. Moreover, there is no MRI or CT feature that can clearly distinguish between a benign and a malignant meningioma (9). Concerning the prognostic value of the appearance of tumor margins, previous studies have reported that the irregular margins of meningiomas and their lobulated appearance are associated with brain invasion and denote malignant behavior of the tumor (10–14).

The development of imaging techniques in recent years, especially MRI, allowed to perform a predictive analysis of malignancy degree. This was posible corroborated with clinical data, tumor morphology and also with imaging characteristics (study of perfusion, diffusion coefficient, spectroscopy - in MRI imaging) (15). It seems that these preoperative imaging studies can improve both the management strategy and the prognosis of these patients (16,17).

The aim of our article is to identify in a group of atypical meningiomas (AMs), the prognostic value of margins for recurrence and progression-free survival (PFS), but also to analyze the correlations between the tumor margins and other neuroimaging features (brain edema and contrast enhancement) and pathological characteristics such as brain invasion and the mean value of Ki-67 labeling index (LI).

Materials and methods

In this study we evaluated the imaging characteristics in 81 patients with AMs, who had undergone surgery in the Department of Neurosurgery, from Prof. Dr. N. Oblu Emergency Clinical Hospital, and the patients were followed between January 1, 2010 - December 31, 2019. The preoperative MRI factors assesed were: (1) tumor margins (regular vs. irregular), (2) the grade of peritumoral brain edema (absent, mild, moderate or severe), (3) contrast enhancement (homogeneous vs. heterogeneous), (4) anatomical location, (5) tumor volume and (6) recurrence. We also evaluated pathological characteristics such as brain invasion and the mean value of the Ki-67 LI. The tumor margins were delineated on preoperative MRI (contrast-enhanced T1WI) and were classified as regular or irregular. Brain edema was evaluated in the T2WI sequence, as hyperintense extension adjacent to the tumor and for grading, we used Hale scale: (0) no cerebral edema - absence of high T2WI signal around the meningioma, (1) mild edema - ring of high T2WI signal surrounding the meningioma, but without mass effect, (2) moderate edema - more extensive edema, but without mass effect, (3) severe edema - mass effect on neighboring structures or deep digitiform edema in the white matter (16,18). Regarding the anatomical classification, meningiomas were classified as follows: (1) skull base meningiomas, (2) convexity meningiomas, (3) parasagittal-falcine meningiomas, (4) posterior fossa meningiomas and (5) intraventricular meningiomas. Tumor volume was calculated according to the formula = π/6 x length x width x height (18–21), and mean tumor volume was 26.4 cm3. Patients underwent MRI imaging annually, for a period of 5 years, and tumor recurrence/progression was defined as any contrast-enhancement at the level of the remaining tumor bed, or the increase in volume of the remnant tumor (18).

The statistical data processing was made in SPSS 24.0 (SPSS Inc., Chicago, IL). The data were characterized through descriptive statistics and frequency distributions. We used the following tests: Kolmogorov-Smironov test, t-Student, ANOVA tests, Mann-Whitney and Kruskal-Wallis tests and Chi-squared test. A p value of 0.05 was considered

significant. The actuarial data were represented with Kaplan-Meier plots, and the cumulative incidence curves were compared using the log-rank test. The study was approved by the Reasearch Ethics Committee of the "Grigore T. Popa" University of Medicine and Pharmacy.

Results

The study group included 81 patients of which 53.1% (n=43) were male. The mean age was 61 years (range 37-87 years). In the study group we observed that 59.3% (n=48) of meningiomas had irregular margins. This appearance of irregular margins was mainly in the male population, in a percentage of 65.1% (28 patients out of a total of 43 men male).

Results concerning preoperative imaging features

The appearance of the tumor margins were found to have a significant statistical influence on brain edema (p<0.001). In the study group, 73.3% (n=22) of patients with severe brain edema had irregular margins and 72.2% (n=13) of patients with moderate edema had irregular margins. Beside this, 86.7% of patients without brain edema had regular margins (Table 1). Between the appearance of tumor margins and contrast enhancement we identified a statistically significant correlation (p<0.01). Also, 72.7% of tumors with regular margins were homogeneous.

Between the tumor margins and the anatomical location of meningiomas, we observed a statistically significant difference (p<0.014). Thus, in the cases of parasagical-falcine meningiomas, 90.5% (n=9) had irregular margins, as well as 52.9% (n=9) of the skull base meningiomas. 50% (n=7) of all convexy meningiomas had irregular margins. There were no statistically significant differences between the tumor margins and tumor volume (p<0.221). We noticed instead that 65.9% (n=27) of patients with tumor volume > 26.4 cm3 had irregular margins (Table 1).

Results concerning pathological aspects

Of the 12 patients with brain invasion, 9 of them had irregular margins. However, we did not identify a statistically significant correlation between the tumor margins and brain invasion. Between the mean value of Ki-67 LI and the appearance of tumor margins we found a statistically significant correlation (p<0.01). 78.9% of patients with regular margins had Ki-67 LI <7% of the (Table 1). On the other hand, 15 patients with irregular marginis, out of 19, had Ki-67 LI > 8%.

Recurrence and progression-free survival

The tumor margins did not statistically significantly influenced the recurrence rate (p<0.111). However, of patients with irregular margins, 60.4% (n=29) relapsed in the 5-year follow-up period, in contrast to patients with regular margins, who relapsed less (42.4%; n=14). Although we did not identify statistically significant differences between the tumor margins and PFS (p<0.067), we observed that patients with regular margins had a better mean PFS (52 months), in contrast to patients with irregular margins, who had had a lower mean PFS (43.7 months). All the results are presented in Table 1.

Characteristics	**Tumor margins**		***p*-Value**
	Irregular n (%)	**Regular n (%)**	
Brain edema			p<0.001
Absent	2 (13.3%)	13 (86.7%)	
Mild	11 (61.1%)	7 (38.9%)	
Moderate	13 (72.2%)	5 (27.8%)	
Severe	22 (73.3%)	8 (26.7%)	
Enhancement			p<0.01
Homogeneous	27 (56.3%)	9 (27.3%)	
Heterogeneous	21 (43.8%)	24 (72.7%)	
Tumor location			p<0.0014
Parasagital-falcine	9 (90.5%)		
Skull base	9 (52.9%)		
Convexity	17 (50%)		
Posterior fossa	2	4	
Volume			
> 26.4 cm^3	27 (65.9%)		
< 26.4 cm^3	21 (52.5%)	19 (47.5%)	
Pathological aspects			
Brain invasion present (*n=12*)	9 of 12 (75%)	3	
Ki-67 LI >8% (*n=45*)	15	4	p<0.01
Recurrence (*5 years*)	29 (60.4%)	14 (42.4%)	
Progression-free survival (*months*)	43.7	52	

Table 1. Imaging and pathological characteristics in relation to tumor margins.

Discussions

In this retrospective study from a single-institution case series of AMs, we analyzed the usefulness of evaluating the appearance of tumor margins for tumor recurrence and PFS, but also the correlations between the tumor margins and other radiological

features (brain edema and contrast enhancement) and pathological findings (brain invasion and the mean value of Ki-67 LI).

Correlations between the tumor margins and brain edema

Analyzing the correlation between tumor margins and the degree of peritumoral cerebral edema, we observed statistically significant differences (p<0.001). Thus, almost half of the patients with irregular margins (45.8%) had severe brain edema, while 39.4% of patients with regular margins have no cerebral edema, or it was minimal (21.2%). Thus, we can consider that the irregular margins of a meningioma may be a predictor of the occurrence of brain edema (Figure 1).

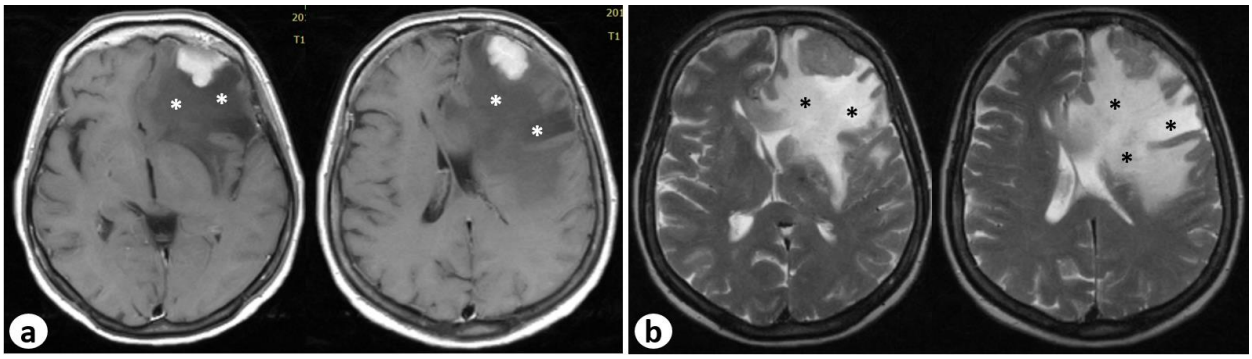

Figure 1. Illustrative examples of the analysed MRI variables: (a) axial T1-weighted MRI shows an irregular tumor shape with mushroom-like growth and peritumoral edema (white asterisk). (b) T2-weighted MRI shows the same tumor, with severe peritumoral edema which compresses the lateral ventricles (Hale 3 grade) (*black asterisk*).

Consistent with our results, Lobato *et al.* reported a statistically significant difference between the tumor margins and brain edema. He found that patients who had meningiomas with an irregular margins, had a 2.9 times higher risk for brain edema (10). Although cerebral edema can also occur as a result of brain invasion, there are additional biological mechanisms involved in the occurrence of this phenomenon, such as ischaemia from tumor mass effect or venous congestion (5, 22). Also, Nakano observed with his collaborators a statistically significant correlation between brain edema and meningioma margins, both in univariate analysis and in multivariate analysis (23). The conclusion of his study was that the incidence of brain edema was significantly higher in the group of tumors with irregular margins (23).

Correlations between the tumor margins and contrast enhancement

In our study, we identified a statistically significant correlation (p<0.010) between the tumor margins and contrast enhancement. Thus, 72.7% of tumors with regular margins was homogeneous (Figure 2). The heterogeneous aspect of meningiomas can also be given by the presence of intratumoral necrosis (24), and this can also indicate a malignant histology of the tumor (10, 25). The most common mechanism of necrosis in meningiomas is due to hypoxia (26), and in turn, this occurs due to high metabolic demands, and may be related to a more aggressive tumor progression (27).

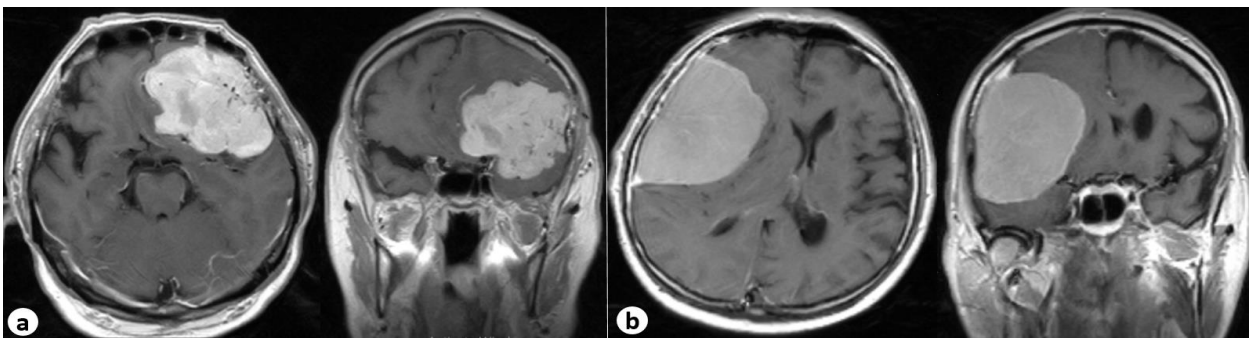

Figure 2. Illustrative examples of the analyzed MRI variables: (**a**) Axial and coronal contrast enhanced T1- weighted MRI showing a sphenoid wing meningioma with irregular margins and heterogeneous enhancement. (**b**) Axial and coronal contrast enhanced T1-weighted MRI showing another sphenoid wing meningioma with regular margins and homogeneous enhancement.

Correlations between the tumor margins and brain invasion

Analyzing the correlation between the margins and brain invasion, although there was no statistically significant difference between the two variables, we found that of the 12 patients with brain invasion, 9 of them had irregular margins (Figure 3, Figure 4.b.).

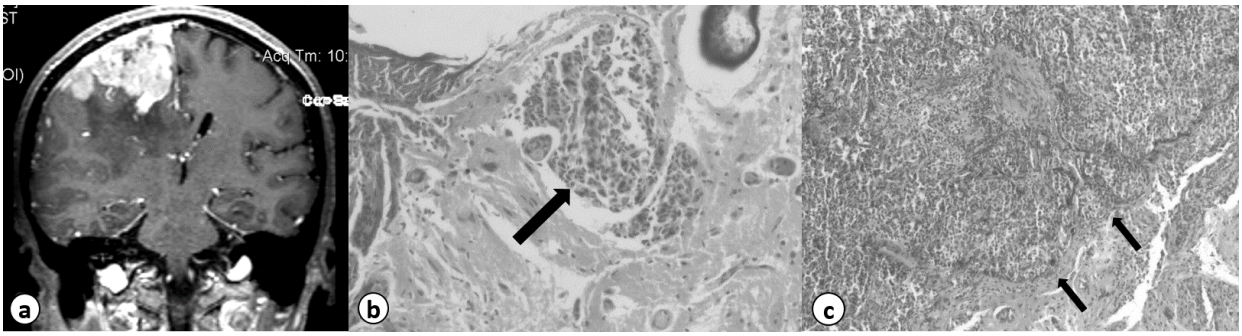

Figure 3. (**a**) Illustrative examples of the analyzed MRI variables: axial T1-weighted MRI shows an irregular tumor shape with mushroom-like growth. (**b**) Brain invasion revealed as small "islands" of tumor cells (*black arrow*) into adjacent nervous tissue, which also shows astrocytic gliosis (*HE, x200*). (**c**) Brain invasion as irregular projections of the tumor into adjacent nervous tissue without an intervening layer of leptomeninges at the tumor to brain interphase (*black arrows*). The adjacent brain parenchyma also exhibited astrocytic gliosis (*HE, x100*).

Some authors consider that the presence of irregular margins, as well as their lobulated appearance with fringed extensions to the brain parenchyma is associated with brain infiltration and denotes malignant tumor behavior (10–14,28). Among these authors, Adeli *et al.* observed a statistically significant correlation between irregular margins and brain invasion in 4% of 617 grade I, II and III meningiomas (28). In relation to brain invasion, in the evaluation of imaging factors, some authors observed that the absence of a cerebrospinal fluid rim separating the meningioma from brain, would suggest a higher histological degree of the tumor, due to the possibility of invasion of the adjacent brain tissue.

Correlations between the tumor margins and the mean value of the Ki-67 LI

Correlating the tumor margins with the value of the marker Ki-67 LI, we identified a statistically significant difference ($p<0.01$). Thus, 78.9% of patients with regular margins had Ki-67 LI <7% On the other hand, out of 19 patients with Ki 67 LI> 8%, 15 of them had meningiomas with irregular margins. Statistical significant differences were also reported by Beculic *et al.* between the two variables, noting that irregular margins were associated with higher Ki-67 LI values (30). Moreover, immunohistochemical detection of Ki-67 LI remins an important tool in addition to routine histopathological evaluation that can be used to predict tumor behavior of AM (31,32) (Figure 4).

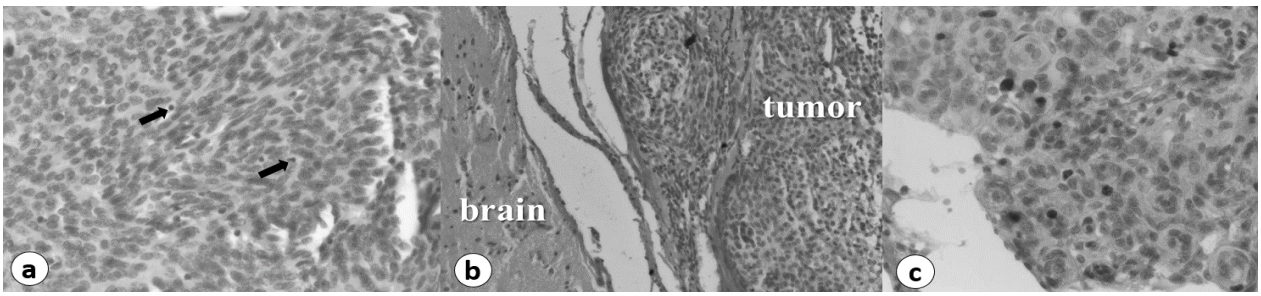

Figure 4. (**a**) Meningothelial tumor with sheet-like growth, increased cellularity and two mitotic figures/ high power field (*black*

arrows) (*HE, x400*). (**b**) Leptomeningeal tumoral invasion with a thin intervening layer of pia mater at the tumor (*black arrow*) to brain interphase (*white arrow*) (*IHC, anti-Ki67 antibody, x200*). (**c**) Nuclear immunoreactivity (8%) for Ki-67 LI in atypical meningioma, grade II of malignancy (*IHC, anti Ki-67- antibody, x200*)

The influence of tumormarginson recurrence

Until now, several authors have shown that grade of lobulation of a meningioma increases with the malignancy (33,34), so implicitly the irregular appearance of the tumor margins.

Irregular margins of meningiomas have been attributed to different growth rates in certain regions of the tumor (35) and are associated with increased cell proliferation (33) and an increased risk of tumor recurrence (7). In this regard, Zhang *et al.* demonstrated in a study of 33 AMs that tumors with irregular margins are more prone to malignant progression compared with AMs with regular margins (36). Also, Gobran *et al*. observed in its series of 138 intracranial meningiomas (all grades), that lobed-looking meningiomas had a recurrence rate of 23.5%, and mushroom meningiomas had a recurrence rate of 62.5% over a five-year period, observing a statistically significant correlation (37).

When we evaluated the relationship between the tumor margins and the recurrence, although we did not find any statistical corellation between tumor margins and recurrence, according to other studies (6, 38). However, we observed that the majority of meningiomas that recurred had irregular margins (60.4%). Moreover, 57.6% of regular-margin tumors did not recur over a 5-year follow-up period.

In the literature, the existence of irregular margins or "mushrooming" is considered to be an important prognostic factors for recurrence, as it could reflect the high proliferative potential of the tumor (7). Also, Nakasu *et al.* noted that tumors "mushrooming" tumors had the highest recurrence rate, followed by lobulated tumors and then tumors with smooth and irregular margins (7). Also Ildan *et al.* observed in 137 patients with grade I-III meningiomas, that mushroom - shaped meningiomas was associated with a significantly higher risk of recurrence than those with smooth margins (39). However, this atypical imaging feature of irregular margins cannot be considered as an indicator of a higher-grade behavior, and cannot be reliable and specific in differentiating benign and malignant meningiomas (40).

The influence of tumor margins on the progression-free survival

In our study, we observed that patients who had meningiomas with irregular margins had a lower rate of survival than those with regular margins (43.75 months vs. 52 months) (Figure 5). As we did not identify a statistically significant difference between the two variables in agreement with other authors (6), we can consider that the irregular appearance of meningiomas did not influence the PFS. However, other authors such as Nakasu *et al.* observed that irregular margins correlates with PFS (7, 41).

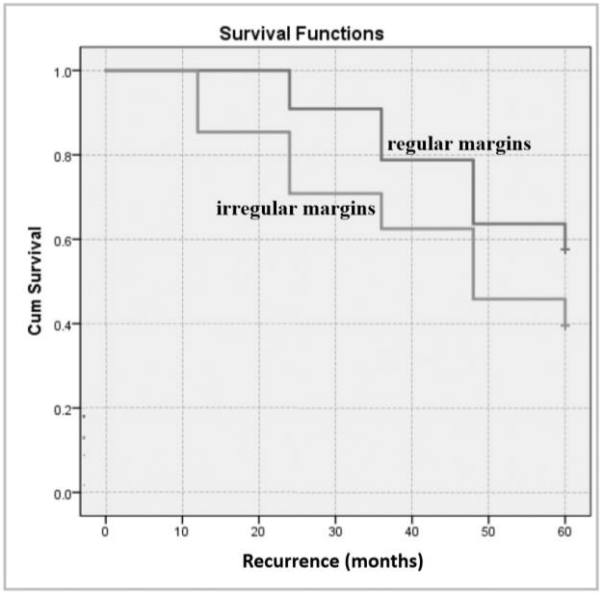

Figure 5. Progression-free survival depending on the appearance of meningioma margins. It is notable that patients with regular margins (blue line) had a better progression-free survival (52 months vs. 43.75 months).

Conclusions

We found that in our series of patients, that irregular margins has no prognostic value for tumor recurrence over a period of 5 years follow up and also for PFS, but instead correlates statistically with grade of brain edema, contrast enhancement and the mean value of Ki-67 LI. Even so, the appearance of tumor margins must be a factor to consider when evaluating neuroimaging of meningiomas and such studies should be extended to other types of intracranial tumors.

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The role of MRI-guided focused ultrasound in neurosurgery. A narrative review

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Keywords
MRgFUS,
movement disorders,
blood-brain barrier,
high focused ultrasound

ABSTRACT

Introduction. MRgFUS is a novel technology, which can have profound implications in the current treatment of neurological disorders. Its applications range widely, from the alteration of the blood-brain barrier, ablation of tumours to the treatment of movement disorders.

Objective. To review, following thorough research of the literature, the principles of its use in the treatment of neurological diseases and the main reported evidence of its clinical implementation.

Material and method. Interrogation of the MEDLINE database, using the PubMed search engine, for the following MESH words: "MRgFUS", "FUS" "BRAIN", from 2000 to the current year.

Conclusion. MRgFUS can be safely used today for the treatment of Essential Tremor. New research is warranted for the evaluation of its safety and effectiveness in other neurological disorders.

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INTRODUCTION

MRI guided focused ultrasound (MRgFUS) of the brain is a novel technology which has the potential to be implemented successfuly in our modern neurosurgical practice. Because of its capability to alter the blood brain barrier, ablate tumors and proven to be effective as a treatment of different movement disorders, it is worthy for us to gain familiarity with this technique. Unfortunately, novelty and the specific technicality of this instrument confuses the clinician. Therefore, we aim in this paper, by the means of a narrative review, to provide an insight on the working mechanism and the uses of the technology and to address the benefits and limitations of its applicability in the clinical practice.

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Method

Research of the MEDLINE database, using the PubMed search engine, for the following MESH words: "MRgFUS", "FUS" "BRAIN", from 2000 to the current year.

Background.

First studied by Lynn (1) at the start of the 20th century, the ability to focus ultrasound waves in order to produce a biological effect on the intracranial content was a tempting idea. Aided by the recent advances in high resolution MRI imaging, neuronavigation and the development of hemispheric piezoelectric transducer systems, we are now able to accurately focus the ultrasound waves intracranially, as demonstrated by the commercially available system ExAblate 4000 (InSightec LTD). The result of their application on the tissue can be divided into thermal and mechanical effects. As ultrasounds propagates through the tissue, they raise the local temperature and interact with the gas molecules, producing bubbling, oscillation and finally cavitation with the stretching of the cellular membrane as a result (2) . Based on these mechanical and thermal effects they can reversibly or irreversibly alter the brain tissue, depending on their strength and frequency.

The role of MRgFUS in tumor ablation

Ultrasound can aid in the treatment of deep brain neoplastic lesions, considered unresectable, or in patients that are unfit for surgery. Unfortunately, the data is scarce due to the relative novelty of the technology and the absence of clinical trials (3), (4).

In 2014, Daniel Coluccia published the results regarding the thermoablation of a left thalamic recurrent glioma, using ultrasound. He noticed a 10% reduction in tumoral volume at 5 days post procedure, with improvement in the neurologic status of the patient. At the 21th day check-up no increase in the volume of the tumor was observed (5).

Preliminary results, published by Ernst Martin, creates an insight on the thermoablative tumoral effect of the HIFUS system. Although the author reported clinical improvement in only one patient, it opens the pathway to the development of new clinical trials (6).

The role of MRgFUS on the permeability of the blood-brain barrier

The BBB is a complex structure serving the role of an interface between the blood and the cerebral tissue. Its cytoarchitecture is mainly represented by a layer of endothelial cells, binded one to another by tight junction proteins, interconnected with neurons, perycites and astrocytes (7). This renders it virtually impermeable to exogeneous molecules and thus limiting the effectiveness of different pharmaceuticeuticals. MRgFUS can be used to transiently open the BBB. Hynynen et.al, in his in vivo study, demonstrated that the BBB can safely be opened in rabbits, by applying low strength ultrasounds combined with the intravenous administration of preformed microbubbles. After applying the ultrasound field, these microbubbles oscillate, modify their form, thus stimulating the cerebral blood capillaries and opening the BBB. The effects are transient without significant side-effects (8) (fig 1.). Combining the microbubbles with contrast agent, enables us to accurately pinpoint the target anatomic structure, with the aid of imaging (9).

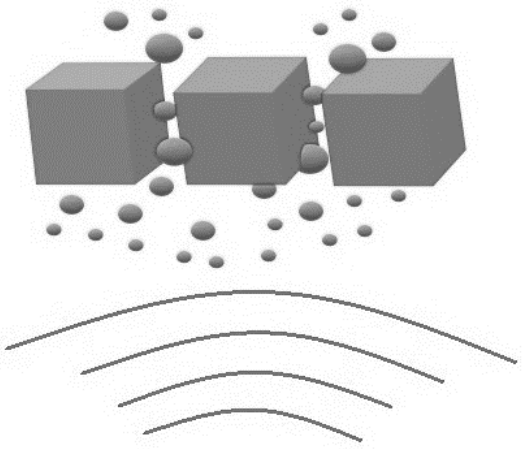

Figure 1. Vascular cells being stimulated (red cubes) by the ultrasound induced cavitation of the microbubbles (green spheres).

Agessandro Abrahao et al, in their human trial of 4 participants suffering from ALS, demonstrated the successful opening of the BBB, after sonification, without side effects (10). MRgFUS can be used in conjunction with systemic chemotherapy in the treatment of intracranial neoplasms. Liu HL et al, in their rat glioma model study, demonstrates a significant survival improvement in the combined

treatment group versus the single treatment group (53 days versus 29 days) (11). It appears that the opening of the barrier can significantly enhance the effect of immunotherapy on brain metastases, as demonstrated by Thiele Kobus et al, in their study (12). Finally, it has been shown that MRgFUS cand aid gene therapy pharmaceuticals in their permeation of the BBB as shown by Liu et al in their study (13).

The role of MRgFUS in the treatment of movement disorders and chronic neuropathic pain

Lesioning of the brain by stereotactic techniques along with DBS represent the mainstay of neurosurgical treatment in movement disorders. However, despite their effectiveness, they are not without potential side effects and contraindications. MRgFUS can be a valuable alternative tool in the treatment of these pathologies. Based on the principle of cavitation and thermoablation they can produce discrete lesioning of target anatomical areas, similar with stereotactic radiosurgery, but without harming the surrounding healthy tissue (14). Clearly, a positive ratio of reward versus risk associated with the technique has led different authors to implement it into clinical practice.

Zaaroor et al, in their study investigating the treatment of symptomatic Parkinson Disease and Essential tremor by HIFU VIM thalamotomy, reported a significant improvement in quality of life and reduction of symptomatology by approximatively 50% in the treated subjects. The effects persisted in all but 6 patients, at the 24th month follow-up. Common side effects were transient and represented by gait ataxia, hand paresthesia and asthenia (15).

Martínez-Fernández et al, in their randomised trial investigating the role of HIFU sub-thalamotomy for the treatment of Parkinson Disease numbering 40 subjects, 27 assigned to the procedure group versus 13 to the sham procedure, reported improvement of symptoms at 4 months post procedure by approximatively 50% in the treated subjects vs. the placebo. Common reported side effects are represented by slurred speech, dyskinesia and gait disturbance, with long term persistence in 6 treated patients (16).

Elias et al, in their trial with 76 enrolled participants, investigating the role of HIFU VIM thalamotomy in the treatment of patients suffering from essential tremor refractory to conservative therapy, reported a 41% improvement of the tremor at 3 months post procedure, respectively a 35% percent improvement in the treated group versus the placebo group. Common adverse effects included gait ataxia and paresthesias ,these being present in approximative 36% of the treated subjects (17).

Jin Woo Chang et al, which investigated the use of HIFU VIM thalamotomy in the treatment of refractory essential tremor in 76 patients, reported an overall of 53% improvement of the tremor at one year post procedure. Gait disturbances and paresthesias are reported as the most common adverse effects (18).

Another study investigating the role of HIFU thalamotomy in the treatment of Essential Tremor, with 26 participants, published similar results (19).

The evidence offered by the literature, which proves that HIFU thalamotomy is safe and efficient has led the FDA to approve it, in 2016, for the treatment of Essential Tremor (20), marking a cornerstone in it's pathway for clinical implementation.

It has been proven that MRgFUS can be used in the treatment of chronic neuropathic pain. First described in 2009, FUS medial thalamotomy can be a viable therapeutic approach of chronic neuropathic pain (21). Marc N Gallay et al, reports improvement of trigeminal neuralgia after central lateral FUS thalamotomy (22). Further clinical trials are needed in order to adequatly asses the possibility of these technique to be safely and successfully used.

Discussion

As previously shown focused ultrasound therapy has the capability to significantly alter the current paradigm of treatment used in neurological diseases. Regarding it's use on opening the BBB, it is possible that the translation of fundamental science into clinical practice, aided by the future realisation of clinical trials, will usher a new era in Neuro-Oncology (23), (24) and in the treatment of neurodegenerative disorders.

Several studies are currently investigating its role in the treatment of brain ischemia (25), (26). It remains to be seen if it will be effective.

In the field of movement disorders, unfortunately it is now limited only to the treatment of Essential tremor, but probably in the near future, will be extended for Parkinson Disease (27).

New progress in our understanding of the neurological pathology combined with technical improvements will probably advance this technology as a treatment for chronic pain (28) and other neuropsychiatric disorders, such as obsessive-compulsive disorder and depression (29), (30).

Conclusion

MRgFUS is a promising technology in the field of neuroscience. Although currently used in the treatment of movement disorders, further studies are needed for clear identification of its role in the treatment of different neurological diseases.

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The stent-assisted coil-jailing technique for very small intracranial aneurysm treatment

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ABSTRACT
The stent-assisted coil-jailing technique was initially introduced as an effective and secure method in the treatment of large wide-necked intracranial aneurysms. Later on, this technique has proved its efficiency in the safety and optimal treatment of very small aneurysms. In this article, we will present the successful treatment of a very small middle cerebral artery aneurysm using the stent-assisted coil-jailing technique and review the current trends in this type of treatment.

Keywords
very small aneurysm, stent-assisted coil-jailing technique

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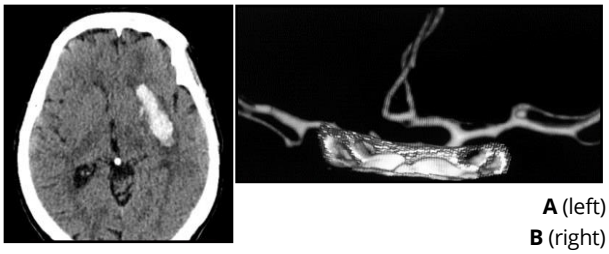
INTRODUCTION

With the advances in endovascular technologies, endovascular coil embolization of ruptured cerebral aneurysms has become the first efficient treatment option. Nevertheless, endovascular coiling of very small aneurysms remain controversial. Most of these particular vascular lesions are conformational characterized by a small dome and large-neck. The technical difficulties are represented by the high risk of procedure-related rupture and coil migration due to a very limited aneurysm volumes and structural restriction of embolization coils. Stent-assisted coil-jailing technique is a very popular endovascular method that could be feasible and effective for such structural complicated aneurysms. However, the technique should be used carefully and above all, its usage must be safe and lead to good clinical results with regard to aneurysm occlusion. In this report, we describe a successfully treated very small middle cerebral artery aneurysm using the stent-assisted coil-jailing technique in order to provide a more comprehensive view of this challenging endovascular treatment and eventually to offer helpful clinical information for the management of such cases [8].

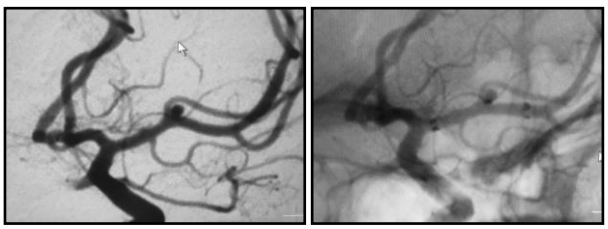
CASE PRESENTATION

A 50-year-old woman presented with a sudden-onset headache for which she addressed the emergency department at a local hospital. A

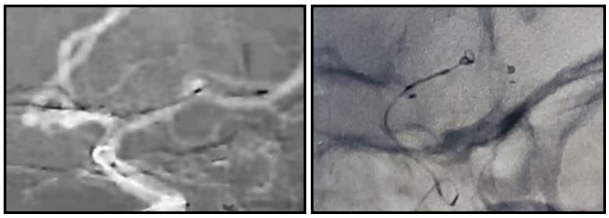
head CT-scan investigation was performed immediately and showed a lenticular hematoma and mild subarachnoid haemorrhage in the left Sylvian fissure. Due to the suspicion of an aneurysmal cerebral hemorrhage, the patient was immediately transferred to our hospital for further diagnosis and treatment. At admission she was confused and with right hemiparesis. Her past medical history included hypertension with no regular treatment. The brain CT angiography raised the suspicion of an aneurysmal dilatation on M1 segment of left middle cerebral artery. A subsequent subtraction catheter cerebral angiography confirmed a very small aneurysm at the origin of left Charcot artery. Due to the very small dimension of the aneurysm (2.3 mm × 2.0 mm) and relatively large neck a stent-assisted coil-jailing technique was proposed for the occlusion of the lesion.



A (left)
B (right)



C **D**



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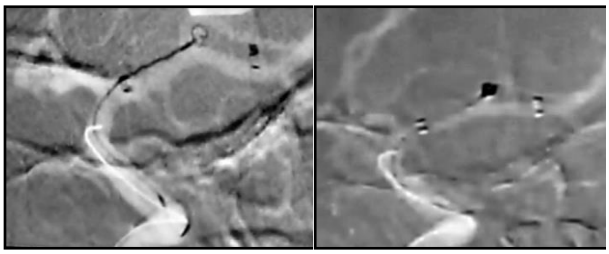

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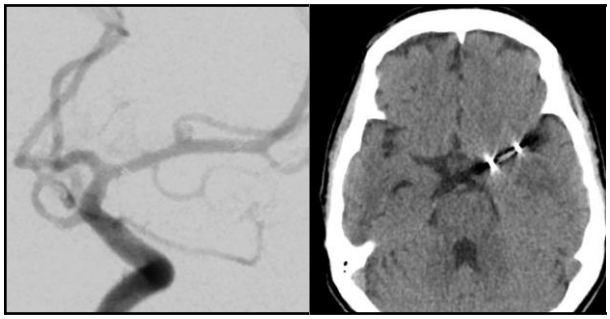
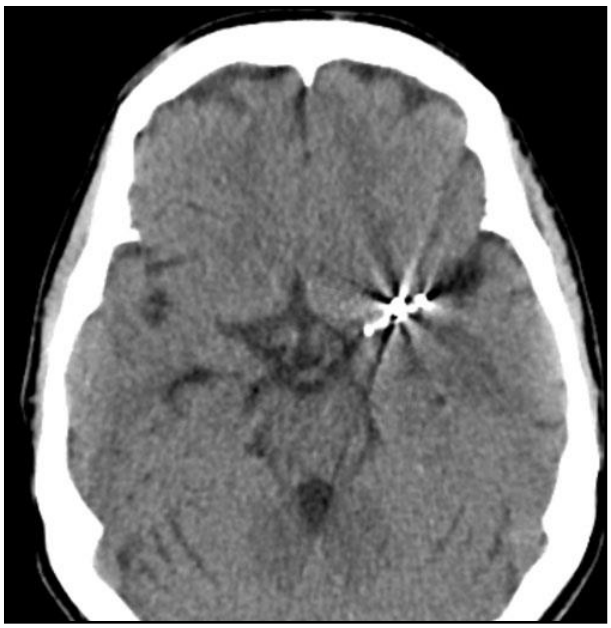


I **J**



K

Figure 1. A, B – Diagnostic cerebral CT and Angio-CT images; **C, D, E, F, G, H, I** – Intraprocedural DSA images; Postprocedural Cerebral CT Images.

The intervention performed the next day on a biplane angiography system (INFINIX, Toshiba, Canon Medical System) under general anesthesia by our neurosurgical team with many years of experience in neuroendovascular interventions. Written informed consent was obtained prior to the treatment. Commercially available 6F introducer sheath from Merit Medical was placed into the right femoral artery. A 6F Chaperon guiding catheters (Microvention) was carefully advanced over 0.035 glidewire up to the proximal segment of the left internal carotid artery. Using the 3D-CT images analysis a favourable working angle roadmap for the target aneurysm was obtained. A Prowler 10 microcatheter (Codman J&J) was then very carefully advanced over a 0.014 Transed microwire (Boston

Scientific) and positioned into the aneurysm sac. Keeping the microcatheter in this fixed position a second Prowler Select Plus microcatheter (Codman J&J) was inserted up to the M1 / M2 bifurcation level of the left middle cerebral artery. With its help a 4/16 mm Enterprise 2 intracranial stent (Codman J&J) is deployed over the aneurysm neck and the first microcatheter in a jailed configuration. After the Prowler Select Plus microcatheter withdraws, two Galaxy G3 MINI microcoils (Cerenovus Johnson&Johnson) were then inserted and detached into aneurysm. The coils placement was done very slowly, and gentle handling of the microcatheter was used to avoid tension build-up in the aneurysm and to allow the coil loop to form inside the aneurysm. After detaching the last coil, the microcatheter is carefully retracted so as not to cause any movement of the stent. A DSA acquisition is performed to check the permeability of all vessels and complete occlusion of the aneurysm. Finally, the entire guiding system is retracted with a compressive dressing of the femoral puncture site. The patient was placed into intensive care and received 75mg clopidogrel and 100mg aspirin daily. A cerebral CT scan was performed 7 days postoperatively and showed the lenticular hematoma resorption. The patient was discharged home after 3 days in good neurological condition.

Discussions

The literature reports that very small intracranial aneurysms (≤3 mm) represent 13.2%–15.1% of all intracranial aneurysms. On the other hand, according to ISUIA study only 0.1% (per year) of small aneurysms (<5 mm) of the anterior circulation will manifested by rupture. There have been also several particular studies that have reported incidences of small aneurysms of up to 7% of all ruptured aneurysms[s]. In this clinical situation an emergency treatment must be initiated. Endovascular coil embolization or microsurgical clipping of ruptured very small cerebral aneurysms are still challenging methods due to distinctive technical difficulties [t,x,s]. If in the case of endovascular treatment the very small size of the aneurysmal dome frequently associated with a wide neck make it difficult to place a coil safely, in the case of microsurgical treatment the thin-walled and too small neck make it difficult to accept a clip without narrowing or tearing the parent artery [3,6,9].

The stent-assisted coiling technique represents an efficacious adjuvant technique for treating wide-necked aneurysms. The advent of these adjuvant techniques has made possible the endovascular occlusion of an increasing number of very small aneurysms. The stent-assisted coil-jailing technique has become often considered as the most efficient option for the embolization of very small aneurysms. This technique allowed, not only to provided the necessary support to achieve a stable coil arrangement, but also solved the problem of overestimating the coil length in small aneurysms. By this technique, if the coil is too long for a small aneurysm, the remaining coil segment (tail) could be purposely left and jailed between the stent and the parent artery wall at the end of the embolization procedure.

The main complication reported in very small aneurysms was intraprocedural rupture. If the first studies reported significantly higher rates of procedural rupture, with the continuing development of endovascular devices and greater operator experience, the last ones did not show a significant association between very small aneurysms and intraprocedural rupture. It seems that the preferred use of stent-assisted coil-jailing technique might explain the evolution of the previously mentioned results. Obtaining a stable position of the microcatheter by fixing it between the arterial wall and the stent, as well as the possibility of coils insertion into aneurysm with the tip of the microcatheter in its neck area, without the need of navigation in the aneurysmal sac caused a significant reduction in the risk of intraprocedural rupture in very small aneurysms [1,3,6,9]

Another complication described in very small aneurysms was that of thrombemolism. Because of a restricted intra-aneurysmal space and an improper dome/neck ratio, coil migration and coil loop protrusion may frequently occur in very small aneurysms embolization. The thromboembolic complications rate for such events has been reported in the literature as varying between 2.1%–12%. The new designs of the intracranial stents and development of the assisted coil techniques have allowed the significant reduction of these complications by their ability to prevent the herniation of the coils and at the same time to fix outside the blood flow the possible oversized coils. These have also simplified the procedure and

prevent possible complications caused by the replacement of the coils [2,4,6].

The recurrence rates of previously coiled vary small intracranial aneurysms in early published reports were variably, in a range approximately similar to those of larger intracranial aneurysms (range from 21% - 15%) [s,t,x].With the increasing use of the jail technique in cases of embolization of very small aneurysms, new studies have reported much lower recurrence rates in these vascular lesions (range from 7.5 % - 1.5%.) [3.5.6.9].This technique has proven useful for the dense packing of the very small aneurysm and avoiding the recoiling of an inappropriate aneurysm occlusion.

Conclusions

The stent-assisted coil-jailing technique has been proven as an efficient approach for the treatment of very intracranial aneurysms with excellent and safety profiles. This technique allowed us both to support the coil loops in the aneurysmal sac by stabilizing the microcatheter and to solve the problem related to the possible oversizing of the length of a coil.

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Endovascular treatment options for carotid-cavernous fistulae

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ABSTRACT

A carotid-cavernous fistula is a pathological shunt between the internal or external carotid arteries and the cavernous sinus (CS). The arteriovenous shunt can be direct, between the internal carotid artery and the CS, or indirect, between meningeal branches from the carotid arteries and the dural coverings of the CS. Direct fistulas occur most commonly after craniofacial trauma, while indirect shunts result from various chronic diseases. Signs and symptoms depend on the venous drainage routes. Exophthalmos, chemosis, and diplopia are caused by venous drainage through the superior and inferior ophthalmic veins. If venous egress is mainly through the inferior petrosal sinus, patients complain of pulsatile tinnitus. Cortical venous drainage is the most dangerous route because it can lead to focal neurological deficits and intracerebral haemorrhage. Treatment of carotid-cavernous fistulae can be achieved through different endovascular techniques, using detachable balloons, coils, liquid embolic agents, covered stents, and flow-diverters. This paper aims to report three cases with carotid-cavernous fistulae, which were successfully cured using different transarterial and transvenous modalities.

Keywords
carotid-cavernous fistula, endovascular treatment, transarterial, transvenous

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INTRODUCTION

Carotid cavernous fistula (CCF) refers to an aberrant arteriovenous communication between the carotid arterial system and the venous compartments of the cavernous sinus (CS). Based on the arterial feeding source, CCF's can be direct or indirect.[1] According to the Barrow classification of CCF's, a direct, high-flow connection between the internal carotid artery (ICA) and the CS is regarded as a "type A" fistula. Indirect CCFs, which typically have a low flow, are classified as type B if they are supplied only by the dural branches of the ICA, type C by dural branches of the external carotid artery (ECA), and type D by both ICA and ECA dural branches. The majority of type A CCF's are more commonly a result of blunt or penetrating trauma, accounting for 75% of all CCF cases.[1] Clinical manifestations of type A fistulas depend on the venous outflow from the CS and include ocular pain, exophthalmos, chemosis, ocular foreign body sensation, visual disturbances, and headaches for an anterior superior ophthalmic venous route. Drainage

to the posterior venous outflow channels can lead to neurologic symptoms, such as aphasia and confusion.[2] Digital subtraction angiography (DSA) is the gold standard in the diagnosis of CCF. It must be performed before any potential intervention. Endovascular treatment is now the first therapeutic option for CCFs because it is associated with high occlusion and low complication rates.[3] Depending on the angioarchitecture of the fistula, endovascular obliteration can be achieved by a combination of coils, detachable balloons, liquid embolic agents, and stents.[4] This paper aims to present a case series of three patients with CCF's occluded using different transarterial and transvenous treatment strategies.

CASE DESCRIPTIONS

Case 1

A 17-year-old female patient was admitted in July 2020 to the emergency department of an outside hospital for craniofacial trauma with multifocal, displaced mandibular fractures, active bleeding in the oral cavity, and marked facial edema after a motor vehicle accident. Urgent maxillofacial surgery was performed to stop the bleeding and treat the mandibular fractures.

After several days the patient complained of left ocular pain. Periorbital edema, chemosis, and exophthalmia developed gradually afterward. CT angiography showed an enlarged left cavernous sinus compared to the contralateral side (Fig. 1, a) and a dilated, engorged superior ophthalmic vein. (Fig. 1, b, c). Five days later, she was transferred to our hospital for further investigations.

Catheter angiography confirmed a high-flow, type A, left carotid-cavernous fistula with a 4.2 mm direct "communication" between the ICA and the CS, located on the horizontal part of the cavernous segment (Fig. 1, d, e, f). Venous drainage was mainly through the superior ophthalmic vein, markedly enlarged, explaining her main signs and symptoms (Fig. 1, e). Additionally, drainage occurred in the pterygoid venous plexus, inferior petrosal sinus, and jugular vein, and through the coronary sinus in the contralateral cavernous sinus (Fig. 1, d). Based on the angioarchitecture of the fistula, a decision was made to occlude the fistula with coils through a transarterial approach using the balloon-remodeling technique.

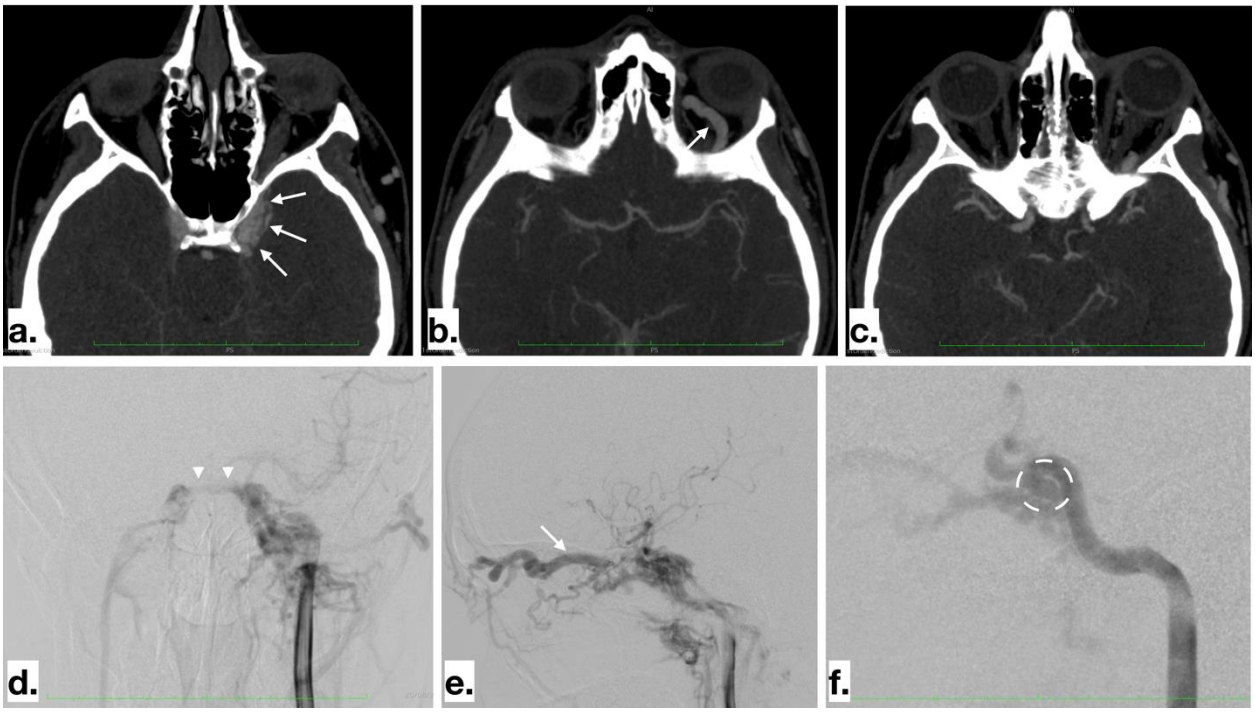

Figure 1. Axial CT angiogram images in **a.** enlarged left CS (white arrows), **b.** engorged left SOV (white arrow), **c.,** and left exophthalmia. DSA images in **d.** frontal projection, the drainage through the coronary sinuses (arrowheads) in the contralateral CS, IPS, and internal jugular vein, **e.** lateral projection, engorged SOV (white arrow), **f.** lateral projection, the "venous pouch" connected to the ICA (white circle). CS=cavernous sinus; SOV=superior ophthalmic vein; DSA=digital subtraction angiogram; IPS=inferior petrosal sinus; ICA=internal carotid artery.

On the following day, under general anesthesia, through a right femoral approach, a 6F guiding catheter was placed in the distal cervical ICA, followed by navigation of a microcatheter in the CS and a hypercompliant balloon in the carotid siphon (Fig. 2, a). While the balloon was inflated over the arterial "tear," six bare platinum, detachable coils were implanted through the microcatheter into the left cavernous sinus (Fig. 2, b). No antiplatelet therapy was used during the procedure. After the first coil was deployed, a bolus of 5000 IU of unfractionated heparin was administered intravenously. After the 6th coil was introduced, complete obliteration of the fistula was obtained (Fig. 2, c, d). There were no periprocedural complications. Immediately after the procedure, the patient was extubated. Her symptoms regressed completely over the following days, and she was discharged four days later. A control angiogram was performed three months later, confirming the total exclusion of the fistula without additional sequelae (Fig. 2, e, f).

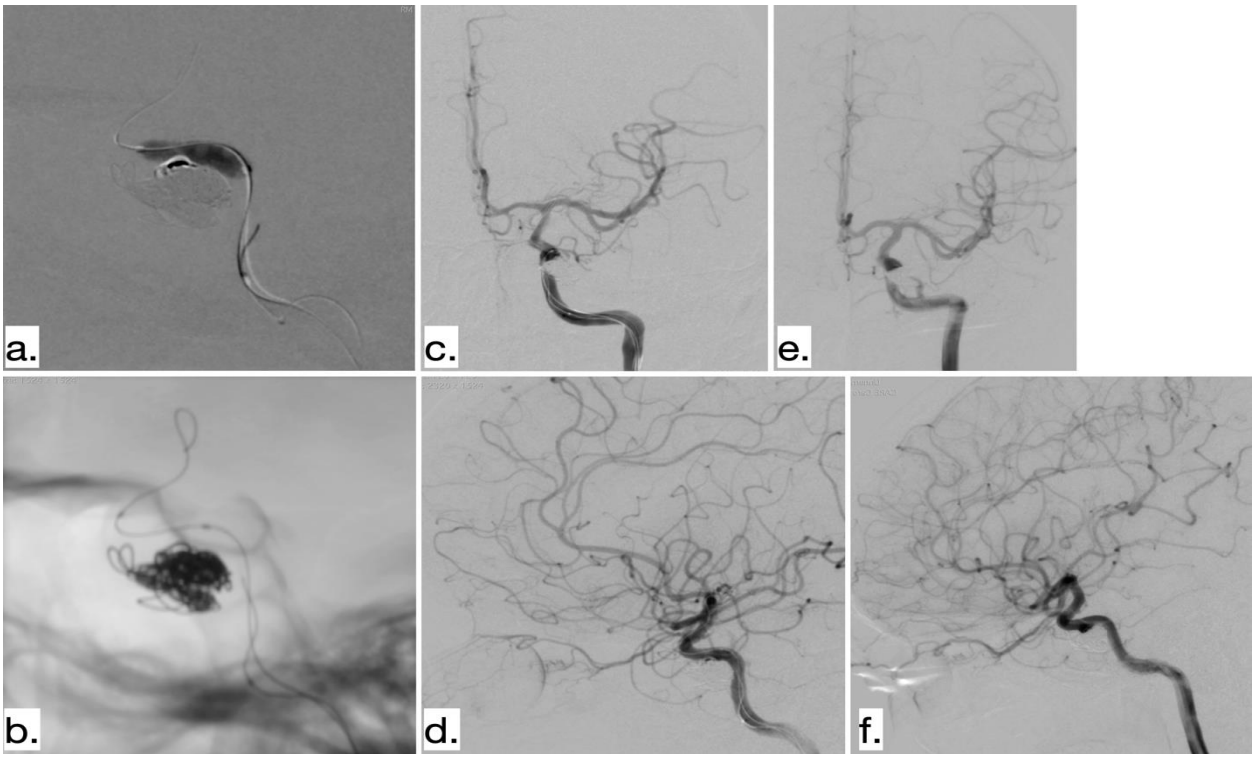

Figure 2. a. blank roadmap image shows the inflated balloon in the ICA, overlying the coil mass; **b.** lateral projection fluoroscopy image: the coil mass is better seen; **c, d.** frontal and lateral projection DSA images immediately after the procedure showing complete obliteration of the fistula; **e, f.** control angiogram after three months demonstrating cure of the fistula. ICA=internal carotid artery, DSA=digital subtraction angiogram.

Case 2

An 8-year-old boy was admitted to our hospital with exophthalmos and chemosis of the left eye, which developed gradually for the last week before admission. Upon neurological examination, the patient was conscious, cooperative, with motor aphasia and right hemiparesis. His neurological deficits resulted from a left hemispherectomy, which he received after significant head trauma during a motor vehicle accident seven months prior. The following day, under general anesthesia, a catheter angiography revealed a left high-flow Barrow type A carotid-cavernous fistula (Fig. 3 a, b). The fistula was also opacified retrogradely from the vertebral artery (Fig. 3 c, d). In addition, due to the high flow, aspiration from the external carotid artery via artery of foramen rotundum was evident (Fig. 3, g).

A decision was made to cure the fistula by sacrificing the left ICA with coils. A 6F guiding catheter was placed in the left ICA, followed by navigation of a microcatheter in the supraclinoid segment. Two Penumbra Occlusion Devices were deployed distal and proximal to the fistula (Fig. 3, e), achieving complete obliteration of the ICA and fistula. The

enlarged artery of the foramen rotundum was occluded with a 1mm Target Nano coil (Fig 3. g, h). A cure of the fistula was immediately seen upon contrast injection in the vertebral artery (Fig. 3, i). Chemosis and exophthalmia gradually improved following the procedure, and the patient was discharged three days later.

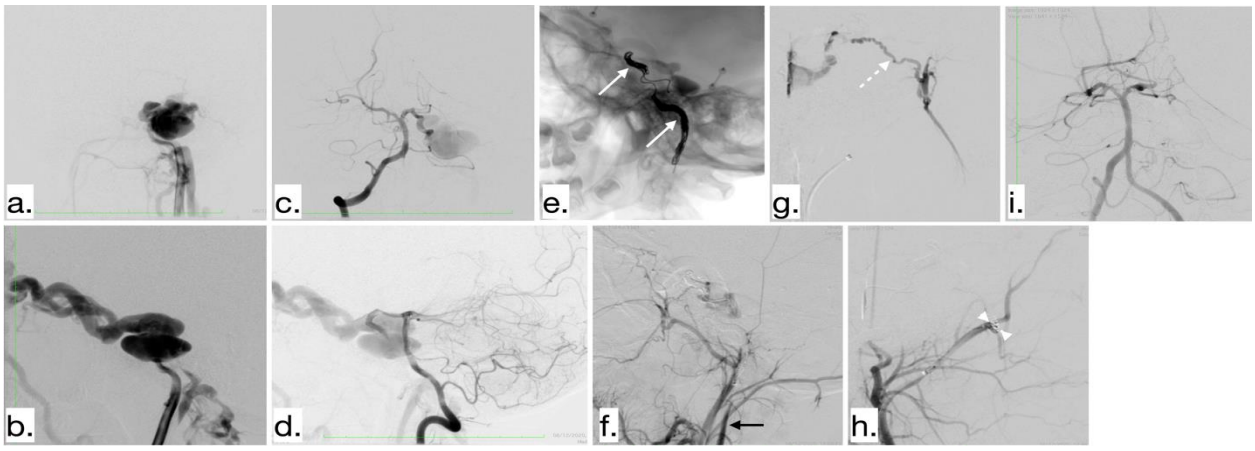

Figure 3. DSA images showing **a, b.** frontal and lateral projections, high-flow fistula with a large venous pouch, draining in the SOV; **c, d.** the fistula is opacified retrogradely through the PCom, during contrast injection in the right VA; **e, f.** Two Penumbra Occlusion Devices (white arrows) were deployed in the ICA distal and proximal to the fistula, with immediate occlusion of the ICA; **g, h.** aspiration through an enlarged artery of the foramen rotundum (dashed arrow) was interrupted by occluding the artery with a 1mm Target Nano coil; **i.** final contrast injection in the VA shows no residual filling of the fistula.
DSA=digital subtraction angiogram; SOV=superior ophthalmic vein; PCom=posterior communicating artery; VA=vertebral artery; ICA=internal carotid artery.

Case 3

A 33 years-old male patient was admitted to our hospital with diplopia, ptosis of the left eyelid, exophthalmia, and chemosis of the left eye. The symptoms had a gradual onset in the last two weeks before admission. MRI performed at another institution revealed enlarged left CS and SOV (not shown). Upon admission, his blood pressure and other laboratory findings were within normal limits. Neurological examination was also normal. The only significant information that he recalls was an abrupt deceleration from 100km/h, without head trauma, while driving a truck, two weeks before symptom onset. Catheter angiogram performed the following day revealed a left, indirect, Barrow type D dural CCF, opacified through meningeal branches from the ICA and ECA (Fig. 4 a, b, c, d). Venous drainage occurred through the SOV and IOV.

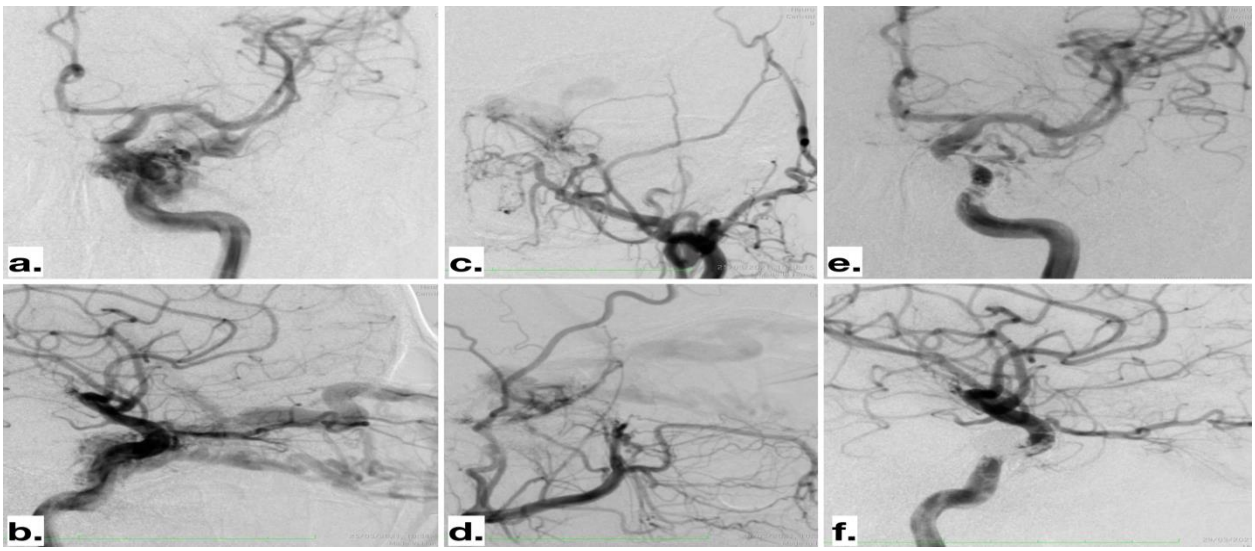

Figure 4. a, b. frontal and lateral projection DSA images showing a left dural, indirect CCF, and venous drainage through the SOV and IOV; **c, d.** the fistula is opacified through meningeal branches from the ECA; **e, f.** complete cure of the fistula obtained with transvenous Onyx injection.
DSA=digital subtraction angiogram; CCF=carotid-cavernous fistula; SOV=superior ophthalmic vein; IOV=inferior ophthalmic vein; ECA=external carotid artery

Under general anesthesia, super-selective catheterization of the ECA and its meningeal branches was performed with a 1.3F Headway Duo microcatheter (Microvention, California, USA) with the goal of occluding the fistula trans arterially (not shown). However, a sufficiently distal position could not be obtained, raising the concern of an incomplete obliteration. Therefore, a combined transarterial and transvenous route was chosen to occlude the fistula by injecting a liquid embolic in the CS while preventing its reflux with a compliant balloon inflated in the ICA.

The left internal jugular vein was punctured under roadmap guidance, followed by the placement of a 6F sheath (Fig. 5, a). A Scepter C compliant balloon (Microvention, California, USA) was navigated in the ICA (Fig. 5, b) and inflated to prevent reflux of the liquid embolic. A 4F diagnostic catheter was placed at the level of the left IPS, which was not visible. After multiple failed attempts to recanalize the IPS with a Terumo 35 guidewire, we managed to cross the IPS and reach the CS with a coronary angioplasty wire, Pilot 14 (Abbott, Chicago, USA) (Fig. 5, c, d) and a Headway Duo microcatheter. Superselective contrast injection confirmed the position inside the CS and the enlarged SOV (Fig. 5, e, f). With the balloon inflated in the cavernous ICA, two vials of Onyx (Medtronic, Dublin, Ireland) were slowly injected through the Headway Duo microcatheter until the fistula was no longer visible (Fig. 4, e, f). No complications occurred during or after the procedure. Symptoms improved almost immediately on the angiographic table. The patient was discharged five days later with residual diplopia.

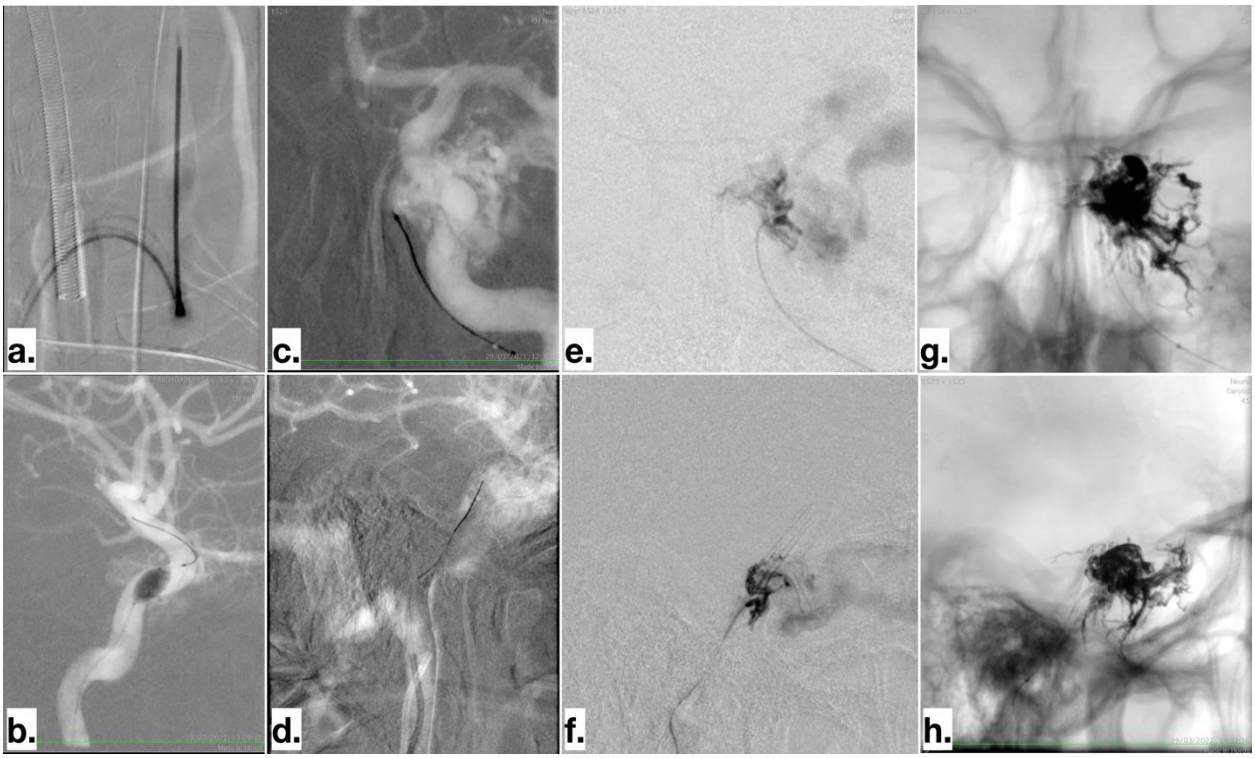

Figure 5. a. A 6F sheath was placed in the IJV under roadmap guidance; **b.** the compliant balloon inflated had the role in preventing reflux of the liquid embolic in the cavernous ICA; **c, d.** frontal and lateral projection roadmap images: a coronary wire was successfully navigated from the IJV through the IPS in the CS; **e, f.** frontal and lateral projection DSA images confirming the microcatheter position in the CS; **g, h.** frontal and lateral fluoroscopy images showing the final Onyx cast.
IJV=internal jugular vein; ICA=internal carotid artery; IPS=inferior petrosal sinus; CS=cavernous sinus; DSA=digital subtraction angiogram.

Discussion

Endovascular treatment of carotid-cavernous fistulae can be achieved by transarterial or transvenous approaches. Furthermore, multiple devices and occlusion strategies are available. The selection of a treatment strategy depends mainly on the angioarchitecture of the fistula. In the first case presented, transarterial occlusion with coils was, in our opinion, the safest plan due to a good visualization of the shunt and the easy access to the enlarged venous pouch. The treatment strategy in the second case was dictated by the absence of the left hemisphere, such that sacrifice of the ICA was deemed the safest and fastest cure possible.

Transarterial treatment of direct CCF's using detachable coils was first reported by Halbach et al. in 1991.[5] Since then, this technique has been assessed in multiple retrospective cohort studies. The reported immediate complete obliteration rate was around 70%, and up to 90% after later reinterventions, with no periprocedural morbidity or mortality.[5–7] The main reasons behind incomplete obliteration were a large arterial defect or a large aneurysmal dilation of the cavernous sinus.[6] To preserve the parent artery and prevent coil herniation in the ICA, non-detachable balloons or intracranial stents can be used as reconstructive treatment options.[6,8] In addition, incomplete closure of the fistula can lead to a change in hemodynamics, leading to a redirection of blood drainage, e.g., from the SOV to cortical cerebral veins, which can rupture and cause an intracerebral hemorrhage.

Detachable coils have potential disadvantages in the treatment of CCF's. Due to the dense packing needed to occlude the fistula, the coil mass can cause mechanical compression on the nerves that travel in the CS, with subsequent cranial nerve palsy (CNP). Worsening or developing new CNP after fistula closure seems to be associated with the total volume of coils used. Almost 80% of patients who needed a coil volume larger than 0.2 cm^3 developed new or worsening previous CNP. Only 70% of these patients recovered completely, requiring a more extended period than patients with lower coil volumes.[9] To achieve such a dense packing necessary to cure the fistula, a mean number of 14-22 coils are needed per patient.[6,7] This large number of coils increases the cost of the procedure and the irradiation to the patient.

If obliteration of the fistula with coils cannot be obtained transarterial, transvenous access is a viable alternative. It can be achieved by a posterior route to the CS through the internal jugular vein and inferior petrosal sinus or an anterior approach through the facial or superior ophthalmic vein.[4,9] Considering the internal trabecular structure of the CS, using only detachable coils might be partially responsible for the relatively low immediate occlusion rate. Consequently, coils can be combined with liquid embolic agents, either as a first-line approach or as a bail-out strategy to achieve complete obliteration.[4] This technique requires a combined transarterial and transvenous access. Usually, embolic agents are injected into the coil mass. At the same time, a non-compliant balloon is inflated in the ICA, covering the laceration to prevent emboli from occluding ICA branches. Immediate obliteration rates reported for this technique are higher than those for coiling alone, reaching 90%.[10] However, care should be taken when injecting liquid embolic in the CS, not to occlude normal draining veins and to cause a hemorrhagic infarct. In the third case reported, the structure of the fistula was so diffuse that we considered coils impossible to position properly. Therefore, only liquid embolic was slowly injected into the CS. Concomitantly, a compliant balloon was inflated in the cavernous segment of the ICA to prevent liquid from refluxing into the artery, causing an ischemic stroke.

Covered and flow-diverting stents can also occlude the tear in the cavernous segment of the ICA while preserving its patency.[4] However, covered stents are rigid, not designed for intracranial arteries, making them difficult to navigate and deploy. The first report of a direct CCF, caused by a ruptured aneurysm in a 72 years-old female patient, successfully obliterated with a Flow-Redirection Endoluminal Device (FRED) flow-diverter, was presented in 2012 at the ABC-WIN, Val d'Isere meeting by Stefanita Dima and Lucian Marginean. Since then, other reports have shown that transvenous or transarterial coiling of the cavernous sinus, with simultaneous flow-diverter implantation in the ICA, achieves a 100% obliteration rate.[11,12]

Conclusions

Carotid-cavernous fistulae represent a heterogeneous disease. This heterogeneity is caused by the different angioarchitecture of each fistula. These architectural particularities dictate the best

endovascular treatment modalities. Transarterial balloon-assisted coiling is associated with relatively high immediate obliteration rates and a low number of complications. However, due to the large volumes of coils needed to occlude the fistula and their subsequent mass effect, cranial nerve palsies can persist for more extended periods. Transvenous occlusion with coils and liquid embolic has a higher cure rate than coiling alone; however, inadvertent reflux of liquid embolic into normal arteries can lead to devastating ischemic complications.

As technology evolves, endovascular choices will continue to expand, allowing higher immediate cure rates and shorter recovery intervals. Flow-diversion devices are promising adjuncts to the arsenal of devices aimed at carotid-cavernous fistulas. They can promote a faster thrombosis of the fistula, and more importantly, offer a scaffolding surface over the arterial laceration that can serve as a platform for endothelial growth and complete reconstruction of the internal carotid artery.

Ethical requirements

No personal data of the patient is available for identification.

Conflicts of Interest

The authors declare that there is no conflict of interest.

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Deep cerebral vein thrombosis due to anaemia in a child

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ABSTRACT

An eighteen-month-old child presented with vomiting, fever and altered sensorium of two days duration. He had anaemia and computed tomography of head revealed hyper-dense internal cerebral veins, vein of Galen and inferior sagittal sinus and bilateral thalamic hypo-density. The child improved with anti-coagulants and packed cell transfusion.

Keywords
anaemia,
computed tomography,
deep cerebral vein
thrombosis.

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INTRODUCTION

Deep cerebral veins include the internal cerebral vein, vein of Galen, basal vein of Rosenthal and the straight sinus. Approximately 10% of the cases of cerebral venous thrombosis are contributed by deep cerebral venous system, the remainder being that due to superficial system [(1)]. Symptoms of Deep Cerebral Venous Thrombosis (DCVT) are confusing and non-specific. Hence the diagnosis is often delayed. A high index of suspicion can save valuable lives if proper treatment is initiated at an early stage. Recently we came across a case of DCVT with anemia which is unusual and hence is being reported.

CASE REPORT

An 18-month-old child presented with 3-4 episodes of vomiting since 2 days, fever and tonic posturing of all four limbs since one day. On examination, the child had fever, tachycardia of 150/min, respiratory rate of 44/min. He was in altered sensorium. Fundus was normal and the deep tendon reflexes were brisk. The plantar were extensor. Investigations revealed Hb of 6.34 g/dL, RBC Count of 4.43* $10^6/mm^3$, WBC 17.6*$10^3/mm^3$, with a differential count of NE 64.4%, L28.2%, Mo. 7.1%, EO 0.3%; Hct 23.7%, MCV 53.4fL, MCH 14.2pg, MCHC 26.6g/dL, Platelet count 1236*10^3/microlitre, MPV 6.4, Procalictonin 0.797. Peripheral smear showed anisocytosis, hypochromia, microcytosis, poikilocytosis, and target cells. Serum electrolytes, LFTs, KFTs were normal. CSF was colorless, clear and on microscopy, contained 22 cells/microlitre with 98% polymorphs, 2% lymphocytes with RBC+ve, Gram staining was negative and culture was sterile after 72 hours.

Computed tomography revealed hyperdensity in the internal cerebral vein of Galen and the straight sinus (Fig. 1). There were bilateral

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thalamic hypodensities and hydrocephalus. Radiologists were sure of thrombosis of deep cerebral venous system and advised a follow up MRI in the follow up period.

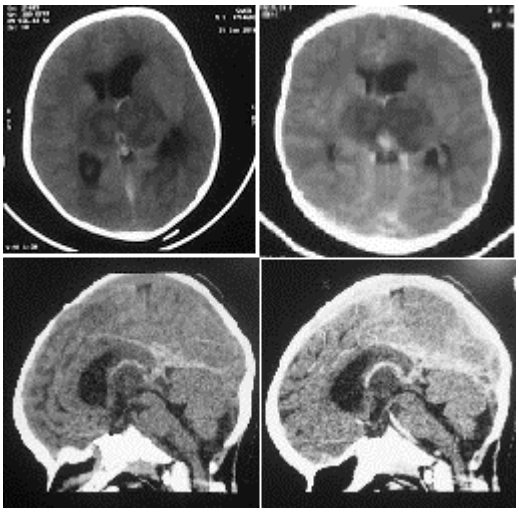

Figure 1. (Top row) Non-contrast (left) and contrast (right) axial computed tomography scan showing bilateral thalamic hypo-density and hyper-dense deep cerebral venous system (on plain scan).
(Bottom row) Non contrast (left) and contrast(right) sagittal CT showing hyper dense deep cerebral venous system on non-contrast scan which remains as such with contrast.

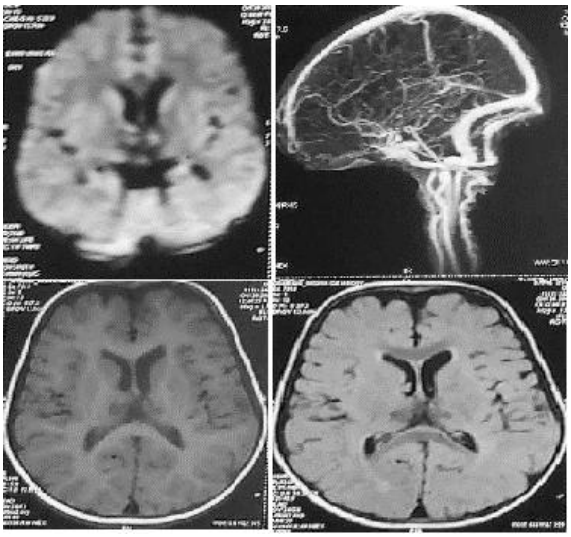

Figure 2. (Top row) Follow up MR showing very small area of infarct (DWI on left) surrounded by a ring of edema and patency of deep venous system demonstrated in MRV (right).
(Bottom row) Follow up MRI demonstrating small hypo-intense areas on T(left) and FLAIR (right) in bilateral thalami.

The patient was started on Acylovir and anticoagulants (enoxaparin). External ventricular drainage was instituted. He had recurrent seizures which were controlled with anti-epileptics. Sensorium improved over a period of time and the EVD was removed. He was discharged after 20 days of hospitalization in conscious state with power of 4/5 in all limbs with mild hypotonia.

Investigations for possible thrombophilia were normal. These included cardiolipin antibodies (6.03-Normal <12 MPL),Homocysteine(11.62micromol/L-Normal 5.46-16.2), Protein C (67-Normal 70-140 IU/dL),MHFTR mutation(+ve),Phospholipid IgG(1.52-Normal <10), Phospholipid IgM(2.42, Normal <10).On follow up, he was ambulant with mild dystonia and MRI done at 3 and 9 months revealed recanalization of the deep cerebral venous system (Fig. 2).

Discussion

Deep cerebral venous thrombosis is a rare cause of stroke in children and may be associated with poor prognosis [2]. The diagnosis is often delayed as the symptoms of venous occlusion are varied and non-specific. Children may present with encephalopathy as seen in our case or may have headache, seizures or raised intracranial pressure.

In our patient, all the biochemical parameters were normal. Hematological investigations revealed microcytic, hypochromic anemia and the diagnosis cerebral DVT was established with a non- contrast computed tomography (CT).CT may be normal in 30% of the cases [2, 3]. The thalami only or the basal ganglia may show edema or infarction. At times, the thalamic involvement may be unilateral even with bilateral DCVT [4]. Sidek et al in 2015 could collect 24 cases of isolated deep cerebral vein thrombosis and added one of their own. Out of 25 cases, 15 were bilateral infarctions [5].

Hyper-density in the deep venous system on CT is suggestive of the diagnosis. MRI can serve as a contributory tool by demonstrating hypo-intense lesion on T2WI and hyper-intense image on T1WI[6, 7]. Though MRI appears to be sensitive for detection of cerebral deep vein thrombosis, it could provide additional diagnostic benefit in only two cases of CDVT,where thrombosis could not be suspected on CT[8].

Hydrocephalus was due of thalami causing occlusion of the third ventricle. Recanalization can occur [9] and was seen in our patient as well. Our patient was treated with low molecular weight heparin,Vitamin K and packed cell transfusion.

Clinical outcome was favorable. Thrombosis resolved at 5 months.

Onset may be acute (less than 48 hours), subacute (48hrs to 1 month) and more chronic disease. Mortality was reduced from 48% to 13% with the use of heparin, increasing the importance of early diagnosis[10].The predisposing factors include dehydration, hypercoagulable state, states of infection and malignancy[2].

Acute thrombosis decreases the level of anti-thrombin, protein C, and protein S. Therefore the tests for thrombophilic states should be performed at least 6 weeks after an acute thrombotic event and INR should be maintained between 2-3. Investigations for hypercoagulability panel were negative in our patient except anemia.

Various mechanisms have been postulated to explain iron deficiency leading to CSVT.Serum iron prevents thrombopoiesis [11] and acts as an inhibitor of thrombocytosis.Therefore, iron deficiency leads to increased platelets and results in a hypercoagulable state .Increased erythropoietin activity during iron deficiency anemia stimulates megakaryocytosis. Microcytosis decreases cell deformability and increases viscosity leading to deranged flow pattern [12]. In the presence of infection, increased metabolic demand can create anemic hypoxia with predisposition to venous thrombosis [13].

Ourpatient, had anemia with occult infection as indicated by high TLC.This, in our opinion was responsible for the DCVT. He did not have any evidence of dehydration or thrombophilic state (Cardiolopin antibody was negative and homocysteine, Protein C, Phospolipid IgG and IgM levels werereported to be normal). Early diagnosis coupled with institution of low molecular weight heparin and blood transfusion resulted in good outcome.

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Long term clinical outcome following decompressive surgery for Cauda Equina Syndrome. A single centre experience from India

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Keywords
Cauda Equina Syndrome, long term follow-up, surgical decompression, time to surgery

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ABSTRACT

Study design: Retrospective study with prospective long-term clinical follow-up.

Background: Cauda equina syndrome (CES) is a neurosurgical emergency, mostly caused by herniated lumbar disc for which urgent surgical decompression is indicated. Data on long-term clinical outcome of bladder, bowel & sexual function following decompression are elusive.

Aim: To evaluate the effectiveness of surgical decompression on recovery of CES symptoms at long-term follow-up & role of timing of surgery on the outcome.

Methods: Records of 35 CES patients who underwent surgical decompression for herniated lumbar disc during a five years period retrospectively analysed & patients called for follow-up visits. Outcome measures comprised of history & clinical examination pertinent to bladder, bowel & sexual function.

Results: Twenty-four patients (68.5%) were included for final evaluation who attended follow-up visits, with a minimum follow-up period of one year. Most common complaint at presentation was bladder dysfunction (100%) with urinary retention in 16 patients (66.6%), faecal incontinence in 11 (45.8%), saddle anaesthesia in 22 (91.6%) & erectile dysfunction in 6 patients (out of 15 males). Only four patients underwent surgery within 48 hours of CES symptom onset, rest cases after 48 hours duration. At follow-up, bladder dysfunction present in 33.3% with urinary retention in 16.6%. Faecal incontinence persisted in 4 patients (16.6%) & saddle anaesthesia in 7 (29.1%). Sexual dysfunction was the most persistent complaint.

Conclusion: Long-term follow-up shows significant recovery of sphincteric function in CES patients after surgical decompression. Urinary & bowel dysfunction improve significantly. Timing to surgery didn't affect the long-term outcome.

INTRODUCTION

Cauda equina syndrome (CES) is clinically characterized by varying degree of loss of bladder, bowel & sexual function & is often associated with one or more of features like low back pain, unilateral or bilateral

sciatica, leg weakness & is caused by compression of lumbar and sacral nerve roots in cauda equina [1, 2, 25, 33, 35].

It is considered a neurosurgical emergency & prompt surgical decompression represents the therapeutic gold standard [1, 18, 28]. The most common cause of CES is herniated lumbar disc (HLD) & CES is considered the only primary absolute indication for surgery in HLD patients [1, 8, 18, 28].

There are differing reports in the literature regarding the optimum time to surgery but because of the rare occurrence of this syndrome, there is a lack of unified criteria for deciding the best timing for surgery and determining factors that positively influence the clinical outcome.

Hence, the influence of timing of surgery on outcome has been a topic of debate in literature and most studies show that decompression within 48 hours yield better outcome [1, 3, 18]. But many others disagree & indicate that timing of surgery does not appear to significantly improve the outcome [4, 14, 25, 26, 28]. Regardless of the disease onset, it is logical to conclude that operating sooner rather than later is better.

Long term follow-up of CES patients is required for evaluation of bladder, bowel & sexual function recovery following surgical decompression and several studies do include individual population with follow-up of several years, however, those patient numbers are small and evaluation of outcome seldom includes defecation and sexual function [20].

Aim of this study was to present our experience at this institute and assess the effectiveness of surgical decompression on functional recovery of CES symptoms after long term follow-up with regards to bladder, bowel as well as sexual dysfunction & evaluate the factors affecting the long-term outcome after surgery following development of CES symptoms, together with a thorough review of literature.

Materials & methods

Study design

Medical records & clinical data of consecutive patients operated for lumbar herniated disc at this tertiary care regional Government hospital during a five years period from July 2014 to June 2019 with coded admission diagnosis & clinical presentation of CES were retrospectively reviewed for their baseline characteristics, presenting complaints, pre-operative neurological status, surgical complications, clinical parameters at the time of discharge from the hospital. Then selected patients included in the study were called upon telephonically for follow-up visits arranged in outpatient care clinic. All patients had pre-operative MRI of lumbosacral spine for definitive diagnosis of herniated disc causing clinical cauda equina syndrome. The minimum follow-up period was set to one year with mean follow-up of 28 months and maximum of 5 years. Patients were evaluated for clinical improvement & outcome of micturition, defecation, and sexual function and possible predictors of outcome. The study was approved by Institutional Review Board.

Inclusion criteria

- Patients with newly diagnosed CES operated within the study period.
- Pre-operative MRI suggestive of herniated lumbar disc causing cauda equina nerve root compression (Figure 3 & 4).
- Follow-up of at least one year.

Exclusion criteria

- Cause of CES other than HLD, like tumors or degenerative lumbar stenosis.
- Patients with re-operation for persistent symptoms with post-operative MRI suggestive of residual/recurrent disc herniation.
- Didn't attend the follow up clinic.

A total of 35 patients were identified by screening the records of all patients operated by the two experienced senior neurosurgeons for lumbar herniated disc at this institution & out of these, 24 patients were included for the final evaluation. Rest eleven patients didn't meet the inclusion criteria due to various reasons & were excluded.

Operative procedure

All patients underwent standard laminectomy & removal of herniated lumbar disc causing compression of lumbosacral nerve roots. No patient in this study had spinal fusion or any instrumentation for instability.

Demographic & clinical data

Baseline parameters like age, sex, level of disc, associated comorbidities, smoking status, presenting symptoms, duration of symptoms of CES

& time to surgery were analyzed (table-1). Limb weakness was graded according to MRC (Medical research council) scale. Symptoms of bladder, bowel & sexual dysfunction were separately measured. Patients who were catheterized at the time of presentation were considered having urinary retention. Incontinence of faeces due to sphincteric dysfunction & saddle anesthesia were included as symptoms of bowel dysfunction relevant to CES & were evaluated. Sexual dysfunction was present in male patients as erectile dysfunction. Post-operative complications were also noted & patient-related clinical data at the time of discharge from the hospital were analyzed.

Characteristics (n=24)	
Median Age (in years)	40.0 years (Range 30-65)
Sex – Male Female	15 09
Level of HLD	L2-3 1 (4.1%) L3-4 5 (20.8%) L4-5 11 (45.8%) L5-S1 9 (37.5%) Two level HLD 2 (8.3%)
Comorbidities	DM-2 3 HTN 4
Smoking status	Smoker 8 Non-smoker 16
(HLD Herniated lumbar disc; DM-2 Diabetes mellitus type-2; HTN Hypertension)	

Table 1. Pre-operative patient related parameters.

Outcome Measures

A follow-up visit was arranged during a period between July to August 2020 for all screened patients of CES as per their convenience to attend the outpatient care & relevant clinical history was taken regarding present status of pain, limb weakness & improvement in bladder, bowel & sexual function. Thorough neurological examination was performed in all patients including presence of motor deficit, anal tone & perineal sensation. Improvement in limb weakness was considered significant if it upgraded at least two MRC (Medical research council scale) grades from the pre-operative record.

Outcome of individual parameters was assessed & compared between two intergroups of chronological order 1) pre-operative v/s at discharge & 2) at discharge v/s long term follow-up. This comparison was done to evaluate the importance of a long-term follow-up & long recovery time required to see the results of surgical decompression.

Statistical analysis

The recorded data were analyzed using IBM-SPSS software version 24.0 for windows OS 10 (SPSS Inc. Chicago). Comparing independent groups with categorical variables was done with Chi Square test. For comparisons between paired groups of categorical variables, McNemar's test was done with Yates correction for continuity and validated with a binomial exact test. Binary logistic regression models were used to evaluate predictors for bladder, bowel and sexual dysfunction at long term follow-up, with inclusion of the following variables: age, sex, level of herniated disc at presentation, duration of complaints of CES at presentation & time to decompression. Statistical significance determined by a p value < 0.05.

Results

A total of 594 patients underwent laminectomy with discectomy surgery for herniated lumbar disc during the five years study period at this institution, out of which thirty-five (35) patients were diagnosed having CES. So, the incidence of CES among patients operated for lumbar herniated disc was 5.9% at our center. Out of these 35 patients, eight didn't attend the follow-up visit due to various reasons (three of them couldn't be contacted, five didn't came for follow-up even after several requests made telephonically & so couldn't be examined at follow-up). Three patients demonstrated significant residual or recurrent disc herniation in the follow-up MRI scans and were re-operated, so excluded from the final evaluation. Hence, twenty-four patients (68.5%) with CES were included in our study for evaluation.

Demographic parameters of the patients who were included are summarized in table-1. The median age was 40 years with 15 males & 9 females. The most common level of disc herniation was L4-5 (in 45.8%) followed by L5-S1 (37.5%) & two-level disc herniation in two cases (8.3%), one with L2-3 & L3-4 levels & other one with L3-4 & L4-5 levels, & these

two patients underwent laminectomy & discectomy at both levels simultaneously.

Pre-operative clinical parameters

The common presenting clinical features are listed in Table-2. The most common presenting symptoms were radicular leg pain (87.5%), urinary dysfunction (100%) & saddle anesthesia (91.6%). Other common complaints were weakness of either or both legs (54.1%) & bowel dysfunction in form of faecal incontinence of varying severity (45.8%). Two patients had partial foot drop at presentation which improved at long term follow-up. The least common complaint reported was sexual dysfunction (25% in whole sample) as 6 male patients having erectile dysfunction (40%). None of the females reported any sexual dysfunction. Sixteen patients (66.6%) were catheterized either at the time of admission or before surgery for urinary retention. Per-rectal examination revealed perineal hypoesthesia in thirteen (54.1%) & decreased anal tone in nineteen (79.2%) patients. Three patients who reported absence of radicular pain, also had bilateral lower limb weakness, complete saddle anesthesia with urinary retention.

Symptoms/signs	Overall (n=24)
Low back pain	22 (91.6%)
Radicular leg pain	21 (87.5%)
- Unilateral	16 (66.6%)
- Bilateral	5 (20.8%)
Motor deficit	13 (54.1%)
- U/l leg weakness	8 (33.3%)
- B/l leg weakness	3 (12.5%)
- Foot drop (U/l & partial)	2 (8.3%)
Bladder dysfunction	24 (100%)
- Urgency/dysuria	3 (12.5%)
- Overflow incontinence	5 (20.8%)
- Retention	16 (66.6%)
Bowel dysfunction	
- fecal incontinence	11 (45.8%)
Sexual dysfunction (Male)	
- Erectile dysfunction	6/15 (40.0%)
Perineal hypoesthesia	13 (54.1%)
Saddle anesthesia	22 (91.6%)
- Complete	15 (62.5%)
- Partial	7 (29.1%)
Anal tone	
- Normal	5 (20.8%)
- Decreased	19 (79.2%)

Table 2. Pre-operative clinical parameters.

Disease duration and time to surgery

The duration of complaints related to herniated lumbar disc disease with low backache &/or radicular leg pain are summarized in Table-3. The most important parameter to be measured was the mean duration of onset of cauda equina syndrome symptoms (bladder &/or bowel dysfunction with or without leg weakness) to surgical decompression. For this, the duration of symptoms at admission was added to the duration from admission to surgery. The mean duration was 117 hours (approximately 5 days) with only four patients (16.6%) undergoing surgery within 48 hours from symptom onset. We do not have emergency spine surgery unit at this institution; hence all cases were posted for surgery on urgent priority basis in the elective theatre on the same day or within 48 hours of admission. The time to surgical decompression from onset of CES symptoms of all included patients is shown in Figure-1 & the time to surgery from admission to the hospital in Figure-2. The average duration of hospital stay was 6.5 days. Mean follow-up period was 28 months with range from 12-60 months. The duration of symptoms relevant to herniated disc like low backache and radicular pain with or without limb weakness were also noted from patient's history sheets. Many of these were on conservative approach of management with analgesics alone. Those cases first presented to us with acute involvement of bladder & bowel function. Some cases developed CES without prior symptoms of HLD. The longest duration of CES symptoms recorded was 15 days in two cases (Figure-1).

	Duration (Range)
Mean duration from onset of symptoms of HLD to presentation (in days)	152.3 (10-730)
Mean duration of onset of CES complaints to surgery (in hours)	117.0 (36-360)
Mean duration from admission to surgery (in hours)	33.5 (12-48)
Average duration of hospital stays (in days)	6.5 (3-13)

Table 3. Duration of symptoms & time to surgical decompression.

Surgical complications

All patients underwent standard laminectomy & discectomy surgery to decompress the cauda equina

nerve roots, intraoperatively dural tear was encountered in two cases but they were recognized & managed intraoperatively without closure of dura required & they had no post-operative CSF leak. Post-operatively no major complications were reported before discharge except one patient having diabetes developed superficial wound infection on post-operative day-4 which was managed conservatively with antibiotics alone. No worsening of neurological status reported in the post-operative period & at discharge from hospital. All patients were shifted to elective ICU care at least for 24 hours post-operatively, no patient required ventilatory support or prolonged ICU stay. Injectable antibiotics were given routinely to all patients for a minimum of three days post-operatively, no steroid use documented for any patient.

Clinical outcome at long-term follow up

At a minimum follow-up period of one year, most of the patients had significant improvement in their pre-operative deficits (Table-4). Age at onset of CES, sex, comorbidities, smoking status & level of disc were not found to influence the outcome (not statistically significant).

The assessment of pain relief was subjective & patient reported & this was not quantified on pain scale. Our study shows that a significant number of patients (37.5%) still complain of radicular leg pain at follow up. Patients who had limb weakness show significant improvement when compared to pre-operative & discharge records, & only 4 patients (16.6%) had reported residual deficits.

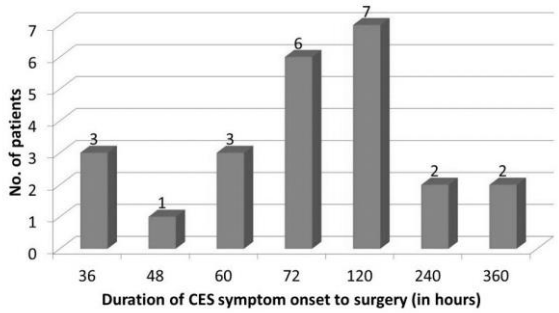

Figure 1. Duration from CES symptom onset to surgery of all patients.

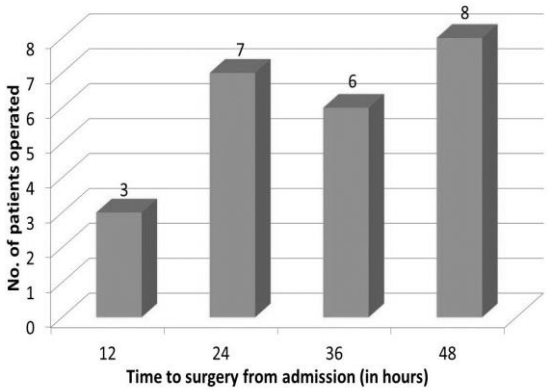

Figure 2. Time to surgery after admission of all patients.

	Pre-operative	At discharge (average 6.5 days)	At long-term follow up	p-value**
Radicular leg pain	21 (87.5%)	15 (62.5%)	9 (37.5%)	MNY 0.003
- Unilateral	16 (66.6%)	11 (20.8%)	6 (25.0%)	BE <0.001
- Bilateral	5 (20.8%)	4 (8.3%)	3 (12.5%)	
Motor deficit*	13 (54.1%)	12 (50.0%)	4 (16.6%)	MNY 0.016
-U/l leg weakness	8 (33.3%)	8 (33.3%)	3 (12.5%)	BE <0.001
-B/l leg weakness	3 (12.5%)	3 (12.5%)	1 (4.1%)	
-Foot drop	2 (8.3%)	1 (4.1%)	0 (0.0%)	

* if no improvement in motor power by at least 2 MRC grades; **outcome at long-term; MNY – McNemar's test with Yates correction; BE – Binomial Exact test

Table 4. Long-term outcome of leg pain & motor deficits.

	Pre-operative	At discharge (average 6.5 days)	At long-term follow up	p-value[#]
Urgency/dysuria	3 (12.5%)	3 (12.5%)	2 (8.3%)	-
Overflow incontinence	5 (20.8%)	4 (16.6%)	2 (8.3%)	-
Retention	16 (66.6%)	14 (58.3%)	4 (16.6%)	-
Total	**24 (100%)**	**21 (87.5%)**	**8 (33.3%)**	MNY <0.001 BE <0.001

outcome at long-term; MNY – McNemar's test with Yates correction; BE – Binomial Exact test

Table 5. Long-term outcome of bladder dysfunction.

Long-term outcome of bladder dysfunction

At follow-up, 33.3% of patients complained of bladder involvement at follow-up & this improvement, when compared with either pre-operative or at discharge data using McNemar's test with Yates correction for continuity, was statistically significant (Table-5). Binomial exact test was used to check the validity of this calculation. Out of 16 patients with retention initially, 12 were free from catheter at long-term & only 16.6% were still dependent on it despite proper bladder training in post-operative period.

Two of the cases who had retention before surgery, however, reported complaints of dysuria or urgency at follow-up but were not catheter-dependent. Out of the four patients operated within 48 hours after CES symptom onset, three had retention & one had incontinence pre-operatively, out of which one patient still had retention at the follow-up visit. When compared with the group of rest of the 20 patients operated >48 hours after CES onset, no statistically significant difference was observed in outcome of bladder function between the two groups.

	Pre-operative	At discharge (average 6.5 days)	At long-term follow up	p-value[##]
Saddle anaesthesia	22 (91.6%)	19 (79.1%)	7 (29.1%)	MNY <0.001
- Complete	15 (62.5%)	13 (54.1%)	4 (16.6%)	BE <0.001
- Partial	7 (29.1%)	6 (25.0%)	3 (12.5%)	
Faecal incontinence	11 (45.8%)	11 (45.8%)	4 (16.6%)	MNY 0.046 BE 0.004
Perineal hypoaesthesia	13 (54.1%)	11 (45.8%)	8 (33.3%)	MNY 0.131 BE 0.016
Anal tone -decreased	19 (79.2%)	15 (62.5%)	7 (29.1%)	MNY 0.005 BE <0.001
Sexual dysfunction in males (ED), n=15	6 (40.0%)	6 (40.0%)	4 (26.6%)	MNY 0.479 BE 0.50

outcome at long-term; MNY – McNemar's test with Yates correction; BE – Binomial Exact test

Table 6. Long-term outcome of bowel & sexual dysfunction.

Bowel & sexual dysfunction

Bowel dysfunction was measured with four different parameters (Table-6). Two subjective parameters including saddle anaesthesia & faecal incontinence as reported by the patients. Saddle anesthesia present pre-operatively in 22 cases (91.6%) including 15 complete & 7 partial loss of sensation in saddle region. It improved at follow-up visit to seven (29.1%), four (16.6%) & three (12.5%) respectively. Faecal incontinence with partial or complete loss of control over defecation including either intermittent incontinence or soiling was reported by 11 patients (45.8%) before surgery which improved significantly at follow-up & prevalent in only 4 cases (16.6%) at follow-up.

Objective parameters of bowel dysfunction included presence or absence of perineal hypoaesthesia & demonstration of anal tone. At presentation, hypoaesthesia was present in 13 patients & decreased anal tone i.e. lax anal sphincter in 19 patients, which improved at follow-up. The association of saddle anaesthesia & decreased anal tone with presence of urinary retention at presentation & follow-up was statistically significant (p-value < 0.05) & all 4 patients with retention at follow-up had saddle anaesthesia, perineal hypoaesthesia & decreased anal tone. Hence, presence of saddle anaesthesia with perineal hypoaesthesia and a lax anal tone was a predictor of urinary dysfunction.

Sexual dysfunction which was prevalent in 25% of the study cohort & reported by 6 male patients (40%) having erectile dysfunction at presentation was still present in 4 of them at follow-up. The lower initial incidence of this complaint as compared to other sphincteric disturbances may be due to response bias, as none of the females complained any form of sexual dysfunction, possibly reflecting some form of barrier on both patient's side as well as on doctor's side regarding the discussion of sexual health.

Discussion

This study is one rare of its kind to prospectively assess the long-term outcome following surgery for CES secondary to herniated lumbar disc by directly obtaining patient history & performing clinical examination in the outpatient care clinic after a minimum of one year.

The primary aim of this study was to evaluate clinical outcome after a long period following surgery, specifically the outcome of sphincteric function. This long term follow-up is required for neurological recovery which tends to occur many years after decompression [5, 25]. Some previous studies by Korse et al. & Hazelwood et al. have evaluated outcomes at relatively longer duration [13, 20]. Together with highlighting the importance of a long term follow up, we also reviewed the literature to describe other features relevant to the context of cauda equina syndrome and their possible association with the outcome.

The sample size (n=24) in our study was relatively small but considering the rare occurrence of this syndrome [9, 15, 23], number of patients in this study were considerable. We achieved a response rate of 68.5% due to unwillingness of many patients (31.5%) to participate for the follow-up evaluation for various reasons, personal or social. This shows a significant number of patients were lost to follow-up & indicates towards an attrition bias, but it could well be because of dissatisfaction from the delivered care also & must have been a major factor affecting the overall outcome assessment.

The incidence of CES in patients undergoing surgery for lumbar disc herniation in this study was 5.9%, which is slightly higher than previous literature that quotes approximate incidence of 1-3% [8, 9, 14, 16, 19, 23, 25]. Recently Korse et al. quoted a higher incidence of 10.8% in their study on 75 patients [19].

The most common cause of CES is lumbar disc herniation [18, 34]. Others include tumors, spinal stenosis, hematomas, trauma, and iatrogenic causes [21]. The most common level of cauda equina nerve root compression is L4-5 or L5-S1 level [6, 8, 16] and our study population also reflects the same with almost 83.3% (20/24) of cases demonstrating disc at these two levels. We couldn't demonstrate a correlation between the level of disc and long-term outcome.

The exact definition of cauda equina syndrome is not available. It is described by various authors in different terms and there is no agreed definition [32]. There have been attempt to quantify the clinical aspects of Cauda equina syndrome by N. V. Todd based on bladder and bowel dysfunction but has not been validated for clinical practice [2, 35]. The five characteristic features of CES are bilateral neurogenic sciatica, reduced perineal sensation, altered bladder function ultimately to painless urinary retention, loss of anal tone and sexual dysfunction. Not all will be present in any individual patient [8, 32]. Results demonstrated that bladder dysfunction, radicular leg pain, saddle anaesthesia with decreased or loss of anal tone are the most prevalent complaints within this population, while leg weakness & bowel dysfunction being comparatively less common and sexual dysfunction reported least frequently. Bilateral sciatica also, was a less common feature (in 20.8%). Unilateral foot drop is also described as a feature of CES & two patients in this study had partial unilateral foot drop along with sphincter dysfunction with evidence of disc herniation at L3-4 & L4-5 levels respectively. These two patients recovered at follow-up. Bilateral foot drop can also occur but is an extremely rare

condition as described by Mahapatra et al. in a case of CES due to L3-4 prolapsed disc [24]. Low-backache being non-specific, was not assessed as an independent outcome measure, though many cases still had this complaint in post-operative and follow-up period.

There has also been an attempt to classify CES by 'The British Association of Spinal Surgery' into three subgroups as CESS (suspected CES with absence of sphincter dysfunction), CESI (CESS plus dysuria, urgency or altered urinary sensation) and CESR (painless retention with faecal or urinary overflow incontinence) [10, 14]. However, classification into two broad groups of incomplete (CESI) and complete (CESR) cauda equina syndrome seems more realistic for the true evaluation of the clinical outcome, as these two groups represent the definite involvement of sphincter function, specifically the bladder function. We followed the same criteria to describe CES clinically. All the 24 patients in our study cohort had some form of bladder dysfunction and 21 of them fall into CESR subgroup (16 with retention & 5 with overflow incontinence). Thereby, a comparison couldn't be made with the rest of the three patients falling into CESI subgroup due to such skewed distribution of variables.

The long-term outcomes related to bladder, bowel & sexual dysfunction in this study broadly agree with previous literature. However, similar to previous studies, the proportions of patients with residual symptoms differ in individual categories. Our study noted a lower rate of bladder dysfunction (33.3%) at long term follow up than previous studies, with Hazelwood et al. finding 76%, Korse et al finding 36.1% & McCarthy et al finding 43% of patients to have bladder dysfunction at long term follow-up [13, 20, 25]. The higher incidence of bladder dysfunction by Hazelwood et al. may be due to use of the objective USP score (Urinary symptoms profile score) which have a high sensitivity to a range of urological symptoms and patients would often report a symptom-free bladder, only to show dysfunction on the USP [5, 36]. This is likely due to the neural damage sustained in CES that would preferentially affect detrusor innervation and function over pelvic floor strength or urethral patency [10]. Olivero et al. have described an improvement of bladder function in more than 90% of their cases with a sample size of 31 patients [26]. Kaiser et al. noted good outcomes in 70% of their patients with CESR [16]. Similar to these, patients in the retention group also had good recovery patterns in our study with a prevalence of 66.6% reducing to 16.6% at follow-up. This improvement is significant considering the generally described poor outcome in previous studies [18, 20]. Konig et al. found no improvement in bladder dysfunction in any case of a grade-4 CES (based on Shi classification) regardless of the timing of surgery [18, 31]. We did not classify our patients into these grades as described by Shi et al. but the classification seems promising and further prospective studies on its application in prognostication of CES patients are recommended [31].

Two important aspects of bladder dysfunction not sufficiently mentioned in the previous literature are the pre & post-operative urodynamic study (UDS) and electromyography of bladder musculature. Uroflowmetry and post-void residual urine (PVR) are simple objective tests to establish the neurovesical involvement in CES [17]. These can be further confirmed with invasive multichannel UDS to exclude other possible causes responsible for persistent bladder dysfunction in the post-operative period. Yamanishi et al. in their study on urodynamic evaluation of surgical outcome of CES stated that most of the patients could empty their bladder only by straining or changing their voiding postures postoperatively [37]. This adaptation by the CES patients in post-operative period could well be a reason for the subjective improvement of bladder dysfunction in the present study and their catheter-free status at follow-up, despite the presence of a residual bladder dysfunction on objective assessment. Lee et al. have evaluated the role of electromyography as a tool for evaluating the integrity of sacral spinal segments 2 to 4 to predict the outcome of bladder dysfunction in CES & found that results of electrically induced bulbocavernosus reflex (E-BCR) examination seemed to give excellent positive and negative predictive values for the recovery of bladder function in patients with CES [22]. These two factors should be considered relevant predictors of bladder dysfunction and should be evaluated in the follow-up.

Bowel dysfunction is a complex domain of Cauda equina syndrome and includes two subjective and two objective parameters as previously mentioned. We describe a high prevalence of 91.6% saddle anaesthesia and 45.8% faecal incontinence. This incontinence of varying degree was strongly related

to the presence of two objective parameters of perineal sensory loss and decreased anal tone. All patients having some form of faecal incontinence also had both these findings present. Most of the previous studies report poor outcome of bowel disturbances with Korse et al. finding a prevalence of 43% at long term follow-up from 47% at initial follow-up and McCarthy et al. finding 60% bowel disturbance at follow-up & one-third of these having intermittent faecal incontinence or soiling [20, 25]. Our findings correlate with the previous studies but since there is no unified criteria of defining bowel dysfunction or disturbance in different studies [4, 13, 20] we could not compare individual parameters, however, the overall recovery is significant for all these 4 parameters. The role of rectal examination testing the anal tone is described in previous studies. Sphincter disturbance and saddle anaesthesia appear to be the most reliable predictors of outcome after surgery [7, 12, 21, 25]. There are few studies suggesting that early surgery increases the likelihood of an improvement in bowel dysfunction [8, 18, 25]. However, we could not verify this association.

Sexual dysfunction was reported less commonly and complained only by the male population with erectile dysfunction. There was no patient showing any functional recovery at the time of discharge but 33.3% (2 of 6) patients had reported improvement in erection at long term follow-up though it was not statistically significant (p value 0.479). None of the females reported any form of sexual dysfunction, however this doesn't rule out its prevalence in this population considering the under-reported complaints related to sexual dysfunction. McCarthy et al. reported 50% of patients had some degree of sexual dysfunction, and Korse et al. reported dysfunction prevalence of 56% at 2 months, marginally improving to 53% at 13 years [20, 25].

In our study, patients operated before 48 hours fared no better than those operated after 48 hours, specifically the sphincter function. However, since only four cases were operated before 48 hours, this conclusion didn't reach a statistical significance. But, considering the significantly good recovery in those operated after 48 hours, it can be concluded that a more important factor predicting the outcome is 'time factor' post-surgery, thus emphasizing the role of a long-term follow-up of these cases. Four cases presented more than 10 days after the onset of their CES symptoms (figure-1), but had no statistically significant difference between the outcome when compared with those operated early upon. What are the factors then, governing the neurological recovery in such patients remains unanswered.

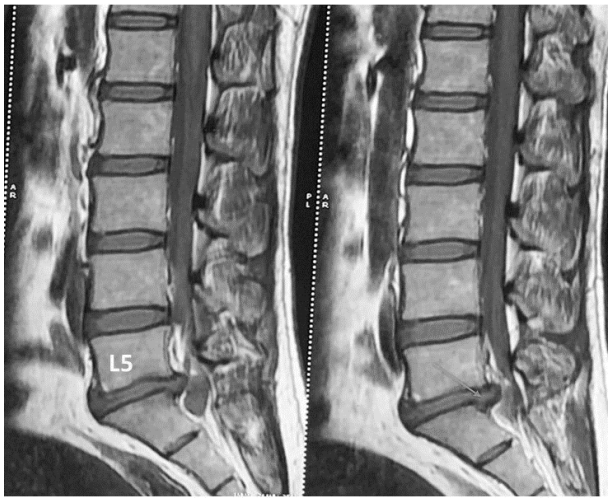

Figure 3. Pre-operative T1-weighted sagittal MRI image of a 36 years old male patient showing a large herniated disc at L5-S1 level (yellow-coloured arrow mark).

Recently, Bydon et al. in their study on 45 patients of CES have stated that determinants of outcome in CES are elusive, similar to the state of the literature on surgical management of acute spinal cord injury, in which the timing of surgery has not been conclusively correlated with outcome [4]. Studies in the porcine model have shown that cauda equina compression can cause injury after as little as 2 hours [4, 27, 29]. They have further postulated that time-dependent cellular and physiologic effects of cauda equina impingement are irreversible well before patients reach surgery, leaving outcome dependent on other factors. This together with the delayed presentation of patients to seek medical help, unavailability of adequate medical facilities in the developing countries and delayed diagnosis by primary care physician leads to a significant delay in time to surgery. Heyes et al. in their recent series of 136 patients, demonstrated that regardless of type of CES and independent of timing of surgical intervention, most patients see a significant improvement in bowel and bladder function following surgical decompression [14]. The majority of patients in their series also presented with symptom duration of greater than 48 hours. We consider this related to the long time required for natural recovery of damaged nerve fibers after

decompression. Nerve injury is not necessarily a direct result of injury to the nerve at the level of the Cauda equina but more a mechanical injury to the bladder wall musculature. Schoenfeld AJ & Bono CM stated in their systematic review of timing on post-operative recovery in Lumbar discectomy, functional outcome was only adversely affected if decompression was carried out 6 months post onset of symptoms [30]. Considering all these facts, outcome in our study were fairly good irrespective of duration of CES symptoms & time to surgery.

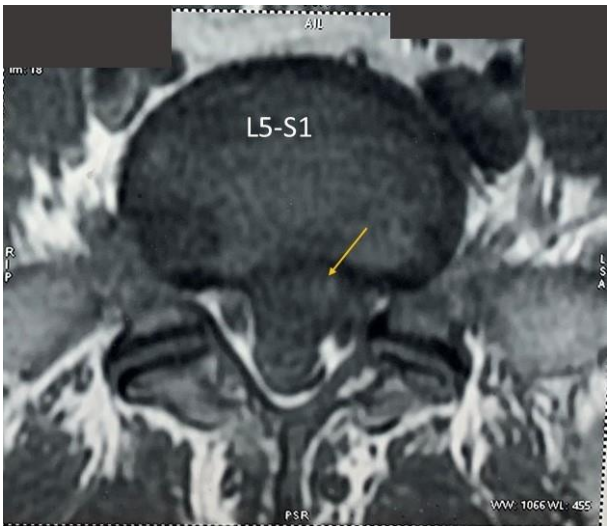

Figure 4. Pre-operative axial MRI image of the same patient as in figure-3, showing large postero-central disc herniation at L5-S1 level causing compression over ventral thecal sac (yellow-coloured arrow mark).

We also reviewed the pre & post-operative MRI scans wherever available to evaluate the possible role of MRI findings in clinical outcome (figure-3 to 6). Three of the cases not included in our study cohort but were first operated during the study period, had evidence of significant residual or recurrent disc herniation on post-operative MRI, were re-operated for their persistent sphincteric dysfunction. This role, of ineffective decompression or recurrence of disc herniation, has not been considered in most of the previous studies. Residual disc or recurrent disc herniation can be a cause of long term sphincteric dysfunction in these population of patients and should not be overlooked. Another factor which can influence the outcome is disc herniation size and degree of compression of cauda equina nerve roots. A previous study by Kaiser et al. however, found no significant correlation between the size of disc herniation relative to size of spinal canal and post-operative urinary function in patients with CES [16]. Further research is recommended to evaluate this probable association.

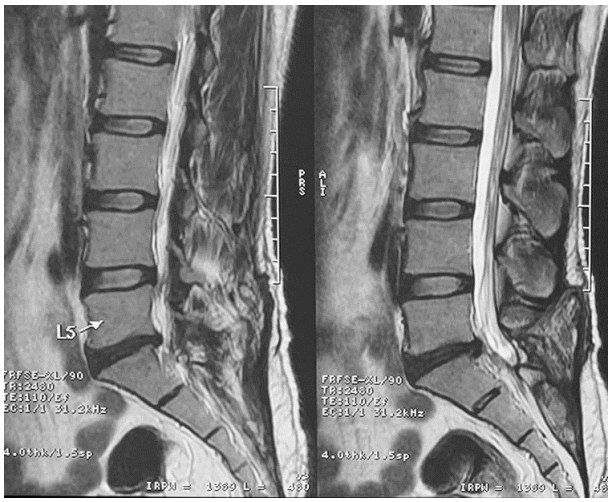

Figure 5. Post-operative sagittal MRI image of same patient as in Figure-3.

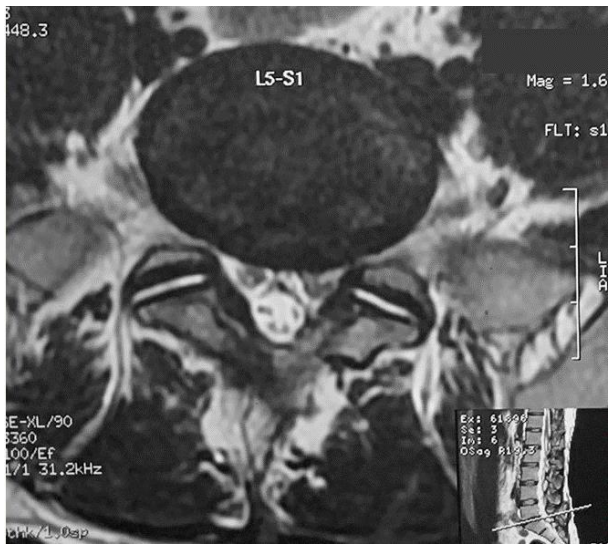

Figure 6. Post-operative axial MRI image of same patient as in Figure-4.

We also reviewed the literature for comparison of different surgical techniques and found that most of the previous studies recommend a wider decompression [11]. There is no significant difference with either bilateral laminectomy or hemilaminectomy or interlaminar fenestration with discectomy, with fusion or without fusion. Dave et al. found patients operated with trans-foraminal lumbar interbody fusion (TLIF) have decreased

incidence of surgical complications but similar neurological outcome compared with non-fusion group [6]. All the patients included in current study underwent standard unilateral or bilateral laminectomy with discectomy and without fusion.

Overall, the outcome predictors of CES surgery are difficult to prognosticate. Timing of surgery is the most extensively studied parameter in CES patients but till now no consensus exists for the optimum time window of surgery. However, we still recommend urgent surgical decompression once the patient presents with CES symptoms. We also recommend a strict follow-up schedule for all operated patients of CES till recovery of sphincteric dysfunction achieved so as to further evaluate the other causes responsible for delayed long-term outcomes.

Limitations

All pre-operative data were obtained retrospectively from the history files of the patients from hospital's medical record section. This implicates an observer's bias & limitation of the data quality. Most of the recorded parameters were patient reported & subject to individual variation.

Conclusion

This study assesses most of the issues relevant to CES & demonstrated that regardless of timing of surgical intervention, most of the patients see a significant improvement in pain, limb weakness, bowel and bladder function following surgical decompression & this requires a long-term follow-up. Recovery is not complete in all patients but urinary & bowel dysfunction improve significantly. Sexual dysfunction, however, have poor recovery. This long-term outcome after surgery has highlighted the importance of a strict schedule of follow-up of all CES patients. Timing of surgery was not shown to influence the clinical outcome in this study. This doesn't mean surgery should be deferred, but better outcomes are not guaranteed even after earlier surgical decompression. Since it is not always practical for most of the patients of CES to operate within the first 48 hours after symptom onset, especially in the developing countries, we should focus further research on other relevant outcome parameters to prognosticate this rare neurosurgical disease entity.

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Visual outcome analysis in patients with posterior fossa tumours undergoing surgical treatment

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ABSTRACT

Background: In the past, there were studies done to assess visual outcomes like visual acuity, fundoscopic findings and visual field mainly in pediatric patients with posterior fossa tumours (PFT). We assessed the above parameters pre- and post-operatively in all age group patients including both extra and intra-axial PFT. We also assessed visual outcome in patients with or without hydrocephalus.

Objectives: To analyze "visual outcomes in patients with posterior fossa tumours undergoing surgical treatment". The effect of hydrocephalus on the visual outcome was also analyzed.

Materials and Methods: This prospective study including 107 patients with PFT undergoing definitive surgery was conducted in the Department of Neurosurgery at Dr Rmlims, Lucknow. Pre-op and post-op (six weeks after tumour resection) visual examinations were done and compared.

Results: A shifting trend towards normalization of visual acuity (VA) was seen post-surgery in all age groups. Overall improvement was seen in the majority of cases having pupil normal size sluggish reactive (NSSR) after surgery. Papilledema improved in the majority of patients in all age groups and patients having hydrocephalus. Colour vision and night vision also improved in the majority. The field of vision cut was not improved postoperatively in the majority.

Conclusion: Visual parameters like visual acuity, pupil size and reactivity to light; colour vision and night vision were improved significantly after surgery whereas cut field of vision did not improve. All fundoscopic findings like papilledema, retinal venous dilation and retinal splinters haemorrhage disappeared in a significant number of patients post-operatively. In cases with obstructive hydrocephalus, these parameters also improved significantly after Ventriculo-peritoneal shunt/ ETV or definitive surgery.

Keywords
posterior fossa tumors, hydrocephalus, visual acuity, papilledema

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INTRODUCTION

Posterior fossa tumors (PFT) cause symptoms due to compression over brainstem, cerebellum and raised intracranial pressure (ICP).[1,2,3,4] . This can lead to obstructive hydrocephalus and papilledema leading to secondary optic nerve atrophy and permanent vision loss.[5] Hydrocephalus may cause Abducens palsy leading esotropia, and

horizontal diplopia. Trochlear nerve palsy may cause vertical/oblique diplopia, with hypertropia. These tumors may disrupt visual fixation and vestibular and/or gaze-stabilization mechanisms, resulting nystagmus, skew deviation, and complex gaze palsies Vth and VIIth nerve palsy may lead to corneal damage.[6] In children, cerebellar mutism may result after surgery.[7] Specially pediatric PFT with ophthalmic complications need more attention.[8]

This study was done to prospectively analyze visual outcome after surgery in PFT (extra-axial/intra-axial) patients in all age group.

Aims

To analyze "visual outcomes in patients with posterior fossa tumors undergoing surgical treatment" and also to analyze the effect of hydrocephalus on the visual outcome.

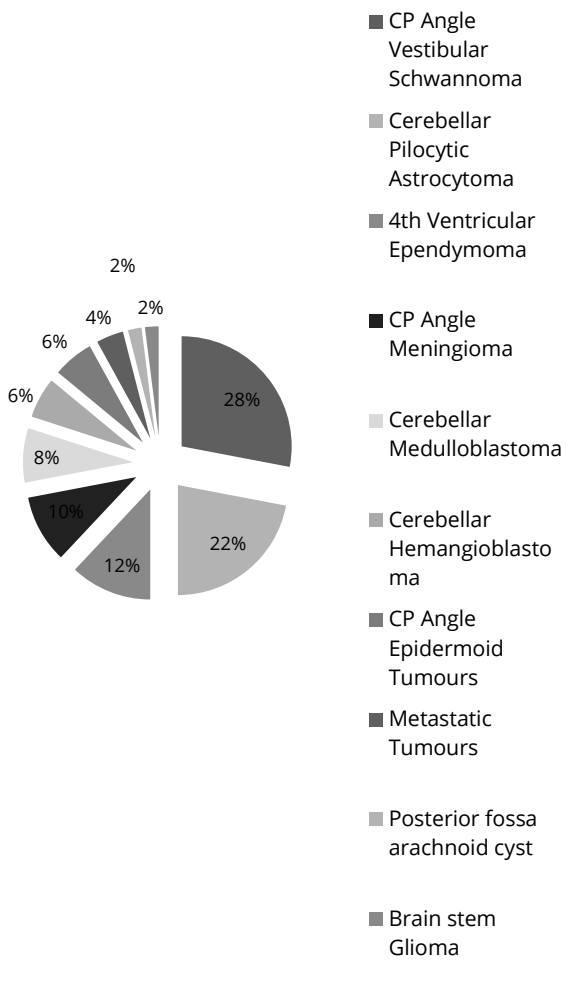
Materials and methods

This prospective study included 107 patients was conducted in the department of Neurosurgery Dr.RMLIMS Lucknow. Those patients presenting with symptoms of hydrocephalus underwent cerebrospinal fluid (CSF) diversion procedure e.g. ventriculo-peritonial (VP) shunt/endoscopic third ventriculostomy (ETV) as emergency procedure. Inclusion criteria were PFTs with or without hydrocephalus. Exclusion criteria were patients with recurrent PFT, visual and ocular motor dysfunction unrelated to their tumor, patients undergoing primary radiotherapy treatment, non-co-operative and not following commands. Most common procedures performed for definitive surgery were retro-sigmoid sub-occipital craniotomy/craniectomy or midline suboccipital craniotomy/craniectomy with gross total resection or subtotal resection of tumor. Pre-op and post-op (after six weeks of tumor resection) visual acuity on Snellen chart, pupillary function (size, reactivity), color vision on Ishihara test (present/absent), night vision (present /absent), visual field by confrontation test, fundoscopy, papilledema grade (modified Frisen scale), retinal findings (venous dilatation and splinter hemorrhage present/absent) were examined. Hydrocephalus (present/absent), CSF diversion procedure in the form of VP shunt/ETV done or not, were also examined. Visual acuity outcomes of various age groups, extra-axial and intra-axial posterior fossa tumors and patients with or without hydrocephalus compared with Wilcoxon signed-rank test. Analysis was performed on STATA software.

Results

Sample size was 107, out of which 3 patients died due to brainstem injury, infarction and edema. Four cases lost follow up due to unknown reasons. Total 100 patients were followed up to 6 months. 46 (46%) patients were found to be having extra-axial tumors and 54 (54%) intra-axial tumors (Figure 1). Total 20 (20%) patients having PFTs were found in pediatric age (<20years) group, 70 (70%) patients in middle (20-50 years) age group and remaining 10 (10%) in old age group (>50 years). Out of 100, 74 (74%) with obstructive hydrocephalus underwent VP shunt/ETV in emergency.

Figure 1: Pathological Diagnosis

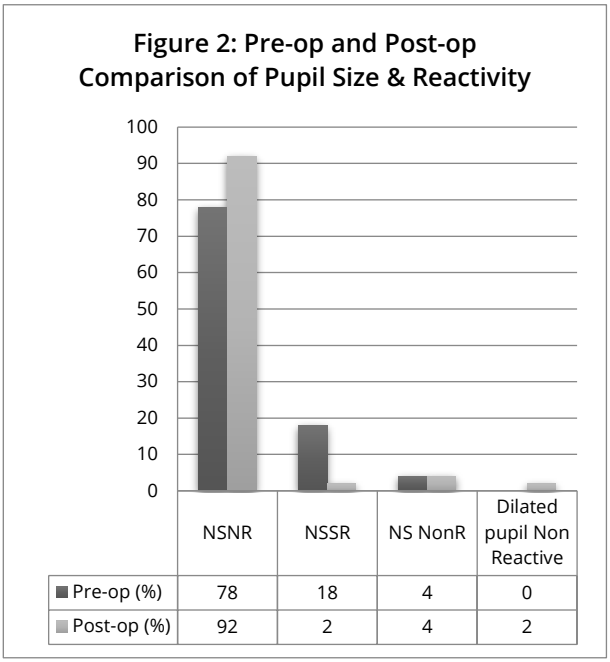


Visual acuity was categorized arbitrarily as normal (6/6), good (6/9 to 6/12 in both eyes), moderate (6/18 to 6/60 in at least one eye), and poor (<6/60 in at least one eye) (Table 1). Using Wilkoxan signed-rank test assessed VA outcomes in patients with extra-axial, intra-axial tumor, with/without hydrocephalus and in different age group.

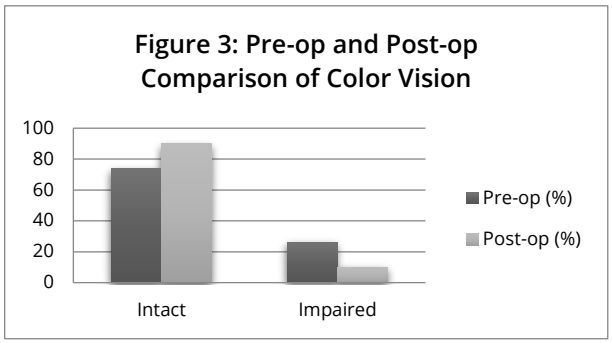
S. No.	Visual Acuity Category	Pre-op		Post-op	
		No. of Cases	%	No. of Cases	%
1.	Normal Vision (6/6)	48	48	66	66
2.	Good Vision (6/9 to 6/12)	22	22	10	10
3.	Moderate Vision (6/18 to 6/60)	12	12	10	10
4.	Poor Vision (<6/60)	18	18	14	14
Total		100	100	100	100

Table 1. Pre-op and post-op comparison of visual acuity.

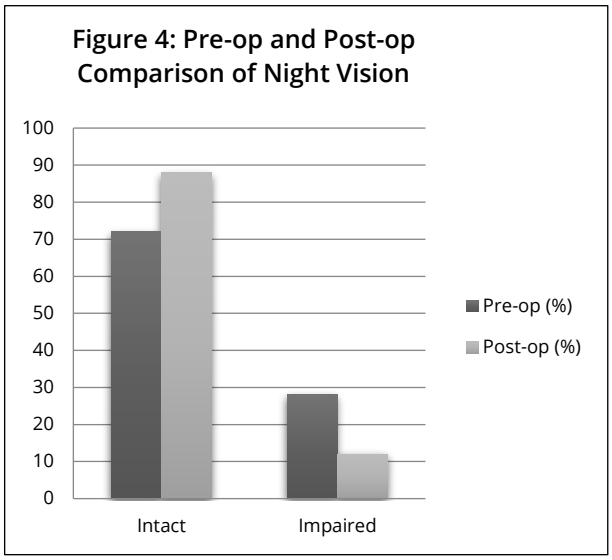
Pupil size and reactivity measured as normal size of pupil and normal reactivity (NSNR), normal size sluggish reactive (NSSR), normal size nonreactive (NSNoR) and dialated pupil (Figure.2) and outcome analysed. Overall improvement was seen in majority of cases having pupil NSSR post-surgery.



Out of 100, 26(26%) patients had impaired color vision on pre-op examination, which decreased to 10(10%) after surgery. Total number of cases having normal color vision was increased to 90(90%) after surgery but remain impaired or absent in 10(10%) cases. (Figure.3)



Total 72 (72%) patients were found to have normal night vision pre-operatively. Patients having normal night vision were increased to 88(88%), after surgery. Remaining 12(12%) patients did not improve even after surgery (Figure 4).



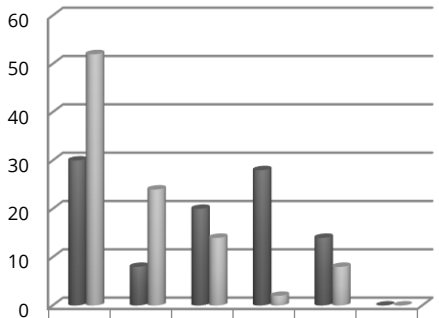
Vision field by confrontation outcome is given in Table 2.

S. No.	Vision Field	Pre-op		Post-op	
		No. of Cases	Percentage	No. of Cases	Percentage
1.	Intact	96	96	96	96
2.	Impaired	4	4	4	4
Total		100	100	100	100

Table 2. Pre-op and post-op comparison of vision field by confrontation.

Out of 100 patients, 30(30%) patients were found to have normal fundoscopic findings (Grade 0), which increased to 52(52%) on post op examination. Grade IV papilledema was found in 14(14%) patients on pre-op examination which decreased to 8(8%) after surgery. Total no of patients having grade III papilledema was 28(28%) on pre-op examination which decreased to one after surgery(Figure.5). Likewise total number of patients with grade II papilledema decreased post operatively. However in 12(12%) patients, either in one or in both eye, optic atrophy was seen on follow up examination.

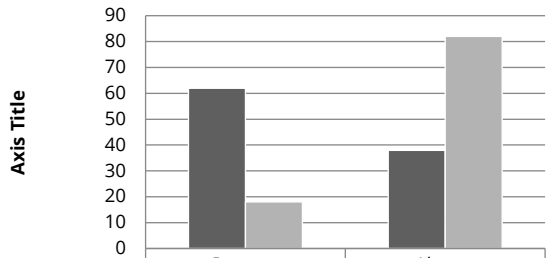
Figure 5: Pre-op and Post-op Comparison of Papilledema



	Grade 0	Grade I	Grade II	Grade III	Grade IV	Grade V
Pre-op (%)	30	8	20	28	14	0
Post-op (%)	52	24	14	2	8	0

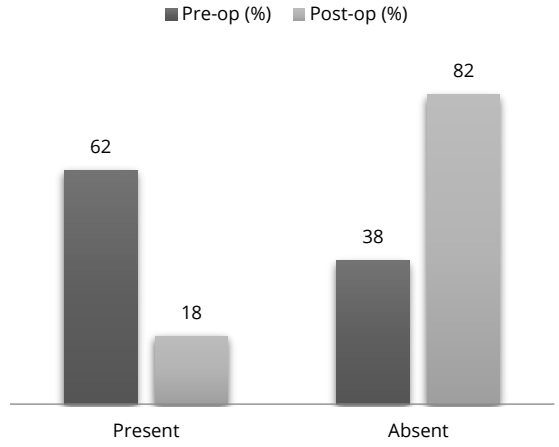
Retinal venous dilation and splinter hemorrhage examined on fundoscopy and outcome given in figure 6 and 7 respectively. After surgery one case was complicated with III[rd] nerve palsy.

Figure 6: Pre-op and Post-op Comparison of Retinal Venous Dilatation



	Present	Absent
Pre-op(%)	62	38
Post-op (%)	18	82

Figure 7: Pre-op and Post-op Comparison of Splinter Haemorrhage



Discussion

Clinical profile and presentation: Total 100 patients were followed up in this study out of which 20 (20%) patients having PFTs were found in pediatric age (<20years) group, 70(70%) patients were in middle (20-50 years) age group and remaining 10(10%) patients were in the age group of >50 years. Most common extra-axial tumor was cerebellopontine angle vestibular schwannoma whereas most common intra- axial tumor was cerebellar pilocytic astrocytoma. Extra-axial tumors were diagnosed pathologically as cerebellopontine angle vestibular nerve schwannoma (28%) patients, cerebellopontine angle meningioma (10%) patients, cerebellopontine epidermoid tumors (6%) patients and posterior fossa arachnoid cyst (2%) patients. Intra-axial tumors were diagnosed pathologically as cerebellar pilocytic astrocytoma (22%) and fourth ventricular ependymoma (12%) cerebellar medulloblastoma (8%) cerebellar hemangioblastoma (6%) cerebellar metastatic tumors (4%) and brainstem glioma in one patient (Figure 1). Most common symptoms were headache (80%), nausea or vomiting (69%), ataxia (61%), ophthalmologic symptoms (31%) hearing loss (28%) and other cranial nerve involvement. Visual and oculomotor disturbance was the fourth most common symptoms (27%), which is similar to a study done by Nisha Gadgilet al. [8] Patients with hydrocephalus (75%) underwent CSF diversion procedure, either VP shunt or ETV in emergency followed by definitive surgery. Patients with persistent ophthalmological complications were consulted 6 weeks post-surgery.

Visual acuity outcome: In our study 48% cases had normal vision (6/6) in both eyes pre-operatively which increased to 66% post surgery. Poor visual acuity (<6/60) was observed in 18% patients in pre-op examination, which decreased post-operatively to 14%. Good visual (6/9 to 6/12) acuity was found in 22% patients pre-operatively, which decreased to 10% after surgery. The sum total of patients having normal visual acuity and good visual acuity was found to be 76% after surgery. Likewise, total no of cases having moderate visual acuity (6/18 to 6/60) was also decreased from 12% to 10% post-surgery. Over all shifting trend towards normalization of visual acuity was seen in majority, post-surgery. According to Peeler et al (2017) VA was good in 82.8%, fair in 9.8%, and poor in 7.4%. 9.4% cases had optic atrophy on follow up.[9] However, this study was done only in pediatric patients having PFT.

Recently Nisha Gadgil et al (2018) concluded that 88% had good visual acuity; 5% had moderate and 5% had poor visual acuity. Optic atrophy due to prior hydrocephalus was noted in 13% cases but this resulted in persistent loss of visual acuity only in 2% cases. [8]

In those patients presenting with obstructive hydrocephalus, urgent neurosurgical intervention was needed to decrease intracranial pressure for saving vision. Patients with poor visual acuity pre-operatively, having long duration of raised ICP improved little or none after surgery.

The median pre-op visual acuity in patients with extra-axial tumors (6/9; IQR 6/6 – 6/12) was better than patients with intra-axial tumors (6/12; IQR 6/6 – FC at 1 mt), but statistically non-significant difference was observed with KW test (p=0.376). Similarly, no statistical difference (p=0.182) was observed in the median post-op visual acuity in patients with extra-axial tumors (6/6; IQR 6/6 – 6/9) and patients with intra-axial tumors (6/6; IQR 6/6 – 6/36). Wilcoxon signed-rank test revealed statistically significant improvement in visual acuity after surgery in extra-axial tumors (p=0.001) and intra-axial tumors (p=0.005).

The median pre-op VA in patients without pre-op hydrocephalus (6/6; IQR 6/6 – 6/6) was better than patients with pre-op hydrocephalus (6/12; IQR 6/6 – 6/60), and this difference in visual acuity was found to be statistically significant with KW test (p=0.000). Similarly, statistically significant difference (p=0.004) was observed in the median post-op visual acuity in patients without pre-op hydrocephalus (6/6; IQR 6/6 – 6/6) and patients with pre-op hydrocephalus (6/6; IQR 6/6 – 6/24). Wilcoxon signed-rank test revealed statistically significant improvement in visual acuity after surgery in patients with pre-op hydrocephalus (p=0.000) and patients without hydrocephalus already had normal median visual acuity.

The median pre-op visual acuity in patients aged <20 yrs.', 20 to <50 yrs.' and ≥50 yrs.' was 6/6 (IQR 6/6 – 6/12), 6/9 (IQR 6/6 – 6/60) and 6/24 (IQR 6/36 – 6/12), but this difference in visual acuity by age was found to be statistically non- significant with KW test (p=0.153). Similarly, the median post-op visual acuity in patients aged <20 yrs.', 20 to <50 yrs.' and ≥50 yrs.' was 6/6 (IQR 6/6 – 6/6), 6/6 (IQR 6/6 – 6/24) and 6/12 (IQR 6/6 – 6/12), and this difference in visual acuities by age too was found to be statistically non-significant with KW test (p=0.200). Wilcoxon signed-rank test revealed statistically significant improvement in visual acuity after surgery in patients of all age groups ('p' values for <20 yrs.', 20 to <50 yrs.' and ≥50 yrs.' are 0.047, 0.001 and 0.046 respectively).

Pupil size and reactivity to light: On pre-op examination NSNR to light was found in 78% cases, which increased to 92% after surgery. NSSR was seen in 18% cases pre-operatively, which decreased to 4% post surgery. However, 4% cases having NSNoR did not improve even after surgery. One case with NSNoR, complicated with third nerve palsy with dilated pupil (Figure 2).

Color vision: 26% patients were found to be having impaired color vision on pre-op examination, which decreased to 10% after surgery. Total no. of cases having normal color vision increased to 90% after surgery. In remaining 10% cases color vision was either impaired or absent even after surgery (Figure 3).

Night vision: 72% patients were found to have normal night vision pre-operatively. After surgery, total number of patients having normal night vision increased to 88%. Improvement was observed in majority of cases with impaired night vision (Figure 4).

Vision field by confrontation: On pre-op examination 4% patients were found to have field vision cut, which did not improve even after surgery.

All patients with field vision cut had visual acuity PL-ve preoperatively.

Similarly field cut was observed in 2.7% patients in study done by Nisha Gadgil et al.[8] In our study defect in field vision was due to optic atrophy. The limitation of this study was inability to report on visual field outcomes in all pediatric patients, because quantitative subjective visual field testing could not consistently performed and better method of measurement of vision field like perimetery could not be done.

Papilledema: According to study done by M.S. Girwan et al papilledema was observed in 94.2% in their experience. [10] In our study, on pre-op examination 30% patients were found to have normal fundoscopic findings (Grade 0) while 70% patients were having papilledema (Modified Frisen Scale). The number of patients having normal fundoscopic findings increased to 52% on post op examination. Grade IV papilledema was found in 14% patients on pre-op examination which decreased to 8% on post op examination. Total no of patients having grade III papilledema was 28 (28%) on pre-op examination, which decreased to two after surgery. Likewise total number of patients with grade II papilledema decreased post operatively. The trends toward normalization were seen in majority of patients. However in 12(12%) patients, either in one or both eyes, optic atrophy was seen on follow up examinations (Figure5).

Retinal venous dilation: On pre-op fundoscopic examination retinal venous dilation was seen in 62% cases, which decreased to 18% after surgery (Figure 6). Better outcome was observed in patients who underwent earlier neurosurgical intervention.

Splinter hemorrhage: Total number of patients having retinal splinter hemorrhage was 62(62%), which decreased to 18(18%) after surgery. Splinter hemorrhage disappeared in 44% patients after neurosurgical intervention (Figure 7)

Conclusion

Conclusively, visual parameters like visual acuity, pupil size and reactivity to light; color vision and night vision were improved significantly after surgery whereas cut field of vision did not improve. Significant improvement in the visual acuity and papilledema in patients with pre-op hydrocephalus, irrespective of extra or intra axial location of tumor, age group, were observed after surgery. Other fundoscopic findings like retinal venous dilation and retinal splinters hemorrhage disappeared in significant number of patients post-operatively.

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Single versus double burr holes evacuation in the treatment of chronic subdural hematoma. A tertiary centre experience

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Keywords
single burr hole craniostomy (SBHC), double burr hole craniostomy (DBHC), chronic SDH (CSDH)

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ABSTRACT

Background: Chronic subdural hematoma (CSDH) is a well-known entity and common surgical disorder managed by the neurosurgeon and, if not recognized and treated timely, may prove fatal. It can be non-traumatic or post-traumatic and all of them need urgent attention irrespective of aetiology. It manifests with a progressive neurologic deficit that occurs ≥3 weeks following head injury. The principal techniques used in the treatment of CSDHs presently are burr hole, twist drill craniostomy, craniectomy and craniotomy.

Objective: The aim of this study was to assess clinical outcome in unilateral chronic subdural hematoma patients treated by single or double burr-hole drainage. This prospective study was carried out at the Department of Neurosurgery, IMS, BHU, Varanasi from September 2016 to August 2018. A total of 60 patients with their age ranged from 22to 88 years with GCS 6 to 15 & hematoma thickness 10mmc were included in this study and randomly divided into two groups using random allocation software. In group A, patients with chronic subdural hematoma (CSDH) were managed with single burr-hole drainage. In group B, patients were managed with double burr-hole drainage. Clinical outcome was measured on the1st postoperative day, 3rd postoperative day and 7th postoperative day by GCS and at 1month follow-up by measuring the Glasgow outcome scale (GOS).

Result: In this study double burr-hole drainage and single burr-hole drainage surgery shows equal success in the management of CSDHs with single burr hole taking less operative time.

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INTRODUCTION

Chronic subdural hematoma (CSDH) is a common neurosurgical disorder managed by neurosurgeons and if not recognized and treated timely, may prove fatal. It can be non-traumatic or post traumatic and all of them need urgent attention irrespective of etiology. [1]It manifest with progressive neurologic deficit that occur ≥3 weeks following head

injury.[2]Besides clinical suspicion various modalities has been used to diagnose CSDH but CT scan of head is the investigation of choice. CT scan has revolutionized the ways in which patients with CSDH may best be managed. [3]Some CSDH known to resolve spontaneously as seen by the existence of calcified "hematomas". Medical management has been advocated for old debilitating patient with CSDH included bed rest, steroids and mannitol but it needs prolonged hospitalization for these patients. [4]It is a common consensus that operative treatment would be more quickly, safely and effectively remove the mass. [5]Most of the neurosurgeons prefer to place two burr holes on the side of lesion and irrigate through small silicon catheters to wash out the subdural space with or without use of sterile closed drainage system.[6]Few authors have suggested the use of a single burr hole and thorough irrigation for evacuation of CSDH. Instead of evacuation through a burr hole, evacuation through a twist drill hole in critically ill patients was found to be equally satisfactory by some surgeons.[7]Evacuation of CSDH by craniotomy is also indicated in certain situations and there are few surgeons who feel craniotomy has still a definite role in management of CSDH. Endoscopic evacuation of CSDH can also be done.[8]In the light of current knowledge, there are various methods for surgical evacuation of CSDH. Described by different authors, all the methods have its merits and demerits. It is still debated that which is the best method for CSDH. This study is planned to compare the intraoperative, postoperative complications and outcome of evacuation of CSDH by two different techniques in the same set up ie single vs double burr hole evacuation of CSDH.

MATERIAL AND METHODS

This prospective study was conducted on patients with CSDH, admitted to Trauma Centre and SSH Hospital(Sir Sundar Lal hospital) Department of Neurosurgery IMS, BHU Varanasi, from september2016 to August2018. Total 60 patients were enrolled in the study and divided in two groups .Informed consent was taken from the patients or immediate relatives (first degree) .The patients who underwent single burr hole drainage were labeled as Group A and those with a double burr holes were designated as Group B. Both groups included '**thirty'** patients each who presented with diagnosis of CSDH on Monday, Wednesday, Saturday and on alternate Sundays.

All patients admitted in neurosurgery ward were evaluated by taking detailed history, clinical examination and investigations. Diagnosis of CSDH was confirmed by radiological (CT,MRI) investigation. Incidence of the CSDH was recorded out of all admitted patients in a particular time period. After confirmation of CSDH by CT/MRI scan patients were operated alternatively by single and double burr holes respectively.

Inclusion criteria**:**

- CT/MRI proved symptomatic cases of CSDH.
- Patients of both sexes and all age groups .
- All the patients who were operated for the first time for the disease (CSDH).
- All CSDH patients with midline shift of 10 mm or more.
- Unilateral chronic SDH patients
- Hematoma thickness of 10 mm or more.

Exclusion criteria**:**

- Patients with recurrent disease after previous operation.
- Asymptomatic patients with very thin CSDH (conservatively managed)
- ventriculoperitoneal shunt in situ.
- hematological disorder/anticoagulant drug use.
- bilateral CSDH.

Operations by "Two burr holes technique" and "Single burr hole were done under general anesthesia on emergency basis.

PROCEDURE

A written consent was taken from the patient or patient party after explaining the procedure. Patients with CSDH, treated at trauma centre & SSH, BHU Varanasi in a neurosurgical unit during the years September 2016 to August 2018. On admission, in addition to the presenting history, details were obtained regarding previous head injury, alcohol abuse and medication. The patients underwent a neurological examination. Routine laboratory tests, along with a complete coagulation profile and liver function tests, were done. Radiological investigation of the brain ie CT and MRI were the investigation to diagnose the CSDH. The size, extentand density/intensity of the contents of the CSDH were recorded.general anesthesia was given as the

standard modality for anaesthesia. Single and double burr hole procedure were performed randomly. The patients who underwent single burr hole drainage were labeled as Group A and those with a double burr holes were designated as Group B. The surgical procedure was as follows.

Double burr holes technique

Patient lied supine on operation table. Head turned to side on which burr holes were made. Parts cleaned and draped. Two linear skin incision of two to three centimeters for burr holes were given on frontal and parietal region (precoronal and post coronal) along mid papillary line which correspond to maximum thickness of CSDH NCCT head.

After the burr holes were made of dm 2.5 cm each , the dura was opened in a cruciate manner. The dural edges were coagulated completely. The subdural space was liberally irrigated with normal saline till the refluxing fluid started coming out clear. Skin closure was done in two layers with vicryl 2-0 rb and nylon 2-0 cutting sutures respectively.

No post-operative drains were used in our cases.

Single burr hole technique

Patient lied supine on operation table. head turned to side on which burr hole was made. Parts cleaned and draped. Single linear skin incision given after local infiltration along mid pupillary line over parietal bone correspond to maximum thickness of CSDH over NCCT head.

After the burr hole was made of dm 2.5, the dura was opened in a cruciate manner. The dural edges were coagulated completely. The subdural space was liberally irrigated with normal saline till the refluxing fluid started coming out clear.

Skin closure was done in two layers with vicryl 2-0 rb and nylon 2-0 cutting sutures respectively

No post-operative drains were used irrespective the fact weather brain expanded or not.

Post-operative course

Patients advised complete bed rest and were kept supine post-operatively for 3 days. The patients did not receive any specific medication, including steroids, anticonvulsants or excessive hydration. The operative procedure was standardized between the study groups. A repeat CT scan of the brain was performed in all patients on post-operative day 3 to confirm adequate drainage of the CSDH.Patients were discharged after first Ct scan if no complication was found. In addition, a CT scan of the brain was performed at day 7 and 1-month after evacuation of the hematoma. All patients were followed-up for at least 1 month after surgery. Both clinical and radiological criteria were used to evaluate the recurrence of CSDH.

The clinical criteria suggestive of a recurrence**:**

- altered level of consciousness
- persisting headache
- appearance of new or worsening pre-existing neurological deficits.

The radiological criteria of recurrence**:**

- increased volume of subdural fluid
- mass effect on the ipsilateral brain or ventricular system,
- effacement of cerebral sulci to gross subfalcine herniation.

Reoperation in the form of rewashing ,craniectomy or additional burr hole was done in cases with recollection/recurrence on post operative NCCT head.

RESULTS

The age ranges from 28 to 88 years in Group A with mean of 58.77 ± 14.29 years while it is 30 to 88 years in Group B with mean age 57.07 ± 15.02 years. Out of total patients 44(73.3%) were males and 16 (26.7%)were females.In Group A, 24(80%) were males and 6(20%)patients were females while in Group B 20 (66.7%) were males and 10(33.3%) patient were females. Headache was the most common presentation in both the groups with total 27 (45%) presented with it out of which 11(36.6%) were in Group A and 16(53.3%) were in Group B followed by Altered sensorium which was presented by 5(16.7%) and 3(10%) patients in Group A and B respectively. Other presentations were Hemiparesis presented in 4(13.3%) and 2(6.7%) ,aphasia (0%) and (3.3%), coma (10%) and (10%), gait disturbance (6.7%) and (3.3%), visual disturbance(6.7 & 3.3%), incontinence (6.7% & 3.3%) and seizure (3.3 & 6.7%) patients of Group A and B respectively (Figure1).

Trauma was the most common etiology in both Groups with total 48(80%) patients suffered with it.23(76.7%) in Group A and 25 (80%) in Group B patient gave history of trauma, while 6(20%) and 5 (18.3%) in Group A and B respectively had history of

CVA (cerebrovascular accident). History of AVM (arteriovenous malformation) bleed was presented in one patient of Group A.

Hypertension was the most common associated comorbidity found in 20% of total patients followed by Dementia and Diabetes mellitus (DM) which was found in 15% each in total patients. Other comorbidities were COPD, alcoholic, renal failure respectively. (Figure2)

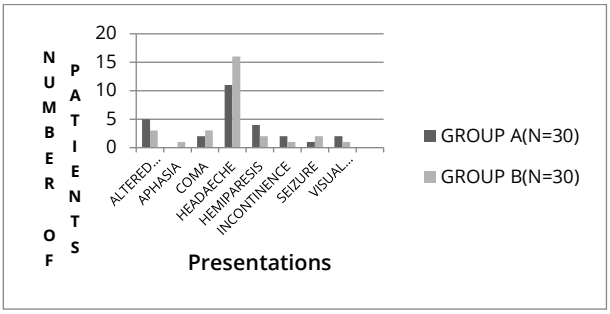


Figure 1.

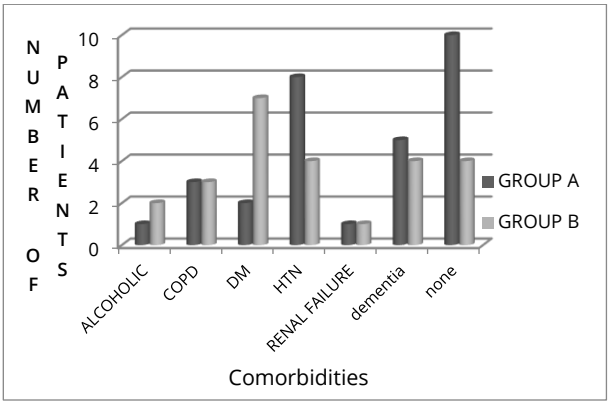


Figure 2.

The Chronic SDH diagnosis was made on CT/MRI brain. The thickness of chronic SDH in Group A ranges from 10 to 18 mm with mean of 14.63± 2.46 mm while in Group B the range was also from 10-18mm with mean of 14.43t± 1. 18mm.The p value for thickness between two Groups was 0.71 which was not significant. Midline shift in Group A ranges from 10-14 mm with mean of 10.80 ±1.03 mm while in Group B the range was 10-14 mm with mean of 10.67±1.18 mm. The p value for midline shift on comparing two Groups came out to be 0.64 which was not significant. On comparing the characteristics on hematoma membrane between two groups both groups had thin membrane in 26(86.67%) patients and thick membrane in 4(13.33%) patients the p value for membrane thickness was not significant. (Table 1)

Hematoma characteristics	GR. A	mean	GR. B	mean	P VALUE (two tailed T test)
Midline shift (mm)	10-14	10.80 ±1.03	10-14	10.67± 1.18	.64
Thickness(mm)	10-18	14.63 ±2.46	10-18	14.43± 1.59	.71

Table 1.

During intraoperative period bleeding from the fragile emissary veins occurred in 3(10%) patients of Group A and 1(3.3%) patients of Group B, while brain contusion during opening up of thick membrane occurred in 2(6.67%) patients' of Group A but none in Group B. The brain after evacuation of hematoma not expanded in 4(13.33%) patients of Group A and 3(10%) of Group B while it expanded over time in 26(86.6%) of Group A and 27(90%) of Group B. the P value for intraoperative complications and non expansion of brain was >.05 which was not significant.

The mean time for the duration of surgery was 31.13±5.01min in Group A while in Group B mean operating time was 47.07±4.75min,showing that the mean operating time in the GroupA was significantly less as compare to the GroupB.(P value=<.001).

In Group A (n=30), before surgery, mean Glasgow Coma Scale (GCS) was 11.90 ± 2.76 (SD) where the range of the GCS was 6-15. In Group B (n=30), mean Glasgow Coma Scale (GCS) was 12.83 ± 2.23 (SD) where the range of the GCS was 8-15. So, the difference of mean pre-operative Glasgow Coma Scale (GCS) between the two Groups was not statistically significant (p-value >0.50).

Patients outcome on day one, three and seven was assessed with GCS. In Group A (n=30), after surgery, mean Glasgow Coma scale (GCS) was 13.00 ± 2.01 (SD) ,13.93± 1.72 1nd 14.47±1.01 on day 1,3 and 7 respectively while it was 13.60±1.67.14.00±1.48 and14.30 ±1.29 respectively inGroup B (n=30). The range of the GCS was 10-15 in both the Groups. So, in post-operative GCS level, there was no significant difference (p-value >0.05). (Table2)

GCS	GR. A (mean ±sd)	GR. B (mean ±sd)	P VALUE
PREOP	11.90 ± 2.76	12.83 ± 2.23	0.15
DAY 1	13.00 ± 2.01	13.60 ± 1.67	0.21

DAY 3	13.93 ± 1.72	14.00 ± 1.48	0.87
DAY 7	14.47 ± 1.01	14.30 ± 1.29	0.58

Table 2.

Clinical outcome of patients at one month on follow up was measured using Glasgow Outcome Scale(GOS) .In Group A 17 (56.7%)&8(26.7%)had GOS of 5 &4 respectively while in Group B 15(50%)&8(26.7%) had gos of 5&4 respectively which is considered favorable GOS score, while GOS of 3 was present in 4(13.3%) patients in Group A and 6 (20%) patients in Group .One patient in Group A died whose GOS was one, while no mortality in Group B.the P value of GOS was s written in table below for various Groups and is more than >.05 and statistically not significant (Table 3).

		GOS	Group A(N=30)	percentage	Group B(N=30)	percentage	P value
Good outcome	Good recovery	5	17	56.7	15	50	.68
	Moderate disability	4	8	26.7	8	26.7	1
Poor outcome	Severe disability	3	4	13.3	6	20	.68
	Persistent vegetative state	2	-		1	3.33	.92
	Death	1	1	3.33	-		.93

Table 3.

In both Group A & B acute rebleed (from the dural stripping, subgaleal vessel) seen in one (3.3%) patient each. ,small brain haemorrhage seen in CVA patients in 1(3.3%) patients of Group A and 2(6.67%) patients of Group B. Pneumocephalus occurred in 3(10%) patients of Group A and 4(13.33%) of Group B. Death(3.33%) occurred in one patient in Group A while no death reported in Group B. Empeyma occurred in a 1(3.3%) patient of Group B only .Rest of complications like new onset seizure ,new focal neurological deficit, wound infection, meningitis also occurred in both Groups as given in table below. On applying fisher exact test no post-operative complication was statistically significant P value >.05 on comparing both Groups. (Figure 3)

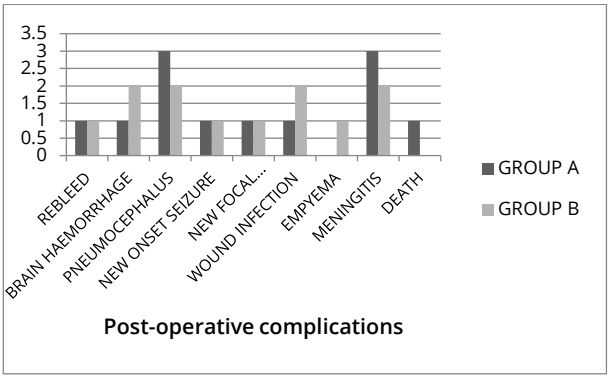


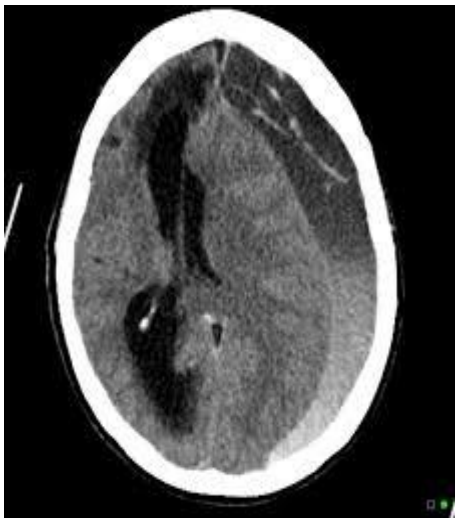
Figure 3.

In Group A 11(36.67%) patients were discharged on post operative day 4 & 5 while in Group B 10(33.33%) were discharged. In 5 to 10 days interval 18(60%) patients were discharged in Group A while in Group B (16%) patients were discharged. After 10 days period only 1(3.33%) patients was discharged in Group A ,while 4(13.33%) were discharged in Group B .Mean hospital stay was 5.67 ±2.15 in Group A while it was 6.60 ±2.97 in Group B.On comparing the hospital stay by T test 2 tailed ,p value was 0.17 which was not significant.

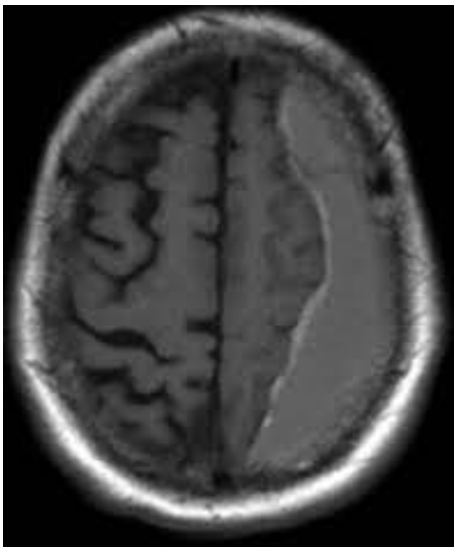
NCCT head was done on day 3 revealed recurrence in 3(10%) patients in Group A while in Group B 5(16.67%) patient had recollection/recurrence. On day 7 only 1(3.33%) patients had recollection in Group A while in Group B no patient had recollection. On follow up on 1 month 2(6.67) patients had recollection Group A while in Group B none had recollection. On comparing the recurrence on day 3,7 and 30 total recurrence was 20 %in Group A and 16.67% in Group Band p value was .067 by pearson chi square test which was not significant.

In Group A, 4(13.33%) patients were reoperated during one month follow up for recurrence/recollection while in Group B Total 3(10%) patients were reoperated during the same period. In Group A ,3(10%) patients were rewashed with the same craniostomy burr hole and improved and 1(3.3%) patients in which membrane was thick and brain not expanding had underwent craniectomy while in Group B 2(6.67%) patients were rewashed for recollection and one (3.33%) patient sunderwent craniectomy for thick membrane and non-expanding brain due to which his GCS was not improving. No Group needed extra burr hole for recollection. On comparing the both Groups for

reoperation the p value for wash Group was .60 and for craniectomy was .37. Both were more than .05 and not statistically significant.



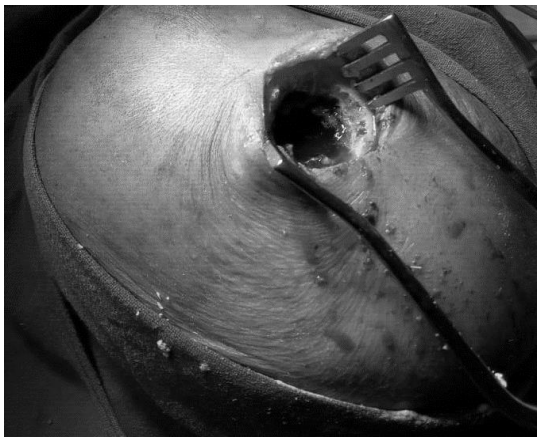
Colour plate 1. Ncct brain showing colour plate 1A: MRI T1 image of brain. Right sided chronic SDH showing right side chronic SDH.



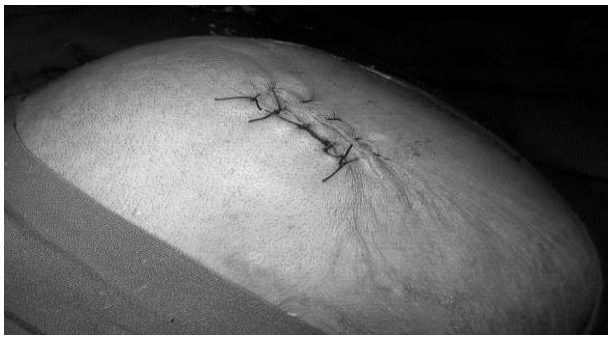
Discussion

The common occurrence of chronic subdural hematomas in older patient raises some diagnostic and therapeutic difficulties. Despite general agreement about the indication of operation, the extent of surgery is still controversial. The treatment of chronic subdural hematomas has drastically evolved over time[9,10,11,12,13,14]. In the management of CSDHs burr-hole craniostomy should be the method of choice for initial treatment. The treatment goal of CSDH is complete drainage of the collection, using the least invasive technique without a high risk of recurrence. Although burr hole drainage remains the commonest form of treatment of CSDH,our literature search failed to yield an article that compared the results of single versus double burr hole drainage of CSDH. However, double burr hole drainage was generally considered a better result, especially regarding recurrence of the subdural collection. The present study was performed to address this issue.

Colour plate 2. Single burr hole incision marking.



Colour plate 3. Single burr hole after dura opening.



Colour plate 4. Single burr hole closure.

Colour plate 5. Double burr holes after dura opening.

The continuous search for the best method of surgery led us to carry out this study in the department of Neurosurgery, IMS, BHU, Varanasi during the period of September 2016 to august 2018 in which we compared two groups of thirty patients each for intraoperative and postoperative complication, postoperative outcome with the help of gcs and gos.

The mean age was 58.77±14.29 years in the group A and57.07 ± 15.02 years in group B respectively. These findings are consistent with the study of Ernestus et al[15] in which the mean age was 60 years, which correlates with this study. The higher incidence among the older age group is because of cerebral atrophy and slow accumulation of blood as well as increased incidences of falling down in elderly population.

In the study out of 60 patients 16 (26.7%) were females and 44(73.3%) were males. In group A, 6(20%) patients were females and 24(80%) were males while in Group B 10(33.3%) patient were females and 20 (66.7%) were males. On comparing. Thus, male were mostly affected in both groups. The male-female ratio was 3:1: which correlates with the study of sanbasivan[16]where male–female ratio was 6:1 showing male preponderance in chronic sdh. Cause of male preponderance could be because they are more prone to injuries because of more outing.
The thickness of CSDH in group A ranges from 10 to 18 mm with mean of 14.63± 2.46 while in group B the range was also from 10-18mm with mean of 14.43t± 1.18..

Midline shift in group A ranges from 10-14 mm with mean of 10.80 ±1.03while in group B the range was 10-14 mm with mean of 10.67±1.18.The hematoma characteristics were similer to the P. Taussky et al.[17] whose study included cases with hematoma thickness of 1.8+0.7 cm and according to him hematoma thickness ,midline shift does not contributes to increased recurrence rate after surgery in both the groups.

During intraoperative period bleeding from the fragile emissary veins occurred in 3(10%) pt. of group A and 1(3.3%) pt. of group B, while brain contusion during opening up of thick membrane occurred in 2(6.67%) pt.'s of group A but none in group B.The brain after evacuation of hematoma not expanded in 4(13.33%) pt. of group A and 3(10%) of group B while it expanded over time in 26(86.6%) of group A and 27(90%) of group B. Thenon expansion of brain is due to long standing CSDH and cerebral atrophy .

The mean time for the duration of surgery was 31.13±5.01 min in group A while in group B mean operating time was 47.07±4.75 min, showing that the mean operating time in the group A was significantly less as compare to the group B. These findings were similer to findings of HAN et al[18] whose study stated that One burr hole craniostomy takes shorter operation time and less invasive than that of two burr-hole craniostomy

In group A (n=30), before surgery, mean Glasgow Coma Scale (GCS) was 11.90 ± 2.76 (SD) where the range of the GCS was 6-15. In group B (n=30), mean Glasgow Coma Scale (GCS) was 12.83 ± 2.23 (SD) where the range of the GCS was 8-15. So, the difference of mean pre-operative Glasgow Coma Scale (GCS) between the two groups was not statistically significant (p-value >0.50). Patients outcome on Day one, three and seven was assessed with GCS.

In group A (n=30), after surgery, mean Glasgow Coma scale (GCS) was 13.00 ± 2.01 (SD) ,13.93± 1.72 1nd 14.47±1.01 on day 1,3 and 7 respectively while it was 13.60±1.67.14.00±1.48 and14.30 ±1.29 respectively in group B (n=30). The range of the GCS was 10-15 in both the groups. So, in post-operative GCS level, there was no significant difference (p-value >0.05. The clinical assessment of patients through GCS findings were similer to findings of AsaduzzamanSM[19]et al who also studied patients preoperative and post operative GCS and find out that clinical outcome of CSDH patients after SBH craniostomy was similer to DBH craniostomy.

Clinical outcome of patients at one month on follow up, measured using Glasgow Outcome Scale(GOS) at 1 month. .In group A 17 (56.7%)&8(26.7%)had GOS of 5 &4 respectively while in group B 15(50%)&8(26.7%) had gos of 5&4

repectively which is considered favourable GOS score.while unfavourable GOS ie GOS of 3 was present in 4(13.3%) patients in group A and 6 (20%) patients in group B .one patient in group A died whose cause of death was old age and poor gcs had GOS 1,while no mortality in group B. the P value of GOS was >0.05 and statistically not significant .The clinical outcome assessment with GOS had proven the fact that single burr hole craniostomy is equally effective and less time consuming as compare to double burr hole craniostomy in selected group of patients as described by kansal et al[20]

In both group A & B rebleed (from the dural stripping, subgaleal vessel) seen in one (3.3%) pt. each, small brain haemorrhage seen in CVA pt. in 1(3.3%) pt. of group A and 2(6.67%) pt. of group B which was due to uncontrolled hypertension. Pneumocephalus occurred in 3(10%) pt. of group A and 4(13.33%) of group B. Death (3.33%) occurred in one patient in group A, who had a preoperative gcs of 6 and after surgery he had rebleed for which washing done but patient dies due to multiorgan failure. Empeyma occurred in a 1(3.3%) patient of group B only who was a known case of diabetes mellitus and prone to postsurgical infections. New onset seizure ,new focal neurological deficit were seen in one patient each(3.3%)of both groups while, wound nfection(3.3%&6.7%),meningitis(10%&6.67%) were also occurred in both groups.

Mean hospital stay was 5.67 ±2.15 in group A while it was 6.60 ±2.97 in group B. The hospital stay was shorter in the SBH group as compare to DBH group can be explained due to less operative time and early recovery of the patients. The study conducted by Gupta Sanja K.[21]had mean postoperative hospital stay was 5 days in single burr hole and 6.5 days in Two burr hole technique. NCCT head was done on day 3 revealed recurrence in 3(10%) patients in group A while in group B 5(16.67%) patient had recollection/recurrence. On day 7 only 1(3.33%) pt. had recollection in group A while in group B no patient had recollection. On follow up on 1 month 2(6.67) pt. had recollection group A while in group B none had recollection. On comparing the recurrence on day 3,7 and 30 p value was .067 by pearson chi square test which was not significant. The study by kansal et al [20]in which they compare SBH with DBH recurrence rates had higher recurrence in SBH group but not statistically significant. In group A, 4(13.33%) patients were reoperated during one month follow up for recurrence/recollection while in group B Total 3(10%) patients were reoperated during the same period. In group A ,3(10%) pts. were rewashed with the same craniostomy burr hole and improved and 1(3.3%) pt. in which membrane was thick and brain not expanding had underwent craniectomy while in group B 2(6.67%) pt. were rewashed for recollection and one (3.33%) .pt.underwent craniectomy for thick membrane and non expanding brain due to which his GCS was not improving. No group needed extra burr hole for recollection. On comparing the both groups for reoperation the p value for wash group was .60 and for craniectomy was .37. Both were more than .05 and not statistically significant. A met analysis comparing single burr hole and double burr hole craniostomy for CSDH was published by Belkhair S[22]et al, whose conclusion was that suggest that SBHC is as good as DBHC in evacuating chronic subdural hematoma and is not associated with a higher revision rate compared to DBHC. No group needed second reoperation and recovered well.

Conclusion

This study was undertaken with the aim to evaluate the results of treatment of CSDH with Single vs Double burr hole craniostomy. With this study, we have found that single burr hole evacuation is similar to double burr hole evacuation of CSDH in terms of Intraoperative and postoperative complications in selected group of patients. The patients in both groups after intervention had almost similar outcomes and quality of life according to GCS and Glasgow outcome scale also SBHC is a simple, less time consuming and less invasive treatment as it requires only one burr hole to be made.

It was found that double burr-hole procedure is better than single burr-hole procedure in terms of recurrence; but the difference is not statistically significant.

Thus, our study recommends SBHC as equal and a good alternative to DBHC in the management of CSDHs.

Limitations of the study.

The sample size was small and patients with specific conditions were omitted, example- use of anticoagulants. Investigations with larger sample size, inclusion of such patients are required to

further assess the role of number of burr holes as an independent risk factor of CSDH recurrence.

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Upper cervical spine tuberculosis. A case report

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ABSTRACT

Tuberculosis is an infection caused by Mycobacterium tuberculosis; mainly affects the lungs; spinal tuberculosis presents 6 % of the extrapulmonary locations; Upper cervical spine tuberculosis is a rare condition and counts only 0.3 to 1 % of all spinal tuberculosis; that makes it a rare condition studied by few case reports. We report a case of upper cervical spine tuberculosis of the atlantoaxial facet joint.

Keywords
tuberculosis,
upper cervical spine,
atlantoaxial dislocation

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INTRODUCTION

Upper cervical spine tuberculosis is a rare pathology (1,2), although medical treatment is uniformly indicated, surgical management is still debated whether to operate or not patients with poor clinical presentation.

CASE PRESENTATION

The patient is a 19 years old young man without past medical history who was presenting during 3 months a neck pain with a limitation of the neck movement, there was no neurologic deficit at the admission, the cervical spine CT showed a bone lytic lesion interesting the left hemi body of axis, its pedicle and the left atlantoaxial joint; the lesion was hypo intense T1 WI hyper intense T2 on spinal MRI (Figure 1); those images were not specific although an infectious origin was suspected, so first the patient was operated by an anterior approach where we performed total removal of the lesion. Histological examination was in favor of caseo-follicular tuberculosis; immediately anti tuberculosis chemotherapy was started under the protocol 5 RHZE/4 RH (5 months of *Rifampicin, Isoniazid, Pyrazinamide, Ethambutol* and 4 months of *Rifampicin and Isoniazid*). In a second time, the patient was operated and via a posterior approach we performed an occipito- C3-C4 fixation. In post-operative there was a pain relief and images showed a progressive reossification of the lytic lesion (Figure 2).

DISCUSSION

Upper cervical spine tuberculosis is a rare condition and counts only 0.3 to 1 % of all spinal tuberculosis (1,2); it starts frequently unilaterally by involving the cancellous part of the facet of atlas but less frequently

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as in our case, the cancellous portion of the facet of axis and of the odontoid process (3). The upper level is considered to be the highest mobile region of the cervical spine (1,2) and protects a part of the spinal cord that the aggression could jeopardize major functions and even could be fatal. Although progressive, the infectious lesions including tuberculosis cause the same amount of instability as the traumatic lesions (4), and in the most times the lesion itself couldn't be as dangerous on the neurological structures as the spinal instability caused by the destructions of the main bony and ligamentous stability structures; despite that, the presence of a contralateral healthy joint could limit the clinical presentation to neck pain and torticolis and delays the appearance of neurologic deficit (3). On the other side the ligamentous system appears to be unilaterally incompetent even more the obliquity of the inclination of the facet of atlas in the atlantoaxial joint probably resulted in its lateral subluxation over the facet of axis (3); for that the surgical indication is still debated. Other authors proposed classifications based on the presence or not of atlantoaxial dislocation (figure 3) (1), and they propose conservative management in case of minor deficit in absence of atlantoaxial dislocation or an anterior compression due to a large retropharyngeal abscess or granulation destroyed bone (1).

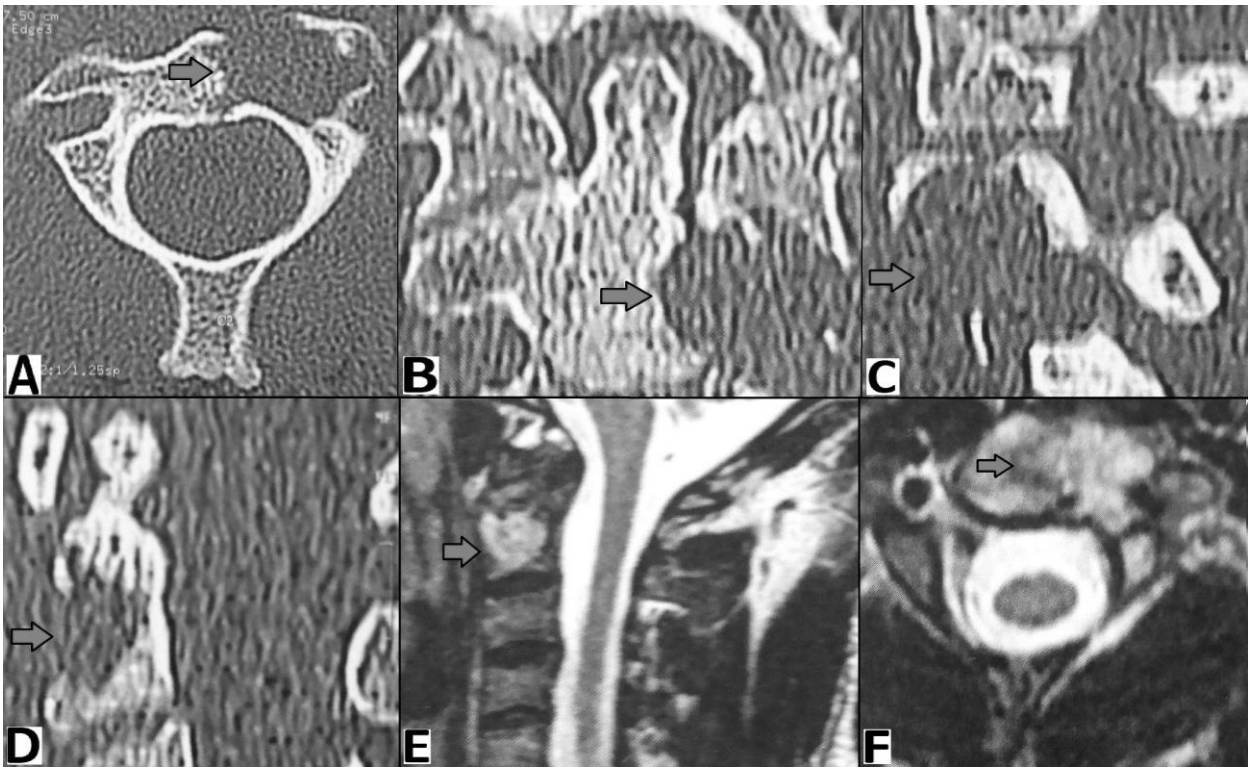

Figure 1. Preoperative images; A: axial CT, B: Coronal CT, C: left parasagittal CT passing through the left C2 pedicle, D: sagittal CT, E: sagittal T2 WI MRI, and F: axial T2 WI MRI; those images show the bone lytic lesion interesting the left hemibody of axis, its pedicle and the left atlanto axial joint; the lesion was hypo intense T1 WI hyper intense T2 on spinal MRI.

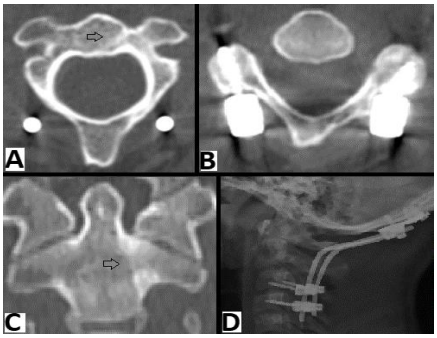

Figure 2. 6 years post operative images; A and C : spiane CT, axial and coronal slides passing through C2 showing a total reosification of the lesion (the arrow); B: axial CT showing the screws placement on C3; D: X-rays of the occipito cervical fixation

Lifeso classification	
Stage 1	Minimal bony or ligamentous destruction; no AAD.
Stage 2	Minimal bony or ligamentous destruction; reducible or irreducible AAD present.
Stage 3	Significant bony or ligamentous destruction evident.
Bhagwati et al. grading system	
Grade I	Merely inflammatory involvement of bony structures of the CVJ with formation of granulation tissue and destruction of bone.
Grade II	Formation of a large retropharyngeal abscess with bony changes.
Grade III	Associated subluxation of the atlantoaxial joint, by bony destruction and/or laxity of apical and transverse ligaments.
Grade IV	Formation of epidural abscess and compression of the cervicomedullary junction and the upper cervical cord, with neurological defi cits that may be mild or severe.

Figure 3. Grading systems for the tuberculosis of the cranio vertebral junction. AAD: atlantoaxial dislocation, CVJ: craniovertebral junction (1).

Conclusion

Upper cervical spine is a rare location of tuberculosis; it is a serious affection that could lead to neurologic deficit or even fatal. In association with medical treatment, surgery is indicated especially if there is a risk of instability.

Declarations of interest

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The use of corticosteroids in autoimmune encephalitis. Basic and clinical considerations

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ABSTRACT

Autoimmune encephalitis (AE) is a brain inflammation caused by autoantibodies that target proteins, intracellular and extracellular antigens, triggering damage in the CNS; AE is classified in various syndromes caused by various antibodies, It is a diagnosis of exclusion. Therefore, it has to be differentiated from multiple causes that could unleash encephalitis. However, its treatment is based primarily on immunotherapy, where corticosteroids as immunosuppressive agents, play a key role in the treatment along with other agents.

INTRODUCTION

The immune system, under certain pathophysiological conditions, is capable of producing antibodies against cells, tissues, or organs, triggering known autoimmune diseases [1]. These reactions are often expressed in the central nervous system, for example, autoimmune encephalitis (AD), which is a brain inflammation due to the presence of freely circulating autoantibodies that affect nerve cells [2]. The advent of technologies that have allowed the detection of antibody subtypes, has modified the classification of autoimmune encephalitis, substantially improving the diagnosis, management, and prognosis of these patients [1,2]. However, one of the current challenges consists of

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as in early diagnosis and management in low-level hospital institutions, which do not have laboratories or specialized equipment that facilitate this type of exam, so the approach in these cases is general, frequently with the isolated use of corticosteroids [3]. Based on the above, the objective of this manuscript is to present evidence on the role of corticosteroids in the treatment of autoimmune encephalitis, highlighting basic and clinical aspects that translate their understanding and usefulness.

Pathogenesis of autoimmune encephalitis

AD is brain inflammation produced by the action of autoantibodies directed against cell surface proteins, intracellular and intracellular antigens [2,4]. Various processes such as paraneoplastic syndromes, molecular mimicry, vaccines, or failure of immune tolerance, might trigger the production of autoantibodies against specific antigens that cause disease [1,4]. For this reason, the identification of autoantibodies constitutes a fundamental step to understand the pathophysiological mechanism of autoimmune encephalitis, its complete understanding will allow choosing the appropriate diagnostic tests and treatment [1,4].

Autoimmune encephalitis is classified taking into account the pathophysiological mechanism that produces it (Figure 1). For this reason, the pathogenesis will be addressed, considering grouping antibodies according to the location of their antigens [5-7].

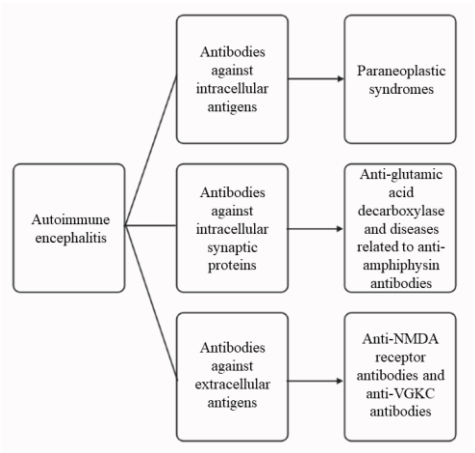

Figure 1. Autoimmune encephalitis classification according to the pathogenetic mechanism [2,4,6,7].

Paraneoplastic syndromes, in which antibodies "Anti-Hu" are directed against intracellular antigens, primarily tissue such as temporal lobe, cerebellum, brainstem, dorsal roots, and autonomic nervous system [8-9]. In other autoimmune systemic syndromes such as Systemic Lupus Erythematosus, where there are antibodies against phosphorylated ribosomal P proteins, neurological and/or psychiatric manifestations may occur, such as psychosis, with a positive correlation between antibody levels and severity of symptoms [10,11].

The binding of antibodies to antigens, whether at the intracellular or extracellular level, causes alteration of synaptic interactions and prevents the expression of these receptors; if this happens for a long time, irreversible damage to the central nervous system could be generated [12].

Clinical manifestations

AD has a wide clinical spectrum in which they can be found from the typical encephalitis with involvement of the limbic system, to complex neuropsychiatric symptoms. These symptoms are related to the type of antibody and the antigen to which it is directed (Table 1) [1,2,5].

Antigen	Manifestations
NMDA	Psychosis, dystonia, chorea, epilepsy, cognitive impairment, dysautonomia
AMPA	Psychosis, limbic encephalitis, aggressiveness, hallucinations, sleep disorders
GAD 65	Stiff Man syndrome, DM1, cerebellitis
ANNA 1	Cerebellitis
GABA	Psychosis, epilepsy
Caspr2	Neuromyotonia, muscle spasm, fasciculations, insomnia, hallucinations

Table 1. Clinical manifestations related to the type of antigen [2,5].

Symptoms despite being variables, in most adolescents and adults evolve in stages, initially, the symptoms may appear similar to a viral infection in which headache and fever are the most common. Later, between days and weeks, neuropsychiatric

symptoms are triggered. These may include psychosis, euphoria, aggression, inappropriate sexual behaviors, fear, panic attacks, and compulsive behaviors, cognitive impairment, seizures (predominantly in pediatric patients) [13], sleep disturbances, developmental and language regression, catatonia, gait instability, and autonomic instability [14,15].

Subtypes of autoimmune encephalitis

Depending on the presence of specific autoantibodies directed against synaptic and neuronal cell surface antigens [2], the following encephalitis subtypes occur:

Antibodies against intracellular antigens

Anti-Hu encephalitis (ANNA-1)

In Anti-Hu encephalitis (ANNA-1), many patients present with sensory neuropathy, cerebellar degeneration, encephalitis, or encephalomyelitis. Interestingly, this condition is closely related to small cell lung cancer [5]. Other patients with Anti-Hu present with a pattern of encephalitis with greater involvement of the brainstem [16-18] or limbic system [8,18,19].

Antibodies against intracellular synaptic proteins

Anti-GAD65 encephalitis

In Anti-GAD65 encephalitis (glutamic acid decarboxylase 65 kd), the antibody targets the enzyme required for the synthesis of the neurotransmitter GABA [5,20,21]. It is clinically associated with type 1 diabetes mellitus, cerebellar ataxia, Stiff Man syndrome [22,23] and limbic encephalitis [2,8,18,19]. In the paraneoplastic setting, it is related to paraneoplastic cerebellar degeneration [5].

Antibodies against extracellular antigens

Anti-NMDAr encephalitis

Anti-NMDAr (N-methyl-D-aspartate receptor) encephalitis represents 20% of autoimmune encephalitis, being the most frequent [2]. It begins with fever, nausea and diarrhea, 2 weeks later psychiatric and / or neurological symptoms begin, progressing rapidly with a tendency to severity, reaching a comatose phase [14,24,25]. Its classic manifestations are: psychosis, agitation, dyskinesias, sleep disorders, mutism, encephalopathy, faciobrachial seizures, dysautonomia, and cognitive impairment [25].

Anti-LGI1 encephalitis

Anti-LGI1 encephalitis (glioma-inactivated leucine-1) is responsible for most cases of encephalitis attributed to VGKC1 antibodies, its most frequent symptoms are myoclonus, seizures, hyponatremia, limbic encephalitis and fascio-brachial dystonic seizures [26-28].

Anti-Caspr2 encephalitis

Anti-Caspr2 encephalitis is associated with Morvan syndrome and Isaacs syndrome. It may present with confusion and personality change [5.29].

Seronegative Autoimmune Encephalitis

A subgroup of patients, due to their clinical manifestations, presents suspicion of autoimmunity, but the antibody detection test is negative, their main symptoms are of a psychiatric nature, including perceptual alterations, catatonia and agitation [1].

Diagnostic approach

The diagnosis of AD is made based on the clinical characteristics, so it should be suspected in any adult or child with the previously mentioned manifestations. Usually, the diagnosis is accompanied by magnetic resonance imaging, electroencephalography, functional neuro imaging, analysis of systemic tumors, and detection of antibodies.

In Magnetic Resonance, the EA may appear as a completely normal image to an abnormal increase in contrast in the cortical or subcortical area of the brain parenchyma. Positron emission tomography, although not performed routinely, can report an increase in frontal-occipital metabolism. This latter finding is related to longstanding [1,2,3,30] disease.

The most frequently observed changes in cerebrospinal fluid (CSF) are predominantly lymphocytic pleocytosis or oligoclonal bands in the CSF. Another diagnostic tool is the EEG. In this study, a low frequency of disordered activity can be observed, but epileptogenic activity is rarely evidenced. A unique finding, known as a delta brush, is related to prolonged disease [31].

Another useful tool is the detection of autoantibodies in both blood and CSF. One of the most frequent antibodies isolated is the IgG anti-

NMDAr antibody [15]. It should be emphasized that the detection of antibodies in CSF has greater sensitivity and specificity than serum detection [32]. In certain cases, the anti-NMDAr type IgA and IgM may be isolated, but these do not have diagnostic value, however, they are associated with chronic diseases such as schizophrenia [33,34].

In the setting of advanced encephalitis, antibodies tend to remain elevated in CSF, while their titers may be low in serum due to treatment [30,35,36]. The differential diagnosis of AD includes a broad category of psychiatric disorders such as psychosis or schizophrenia (the most common), malignant catatonia, or viral encephalitis. Although not very common, cases of autoimmune encephalitis associated with COVID-19 have been reported [37-39].

PILLARS OF AUTOIMMUNE ENCEPHALITIS THERAPY

There are 2 primary goals in AD therapy: reducing inflammation and slowing the development of the disease, which in turn improves symptoms in patients [1]. A cornerstone of treatment is the early use of immunotherapy when there is a high clinical suspicion of AE, even when the presence of neoplasia or the presence of antibodies has not been identified [40]. However, antibody identification is crucial and that leads to a specific treatment. If there is the presence of tumors, resection This is an important part of treatment [2,3,6].

Immunotherapy

Immunotherapy in AD includes general immunosuppressive agents and others that target phases of pathogenesis [6].

There are 3 lines of treatment; a first-line consisting of steroids, intravenous (IV) immunoglobulin and plasmapheresis (PLEX), a second containing Rituximab and cyclophosphamide, and an alternative therapy that includes agents such as azathioprine, mycophenolate mofetil [1,3,6,41, 42], which are steroid-sparing agents used for maintenance, and tocilizumab for refractory cases [6]. It is important to keep in mind that AE associated with neoplasms has a faster course and is irreversible; in other words, it is difficult for patients to recover even when treatment is started early [43].

In the event of clinical suspicion of AD, empirical treatment should be instituted as quickly as possible, even before the results of antibody tests [40], and may include steroids and/or IV immunoglobulins [5], and if the first-line therapy fails, we should start the second line as quickly as possible. The response to first-line therapy [6] can be observed approximately 2 weeks after starting treatment, so this is the time to take into account for changing therapy, if necessary. However, a significant number of patients with AD will respond to first-line therapy and will have a good outcome within 1–2 weeks after initiation of therapy [3]. Table 2 describes the therapeutic lines available for the management of AD.

Therapy	Therapeutic target	Posology	
		Children	Adults
First line therapy			
Corticosteroids Methylprednisolone (solumedrol) [5]	Cytokines, deplete T cells	30 mg / kg up to 1000 mg IV over 3 to 5 days	1 gram per day for 3-5 days
IV immunoglobuline	Antibodies and autoimmune mediators	2 g / kg over 2 days, followed by weekly dose for the next 4 weeks**	0.4 g / kg / day for 5 days
Plasmapheresis	Antibodies and autoimmune mediators		1 session every 2 days for 5-7 days
Second line therapy			
Rituximab	CD20 + B cells and short-lived plasma cells		375 mg / m2 IV infusion weekly for 4 weeks
Cyclophosphamide	Lymphocytes (alters DNA crosslinking)		750 mg / m2 IV monthly *** for 3-6 months [3,6]
Alternative therapy			
Azathioprine	Lymphocytes (blocks nucleotide synthesis)		Initially 1-1.5 mg / kg once daily or divided twice daily, target 2-3 mg / kg / day

Mycophenolate	Lymphocytes (inhibits IMP dehydrogenase)		Initially 500mg twice daily, target 1000mg twice daily
Tocilizumab	Cytokines		Initially 4 mg/kg, followed by an increase of 8 mg/kg per month based on clinical response
IL-2 (aldesleucina)	Cytokines		1.5 million IU / day, 4 subcutaneous injections 3 weeks apart each other

** If a synaptic antibody/cell surface disorder is detected, administer IVIG, plasmapheresis, and/or steroids. If a synaptic / cell surface antibody is determined and significant symptoms are shown, provide first-line therapy if not provided [5].
** In severe cases, it is given more frequently with the first 2-3 cycles given every 2 weeks [1]
*** Until improvement is observed [5].

Table 2. Therapeutic lines for autoimmune encephalitis [1,5,6].

Symptomatic treatment

It is composed of sedative drugs, to induce and maintain sleep; drugs to manage agitation and emotional instability such as benzodiazepines, clonidine, antiepileptics, choral hydrate, or others, which usually offer benefits [3]. Treatment in the presence of seizures must be carried out aggressively with antiepileptics. The majority of patients do not require long-term seizure treatment [44].

CORTICOSTEROIDS AND ITS MECHANISM OF ACTION IN ENCEPHALITIS

Corticosteroids are the most important first-line agents in AD therapy [3,6], being beneficial in multiple autoimmune disorders [5,6]. Although there is no strong evidence for the superiority of corticosteroids over other therapies, they are the first treatment option, followed by intravenous immunoglobulins and PLEX [6].

Mechanism of action

Corticosteroids are a group of drugs with anti-inflammatory characteristics that act on intracellular glucocorticoid receptors [6], interrupting the transcription of multiple pro-inflammatory genes [6,7] that are activated in chronic inflammatory diseases [7] and that encode cytokines, chemokines, adhesion molecules, inflammatory enzymes, receptors, and proteins [6,7]. They influence almost all cytokines, thus depleting T cells, inhibiting Th1 differentiation, macrophage dysfunction, and eosinophil apoptosis [6]. In high concentrations, they have activity on the synthesis of anti-inflammatory proteins and induce post-transcriptional or post-genomic effects [6,7].

Advantages

They penetrate the brain, an advantage it has over other drugs such as Rituximab, which does not cross the blood-brain barrier (BBB) [6], so they are given as empirical therapy in suspected AD [45]. In addition, they modulate the BBB [3] restoring its integrity and controlling cerebral edema [6].

Goldenholz et al [45] state that corticosteroids as a low-cost therapy could play a role in treatment algorithms for suspected AD cases [45]. Similarly, Prasad et al [46] that in AD a good response to steroids has been shown even when no confirmed serology suggests an autoimmune basis [46].

Disadvantages

Steroids have low specificity on antibody-mediated immune processes, so their efficacy has been debated in AD since they slightly decrease the number of circulating B cells, not contributing much to antibody titers; in addition, they have been associated with systemic side effects [6]. It should be noted that side effects are more frequent with the use of oral steroids than with intravenous [1]. Corticosteroids can also cause or increase the psychiatric symptoms associated with AD, and some clinical studies even suggest neurotoxic and neurodegenerative effects of corticosteroids after chronic exposure [6].

Management

Steroids are administered IV or orally, the former being delivered as “pulse doses” (Table 2). This therapy is not standard and there are no clear treatment regimens [1]. Nosadini et al [47] carried out a systematic review on immune therapy in AD, with the aim of generating evidence on the use, type of treatment and efficacy, finding that as first-line

therapy, it is used in the majority of cases (more than 50% of patients with AD) [47].

Conclusion

Autoimmune encephalitis is a syndrome whose pathogenesis involves different immunological pathways against neuronal surface antigens, for which immunotherapy with various immunosuppressive agents has been proposed as treatment; with a relatively accepted answer. Corticosteroids are consolidated as first-line agents in the treatment of AD, however, better quality studies are needed to demonstrate their superiority over other therapies, and thus identify the safest and most effective system.

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Paediatric brain abscesses in tribal region of India. A single centre experience

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ABSTRACT

Introduction: Brain parenchymal abscesses are relatively infrequent but potentially serious infections in the paediatric population. Surgical intervention in addition to a prolonged administration of antibiotics is generally appropriate management.

Aims and objective: We performed this study to assess the clinical profile, aetiology and outcome of paediatric brain abscess which are treated surgically only by aspiration in the tribal region of Rajasthan.

Material and method: A single-centre retrospective study was conducted over a 5 year period (2014–2019) in the department of neurosurgery in RNT medical college, Udaipur, Rajasthan. We treated approx. 60 patients of which 25 patients treated conservatively and 5 patient treated by craniotomy and abscess excision. So only 30 patient included in our study in which abscess treated by aspiration only. Patients<18 years of age with a confirmed intra-parenchymal abscess were included. Patient records were reviewed for abscess location, microbiology results, Clinical features, Surgical intervention, and outcome using the Glasgow Outcome Score at 3 months.

Result: 11 patients had an abscess in the temporal lobe and Streptococcus was the most common causative micro-organism (n¼15). 25 patients (80%) had an identifiable source which included: ENT infections, congenital cardiac malformations, recent dental surgery and meningitis. The most common symptom is fever f/b headache, seizure and vomiting. But despite previous studies seizure (10/30) presentation is comparatively more. All 30 patients underwent aspiration.

Conclusion: In tribal regions of India ENT infections are a more common source of brain abscess because of poor hygiene and illiteracy and their ignorance of ENT infections and also not taking seriously to fever, headache and other health issues. But at present, there are also decreasing trends of brain abscess by ENT infections and rising trends by congenital heart disease which is a good sign that the health and educational infrastructure is strengthening in the tribal region also.

Keywords
abscess, aspiration, paediatrics, ENT

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INTRODUCTION

A brain abscess is an intra-parenchymal collection of pus in the brain. The incidence of brain abscess among intracranial masses varies from 1-2% in western countries, to about 8% in developing countries[1]. It is still a life threatening and fatal entity and often leads to serious disability and even death if misdiagnosed or treated improperly[2]. Brain abscesses are relatively less common in the paediatric population compared to adults; however, they remain a serious, life-threatening infection[3].

The causes of brain abscesses are highly variable in children. The major predisposing conditions in children are: an adjacent focus of infection, trauma, haematogenous seeding, neurosurgical procedures, cyanotic heart disease and immunocompromised states[4,5,6]. Associated sites of infection commonly include sinusitis, mastoiditis, dental infections and chronic otitis media where aerobic bacterial infections such as Streptococci and Staphylococci predominate[4,7]

The gold standard treatment of brain abscesses continues to be aspiration or excision combined with antibiotic therapy.[5] However the outcome has improved dramatically in recent decades due to improvements in diagnostic techniques and broad-spectrum antibiotics[8.] Magnetic Resonance Imaging is more sensitive at diagnosing early cerebritis[9] and has increased the prognosis of brain abscess by improving the speed of diagnosis.

Despite all of these advances abscesses are still a significant cause of morbidity and mortality[10]. In addition, abscess growth can result in rupture of the abscess into the ventricular system. This life-threatening event will result in an acute decompensation and symptoms of a purulent meningitis[11].

We performed this study to assess the clinical profile, aetiology, and outcome of paediatric brain abscess in the tribal region of Rajasthan.

Material and method

A single-centre retrospective study was conducted over a 5-year period (2014–2019) in department of neurosurgery in RNT medical college, Udaipur, Rajasthan. We treated approx. 60 patients in which 25 patients treated conservatively and 5 patients treated by craniotomy and abscess excision. So only 30 patients included in our study in which abscess treated by aspiration only.

The final cohort of 30 patients comprised 20 male patients (45.8%) and 10 female patient and had a mean age of 6.5 ± 4 years Patients < 18 years of age with radiological confirmed intra-parenchymal abscess were included. Patient records were reviewed for abscess aetiology, location, size, microbiology results, surgical intervention, and outcome using the Glasgow Outcome Score at 3 months.

We include the patients in which abscess treated only by aspiration and then antibiotics. Aspiration of abscess may be single or multiple times. Size of abscess is more than 2.5 cm. The total antibiotic duration was discernible from the medical notes for all patients and the mean time was 5.8 ± 2.0weeks. This comprised a mean of 2.9 ± 1.5 weeks intravenous and3.0 ± 1.8 weeks oral antibiotics. White cell count >11109/L and/or C-Reactive Protein >5mg/L was classed as raised inflammatory markers. Functional outcome was measured using the Glasgow Outcome Score (GOS) at 3 months from discharge. Those with isolated subdural empyema, extradural abscess, or an unknown abscess location were excluded from the study.

Result

Most common symptom is fever followed by headache, seizure and vomitting. (Table-3). The classic triad of headache, fever and focal neurological deficit was seen in two patients (8.6%). Drowsiness or reduced level of consciousness on presentation was recorded in 6 patients (34.8%). Age of patients are mostly 5-10 years. (Table-1)

The Temporal lobe was the most common abscess location (11). The remainder of the abscesses were in the parietal lobe (8), frontal lobe (7), cerebellum (2), thalamus (1), pons (1) (Table 4) .22 patients had a solitary lesion at presentation and rest 8 has more than one lesion. The patient with aspergilloma had two lesions in the same location.

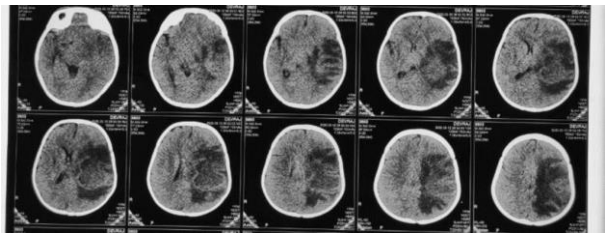

Figure 1. Pre-operative scan of 10-month male child left temporo-parietal brain abcess (original pics).

S. N.	Age	Number	Percentage
1	<5 year	6	20%
2	5-10 yr	15	50%
3	10-18 yr	9	30%

Table 1.

25 patients (80 %) had an identifiable source which include post meningitic (4), congenital cardiac malformations (7), Otogenic and mastoditis (11), Post

traumatic (3). Rest 5 has other non-identifiable sources (Table-2). Streptococcus was the most common organism cultured from the abscesses (18). Other microorganisms include Staphylococcus aureus (5), Coliforms (1), Propriobacterium (1), Mycobacterium tuberculosis (2), Gram negative rods (1) and mixed anaerobes (2).

All 30 patients underwent surgery. All 30 patients had Burr hole aspirations (Figure 1 and 2) (17 patients had single aspiration). More than 2.5 cm size of abscess aspirated or treated surgically, rest were treated conservatively. Pre-operative imaging was available for all 30 patients and volumetric analysis showed an average pre-operative volume of 16.3ml.

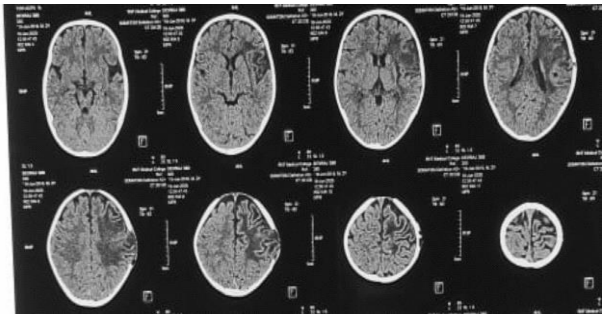

Figure 2. Post-operative scan of this 10-month male child after single burr hole aspiration (original pics).

S. N.	Predisposing Factor	No.	Percentage
1	Otitis Media and mastoditis	11	36.66%
2	Congenital heart disease	7	23.33%
3	Meningitis	4	13.33%
4	Posttraumatic	3	10%
5	Others	5	16.66%

Table 2.

According to size 2.5- 3.5 cm total 16 cases in which 4 cases require single re aspiration (28.57%) , but in 3.5-4.5 cm size total 10 cases in which we require 6 re aspiration (60%) , in which 4 cases require single reaspiration and 2 require two reaspiration. More than 4.5 cm total 4 cases in which 3 patients requires re aspiration. (75%), in which 1 case require two re aspiration and rest 2 cases required three re-aspiration (Figure-3). But the good thing is that all treated with aspiration and antibiotics. Location dose not significantly co-relate with re –aspiration.

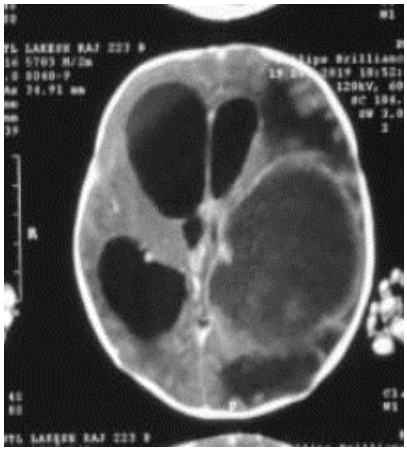

Figure 3. Huge abscess in left temporoparietal region in 2.5month old child (Original Pics).

GOS score at 3-month -22 patient has 5, 3 patients has score 4 and 3 patient had score 3 or less. 2 patients expired – 1 due to some cardiac problem in congenital heart disease, second is due to severe sepsis in otitis media patient. Rest 28 patients survived.

According to symptoms fever resolved in all patients. Seizure resolved in 6/8 patients in 3 months follow up. Motor deficit corrected in 6/8 patients in 3 months follow up.

S.N.	Symptoms and Signs	Number	Percentage
1	Fever	14	46.66%
2	Headache	11	36.66%
3	Seizure	10	33.33%
4	Altered Sensorium	6	20%
5	Vomitting	5	16.66%
6	Meningism	5	16.66%
7	Motor deficit	8	26.66%
8	Sensory deficit	4	13.33%

Table 3.

S.N.	Site of abscess	Number	Percentage
1	Temporal	11	36.66%
2	Frontal	7	23.33%
3	Parietal	8	26.66%
4	Cerebellum	2	6.66%
5	Others(pons,thalamus)	2	6.66%

Table 4.

Discussion

The change in practice towards early prescription of antibiotics for oto-sinogenic infections has resulted in a change in the infective etiologies associated with brain abscess[12]. In studies from the pre-CT era ENT infections were the cause in 38-76% of brain abscesses in children; however this has fallen to 8-36% .In the modern era with congenital heart disease and immunosuppression becoming a more commonly recognized causative factor[11,12,13,14].But in the present study, Temporal lobe abscess following middle ear infection and mastoiditis was the commonest finding[15,16]. Temporal lobe abscess following otogenic infection has been found in previous studies[22]. In tribal area due to poor hygine and others late responding to fever and ignorance of ear infection or maltreatment of ear infection develop a simple meningitis and ear infection into a brain abscess[15,16].

In our study, males are more affected than females. Males are more exposed to outdoor activities with greater chance of ear infection and predisposing to brain abscess [17]. Regardless of the changes in etiology, Streptococcus remains the most commonly reported causative microbe both in this series and those published in the literature[17,18]. The presentation of brain abscesses is non-specific but most commonly includes, headache, fever, altered mental status, meningism and seizures[5,]According to Samull et al nowadays suggest that headache and fever is the most common symptoms and seizures is not so common in abscess but in this study seizure is also common complain (10/30-30%) because involvement of temporal lobe is more .

Those who present with altered mental status and rapid neurological deterioration are more likely to have an increased mortality rate[19]. 2 patient expired in this study had low GCS and altered mental status. So preoperative GCS is important for prognosis. Multiple aspirations were associated with a larger initial abscess volume. These will leave a larger cavity that is slower to involute and thus leave a nidus of infection that can re-accumulate. Half of the patients in this series required more than one aspiration and thus patients should be counselled accordingly.[12]

Modern series report lower mortality rates than the pre-CT era ranging from 8 to 25%[20] and the large series by Tekkok and Erbengi[21] even managed 0% mortality at the end of their study period. Neuroimaging was done in all cases. CT scan was done in 25 cases and MRI was done 5 cases. The only added advantages of MRI over CT Scan are: better differentiation of edema from necrosis, more sensitivity in detection of early cerebritis, greater sensitivity for early satellite lesion[23.] Most common neuroimaging finding was ring enhancing lesion. This has been reported in previous studies from India and abroad[24,25].

One reason for a low mortality rate may be an aggressive approach towards abscess drainage and also sepsis source control. Poor Glasgow coma scale (GCS) at time presentation has been associated with poor outcome. Previous studies in India, Nepal and Pakistan have also reported poor GCS as negative prognostic factor in their studies[24,25]

Conclusion

This study demonstrates that in the modern era with ready access to CT imaging and broad-spectrum antibiotics, low rates of morbidity and mortality can be achieved. Drainage of paediatric abscesses remain the mainstay of treatment both to relieve mass effect and provide a microbiological diagnosis. Patients and their families should be counselled to expect multiple procedures.

But in this study most common predisposing factor for abscess is otitis media than congenital heart disease. Because in tribal region exposed to outdoor activities with greater chance of ear infection and predisposing to brain abscess. Also, illiteracy and poor hygiene leads to more chances of chronic ear discharge and brain abscess formation in future.

So we need to educate the people of tribal region for proper hygine and also early consult to doctor for any ear infection. We have to educate them about their proper health checkup and consult if child had fever, seizure, headache and vomitting. If infant and less than 3 yr age child had excessive irritability then also take consultation. We can also promote pneumococcal vaccination.

But at present there are also decreasing trends of brain abscess by ENT infections (11/30 -36.66%) and rising trends by congenital heart disease (7/30-23.33%) which is a good sign that the health and educational infrastructure is strengthening in tribal region also.

Conflict of interest

There is no conflict of interest to disclose.

Informed Consent

Informed consent was obtained from all individual participants included in this study.

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Lateral orbitotomy in the management of an intra-orbital lipoma. A case report

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Abstract

Introduction: Lipomas are benign subcutaneous mass, but the intra-orbital location is rarely reported in the literature and it can resemble a variety of other orbital lesions.

Case report: We describe a 15-year-old girl who presented with left exophthalmia. Orbital magnetic resonance imaging showed an encapsulated intra-conal mass displacing the optic nerve medially, the external right muscle laterally and the globe anteriorly. Excisional biopsy of the mass by lateral orbitotomy approach resolved the exophthalmia, and histology revealed a primary orbital lipoma.

Conclusion: The diagnosis of an intra-orbital lipoma is not easy and the surgical approach represents a challenge to achieve a total excision while avoiding complications.

Keywords
exophthalmia,
lateral orbitotomy,
lipoma,
orbital

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Introduction

Lipoma is a benign mesenchymal neoplasm composed of mature adipose tissue surrounded by a fibrous tissue capsule[1]. The majority is developed in the subcutaneous soft tissue in the neck, shoulder and back, but it is uncommon in the orbital region[2]. We describe a case of exophthalmia caused by an intra-orbital lipoma and review of the literature.

Case report

A 15-year-old Moroccan girl, admitted to our department for treatment of a progressive left exophthalmia for 06 months. There was no history of trauma, visual disturbances, and significant ocular or medical histories. On ocular examination, she had visual acuity of 20/20 in both eyes with a left axile, reducible and non-pulsatile exophthalmia. Orbital Magnetic Resonance Imaging (MRI) revealed an encapsulated intra-conal mass (2.5 x 1,7 x 0,5 cm) in the posterolateral compartment of the left orbit. The mass was displacing the optic nerve medially, the external

right muscle laterally and the globe anteriorly with resultant exophthalmia. Hypointense at T1 and hyperintense at T2 taking the contrast (Figure 1-2). A left lateral orbitotomy approach was utilized with an excisional biopsy (Figure 3-4). Histopathological evaluation revealed well-encapsulated, mature adipose tissue consistent with a primary orbital lipoma. After surgery, exophthalmia had subsided with a normal ocular motility.

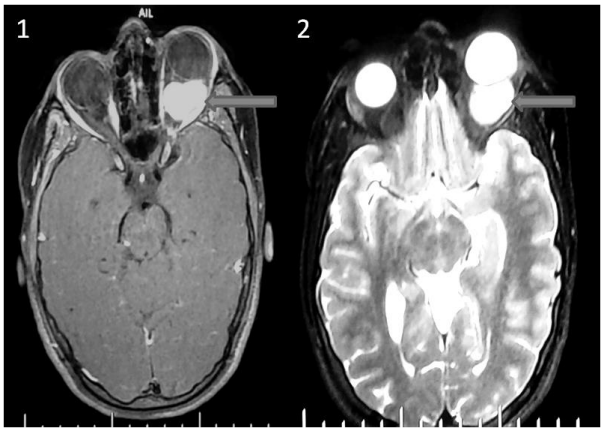

Figure 1. Post contrast axial T1-weighted MRI showing hyper intense lesion (arrow).
Figure 2. Axial T2-weighted MRI showing hyper intense lesion (arrow).

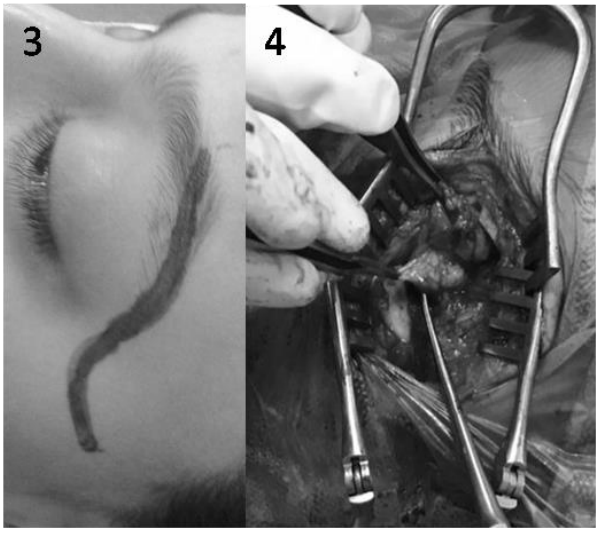

Figure 3. Preoperative photograph showing the incision for a left lateral orbitotomy.
Figure 4. Intra-operative photograph showing tumor excision.

Discussion

Lipoma is a benign lobulated tumor composed of mature adipose tissue surrounded by a fibrous tissue capsule. Frequently it is localized subcutaneously around the torso, neck, and proximal limbs[3], but in the orbital region is uncommon with the reported incidence of 0.6% in adults and 2.8% in children[4].

The exact etiology of lipoma formation is unknown, but there are instances following trauma[4,5]. Also some hypotheses have been mentioned as hypertrophy theory (the growth of the tumor is caused by obesity) and metaplasia theory (the growth of lipoma occurs due to differentiation of mesenchymal cells into lipoblast) [6].

Generally, orbital lipoma slow growing and often asymptomatic until large enough to be palpable, visible or cause mass effect. Rarely grows and compresses the optic nerve causing disturbance in visual function[7].

The radiological appearance of orbital lipoma, on computed tomography the tumor has a distinctive low attenuation with a finely defined border. On MRI it is generally hyperintense on T1-weighted imaging and indistinct to orbital blood on T2-weighted images, hypointense after fat suppression. However, it is not enhanced after contrast images[8], but in our case the lesion was hyperintense.

Due to the various presentations of lipoma, the diagnosis is not always easy and other orbital masses should be considered in the clinical differential diagnosis, such as dermoid cyst, fibrous histiocytoma, schwannoma and cavernous hemangioma[9].

The recommended treatment is the surgical excision and it is a challenge because of the complex anatomy of the orbital structures[10,11]. In our case, the patient was operated by a lateral orbitotomy with removal of the tumor. The long-term outcome after surgery is seen to be excellent however, recurrence of the tumor may occur due to incomplete excision[12].

Conclusion

We present a case of a rare intra-orbital tumor whose surgical approach such as lateral orbitotomy is a real challenge for neurosurgeons.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Abbreviations

MRI: Magnetic resonance imaging

Author's contributions:

C M: manuscript writing; A L and A K: manuscript preparation; B E and M G: manuscript analysis. All authors read and approved the final manuscript.

Acknowledgements

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Conflicts of interest

The authors declare no potential conflict of interest

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Primary calvarial cavernous haemangioma in a child. A case report

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Abstract

A wide variety of bone lesions is encountered on the skull and usually with poor clinical presentations and non-specific radiological features. Primary cavernous hemangioma is one of these rare calvarial lesions that the symptoms are limited to a simple subcutaneous mass frequently neglected by the patient. Although seen in all ages from neonate to elderly; few cases were reported in the literature of patients in the first decade of life. We report a case of four years old boy with primary calvarial cavernous hemangioma in order to help to understand this pathology and to urge physicians to explore any chronic subcutaneous mass at any age.

Keywords
hemangioma,
bone tumours,
skull tumours

Introduction

Skull hemangioma is a rare pathology with minimal clinical presentation and non-specific images. The first known description of this lesion in literature was in 1845 by Toynbee [1]. Skull hemangiomas are classified into capillary and cavernous types; with cavernous type being more frequently seen [1,2,3,4,5,6]. We present a case of four years old boy with primary calvarial cavernous hemangioma.

Case presentation

The patient is a four years old boy with trisomy 21. The parents consulted for the appearance of a right fronto parietal subcutaneous mass; of barely 1 cm of diameter. A brain CT was performed objectified an extra axial right fronto parietal lesion of 42 x 29 mm; isodense, with intense homogenous enhancement after contrast injection, and bone destruction from where the lesion get through to the subcutaneous region; there was also a circumferential osteophytic bone reaction (Figure 1). The patient was operated and the lesion was totally removed through a frontoparietal bone flap. In post-operative there were no complications. Pathology study was in favor of bone cavernous hemangioma. No supplementary management was necessary. Control images performed nine years later, showed no residual tumor or recidivism (Figure 2).

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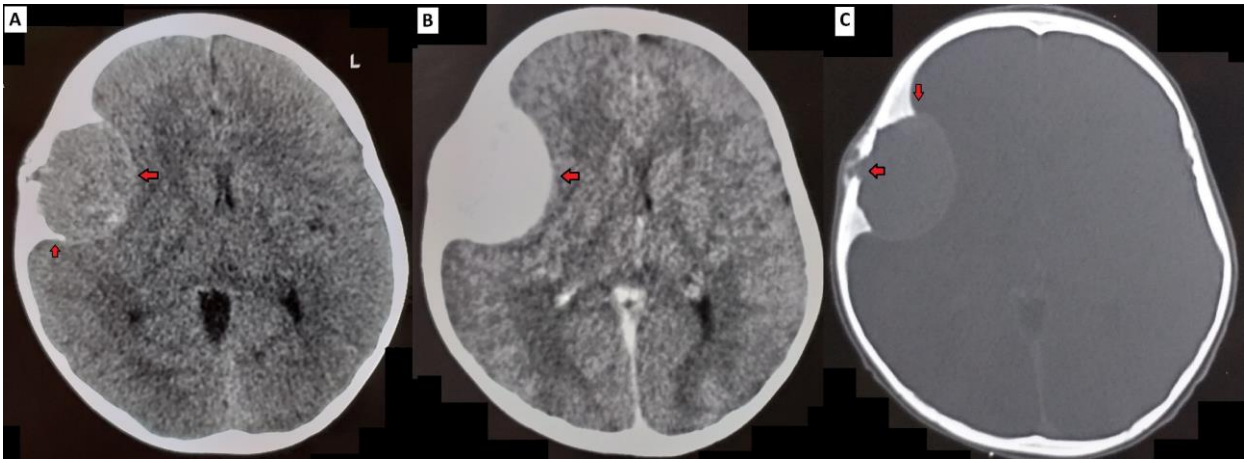

Figure 1. Preoperative brain CT; A: before injection; B: after injection; C: bone window. The images objectify an extra axial right fronto parietal lesion; it appears spontaneously isodense (A, horizontal arrow), with intense homogenous enhancement after contrast injection (B, horizontal arrow), and bone destruction from where the lesion get through to the subcutaneous region (C, horizontal arrow). There was also a circumferential osteophytic reaction from the inner calvarial bone (A and C, vertical arrows).

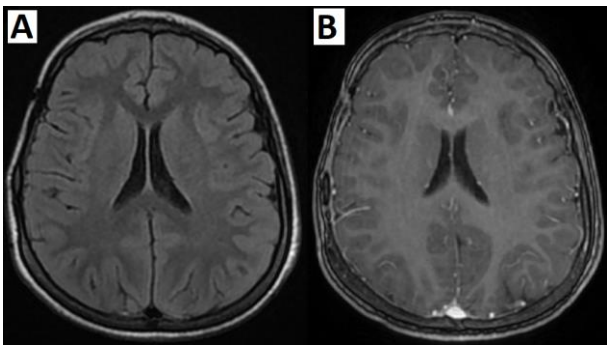

Figure 2. Nine years post-operative MRI showing no tumor recidivism. A: axial FLAIR sequence; B: axial T1 injected image.

Discussion

Primary calvarial hemangiomas (PCHs) are rare lesions; they account of 0.2 % of all bone neoplasm [1,3,5,6,7,8]. Yang *et al.* reviewed 93 cases of PCH reported in the literature from 1845 to 2015; according to this paper most patients were in the fourth and the fifth decade [1,2]. Only 0.9 % of PCHs were seen in the first decade of life as in our case [2]. Frontal bone is a predilection location for PCHs with 44.1% of all cases [1,2]. Clinical presentation depends on the topography of the lesion. Subcutaneous mass and headaches were the most frequent reasons for consultation [1,2]; neurologic deficit is rarely seen [1,2,4,5,6,7,8]. Proptosis, impaired vision, facial nerve paralysis, tinnitus, and hearing loss are seen in orbital and skull base locations [1,2]. Bleeding from the lesion may be seen in the epidural or subarachnoid spaces [1,3,7]. On plane X-Rays and on CT scan, PCH is a lytic lesion with sclerotic rim; after contrast injection the enhancement is constant it could be heterogeneous or homogenous as in our case [2,3]. For us those finding were sufficient to indicate the surgery and to plan the resection strategy. Although not specific, MRI affords supplementary information about the relation of the lesion with the underlying dura, parenchyma, and vascular structures; it shows hypo to iso intense mass on T1 weighted images, hyperintense on T2 weighted images and on FLAIR sequences; there is a large enhancement after gadolinium injection [1,3]. PCHs are accessible lesions for surgical resection, thus total removal with acceptable margin is the treatment of choice [1]; this could be achieved through a skin incision and craniectomy centered on the lesion. In Adult the bone defect is correct usually with cranioplasty. As in our case the management of many other pediatric cases in the literature was limited to lesion removal without bone correction due to the young age face to future skull changing [4,8]; other teams preferred cranioplasty [6] or remodeling [5].

Conclusion

Subcutaneous mass could underestimate deep infiltrating and brain compressive lesion. This is the case of rare lesions like calvarial cavernous hemangioma which is seen in any age. This lesion is associated with the best prognostic if totally removed.

Conflicts of interest

None.

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A solitary case of gliosarcoma an indication for TP53 mutation analysis: a non-concordant finding. Case report

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ABSTRACT

Background: Li-Fraumeni syndrome (LFS) is a hereditary, autosomal dominant malignancy predisposition induced by a mutant TP53. Here, we describe a gliosarcoma (GS) case with a clinical family history impressive for an LFS case in the absence of inherited germline TP53 mutations.

Case description: We present a 44-year-old female with a right high parietal mass. The mass proved pathologically to be GS with an isocitrate dehydrogenase-1 (IDH1) mutation. Pedigree analysis identified five first-degree and second-degree relatives with LFS spectrum malignancies. The patient tested positive for TP53 mutation; however, her family tested negative.

Conclusion: Of all the tumours, GSs are the least described entity with LFS. We are highlighting the need to do a genetic survey in family members of the patient who has been diagnosed to have gliosarcoma and other tumours consistent with LFS.

Keywords
gliosarcoma,
IDH-1 mutation,
Li-Fraumeni Syndrome,
TP53

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INTRODUCTION

Gliosarcoma (GS) is an infrequent malignancy that is made up of glial and sarcomatous components (3). According to the WHO classification (2016), GS falls under the umbrella of isocitrate dehydrogenase (IDH)-wild type Glioblastoma (GBM) (8). The distinction of primary GS is given to GS tumours that arise without the presence of previous GBM (3). Despite being known for over a century, many aspects of GS remain ill-defined (7) (13). The median age for GS patients at diagnosis ranges from 55 to 61 years (3) (7). GS has a male predominance and a predilection for the temporal lobe (7).

Currently, GS tumours are treated in accordance with Stupp's trimodal regimen originally designed for GBM; the regimen entails the combination of maximum safe surgical resection, radiation therapy, plus concomitant and adjuvant temozolomide (16). Despite the absence of solid evidence to support Stupp's regimen for GS, several

studies have reported encouraging results (3) (4) (15) (17). Even in the era of multimodality therapy, the prognosis of GS tumours remains grim, with the median survival ranging between 8.3 and 16.7 years (5-7) (17). Factors impacting GS's survival include age at presentation, the extent of surgical resection, and adjuvant radiotherapy (7).

We aim to describe a case of GS with a clinical family history impressive for a LFS case; However, no inherited germline TP53 mutations have been detected.

CASE DESCRIPTION

A previously asymptomatic 44-year-old female was introduced to our institution after experiencing a fall. She complained of progressive weakness of her left arm and leg over the course of one month, which had led to a worsening ability to walk and handle items (Figure 1). She denied any other limb weakness or paraesthesia, speech or visual disturbances, nausea, vomiting, or headache. Throughout this period, she also denied any episodes of seizures or alteration in mental status.

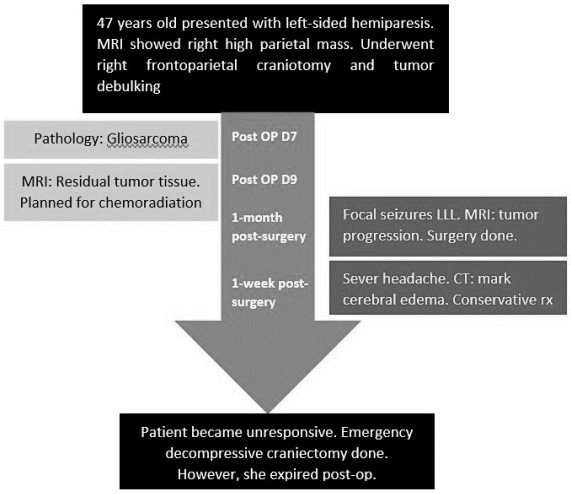

Figure 1. Timeline showing the course of the patient during the follow-up and outcome. ***Keys:*** *OP: operative; LLL: left lower limb; Rx: treatment.*

The patient was presented with left breast cancer with stage III (aT3N2M0) of invasive ductal carcinoma metastasized to the ipsilateral axillary lymph nodes, for which she had modified radical mastectomy and axillary clearance followed by adjuvant radiation therapy two years back. Pathological evaluation was negative for oestrogen receptor, progesterone receptor, and human epidermal growth factor receptor-2 defined by immunohistochemistry and fluorescent in situ hybridization.

On physical evaluation, she was grossly intact, aside from left-sided hemiparesis (Grade II Medical Research Council) and left-sided deep tendons hyperreflexia. Cranial magnetic resonance imaging (MRI) (Figure 2) verified the presence of a 3.4×3.3 cm right high parietal mass with surrounding hyperintensity on T2-weighted sequence, representing vasogenic oedema. Postcontrast images revealed thick irregular peripheral enhancement with central hypointensity representing central necrosis.

Right frontoparietal craniotomy and brain tumour debulking with stereotactic computer-aided navigation was performed. Histopathology (Figure 3) revealed a high-grade glial neoplasm admixed with an area comprising of spindle-shaped cells arranged in fascicles. The glial area of the tumour was positive for glial fibrillary acidic protein (GFAP) immune stain and showed poor reticular network. The spindle-shaped area was negative for GFAP and showed a rich reticular network. The specimen was immunoreactive for IDH-1. Based on the presence of both glial and sarcomatous areas in the tumour, a diagnosis of GS was established.

The patient was offered genetic counseling; her family history revealed that her oldest sister was diagnosed with breast cancer at 39 years old (yo) and synovial sarcoma of the foot at 42 yo. Her other sister was diagnosed with primary spinal osteosarcoma at 40 yo and breast cancer at 44 yo. Among her maternal uncles, one developed leukaemia at 35 yo, and another one had lymphoma at 55 yo. Her paternal uncle was diagnosed with lung cancer at 50 yo. Based on the clinical family history in the context of GS, a diagnosis of LFS was highly suspected. Genetic testing revealed a presence of a mutated TP53 in our patient with an absence of germline TP53 mutations in her family. The BRCA1, BRCA2, and PTEN mutations were not identified.

Postoperative MRI (Figure 4) showed 1.3×1cm residual tumour tissue, for which she received adjuvant temozolomide and radiotherapy. At the one-month follow-up, the patient endorsed focal jerky movements in her left leg. Cranial computerized tomography (CT) scan revealed a further progression of the previously seen residual

tumour tissue with significant midline shift and surrounding vasogenic oedema. Surgical extirpation of the brain tumour was done. She had recovered from surgery with persistent left-sided hemiparesis and discharge on dexamethasone. One week later, she endorsed severe headaches and episodes of vomiting. A cranial CT scan (Figure 5) revealed marked cerebral oedema. Her family refused the decompressive craniectomy option. She was started on mannitol and dexamethasone. However, two-day after, she became unresponsive and developed a right fixed dilated pupil for which she had an emergency decompressive craniectomy. Unfortunately, her clinical status progressively deteriorated till she expired.

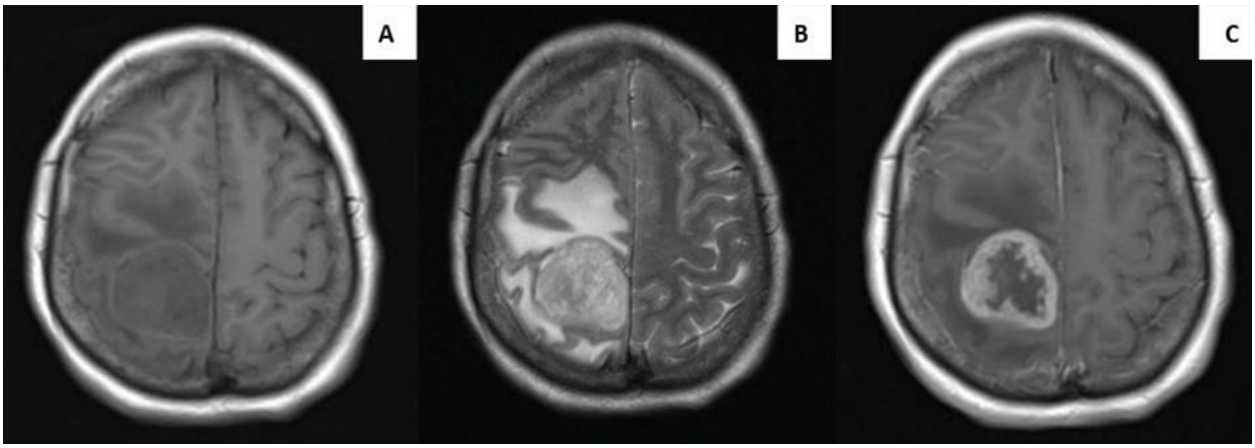

Figure 2. Brain MRI demonstrates a right high parietal lesion with surrounding vasogenic oedema. The mass shows isointensity on the sagittal T1-weighted sequence (**A**), heterogeneous hyperintensity on the sagittal T2-weighted sequence(**B**), and thick irregular peripheral enhancement in the postcontrast T1-weighted sequence (**C**).

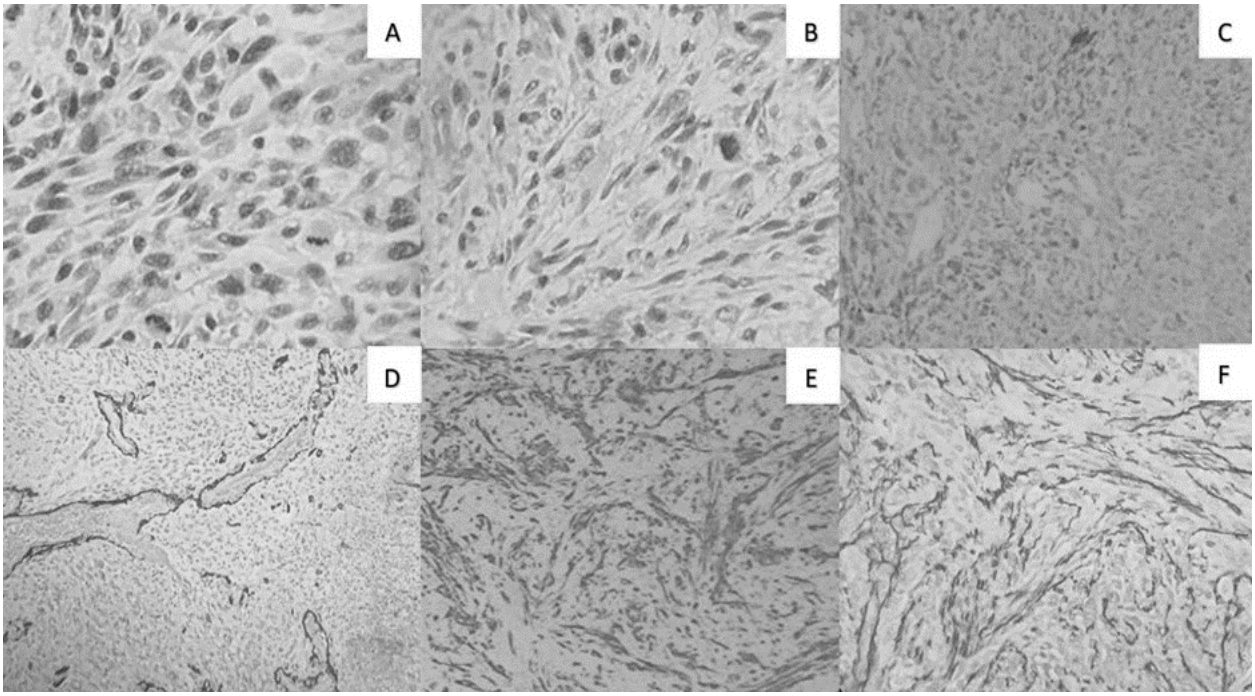

Figure 3. The histopathology revealed a brain tumour tissue comprising two cells types. Area of neoplasmic glial cells depicting moderate nuclear pleomorphism and frequent mitosis (**A**) admixed with area comprising of spindle shaped cells arranged in fascicles (**B**). Glial area of tumour was positive for GFAP immunostain and showed a poor reticular network (**C&D**). Spindle shaped area were negative for GFAP and showed a rich reticulin network (**E&F**).

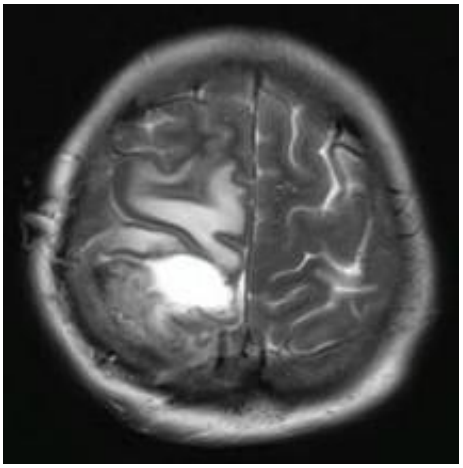

Figure 4. Postoperative Brain MRI demonstrates a 2.8×1.7×2.7 cm fluid filled cystic cavity at the operative bed with 1×1.3cm peripherally irregular enhancing lesion at its anterior-inferior border suggestive of residual tumour tissue.

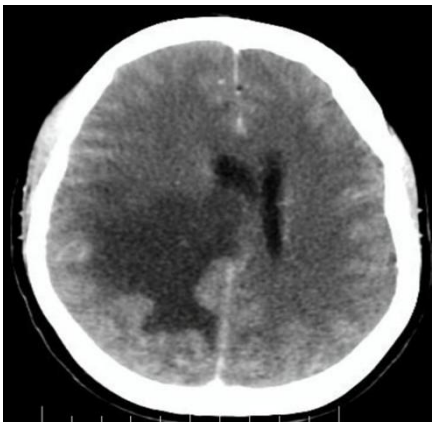

Figure 5. Cranial CT scan revealed mark cerebral oedema.

Discussion

LFS is an inherited autosomal dominant cancer predisposition triggered by a mutant TP53 (9). TP53 is a transcription factor located on chromosome 17 (17p13.1), which normally controls the cell cycle, genomic stability, and cell death (2) (14). Accumulation of secondary mutations over and above the mutated TP53 attributes to the fact that LFS is characterized by unusual patterns of cancer incidence (11).

The Chompret Criteria allows the clinical identification of LFS. The three clinical presentations are taken into consideration: 1. Family presentation of LFS cancers such as breast cancer, soft tissue sarcoma, central nervous system cancer, adrenocortical carcinoma, leukaemia, and bronchoalveolar lung cancer under the age of 46 and one first or second degree relative with an LFS cancer under the age of 56. 2. Multiple primary tumours related to the LFS spectrum with the first diagnosis before the age of 46. 3. Rare cancers such as adrenocortical carcinoma or choroid plexus carcinoma irrespective of family history (1) (12).

Full-body MRI is the currently used screening modality for LFS patients with high sensitivity and specificity in detecting various tumours (10). 18F-fluorodeoxyglucose positron emission tomography and full-body CT scan as screening modalities are not recommended as they increase the risk of radiation-induced tumours (10).

Genetic testing and counseling should be offered to the LFS patient's family. Using basic Mendelian genetics, the probability of inheritance can be determined, assuming that the mutant allele is inherited in an autosomal dominant fashion. Siblings of an affected patient have a 50% chance of having LFS. If neither parent has LFS, the mutation is assumed to be de novo, and the risk to siblings is lower. However, the risk to siblings is higher than the general population due to the possibility of germline mosaicism (10).

In this specific instance, the clinical family history was impressive for a LFS case according to Chompret criteria; however, no inherited TP53 alterations have been found except for the patient. We believe that this lack of an absolute phenotype-genotype concordance could be ascribed to other, as yet unidentified mutations involved in the pathogenesis of LFS. Further genetic studies involved in cell growth regulation and proliferation may be efficient in deciphering such aggregations and addressing the genetic events involved in cancer predisposition in families suspected to have LFS.

Conclusion

The description of this case highlights the importance of genetic family counseling of patients diagnosed to have GS and other tumors consistent with LFS. Early identification of high-risk subjects will provide appropriate lifelong monitoring within clinical and psychological programs. Importantly, sporadic cases should not be dismissed.

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C7 contribution to the ulnar nerve. Literature review

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Keywords
ulnar nerve, brachial plexus, neuroanatomy

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ABSTRACT

Introduction. Classic anatomical literature frequently describes C7 contribution to ulnar nerve (UN) formation as a casual event. However, surgical practice and dissections frequently reveal a recurrent presence of a lateral cord component of the UN. This study aimed to seek through literature to establish the frequency and degree of this contribution.

Methodology. We ran a literature review searching on Pubmed, MEDLINE, Embase and Web of Science databases for ulnar nerve anatomy and described discursively the results.

Results and discussion. We found 9 articles that described quantitatively and qualitatively the contribution of C7 on the formation of the UN. The prevalence described ranged from 2 to 100%, depending on the methodology used and population characteristics. When present, studies described a contribution from 9,9% to 30,4%, sending even more fibres than T1 root on average.

Conclusion. The C7 root can be considered a frequent and important component of the ulnar nerve, explaining UN territory repercussions on C7 radiculopathies. This knowledge is important on surgical approaches, maybe avoiding iatrogenic lesions and negative outcomes.

INTRODUCTION

The anatomical literature reports the origin of the ulnar nerve (UN) as the medial fascicle (C8-T1), but often receiving fibers from the ventral branch of C7. It is also mentioned its path through the axilla, initially

medial to the axillary artery and between this and the vein, continuing distally medial to the brachial artery up to the middle third of the arm, where the UN punctures the medial intermuscular septum and leans medially as it descends anteriorly to the medial head of the triceps muscle towards the interval between the medial epicondyle and the olecranon, with the superior ulnar collateral artery. Its relationship with the brachial artery and medial epicondyle makes it easy to map in its proximal path; a line from the medial epicondyle to the lateral margin of the pisiform bone represents its distal path[1,2,3,4,5].

Although its path and function are known, there are few records in the literature about the frequency and the way C7 contributes to the formation of the UN. It should also be noted that there are differences between the anatomical study and the electromyographic diagnosis of the nerve. The objective of this study was to seek, through a literature review, to clarify the frequency and the degree of C7's contribution to the formation of the UN.

Methods

An integrative review of the literature was carried out, seeking articles that described qualitatively and/or quantitatively the formation of the UN from the brachial plexus. For this, we searched at MEDLINE, Embase and Web of Science, using the descriptors "Ulnar Nerve" and "Anatomy", with no language or publication date restrictions. The results of the search were discursively described.

Results and discussion

Hur et al. (2013) analyzed 100 brachial plexus (BP) from Korean adult cadavers. The extracted samples were immersed in Guanidine-HCl for 2 weeks. After the contribution of C7 was proven, 20 samples were processed with a routine histological staining (H&E) procedure to count the number of myelinized axons using Imbroglio Modometer software. In all 100 BPs, there was a contribution of C7 to the formation of the ulnar nerve. Moreover, it was unanimous the ramification of the C7 fascicles in the distal portion of the fascicles that compose the lateral root of the median nerve, decussing with the medial root of the median nerve. The contribution of C7 to the ulnar nerve was 1.452 ± 429 (9.9%) myelinized axons, C8 was 11.448 ± 1.473 (78.3%) and T1 was 1.720 ± 382 (11.8%) in the 20 samples processed in H&E[6].

In contrast, Fuss (1989) investigated 158 BPs and reported in his study a 56% contribution of C7 to the formation of the ulnar nerve, highlighting that this collaboration may be accompanied by fibers of the median nerve (type 1) or may occur separately (type 2). Considering the 56:44% relationship between ulnar nerves with and without lateral root, the author highlights that both possibilities should be considered as normal variations[7].

Pyun, Kang and Kwon (2010), after dissection of 38 BPs, reported 13.1% contribution of C7. It is worth mentioning that, for having performed an associated electrophysiological study, this study showed a high prevalence of alterations in the electromyography of M. flexor ulnar carpi in patients with C7 radiculopathy (13/17 = 76.5%)[8].

Kumar and Ranganath (2014) also described only 1 (2%) out of 100 BPs with the contribution of the lateral cord of C7 to the formation of the UN; more precisely, the branches for the UN came from the union of the medial and lateral roots of the median nerve[9].

Guru et al. (2015) dissected 50 upper limbs to observe UN variations. In all, 4 variations were observed, all on the right side. The notable contribution of the BP side cord to the formation of the UN was observed unilaterally in 2 (4%) members. The contributing branch passed from the lateral side to the medial side deeply to the formation of the median nerve and joined the ulnar nerve at its lateral aspect. In the two remaining cases, the ulnar nerve had abnormal communications with the neighboring nerves, radial nerve, and medial cutaneous nerve of the forearm nerve[10].

Emamhadi et al. (2016) dissected 64 fresh BPs in order to evaluate possible anatomical variations, excluding damaged specimens or ante mortem surgical interventions. During the investigations, it was found collaboration of the lateral cord of BP for the formation of the UN in 3 (9.38%) of the 32 cadavers[11].

Koo and Lee (2007) analyzed the composition of the terminal branches of BP, dissecting 32 upper limbs. Regarding the UN, four different patterns were observed. The most frequent type was C7, C8 and T1 (75% of cases). In the average diameter, C8 was the thickest, measuring 2.64 ± 0.57 mm, and T1 was the thinnest with 0.06 ± 0.56 mm[12].

The oldest studies found, performed with even more rudimentary cadaveric dissection techniques, were those of Harris (1904)[13] and Linell (1921)[14], which showed the presence in, respectively, 86% and 57% of the brachial plexus of an exchange of fibers between the medial and lateral plexus strands, specifically the C7 fibers contributing to the formation of the ulnar nerve.

Author, Date	Sample (n)	Methodology	Qualitative Analysis	Quantitative Analysis
Hur et al., 2013	100 BPs	H&E + Imbroglio Modometer	100 (100%, C7)	1,452 ± 429 (9,9%) axônios
Koo, Lee, 2007	32 BPs	Cadaveric dissection	24 (75%, C7)	1,18 ±0.59 mm
Fuss, 1989	158 BPs	Cadaveric dissection	56% (lateral cord)	N/A
Pyun et al., 2010	38 BPs	Cadaveric dissection	13,1% (lateral cord)	N/A
Kumar, Ranganath, 2014	50 BPs	Cadaveric dissection	1 (2%,lateral cord)	N/A
Guru et al., 2015	50 BPs	Cadaveric dissection	2 (4%, lateral cord)	N/A
Emamhadi et al., 2016	64 BPs	Cadaveric dissection	3 (9,38%,lateral cord)	N/A
Ramchandran et al., 2006	1 BP	Case Report	1 (lateral root of the median)	N/A
Linnel, 1921	42 BPs	Cadaveric dissection	57%, C7	N/A
Harris, 1904	60 BPs	Cadaveric dissection	86%, C7	N/A

Figure 1. Summary of the findings of the review on C7 contribution

It is noticeable that the studies that performed quantitative analysis, especially Hur et al. (2013) and Koo and Lee (2007), showed a higher prevalence of C7 contribution than the studies with cadaveric dissection, except for those of Harris (1904) and Linnel (1921) [6,12,13,14]. This can be justified by an eventual iatrogenic loss of the lateral contribution during dissection or by the sophistication of quantitative methods.

In this context, it is frequent a sub-quantification of the contribution of C7 to the nerve during dissection, justifying the absence of root representation in most of the classic anatomic literature [1,2,3,4,5]. In practice, however, the repercussions of C7 radiculopathies on electromyographic variables in part of the UN territory can be seen, as Pyun et al. (2010) have shown[8].

This knowledge becomes essential in neurosurgical practice, since unadvised dissection can cause iatrogenicity. The authors themselves came across the contribution of the lateral cord to the formation of the UN during surgical dissection in the treatment of a brachial plexopathy (Figure 2), which motivated this review.

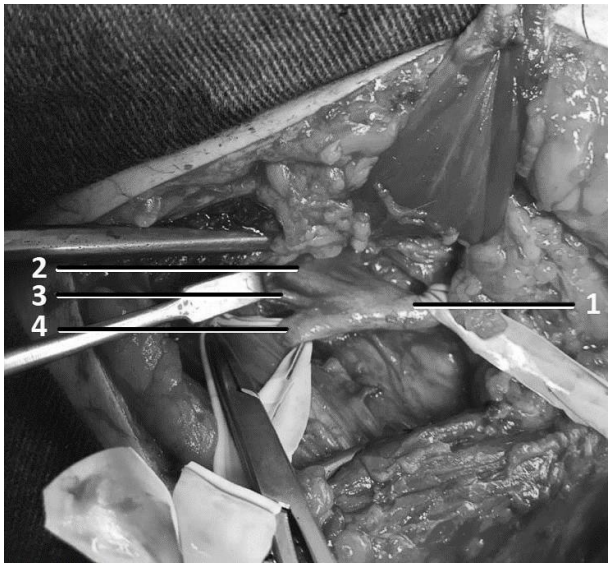

Figure 2.

Conclusion

The C7 root can be considered a frequent component of the ulnar nerve, although its contribution may be underestimated in less sophisticated dissection studies. There is even a high incidence of C7 radiculopathy causing repercussions in the nerve territory. Knowledge of this participation is indispensable for peripheral nerve surgery, avoiding iatrogenic lesions and possible negative outcomes for the patient.

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Burr-hole craniostomy versus mini-craniotomy in the treatment of chronic subdural hematomas. Analysis of clinical results

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burr hole,
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Abstract

Although cases of spontaneous recovery or under medical treatment have been reported, the treatment of chronic subdural hematoma is mainly surgical. The optimal surgical technique for the treatment of chronic subdural hematomas is still open to debate. The purpose of this study was to compare the clinical outcomes between burr-hole craniostomy and craniotomy in patients with chronic subdural hematoma. Materials and methods: we have performed a retrospective study in patients operated for chronic subdural hematoma in the neurosurgery department of the teaching hospital of Bouaké between July 1, 2016, and June 30, 2020. We compared the data of patients operated by a single burr-hole craniostomy (group A) and those operated by minicraniotomy (group B). Demographic parameters, clinical signs, complications and neurological findings were analyzed. Fisher's exact test, Chi-squared, and student's t-test were performed. Results: group A included 46 patients and group B 55 patients. There was no significant difference between the two groups about age (59.5 years vs 59.8 years p = 0.89), sex (man: 74% vs 78.2%, P = 0.645), comorbidities, clinical signs on admission and location of the hematoma. There was also no significant difference between recurrence rates (4.3% vs 3.6% p = 0.55), postoperative complications (15.21% vs 7.27% p = 0.172) and neurological findings between the two groups. Conclusion: patient outcomes are similar in the treatment of chronic subdural hematomas by craniostomy and minicraniotomy.

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Introduction

Chronic subdural hematoma (CSDH) is a collection of aged blood that lies between the dura mater and the arachnoid. In many patients, it develops slowly after a mild head trauma often overlooked by them [9], but the number of patients without a history of trauma is increasing, probably due to anticoagulant or antiaggregant treatment [8]. Although

cases of spontaneous recovery [1,10] and recovery with medical treatment (corticosteroid or atorvastatin-based) [6] have been reported, the treatment of CSDH is mainly surgical. Surgery for chronic subdural hematoma itself is based on several techniques, including evacuation through a small bone flap associated or not with a drainage system or through one or more burr-holes also associated or not with a system of continuous drainage or percutaneous twist drill craniostomy. The optimal surgical procedure is still subject to debate.

The purpose of this study was to compare the clinical outcome of patients who had chronic subdural hematoma evacuation and drainage through a single burr hole craniostomy and those who had chronic subdural hematoma evacuation and drainage through a minicraniotomy.

Materials and method

We carried out a retrospective study on 101 patients who were hospitalized in the neurosurgery department of the teaching hospital of Bouaké between July 1, 2016 and June 30, 2020 for the management of a chronic subdural hematoma. Due to the retrospective nature of this study, no consent was given and all records have been anonymised. The diagnosis of chronic subdural hematoma was made by CT scan without injection of contrast medium. We compared the data of the patients who had been operated by a burr hole craniostomy (group A) and those of those who had been operated by a minicraniotomy (group B). Patient data was collected from records available in the neurosurgery department. The following parameters were analyzed: age, sex, history, clinical and paraclinical signs, the etiology retained, the surgical technique used, the complications and the clinical course. During the postoperative period, regression of signs and symptoms of CSDH was expected as clinical improvement. Data were entered and statistically analyzed using IBM SPSS 22.0. Fisher's exact test, chi-squared and Student's t-test were performed to compare the 2 groups. All the tests were bilateral. The P-value (P) <0.05 was considered statistically significant.

Surgical technique

In group A a single burr-hole was made while in group B it was a minicraniotomy. The technique used was the choice of the surgeon. All patients (regardless of the technique) were operated under general anesthesia with endotracheal intubation. A skin incision of 4 to 5 centimeter was made across the maximum thickness of CSDH. A burr hole craniostomy of 1 centimeter diameter was performed in group A, followed by a cruciform opening of the dura mater and outer membrane of CSDH after thermo coagulation. In group B, instead of the burr hole craniostomy, a bone flap of 3 centimeter diameter was cut with the trephine. Subsequently, like group A, the dura mater and the outer membrane of the hematoma were incised crosswise after their thermo coagulation. whatever the group, rinsing of the subdural space was performed with isotonic saline (0.9%) until the rinsing liquid returned clear followed by drainage of the subdural space with a closed system. by siphoning (depending on gravity without continuous suction). In group B, the dura is sutured around the drain followed by placement of the bone flap. In group A, the same closed siphoning subdural drainage system is put in place but the dura is left open. In bilateral subdural hematoma, surgery was done bilaterally. Regardless of the technique used, the inner membrane of the hematoma as well as the arachnoid were not open. The rest of the care is identical in both groups. It consisted of suturing the surgical wound followed by the dressing. Patients were strictly bedridden for 48 hours and, the drainage bag is placed on the patient's bed. The drains were removed in all the patients after 48 hours.

Results

During our study period 102 patients were treated for a chronic subdural hematoma, including 1 patient treated medically (corticosteroid therapy) and 101 others treated surgically, i.e. 99%.

A total of 101 patients were included in this study, 46 in group A (patients who had burr hole craniostomy) and 55 in group B (patients who had mini-craniotomy). Our study population had a mean age of 59.7 +/- 13.35 years with extremes of 24 and 100 years. Patients under the age of 65 years accounted for 69.3% and those aged 65 years and over represented 30.7%. There were 24 women (23.8%) and 77 men (76.2%).

The demographic, clinical and paraclinical characteristics of patients before their surgical

treatment are summarized in Table 1.

The clinical evolutionary aspects of the patients are presented in Table 2.

Clinical examination at 3 months and 1 year postoperatively showed full recovery in the 97 patients who survived.

Table 1. Characteristics of patients before their surgical treatment.

variables	Group A(burr hole craniostomy), N = 46 (45.5%)	Group B (mini-craniotomy), N = 55 (54.5%)	Total (N = 101)	test	P value
Age (years)	59.5 +/-14.56 (min = 24 and maxi = 100)	59.8 +/-12.396 (min = 26 and maxi = 84)	59.7 +/- 13.35 (min 24 and maxi = 100)	t-student = 0.139	P = 0.89
gender				X^2 = 0.252	P = 0.645
male	34 (74)	43 (78.2)	77(76.2)		
Female	12 (26)	12 (21.8)	24(23.8)		
Aetiology				Fisher = 2.134	P = 0.372
Head trauma	31 (67.4)	40 (72.7)	71(70.3)		
Hemostatic disorder	0	2 (3.63)	2(1.98)		
No cause identified	15 (32.6)	13(23.6)	28(27.72)		
delay (trauma and diagnosis (days)	31	30.7			
Symptoms					
headache	35(76%)	42(76.3%)	77(76.2%)		
vomiting	9(19.5%)	11(20%)	20(19.8%)		
behavior disorder	7(15.2%)	8(14.5%)	15(14.8%)		
Epileptic seizure	1(2.1%)	1(1.8%)	2(1.9%)		
mean Glasgow score on admission	13.22 +/-2.511 min = 6 et max = 15	13.4 +/- 2.257 min = 7 et max = 15	13.32+/-2.366 Min = 6 Max = 15 Mode = 15	t-student = 0.385	P = 0.701
Motor deficit on admission	34 (74%)	46 (83%)	80(79.2%)	X^2=1.438	P = 0.23
Co-morbidities				Fisher = 12.51	0.27
Chronic arterial hypertension	6(13%)	8(14.5%)	14(13.8%)		
Chronic alcoholism	8(17.4%)	5(9%)	13(12.8%)		
Parkinson disease	0	1(1.8%)	1(0.9%)		
Hepatocellular insufficiency	0	1(1.8%)	1(0.9%)		
HIV Infection	0	2(3.6%)	2(1.9%)		
tuberculous Meningitis	1(2.1%)	0	1(0.9%)		
Heart disease under diuretics	0	1(1.8%)	1(0.9%)		
Stroke and chronic hypertension	1(2.1%)	1(1.8%)	2(1.9%)		
blindness	0	2(3.6%)	2(1.9%)		
prostatic Adenocarcinoma	1(2.1%)	0	1(0.9%)		
No comorbidity	27(58.7%)	34(61.8%)	61(60.4%)		
location				Fisher = 1.787	P = 0.455
Right	16 (15.8%)	22 (21.8%)	38(37.6%)		
left	24(23.8%)	30(29.7%)	54(53.4%)		
bilateral	6 (5.9%)	3 (3%)	9(8.9%)		

Table 2. Evolution of patients according to the surgical technique used.

variable	Group A (burr hole craniostomy), n = 46 (45.5%)	Group B (minicraniotomy), n = 55 (54.5%)	Total (n= 101)	test	P value
Evolution of consciousness 48 hours postoperatively	14.58 +/- 1.59	14.65+/-1.30			P = 0.81
Improvement in motor skills 48 postoperatively	31(67.39%)	44(80%)	75(74.25%)	X^2= 4.03	P = 0.133
immediate post-operative Complications	7(15.21%)	4(7.27%)	11(10.89%)	Fisher = 6.223	P = 0.172
Clinically manifested Pneumencephaly	3(6.5%)	2(3.6%)	5(4.9%)		
Acute bleeding	0	2(3.6%)	2(1.9%)		
Brain Contusion	1(2.1%)	0	1(0.9%)		
Brainstem haemorrhage	2(4.3%)	0	2(1.9%)		
post-operative Epilepsy	1(2.1%)	0	1(0.9)		
Recurrence during the first year	2(4.3%)	2(3.6%)	4(3.96%)	Fisher = 1.57	P = 0.55
3 months Outcome				X^2 = 0.483	P = 0.328
mortality rate	3(6.5%)	1(1.8%)	4(3.9%)		
Full recovery	43(93.4%)	54(98.1%)	97(96%)		

DISCUSSION

Chronic subdural hematoma (CSDH) is one of the most common neurosurgical conditions. Its incidence increases considerably with age and ranges from approximately 3.4 per 100,000 in patients younger than 65 years old to 8 to 58 per 100,000 among those over 65 years [2,16]. Contrary to observations made in developed countries, our study population consists mainly of patients under the age of 65 (approximately 70% of our patients). This is partly explained by the characteristics of the Ivorian population, which is made up mainly of young people. Indeed 97.15% of the Ivorian population is under 65 years old with a life expectancy of 61.8 years [17]. Karibe H et al like Rauhala M et al. in their various studies carried out in Japan and Finland respectively, showed that the incidence of chronic subdural hematoma increased with age [7,13]. Some authors have also found an average age of occurrence of chronic subdural hematomas less than 65 years, such as Mwanyombet et al in Gabon [9] who observed that 80% of their patients were between 60 and 65 years old; Jaiswal et al in India reported in their series an average age of 53 years [5]. We also observed a male predominance. The sex ratio in our study was 3.2: 1. The higher incidence in men may be due to higher rates of head trauma in them. Head trauma has been identified as the most common factor associated with 25% to 75% of cases of CSDH in most studies. In our study, a head trauma was reported in 70% of patients. This proportion varied according to the studies: in that of Goyal RK, it was 75% [3], in that of Santarius et al. it was 61% [15], in that of Zumofen et al. it was 79.6% [20] and in that of Ramachandran and Hegde it was 56% [12].

Although spontaneous resolutions [10] or under medical treatment of chronic subdural hematomas [4] have been reported, the treatment of chronic subdural hematomas is resolutely surgical. The treatment decision is based on clinical manifestations and radiological signs including the volume of the hematoma and its mass effect on the parenchyma [18]. Several surgical techniques have been described, however, no study can formally conclude the superiority of a technique in terms of efficiency and safety. In our study, we concluded that the two evacuation and drainage procedures that are burr hole craniostomy and minicraniotomy gave similar results in terms of complications, recurrence rate and neurologic course.

No statistically significant difference was observed in the clinical course of patients either in the immediate postoperative period or in the medium and long term. In fact, there was no statistically significant difference in the evolution of the consciousness and motor deficit in the two groups. The occurrence of postoperative complications were also statistically superimposable in the two groups as were the recurrence rates. Therefore, the two techniques had identical efficiencies. Regan M. et al, after a comparative study of these 2 surgical techniques, concluded that evacuation by craniotomy was associated with a higher re-operative rate (24.1%) than evacuation by burr hole craniostomy with P = 0.0156 [14]. They argued that the re-operation was mainly due to a residual chronic subdural hematoma or secondary to one or more acute haemorrhages. Their result was related to the lack of drainage in their patients who had had craniotomies. Weigal and. Al. Had shown in a study that the use of a closed drainage system reduced the risk of recurrence of hematoma [19] and therefore of the need for re-operation. Santarius et al. in a randomized study comparing two groups of patients treated for CSDH by burr holes craniostomy, one group having had drainage and the other not. Those with drain were found to have a lower reoperation rate due to a decrease in hematoma recurrence [15]. However, Raghavan A et al. for their part found that burr hole craniostomy was associated with a higher re-operative rate [11]. The recurrence rate was relatively low in our series compared to that reported in the literature, especially the series from developed countries. The low rate of recurrence in our series could be explained by the characteristics of our population which was essentially made up of young adults with very little cerebral atrophy on the one hand and on the other hand by a low rate of comorbidity requiring the taking antiaggregant or anticoagulant. Indeed, it is accepted that cerebral atrophy and increased subdural space observed in elderly patients make them vulnerable to the development of chronic subdural hematomas [5]. Also according to Regan M. et al. in their series, there was a higher incidence of postoperative complications in the craniotomy group than in the burr hole craniostomy group. Moreover, it clearly appears that the duration of the procedures was significantly longer in craniotomies than burr holes craniostomies [14]. We were unable to compare the duration of different surgeries in our study due to unavailability of data.

Conclusion

Evacuation and drainage of chronic subdural hematoma by burr hole craniostomy or mini-craniotomy are comparable in terms of clinical outcome. However, other factors not analyzed in our study, such as surgical procedure duration and the type of anesthesia, could help surgeons to choose the appropriate surgical technique on a case-by-case basis. Future prospective, randomized, multicenter studies taking into account several factors that may influence surgery for chronic subdural hematoma and the vital and functional prognosis of patients are needed.

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Shunt in scrotum: unusual shunt complication in an operated case of post TBM hydrocephalus

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ABSTRACT

The role of shunt placement is to divert cerebrospinal fluid (CSF) from within the ventricles to an alternative location most commonly peritoneal space. Ventriculo Peritoneal Shunt (VPS) is associated with many complications viz over drainage, valve failure, breaking of catheter, catheter obstruction, coiling of catheter, spontaneous knot formation, infection and migration of distal catheter and all of them finally leading to obstructive hydrocephalus. One such complication is distal catheter migration to a rare but possible site i.e. scrotum. We reported a case of scrotal migration of shunt as a late complication of VPS insertion.

Keywords
Ventriculo Peritoneal Shunt (VPS), complications, distal catheter migration, scrotum

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BACKGROUND

The role of shunt placement is to divert cerebrospinal fluid (CSF) from within the ventricles to an alternative location (most commonly peritoneal space, rarely to atria, pleural space) and from lumbar space to peritoneal cavity.

Ventriculo Peritoneal Shunt (VPS) is associated with many complications namely over drainage, valve failure, breaking of catheter, catheter obstruction, coiling of catheter, spontaneous knot formation, infection and migration of distal catheter and all of them finally leading to obstructive hydrocephalus [1,2]. One of the rare sites of distal catheter migration is scrotum. Scrotal migration of distal shunt catheter is more common in children due to patent processus vaginalis [3]. We reported a case of scrotal migration of shunt as a late complication of VPS insertion.

CASE PRESENTATION

An eighteen months old male child, a follow up case of tubercular meningitis (TBM) with hydrocephalus was operated by right VPMP shunt via right Keens point in January 2020 at our tertiary care centre. Post operatively patient's GCS improved and patient was discharged. After approximately 03 months patient presented with gradual increase in size of bilateral scrotum in the past 2 months, intermittent

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fever and on & off vomiting and was admitted (Fig.1). On local examination cough impulse was present in the right inguinal region & a tube like structure was palpable in the right hemiscrotum, external genitalia was normal. Neurological examination was normal with no focal neurological deficit, GCS was E4V5M6, head circumference was normal for age, no signs of shunt obstruction were present.

Investigations

X-ray of neck, chest, abdomen & pelvis were conducted which showed an intact VP shunt with extension of the peritoneal end into the right hemi scrotum. USG of inguinoscrotal region was also suggestive of same.

Treatment

Surgical intervention was planned in this rare case. Re-exploration of the abdominal wound was done, the peritoneal end of the shunt was identified and it was pulled and repositioned in peritoneal cavity under C-ARM guidance and the abdominal wound was closed in layers. Post-operative X-ray of chest, abdomen & pelvis showed normal position of peritoneal end of VP shunt (Fig.2).

Outcome and follow up

The child was kept under observation and discharged after 48 hours since the postoperative period was uneventful and was advised for follow up in general Surgery OPD and Neurosurgery OPD.

Discussion

The most common surgery performed worldwide for hydrocephalus is VP shunt [3]. Shunting is performed to divert the CSF from dilated ventricles to peritoneal cavity from where CSF is absorbed. Apart from the morbidity associated with hydrocephalus, shunt surgeries have their own complications which are well known [2-6].The reported incidence of shunt-related abdominal complications is 10-30%[7] Various authors have reported migration of the distal end of peritoneal catheter into the scrotum through a patent processus vaginalis[8-11]. The processus vaginalis may remain patent until 1 year of life in 50-60% cases and until 2 years of life in 40-50% of cases [3]. Rowe et al[12] have explained the aetiology of peritoneal catheter migration, which has been universally accepted over the years by various authors[13]. Peritoneal cavity distension due to draining CSF also prevents the obliteration of processus vaginalis which had also been reported by Ho et al [14] and Ozveren et al[15]. In the present case, a male child had a patent processus vaginalis which was either congenital or because of peritoneal CSF drainage. In our case, right-sided VP shunt was performed and it would be difficult to comment and is another research study topic whether the side has something to do with the shunt migration as there is no such report in the literature comparing the right and left patent processus vaginalis. We used Chabbra medium pressure VP shunt in our case. Shunt migration can occur either as an early or a late complication. Ozveren et al[15] have reported shunt migration within 24 h, while the average length of time reported in other series was 6.8 months. In our case, the time interval was approximately 3 months. Thus this kind of shunt complication needs to be reported and should be kept into mind in dealing with cases who had undergone shunt insertion surgery.

Scrotal VP shunt migration has been reported in 26 children, and the time of presentation varies from 1 month to 2.5 years (mean 3.8 months, median 1 month) after shunting, with 21 out of 26 migrations occurring within 6 months, 88% involving the right side [16].

Ramareddy RS describe the spontaneous resolutionof hydrocele and retreat of migrated peritoneal portion of VP shunt, and also discuss the pathogenesis and management [16].

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Spectrum of non-traumatic craniovertebral junction disorders. Diagnosis and demonstration with magnetic resonance imaging and multidetector computed tomography

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Keywords
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ABSTRACT

Introduction: Craniovertebral junction is the "zone of transition" between the skull and cervical spine so its detailed discussion is lacking in so many standard textbooks addressing these regions. These anomalies are especially common in the Indian subcontinent. Accurate diagnosis, probable aetiology and pre-treatment evaluation considerably affect the prognosis of patients. The aim of this study was to classify various Craniovertebral junction disorders according to their aetiology and to correlate the imaging findings with the clinical profile of the patients and histopathology whenever possible.

Methods: This prospective observational study was done in our department over the period of one year from August 2016 to July 2017. 57 North Indian patients from all age groups and both sex, who had imaging features suggesting craniovertebral junction pathology were selected for the study.

Results: Our study group comprised 34 males and 23 females with a male to female ratio of 1.47: 1. The most common age group was 11-20 years and the most common aetiology being developmental followed by infective, autoimmune and inflammatory disorders.

Conclusions: CVJ abnormalities are a group of treatable neurological disorders, and are approached with much caution by clinicians. Thus, it is crucial that radiologists should be able to make a precise diagnosis, categorize them into etiological groups, and give precise anatomical information on MDCT and/or MRI, as this information ultimately helps determine the management of such abnormalities and their prognosis.

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INTRODUCTION

The term craniovertebral junction (CVJ) refers to a cone shaped area, the upper limit of which is a line joining the internal occipital protuberance to the spheno- occipital synchondrosis& the lower limit is inferior margin of the body of axis.[15] It is a transition site between

mobile cranium and relatively rigid spinal column. Disorders of the CVJ present a dilemmatic problem due to presence of neurologically vital structures in the vicinity, potentially unstable articulation and grave prognosis, if gone untreated and undetected.

Our study is an attempt to systematically classify different CVJ abnormalities according to their etiopathogenesis and to describe the importance of accurate diagnosis and precise anatomical information for pretreatment evaluation with Multidetector computed tomography (MDCT) and/or magnetic resonance imaging (MRI).

The main objectives of our study were:

1. To evaluate the patients with non traumaticcraniovertebral junction disorders by multiplanar and dynamic imaging utilizing MRI and/ or Multidetector CT.
2. To classify various craniovertebral junction disorders according to their etiology.
3. To correlate the imaging findings with clinical profile of the patients.
4. To correlate radiological diagnosis with diagnosis after medication /surgery / biopsy whenever undertaken.

Methods

This prospective study was done in Department of Radiodiagnosis & Imaging, Ram Manohar Lohia Institute of Medical sciences, Lucknow, over the period of one year from August 2018 to July 2019.The Permission from Ethics Committee of our institute was taken. Written informed consent for the study was obtained from each patient prior to the examination.

North Indian Patients from all age groups and both sex, who underwent MRI and / or CT for clinical suspicion of non-traumaticCranio-vertebral junction disorder were evaluated. Out of these, 57 patients who had imaging features suggesting cranio-vertebral junction pathology were selected for the study. Contrast enhanced imaging was restricted only to those with suspicion of infective, inflammatory or neoplastic etiology. Dynamic scanning in neutral, active flexion and extension posture was done in all cases except in those with atlanto-axial instability. Only exclusion criterion was presence of at least one absolute contraindication for MRI.

MR imaging was performed with a 1.5 T whole body MR imaging system (SIGNA EXCITE GEMSOW) and the following sequences were obtained:

1. Sagittal -T1-weighted spin echo (T1W SE), T2-weighted turbo spin echo (T2W TSE) and T2-weighted fat suppressed.
2. Axial- T1-weighted spin echo (T1W SE) & T2-weighted turbo spin echo (T2W TSE).
3. Coronal - T2-weighted turbo spin echo (T2W TSE).
4. T2W TSE in flexion and extension whenever required.
5. Contrast enhanced T1W fat saturated (FS) images in axial, coronal and neutral sagittal planes.

Scanning parameters used for T1W SE sequence were a repetition time (TR) of 600 ms and an echo time (TE) of 9.7 ms; for T2W TSE sequence TR of 4,000 ms and TE of 100 ms; for T2W fat suppressed sequence TR of 3,300 ms, TE of 110 ms. These sequences were done with slice thickness of 4 mm and spacing of 0.5 mm.

CT examination was done on a Multislice spiral CT scanner (BRILLIANCE CT, Phillips medical system, Nederland, B.V.5684 PC Best). After acquisition of thin axial images, multiplanar reconstruction into sagittal and coronal planes was obtained.

Craniometric measurements used for radiologic assessment of CVJ abnormalities include Chamberlain's line, McGregor line, McRae line, Wackenheimclivus line, Fishgold digastric line, Fishgoldbimastoid line, Welcher basal angle, and atlantooccipital joint axis angle.

Detailed history of the patients was taken with respect to age, sex, socio-economic status, clinical profile & correlated with the spectrum of cranio-vertebral junction finding on MRI and Multislice CT. These patients were followed up to look for clinical outcome after conservative or surgical treatment.

Statistical Methods: Statistical analysis was done using ratio and percentages for age and gender distribution. Percentage distribution was calculated for each disease affecting the CVJ. Pearson's chi square test was used to establish the association between two different anomalies.

Results

Our study group comprised of 34 males and 23 females with a male to female ratio of 1.47: 1. Maximum number of patients (21) was in the age group between 11-20 years, which included 8 females (34.78% of all females) and 13 males (38.24% of all males). This was followed by 21-30years age

group (12 patients) comprising of 3 females (13.04% of all females) and 9 males (26.47% of all males).

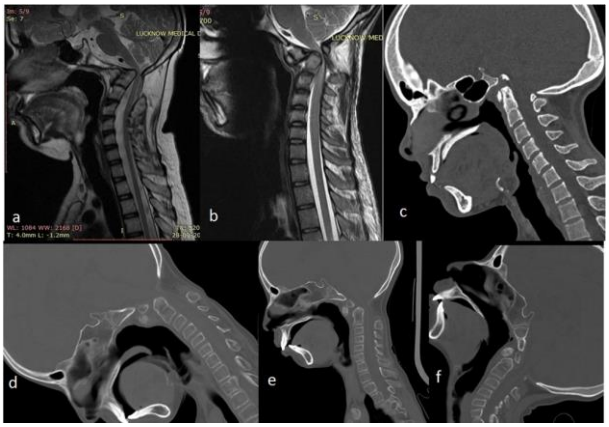

Figure 1. a) Sagittal T2W MRI shows Platybasia with flattened clivus, blocked C2- C3 complex with atlanto-occipital assimilation, AAD and BI causing compression over cervico-medullary junction **b)** Sagittal T2W MR shows Osodontoideum with AAD causing compressive myelopathy. **c)** Sagittal NCCT shows shallow posterior fossa with hyoplasticclivus related to basioccipital hypoplasia. A bony arch is noted at the tip of clivus which is continuous laterally with occipital condyles consistent with prebasioccipital arch. **d, e, f)** Sagittal dynamic NCCT shows mobile type atlantoaxial dislocation with ossiculumterminale causing cord compression.

Developmental cause of atlanto-axial diseases most commonly presented in 11-20 year age group (18 patients-40.91%), followed by 21-30 year age group (12 patients-27.27%). None of the patient of 51-60 years presented with a developmental cause, while one of these (2.27%) presented in 61-70 years age group. Patients with acquired causes of atlanto-axial diseases most commonly presented in 41-50 years age group (4 patients-30.77%) followed by 3 patients each (23.08%) in 11-20 and 51-60 years age group and 2 patients (15.38%) in 31-40 year age group [Table 1].

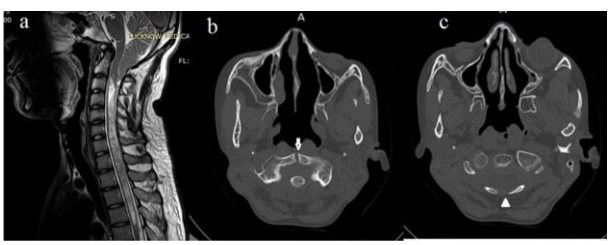

Figure 2. a) Sagittal T2W MRI shows small posterior fossa with hypoplasticclivus and cerebellar tonsillar herniation causing crowding at foramen magnum with compression over proximal cervical cord causing syringomyelia in cervico-dorsal cord. **b)** Axial non contrast bone window image shows anterior and posterior rachischisis with atlanto-axial dislocation and hypoplastic posterior arch of atlas.

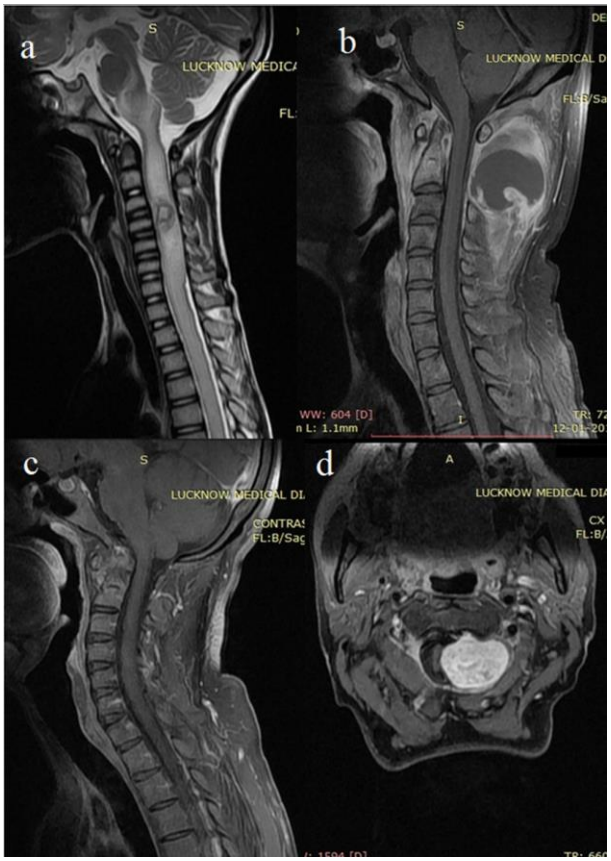

Figure 3. a) Sagittal T2W MR Image shows inflammatory granuloma in cervical cord with marked edema involving cord and brainstem. T1W Fat sat contrast enhanced **b)** sagittal image showing contrast enhancement in atlas and axis vertebra with erosion of dens. Enhancing granulation tissue is noted adjacent to atlanto-axial joint with a large abscess in paraspinal soft tissue. **c)** Sagittal image showing erosion of dens with mild heterogenous contrast enhancement in anterior atlas arch and axis vertebra. Enhancing soft tissue s/o pannus is noted adjacent to atlanto-axial joint with increased atlantoaxial interval. **d)**axial image shows a well defineddural based lesion with strong homogenous contrast enhancement at C1- C2 level on left side causing right lateral displacement and compression of cord. Radiological diagnosis of meningioma was made.

Most common presenting symptom was neck pain seen in 33 patients (57.89%), followed by weakness of both upper and lower limb in 24 patients (42.11%) and neck stiffness in 23 patients (40.35%). These were followed by fever, hemiparesis, sensory symptoms, paraparesis, headache and upper limb weakness. However, weakness of limbs (motor

symptoms) was overall the most common clinical feature present in 35 patients (61%).

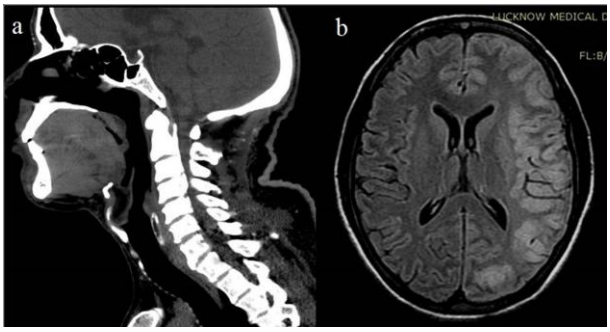

Figure 4. a) Sagittal CT shows thickened and ossified posterior longitudinal ligament causing spinal canal narrowing. **b)** Axial T2 FLAIR shows hyperintense signals in left cerebral hemisphere involving cortex and subcortical white matter. Diagnosis of Acute disseminated encephalomyelitis was made.

Age	Developmental	Percentage (%)	Acquired	Percentage (%)
0-10	4	09.09%	1	07.69%
11-20	18	40.91%	3	23.08%
21-30	12	27.27%	0	00.00%
31-40	4	09.09%	2	15.38%
41-50	5	11.36%	4	30.77%
51-60	0	00.00%	3	23.08%
61-70	1	02.27%	0	00.00%
TOTAL	**44**	**100.00%**	**13**	**100.00%**

Table 1. Age wise distribution of developmental and acquired abnormalities of cranio-vertebral junction.

Abnormality	No. of cases	Percentage (%)
Clivus segmentation	6	10.53%
Basilar invagination	31	54.39%
Condylar hypoplasia	1	01.75%
Platybasia	1	01.75%
Occipitalization	21	36.84%
Hypoplasia/aplasia of atlas arches	3	5.26%
Atlantoaxial fusion	0	00.00%
Fixed atlantoaxial instability	31	54.39%
Mobile atlantoaxial instability	4	7.01%
Cord compression with myelopathic changes	30	52.63%
Os- odontoideum	8	14.02%
Os- terminale	1	01.75%
Syrinx	4	07.02%
Tuberculosis	6	10.53%
Spondyloarthropathy	1	01.75%
Neoplasms	1	01.75%
Chiari malformation	7	12.51%
Inflammatory granuloma with myelitis	1	01.75%
C2/c3 block vertebra	5	08.77%
Thickened calcified pll	1	01.75%
Adem	2	03.51%

Table 2. Spectrum of cranio-vertebral junction diseases

Most common disorder was developmental anomalies (46 patients, 80%) followed by infective (7patients, 12.2%), autoimmune (2 patients, 3.5%), inflammatory (1 patient, 1.7%) and neoplastic (1 patient, 1.7%) etiology [Table 2]. The developmental anomalies were co-existing and were found in various combinations. Overall, Atlanto-axial instability was the most common abnormality found in 35 patients (fixed in 54.39% + mobile in 7.02%= 61.4% total) followed by Basilar invagination (31 patients, 54.39%) and Atlanto-occipital assimilation (21 patients, 36.84%) whether partial or complete (figure 1a). Osodontoideum was noted in 8 patients (14.04%) (figure1b) and Chiari malformation in 7 (12.5%) (figure 2a). Others being, C2/C3 block vertebra in 5 cases (08.77%) (figure 1a). Syrinx was found in 4 patients (07.02%) each (figure 2a) and hypoplasia/aplasia/rachisis of atlas arches in 3(5.26%) (figure 2b,c), clivus hypoplasia (figure 1a, 1c,2a) and tuberculosis found in 6 patients (10.53%) each (figure 3b).

ADEM were found in 2 patients each (03.51%) (figure 4b), while condylar hypoplasia, platybasia (figure 1), os-terminale (figure 1 d, e, f), spondyloarthropathy, neoplasm, inflammatory granuloma (figure 3) and thickened calcified posterior longitudinal ligament were found in only 1 patient each (1.75%) (figure 4 a).

Cord compression with myelopathic changes were observed in abovementioned abnormalities in 30 patients (52.63%) and were most frequently associated with atlanto-axial instability and basilar invagination (figure 1).

Out of 21 patients with Occipitalization, basilar invagination was seen in 19 patients (90.48%) with a p value of <.001 indicating a significant association between the two.

Basilar invagination also had an important association with atlantoaxial instability as Out of 31 patients presenting with basilar invagination, 26 also had atlantoaxial instability with a p value of <.001.

Out of 23 patients who were operated, 22 completely recovered, while partial recovery and post operative worsening was noted in one patient. Rests of the patients were managed conservatively.

One of the patients expired while one patient who presented with isolated syrinx was kept on monitoring.

Discussion

Craniovertebral junction (CVJ) is a collective term for occipital bone, clivus, atlas, axis, supporting ligaments and underlying part of neural axis (medulla, spinal cord and lower cranial nerves)[2]. Any process congenital, developmental or acquired, which affects these structures, can give rise to abnormalities of CVJ. CVJ has intricate relationship with the major neurovascular structures which can lead to compression over cervico-medullary junction, lower cranial or spinal nerve and vertebral artery [10]. Due to its complex anatomy and relationships, CVJ disorders are difficult to treat, so, their proper classification, accurate diagnosis and precise anatomical information is of utmost importance as shown in our study.

Our study group of 57 patients, revealed male to female ratio of 1.47:1 which correlated well with the study done by Rajshree U. Dhadve et al & N.J.M. Mwang'ombe et al which also showed male predilection and a ratio of 1.6:1 and 2:1 respectively.[6,13] In our study, the most common age of presentation was 11-20 years followed by 21-30 years (21 patients, 37%) as compared to the studies by N.J.M. Mwangómbe et al and De Barrorswhich had a peak in third decade.[13,5] Most common presenting complaint in our study was neck pain followed by limb weakness and neck stiffness which was in accordance with most of the previous studies.[6,14]

However. Mwang'ombe stated that most common symptom was weakness of limbs followed by sensory disturbances, headache and neck pain.[13] The imaging features of cranio-vertebral junction in first decade are confusing as ossification is completed only after 12 years of age[11].

These composite disorders need accurate diagnosis and precise anatomical information by experienced radiologists so that decision for management can be tailored on individual basis. Due to complex anatomy of CVJ and overlap of many soft tissue structures, plain radiographs create limitations in diagnosis and anatomical delineation.[3] So, we used cross-sectional imaging (MRI and CT) for its evaluation. Due to its capability of volume rendering and multiplanar reformations, MDCT is "state of the art" imaging technique for evaluation of complex osseous anatomy of CVJ. MRI, due to its high soft tissue contrast resolution and multi-planar capabilities, has turned into the mainstay in radiological evaluation of this region [18]. Quantitative assessment of the CVJ uses a series of lines and angles, as discussed in material and method, to describe various anatomic relationships. [14]

In our study, developmental anomalies were the most frequent etiological group, followed by infective, autoimmune, inflammatory and neoplastic which correlated well with the studies done by Bhagwati et al [1] and Kale.[10] In our study, Atlantoaxial dislocation was most common etiology seen in 61.4% cases which was comparable with results produced by J.S. Chopra et al who stated that congenital AAD accounted for 51.5–68% of all CVJ anomalies.[3] Atlantoaxial instability was followed by basilar invagination and occipitalization which correlated well with study by Rajshree U. Dhadve.[6] Compressive myelopathic changes were seen in 52.63% cases which was in accordance with studies by Ramen Talukdar.[17] Os-odontoideum was found in 14.02% which was in correspondence with previous studies.[4] Os-terminale was seen in 1.75% of the cases

Among acquired disorders, tuberculosis was most common entity seen in 6 patients (10.5%) which may be explained by high prevalence of the disease in Indian subcontinent and correlated well with study done by Ramen Talukdar.[17] Out of these 6 cases, 4 patients showed erosions and destruction of dens and 2 of anterior atlas arch. Atlanto-axial dislocation was noted in 5 patients and basilar invagination in two. Prevertebral and paravertebral granulation tissue was seen in 5 cases and frank abscess formation in 2 cases. 3 patients showed extension of granulation tissue/ abscess in anterior epidural space and compressive myelopathy was seen in 2 patients. 2 cases showed involvement of the skull base in form of marrow edema and post contrast enhancement in clivus. Involvement of occipital bone was not seen in any of these patients. These findings were in accordance with study by Rajshree U. Dhadve.[6]

CVJ involvement in Rheumatoid arthritis was noted in one patient who showed erosions of dens and associated fibrous pannus resulting in atlanto-axial dislocation.

In our series of 59 patients, four had Syringomyelia and two had Chiari I malformation. The later entity was associated with platybasia, flattened clivus, blocked vertebra and atlantoaxial dislocation in 100 % of the cases. Scoliosis and platybasia were seen in two patients each which was in accordance with previous studies.[17] One patient had neoplastic etiology of CVJ, an extra-axial dural based meningioma. Elderly patients (between 50-70 years), who presented with complains of neck pain, headache and walking difficulty, developmental cause was seen in only one patient and acquired causes in 3 patients. Bony and ligamentous degeneration explained the above complaints in one patient as imaging revealed ossified posterior longitudinal ligament.

Our study showed basilar invagination in 90% of the cases who had atlanto-occipital assimilation indicating strong association between these two entities. This association was first noted by by Grawitz[9] and has since been reported frequently. [2,12,16,19,7] Many articles have regarded atlanto-occipital assimilation as a characteristic feature of basilar invagination.

Similar association was also noted between atlanto-axial instability and basilar invagination. Previous studies state micro-trauma due to instability related repeated cord injuries to be the defining factor in the entire pathophysiology of basilar invagination. [8]

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Possibilities of endoscopic endonasal transsphenoidal surgery in treatment of growth-hormone pituitary adenomas

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Abstract

Pituitary adenomas are one of the most common primary central nervous system tumours and have an estimated prevalence of 17%. Management of hormone-secreting pituitary adenomas involves a multidisciplinary approach that can incorporate surgical, medical, and/or radiation therapies. Acromegaly is a rare, chronic disorder that mostly results from growth hormone (GH)-secreting pituitary adenoma. We analyzed the outcomes of surgical treatment for growth hormone (GH) pituitary adenomas based on 28 cases and determine factors that lead to biochemical remission.

Keywords
endoscopic, endonasal, transsphenoidal, pituitary adenomas

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Introduction

Growth-hormone (GH) pituitary adenomas occur in 13-20% of all hormonally active pituitary adenomas [1, 21]. Increased levels of GH can cause the progression of cardiovascular and cerebrovascular diseases, which leads to increased mortality [4, 5] These pituitary adenomas are invasive to the surrounding structures around the sellar area, which reduces the radicality and makes hormonal remission unattainable. [6, 15]. GH- pituitary adenomas treatment includes surgery, radiotherapy and medical therapy. Surgery allows to reduce the GH level insulin-like growth factor 1 (IGF-1) rapidly and is the primary method in GH pituitary adenomas [10, 11]. Currently, almost all pituitary adenomas are removed by endoscopic endonasal route which is highly effective and allows to achieve a high remission rate with a low number of complications [6, 12].

Material and methods

A retrospective analysis of 28 patients with GH pituitary adenomas in the period from 2013 to 2019. All patients underwent surgical treatment by endoscopic endonasal route. Information about patients, tumor characteristics, clinical symptoms and biochemical remission is shown in Table 1. Patients were divided by age and gender: men – 12

(42.9%), women - 16 (57.1%), the average age was 40.67 years. GH pituitary adenomas were classified by size: microadenoma (up to 10 mm) - 5 (17.9%) patients, macroadenoma (10-39 mm) - 21 (75%) patients, giant pituitary adenoma (> 40 mm) - 2 (7,1%) patients. Cavernous sinus extension was classified according Knosp scale [18]: grade 0, 1 and 2 are defined as noninvasive tumors, grade 3 and 4 are defined as invasive tumors.

Age (mean, range)	40,67 (18-64)
Male	12 (42,9%)
Female	16 (57,1%)
Tumor size	
- Micro	5 (17,9%)
- Macro	21 (75%)
- Giant	2 (7,1%)
Cavernous sinus invasion	
- No invasion	18 (64,3%)
- Invasion	10 (35,7%)
Pre-GH level (mean, range)	39, (5,7 – 252) ng/ml
Symptoms and signs	
- Acromegaly	28 (100%)
- Visual field defect	9 (32,1%)
- 6 nerve palsy	1 (3,6%)
- Headache	11 (39,3%)
Long term follow-up results	
- Remission	23 (82,1%)
- Persistence	3 (10,7%)
- Recurrence	2 (7,1%)

Table 1. Patients, tumor characteristics, clinical symptoms and biochemical remission for 28 patients.

There were 18 (64,3%) cases with noninvasive cavernous sinus extension and 10 (35,7%) cases with invasive tumors. All patients were tested for GH and IGF-1 level before surgery, 3 months after surgery, and annually. Acromegaly was diagnosed on the basis of relevant clinical features: mean GH level >5 μg /l, plasma IGF-1 level greater than normal appropriate to age and gender. The serum GH level ranged from 5.7 to 252 ng / ml (at average 39), IGF-1 level ranged from 592 to 1506 ng / ml (at average 960.9). Preoperative clinical manifestations were observed in all 28 cases. All patients had clinical signs of acromegaly, visual impairment were found in 9 (32.1%) patients, oculomotor disorders in one patient (3.6%), headache was observed in 11 (39.3%) cases. All patients underwent magnetic resonance imaging (MRI) with intravenous contrast enhancement. The endoscopic endonasal transsphenoidal (EET) approach was used in all cases. Surgery was performed using an endoscopic stand based on the HD-endoscope “Image-1HD” (Karl Storz, Germany). Rigid endoscopes "Karl Storz" 4 mm in diameter with viewing angles of 0 and 35 degrees were used as the main tool for visualization of the operating field. The follow-up ranged from 12 to 60 months, at average 25.4 (2.1 years) months. The serum level of GH and IGF-1 was determined in 3 months after surgery and annually. The criteria for endocrine remission or treatment were the lowest serum GH level of <0.4 ng/ml after oral glucose challenge, and subsequent normal IGF-1 levels appropriate to age and gender.

Results

Radical removal: complete resection of somatotroph pituitary adenomas (PA) was achieved in 22 (78.6%) cases, of which in 19 (86.4%) patients - without invasive extension to the cavernous sinus, and in 3 (13.6%) patients - with invasive extension of Knosp 3. Subtotal resection was in 5 (17.8%) cases, of which non-invasive extension was found in 2 patients, in one of which the growth of PA was prolonged. The size of these tumors was from 30 to 40 mm. Invasive extension with subtotal resection of somatotroph PA Knosp 3 and Knosp 4 was revealed in 3 cases. Partial removal in 1 (3.6%) case, where there was extension to the cavernous sinus during Knosp 3.

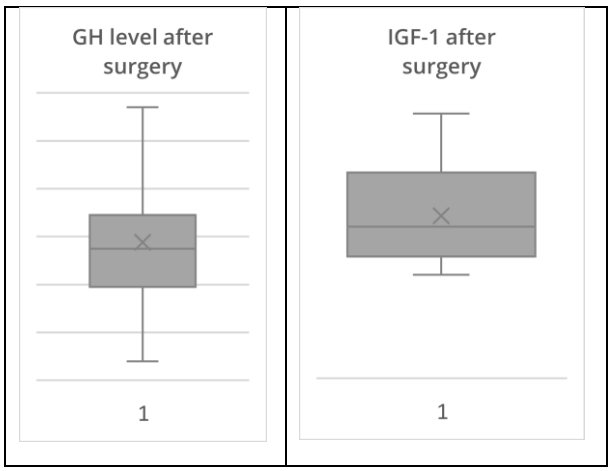

Figure 1. Range of GH and IGF-1 serum level after surgery.

Postoperative radiation therapy was performed in 4 cases, in 3 of them subtotal resection was performed, in one case due to partial removal. Growth recurrence after radiation therapy was observed in 2 (7.1%) cases, resulting in repeated

surgery. Clinical laboratory remission (CLR) was achieved in 23 (82.1%) patients. IGF-1 serum level ranged from 1 to 649 (mean 378,) GH level ranged from 0,4 to 5,7 (mean 2,9) (Fig. 1). In patients who underwent only radiation therapy after surgery, CLR was achieved in 2 patients. In patients who underwent radiation therapy and repeated surgery for a prolonged growth of PA, CLR was achieved in 1 case (out of 2 patients), which is associated with radical removal of PA. Postoperative nasal cerebrospinal fluid was observed in 3 (10.7%) cases, for which lumbar drainage was inserted in all 3 cases. Diabetes insipidus was detected in 1 (3.6%) case, which required the assignment of replacement therapy. There is no postoperative mortality.

Discussion

Currently, in the treatment of tumors sellar region transsphenoidal approach is generally accepted and widely used in surgical practice [1,9,10,17]. Pituitary adenomas of various sizes and hormonal activity can be completely removed using EET approach [6, 22]. EET approach is currently the main method of surgical treatment of somatotroph pituitary adenomas [2].

The use of EET approach allows to achieve rapid decompression of the optic nerves and chiasm, affect the regression of acromegalic changes, reduce the risk of cardiovascular diseases and decrease mortality due to the rapid release of GH excess [22]. Compared to the microsurgical transsphenoidal approach, the EET approach is effective and allows one to achieve a larger number of totally removed pituitary adenomas and achieve biochemical remission surgically [6]. In our study, radical resection was achieved in 22 (78.6%) cases, of which 19 (86.4%) patients without invasive extension to the cavernous sinus, 3 (13.6%) patients with invasive extension Knosp3, subtotal resection - 5 (17.8%) cases, of which non-invasive extension was found in 2 patients. The size of these tumors was from 30 to 40 mm. Invasive extension with subtotal resection of these tumors was found in 3 cases. Partial removal in 1 (3.6%) case, where there was a spread to the cavernous sinus during Knosp3. Biochemical remission in endoscopic endonasal transsphenoidal removal of somatotroph pituitary adenomas was achieved in 23 (82.1%) patients.

According to the literature, biochemical remission in surgical series can be achieved in 60% -86% of cases [13, 16, 22]. It is noted in studies that biochemical remission is influenced by the invasiveness of somatotroph pituitary adenomas, the level of preoperative GH [20]. In our series of observations, the radical removal of somatotroph pituitary adenomas depended on the invasive extension of these tumors to the cavernous sinus. At the same time the achievement of hormonal remission depended on the degree of removal of pituitary adenomas and their extension to the cavernous sinus. It was noted that hormonal remission was different depending on the size of somatotroph pituitary adenomas ($p < 0.05$). In pituitary microadenomas, hormonal remission was achieved in all patients (5 cases), in macroadenomas - 18 (85.7%), in giant pituitary adenomas - in one (out of two cases).

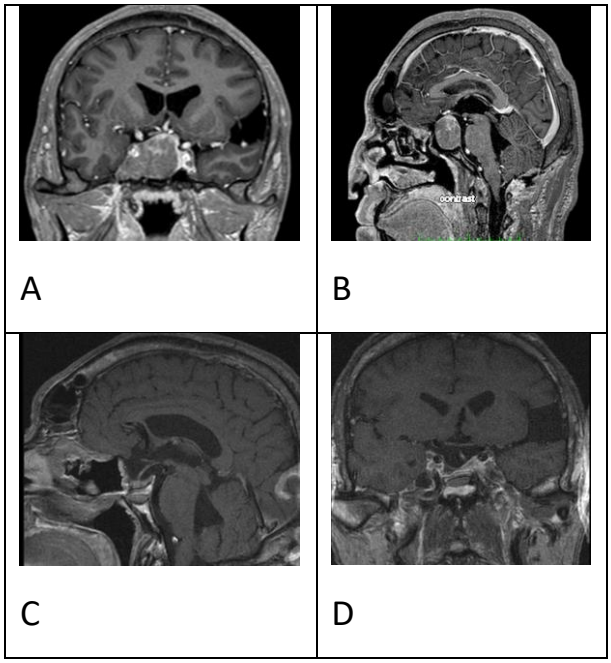

Figure 2.
A-B preoperative MRI scans with gadolinium. Macroadenoma 27x25x38 mm in size with Knosp 3B extension into the cavernous sinus.
C-D MRI scans with gadolinium after surgery, follow-up 5 years. GH level – 4,6 ng\ml.

Among invasive GH pituitary adenomas, biochemical remission was achieved in 8 (72.7%) patients, among noninvasive tumors, biochemical remission was achieved in 16 (94.1%) patients. As a clinical case we illustrate outcome of surgical treatment patient with large GH pituitary adenoma (Fig. 2). Patient with clinical manifestation of acromegaly, visual

disturbances, high level of GH -233 ng\ml and increased IGF-1 - 1288 ng\ml. Preoperative MRI scans with gadolinium shown large pituitary adenoma 27x25x38 mm in size with Knosp 3B extension into the cavernous sinus. Endoscopic endonasal approach was used to remove the tumor. Visual disturbances regressed after surgery. CLR was achieved after surgery in a few months and stay stable during all follow-up period (5 yeas). MRI scans with gadolinium after surgery and 5 years after shown gross-total tumor resection and no recurrence. Serum GH level – 4,6 ng\ml, IGF-284 ng\ml.

Recurrence and low level of hormonal remission are associated with the volume of tumor removal, its extension to the cavernous sinus. Thus, in 6 patients there was incomplete resection of GH pituitary adenoma. The size of these tumors was more than 3 cm in diameter. In 4 cases there was an invasive extension to the cavernous sinus. In two cases, there was a prolonged growth of tumors which were operated on at another center.

Adjuvant therapy, which includes drugs that reduce GH, repeated surgery or radiation therapy, plays an important role in the long-term treatment of patients who have not achieved hormonal remission after surgery [8, 9]. Postoperative radiotherapy was performed in 4 cases. Recurrence of growth after radiation therapy was observed in 2 (7.1%) cases, resulting in repeated surgery. Thus, hormonal remission in the group of patients with incomplete resection of GH-pituitary adenoma was achieved in 4 (66.7%) patients.

According to the literature, complications during pituitary adenoma surgery occur on average in 10% of cases, hypopituitary syndrome is manifested in less than 10% of cases, nasal cerebrospinal fluid - 13.9%, oculomotor nerve injury- in 6% [3, 17, 19]. Postoperative nasal cerebrospinal fluid was observed in 3 (10.7%) cases. Diabetes insipidus - 1 (3.6%) case, for which was prescribed the replacement therapy. There is no postoperative mortality.

Conclusions

1. Endoscopic endonasal transsphenoidal approach in the treatment of GH pituitary adenomas is effective, allowing to achieve hormonal remission in 82.1%, and is safe method reducing the number of postoperative complications.

2. Cavernous sinus extension of GH pituitary adenomas reduces the possibility of radical removal of these tumors, clinical and laboratory remission can be achieved in 85.7% of patients.

3. Radiotherapy can reduce the number of recurrences, while clinical laboratory remission was achieved in 66.7% of patients.

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Letter to the editor. Intracranial aneurysm: research in preclinical outcome models and human effectiveness of intraluminal devices

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Keywords
intracranial aneurysm, preclinical outcome models, intraluminal devices

ABSTRACT
Endovascular treatment of intracranial aneurysms has become one of the most important preclinical research arenas. This influential progress is due to the incredible development of new devices and catheters technologies. One of the main outcomes for intraluminal devices used for treatment is the rate of occlusion of the aneurysm.

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Dear Editor,

The endovascular treatment of intracranial aneurysms has become one of the most important preclinical research arenas. [1] This influential progress is due to incredible development of new devices and catheters technologies. One of main outcome for intraluminal devices used for treatment is the rate of occlusion of the aneurysm. Coil embolization, stenting, flower diverter and intrasaccular disruptors cause progressive healing of the aneurysm.[2] One of the most important challenges is recanalization resulting in retreatment in up to 20% of cases. [2] Although the mechanisms of aneurysm healing are poorly understood, much of the information has been obtained from preclinical animal models. The latter do not emulate the conditions of the healing process that occurs in humans. [3] One recent biggest problem facing the world today is SARS-CoV-2 epidemic and the capability of SARS virus to infect multiple cell types and thus several organs [4] Varga et al, showed evidence of direct viral infection of the endothelial cell and diffuse endothelial inflammation. [5] Although the 3 cases mentioned in the report did not include any cerebral vasculature histology though the same impact of

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virus can be there. This endotheliitis associated with COVID-19 may have relevant implications for preclinical investigation, usually in animal models capable of being coronavirus-infected and in humans receiving treatment with devices such as stents, flow diverters, and intrasaccular disruptors.

Ravindran et al, published a systematic review where they evaluated the published literature regarding endothelialization after flow diverter deployment.[6] For example, after pipeline embolization device (PED) deployment, progressive endothelialization occurs in two forms rapidly, at the parent artery and slowly at the aneurysmal neck. [7] At the histopathological level, the presence of inflammatory cells and thrombi have been determined, all of which contribute to the effectiveness of the devices. [8] The infection associated with SARS-CoV-2 leads to a hyperinflammatory response.[9] The presence of a dysregulated macrophage response that injures the host. The role of this inflammatory response and its effect must be established on the endothelialization and healing process of intracranial aneurysms after treating with endovascular devices. [9] The clinical implication at this time is unknown with pandemic in full force. With time, patients who are getting devices placed for aneurysm treatment might not heal these aneurysms fully. More research is necessary to establish the effect of coronavirus on the healing and endothelialization of intracranial aneurysms.

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