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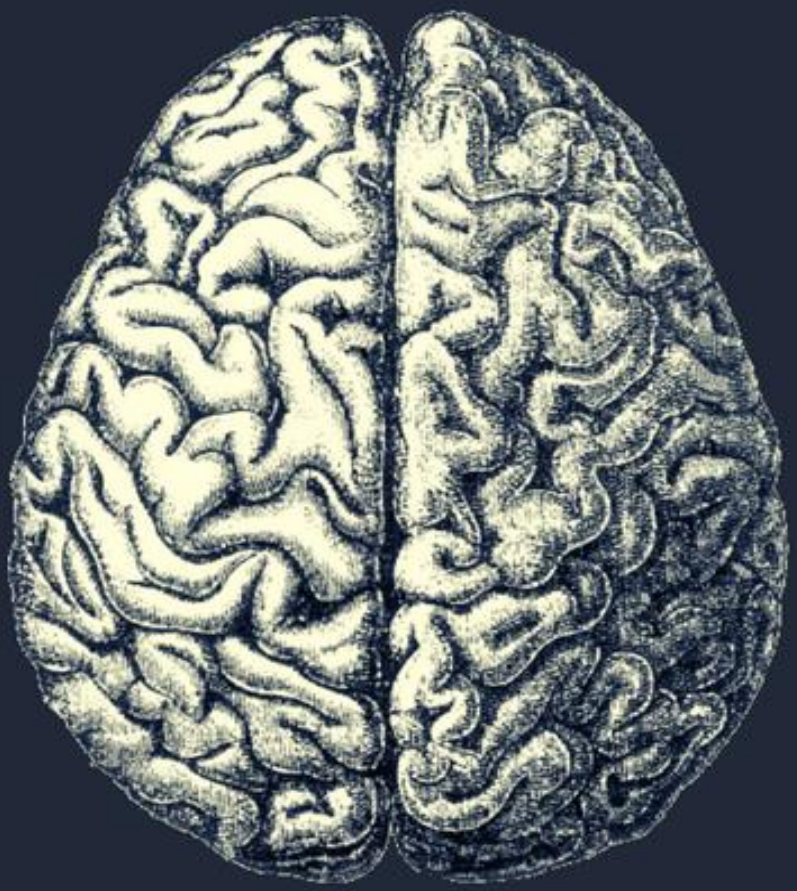

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Troponin and non-traumatic subarachnoid haemorrhage. Results from a study of 243 consecutive patients

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Keywords
aneurysmal subarachnoid haemorrhage, non-aneurysmal, non-traumatic subarachnoid haemorrhage, cardiac troponin, cardiac markers, neurogenic cardiac dysfunction, stress cardiomyopathy

ABSTRACT

Introduction: Subarachnoid haemorrhage (SAH) is a devastating event, with a mortality of up to 50%. Acute cardiac dysfunction is common after such an event, and it is known to have a negative impact on the outcome of these patients. Cardiac troponin release occurs frequently after SAH and represents an early biomarker for neurogenic cardiac dysfunction.

Objective: The present study aimed to evaluate the impact of a raised troponin value on the outcome of SAH patients.

Methods: This is a prospective observational study held between 2014-2017 at the University Emergency Hospital, Bucharest. Data on clinical admission status, high-sensitivity troponin I, ECG and echocardiographic evaluation results, ICU length of stay and in-hospital mortality rate. Statistical analysis was performed using non-parametrical Mann-Whitney and chi-square tests. The results were considered significant at $p<0.05$.

Results: A total of 335 consecutive patients with non-traumatic SAH were admitted during the study period. 92 of them were excluded and 243 were analyzed, 203 with aneurysmal SAH and 40 with non-aneurysmal, non-traumatic SAH. High-sensitivity troponin I reached its peak level 48 to 72 hours after SAH and was higher in patients with aneurysmal SAH. For all SAH patients, its median and peak values on days 1 and 2 were correlated with the ICU length of stay and inversely correlated with in-hospital length of stay. For the first 3 days, the median and maximum troponin values are higher in patients who died compared with those who survived and were discharged home (p-value < 0.001). Predictors of an elevated troponin on day 1 are loss of consciousness at ictus, a high Hunt and Hess and Fisher Scale grade, intraventricular haemorrhage and cerebral midline shift.

Conclusions: The release of cardiac troponin is a valuable marker of neurogenic cardiac dysfunction in the first 3 days after SAH. The study replicates other data in the literature and highlights the association between SAH severity, early troponin elevation and in-hospital death.

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Introduction

Subarachnoid hemorrhage (SAH) is a medical emergency, still associated with a high morbidity and mortality, despite the recent advancement in its treatment. The fact that it affects people in the prime of their lives makes it an important public health concern. It is a well-known fact that subarachnoid hemorrhage is associated with neurogenic myocardial dysfunction, of which cardiac troponin is a reliable marker. Up to 63% of aneurysmal SAH patients have a cardiopulmonary involvement and 23% of them die as a result of such a complication (1-3). The cardiac dysfunction becomes a sign of the severity of SAH, as well as a marker of bad outcome. It is associated with neurologic complications, such as vasospasm and delayed cerebral ischemia, and with a high in-hospital mortality (4-6). The diagnosis of such a myocardial dysfunction is made taking into consideration the early electrocardiographic changes, the release of cardiac troponin and NTproBNP and the echocardiographic wall motion anomalies.

Moreover, this stress cardiomyopathy is encountered early in the clinical evolution of aneurysmal SAH, as the majority of patients who are diagnosed with such a complication have a lower arterial blood pressure and thus a higher need for vasopressors, more ST-T anomalies and even a high value of the cardiac troponin at the moment of their hospital admission (7). Troponin has a high sensibility for detecting the cardiopulmonary stress encountered in SAH, with up to 70% of patients having a rising troponin value in the first two days from the aneurysmal rupture. Furthermore, a high troponin value is corelated with a prolonged corrected QT interval on the electrocardiography and echocardiographic anomallies (3)(4)(7-12).

Materials and method

We conducted a prospective observational study. All consecutive adult patients admitted to the Neurosurgical or the Intensive Care Unit of the University Emergency Hospital, Bucharest, between December 2014 and December 2017 were included. Their identity was anonymized and all of them were treated by their attending doctors according to national and international protocols for SAH, without any interference from the lead author of this paper, who collected the data. A series of data were collected, among them preexisting pathologies and known SAH risk factors, clinical status on admission (neurological and cardiovascular parameters, such as Glasgow Coma Scale grade, arterial pressure and heart rate) vasopressor requirement, oxygenation index, SAH extension on CT (Fisher Scale grade, intracerebral and intraventricular hemorrhage extension), ECG and echocardiographic evaluation results, high-sensitivity troponin I value, ICU length of stay and in-hospital mortality. Exclusion criteria were represented by: traumatic SAH, preexisting cardiac disease (ischemic heart disease, congestive heart failure, cardiac pacing, atrial fibrillation or atrial flutter), chronic renal failure, fluid balance and electrolytic anomalies or treatment with drugs that might affect the ECG or a period longer than 24 hours between the debut of symptoms and the transfer to the University Emergency Hospital. Statistical analysis was performed using SPSS v27.01.0 (SPSS Inc., Chicago, Ill., USA). Data was represented using means or medians and non-parametric Mann-Whitney tests were performed to analyze the difference between groups. Categorical data was assessed using chi-square tests. A p value <0.05 was considered statistically significant.

Results

Between December 2014 and December 2017, there were 335 adult patients with SAH admitted to the University Emergency Hospital in Bucharest. We excluded 92 of them due to criteria mentioned above, so 243 of them were studied – 203 with aneurysmal SAH and 40 with non-aneurysmal, non-traumatic SAH.

Aneurysmal SAH

Of the 203 patients with aneurysmal SAH, the majority were women (55.17%) and lived in an urban area (61.58%). The mean age was 51.4±12.1 years old, with the youngest patient being 20, and the oldest 79 years old. The mean age was 52 years old for women and 49 years old for men. The mean body mass index was 28 (interquartile range IQR 26, 31), 102 patients (50,2%) were smokers and 42 (20.7%) were using alcohol. 45 patients (22%) were dyslipidemic, 48 (23.6%) were hypertensive, 11 (5.4%) had a history of stroke and 20 patients (9.9%) had diabetes. The mean duration from symptom debut to hospital admission was 2.67 hours for people coming from rural areas, and 1.64 hours for people coming from urban areas. The median for the

admission Glasgow Coma Scale score was 7.5 (IQR 5, 14). Most of the patients with a ruptured aneurysm (135 or 66.5%) were admitted to the Intensive Care Unit, with a median ICU stay of 1 day (IQR 0, 4) and a median hospital stay of 9 days (IQR 1, 19). More than half of them (113 or 55.7%) died during their hospital stay.

Table 1. Data for day 1

Parameter	All patients (n=243)	Non-aneurysmal SAH (n=40)	Aneurysmal SAH patients (n=203)
Median for systolic arterial pressure (IQR)	135 (125,155)	140 (135,150)	135 (125,155)
Median for mean arterial pressure (IQR)	101.67 (88.34,11)	105.83 (94.6,113)	101.67 (85,115)
No. and percentage of patients with vasopressor treatment	42 (17.3%)	1 (2.5%)	41 (20.2%)
Median for heart rate (IQR)	85 (70, 95)	80 (71.25, 90)	85 (70, 95)
Median for oxygenation index (IQR)	300 (263.5, 327)	371.5 (321.5, 448.5)	290 (260, 321.75)
Mechanically ventilated	145 (59.7%)	20 (50%)	125 (61.6%)
Median for troponin level (IQR)	0. 62 (0.02,1.24)	0.36 (0.17,0.59)	0.63 (0.09,1.24)
No. and percentage of patients with high troponin value	113 (74.8%)	6 / 9 (66.7%[1])	107 / 142 (75.4%[1])
Median for corrected QT interval (IQR)	410 (378, 448)	386 (372, 418)	416 (380, 452)
No. and percentage of patients with prolonged corrected QT interval	47 (19.3%)	0	47 (23.2%)

[1] Percentage based on total number of patients with available troponin value for day 1

Other data collected for day 1 are shown in table 1. The median for the maximum high-sensitivity cardiac troponin I level was 1.02 ng/ml, with an interquartile range of 0.26 to 1.96 ng/ml. For those patients in whom high-sensitivity cardiac troponin I level was measured, its value increased from day 1, reaching a peak value on day 3 (48 to 72 hours from the rupture of the aneurysm). Table 2 shows data regarding the high-sensitivity cardiac troponin I values for patients with aneurysmal SAH.

Table 2. High-sensitivity cardiac troponin I level

	Day 1	Day2	Day 3
Median for troponin level (IQR)	0.63 ng/ml (0.09,1.24)	0.98 ng/ml (0.29,1.91)	1.7 ng/ml (0.85,2.63)
No. and percentage of patients with high troponin value	107 / 142 patients (75.4%[1])	67 / 84 patients (79.8%[1])	41 / 41 patients (100%[1])

[1] Percentage of the patients with available troponin value for day

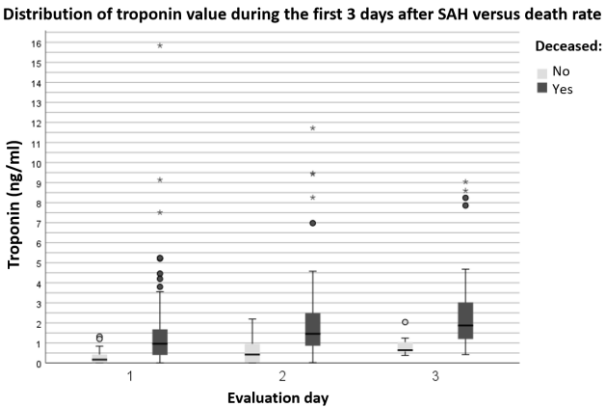

Figure 1. Distribution of troponin value during the first 3 days after SAH versus death rate

For all patients (aneurysmal and non-aneurysmal, non-traumatic SAH), both maximum troponin value ($p<0.001$) and troponin value from day 1 ($p<0.028$) and day 2 ($p<0.001$) were correlated with their ICU stay, and inversely correlated with their in-hospital stay ($p<0.001$ for all). Moreover, for patients with aneurysmal SAH, these values were correlated with

their in-hospital stay (p<0.001) and not with their ICU stay. Furthermore, the maximum troponin value and the troponin level during the first 3 days were significantly higher in patients who died during their hospital stay compared with those who were discharged (p<0.001 for all) (Figure 1).

Table 3. Predictors of elevated troponin (troponin >0.03 ng/dL) on day 1

Variable	No of patients with elevated troponin on day 1 N=107 (%)	OR (95%CI)	P value
Loss of consciousness at ictus	68 (63.6%)	5.03 (2.14, 11.83)	<0.001
Hunt&Hess grade IV or V	86 (80.4%)	4.86 (2.14, 11.02)	<0.001
Fisher Scale grade III or IV	84 (80%)	10 (4.16, 24)	<0.001
Intraventricular hemorrhage	51 (47.7%)	5.46 (1.97, 15.15)	<0.001
Midline shift	51 (47.7%)	4.4 (1.69, 11.46)	0.001

Admission clinical and radiographic variables (CT) predictive of increased day 1 high-sensitivity cardiac troponin I levels included: loss of consciousness at ictus, higher Hunt and Hess grade (IV and V), higher Fisher scale grade (III and IV), intraventricular hemorrhage and midline shift on admission CT.

Non-aneurysmal, non-traumatic SAH

This group consists of 40 patients, with 57.5% originating from urban areas and 42.5% of them being women. The mean age was also 51.48±11.87 years old, with the youngest being 28, and the oldest 71 years old, in both men and women. The mean body mass index was also 28 (IQR 26, 31), 15 patients (37.5%) were smokers and 6 (15%) were using alcohol. 14 patients (35%) were dyslipidemic, 9 (22.5%) were hypertensive, and 13 patients (32.5%) had diabetes. None had a history of stroke. The mean duration from symptom debut to hospital admission was 4.4 hours for both rural and urban areas, but with a median value of 2 hours for people coming from rural areas, compared with 5 hours for people coming from urban areas. The median for the admission Glasgow Coma Scale score was 11.5 (IQR 5.25,15). Just like patients with aneurysmal SAH, more than half of the people in this subgroup were admitted to the Intensive Care Unit (21 or 52.5%), with a median ICU stay of 1 day (IQR 0, 4) and a median hospital stay of 18.5 days (IQR 5.25, 26).Less than half of them (17 or 42.7%) died during their hospital stay.

Discussion and conclusions

Our data correlate well with those found in the literature when it comes to the general characteristics of the people in the 2 subgroups: women are more affected by SAH caused by aneurysm rupture, while more men are affected by non-aneurysmal, non-traumatic SAH. Both subgroups are represented by people in their prime (about 51 years old), coming from urban areas (13)(14). As expected, smoking was the most prevalent risk factor encountered in our cohort, in half of the patients. A series of studies cites smoking as the most important modifiable risk factor for aneurysmal rupture (15-20). The fact that alcohol consumption was declared by only about a quarter of the patients may be so because of the social stigma associated with it, or because of the underreporting bias – people tend to underestimate their alcohol intake. A high alcohol consumption represents an important risk factor for aneurysm rupture (15)(17)(21)(22). In contrast to the literature (15)(17)(21-23), not finding hypertension as a main risk factor for SAH may be explained by the general lack of preventive medicine in our country, with a certain number of people believing that you should visit a doctor only when you are “sick”, without realizing that a lot of diseases are, in fact, “silent killers”.

It was important to study all of these risk factors, as all of them are also risk factors for cardiac disease, where troponin plays a key role. On the one hand, for aneurysmal SAH, the more rapid hospital admission for people coming from urban areas compared to those from rural areas could be easily explained by their proximity to a hospital. On the other hand, vice-versa was observed for non-aneurysmal, non-traumatic SAH. This seems to represent a paradox – lighter symptoms compared to those produced by the rupture of an aneurysm make people living in an urban area ignore them for a longer period of time, precisely because they can access medical support at any time they feel they finally need to. Nevertheless, the time frame between symptom debut to hospital

admission remains short in terms of troponin release and detection. This is important as it did not interfere with the trend of our troponin results.

A lower median value of the Glasgow Coma Scale Score, a higher percentage of ICU admission and a higher death rate for patients with aneurysmal SAH versus non-aneurysmal, non-traumatic SAH was observed, as expected, due to its more severe evolution, with a known high mortality (1)(24)(25). The cardiac dysfunction in patients with SAH was readily apparent when analyzing general data, like mean arterial pressure, need of vasopressors, heart rate, and even oxygenation index and need of mechanical ventilation, or specific parameters like, troponin level and corrected QT interval on the electrocardiogram. The subgroup of aneurysmal SAH patients had a lower mean arterial pressure and a higher need of vasopressor treatment, a lower oxygenation index and a higher percentage of mechanically ventilated people, all of which are markers of a cardiac involvement. Moreover, a higher percentage of aneurysmal SAH patients had an abnormal troponin level, with a median troponin value almost double the one observed in non-aneurysmal, non-traumatic SAH. The fact that troponin elevation is detected early in the evolution of SAH is very useful in order to detect the incidence of cardiac dysfunction immediately after SAH.

For the first day of hospital admission, our study revealed a high frequency of high-sensitivity cardiac troponin I elevation - 74.8% out of the 151 patients who were tested in the entire SAH group, with a higher percentage in the aneurysmal SAH subgroup (75.4% out of the 142 patients who were tested) compared to the non-aneurysmal, non-traumatic subgroup (66.7% out of the 9 patients who were tested). We may have overestimated the true incidence of an elevated troponin I value, due to the fact that not all patients included in the study were tested. On the one hand, other studies (8)(26-28) revealed that only 20% to 40% of the patients with aneurysmal SAH had a detectable troponin I release. On the other hand, all these other cited studies used cardiac troponin I assays, whereas we investigated the dynamics of high-sensitivity cardiac troponin I, which, as its name suggests, has much lower limits of detection (29). Therefore, new studies may be needed in order to describe de dynamics of high-sensitivity cardiac troponin I assays in patients with SAH. Troponin reaching a peak on day 3, that is 48 to 72 hours after aneurysmal rupture in our study, is also well correlated with other literature references (30).

We found that high-sensitivity cardiac troponin I measurements after SAH have prognostic significance. A raised value on day 1 and 2 (which represent the first 48 hours after SAH) is significantly correlated with the ICU stay, and inversely correlated with in-hospital stay. This suggests a more severe clinical evolution for patients with a high troponin value and supports the idea that cardiac dysfunction associated with SAH may be involved in their poor outcome. Moreover, the fact that maximum troponin level, as well as troponin values during the first 3 days after SAH are significantly higher in patients who died, versus patients who were discharged home suggests that cardiac troponin should be routinely measured in SAH patients, in order to be able to offer a more intensive management for these patients. Furthermore, these results reinforce the general recommendation of a thorough cardiac monitoring, including serial troponin measurements, especially during the first 3 days in all SAH patients.

Patients with more severe SAH grades should be primarily monitored closely for cardiac dysfunction, as they demonstrated to be more likely to develop an elevated level of serum cardiac troponin I. There was a strong correlation between the extent of cardiac troponin I elevation and various parameters of SAH severity, such as loss of consciousness at ictus, a high Hunt and Hess grade, intraventricular hemorrhage, midline shift and a high Fisher scale grade. These results demonstrate the neurogenic origin of heart injury in aneurysmal SAH patients. Further research is needed to investigate whether certain measures to optimize cardiac treatment after SAH improve outcome.

References

1. Okabe T, Kanzaria M, et al. - Cardiovascular protection to improve clinical outcomes after subarachnoid hemorrhage: is there a proven role? Neurocrit Care 2013, 18(2), 271-284.
2. Chen WL, Huang CH, et al. - ECG abnormalities predict neurogenic pulmonary edema in patients with subarachnoid hemorrhage. Am J Emerg Med, 2016, 34(1), 79-82.
3. Zahid T, Eskander N, et al. - Cardiac Troponin Elevation and Outcome in Subarachnoid Hemorrhage. Cureus 2020, 12(8), e9792.
4. Mavridis I, Meliou M, et al. - Troponin elevation in

subarachnoid hemorrhage, Journal of Acute Disease 2015, 21, 10, 1016/S2221-6189(14)60074-3.
5. Oras J, Grivans C, et al. - Lodding H. Elevated high-sensitive troponin T on admission is an indicator of poor long-term outcome in patients with subarachnoid haemorrhage: a prospective observational study. Crit Care, 2016, 20, 11.
6. McAteer A, Hravnak M, et al. - The Relationships Between BNP and Neurocardiac Injury Severity, Noninvasive Cardiac Output, and Outcomes After Aneurysmal Subarachnoid Hemorrhage, Biol Res Nurs. 2017, 19(5), 531-537.
7. Oras J, Grivans C, et al. - High-Sensitive Troponin T and N-Terminal Pro B-Type Natriuretic Peptide for Early Detection of Stress-Induced Cardiomyopathy in Patients with Subarachnoid Hemorrhage, Neurocrit Care 2015, 23(2), 233-242.
8. Parekh N, Venkatesh B, et al. - Cardiac troponin I predicts myocardial dysfunction in aneurysmal subarachnoid hemorrhage, J Am Coll Cardiol. 2000, 36(4), 1328-1335.
9. Naval NS, Stevens RD, et al. - Controversies in the management of aneurysmal subarachnoid hemorrhage, Crit Care Med.2006, 34(2), 511-524.
10. Stevens RD, Nyquist PA. - The systemic implications of aneurysmal subarachnoid hemorrhage, J Neurol Sci. 2007, 261(1-2),143-156.
11. Ripoll JG, Blackshear JL, et al. - Acute Cardiac Complications in Critical Brain Disease, Neurol Clin.2017, 35(4), 761-783.
12. Kagiyama N, Sugahara M, et al. - Neurocardiac Injury Assessed by Strain Imaging Is Associated With In Hospital Mortality in Patients With Subarachnoid Hemorrhage, JACC Cardiovasc Imaging, 2020, 13(2 Pt 2), 535-546.
13. Sarti C, Tuomilehto J, et al. - Epidemiology of subarachnoid hemorrhage in Finland from 1983 to 1985, Stroke 1991, 22(7), 848-853. 1991.
14. Vlak MH, Algra A, et al. - Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis, Lancet Neurol. 2011, 10(7), 626-636.
15. van Gijn J, Rinkel GJ. - Subarachnoid haemorrhage: diagnosis, causes and management. Brain 2001, 124(Pt 2), 249-278.
16. Anderson CS, Feigin V, et al. - Australasian Cooperative Research on Subarachnoid Hemorrhage Study (ACROSS) Group. Active and passive smoking and the risk of subarachnoid hemorrhage: an international population-based case-control study, Stroke 2004, 35(3), 633-637.
17. Feigin VL, Rinkel GJ, et al. - Risk factors for subarachnoid hemorrhage: an updated systematic review of epidemiological studies, Stroke 2005, 36(12), 2773-2780.
18. Feigin V, Parag V, et al. - Asia Pacific Cohort Studies Collaboration. Smoking and elevated blood pressure are the most important risk factors for subarachnoid hemorrhage in the Asia-Pacific region: an overview of 26 cohorts involving 306,620 participants, Stroke 2005, 36(7), 1360-1365.
19. Sandvei MS, Romundstad PR, et al. - Risk factors for aneurysmal subarachnoid hemorrhage in a prospective population study: the HUNT study in Norway, Stroke 2009, 40(6), 1958-1962.
20. Korja M, Kivisaari R, et al. - Size of Ruptured Intracranial Aneurysms Is Decreasing: Twenty Year Long Consecutive Series of Hospitalized Patients, Stroke 2018, 49(3),746-749.
21. Andreasen TH, Bartek J Jr, et al. - Modifiable risk factors for aneurysmal subarachnoid hemorrhage, Stroke 2013, 44(12), 3607-3612.
22. Vlak MH, Rinkel GJ, et al. - Lifetime risks for aneurysmal subarachnoid haemorrhage: multivariable risk stratification, J Neurol Neurosurg Psychiatry 2013, 84(6),619-623.
23. Ruigrok YM, Buskens E, et al. - Attributable risk of common and rare determinants of subarachnoid hemorrhage, Stroke 2001, 32(5), 1173-1175.
24. Anderson T. - Current and evolving management of subarachnoid hemorrhage, Crit Care Nurs Clin North Am.2009, 21(4), 529-539.
25. Carpenter CR, Hussain AM, et al. - Spontaneous Subarachnoid Hemorrhage: A Systematic Review and Meta-analysis Describing the Diagnostic Accuracy of History, Physical Examination, Imaging, and Lumbar Puncture With an Exploration of Test Thresholds, Acad Emerg Med. 2016, 23(9), 963-1003.
26. Deibert E, Barzilai B, et al. - Clinical significance of elevated troponin I levels in patients with nontraumatic subarachnoid hemorrhage, J Neurosurg. 2003, 98(4):741-746.
27. Tung P, Kopelnik A, et al. - Predictors of neuro cardiogenic injury after subarachnoid hemorrhage, Stroke 2004, 35(2), 548-551.
28. Naidech AM, Kreiter KT, et al. - Cardiac troponin elevation, cardiovascular morbidity, and outcome after subarachnoid hemorrhage, Circulation 2005, 112(18), 2851-2856.
29. Reichlin T, Hochholzer W, et al. - Early diagnosis of myocardial infarction with sensitive cardiac troponin assays, N Engl J Med. 2009, 361(9), 858-867.
30. Macrea LM, Tramèr MR, et al. - Spontaneous subarachnoid hemorrhage and serious cardiopulmonary dysfunction - a systematic review, Resuscitation 2005, 65(2), 139-148.

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Clinico-pathological features and molecular background of oligodendrogliomas. A single centre retrospective study

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Keywords
oligodendrogliomas, clinico-pathological features, molecular background

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ABSTRACT

Background: Diffuse gliomas are the most frequent primary central nervous system (CNS) neoplasms, originating from the parenchyma itself, oligodendrogliomas accounting for approximately 10% of cerebral gliomas. For the past 20 years, the study of genetic/molecular mechanisms of glioma genesis and progression has gradually come into focus. However, the biological and clinical significance of these mutations are still to be completely characterized. The purpose of this article is to describe our clinical experience with oligodendrogliomas and to review the current literature, in order to better describe the characteristics of the molecular/genetic oligodendroglioma subgroups.

Methods: We performed a single-institution retrospective study that included 66 patients with oligodendrogliomas operated in our department between January 2011 and December 2018.

Results: Our study included 26 female patients (39%) and 40 male patients (59%). The mean age at presentation was 39.9year-old (range 26-59year-old). The tumours were located predominantly in the right hemisphere (53%), the majority being situated in the frontal lobe (59%). 64% of the patients had signs of mass effect on the imaging studies, 13% presented with brain herniation syndromes, and 16 % of the surgically treated patients had a relapse with regrowth and malignant transformation of the tumour. The most common complaint that the patients had at admission was a headache. Seizures were the second most common symptom that determined the patients to seek medical attention.

Conclusion: The expanding knowledge regarding the genetic alterations of oligodendroglial tumours could lead to significant changes in treatment strategies. However, the utility of each particular marker in planning the treatment has yet to be

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established. Emerging data will, most likely, improve outcome prediction and adjuvant therapy strategies by identifying the patients most likely to benefit from a particular treatment.

Introduction

Diffuse gliomas are the most frequent primary central nervous system (CNS) neoplasms, originating from the parenchyma [1]. About 75% of gliomas in adults are astrocytic, two-thirds being glioblastomas, the most malignant form. Oligodendroglial tumors account for than 10% of the gliomas [2]. For the largest part of the last century, the diagnosis of oligodendrogliomas has been based on histopathological aspects alone. For the past 20 years, the study of genetic/molecular mechanisms of glioma genesis and progression has gradually come into focus. The 2021 World Health Organization (WHO) Classification of Tumors of the CNS includes molecular features for diagnosis and further classification of oligodendroglioma into IDH-mutant and 1p/19q-codeleted [3]. The biological and clinical significance of these mutations are still to be completely characterized. The purpose of this article is to describe our clinical experience with oligodendrogliomas and to review the current literature, in order to better describe the characteristics of the molecular/genetic oligodendroglioma subgroups.

Materials and methods

We performed a single institution retrospective study that included the patients of the 4th Clinical Department of Neurosurgery of the Bagdasar-Arseni Clinical Emergency Hospital.

We retrospectively reviewed the case files of 66 patients with oligodendrogliomas operated in our department between January 2011 and December 2018. We only included patients operated for oligodendrogliomas with a positive anathomopathological examination for a “classical” oligodendroglioma. Exclusion criteria were diagnosis of primary glioblastoma, oligoastrocitoma with important oligodendroglial compound or patients with a high suspicion for oligodendroglioma, that refused surgery or biopsy for diagnosis. Data were obtained by studying patient files.

Results

Our study included 26 female patients (39%) and 40 male patients (59%). The mean age at presentation was 39.9year-old (range 26-59year-old). The tumors were located predominantely in the right hemisphere (53%), the majority being situated in the frontal lobe (59%). 64% of the patients had signs of mass effect on the imaging studies, 13% presenting with brain herniation syndromes (Figure 1).

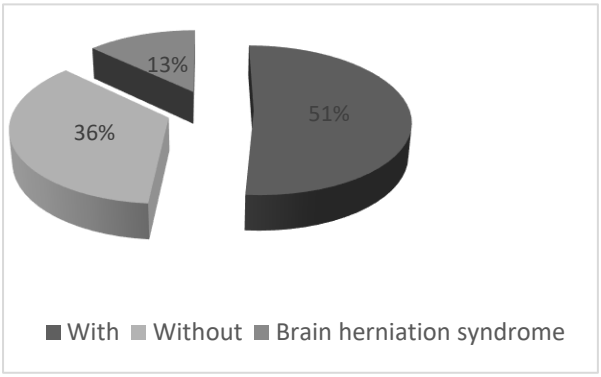


Figure 1. Distribution of patients based on the presence/absence of mass effect on imaging studies.

16 % of the surgical treated patients had a relapse with regrowth and malignant transformation of the tumor (Figure 2).

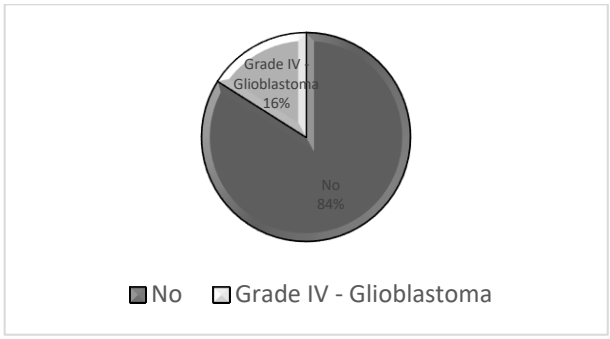
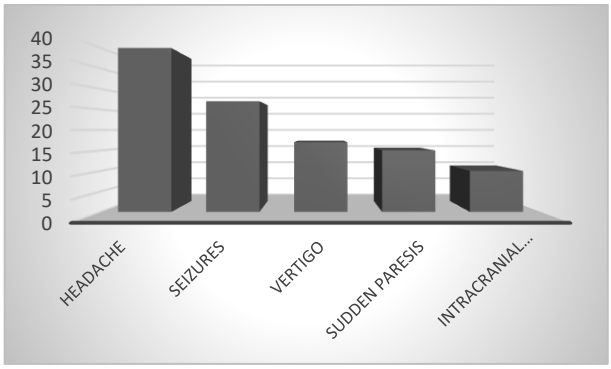


Figure 2. Distribution of the patients based on the presence/absence of relapse with malignant transformation.

Figure 3. Distribution of the patients based on the clinical symptoms at admission.



The most common complaint that the patients had at admission was headache. Seizures were the second most common symptom that determined the patients to seek medical attention (Figure 3).

Illustrative case

A 30-year-old male with no significant medical history was referred to our clinic for intense headache, progressively worsened during the month prior to admission. Clinical examination showed no neurological deficit. Gadolinium-enhanced MRI scan revealed a right fronto-temporal tumor, measuring 9.5 cm in diameter, compressing the adjacent structures and producing mass effect on the right lateral ventricle (Figure 4).

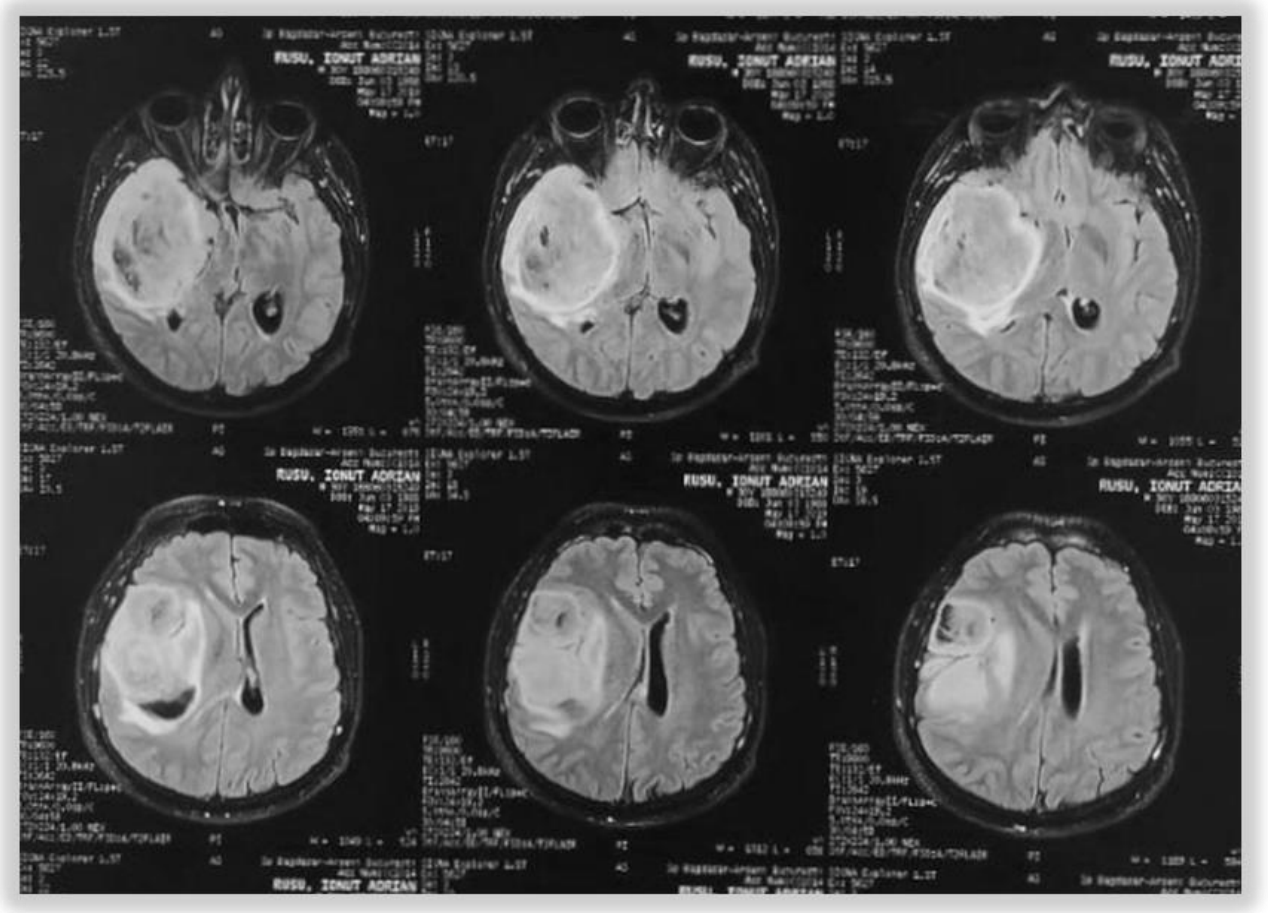


Figure 4. Gadolinium enhanced MRI scan, axial section, showing a right fronto-temporal tumour, measuring 9.5 cm in diameter, compressing the adjacent structures with inhomogenous enhancement.

Figure 5. Intraoperative aspect showing the yellow-grey tumour.

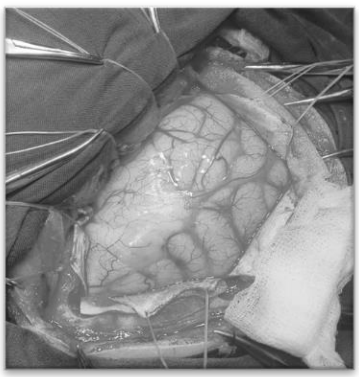
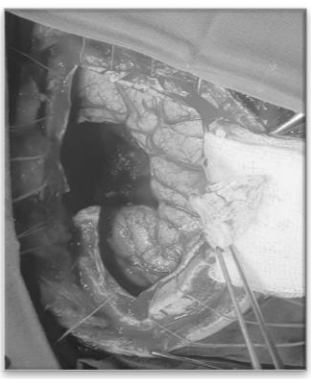


Figure 6. Intraoperative aspect showing the resection cavity.



We performed a gross total resection through a pterional approach (Figure 5, Figure 6). The patient was discharged 7 days later, with no postoperative neurological deficits. Control CT scan showed a gross total resection of the tumor (Figure 7).

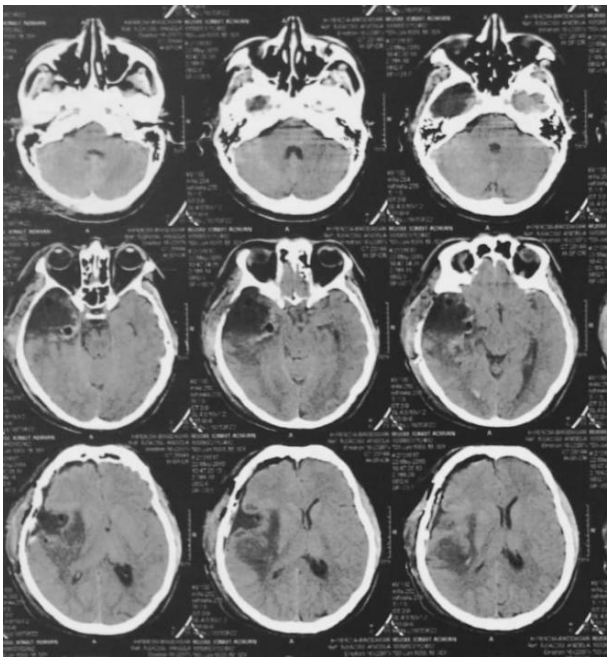


Figure 7. Postoperative CT scan showing the resection cavity.

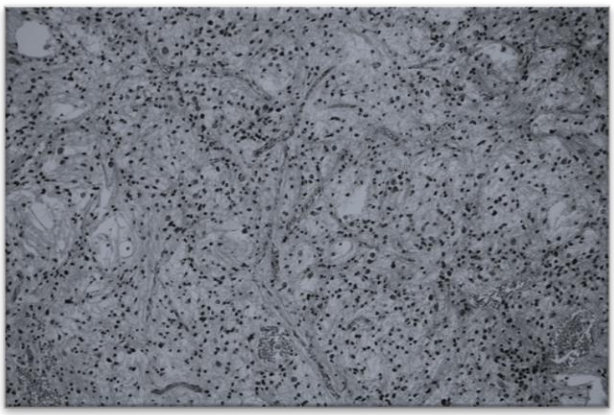


Figure 8. Histopathological specimen showing arciform vascularization.

Histopathological examination showed arciform vascularization (Figure 8), "boiled egg cells" (Figure 9) and high fibrilarity (Figure 10).

MLPA analysis of the tumor sample identified a codeletion of 1p19q and a c.395G>A (p.R132H) mutation in the exon 4 of IDH1 gene. The analysis was negative for mutations of exons 11 and 15 of BRAF gene, EGFRvIII, MGMT promoter methylation and TERT promoter mutation.

The patient had a favorable evolution, with no neurological deficits and was discharged in the seventh postoperative day.

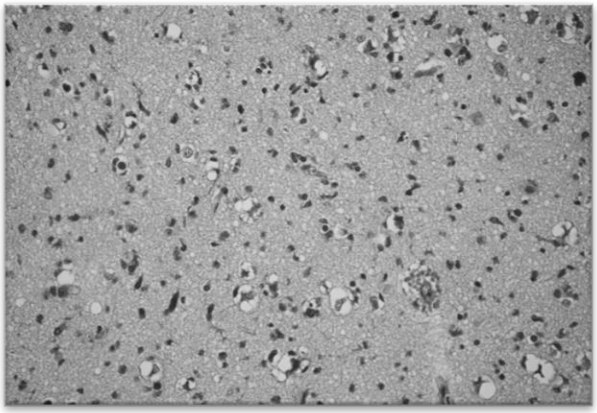


Figure 9. Histopathological specimen showing "boiled egg cells" aspect.

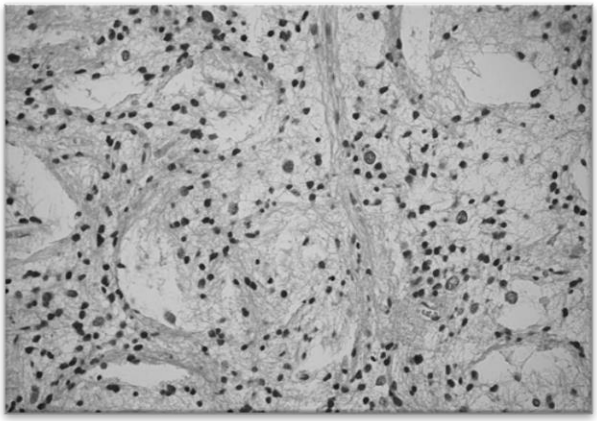


Figure 10. Histopathological specimen showing high fibrillarity.

Discussion

Under the generic term "oligodendroglioma" is a heterogenous group of tumors, with a variable response to adjuvant therapy. This variance highlights the need for markers that can guide the clinical decision-making. Codeletion of 1p19q occurs in 50 to 76% of oligodendrogliomas [4] [5]. EORTC 26951 and RTOG 9402 studies proved that combining radiation therapy with procarbazine, vincristine and lomustine chemotherapy protocol drastically increased overall survival in 1p19q codeleted anaplastic oligodendroglioma patients compared to radiotherapy alone [6] [7]. The EORTC 26951 trial investigated the adding of six cycles of standard procarbazine, vincristine and lomustine to

radiation therapy of 59.4 Gy in 33 fractions in anaplastic oligodendroglioma patients and reported a significant difference in overall survival [7] [8]. Patients with 1p19q codeleted oligodendrogliomas benefitted more from the addition of chemotherapy to radiotherapy, the risk reduction in patients with non-codeleted tumors being significantly lower [7]. Regarding both trials, it is also notable the fact that patients with 1p19q codeleted oligodendrogliomas who were treated with adjuvant radiotherapy alone initially, had a lower survival rate at progression, despite being administered a heightened chemotherapy regimen [4] [7]. The CODEL trial has been designed to compare administration of adjuvant therapy consisting of either radiotherapy alone, themozolomide alone or radiotherapy combined with themozolomide. The analysis from the initial study design showed that themozolomide-alone patients experienced a significantly shorter progression free survival, compared to either one of the radiotherapy arms [9]. The study has been subsequently redesigned to compare radiotherapy combined with procarbazine, lomustine and vincristine to radiotherapy and themozolomide regimens and is still ongoing.

Mutations of IDH1 and IDH2 seem to occur in about 70% of oligodendroglioma tumors, mainly affecting amino acid 132 of IDH1 or IDH2 [10] [11]. IDH1 is known to function as a tumor suppressor, its mutational inactivation leading to tumorigenesis, partially through the induction of the HIF-1 pathway [12] [13]. IDH mutations have been reported in several studies to produce a favorable prognostic impact [7] [10] [14]. However, despite the more favorable prognosis of patients with oligodendrogliomas harboring IDH mutations, it hasn't been proven yet that the treatment strategy should be changed regarding the IDH status.

Conclusion

The expanding knowledge regarding the genetic alterations of oligodendroglial tumors could lead to significant changes in treatment strategies. However, the utility of each particular marker in planning the treatment has yet to be established. Emerging data will, most likely, improve outcome prediction and adjuvant therapy strategies through identifying the patients most likely to benefit from a particular treatment.

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Multimodal treatment of glomus jugular tumours. Case series and literature review

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ABSTRACT

Glomus jugulare tumours are extremely rare, slow-growing, hypervascular tumours that arise within the jugular foramen of the temporal bone and frequently involve the lower cranial nerves. We performed a retrospective study for patients treated between January 2005 and December 2019, reviewing clinical and radiological data for 91 cases of glomus jugulare tumours. Data were available for 91 patients presenting with 96 tumours. Surgery was 1st intention of treatment for 13 cases, the endovascular approach was 1st intention for 6 cases and GKRS was primarily performed in 72 cases. Combined treatment options were used in 19 cases. The median age at the time of treatment was of 57 years. The tumour volume varied between 0.5 and 73.4 cm3 with a median value of 8.3 cm3. For the cases treated with GKRS, the peripheral dose ranged between 8 and 35 Gy on the 35% to 65% isodose, with a median of 14 Gy on the 45% isodose. The average follow-up was 38 months with a maximum of 94 and consisted of contrast-enhanced MRI every six months in the first year after the procedure and every 1 to 2 years afterwards. The overall tumour control rate was 95.6% using multimodal treatment options for glomus jugulare tumours. Multimodal treatment for glomus jugulare tumours offers the patient the chance for the best possible outcome and long-term survivability. An individual treatment approach for this kind of very rare head and neck tumour (0,6% of all head and neck tumours) is recommended to choose the best risk-versus-benefit treatment option.

Keywords
tumour,
glomus,
jugular

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BACKGROUND

Glomus jugulare tumor is a benign neuroendocrine tumor that arises from the jugular foramen. This tumor characterized by a slow-growing pattern. Paragangliomas, also known as chemodectomas represent benign tumors with the origin from neural crest derivates also known as the parangalia [1],[2],[3]. These tumors are highly vascularised. They can receive blood supply from both from the external carotid artery and internal carotid artery. The localization of these tumours can widely

vary, from carotid bifurcation to the auricular branch of the vagus nerve. The most frequent localization is the carotid body, accounting for almost half of the tumors [5], [6] whereas glomus jugulare tumors represent 24% of them [6]. Even though they are benign tumors, the symptomatology can be the cause of the mass effect [2].

Usually, these tumors are diagnosed in the fourth to sixth decade of life, with a moderate female predilection. Most of the glomus jugulare tumors are isolated lesions but around 20% of them present hereditary components [4]. The inherited tumors are usually bilateral and the onset of the symptoms is reported to be earlier than the onset symptomatology of the sporadic tumors. The reported malignancy of these tumors is less than 5% [2].

Around 25% of the paragangliomas remain silent and are incidentally discovered. The symptoms caused by these tumors depend on their location. Lower cranial nerves impairment is reported in more than 10% of patients [8]. The most common neurological deficits reported are tongue deviation, hoarseness, facial palsy, dysphagia, and shoulder weakness [2],[7],[8]. Additionally, patterns of cranial nerve palsies were described and these include [12]:

- Vernet syndrome that represents motor paralysis of cranial nerves IX, X and XI; [9]
- Collet- Sicard syndrome described as the palsy of cranial nerves IX,X,XI and XII; [10]
- Horner syndrome – oculosympathetic palsy. [11]

Due to its slow-growing pattern and the complex anatomy of the skull base and neck, observation of the patient is considered a good treatment alternative. In more than 60% of the cases, tumor volume remains stable or decrease in size [14]. However, if the tumor tends to be symptomatic, surgical excision or stereotactic radiosurgery will be take into account.

Case series

We performed a retrospective study for patients treated between January 2005 and December 2019, reviewing clinical and radiological data for 91 cases of glomus jugulare tumors. Data were available for 91 patients presenting with 96 tumors.

Surgery was the treatment of choice for 13 cases, endovascular embolization was performed as first intention treatment for 6 cases and GKRS was primarily performed in 72 cases.

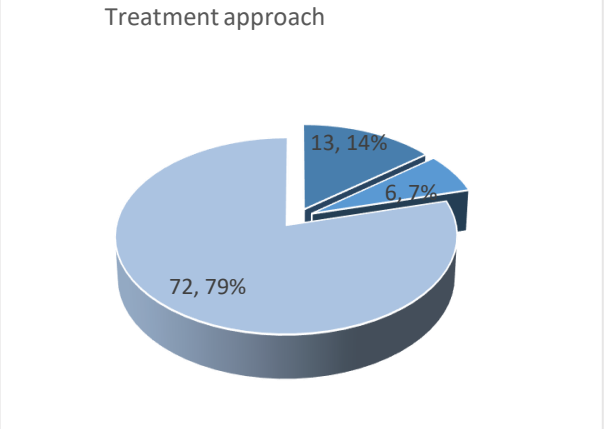

Figure 1. Distribution of the treatment option

Combined treatment options were used in 19 cases (1 surgery with GKRS, 18 endovascular with GKRS). 44 glomus jugulare tumors were identified on the right side, and 47 on the left side. In the study group, we had 23 male patients and 63 female patients. 11 patients were in the 15-39 age group while 80 patients were older than 40 yrs. The median age at the time of treatment was of 57 years. The tumor volume varied between 0.5 and 73.4 cm3 with a median value of 8.3 cm.

For the cases treated with GKRS, the peripheral dose ranged between 8 and 20 Gy on the 35% to 65% isodose, with a median of 14 Gy on the 45% isodose. The average follow-up was 38 months with a maximum of 94 and consisted of contrast-enhanced MRI every six months in the first year after the procedure and every 1 to 2 years afterward. Overall tumor control rate was 95.6% using multimodal treatment options for glomus jugulare tumors.

Table 1. Most common comorbidities

COMORBIDITY
Lower cranial nerves deficits
Dizziness
Tinnitus
Hearing impairment
Hemorrhages
Hydrocephalus
Hemiparesis

Comorbidities were noted in 37 patients (40.6%) and consisted of lower cranial nerves deficits (26.4%), dizziness, tinnitus, partial or complete hearing loss in 21.9% of cases, 2 hemorrhages, 2 secondary hydrocephalus, and 1 hemiparesis. 23 patients (24.3%) presented recurrences: 13 after surgery, 6 after embolization, and 4 after GKRS. However, the mortality rate was 0.

CASE 1

The first case is represented by a female patient of 53 years old, whose symptoms are vertigo, hearing loss, and pulsating tinnitus. Soon it is discovered the typical aspect of "salt and pepper" for a glomus tumor with temporal localization, millimetric extracranial extension into jugular vein lumen and damage to the structures of the inner ear. 9 years after GKRS, a cerebral MRI was performed, which showed that the irradiated tumor volume has been reduced in circumferential dimensions, with a homogeneous intake of contrast substance ("densified" appearance due to sclerosis and obliteration of intratumoral blood vessels) without adverse reactions due to irradiation. No new neurological deficits were recorded after GKRS.

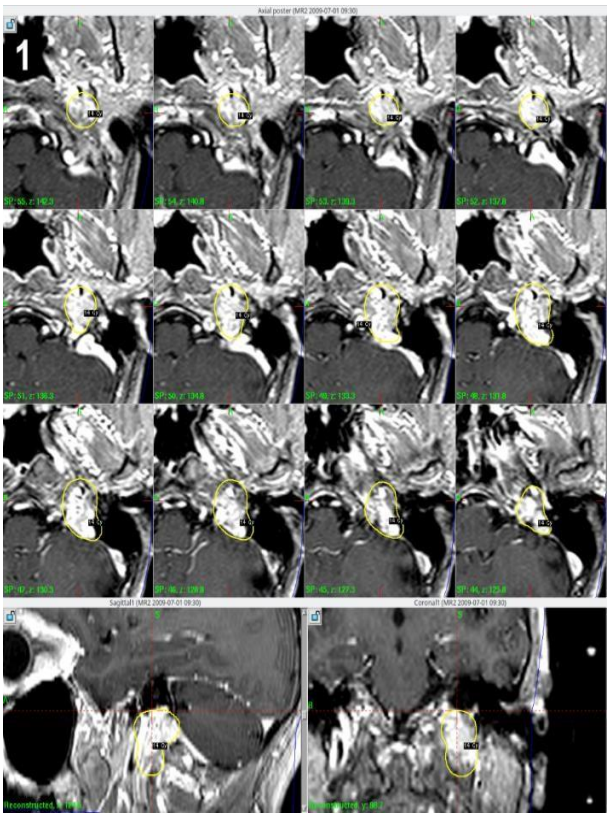

Figure 2. Preoperative aspect of the tumour

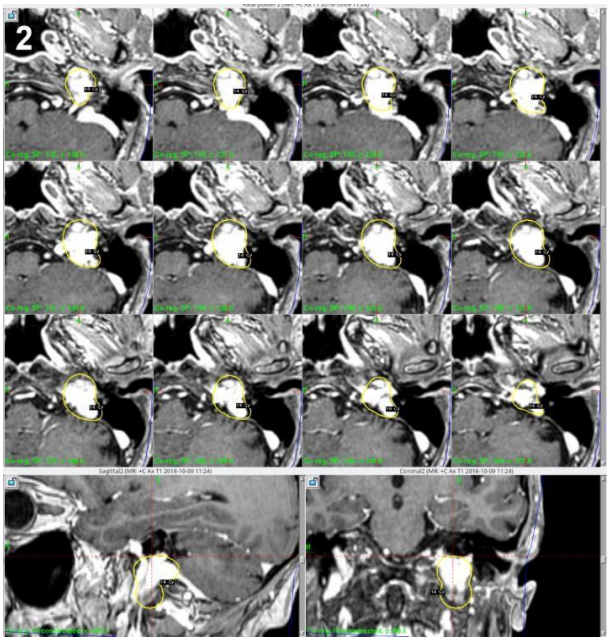

Figure 3. Postoperative aspect after Gamma Knife Radiosurgery

CASE 2

The second case is represented by a 62 years old female patient, whose symptoms onset with injury to multiple cranial nerves (VII, VIII, IX, XI, XII). The diagnosis was represented by a large glomic tumor with an important intracranial component with a mass effect on the brainstem.

A cerebral MRI was performed 4 years post GKRS, showing a marked reduction in the size of the irradiated tumor, especially in the intracranial component, with a significant decrease in the mass effect, without perilesional reactive edema.

No new neurological deficits were recorded. 18 months after irradiation, a complete remission of facial paresis has been noticed and other cranial nerves neurological status remained stationary.

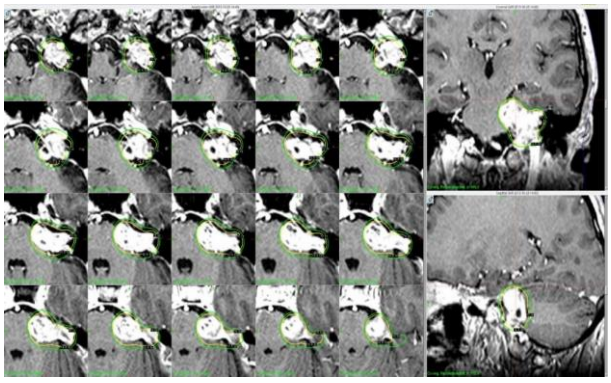

Figure 4. Preoperative aspect of the tumour

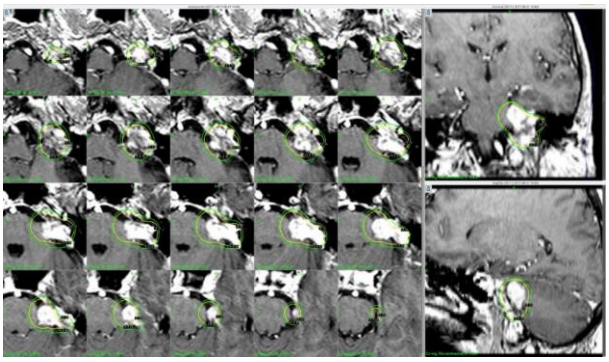

Figure 5. Postoperative aspect after Gamma Knife Radiosurgery

Case 3

For the third case, we have a 35 years old male patient, who presented with glomic tumor located in the temporal bone, onset with hearing disorders (hearing loss and pulsating tinnitus).

6 years after GKRS, a periodic follow-up MRI has been performed. the inferior recurrence in the lumen of the jugular vein was identified outside the irradiation field with a volume of 4.6 cm3, asymptomatic. The decision is made in order to irradiate the recurrence with 14 Gy on 47% isodose.

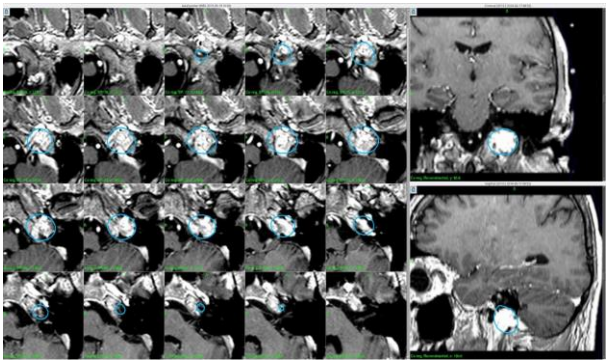

Figure 6. Preoperative aspect before Gamma Knife Radiosurgery

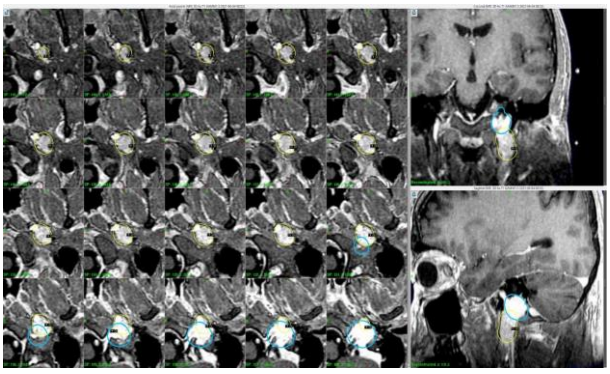

Figure 7. The recurrence aspect, 6 years after GKRS

Discussions

The best treatment option for glomus jugulare tumors is yet to be debated. Due to their localization, surgical treatment does not represent the gold standard because of the complex anatomy of the region, high rates of morbidity, subtotal resection, and the alternative behavior of the tumors that could be very aggressive in some cases. In 2003, Roberto Pareschi et al [15] described their experience in the surgical treatment of glomus jugulare tumors. 42 patients with glomus jugulare tumors were identified, 3 of them previously undergone surgery for this pathology, and 3 patients presented bilateral temporal lesions. The otoscopic evaluation revealed in 80% of the patients the typical red middle ear mass. 70% of the cases had no preoperative cranial nerve deficit. 37 seven patients were elected for surgical intervention. In 33 cases, infratemporal fossa approaches were used and in 4 cases, conservative jugulopetrosectomy was performed, in order to preserve the facial nerve. In 20% of the cases, cranial nerves IX and X were injured. No recurrence after total resection was reported. An extensive dissection of the posterolateral skull base is required for surgery of glomus jugulare tumors [15]. Even though cranial nerve preservation is an extremely important goal in the surgical approach, in 22% of the cases facial nerve is sacrificed [15]. The authors concluded that the focus should drift away from total resection to increasing the quality of life of the patient, a philosophy that our clinic shares. Only 14% percent of our cases were surgically treated, in order to avoid the decrease in the quality of patient`s life.

Endovascular treatment is an alternative treatment approach for patients with glomus jugulare tumors. In 2017, Kocur et al [17] presented their experience and the outcome of embolization in 3 cases of glomus jugulare tumors. They described the technical difficulty of achieving complete obliteration of the glomus jugulare tumors and concluded that increased risk of revascularization is not beneficial compared to the diminished clinical symptoms. In our clinic, only 6 endovascular treatments were performed.

A promising approach for this pathology is represented by radiosurgery. Due to the high degree of accuracy, rapid radiation dose falloff at the periphery of the target tumor, and their high precision, radiosurgery became a popular treatment

choice. In their meta-analysis, Guss et al [13] included 19 studies, compounding 335 glomus jugulare patients. They reported a reduced or unchanged tumoral volume after radiosurgery, sustained by imagistic findings. Clinical control was reported as improved or unchanged after radiosurgery in 95% of the cases. The authors emphasized the effectiveness of this treatment option. In our clinic, 72 patients benefited from radiosurgery.

Conclusions

Multimodal treatment for glomus jugulare tumors offers the patient the chance for the best possible outcome and long-term survivability. Individual treatment approach for this kind of very rare head and neck tumor (0,6% of all head and neck tumors) is recommended to choose the best risk-versus-benefit treatment option. GKRS in these kinds of tumors seems to be the option of choice, considering that in our experience, has the lowest comorbidity, recurrence rate and mortality.

References

1. Fussey JM, Kemeny AA, Sankar S, Rejali D. Successful management of a catecholamine- secreting glomus jugulare tumor with radiosurgery alone. J Neurol Surg B Skull Base. 2013 Dec;74(6):399-402.
2. Ramina R, Maniglia JJ, Fernandes YB, Paschoal JR, Pfeilsticker LN, Neto MC, Borges G. Jugular foramen tumors: diagnosis and treatment. Neurosurg Focus. 2004 Aug 15;17(2):E5.
3. Petropoulos AE, Luetje CM, Camarata PJ, Whittaker CK, Lee G, Baysal BE. Genetic analysis in the diagnosis of familial paragangliomas. Laryngoscope. 2000 Jul;110(7):1225-9.
4. Semaan MT, Megerian CA. Current assessment and management of glomus tumors. Curr Opin Otolaryngol Head Neck Surg. 2008 Oct;16(5):420-6.
5. Tokgöz SA, Saylam G, Bayır Ö, Keseroğlu K, Toptaş G, Çadallı Tatar E, Akın İ, Korkmaz MH. Glomus tumors of the head and neck: thirteen years' institutional experience and management. Acta Otolaryngol. 2019 Oct;139(10):930-933.
6. Singh S, Madan R, Singh MK, Thakar A, Sharma SC. Head-and-neck paragangliomas: An overview of 54 cases operated at a tertiary care center. South Asian J Cancer. 2019 Oct- Dec;8(4):237-240.
7. Wanna GB, Sweeney AD, Haynes DS, Carlson ML. Contemporary management of jugular paragangliomas. Otolaryngol Clin North Am. 2015 Apr;48(2):331-41.
8. Jackson CG, Harris PF, Glasscock ME, Fritsch M, Dimitrov E, Johnson GD, Poe DS. Diagnosis and management of paragangliomas of the skull base. Am J Surg. 1990 Apr;159(4):389-93.
9. Monteiro, F., Oliveira, P., Peneda, J. and Condé, A., 2019. Vernet syndrome: intracranial extension of a slow-growing mass. BMJ Case Reports CP, 12(5), p.e228039.
10. Neo S, Lee KE. Collet-Sicard syndrome: a rare but important presentation of internal jugular vein thrombosis. Practical Neurology. 2017 Feb 1;17(1):63-5.
11. Spector GJ, Druck NS, Gado M. Neurologic manifestations of glomus tumors in the head and neck. Archives of Neurology. 1976 Apr 1;33(4):270-4.
12. Spector GJ, Gado M, Ciralsky R, Ogura JH, Maisel RH. Neurologic implications of glomus tumors in the head and neck. The Laryngoscope. 1975 Aug;85(8):1387-95.
13. Guss ZD, Batra S, Limb CJ, Li G, Sughrue ME, Redmond K, Rigamonti D, Parsa AT, Chang S, Kleinberg L, Lim M. Radiosurgery of glomus jugulare tumors: a meta-analysis. International Journal of Radiation Oncology* Biology* Physics. 2011 Nov 15;81(4):e497-502.
14. Prasad SC, Mimoune HA, D'Orazio F, Medina M, Bacciu A, Mariani-Costantini R, Piazza P, Sanna M. The role of wait-and-scan and the efficacy of radiotherapy in the treatment of temporal bone paragangliomas. Otol Neurotol. 2014 Jun;35(5):922-31.
15. Pareschi R, Righini S, Destito D, Raucci AF, Colombo S. Surgery of glomus jugulare tumors. Skull Base. 2003 Aug;13(03):149-58.
16. Kocur D, Ślusarczyk W, Przybyłko N, Hofman M, Jamróz T, Suszyński K, Baron J, Kwiek S. Endovascular approach to glomus jugulare tumors. Polish journal of radiology. 2017;82:322.

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Cervicomedullary junction intramedullary hemangioblastoma. A 10 years report of cases and review of literature

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Keywords
cervicomedullary, intramedullary, hemangioblastoma

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ABSTRACT

Hemangioblastoma is a rare, benign, highly vascularized tumour, that usually presents a muriform nodule. The most frequent localization is the posterior cranial fossa. The frequency of this spinal lesion is very low, representing less than 5% of spinal cord tumours. The presentation of hemangioblastoma can widely vary, from a solid tumour to a lesion with a cystic component. We present the case of a 43 years old patient, admitted to our clinic for left hemiparesis, swallowing disorders, and dysphonia. An MRI is performed and it showed a cervicomedullary junction tumour with a solid nodule and an anterior cystic cavity pushing towards the 4th ventricle. The patient underwent surgery for the total removal of the tumour. Post-operative CT confirmed the total ablation of the tumour. The patient is discharged with improved symptomatology. In the last 10 years, in our clinic were admitted 23 cases of hemangioblastoma, 14 males (61% of the patients) and 9 females (39%) with an age at presentation varied from 14 to 78 years (mean 48,2 years). Only 3 patients (13%) out of the 23 had associated von Hippel–Lindau syndrome, with hemangioblastomas also present in other locations. The most common location was the posterior fossa, in 13 cases (56,6%). Headache (69,5%), ataxia (56%) and balance disorders (52%) were the most common symptoms accused by patients. The follow-up varied from 6 to 84 months (mean 20 months). Only one patient died during hospitalization and one tumour recurrence was noted. Most patients improved or remained clinically stable postoperatively.

BACKGROUND

Hemangioblastoma is a rare, histologically benign, highly vascularized tumor, that usually presents an enhancing muriform nodule, having the most frequent localization in the posterior cranial fossa [1].

Moreover, hemangioblastoma is the most common primary intra-axial posterior fossa tumor in adult population. It is usually identified in the cerebellar hemisphere (including vermis) and brainstem [2], [3], [4]. On the other hand, supratentorial localization is rare, in the literature being described less than 100 cases. Furthermore, only 3-13% are reported in the spinal cord [5].

The presentation of hemangioblastoma can widely vary, from a solid tumor to a lesion with a cystic component. Usually, sporadic hemangioblastoma is a solid tumor with a pseudocapsule. Despite the lack of a proper capsule, the lesion is well circumscribed. The solid nodule is red and very well vascularised, localized close to the pial layer. The cystic cavity usually occurs due to the thinness of the vessel wall that allows water to leak [5], [6]. The walls of the cyst are tapped with non-neoplastic compressed cerebellum cells and the cyst fluid is usually yellow with a high concentration of proteins [6], [7].

Both CT (computed tomography) scan and MRI (magnetic resonance imaging) can be useful for emphasizing the lesion. On CT scan, the mural nodule is isodense with fluid density surrounding the cyst [8], [20]. On contrast scan, cyst walls usually not enhance and the presence of calcification is rare. The MRI scan is superior to the CT scan and it shows vascular signal voids, especially in the periphery of the lesion, as well as, the hemosiderin deposits that can occur due to recurrent hemorrhages [6], [8], [9].

The most common symptoms determined by these tumors are: headaches, hydrocephalus, cerebellar dysfunction and altered mental state.

Surgical approach is the gold standard for sporadic cases of hemangioblastoma, but not for multiple lesions associated with von Hippel Lindau syndrome. The outcome of the surgery is good, given that hemangioblastomas are benign lesions [10]. Despite that tumoral cells may be spreaded through CSF, it still remains a benign tumor. Solid lesions are more difficult to excise compared to cystic ones [11].

Hemangioblastomas are usually sporadic lesions but around 20% of them are associated with Von Hippel Lindau syndrome [5]. Moreover, 6% of cerebellar hemangioblastomas are associated with retinal hemangioblastoma. The retinal hemangioblastoma is usually placed peripherally. It tends to rupture and cause hemorrhage that can lead to retinal detachment.

Von Hipple Lindau syndrome is a multysistem neoplastic condition with autosomal inheritance, described by the occurrence of multiple hemangioblastomas in different localisation such as brain, spinal cord and retina [12]. In these cases, individual resection of the central nervous lesions is not the optimal treatment until it became symptomatic, due to the tendency of reccurence and the inconsistent growth pattern of tumor [13], [14].

Case presentation

We present the case of a 43 years old patient, admitted to our clinic for left hemiparesis, swallowing disorders, and dysphonia. The first symptoms occurred 8 months ago with left intercostal neuralgia.

An MRI is performed and it shows a cervicomedullary junction tumor with a solid nodule and an anterior cystic cavity pushing towards the 4th ventricle, which lead to our presumptive diagnosis of hemangioblastoma. In order to rule out von Hipple Lindau syndrome, a whole-body CT scan was performed. No other lesions were identified. The decision was made to perform surgery in order to remove the tumor.

The patient was placed in the prone position, and a midline incision was made, with a standard occipital craniectomy and resection of the C-1 posterior arch. After the dura mater was opened, the tumor was identified on the midline, at cervicomedullary junction. Under the operating microscope, the hemangioblastoma was dissected, the integrity of the lesion was preserved. The tumor was gently retracted laterally, and the feeding vessels were identified coagulated with bipolar forceps and divided sharply. The main feeder is exposed, clipped, coagulated, and cut. The tumor was sent for pathologic examination and the diagnosis of hemangioblastoma was confirmed. Closure of the surgical wound was performed respecting the anatomical planes and leaving an epidural external drain in place. Finally, the skin suture was draped in a sterile fashion. After careful hemostasis, the surgical wound is closed layer by layer. No perioperative incidents were reported. The post-operative MRI confirmed the total resection of the tumor.

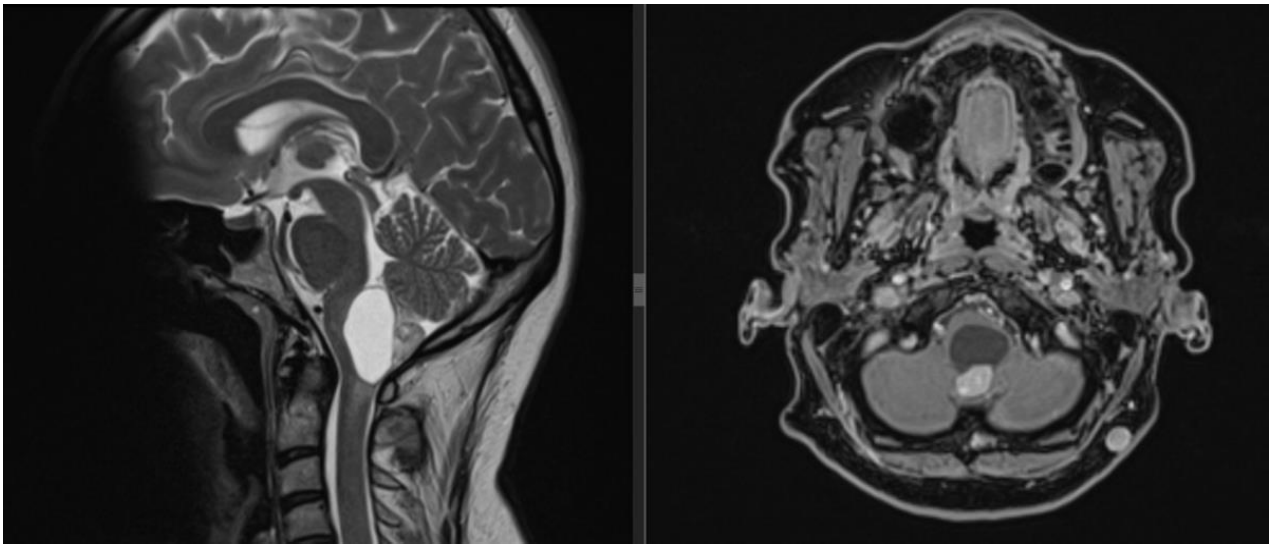

Figure 1. Cervicomedullary junction tumor with a solid nodule and an anterior cystic cavity pushing towards the 4th ventricle.

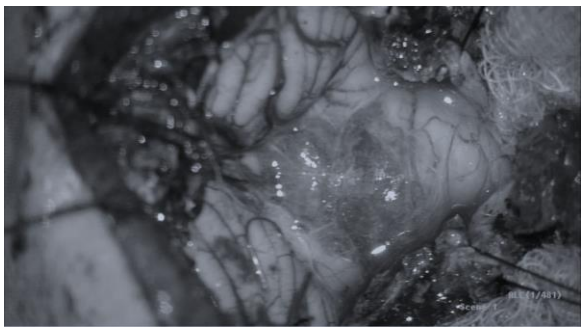

Figure 2. The cervicomedullary junction lesion, after dura mater was opened.

Figure 3. Gently dissection of the lesion. The feeders are coagulated and sharply cut.

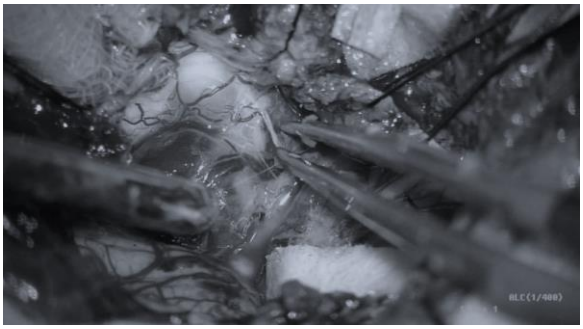

Figure 4. After circumferential dissection, the main feeder is exposed.

Figure 5. The main feeder is clipped and cut. The tumor is removed "en bloque".

The external drain was removed 24 hours later. Symptomatology was improved in the first week postoperative by the patient. Mobilization of the patient was allowed 24 hours after the surgery. The skin sutures were suppressed at seven days postop.

This is just one out of 23 cases we had in our clinic in the last 10 years. 14 men (representing more than 60% of the study group) and 9 women. Their median age was 48, ranging from 14 to 78 years. The average time of hospitalization was 15 days, between 7 to 20 days.

Headache and ataxia were the most common symptoms accused by patients, accused by more than 70% of the patients. Other symptoms were dysphonia, dysphagia, seizures, cecity and hearing loss.

Table 1. Table of the main symptoms accused by patients

Symptom	Cases	Percentage
Headache	18	78,2
Ataxia	17	73,9
Dysphonia	2	8,69
Dysphagia	2	8,69
Seizures	2	8,69
Loss of visual acuity	1	4,34
Hearing loss	1	4,34

MRI was performed in all cases. It is worth mentioning that in 17 cases hemangioblastoma presented a cystic component. Also, in 3 cases were identified multiple lesions. There were 16 cases of intracranial hemangioblastoma, 2 with supratentorial location (frontal and parietal lobe), and in 14 cases, the tumor was located in the posterior fossa, in the cerebellum. Just 4 craniospinal junction cases were identified. At the spine level, there were 3 tumors, 2 located in the thoracic spine and 1 in the cervical spine.

All of the patients underwent surgery. In 22 out of 23, complete ablation of the tumor was performed. In just one case, total excision was not possible, and a subtotal ablation was performed. The postoperative evolution was good, without complications in 20 cases. 3 patients developed hydrocephalus and in one case a recurrence occurred, a few months after the surgical intervention. Postoperative follow-up was between 6 months to 7 years, with a mean follow-up of 20 months. Neurological improvement was noted in 18 cases, whereas in 2 cases, the neurological state remained stationary and in 3 cases, the neurological status had worsened. One patient died.

As we mentioned before, hemangioblastoma can be associated with von Hipple Lindau syndrome, a rare genetic disorder with multisystem involvement. It is characterized by visceral cysts and benign tumors with the potential for malignant transformation. 3 patients had associated this syndrome with pancreatic and kidney cysts.

Discussions

One of the greatest complications of hemangioblastomas is the risk of hemorrhage. However, the risk of hemorrhage is lower for the lesions of the spinal cord, where catastrophic neurological impairment is the main risk [6], [15], [16]. In 2007, Dr. Cornelius et al [17] compared the outcome of perioperative embolization of hemangioblastomas for spinal and cerebellar lesions. The result of embolization was favorable in patients with spinal cord hemangioblastomas, but, for the hemangioblastomas located at the cerebellar level, there were reported acute tumoral bleeding that led to death of the patients. The outcomes following embolization are very different for these two locations possibly because of the different capillary sizes. Due to high mortality, the procedure is no longer used.

In some cases, due to the clinical state of the patient or the localization of the tumor, surgical intervention cannot be achieved. In 2020, Mak et al[18] published the case of an immunocompetent patient that presented with a one-year history of progressive nausea and vomiting. After an MRI scan, a homogeneous enhancing intra-axial mass located at cervicomedullary junction was revealed. The surgical removal attempt failed due to multiple bradycardia episodes. However, a biopsy was performed and it confirmed that the lesion was a hemangioblastoma. Conservative treatment with bevacizumab, a humanized monoclonal antibody that targets vascular endothelial growth factor (VEGF) was initiated and the neurological status of the patient had been improved and the size of the tumor remained stable. Moreover, the reduction of the surrounding edema was noticed. Hemangiobalstomas are highly vascularized tumors with a rich capillary network. The endothelial cells express the VEGF receptor. Based on the histopathological characteristics, new treatment approaches are proposed for patients that are not suitable for surgical intervention.

In the last couple of decades, stereotactic radiosurgical treatment represented an alternative for the surgically inaccessible locations or for multiple localisations that typically occur in von Hippel-Lindau disease. Moss et al [13] published their almost 20 years experience of radiosurgical treatment for hemangioblastomas. Their study comprehends 92 hemangioblastomas from 31

patients, 26 of them being diagnosed with von Hipple Lindau syndrome. The mean age of the patients was 41 years. The radiation dose used to the periphery of the tumor average 23,4 Gy with a mean tumor volume of 1,8 cm3. The tumoral response was measured with contrast-enhanced computed tomography scans. In 62% of the cases, the tumor volume remained stable, in 22% the tumor shrank, and 16% of the cases, hemangioblastoma contiuned to grow. These results emphasized that stereotactic radiosurgical treatment is a safe and effective alternative to open surgery.

Even though there are multiple approaches for the treatment of hemangioblastoma, surgical treatment remains a safe option for patients with a good outcome. In 2020, Xiangdong Yin et al [19] published a meta-analysis composed of 13 studies that included 473 cases. In this paper, they analyzed the surgical outcomes, including gross total resection, mortality, neurological morbidity, and functional outcome. Gross total resection was performed in 98% of the cases. In our study, total resection was achieved in 95,6% of the cases (22 out of 23). Neurological improvement was reported in 85% of the cases in their study, compared to our clinic, where 86% of the patients reported an improved neurological state. Mortality was also similar between the statistics of meta- analysis and our clinic. In the mentioned study, mortality was 4% (23 out 473) compared to the 4,4% (1 out 23) mortality rate in our clinic. Xiangdong Yin et al postulated that surgical treatment for hemangioblastomas is still feasible and effective, a statement supported by good statistical outcomes from both their study and from our clinic experience.

Conclusions

Hemangioblastoma is a benign, highly vascularized tumor that usually occurs in the posterior fossa but its localization may widely vary. In the most cases, total resection is possible with a significant improvement of the neurological state of the patient. The rate of recurrence is low, even though tumoral cells can be spread by CSF. Nowadays there are multiple treatment options and every case should be carefully investigated in order to choose the best approach for improving the quality of the patient`s life.

References

1. Wilkins RH, Rengachary SS. Neurosurgery. New York 1985.
2. Conway JE, Chou D, Clatterbuck RE, Brem H, Long DM, Rigamonti D. Hemangioblastomas of the central nervous system in von Hippel-Lindau syndrome and sporadic disease. Neurosurgery. 2001 Jan 1;48(1):55-63.
3. Lindqvist M, Steiner L, Blomgren H, Arndt J, Berggren BM. Stereotactic radiation therapy of intracranial arteriovenous malformations. Acta radiologica. Supplementum. 1986 Jan 1;369:610-3.
4. Neumann HP, Lips CJ, Hsia YE, Zbar B. Von Hippel-Lindau Syndrome. Brain pathology. 1995 Apr;5(2):181-93.
5. Lee SR, Sanches J, Mark AS, Dillon WP, Norman D, Newton TH. Posterior fossa hemangioblastomas: MR imaging. Radiology. 1989 May;171(2):463-8.
6. Gläsker S, Van Velthoven V. Risk of hemorrhage in hemangioblastomas of the central nervous system. Neurosurgery. 2005 Jul 1;57(1):71-6.
7. Jeffreys R: Clinical and surgical aspects of posterior fossa haemangioblastomata. J Neurol Neurosurg Psychiatry 38:105–111, 1975.
8. Bonneville F, Sarrazin JL, Marsot-Dupuch K, Iffenecker C, Cordoliani YS, Doyon D, Bonneville JF. Unusual lesions of the cerebellopontine angle: a segmental approach. Radiographics. 2001 Mar;21(2):419-38.
9. Silver ML, Hennigar G. Cerebellar hemangioma (hemangioblastoma): a clinicopathological review of 40 cases. Journal of neurosurgery. 1952 Sep 1;9(5):484-94.
10. Wang C, Zhang J, Liu A, Sun B. Surgical management of medullary hemangioblastoma: report of 47 cases. Surgical neurology. 2001 Oct 1;56(4):218-26.
11. Resche F, Moisan JP, Mantoura J, de Kersaint-Gilly A, Andre MJ, Perrin-Resche I, Menegalli-Boggelli D, Lajat Y, Richard S: Haemangioblastoma, haemangioblastomatosis, and von Hippel-Lindau disease. Adv Tech Stand Neurosurg 20:197–304, 1993.
12. Takeuchi S, Tanaka R, Fujii Y, Abe H, Ito Y. Surgical treatment of hemangioblastomas with presurgical endovascular embolization. Neurologia medico-chirurgica. 2001;41(5):246-52.
13. Moss JM, Choi CY, Adler Jr JR, Soltys SG, Gibbs IC, Chang SD. Stereotactic radiosurgical treatment of cranial and spinal hemangioblastomas. Neurosurgery. 2009 Jul 1;65(1):79-85.
14. Jagannathan J, Lonser RR, Smith R, DeVroom HL, Oldfield EH. Surgical management of cerebellar hemangioblastomas in patients with von Hippel–Lindau disease. Journal of neurosurgery. 2008 Feb 1;108(2):210-22.
15. Koda M, Mannoji C, Itabashi T, Kita T, Murakami M, Yamazaki M, Aramomi M, Ikeda O, Furuya T. Intramedullary hemorrhage caused by spinal cord hemangioblastoma: a case report. BMC Research Notes. 2014 Dec;7(1):1-3.
16. Kiyofuji S, Graffeo CS, Yokoyama M, Sora S. Intramedullary and intratumoral hemorrhage in spinal

hemangioblastoma: Case report and review of literature. Surgical Neurology International. 2018;9.
17. Cornelius JF, Saint-Maurice JP, Bresson D, George B, Houdart E. Hemorrhage after particle embolization of hemangioblastomas: comparison of outcomes in spinal and cerebellar lesions. Journal of neurosurgery. 2007 Jun 1;106(6):994-8.
18. Mak G, Algird A, Greenspoon J, Provias J, Hirte H. Cervicomedullary hemangioblastoma treated with bevacizumab. Neuro-Oncology Advances. 2020 Jan;2(1):vdaa076.
19. Yin X, Li C, Li L, Duan H. Safety and efficacy of surgical treatment for brainstem hemangioblastoma: a meta-analysis. Neurosurgical review. 2021 Apr;44(2):799-806.
20. Ho VB, Smirniotopoulos JG, Murphy FM, Rushing EJ. Radiologic-pathologic correlation: hemangioblastoma. AJNR: American Journal of Neuroradiology. 1992 Sep;13(5):1343.

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Lumbar disc herniation presenting with contralateral neuropathy. Case report

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ABSTRACT

We admitted a unique case of right lumbar disc herniation at L4L5 who presented with contralateral symptoms and was successfully treated with a right large L4/L5 fenestration and microdiscectomy.

When the operation is considered, intervention only from the herniation side is sufficient.

In the case presented, it is probable that Kernohan notch-like phenomenon, venous engorgement and congestion at the contralateral side of the herniated lumbar disc and the contralateral migrated epidural fat are responsible for the emergence of contralateral symptoms.

Keywords
herniated disc,
intervertebral disc displacement,
contralateral symptoms

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INTRODUCTION

Lumbar disc herniation usually presents with varying degrees of pain, numbness and weakness in the distribution of the affected nerve root.

CASE PRESENTATION

A 46 year-old gentleman who performed intense physical work presented a 6 months old history of low back pain radiating down to his left buttock , posterior thigh, lateral and posterior leg (L5 and S1 dermatomas). Examination revealed intense algoparesthesias on the left L5 and S1 dermatomas (VAS 8/10), are refractory to conservative management and acupuncture, rotulian and achilian reflexes were absent bilaterally. Straight leg raise was positive at 30 degrees on the left side and 40 degrees on the right side.

Anamnesis revealed L4-L5 disc hernia operated on the right side in 2020 with very good postoperative evolution.

MRI of his lumbar spine showed a central and right-sided paracentral disc herniation at L4/L5 causing cauda equina compression (blue arrow) rupture of fibrous ring and posterior longitudinal ligament in the midline (red arrow) - Figures 1,2) .

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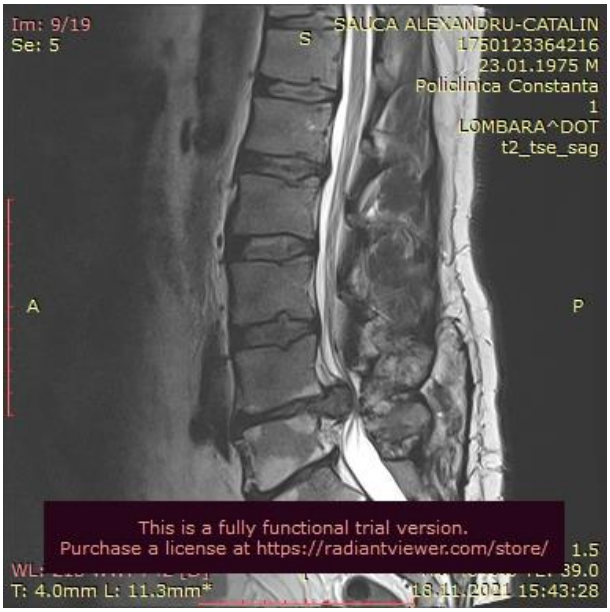

Figure 1. Sagittal cut of lumbar spine (T2) L4-L5 disc hernia, ruptured, huge, compressive on the cauda equina

Figure 1. Axial cut at L4/L5 disc level, the right side (T2). central and right-sided paracentral disc herniation at L4/L5 causing cauda equina compression (blue arrow), rupture of fibrous ring and posterior longitudinal ligament in the midline (red arrow), operated (2020) L4-L5 fenestration (yellow arrow).

The patient was emergently operated on (enlargment of fenestation L4-L5 on the right side, microsurgical discectomy). Postoperative results were very good with dissapearance of the pain and paresthesis.

Postoperative follow-up period: 6 months.

Discussion

There is no consensus about surgical approac; side or sides and the pathophysiology. Some authors like Choudhury et al[1], Kornberg[2] , Mirovsky and Halperin[3] performed bilateral explorations not to miss a lesion.

However, Sucu and Gelal[4], Akdeniz et al[5], and Karabekir et al[6] performed the operative approach only on the lumbar disc herniated side and reported that exploration of the LDH side was enough for the recovery of the contralateral symptoms.

Radiculopathy from lumbar disc herniation can be a result of mechanical compression[7] , ischaemia[7] or inflammatory irritation[8] of the nerve root.

The mechanism for lumbar disc herniation presenting with contralateral leg symptoms is poorly understood. Kornberg *et al*[2] proposed that inconsistent dural attachments to the posterior longitudinal ligaments holds the lumbar nerve roots at certain levels resulting in a more symptomatic traction of the contralateral nerve root

A radicular pain contralateral to the herniated side is an unusual finding rarely reported in the literature(Safdarian[9]). Safdarian hypothesized that the reason for patients' symptoms contralateral to the apparent compression on imaging studies involves a Kernohan notch-like phenomenon.

Sucu and Gelal[4] presented five patients with lumbar disk herniations and contralateral. The authors observed that the shape of disk herniations in imaging studies was quite similar in these patients. Almost all of them had a broad posterior central-paracentral herniated disk with the apex deviated away from the side of the symptoms.

Kalemci et al[10] reported a case of painless contralateral neurological deficit due to venous engorgement and congestion at the contralateral side of the herniated lumbar disc .

Karabekir et al[6]. concluded that a hypertrophied ligamentum flavum was the likely etiology of contralateral sciatica comparing five patients with only contralateral symptoms, with 200 disc herniated patients with ipsilateral symptoms

According to Jun-Song Yang[11] the migrated epidural fat plays a significant role in the pain mechanism of LDH with contralateral radiculopathy. Only via a surgical approach ipsilateral to the herniated side, could clinical improvement be obtained postoperatively**.**

Conclusions

Patients with lumbar disc herniation may present with radicular symptoms involving the contralateral leg.

In the case presented, the mechanism of contralateral symptoms was Kernohan notch-like phenomenon, venous engorgement and congestion at the contralateral side of the herniated lumbar disc and the contralateral migrated epidural fat.

The operative approach (enlarged fenestration, operative approach of the contralateral disc hernia) was mandatory for a very good postoperative evolution.

References

1. Choudhury AR, Taylor JC, Worthington BS, Whitaker R. Lumbar radiculopathy contralateral to upper lumbar disc herniation: report of 3 cases. Br J Surg. 1978;65:842-4.
2. Kornberg M. Sciatica contralateral to lumbar disk herniation. Orthopedics 1994;17:362-4. [PubMed]
3. Mirovsky Y, Halperin N. Eccentric compression of the spinal canal causing dominantly contralateral-side symptoms. J Spinal Disord. 2000;13(2):174-7
4. Sucu HK, Gelal F. Lumbar disk herniation with contralateral symptoms. Eur Spine J 2006;15:570-4. [Crossref] [PubMed
5. Akdeniz T, Kaner T, Tutkan I,Ozer AF. Unilateral surgical approach for lumbar disc herniation with contraletaral symptoms. J Neurosurg Spine. 2012;17:124-7
6. .Karabekir H. S. , Izhan A Y ,Atar E K ,Yaycloglu S, Gocmen-Mas N, Yazici C. Effect of ligamenta flava hypertrophy on lumbar disc herniation with contralateral symptoms and signs: a clinical and morphometric study
7. Garfin SR, Rydevik B, Lind B, et al. Spinal nerve root compression. Spine (Phila Pa 1976) 1995;20:1810-20. [Crossref] [PubMed]
8. Takahashi H, Wada A, Iida Y, et al. Antimicrobial prophylaxis for spinal surgery. J Orthop Sci 2009;14:40-4. [Crossref] [PubMed]
9. Safdarian M, Farzaneh F, Rahimi-Movaghar V. Contralateral radiculopathy: A kernohan–woltman notch-like phenomenon. Asian J Neurosurg 2018;13:165-7.
10. Kalemci O, Kizmazoglu C, Ozer E, Arda MN. Lumbar disc herniation associated with contralateral neurological deficit: Can venous congestion be the cause? Asian Spine J 2013;7:60-2. [PUBMED]
11. Jun-Song Yang, MD, Dong-Jie Zhang, MS, and Ding-Jun Hao. Lumbar Disc Herniation with Contralateral Radiculopathy: Do We Neglect the Epidural Fat?

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Invasive tumours of third ventricle. The possibilities of endoscopic transventricular surgery

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Keywords
endoscopic transventricular,
invasive tumors,
secondary tumors,
thalamus,
third ventricle,
transforaminal,
ventriculocisternostomy

ABSTRACT

Despite the rapid development of neurosurgery in the 21st century, the invasive (secondary) tumours of the third ventricle have always presented a highly sophisticated challenge in terms of surgical treatment. The question of radical resection of these tumours remains debatable, considering the high risk associated with the possibility of disability, the expected duration and the postoperative quality of life. We conducted a retrospective study of patients with invasive third ventricular tumours that have been treated in our department from 2015 to 2020 reviewing pre- and postoperative clinical and radiological data for 21 cases. The treatment options in all 21 cases included an endoscopic frontal transcortical transventricular transforaminal-transchoroidal tumour removal, achieving gross total and subtotal resection in 86% of the interventions, followed by adjuvant treatment (radiation therapy in all cases, and chemotherapy – for high-grade tumours). An endoscopic third ventriculocisternostomy was performed in cases with partial tumour removal in order to improve the CSF flow. Neurological deficits included permanent hemiplegia – in 3 patients (15%), permanent hemianopia – in 2 patients (10%), transient short-term memory impairment – in 3 patients (15%) with regression in 2-4 weeks after surgery. There was no postoperative lethality. Maximal postoperative survival in our patients with high-grade tumours was 16 months; patients with low-grade tumours are still under supervision. Endoscopic frontal transcortical transventricular transforaminal-transchoroidal approach to resection of third ventricular tumours is an effective surgical modality, that maximizes the possible resection volume with minimal occurrence of postoperative complications, therefore can be recommended for the routine treatment of the aforementioned pathology.

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INTRODUCTION

Despite the rapid development of neurosurgery in the 21st century, surgery of invasive (secondary) tumors of the third ventricle, which are malignant in most cases, remains far from a solution [1-9]. Usually, the zone of primary growth of invasive third ventricular tumors is located in functionally important areas of the brain [2,3-9].

The questions of the radical removal of these tumors [4,7-9] remain debatable, taking into account the possible disability of patients [3-7,9], the expected duration and the postoperative quality of life [1,4,7,12].

Materials and methods

From 2015 to 2020, we have treated 43 patients with tumors of the third ventricle, 21 of which were invasive tumors with predominant growth from the thalamus. All patients underwent complete endoscopic resection using the frontal transcortical transventricular transforaminal approach. If the size of the interventricular foramen was inadequate for the endoscopic intervention, it was expanded by dissection of the anterior portions of the choroid plexus (Fig. 1).

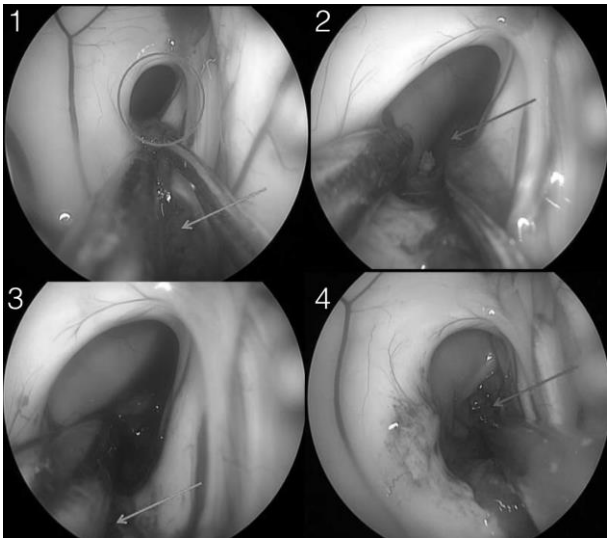


Figure 1. Step-like expansion of the interventricular foramen by dissecting the anterior portions of the choroid plexus: the interventricular foramen is circled in red; the yellow arrow indicates the choroid plexus; the green arrow indicates an invasive third ventricular tumour.

Preoperative neurological status of patients: nonfocal symptoms were present in all patients, central hemiparesis (up to 2/5 points) - in 5 patients, impaired short-term memory - in 6 patients. Occlusive hydrocephalus was diagnosed in all cases.

All patients underwent an endoscopic removal by a frontal transcortical transventricular transforaminal approach, and in 11 cases an additional endoscopic third ventriculocisternostomy was performed.

Results

Radicality of surgical removal of invasive tumors (Fig. 2): Gross total resection (removal within healthy tissues) - 2 patients. Subtotal resection (removal of up to 90% of the tumor) - 16 patients. Partial removal - 3 patients. Partial removal was performed in the cases where an excessive bleeding from the tumor was observed. Endoscopic third ventriculocisternostomy was conducted in 11 cases with a bleeding tumor and limited removal radicality.

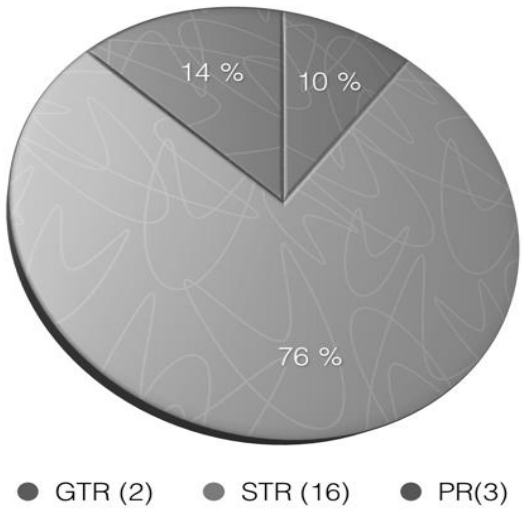
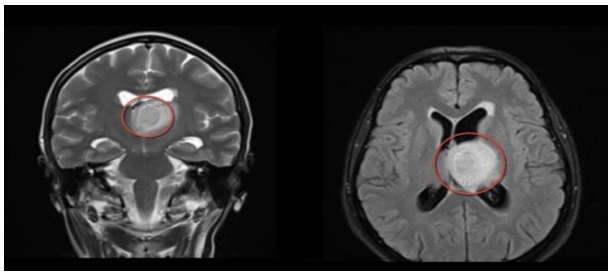


Figure 2. Radical removal of invasive third ventricular tumors: (GTR - Gross total resection - (total) removal of the tumor within healthy tissues; STR - Subtotal resection - subtotal (up to 90%) removal of the tumor; PR - Partial removal.

Histological distribution: low grade tumors (WHO grade 2 - fibrillar astrocytoma) - 3 cases; high grade tumors (WHO grade 3-4 - anaplastic astrocytoma (Fig. 3), anaplastic oligoastrocytoma (Fig. 4), glioblastoma) - 18 cases. The maximum size/diameter of the tumor reached 6.2 cm.



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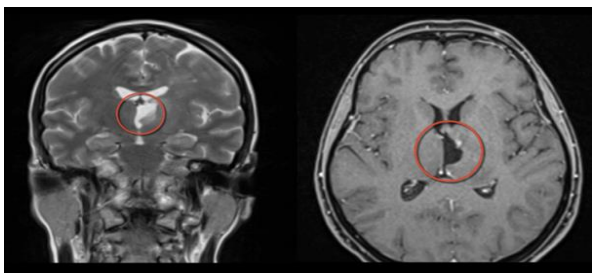
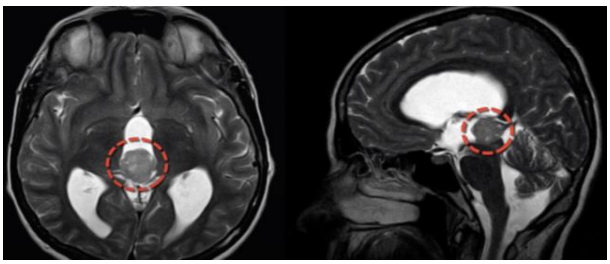


B.

Figure 3. Preoperative brain MRI (A) and 3 months after surgery (B). Total removal of the tumor of the left thalamus (Histological diagnosis – anaplastic astrocytoma, WHO grade 3). Hydrocephalus regressed in the postoperative period.



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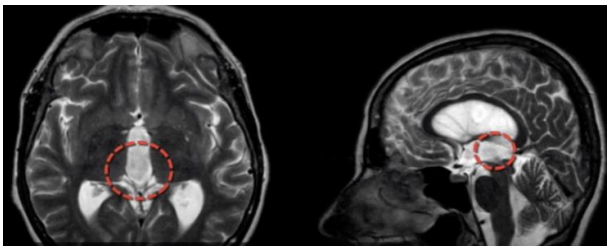

B.

Figure 4. Preoperative brain MRI (A) and 3 months after surgery (B). Total removal of an invasive tumor in the posterior portions of the third ventricle (Histological diagnosis – anaplastic oligoastrocytoma, WHO grade 3). Hydrocephalus regressed in the postoperative period.

Postoperative condition: the postoperative Karnofsky Performance Status in all patients was 70 points or more. Postoperative neurological deficit: permanent hemiplegia – in 3 patients (15%), permanent hemianopia – in 2 patients (10%), transient short-term memory impairment – in 3 patients (15%) with a regression in 2-4 weeks after surgery.

In all patients, nonfocal symptoms regressed. After surgical treatment all patients received adjuvant treatment (radiation therapy in all cases, chemotherapy – for high-grade tumors).

Maximal postoperative survival in our patients with high-grade tumors was 16 months, patients with low-grade tumors are still under supervision. There was no postoperative lethality.

Discussion

The problem of radical gross total resection of invasive tumors of third ventricle is deeply connected to their site of origin, as they predominantly arise from the thalamus. A greater resection volume may jeopardize the integrity of this critical neurostructure, thus leading to a postoperative neurological deficit and disability. Previously, microsurgical technique for resection of third ventricular tumors has been performed with the use of operative microscope. The rapid development of neuroendoscopy in the last 20 years has provided new minimally invasive options for treatment of ventricular pathology, therefore opening new prospects for surgical resection of invasive tumors of third ventricle. Shorter operative time period, minimal invasiveness and better visualization of deep-seated ventricular structures are considered to be the main advantages of neuroendoscopy over microsurgery, although the traditional microsurgery retains its edge in bleeding control [1, 3, 4, 5, 8].

The endoscopic frontal transcortical transventricular transforaminal approach has been used in surgical resection of third ventricular tumors in many institutions worldwide [3, 4, 5, 8]. This approach provides the possibility to utilize a natural pathway such as the foramen of Monro in order to reach third ventricle through established anatomical landmarks, especially in the setting of hydrocephalus, which is habitually present in patients with invasive third ventricular tumors [8]. Achieving gross total and subtotal resection was possible in 86% of the interventions, with minor postoperative complications. Other authors, such as Tawk RG et al. [8] have reported similar results, achieving complete and near complete resection in 84% of the cases. Various endoscopic modalities could be used, when approaching the third ventricular invasive tumors [11]. The endoscopic endonasal approach has similar radical resection success and an ETV procedure could be performed, but it is believed to be associated with higher risk of infectious complications, such as meningoencephalitis, and hormonal disorders (diabetes insipidus, obesity etc.) [10, 12].

The authors believe, that the use of endoscopic frontal transcortical transventricular transforaminal approach in patients with invasive third ventricle tumors and obstructive hydrocephalus may appear to be an effective alternative to microsurgical resection using an operative microscope, although more clinical studies have to be conducted in order to confirm the clinical efficacy of the endoscopic frontal transcortical transventricular transforaminal approach. [1-12]**.**

Conclusions

1. Minor functional disorders and high life expectancy in invasive high-grade tumors make it possible to recommend frontal endoscopic transcortical transventricular transforaminal-transchoroidal approach as an effective method of surgical treatment of these tumors.

2. To prevent the development of a postoperative obstructive hydrocephalus by a blood clot, intraventricular hemorrhages, obstruction of cerebral aqueduct, in patients with invasive third ventricular tumors, it is advisable to perform intraoperative third ventriculocisternostomy.

Disclosures

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

References

1. Ahmed SI, Javed G, Laghari AA, Bareeqa SB, Aziz K, Khan M, Samar SS, Humera RA, Khan AR, Farooqui MO, Shahbaz A. Third Ventricular Tumors: A Comprehensive Literature Review. Cureus. 2018 Oct 5;10(10):e3417. doi: 10.7759/cureus.3417. PMID: 30542631; PMCID: PMC6284874.
2. Chibbaro S, Di Rocco F, Makiese O, Reiss A, Poczos P, Mirone G, Servadei F, George B, Crafa P, Polivka M, Romano A. Neuroendoscopic management of posterior third ventricle and pineal region tumors: technique, limitation, and possible complication avoidance. Neurosurg Rev. 2012 Jul;35(3):331-38; discussion 338-40. doi: 10.1007/s10143-011-0370-1. Epub 2012 Jan 19. PMID: 22258494.
3. Iacoangeli M, di Somma LG, Di Rienzo A, Alvaro L, Nasi D, Scerrati M. Combined endoscopic transforaminal-transchoroidal approach for the treatment of third ventricle colloid cysts. J Neurosurg. 2014 Jun;120(6):1471-6. doi: 10.3171/2014.1.JNS131102. Epub 2014 Mar 7. PMID: 24605835.
4. Chibbaro S, Champeaux C, Poczos P, Cardarelli M, Di Rocco F, Iaccarino C, Servadei F, Tigan L, Chaussemy D, George B, Froelich S, Kehrli P, Romano A. Anterior trans-frontal endoscopic management of colloid cyst: an effective, safe, and elegant way of treatment. Case series and technical note from a multicenter prospective study. Neurosurg Rev. 2014 Apr;37(2):235-41; discussion 241. doi: 10.1007/s10143-013-0508-4. Epub 2013 Dec 19. PMID: 24352893.
5. Ibáñez-Botella G, Domínguez M, Ros B, De Miguel L, Márquez B, Arráez MA. Endoscopic transchoroidal and transforaminal approaches for resection of third ventricular colloid cysts. Neurosurg Rev. 2014 Apr;37(2):227-34; discussion 234. doi: 10.1007/s10143-014-0529-7. Epub 2014 Feb 14. PMID: 24526368.
6. Oppido PA, Fiorindi A, Benvenuti L, Cattani F, Cipri S, Gangemi M, Godano U, Longatti P, Mascari C, Morace E, Tosatto L. Neuroendoscopic biopsy of ventricular tumors: a multicentric experience. Neurosurg Focus. 2011 Apr;30(4):E2. doi: 10.3171/2011.1.FOCUS10326. PMID: 21456929.
7. Roth J, Constantini S. Combined rigid and flexible endoscopy for tumors in the posterior third ventricle. J Neurosurg. 2015 Jun;122(6):1341-6. doi: 10.3171/2014.9.JNS141397. Epub 2015 Mar 27. PMID: 25816082.
8. Tawk RG, Akinduro OO, Grewal SS, Brasiliense L, Grand W, Grotenhuis A. Endoscopic Transforaminal Transchoroidal Approach to the Third Ventricle for Cystic and Solid Tumors. World Neurosurg. 2020 Feb;134:e453-e459. doi: 10.1016/j.wneu.2019.10.099. Epub 2019 Oct 24. PMID: 31669244.
9. Brusius CV, Bianchin MM, Mira JM, Frigeri T, Kruger M, Grudtner MC, Lenhardt R, Maschke S, Wolfsberger S. Single Burr-Hole Extended Transforaminal Approach for Concurrent Endoscopic Surgery in the Third Ventricle Posterior to the Foramen of Monro and Ventriculostomy: Clinical Series and Planning Steps. World Neurosurg. 2021 Jun;150:e1-e11. doi: 10.1016/j.wneu.2021.01.067. Epub 2021 Feb 12. PMID: 33582291.
10. Youngbeom Se, Yong Hwy Kim, Jung Hee Kim, Doo-Sik Kong, Yun-Sik Dho, Ho Kang, Kyung-Min Kim, Jin Wook Kim, Chul-Kee Park Outcomes of the endoscopic endonasal approach for tumors in the third ventricle or invading the third ventricle J Clin Neurosci. 2021 Aug; 90:302-310. doi: 10.1016/j.jocn.2021.06.012. Epub 2021 Jun 21.
11. Changfu Zhang, Zhengcun Yan, Xiaodong Wang, Yuping Li, Hengzhu Zhang Quantitative analysis of exposure and surgical maneuverability of three purely endoscopic keyhole approaches to the floor of the third ventricle J Neurosurg Sci. 2021 Sep 21. doi: 10.23736/S0390-5616.21.05455-2. PMID: 34545733 PMID: 34275567
12. Bolin Liu, Tao Zheng, Wenhai Lv, Yuanzhi Huang, Baofu Li, Baoying Chen, Binrong Wang, Shiming He Endoscopic Endonasal Transsphenoidal Approach for Third Ventriculostomy in the Management of Obstructive Hydrocephalus J Craniofac Surg. 2021 Oct 1;32(7):e609-e612. doi: 10.1097/SCS.0000000000007613 Epub 2021 Feb 12. PMID: 33710059.

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Clinico-radiological factors affecting visual recovery in pituitary tumours

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ABSTRACT

Objectives: It is a prospective, single institute, observational study: primary outcome measure; factors determining visual field improvement and secondary outcome measure; the relationship between severity of visual impairment and duration of symptoms.

Material and Methods: It is a prospective, single institute, observational study that will be conducted between January 2020 and January 2022 in the department of Neurosurgery at the G. R. Medical College &J.A. Group of Hospitals, Gwalior (M.P.), a tertiary centre in India. All patients were admitted to the neuro-surgery department & operated on basis of a CT scan of head/MRI findings. Patients with Laboratory findings having hypopituitarism, diabetes insipidus (DI), and hyperprolactinemia and willing to undergo Endocrinological & visual field tests in inclusion criteria. Data obtained from the study will be analyse by using appropriate statistical tests or methods

Results: At present, series most common age presentation (36.7%) between 21-30 years. In our study, of the total patients, 60% were males and 40% were females. The male to female ratio is 2:1 most common complaint of vision loss and only 50% had hormonal symptoms. In our study 46.7% patients have duration of symptoms < 6 months and 6/6 - 6/24 visual acuity was present in 73.3% patients & 13.3% had optic atrophy(primary/secondary), 43.3%patients had bi-temporal hemianopia.

In our study Suprasellar extension was present in 90% of patients & Vascular invasion was seen in 26.7% of patients.

Conclusion: Good results are seen in patients who have a lesser duration of symptoms, and good pre-operative visual acuity has improved the final visual outcome. Post-operative visual recovery is most promising after 3 months to 1 year of surgery. immediate results of visual recovery should not be expected. Most patients presented with larger adenomas had poor visual recovery as compared to small adenomas. Patients who underwent endoscopic trans-nasal, trans-sphenoidal resection had better post-operative recovery.

Keywords
pituitary adenoma,
tumours,
visual field defect,
harmonal symptoms

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INTRODUCTION

Pitutary adenomas account for 10-15% of all brain tumours, it is the third most frequently diagnosed brain tumour [1].

Pitutary tumours can be clinically Classified as functioning & non-functioning pituitary adenomas [2].

Non-functioning pituitary adenomas are not usually associated with

clinical syndromes related to hormone excess and may be discovered occasionally.[3]

When they exert mass effects on surrounding tissues leading to visual impairments, headache and hypopituitarism and hydrocephalus.[4]

The growing of pituitary tumors may compress the surrounding structures especially optic nerve, cause visual field defects including bitemporal hemianopia, visual disturbance. The frequency of visual field defects in pituitary adenomas varies from 37% to 96% in different studies.[5]

The symptoms due to pituitary hormonal dysfunction are not the one for which the patient seeks medical attention.

The presence of a visual field defect is one of the common indications for surgery in patients with pituitary tumors, and the degree of the visual field defect should be identified through a preoperative visual field examination, even if the patient does not complain of symptoms [6]

If the tumor is accompanied by a visual field defect, it is clinically important to predict the prognosis for postoperative visual field recovery.[7]

The typical visual field defect, bitemporal hemianopia, is due to anatomical compression of the optic chiasm, which contains the crossing nasal fibres of each optic nerve fibres.[8]

Materials and method

Study Design

It is a prospective, single institute, observational study will be conducted between January 2020 and January 2022 in the department of Neurosurgery at the G. R. Medical College &J.A. Group of Hospitals, Gwalior (M.P.), a tertiary centre in India. The study protocol will be approved by the Institutional Ethics Committee and written informed consent will be obtained from all participants.

Sample Size

30 and above Patients

Inclusion criteria

1. All patients admitted in neuro-surgery department & operated on basis of CT scan of head/MRI findings.
2. Patients with Laboratory findings having hypopituitarism, diabetes insipidus (DI), and hyperprolactinemia.
3. Patients willing to undergo Endocrinological & visual field tests.
4. Patients with visual field defect induced by pituitary tumors.

Exclusion criteria

1. Severe co-morbid illness
2. Patients having past h/o of surgery or treatment adjacent to Sellar lesion.
3. Patients excluded who refused Endocrinological Evaluation.
4. Patients not willing for operation.
5. Patients less than 15 years of age.
6. Cases with other causes of visual loss such as cataract, Glaucoma, and Retinal detachment.

Study Protocol and Data Collection

All patients of pituitary tumour admitted in department of Neurosurgery. A written consent will be taken from the patient or their attendants for the study. Details of demographics and detailed history of event, presenting symptoms and signs, laboratory parameters (Serum prolactin, Growth hormone, ACTH, TSH, Cortisol) and imaging findings (size of tumour, invasion of surrounding structures) A contrast-enhanced magnetic resonance imaging (MRI) of the sella was performed in all these patients preoperatively. The adenoma volume was calculated by the De Chiro and Nelson formula [volume = (sagittal × coronal × axial diameters) × π/6]. Modified Hardy's classification was used for staging (extension) and grading (degree of sellar destruction) of the pituitary adenomas. We also used Knosp grading to document the parasellar extension, Ophthalmologic evaluation (Visual acuity, Visual field, Fundus) VA was determined by the Snellen's chart, and VF testing was performed by Humphrey automated computerized perimeter, C76 Panel (Carl Zeiss, Germany). In patients with finger counting, hand movement, and only perception of light, the assessment of VF was done manually using confrontation test before surgery & After 1 month & 3 months of surgery will be noted. The results were recorded as follows: (i) No change, (ii) improved, and (iii) worsened. Significant improvement/worsening was defined as any grade improvement or deterioration in the VA and VF, based upon a 30% change to avoid inter- and intra-individual variation, according to John Thomas Smith's rule of the one-third. Blindness was defined as absence of

perception of light. Management of the patients will be planned and observe in terms of outcome.

Outcome Measure

1. Primary outcome measure- Factors determining visual field improvement.
2. Secondary outcome measure- relationship between severity of visual impairment & duration of symptoms.

Data Analysis

Data obtained from the study, will be analyse by using appropriate statistical test or methods. Data will be entered in Microsoft Word and analyzed using SPSS version 16.0 and EPI INFO version 7.0. Appropriate statistical test will be applied to analyze the data.

RESULTS

In present series (N=4)13.3% patients were up to 20 yrs. of age, (N=11)36.7% between 21-30 years, (N=8)26.7% between 31-40 yrs., (N=5)16.7% were between 41-50 yrs. &(N=2) 6.7% between 51-60 yrs. Our study of the total patient 30, (N=18)60% were males &(N=12) 40% were females. The male to female ratio is 2:1.

In the present study (N=24)80% of patient had complaint of Headache, Vision loss was present in (N=25)83.3% of patients & Features of Raised ICP were present in (n=15)50% of patients**.**

In present study of total patients (N=30) only 50% had hormonal symptoms. Acromegaly was present in (N=5)16.7% patients, Amenorrhea was present in (N=2) 6.7% of patients. Cushing feature was present in (N=3)10% patients. Hirsutism was present in (N=4)13.3% patients. Hypothyroidism was present in (N=1)3.3% patient

In our study (N=14)46.7% patients have duration of symptoms < 6 months, 6 months -12 months (N=6) 20%, 1yr-2yr (N=3)10% & (N=7)23.3% had duration of symptoms more than 2 yr.

Visual Acuity

In our study 6/6 - 6/24 visual acuity was present in 73.3%(N=22) patients, 6/36 - 6/60 visual acuity was present in 13.3%(N=4) patient, Hand movement was present in 6.7%(N=2), perception of light negative in 3.3% (N=1) & perception of light positive in 3.3% (N=1) patients.

Fundus

In our study 70%(N=21) had normal fundus, 16.7%(N=5) had pale optic Disc & 13.3%(N=4) had optic atrophy (primary/secondary).

Visual field

In our study 43.3%(N=13) patients had bi-temporal hemianopia, Normal field of vision in 33.3%(N=10), Blind 13.3%(N=4), Upper Quadrantonopia was present in 6.7%(N=2) & Total field loss in 3.3%(N=1).

In our study Hydodense lesion was seen in 66.7%(N=20) of patients, hyperdense lesion was seen in 6.7%(N=2) & Hetrogenous lesion was seen in 23.3%(N=7). In our study 50%(N=15) were solid lesions, 30%(N=9) were cystic lesions & 20%(N=6) were mixed lesions**.**

In our study vascular invasion was seen in 26.7%(N=8) of patients.

In our study T1-W image 96.7%(N=29) were hypointense & 3.3%(N=1) were hyperintense & on T2-W image 100%(N=30) were hyperintense. In our study 100%(N=30) were macroadenoma pituitary Tumours. Suprasellar extension was present in 90%(N=27) patients & Vascular invasion seen in 26.7%(N=8) patients.

DISCUSSION

Pituitary adenomas can produce visual loss by compression of the optic chiasm or nerves. An extension of >10 mm above the seller diaphragm is necessary to compress the anterior visual system.[9][10]

Pituitary adenoma can be described as microadenoma, macroadenoma, and giant tumors based on size. Microadenoma is a tumor less than 10 mm, while macroadenoma describes a tumor larger than 10mm. Giant pituitary tumors are bigger than 40 mm.

Table 1. Comparison of neurological complaints in various studies

S. NO.	Study	No. of patients	Visual Impairment (%)	Headache (%)
1	Khaled Al dahmani et al (2016)	1005	76	62
2	Elena Valassi et al (2018)	51	51	34

3	Pamela U Freda et al (1999)	62	62	42
4	Mukheraji KK et al (2016)	1007	87.5	87.3
5	Amit Padwal (2017)	80	46	53
6	Present Study	30	83.3	80

Visual symptom is one of the major presenting manifestations of a pituitary macroadenoma causing considerable burden to patients and their families [11]. In present study [Table- 1] vision loss (83.3%) was the most common symptoms followed by Headache (80%) and followed by features of raised ICP (50%) which is consistent with most of the studies of Mukerji K K et al(2016)[12], Khaled Al dahmani et al(2016)[13],Elena Valassi et al(1999)[14], Pamela U Freda et al(1999)[15], Amit Padwal et al (2017)[16]

Table 2. Comparison of Harmonal symptoms in various studies

	Study	No. of patients	Acromegaly	Cushingoid
1	Khaled Al dahmani et al (2016)	1005	6%	0%
2	Mukherji KK et al (2016)	1007	23.9%	8.6%
3	Dong Kyulee (2018)	102	18.3%	0%
4	Present study	30	16.7%	10%

The histologic diversity accounts for its ability to secrete a variety of hormones that include the growth hormone (GH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin (PRL). The median lobe produces melanocyte-stimulating hormone (MSH). The neurohypophysis is composed of the neural stalk and the neural lobe and functions as the primary storage site for antidiuretic hormone (ADH) and oxytocin (OX). These hormones as well as other biologically active substances are released into the adjacent capillaries in response to hypothalamic nerve impulses [17,18,19]. Hypersecretion of prolactin, growth hormone, ACTH and TSH produces corresponding clinical syndromes [19]. In present study 50%tumours were non functional which was not correlating with Mukherji K K et al [12] were 68.8% were non functioning &Dong Kyu lee [20] were 80% were non functioning tumours.[Table- 2].

In present study 16.7% presented with features of Acromegaly being the most commonest followed by cushing features in 10% which is consistent with Khaled Al Dahmani et al[13] 6%, Mukherji KK et al[12] 23.9%, Dong Kyu lee [20] 18.3%.

The most common consistent feature of these tumors is visual loss, a consequence of suprasellar growth and compression of anterior visual pathways. An asymmetric bitemporal hemianopia is the classically observed deficit, although other patterns of visual dysfunction commonly occur such as the junctional scotomas, monocular field defects, papilledema, optic atrophy and total blindness[21]. In the present study on fundoscopic Examination (13.3%) patient had optic atrophy as a result of long-standing chiasmal compression from a pituitary macroadenoma.In a study by Dhasmana et al[22] optic atrophy was seen clearly in 17% of patients with pituitary adenomas and all of them had significantly affected vision. Mukherji K K et al [12] study too, had similar percentage (18.2%) of patients presented with optic atrophy and most of the patients had a poor Visual acuity ranging from 6/36 -6/60 to no light perception.[Table- 3]

Table 3. Comparison of Optic Atrophy in various studies

S. NO.	Study	Optic Atrophy %
1.	Dhasmana et al (2011)	17
2.	Mukherji et al (2016)	18.2
3.	Present Study	13.3

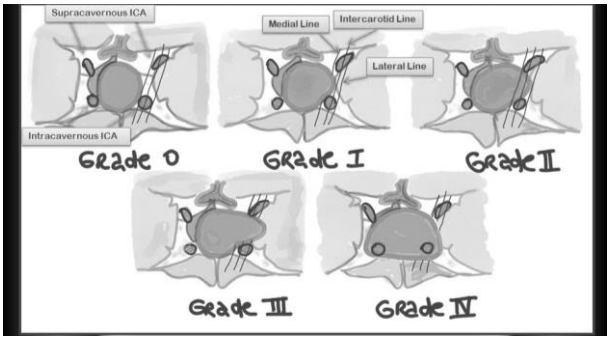
From the surgical stand point sellar and parasellar masses such as pituitary tumors can be can be classified on the basis of their size and growth characteristics as determined by imaging studies.The most enduring classification is that devised by Hardy and modified by Wilson[23].

Grade	Grading
Grade-0	Microadenoma<1cm:No sellar changes
Grade-1	Microadenoma<1cm:Minor sellar changes
Grade-2	Macroadenoma with diffuse enlargement

Grade-3	Macroadenoma with focal destruction
Grade-4	Macroadenoma with extensive destruction of sella

Extrasellar extension
STAGE-A Extending to suprasellar cistern
STAGE-B Extending to third ventricle floor
STAGE-C Extending into the third ventricle
STAGE-D Extensive lateral intradural extension
STAGE-E Extensive lateral extradural extension.

KNOSP Classification



MR imaging is the imaging mainstay of the sellar and parasellar regions. MR imaging has a better soft tissue resolution than computed tomography (CT) and is also not subjected to artifacts from surrounding bony structures.[24]

In our study invasiveness of the lesion was assessed on MRI by Hardy &Wilson classification & Knosp classification. The evidence of carotid encasement in MRI scan is defined invasion of cavernous sinus, in Amit Padwal et al [25] study of 93 patients, 50 patients had invasive adenoma and remaining 43 patients had non-invasive adenoma. This is in agreement with study done by Amit Padwal et al and Ross & Wilson [26] where grade-2 was most common finding. [Table-4]

Table 4. Comparison of Hardy- Wilson Grading in various studies

Study	No. of patients	Grading (most common grade - 2) %
Amit Padwal et al (2017)	93	2-58%
Ross & Wilson (1988)	214	2-60%
Present Study	30	2-47%

CT is better than MR imaging for detecting calcifications, and can be used complementary to MR imaging if a primary bony lesion is suspected (eg, chordoma, chondrosarcoma) and also in defining the sphenoid sinus anatomy if endonasal/sublabial endoscopic or microscopic transphenoidal approach is planned [27,28].CT scan is also beneficial in detecting pituitary apoplexy which will have a hyperdense appearance.

In our study, 29 cases showed hypointensity on T1 Weighted image, while one case showed hyperintensity. All cases showed hyperintensity on T2 weighted image. These MRI Finding are supported by most of other studies, like Pratisruti Hui et al[29] & Kushak Gehlot et al [30], where similar results were obtained.[Table- 5]

Table 5. Comparison of MRI in various studies

Study	T1 MRI	T2 MRI	Contrast
Kushak Gehlot et al (2019)	Hypointense - 84% Hyperintense- 9.2%	Hyperintensity -80%	75.9%
Pratisruti Hui et al (2019)	Hypointense- 100%	Hyperintensity -86%	92%
Present study	Hypointense - 84% Hyperintense- 9.2%	Hyperintensity -100%	80%

Post-operative visual Recovery played a significant role, post-operative assessment was done immediately post-operative, after 1 month & after 3 month of surgery. Most of the patients showed visual recovery after 3 month. A Ashish Suri et al [31] showed visual improvement in 30% patients, Apjit Kaur et al [32] showed visual improvement in 44.8%, Mukherji K K et al [12] showed improvement in 71.1% cases at 3 months which is similar to our study of 83.3% [Table-6].

Table 6. Comparison of post-op visual recovery

Study	Post-op Visual recovery %
Ashish Suri et al (2008)	30%
Apjit Kaur et al	44.8%
Mukherji K K et al (2016)	71.1%
Our study	83.3%

The minimally invasive transsphenoidal approach can be used effectively for 95% of pituitary tumors.

Exceptions are those large tumors with significant temporal or anterior cranial fossa extension. In such circumstances, transcranial approaches are often more appropriate. Occasionally, combined transsphenoidal and transcranial approaches are used. Nevertheless, some surgeons extend the basic transsphenoidal exposure in order to remove some of these tumors and avoid a craniotomy [33,34]

Conclusion

Good results are seen in patients who have lesser duration of symptoms, good pre-operative Visual Acuity have improved final Visual outcome. In our study most cases of pituitary adenoma were functional, so patients with pituitary prolactinoma showed better visual recovery. Post-operative visual recovery is most promising after 3 months to 1 year of surgery. immediate results of visual recovery should not be expected. most of patients presented with larger adenomas with supra-sellar & parasellar extension with encasement of internal carotid artery had poor Visual recovery as compared to small adenomas. Patients who underwent Endoscopic Trans-nasal, trans-sphenoidal resection had better post-operative recovery with less patient morbidity & less post-operative complications and lesser duration of post-operative hospital stay.

References

1. Zacharia BE, Bruce SS, Goldstein H, Malone HR, Neugut AI, Bruce JN. Incidence, treatment and survival of patients with craniopharyngioma in the surveillance, epidemiology and end results program. Neuro-oncol. 2012 Aug;14(8):1070.
2. Olsson DS, Andersson E, Bryngelsson IL, Nilsson AG, JohannssonG. Excess mortality and morbidity in patients with craniopharyngioma, especially in patients with childhood onset: a population-based study in Sweden. J Clin Endocrinol Metab. 2015 Feb;100(2): 467–74.
3. Karavitaki N, Brufani C, Warner JT, Adams CB, Richards P, Ansorge O, et al. Craniopharyngiomas in children and adults: systematic analysis of 121 cases with long-term follow-up. Clin Endocrinol (Oxf). 2005 Apr;62(4):397–409.
4. Pemberton LS, Dougal M, Magee B, Gattamaneni HR. Experience of external beam radiotherapy given adjuvantly or at relapse following surgery for craniopharyngioma. Radiother Oncol. 2005 Oct;77(1):99–104.
5. Wijnen M, van den Heuvel-Eibrink MM, Janssen JA, Catsman-Berrevoets CE, Michiels EM, van Veelen-Vincent MC, et al. Very long-term sequelae of craniopharyngioma. Eur J Endocrinol. 2017 Jun;176(6):755–67.
6. Puget S, Garnett M, Wray A, Grill J, Habrand JL, Bodaert N, et al. Pediatric craniopharyngiomas: classification and treatment according to the degree of hypothalamic involvement. J Neurosurg. 200 Jan;106(1 Suppl):3–12.
7. Müller HL. Craniopharyngioma. Endocr Rev. 2014 Jun;35(3):513–43.
8. Sterkenburg AS, Hoffmann A, Gebhardt U, Warmuth-Metz M, Daubenbüchel AM, Müller HL. Survival, hypothalamic obesity, and neuropsychological /psychosocial status after childhood-onset craniopharyngioma: newly reported long-term outcomes. Neuro- oncol. 2015 Jul;17(7):1029–38.
9. Hudson H, Rissell C, Gauderman WJ, Feldon SE. Pituitary tumor volume as a predictor of postoperative visual field recovery. Quantitative analysis using automated static perimetry and computed tomography morphometry. J Clin Neuroopthalmol 1991;11:280-3.
10. Shults WT. Compressive optic neuropathies. In: Miller NR, Newman NJ, editors. Walsh and Hoyt's Clinical Neuro-Ophthalmology. 5th ed. Baltimore: Williams and Wilkins; 1998. p. 657-8
11. Dutta P, Hajela A, Pathak A, Bhansali A, Radotra BD, Vashishta RK, et al. Clinical profile and outcome of patients with acromegaly according to the 2014 consensus guidelines: Impact of a multi-disciplinary team. Neurol India. 2015;63:360-8.
12. Visual outcome in in 2000 eyes following microscopic transsphenoidal surgery for pituitary adenomas: protracted blindness should not be a deterrent. Dutta p, Gyurmey, T,Banshal R, Pathak A,Dhandapani s, Rai A,Bhansali A, Mukherjee KK,. Neurol india 2016;64:1247-53.
13. Sellar masses : An Epidemiological Study. Al-Dahmani K, et al. Can J Neurol Sci.2016Mar;43(2):291-7.
14. Current openion in Endocrine & metabolic research.Elena Valssi, E Resmini , 63-73,2018.
15. Differential diagnosis of Sellar masses, Endocrionology & metabolism. Palmela U Fareda, Kalmon D. Clinics of north America. 28;1:1999, 81-117
16. Evalution of factors affecting outcome in growth harmonr secreting pituitary adenoma. Amit Padwal, Jagathal Gangadharan, Indian Journal of Neurosurgery2017;06(03):176-183.
17. Wang S, Nie Q, Wu Z, Zhang J, Wei L. MRI and pathological features of Rathke cleft cysts in the sellar region. Exp Ther Med. 2020 Jan;19(1):611–8.
18. Trifanescu R, Ansorge O, Wass JA, Grossman AB, Karavitaki N. Rathke"s cleft cysts. Clin Endocrinol (Oxf). 2012 Feb;76(2):151–60.
19. Mahapatra AK: Does optic nerve injury require decompression? J Indian Med Assoc 88:82–84, 1990.
20. Dong kyu Lee, Mi Sun Sung and Sang Woo park:Factors influencing Visual field Recovery after Transsphenoidal resection of pituitary Adenoma.Korean J Ophthalmol.2018 Dec;32(6):488-496.

21. Marchel A, Bidzinski J, Barczewska M, Dziewiecke C. Meningiomas of sella turcica: some clinical aspects. Neurol Neurochir Pol 30:93–100, 1996 (Pol).
22. Dhasmana R, Nagpal RC, SharmaR, Bansal KK, Bahadur H. Visual fields at presentation and after trans-sphenoidal resection of pituitary adenoma.J Ophthalmic Vis Res 2011;6:187-91.
23. McFadzean RM, Doyle D, Rampling R, Teasdale E, Teasdale G. Pituitary apoplexy and its effect on vision. Neurosurgery 29: 669–675, 1991
24. McGirt MJ, Cowan JA Jr, Gala V, Garton HJ: Surgical reversal of prolonged blindness from a metastatic neuroblastoma. Childs Nerv Syst 21:583–586, 2005.
25. Amit Padwal, Jagathal Gangadharan " evalution of factors affecting outcome in growth harmone-secreting pituitary adenoma" IJN,2017:06(03):176-183.
26. Ross DA, Wilson CB, Results of Transsphenoid microsurgery for growth harmone secreting pituitary adenoma in series of 214 patients. J Neurosurgery 1988;68(06): 854-67.
27. McIlwaine GG, Carrim ZI, Lueck CJ, Chrisp TM: A mechanical therapy to account for bitemporal hemianopia from chiasmal compression. J Neuroophthalmol 25:40–43, 2005.
28. McLarty DG, Kermali W, Makene WJ: Pituitary tumors and blindness: continuation of the pre-Harvey-Cushing era in developing countries. Lancet 2:810–811, 1982.
29. Accuracy of magnetic resonance imaging in evaluation of sellar & juxtra sellar tumours Hui Pratisutri,Parida Sasmita, Mohanty Jayshree, Singh Mamta, Sarangi Pradosh Kumar 2019;3:1: 3-9.
30. Aggrawal,N,Kushal Gehlot,NK Kardam& A.Khan.MRI Characterised of sellar & parasellar lesion & their clinical correlation. 2019
31. Suri A, Narang KS, Sharma BS, Mahapatra AK.Visual outcome after surgery in patients with suprasellar tumours & Pre-operative blindness. JNeurosurg.2008 Jan; 108(1):19-25.
32. Apjit Kaur, Deepu Banerji, Devendra Kumar, Kartikey Sharma. Visual status in suprasellar pituitary Tumours. Indian J opthalmol 1995;43:131-4.
33. Kaptain G.J., et al. Transsphenoidal approaches for the extracapsular resection of midline suprasellar and anterior cranial base lesions. Neurosurgery. 2001;49(1):94–100.
34. Nimsky C., et al. Intraoperative high-field magnetic resonance imaging in transsphenoidal surgery of hormonally inactive pituitary macroadenomas. Neurosurgery. 2006;59(1):105–14.

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Practical concepts in the identification of bilateral chronic subdural hematoma

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ABSTRACT

Bilateral chronic subdural hematoma is a neurosurgical pathology whose incidence in older adults has been increasing, as a consequence of the ageing of the population, added to the factors that are linked to it. Neurosurgical diseases with chronic evolution generate a high burden of disease due to morbidity, disability, mortality and health costs associated with reinterventions and rehabilitation. For this reason, the interest in this disease has been increasing, also justified by the little information there is about it, unlike unilateral chronic subdural hematomas, although it has been described that both may have pathophysiological similarities that help to understand them.

Introduction

The average age of the population has been increasing and with it are associated several pathologies to which the elderly population is exposed, as well as environmental factors [1]. Chronic subdural hematomas (CSDH) are one of the most frequent conditions seen in the population over 65 years of age, however, there are several factors that may predispose to this disease [2,3].

Bilateral CSDH are collections of blood degradation products located between the dura mater and arachnoid, and the denomination of chronicity is given by the amount of time elapsed, which is between 2 or 3 weeks [2,4,5,6,7,8]. It has been described as a pathology that differs from unilateral hematomas in the form of clinical presentation and the rapidity with which it can progress and lead patients to marked deterioration if timely treatment is not carried out [9]. Pathophysiologically, bilateral CSDHs have no clear difference from their unilateral counterparts [9]. The treatment of choice is surgical and ranges from craniotomies and endoscopic treatment to YL-1 type hematoma needle aspiration [4]. Based on the above, the objective of this review is to present practical concepts on the identification and approach to chronic bilateral subdural hematoma.

Epidemiological focus of the disease

The incidence rate of bilateral CSDH ranges from 1-5 cases per 100,000 person-years to 7.4 per 100,000 in the elderly population [10–13]. The most frequent location of CSDH is supratentorial, as opposed to the posterior fossa, whose diagnosis and pathogenesis are poorly understood [14]. Likewise, the average age of patients diagnosed with CSDH has been found to range from approximately 62 to 74 years, and, in the case of bilateral CSDH, a study by Cheng et al found that the average age of patients was 79 years [2].

Predisposing factors of CSDH

Unlike acute subdural hematomas (Acute-SDH), CSDH are poorly associated with head trauma [2,15]. Despite this, trauma is considered to be the primary cause, as it has been reported to be associated with CSDH in 50-80% of cases [2]. On the other hand, antiplatelet and anticoagulant therapies, in addition to alcohol abuse, liver disease, renal disease in hemodialysis patients, and intracranial hypotension associated with ventricular shunt valves have been linked to the development of hematoma [2,3,5].

Pathophysiology of CSDH

In contrast to unilateral CSDH, the pathophysiology of bilateral CSDH is still unknown [9]. However, hypotheses and premises have been established as to what may be occurring, such as the involvement of the bridging veins [9,10]. When bilateral CSDH is present in the posterior cerebral region, blood deposition may be involved with the occipital, sigmoid and transverse sinuses [14]. The development and progression of the hematoma is gradual and slow, initially constituting a thick outer membrane around the hematoma that eventually results in a complete capsule about two weeks later [15], which requires cell proliferation for the formation of a collagen-rich granular tissue [5].

On the other hand, the increase in hematoma size may be related to the increased permeability of capillaries in the outer membrane of the hematoma, which consequently lead to high blood extravasation and plasma exudation [11]. In addition, there is localized inflammation characterized by increased fibrinolysis, release of tissue plasminogen activator and elaboration of angiogenic factors that promote neovascularization [5].

Clinical presentation of CSDH and its diagnosis

The form in which CSDH manifests itself is very variable and can even be confused with other more frequent entities such as stroke, Parkinson's disease, dementia, among others [3,5]. In general, cognitive impairment, headache, and motor deficits are the most common presenting symptoms [3,5,13], although patients have also been shown to manifest nausea, vomiting, mental changes, and convulsions. In a study by Huang Y. et al. in which 25 of the 98 people evaluated had bilateral CSDH, it was observed that headache and mental changes were the most common presenting symptoms, followed by nausea and finally seizures [16].

However, because CSDHs present in most cases with unilateral convexity [16], many studies have relied on the comparison of several clinical features between the two presentations in order to analyze the point differences in the frequency of presentation of a symptom, or other feature, between unilateral and bilateral CSDHs [13,16,17].

In a study by Agawa et al. it was observed that

symptoms such as headache, pupil abnormalities, and acute impairment of consciousness occurred more frequently in patients with bilateral CSDH, while hemiparesis occurred more frequently in patients with unilateral CSDH [13]. Likewise, in the study by Huang Y. et al. it was observed that hemiparesis is more frequently seen in patients with unilateral CSDH since, in the case of patients with bilateral CSDH, there is a lower possibility of the central brain structures being deflected due to the counterbalance of the mass effect on both sides, which is reflected in the radiological findings that showed a lower incidence of midline changes with respect to unilateral [16].

On the other hand, as mentioned above, CSDH are often confused with other diseases, so it is of utmost importance to be really informed about the symptomatology of pathologies with similar clinical presentation to CSDH, in order to be able to make the differential diagnosis together with other complementary diagnostic tests [5,16]. Over the years, cases have been reported in the literature on patients with bilateral CSDH presenting with isolated oculomotor nerve palsy, which is a rare symptom in the atypical clinical presentation of this pathology, as it is commonly associated with vascular disorders, posterior circulation aneurysms or with traumatic, inflammatory or neoplastic diseases [7,18]. Corrivetti et al, by 2016, published two case reports, one of them was about an 81-year-old patient with diabetes and on anticoagulant management who was referred to the hospital with headache and left palpebral ptosis, on physical examination he showed complete oculomotor nerve palsy and mydriasis, and his computed tomography (CT) scan showed bilateral CSDH. He subsequently underwent bilateral surgical evacuation and then, 24 hours after surgery, the ptosis had disappeared and the mydriasis gradually improved [7]. Based on the above, the authors refer that having at least one predisposing factor (diabetes mellitus, hypertension, among others) generates a nervous vulnerability, which is necessary but not sufficient to develop this symptom, in this way, It is suggested that the bilateral pressure exerted on both cerebral hemispheres causes a displacement of the posterior part of the brain causing a compression of the encephalic trunk and this, added to the cisternal compression and the narrow vascular corridor through which the oculomotor nerve passes, stretches and flattens the nerve leading to a nervous alteration [7,18].

On the other hand, Guppy et al, by 2017, reported a rare case of a patient with an abnormal gait, where it was initially thought to be cervical myelopathy due to stenosis, however, he also presented Parkinson's-like symptoms (decreased facial expression, random gait and stooped posture) so a CT scan was requested which subsequently showed bilateral CSDH. After drainage of the CSDHs the symptoms improved, with bilateral CSDH and cervical stenosis being the final diagnosis [19]. Finally, in order to confirm CSDH and to make the definitive diagnosis, patients usually undergo CT or MRI [10,11].

Therapeutic approach

Because bilateral CSDH usually occur in the elderly population with other comorbidities such as coagulation disorders, and because of their rapid clinical evolution compared to unilateral CSDH, it is of vital importance that they are detected early in order to be treated as efficiently and promptly as possible [3,5]. Therefore, two types of treatments have been proposed, which are classified into non-surgical procedures, such as the use of steroids or mannitol, which require a longer recovery time for symptoms and a prolonged hospital stay [3], and surgical procedures (surgical drainage), the latter being the best therapeutic alternative due to its wide range of procedures and the low morbimortality it represents [3,11].

To evaluate the patient's neurological status, the clinical severity of CSDH and the post-surgical evolution, the Markwalder classification system is used, with a scale ranging from grade 0 to 4, the higher the grade, the worse the patient's clinical situation [3,20]. The decision to surgically treat a bilateral CSDH, should be subject to two circumstances which are the clinical manifestations and the radiological findings which include the presence of a mass effect or a midline shift [5,16]. It is generally accepted that symptomatic patients should undergo surgery because surgical evacuation produces an immediate recovery and a favorable evolution in a high percentage of patients [5]. For surgery, neurosurgeons have proposed several surgical techniques such as small craniotomy with endoscopic removal, burr craniotomy with or without continuous drainage of the closed system, large craniotomy followed by hematoma removal

with membranectomy, cranial drilling (twist-drill), and others [5,11,21].

Indications for craniotomy include the presence of any clot causing symptomatology with or without failed conservative or less invasive management, evidence of radiographic progression during a time of conservative observation, and, in addition, craniotomy should be considered in cases of recurrence despite previous surgery or when there are clots with evidence of membranes that may inhibit evacuation [20].

On the other hand, it has been shown that some patients are treated surgically by auger punctures on the side of the subdural hematoma along with irrigation of the subdural space with normal saline, in addition to performing drainage of the closed system by silicone tubes that are removed after the drainage has slowed or stopped, or removal of the hematoma has been confirmed by postoperative CT scanning [10,11,16]. In addition, some patients with coagulation disorders who use anticoagulants as therapy have been shown to have vitamin K, fresh frozen plasma or prothrombin complex administered prior to surgery as a preoperative indication [5,13].

Complications

Recurrence is the most common complication of CSDH with an incidence that can vary from 0% to 31.6% depending on the surgical technique [22,23]. Recurrence is defined as re-accumulation of the hematoma with progressive neurological deficit and represents the main problem after initial trephination because about 20% of patients require at least one re-intervention [22]. A higher recurrence rate has been reported in patients with bilateral CSDH compared to patients with unilateral CSDH [23]. In some cases of bilateral CSDH, when the contralateral hematoma is asymptomatic and thin, trephination surgery is only performed in one side [24]. Up to 20% of these cases may require evacuation of the contralateral hematoma due to subsequent enlargement and appearance of symptoms after a certain period of time [24,25].

The pathophysiology of this complication is not fully understood [22], but in conjunction with bilateral hematoma, many factors have been proposed as predictive of postsurgical recurrence of CSDH [24], such as use and reinitiation of antiplatelet or anticoagulant therapy [22], postoperative midline shift, preoperative hematoma size, mean hematoma density, diabetes mellitus, and postoperative air harvesting [24]. Hematomas that are hypointense or isointense on preoperative MRI on the T1 sequence correlate with a high recurrence rate, because it may reflect intracellular deoxyhemoglobin, signifying relatively recent bleeding [24].

Craniostomy with trephination is a simple surgical procedure; however, postoperative bleeding is another well-known and devastating complication. In a study of 303 patients with CSDH, the incidence of acute postoperative intracranial hemorrhage was estimated to be approximately 4.57% [23]. It was initially attributed to hypertension and anticoagulation therapy in some patients, but later other mechanisms were discussed [22]. It was mainly attributed to a loss of autoregulation of blood vessels with subsequent hypertension and cortical hyperaemia following rapid brain shift after surgery with excessive drainage of the subdural space and hypoperfusion syndrome [22,23]. More studies are needed to be certain about the treatment of acute postoperative bleeding, but many authors recommend slow brain decompression to prevent rapid intracranial changes [22].

Infections are a rare complication of CSDH that can lead to subdural empyema [22,26]. A preexisting subdural hematoma can become infected through hematogenous infection, although the actual incidence rate of this complication is less than 1% of cases [26]. If suspected, it should be investigated with computed tomography as first-line imaging and as treatment, trephination lavage and craniotomy with complete evacuation of the hematoma have been proposed as surgical adjuncts to systemic antibiotic therapy [22,26].

The development of seizures or status epilepticus following CSDH evacuation is a complication with an overall incidence ranging from 1% to 23% [22,27]. Risk factors associated with the development of chronic hematomas are alcohol abuse, change of mental status, previous stroke, and hematoma density on CT scan [27,28].

In this order of ideas, it is necessary to produce more evidence of better quality on the global epidemiology, pathophysiology and management of bilateral chronic subdural hematoma, considering that it is a pathological condition that generates neurological disease burden. Similarly, training in their suspicion and identification, to promote

professionalism and practice in neurosurgery at the different levels of care. It is necessary to know data from low- and middle-income countries, where there are difficulties in the management of pathologies such as these, due to the absence of specialized centers in rural regions [29,34]. Especially in the pandemic and post-pandemic period where funding for research in lines other than emerging infectious diseases has been lost [35-37].

Conclusions

It is important to recognize the differences in presentation between unilateral and bilateral CSDH, as well as with other pathologies of similar presentation that do not require urgent imaging methods, as this may confuse the diagnosis and delay treatment. Bilateral hematoma tends to involve greater mass displacement than unilateral hematoma and reduces the autonomic capacity to buffer increased intracranial pressure, making it even more important to implement early surgical decompression of bilateral mass lesions in order to prevent rapid neurological deterioration. Healthcare professionals should be aware of the higher incidence of recurrence in patients with bilateral treatment, the risk factors and signs for early detection of recurrence, as well as other complications that, although of lower incidence, represent a risk for patient survival.

References

1. Castro-Rodríguez C, Román-Pena P, Arán-Echabe E, Gelabert-González M. Hematoma subdural crónico en pacientes muy ancianos. Rev Esp Geriatr Gerontol. 2016; 51(6):309–16.
2. Hsieh C, Su I, Hsu S, Huang C, Lian F, Chang C. Chronic subdural hematoma: Differences between unilateral and bilateral occurrence. J Clin Neurosci. 2016; 34(2016):252–8.
3. Gelabert-González M, Arán-Echabe E, Bandín-Diéguez FJ, Santín-Amo JM, Serramito-García R, Prieto-González Á, et al. Hematoma subdural crónico bilateral: análisis de una serie de 190 pacientes. Neurocirugia. 2016; 27(3):103–11.
4. Chen L, Dong L, Wang XD, Zhang HZ, Wei M, She L. Bilateral Chronic Subdural Hematoma Treated by YL-1 Type Hematoma Aspiration Needle Complicated by Hemorrhage of the Basal Ganglia and Brainstem. World Neurosurg. 2017; 97:761.e11-761.e13.
5. Gelabert-González M, Rico-Cotelo M, Arán-Echabe E. Chronic subdural hematoma. Med Clínica (English Ed). 2015; 144(11):514–9.
6. Daniel R, Servadei F. 45 - Complications After Surgery for Chronic Subdural Hematomas. Complications in Neurosurgery. Elsevier Inc; 2018. 274–279.
7. Corrivetti F, Moschettoni L, Lunardi P. Isolated Oculomotor Nerve Palsy as Presenting Symptom of Bilateral Chronic Subdural Hematomas: Two Consecutive Case Report and Review of the Literature. World Neurosurg. 2016; 88:686.e9-686.e12.
8. Goodman JC. 338 Neuropathology of Traumatic Brain Injury. Seventh Edition. Youmans and Winn Neurological Surgery, 4-Volume Set. Elsevier Inc.; 2018. 2765-2777.e2.
9. Huang Y, Yang K, Lee T, Liao C. Bilateral chronic subdural hematoma: What is the clinical significance? Int J Surg. 2013; 11(7):544–8.
10. Park HS, Park ES, Park JB, Kwon SC, Lyo IU, Kim M, et al. Chronic Subdural Hematomas: Comparison between Unilateral and Bilateral Involvement. Korean J Neurotrauma. 2014; 10(2):55.
11. Lee J, Park JH. Clinical Characteristics of Bilateral versus Unilateral Chronic Subdural Hematoma. Korean J Neurotrauma. 2014;10(2):49.
12. Luongo M, Grassi M, Godano U. Bilateral Chronic Subdural Nontraumatic Hematoma in a Woman Affected by AL Amyloidosis. J Neurol Surg Reports. 2015 Jun 26;76(01):e164–6.
13. Agawa Y, Mineharu Y, Tani S, Adachi H, Imamura H, Sakai N. Bilateral Chronic Subdural Hematoma is Associated with Rapid Progression and Poor Clinical Outcome. Neurol Med Chir (Tokyo). 2016; 56(4):198–203.
14. Takemoto Y, Matsumoto J, Ohta K, Hasegawa S, Miura M, Kuratsu J. Bilateral posterior fossa chronic subdural hematoma treated with craniectomy: Case report and review of the literature. Surg Neurol Int. 2016; 7(11):255.
15. Herath HMMTB, Matthias AT, Kulatunga A. Acute on chronic bilateral subdural hematoma presenting with acute complete flaccid paraplegia and urinary retention mimicking an acute spinal cord injury: a case report. BMC Res Notes. 2017; 10(1):627.
16. Huang YH, Yang KY, Lee TC, Liao CC. Bilateral chronic subdural hematoma: What is the clinical significance? Int J Surg. 2013; 11(7):544–8.
17. Jukovic M, Petrovic K, Till V. The question is whether hemiparesis is more common in unilateral than bilateral chronic subdural hematoma. Med Pregl. 2014; 67(9–10):277–81.
18. Matsuda R, Hironaka Y, Kawai H, Park Y-S, Taoka T, Nakase H. Unilateral Oculomotor Nerve Palsy as an Initial Presentation of Bilateral Chronic Subdural Hematoma: Case Report. Neurol Med Chir (Tokyo). 2013; 53(9):616–9.
19. Guppy KH, Khandhar SM, Ochi C. Reversible Parkinson-Like Symptoms in Patient with Bilateral Chronic Subdural Hematomas and Cervical Spinal Stenosis. World Neurosurg. 2018; 109:285–90.
20. Abecassis IJ, Kim LJ. Craniotomy for Treatment of Chronic Subdural Hematoma. Neurosurg Clin N Am. 2017; 28(2):229–37.
21. Xu M, Yu B, Wang C, Zhu X, Lu X, Chen P, et al. Minimally invasive approach in bilateral chronic subdural

hematomas: surgical selection and outcome in 74 cases. Turk Neurosurg. 2016; 27(3):380–5.
22. Viaroli E, Iaccarino C, Maduri R, Daniel RT, Servadei F. 45 - Complications After Surgery for Chronic Subdural Hematomas. Complications in Neurosurgery. Elsevier Inc.; 2018. 274–279 p.
23. Hsieh C-T, Su I-C, Hsu S-K, Huang C-T, Lian F-J, Chang C-J. Chronic subdural hematoma: Differences between unilateral and bilateral occurrence. J Clin Neurosci. 2016; 34(2016):252–8.
24. Fujitani S, Ishikawa O, Miura K, Takeda Y, Goto H, Maeda K. Factors predicting contralateral hematoma growth after unilateral drainage of bilateral chronic subdural hematoma. J Neurosurg. 2017; 126(3):755–9.
25. Motiei-Langroudi R, Thomas AJ, Ascanio L, Alturki A, Papavassiliou E, Kasper EM, et al. Factors Predicting the Need for Surgery of the Opposite Side After Unilateral Evacuation of Bilateral Chronic Subdural Hematomas. Neurosurgery. 2018; 1–8.
26. Dabdoub CB, Adorno JO, Urbano J, Silveira EN, Orlandi BMM. Review of the Management of Infected Subdural Hematoma. World Neurosurg. 2016; 87:663.e1-8.
27. Won SY, Konczalla J, Dubinski D, Cattani A, Cuca C, Seifert V, et al. A systematic review of epileptic seizures in adults with subdural haematomas. Seizure. 2017; 45:28–35.
28. Kumar M, Yadav K, Verma S, Maheshwari V. Idiopathic bilateral chronic subdural hematoma with left internal carotid artery infarct in a 3 months infant: A rare case report. J Pediatr Neurosci. 2016; 11(4):364.
29. Lozada-Martínez I, Maiguel-Lapeira J, Torres-Llinás D, Moscote-Salazar L, Rahman MM, Pacheco-Hernández A. Letter: Need and Impact of the Development of Robotic Neurosurgery in Latin America. Neurosurgery. 2021; 88(6):E580-E581.
30. Herrera-Martinez MP, García-Ballestas E, Lozada-Martinez I, Torres-Llinás D, Moscote-Salazar L. Letter to the Editor. Creating the conditions for gender equality to end sexual harassment in neurosurgery. J Neurosurg. 2021 Feb 5:1-2.
31. Gaitan-Herrera G, Lozada-MartÍnez I, Acevedo-Aguilar L, Bohorquez-Caballero A, Moscote-Salazar L. Simulation as a tool to educate the patient about neurosurgical pathology. J Neurosurg Sci. 2021 Jan 22
32. Ortega-Sierra MG, Durán-Daza RM, Carrera-Patiño SA, Rojas-Nuñez AX, Charry-Caicedo JI, Lozada-Martínez ID. Neuroeducation and neurorehabilitation in the neurosurgical patient: programs to be developed in Latin America and the Caribbean. J Neurosurg Sci. 2021 Jun 10.
33. Blanco-Teherán C, Quintana-Pájaro L, Narvaez-Rojas A, Martínez-Pérez R, García-Ballestas E, Moscote Salazar L, et al. Evidence-based medicine in neurosurgery: why and how? J Neurosurg Sci. 2021 Aug 3.
34. Ortega-Sierra MG, Prado-Grajales V, Martinez-Imbett R, Unás-Perea K, Lozada Martinez ID. Research career in neurosurgery: a challenge for future neurosurgeons. J Neurosurg Sci. 2021 Aug 3.
35. Zuluaga-Ramírez P, Lozada-Martínez I, Moscote-Salazar L, Cabrera-Vargas L. Sexual harassment and racism in surgery: A latent problem. Int J Surg. 2021; 86:13-14.
36. González-Herazo MA, Silva-Muñoz DC, Guevara-Martínez PA, Lozada-Martinez ID. Post-COVID 19 Neurological Syndrome: a fresh challenge in neurological management. Neurol Neurochir Pol. 2021;55(4):413-414
37. Llamas-Nieves A, Maiguel-Lapeira J, Lozada-Martinez I, Torres Llinas D, Moscote-Salazar L. The desire to publish a scientific article and the difficulties of publishing it in a highquality neurosurgery scientific journal. J Neurosurg Sci. 2021 Mar 11.

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Posterior fossa extradural hematoma - clinical presentation and outcome. A single centre experience from India

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ABSTRACT

Background: Posterior Fossa Extra Dural Hematoma (PFEDH) is a rare entity but certain crucial structures are supposed to be injured. Because of limited space in the posterior fossa, a clinical small volume of hematoma can deteriorate patients. Therefore, timely diagnosis and prompt intervention are required.

Objective: This study is done to analyse factors like demographic profile, mode of injury, clinical features in relation to PFEDH and its management and how they influence the outcome.

Materials & methods: This is a retrospective analysis of patients who presented with PFEDH from July 2016 to July 2021 at RNT Medical College and M.B. group of Hospitals Udaipur, India. Patients were evaluated on the basis of demographic profile, mode of injuries, GCS on admission & discharge, and associated radiological findings.

Result: A total of 25 patients with PFEDH were included in this study. Amongst these, 18 (72%) were males, and10 (40%) were less than 18 years of age. On admission 19 (76%) had GCS 13-15.22 (88%) patients underwent surgery and 3 (12%) were planned for conservative management. At 6-month follow-up, 22 (88%) patients had good outcomes with GOS 3-5 and 1 was lost to follow up while 2 (8%) had poor outcomes with GOS 1-2.

Conclusion: GCS on admission is a good predictor of outcome. The volume of EDH was one of the key factors in deciding the line of management. PFEDH can sometimes be rapidly fatal due to expansion of hematoma and compression of posterior cranial fossa space which leads to brain stem compression therefore time management is the most important factor for a good outcome.

Keywords
posterior fossa,
extradural hematoma,
EDH

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INTRODUCTION

Extradural hematoma is said to be the most frequently encountered traumatic neurological pathology. But PFEDH has only 4–7% incidence (1.2–15% in various studies for all age groups) of all extradural hematomas.[1,2] EDH comprises the most frequent traumatic space-occupying lesion of the posterior fossa.[12] Posterior fossa is unique

because it contains the brain stem and is smaller in volume than the supratentorial compartment of the cranium.

Though relatively infrequent in occurrence, early identification and immediate appropriate management of Posterior Fossa Extradural Hematoma (PFEDH) is essential for successful neurotrauma management.[4] In PFEDH clinical progress may be silent and slow, but sudden deterioration may occur without significant warning signs. PFEDH can present with quick clinical deterioration because of rapid increasing in size and may cause brain stem compression. Management of PFEDH is either surgical or conservative based on clinical condition and various other factors.

Conservative management has shown good results both in children and in adults in cases of traumatic posterior fossa extra dural hematoma.

Materials and methods

This is a retrospective study from July 2016 to July 2021 at a tertiary care centre, R.N.T. Medical college & M.B. Group of Hospitals, Udaipur, Rajasthan. This study includes 25 cases of traumatic extradural hematoma which were located in posterior fossa.

Patients were categorised on the basis age, sex, mode of injury, GCS on admission, CT findings, volume of PFEDH, type of intervention and post-operative outcome.

Outcome was assessed by GOS at discharge and at 6 months follow-up.

Results

This study includes 25 cases of traumatic posterior fossa extradural hematoma taken over a period of 60 months from July 2016 to July 2021. The mean age of patients was 26.6 (5-48 years).18 (72%) were males amongst these .10 (40%) patients were below 18 years. RTA was found to be the most common mode of injury amongst these patients 18 (72%). Rest were either fall from height or assault. Majority of these patients had GCS 13-15, 19 (76%) when presented to emergency department. 21 (84%) patients were brought within 1 hour of trauma. Headache, vomiting and altered sensorium were few common symptoms found in most of these patients. All patients underwent non contrast CT brain and PFEDH was found in all. PFEDH was unilateral in 23 cases (92%). Occipital bone fracture was found in 17(68%) patients f/b supratentorial extension in 3 (12%) patients, acute subdural hematoma in 1 (4%) patient, frontal contusion in 2 (8%), hydrocephalus and IVH was also present in 1 (4%) patient.Volume of PFEDH was >15 cc in 22(92%) patients and <15 cc in 3 (12%) patients.

Amongst these patients 22 (88%) underwent surgery and 3 (12%) were planned for conservative management. Decesion was based on volume of PFEDH and GSC at admission and associated injuries. Incision and craniotomy were made as per the site and size of EDH.

All operated patients were subjected to early NCCT brain postoperatively.

On discharge 23 (92%) patients had GCS 13-15 and 2 (8%) had GCS of 9-12. Patients who were admitted within 1 hour of trauma had better outcome at discharge, signifying the importance of very early intervention before deterioration. At 6 month follow up 22 (88%) had good outcome with GOS 5, 1(4%) was lost to follow up and 2 (8%) eventually had poor outcome with GOS 2.

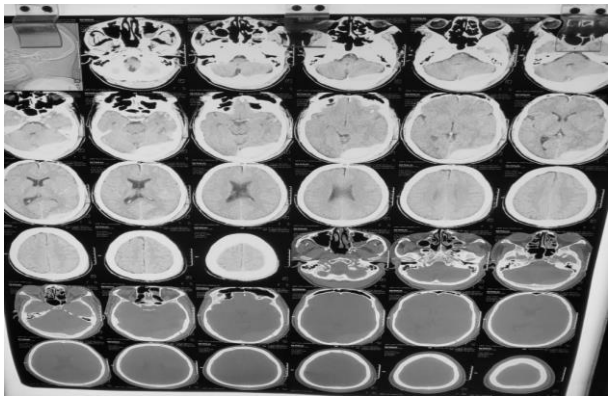

Figure 1. NCCT head showing extradural hematoma in posterior fossa on left side.

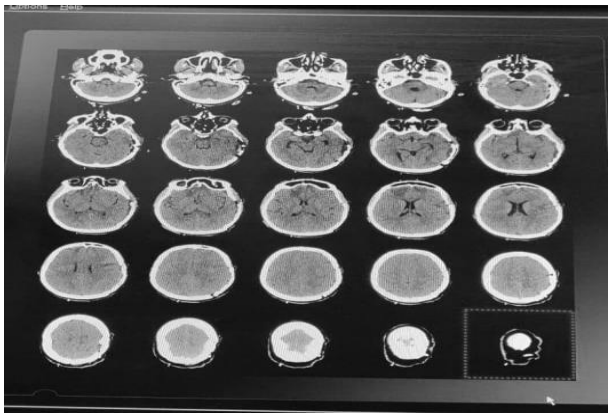

Figure 2. Post-operative NCCT head after evacuation of extradural hematoma.

Discussion

Post-traumatic posterior fossa extradural hematoma is a rare entity. Incidence is 0.3% of all craniocerebral injuries, and 4-12% of all extradural hematomas.[7]

Posterior cranial fossa lodges some important vital structures of brain, like brain stem. If PFEDH is large, it can cause rapid fall in consciousness level and brain stem dysfunction.

PFEDHs have a venous origin in 85% of the cases and develop as a result of injury to the transverse or sigmoid sinuses secondary to occipital bone fracture.[17] For PFEDH, it takes longer to develop clinical picture and it is of vital importance to use imaging methods for early diagnosis. An acute extradural hematoma is seen as a biconvex hyperdense mass located between the duramater and the bone on NCCT. An acute extradural hematoma is demonstrated as a localized extra-axial collection of blood between dura and inner table of skull bones on magnetic resonance imaging. Imaging of dura as a line with very low signal intensity between the hematoma and brain parenchyma is pathognomonic for extradural hematoma. MR imaging modality is more sensitive in detection of parenchymal conditions or dural venous sinus thrombosis possibly associated with PFEDH.[13,14]

Still Imaging of choice and the most commonly used method is NCCT because of a short acquisition time, allowing demonstration of occipital fractures that are associated with great majority of PFEDHs. It also defines the size and mass effects of the hematoma and also provide visualization of possible supratentorial conditions that are reported to be associated with half of the cases in the literature[15,5] and MR imaging study is difficult in unstable trauma patients. Among all the clinico-radiological parameters, volume of PFEDH is the most important factor in deciding the line of management, as also suggested by Prasad et al.[6]

Occipital subgaleal haematoma and Battle's sign can be a clue to the diagnosis of PFEDH. Fracture of the occipital bone is an important sign and it necessitates close observation along with repeat CT scan later to diagnose these haematomas. Change in GCS or severe headache with vomiting and new onset cerebellar signs are associated features that can help to have an idea of diagnosis. Hydrocephalus may be observed in as high as 30% of cases on the CT scan.

All the patients who required surgery in this study had volume of PFEDH more than 15cc. This is similar to the observation of Bozbuga et al.[8] Patients with PFEDH should be operated based on radiological indications without waiting for clinical deterioration, in order to get a good outcome. Paediatric patients with PFEDH require surgery more often than adults because of smaller posterior fossa volume and elderly require surgery less often, as atrophic brain can accommodate more volume.[10]

Admission GCS score is the single most important predictor of outcome, with GCS more than 8 having strong association with good outcome (GOS 5). GCS at admission is found directly proportional to GCS at discharge, better the GCS i.e. >8 better the outcome seen. Our study is also in line with this fact and is consistent with that reported by Balik et al, Jang et al and Prusty et al.[11,16] PFEDH needs more urgent management, before irreversible brainstem herniation occurs. This requires vigilant paramedical and medical care right from the site of accident, early shifting to neurosurgical care, high index of suspicion in cases of occipital trauma and prompt management.

Conservative management can also be an option if the patient is asymptomatic and has good GCS. The patient should be kept under close monitoring in neurosurgical intensive care unit (ICU). There are some case reports in the literature about these haematomas which resolved spontaneously without any intervention.[3]

3(12%) cases in our study were managed conservatively out of which 1(4%) did not report back at follow up of 6 month. In our study, PFEDH was more common among male than female patients Similarly Prashant et al also showed in their study that more males suffered from head trauma as compared to females because of more exposure of males to traffic and outdoor activities than females.[9] RTA being the most common mode of injury in our study was in line with the studies Bavil MS et al[3]and Igun GO et al.[9]

Patients with associated intracranial findings, with mass effect over brainstem had lesser GCS score on admission, increased EDH volume had increased hospital morbidity compared to other patients. Occipital bone fracture was found in 68% patients which was in line with that reported by Karasu et al.

Conclusions

PFEDHs are rare. Early diagnosis and emergent evacuation lead to good outcome and also reduces morbidity. Occipital bone fractures and associated injuries in form of supratentorial or infratentorial subdural hematoma, intraparenchymal hematoma or intraventricular haemorrhage can also be present. Clinical progression of disease is silent and slow, but the deterioration is sudden and quick. It can lead to serious complications if not promptly diagnosed and treated.

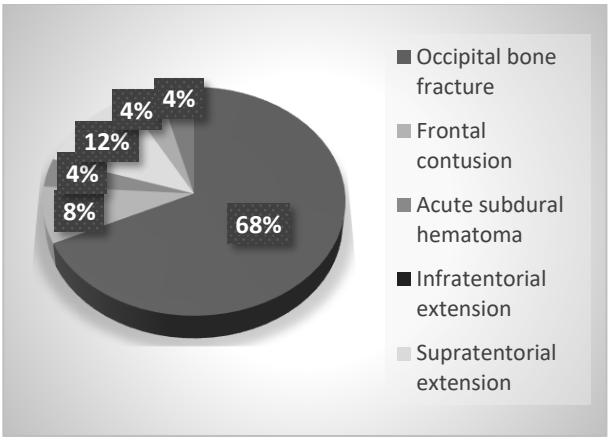

Figure 3. Distribution of radiological findings

Table 1. Demographic data

Gender	Number of cases	Percentage
Male	18	72%
Female	7	28%
Age		
<18	10	40%
>18	15	60%

Table 2. Mode of injury

RTA	18	72%
Fall	6	24%
Assault	1	4%

Table 3. Radiological findings

Occipital bone fracture	17	68%
Frontal contusion	2	8%
Acute subdural hematoma	1	4%
Infratentorial extension	0	0
Supratentorial extension	3	12%
Hydrocephalus	1	4%
Intra ventricular hemorrhage	1	4%

Table 4. GCS

At admission		
13-15	19	76%
9-12	4	16%
<8	2	8%
At discharge		
13-15	23	92%
9-12	2	8%
<8	0	0

Table 5. Volume of PFEDH

<15	3	12%
>15	22	88%

Table 6. Management

Conservative	3	12%
Surgery	22	88%

Table 7. Outcome based on GOS

Outcome based on GOS	At discharge	At 6 month
GOS 5	21(84%)	22 (88%)
GOS 4	2(8%)	1 (4%)
GOS 3	1 (4%)	0
GOS 2	1 (4%)	1 (4%)
GOS 1	0	0

Conflicts of interest
The authors declare no conflict of interest.

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

References

1. Ammirati M, Tomita T. Posterior fossa epidural hematoma during childhood.
2. Asanin B. Traumatic epidural hematomas in posterior cranial fossa. Acta Clin Croat 2009;48:27 30.
3. Bavil MS. Autopsy Findings in Patients with Severe Head Injury. Res J Med Sci 2008;2(4):190.
4. Berker M, Cataltepe O, Ozcan OE. Traumatic epidural haematoma of the posterior fossa in childhood: 16 new cases and a review of the literature. Br J Neurosurg 2003;17:226 9.
5. Bozbuğa, M., İzgi, N., Polat, G., & Gürel, I. (1999). Posterior fossa epidural hematomas: observations on a series of 73 cases. Neurosurgical review, 22(1), 34-40.1.
6. Ersahin, Y., & Mutluer, S. (1993). Posterior fossa extradural hematomas in children. Pediatric neurosurgery, 19(1), 31-33, doi:10.1159/000120697.
7. Garza-Mercado R. Extradural hematoma of the posterior cranial fossa. Report of seven cases with survival. J Neurosurg. 1983;59(4):664-72.
8. Balik, V., Lehto, H., Hoza, D., Sulla, I., & Hernesniemi, J. (2010). Posterior fossa extradural haematomas. Central European Neurosurgery-Zentralblatt Neurochirurgie, 71(04), 167-172, doi:10.1055/s-0030-1249046.
9. Igun GO. Predictive Indices In Traumatic Intracranial Haematomas. East Afr Med J 2000;77(1):9.
10. Jang, J. W., Lee, J. K., Seo, B. R., & Kim, S. H. (2011). Traumatic epidural haematoma of the posterior cranial fossa. British journal of neurosurgery, 25(1), 55- 61, doi:10.3109/02688697.2010.520759 11. Prusty, G. K., & Mohanty, A. (1995). Posterior fossa extradural haematoma. Journal of the Indian Medical Association, 93(7), 255-8.
11. Kang SH, Chung YG, Lee HK. Rapid disappearance of acute posterior fossaepidural hematoma. Neurol Med Chir (Tokyo). 2005;45(9):462-3.
12. Koc RK, Pasaoglu A, Menkii A, Oktem S, Meral M. Extradural hematoma of the posterior cranial fossa. Neurosurg Rev 1998;21:52-7.
13. Osborn AG. Craniocerebral Trauma, Diagnostic Neuroradiology. St. Louis: Mosby; 1994. p. 204 5.
14. Pozzati E, Tognetti F, Cavallo M, Acciarri N. Extradural hematomas of the posterior cranial fossa. Observations on a series of 32 consecutive cases treated after the introduction of computed tomography scanning. Surg Neurol 1989;32:300 3.
15. Prasad GL, Gupta DK, Sharma BS, Mahapatra AK. Traumatic pediatric posterior fossa extradural hematomas: A tertiary-care trauma center experience from India. Pediatr Neurosurg 2015;50:250-6.
16. Prashant G, Atul K, Amit D, Kumkum G, Madhu B, Gouri G, et al. CT Scan Findings and Outcomes of Head Injury Patients: A Cross-Sectional Study. J Pak Med Stud 2011;1(3):78–82.
17. Samudrala S, Cooper PR. Traumatic intracranial hematomas. In: Wilkins RH, Rengachary SS, editors. Neurosurgery. 2nd ed. New York: McGraw Hill; 1996. p. 2797 807.

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Delayed cerebrospinal fluid ascites following ventriculoperitoneal shunt. A case report with literature review

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ABSTRACT

Background: Cerebrospinal fluid (CSF) ascites is an abnormal accumulation of CSF within the peritoneal cavity caused by the peritoneum's inability to absorb the CSF, following a ventriculoperitoneal (VP) shunt surgery. Excessive CSF production (e.g, choroid plexus papilloma and choroid plexus villous hypertrophy), high CSF protein secondary to chronic infection (e.g., tuberculosis), and brain tumours (e.g, optic gliomas and craniopharyngiomas) have all been suggested as contributing factors to the formation of CSF ascites. Peritoneal inflammation as a result of several shunt revisions or some non-specific inflammatory reaction to shunt material has also been explored.

Case Presentation: A 3-year-old girl with lumbar myelomeningocele and delayed CSF ascites following VP shunt is reported. Therapeutic paracentesis was employed to relieve abdominal distension, although recurring accumulation was common. The VP shunt was removed and instead of a Ventriculo-atrial shunt, she underwent Endoscopic Third Ventriculostomy (ETV). CSF ascites gradually disappeared after ETV over a two-week period.

Conclusions: Abdominal paracentesis to relieve ascites and conversion of a Ventriculoperitoneal shunt to a Ventriculo-atrial shunt are commonly used to treat CSF ascites, however Endoscopic Third Ventriculostomy, where feasible, is another alternative treatment that can be performed to treat this condition.

Keywords
hydrocephalus, cerebrospinal fluid ascites, endoscopic third ventriculostomy

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INTRODUCTION

The most frequent procedure for hydrocephalus is a ventriculo-peritoneal (VP) shunt. They have been linked to a variety of issues, including dysfunction, infection, blockage, and migration. Rarely, the patient may develop increasing abdominal distention as a result of cerebrospinal fluid (CSF) accumulation. This is commonly referred to as a pseudocyst. The omentum produces a cyst at the tip of the shunt as a result of inflammation, resulting in a fluid-filled sac. Ascites is caused by a production-absorption mismatch or a non-absorbing peritoneum in very uncommon cases.[46] Ascites owing to hepatic, renal, or cardiac illness must be distinguished from CSF ascites, which is an abnormal buildup of CSF within the peritoneal cavity[38].

CSF ascites is a distinct condition in which there is an excessive

accumulation of CSF in the peritoneal cavity due to the peritoneum's inability to absorb it. This incapacity could be the result of a large amount of CSF being produced.[23] There have been several hypotheses on what factors may lead to the development of CSF ascites. Excessive CSF production (as in choroid plexus papilloma and choroid plexus villous hypertrophy), high CSF protein secondary to chronic infection (e.g. tuberculosis), and brain tumours (e.g, optic gliomas and craniopharyngiomas) have all been suggested as contributing factors to the formation of CSF ascites. Peritoneal inflammation as a result of several shunt revisions or some non-specific inflammatory reaction to shunt material has also been explored.[46] After ensuring that there is no infection, the VP shunt associated CSF ascites is treated by converting the shunt to a Ventriculoatrial shunt. Endoscopic Third Ventriculostomy (ETV) is another treatment option that can be done to treat this condition in selective cases.

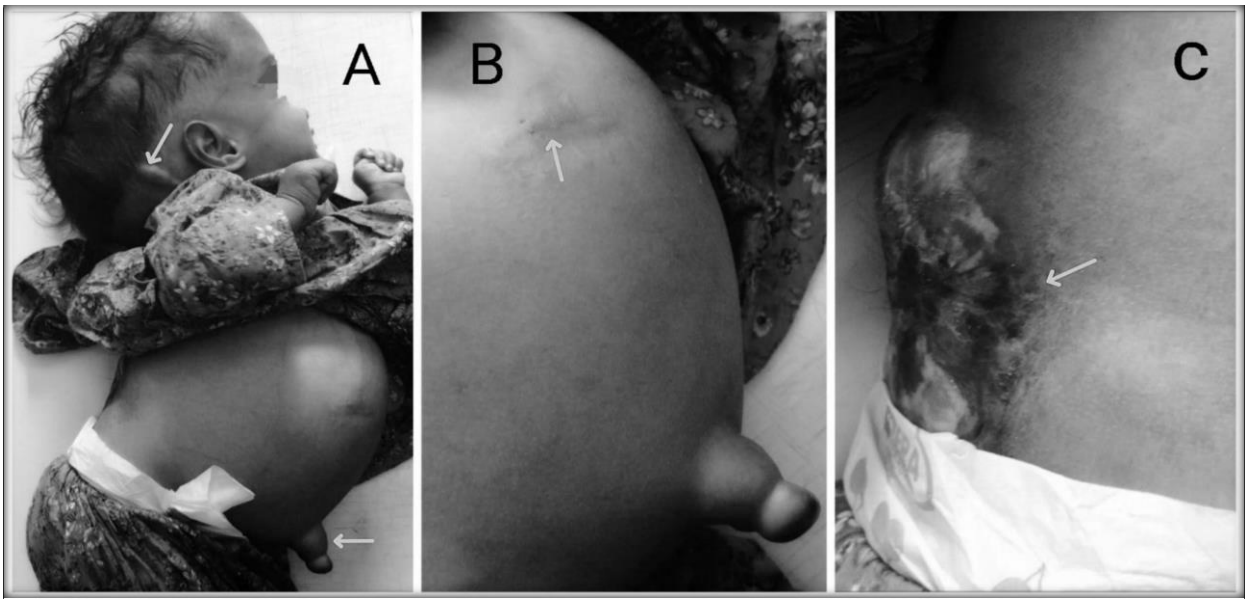

Figure 1. A: CSF swelling at reservoir site of VP shunt with distended abdomen and umbilical hernia due to CSF ascites, **B**: Abdominal incisional scar for VP shunt, **C**: Lumbar Myelomeningocele.

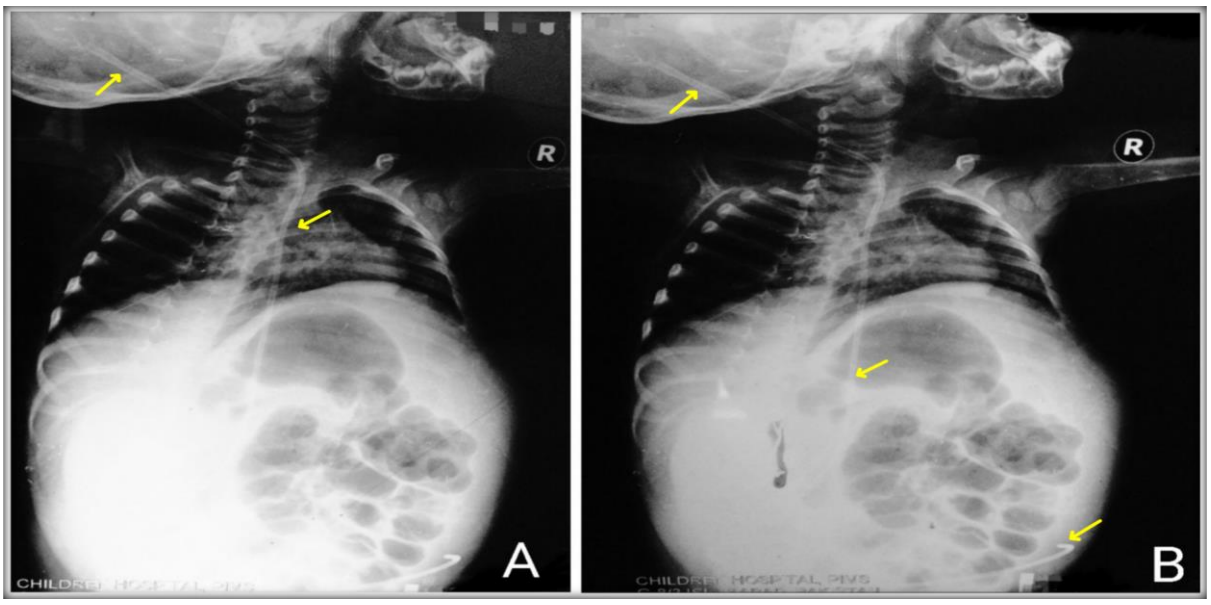

Figure 2. A & B: X-ray shunt series showing VP shunt tubing marked by yellow arrows

Table 1. Detailed literature review of 77 previously reported cases of CSF ascites and their treatment.

S.no.	Author's Name	Year reported	No. of cases reported	Gender/Age	Cause/Type of Hydrocephalus	Treatment for CSF ascites
1	R H Ames[1]	1967	1	M/2 years	Congenital hydrocephalus	Ventriculo-atrial shunt
2	D F Dean[2]	1972	1	M/1 year	Aqueductal stenosis	Ventriculo-atrial shunt
3	J D Rosenthal[3]	1974	1	F/3 years	Suprasellar mass (Astrocytoma)	Ventriculo-jugular shunt
4	Michael J. Weidmann[4]	1975	1	F/3 months	Aqueductal stenosis	Multiple Paracentesis followed by Ventriculo-atrial shunt
5	SW Parry[5]	1975	1	M/7 months	Communicating hydrocephalus	Ventriculo-atrial shunt
6	J Cummings[6]	1976	1	-	Unknown	-
7	R F Lees[7]	1978	2	-	Unknown	-
8	J M Noh[8]	1979	1	-	Unknown	-
9	S C Ohaegbulam[9]	1980	1	-	3rd ventricle compression by recurrent craniopharyngioma	Spontaneous resolution following Paracentesis
10	A B Adegbite[10]	1982	1	F/11 years	Recurrent craniopharyngioma	VP shunt removal leading to resolution of ascites followed by new VP shunt
11	FP Agha[11]	1983	1	M/7 years	Suprasellar astrocytoma	Ventriculo-atrial shunt
12	R A Yount[12]	1984	4	1-F/6 years, 2-F/20 years, 3-M/4 years, 4-F/3 years	1-Communicating hydrocephalus, 2-Unknown, 3-Optic nerve glioma, 4-Optic nerve glioma	1-Ventriculo-cholecystic shunt, 2-Paracentesis and multiple taps of shunt reservoir, 3-Paracentesis and low-sodium diet, 4-Spontaneous resolution with fluid-restricted diet
13	Gairi Tahull JM[13]	1984	1	F/5 years	Communicating hydrocephalus	Ventriculo-atrial shunt
14	DS Rush[14]	1985	4	-	-	VP shunt revisions

15	D Madruga Acerete[15]	1988	1	F/12 years	Dandy-Walker malformation	-
16	G M Goodman[16]	1988	1	F/11 years	Hydrocephalus following lumbar myelomeningocele repair	Ventriculo-atrial shunt
17	S Niikawa[17]	1988	1	F/45 years	Post-infectious obstructive hydrocephalus	-
18	F Pérez Peña[18]	1990	1	M/17 years	Malformation hydrocephalus	-
19	A Suárez[19]	1993	1	M/22 years	Craniopharyngioma	Ventriculo-atrial shunt
20	A West[20]	1994	3	1-M/6 months, 2-M/6 years, 3-M/8 months	Optic pathway gliomas	Ventriculo-atrial shunts
21	A Shuper[21]	1997	1	F/4 years	Optic chiasm glioma	Ventriculo-atrial shunt
22	Michiko Yukinaka[22]	1998	1	F/23 years	Congenital hydrocephalus with spina bifida	Ventriculo-atrial shunt
23	B Chidambaram[23]	2000	2	1-F/3 months, 2-M/7 years	1-Congenital hydrocephalus, 2-Optic chiasm glioma	1-Ventriculo-atrial shunt, 2-Ventriculo-atrial shunt
24	Z Gil[24]	2001	4	1-M/9 years, 2-M/0.5 years, 3-M/0.5 years, 4-M/4 years	1-Optic pathway glioma, 2-Optic pathway glioma, 3-Optic pathway glioma, 4-Chiasmatic glioma	Ventriculo-atrial shunts
25	BH Lee[25]	2001	1	M/68 years	-	VP shunt removal and antibiotics
26	GF Longstreth[26]	2001	1	F/28 years	Communicating hydrocephalus	Ventriculo-atrial shunt
27	GY Lee[27]	2002	1	F/33 years	Congenital hydrocephalus	Ventriculo-atrial shunt
28	Nayyar Yaqoob[28]	2003	1	M/17 years	Tuberculous meningitis	Anti-tuberculous therapy followed by Ventriculo-atrial shunt
29	Raj Kumar[29]	2003	4	1-M/9 years, 2-M/2 years,	1-Thalamic glioblastoma,	1-Paracentesis revealed peritoneal mets,

				3-M/4 years, 4-M/8 years	2-Choroid plexus papilloma of 3rd ventricle, 3-Tuberculous meningitis, 4-Craniopharyngioma	2-Ventriculo-atrial shunt followed by total excision of tumor, 3-Intraperitoneal cyst decompression, 4-Abdominal exploration and VP shunt revision
30	SJ Pawar[30]	2003	2	1-M/8 months, 2-M/2 years	Choroid plexus papilloma of posterior 3rd ventricle	1-VP shunt revision, 2-Ventriculo-atrial shunt
31	Greg Olavarria[31]	2005	4	1-M/8 months, 2-M/8 months, 3-F/12 months, 4-F/12 months	Optic chiasmal hypothalamic astrocytoma	1-Ventricular gallbladder shunt, 2-Ventricular gallbladder shunt, 3-Ventricular gallbladder shunt, 4-Ventricular gallbladder shunt converted to Ventriculo-atrial shunt
32	Michael L Diluna[32]	2006	1	M/4 years	Arachnoid cyst	Ventriculo-atrial shunt
33	Rajeev Kariyattil[33]	2007	5	3 males, 2 females Mean age: 3.7 years	1 Posterior fossa arachnoid cyst, 1 Hemorrhage, 1 Optic chiasm glioma, 1 Craniopharyngioma, 1 Meningomyelocele	4 Ventriculo-atrial shunts, 1 Spontaneous resolution after hypoproteinemia treatment
34	Paik I[34]	2010	1	F/21 years	Myelomeningocele	Ventriculo-atrial shunt
35	S Das[35]	2010	1	M/7 years	Craniopharyngioma	Ventriculo-atrial shunt
36	N Montano[36]	2010	1	F/51 years	Obstructive hydrocephalus due to large Vestibular Schwannoma	VP shunt removal, EVD placement, IV Teicoplanin and multiple ascitic fluid taps
37	WJ Wilma Houtman-van Duinen[37]	2011	1	F/29 years	Congenital Cervical Meningocele	Ventriculo-atrial shunt
38	MWANG'OMBE Nimrod Junius[38]	2012	1	M/7 years	Aqueductal stenosis	Ascites resolved within two weeks of endoscopic third ventriculostomy
39	Yin Yee Sharon Low[39]	2012	1	F/48 years	Brain Mets from Breast Carcinoma with Obstructive hydrocephalus	Peritoneal drain

40	Atakan Comba[40]	2013	1	F/6 years	Myelomeningocele	Ventriculo-atrial shunt
41	J Woodfield[41]	2013	1	F/1 year	Craniopharyngioma	Ventricular gallbladder shunt converted to Ventriculo-atrial shunt
42	Hira Jamal[42]	2016	1	F/37 years	Idiopathic intracranial hypertension	VP shunt removal, antibiotics and Ventriculo-atrial shunt
43	Maheen Siddiqi[43]	2017	1	F/16 years	Congenital hydrocephalus	Ventriculo-atrial shunt
44	D Sachan[44]	2017	1	M/5 years	Choroid plexus papilloma	Tumor resection and VP shunt removal
45	H Han[45]	2017	1	M/20 years	Dandy-Walker Syndrome	Ventriculo-atrial shunt
46	G. Musa[46]	2018	1	F/3 years	Communicating hydrocephalus	Ventriculo-atrial shunt
47	AA Khan[47]	2018	2	-	-	Endoscopic Third Ventriculostomy
48	Darrick K Li[48]	2019	1	F/26 years	Loeys-Dietz syndrome and Congenital hydrocephalus	Multiple therapeutic paracentesis followed by Peritoneovenous (Denver) shunt
49	Saud E. Suleiman[49]	2020	1	F/32 years	Hydrocephalus due to brain malformation (corpus callosum agenesis)	Multiple therapeutic paracentesis followed by Ventriculo-atrial shunt
50	George A.Alexiou[50]	2021	1	F/60 years	Bilateral frontal meningiomas and Obstructive hydrocephalus	Ventriculo-atrial shunt
51	M Mathew[51]	2022	1	F/7 years	Craniopharyngioma	Ventriculo-atrial shunt
52	N Mehta[52]	2022	1	M/29 years	Communicating hydrocephalus	Ventriculo-atrial shunt

CASE PRESENTATION

A 3-year-old girl appeared to us as an outpatient with complaints of frequent episodes of vomiting and reluctance to feed for three days, as well as abdominal distention for two weeks. She was born with a lumbar myelomeningocele and congenital hydrocephalus after a normal vaginal delivery at term. At the age of one month, she had a ventriculoperitoneal shunt placed, but she never had lumbar myelomeningocele repair surgery. She had been doing well since her ventriculoperitoneal shunt surgery until her current presentation. She was lethargic during the physical examination. There was a CSF surge at the VP shunt's reservoir site. Her belly was bloated, and she had an umbilical hernia and rectal prolapse, most likely as a result of excessive

intra-abdominal pressure caused by CSF ascites. (Figure 1; A,B,C). The VP shunt's reservoir was slow. We performed an X-ray shunt series, a Computed Tomography (CT) brain plain, and an abdominal ultrasound. Shunt tubing was found to be totally undamaged on X-ray (Figure 2; A&B). Ventriculomegaly was discovered on a CT scan. An abdominal ultrasound revealed complicated ascites. After a diagnostic paracentesis, the ascitic fluid was revealed to be normal. CSF ascites were confirmed through biochemical analysis. To reduce abdominal distension, therapeutic paracentesis was employed, although recurrent accumulation was common. Instead of a Ventriculo-atrial shunt, the VP shunt was removed, and she underwent Endoscopic Third Ventriculostomy. Following ETV, CSF ascites gradually disappeared over a two-week period.

Discussion

Following the implantation of VP shunts for the treatment of hydrocephalus, a number of abdominal complications have been described. Perforation of the gut, gallbladder, vagina, umbilicus, and volvulus, as well as abdominal CSF encystation and CSF ascites, have all been documented.[5] Infections[12,26], malignancies, particularly choroid plexus papillomas and optico-chiasmatic gliomas[12,20,21,24,31], shunt-disseminated metastasis[39], and foreign body reactivity to the peritoneal catheter have been linked to CSF ascites.[23] High protein content of the CSF, particularly in optico-chiasmatic gliomas[10,20,31]; increased CSF production, as in choroid plexus hyperplasia and papillomas; tumor-secreted vascular permeability factors;[24] and persistent serosal inflammation are among the different causes reported.[26,33] To the best of our knowledge, Akdegbite et al. were the first to identify elevated CSF proteins as a probable cause of ascites.[10]

As little is known about the aetiology of CSF ascites[4], various mechanisms have been proposed, including subclinical peritonitis, which obstructs lymphatic drainage[23], elevated CSF protein, which causes peritoneal malabsorption[10,24,28], and CSF overproduction exceeding absorptive capacity.[38] Multiple shunt revisions[2,22], an immunological reaction to vaccination[2], or shunt degradation[26] can all cause peritoneal irritation. Chronic illnesses such as tuberculosis[28] and brain tumours (e.g. optic gliomas and craniopharyngiomas)[24] have high CSF protein levels. Overproduction of the choroid plexus papillomas causes ascites.[30] A diagnosis of CSF ascites is strengthened by comparing the biochemistry of CSF shunt aspirate and ascitic fluid from paracentesis. CSF ascites resolve spontaneously when CSF flow is redirected using a Ventriculo-atrial shunt or ETV.[38] A previous shunt is linked to a higher rate of ETV failure.[47] In our situation, ETV was used, and symptoms were resolved within two weeks.

A detailed literature review of 77 reported cases of CSF ascites until March 2022 is given in Table 1. Congenital hydrocephalus, obstructive hydrocephalus, choroid plexus papilloma, craniopharyngioma, and posterior fossa tumour were all common etiological causes. Revision of the VP shunt to a Ventricular-atrial shunt is the treatment of choice for CSF ascites, although revision in choroid plexus papilloma will only relieve ascites with the risk of congestive heart failure and bacteremia. The definitive cure is surgical excision of the papilloma.[44] Ascites developed and CSF protein levels increased in a craniopharyngioma instance that underwent VP shunt insertion due to hydrocephalus. CSF protein levels were reduced and ascites was alleviated after the recurring tumour was removed.[10] One patient with ascites and elevated protein levels was treated with a fluid-restricted diet by Yount et al.[12] According to the literature, the most common treatment overall for CSF ascites is abdominal paracentesis and conversion to a Ventriculo-atrial shunt. The time between VP shunt surgery and the onset of ascites might range from 1 day to 12 years.[23,38] It appeared in our patient 2.9 years after the VP shunt.

In VP shunting, the peritoneal lining is particularly effective for quick absorption from the peritoneal cavity because it is made up of specialized mesothelial cells that promote rapid lymphatic drainage from the peritoneal cavity into the adjacent lymphatic lacunae.[39] In dehydrated children, the peritoneum can absorb up to 500 mL of normal saline per 24 hours, and following the osmotic absorption phase, the average fluid absorption rate is 33 mL/h.[51] CSF ascites is defined as an excessive buildup of CSF in the peritoneal cavity due to the peritoneum's failure to absorb the CSF.[23] According to literature study, this state of disequilibrium could be caused by primary peritoneal failure, increased CSF volume, increased CSF protein, infections (peritonitis), eosinophilic catheter rejection, immunological response to immunisation, or in

certain cases, no clear cause. CSF ascites has been linked to tumours such optic gliomas and craniopharyngiomas, possibly due to elevated CSF proteins.[12, 23, 41] In addition to the probable unique proteins produced by optic gliomas, a disruption in the blood-brain barrier could allow tumour proteins to escape into the subarachnoid CSF, resulting in elevated protein levels and impaired CSF absorption through the arachnoid villi.[23]

Patients with CSF ascites have an insidious onset, gradual abdominal distention, and no pain. Hepatic, renal, or cardiac dysfunction are not present. The duration between the shunt being placed and the onset of symptoms might range from days to years. To rule out other probable causes of ascites, a thorough study is required. In patients with a history of VP shunt surgery the likelihood of CSF ascites must be kept in mind, which can be validated by an ascitic fluid β2 transferrin assay. After making the diagnosis of CSF ascites, the treatment includes redirection of CSF flow, preferably Ventriculo-atrial shunt but Endoscopic Third Ventriculostomy is a viable approach in certain circumstances.

Conclusions

Patients with CSF ascites have an insidious onset, progressive and painless abdominal distention. The time between the shunt insertion and the onset of symptoms might range from days to years. An extensive workup is required to rule out other probable causes of ascites. After ensuring that there is no infection, the VP shunt linked CSF ascites is treated by converting the shunt to a Ventriculoatrial shunt. CSF ascites can be treated effectively by abdominal paracentesis and conversion of the VP shunt to a Ventriculo-atrial shunt, but Endoscopic Third Ventriculostomy is a viable approach in some selected cases.

List of Abbreviations:
CSF: Cerebrospinal fluid
VP: Ventriculoperitoneal
ETV: Endoscopic Third Ventriculostomy
CT: Computed Tomography

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References

1. Ames RH. Ventriculo-peritoneal shunts in the management of hydrocephalus. J Neurosurg. 1967;27(6):525-529. doi:10.3171/jns.1967.27.6.0525
2. Dean DF, Keller IB. Cerebrospinal fluid ascites: a complication of a ventriculoperitoneal shunt. Journal of Neurology, Neurosurgery & Psychiatry. 1972 Aug 1;35(4):474-6.
3. Rosenthal JD, Golden GT, Shaw CA, Jane JA. Intractable ascites: a complication of ventriculoperitoneal shunting with a silastic catheter. The American Journal of Surgery. 1974 May 1;127(5):613-4.
4. Weidmann MJ. Ascites from a ventriculoperitoneal shunt: Case report. Journal of Neurosurgery. 1975 Aug 1;43(2):233-5.
5. Parry SW, Schuhmacher JF, Llewellyn RC. Abdominal pseudocysts and ascites formation after ventriculoperitoneal shunt procedures: Report of four cases. Journal of Neurosurgery. 1975 Oct 1;43(4):476-80.
6. Cummings J, Sonntag KH, SCOTT RM. Ascites complicating ventriculo-peritoneal shunting in an adult. Surg Neurol. 1976;6(2):135-136.
7. Lees RF, Harrison RB, Shaffer Jr HA, Hamby LP. Cerebrospinal fluid ascites. Journal of the Canadian Association of Radiologists. 1978 Jun;29(2):132-3.
8. Noh JM, Reddy MG, Brodner RA. Cerebrospinal fluid ascites following ventriculoperitoneal shunt. Report of a case and review of the literature. Mt Sinai J Med. 1979;46(5):475-477.
9. Ohaegbulam SC. Cerebrospinal fluid ascites complicating a ventriculoperitoneal shunt. International surgery. 1980 Sep 1;65(5):455-7.
10. Adegbite AB, Khan M. Role of protein content in CSF ascites following ventriculoperitoneal shunting: Case report. Journal of neurosurgery. 1982 Sep 1;57(3):423-5.
11. Agha FP, Amendola MA, Shirazi KK, Amendola BE, Chandler WF. Unusual abdominal complications of ventriculo-peritoneal shunts. Radiology. 1983 Feb;146(2):323-6.
12. Yount RA, Glazier MC, Mealey J, Kalsbeck JE. Cerebrospinal fluid ascites complicating ventriculoperitoneal shunting: Report of four cases. Journal of neurosurgery. 1984 Jul 1;61(1):180-3.
13. JM GT, JM CC. Ventriculo-peritoneal shunt, hypovolemic shock and cerebrospinal fluid ascites. Anales Espanoles de Pediatria. 1984 Aug 1;21(2):147-52.
14. Rush DS, Walsh JW, Belin RP, Pulito AR. Ventricular sepsis and abdominally related complications in children with cerebrospinal fluid shunts. Surgery. 1985 Apr 1;97(4):420-7.
15. Madruga Acerete D, Vascónez Muñoz F, Práxedes Alonso M, Cincuendez Morcuendez R, Salazar Rojas F, Taracena del Piñar B. Ascitis por líquido cefalorraquídeo como

complicación en derivación ventriculoperitoneal: aportación de un caso y revisión de la literatura [Ascites of the cerebrospinal fluid as a complication of a ventriculoperitoneal shunt: report of a case and a review of the literature]. An Esp Pediatr. 1988;28(6):565-568.

16. Goodman GM, Gourley GR. Ascites complicating ventriculoperitoneal shunts. Journal of pediatric gastroenterology and nutrition. 1988 Sep 1;7(5):780-2.
17. Niikawa S, Hara A, Nokura H, Uno T, Ohkuma A, Yamada H. Central nervous cryptococcosis giving rise to ascites after ventriculo-peritoneal shunting--a case report. No Shinkei geka. Neurological Surgery. 1988 Jun 1;16(7):881-5.
18. Pérez Peña F, Aparicio Campillo G, López Asenjo JA, et al. Ascitis por acúmulo de líquido cefalorraquídeo [Ascites due to cerebrospinal fluid accumulation]. Rev Clin Esp. 1990;187(3):128-130.
19. Suarez A, Riestra S, Navascues CA, Sotorrio NG, Rodríguez M, Alonso JL, Pérez R, Rodrigo L. A ventriculoperitoneal shunt as a rare cause of ascites. Revista Espanola de Enfermedades Digestivas: Organo Oficial de la Sociedad Espanola de Patologia Digestiva. 1993 Apr 1;83(4):285-7.
20. West A, Berger MS, Geyer R. Childhood optic pathway tumors associated with ascites following ventriculoperitoneal shunt placement. Pediatric neurosurgery. 1994;21(4):254-9.
21. Shuper A, Horev G, Michovitz S, Korenreich L, Zaizov R, Cohen IJ. Optic chiasm glioma, electrolyte abnormalities, nonobstructive hydrocephalus and ascites. Medical and Pediatric Oncology: The Official Journal of SIOP—International Society of Pediatric Oncology (Societé Internationale d'Oncologie Pédiatrique. 1997 Jul;29(1):33-5.
22. Yukinaka M, Nomura M, Mitani T, KONDO Y, TABATA T, NAKAYA Y, ITO S. Cerebrospinal ascites developed 3 years after ventriculoperitoneal shunting in a hydrocephalic patient. Internal medicine. 1998;37(7):638-41.
23. Chidambaram B, Balasubramaniam V. CSF ascites: a rare complication of ventriculoperitoneal shunt surgery. Neurol India. 2000;48(4):378-380.
24. Gil Z, Beni-Adani L, Siomin V, Nagar H, Dvir R, Constantini S. Ascites following ventriculoperitoneal shunting in children with chiasmatic-hypothalamic glioma. Child's Nervous System. 2001 Jun;17(7):395-8.
25. Lee BH, Kang SD, Kim JM. CSF Ascites Complicating Ventriculoperitoneal Shunting-A Case Report. Journal of Korean Neurosurgical Society. 2001;30(11):1345-7.
26. Longstreth GF, Buckwalter NR. Sterile cerebrospinal fluid ascites and chronic peritonitis. N Engl J Med. 2001;345(4):297-298. doi:10.1056/NEJM200107263450417
27. Lee GY, Daniel RT, Jones NR. Ventriculoperitoneal shunt failure as a secondary complication of ovarian hyperstimulation syndrome. Case report. J Neurosurg. 2002;97(4):992-994. doi:10.3171/jns.2002.97.4.0992
28. Yaqoob N, Abbasi SM, Hussain L. Cerebrospinal fluid ascites. Journal of the College of Physicians and Surgeons--pakistan: JCPSP. 2003 May 1;13(5):289-90.
29. Kumar R, Sahay S, Gaur B, Singh V. Ascites in ventriculoperitoneal shunt. The Indian Journal of Pediatrics. 2003 Nov;70(11):859-64.
30. Pawar SJ, Sharma RR, Mahapatra AK, Lad SD, Musa MM. Choroid plexus papilloma of the posterior third ventricle during infancy & childhood: report of two cases with management morbidities. Neurology India. 2003 Jul 1;51(3):379.
31. Olavarria G, Reitman AJ, Goldman S, Tomita T. Post-shunt ascites in infants with optic chiasmal hypothalamic astrocytoma: role of ventricular gallbladder shunt. Child's Nervous System. 2005 May;21(5):382-4.
32. DiLuna ML, Johnson MH, Bi WL, Chiang VL, Duncan CC. Sterile ascites from a ventriculoperitoneal shunt: a case report and review of the literature. Child's Nervous System. 2006 Sep;22(9):1187-93.
33. Kariyattil R, Steinbok P, Singhal A, Cochrane DD. Ascites and abdominal pseudocysts following ventriculoperitoneal shunt surgery: variations of the same theme. Journal of Neurosurgery: Pediatrics. 2007 May 1;106(5):350-3.
34. Paik I, Kotler D, Ganjhu L. Cerebrospinal Fluid Ascites as a Rare Complication of Ventriculo-Peritoneal Shunt: A Case Report: 714. Official journal of the American College of Gastroenterology| ACG. 2010 Oct 1;105:S258.
35. Das S, Bhansali A, Upreti V, Dutta P, Gupta SK, Ananthraman R, Walia R. A child with suprasellar mass and ascites. Case Reports. 2010 Jan 1;2010:bcr0620092030.
36. Montano N, Sturiale C, Paternoster G, Lauretti L, Fernandez E, Pallini R. Massive ascites as unique sign of shunt infection by Propionibacterium acnes. British journal of neurosurgery. 2010 Apr 1;24(2):221-3.
37. Houtman-van Duinen WJ, Ende-Verhaar YM, de Ruiter GC, van der Torren-Conze AM. Cerebrospinal fluid ascites from a ventriculoperitoneal shunt. Nederlands Tijdschrift Voor Geneeskunde. 2011 Jan 1;155(50):A4035-.
38. Mwang'ombe NJ, Thiong'o GM, Boore JK. Cerebrospinal fluid ascites. a case report and literature review. African Journal of Neurological Sciences. 2012;31(1):55-7.
39. Low YY, Thomas J, Wan WK, Ng WH. Brain metastases as a cause of malignant cerebrospinal fluid ascites: case report and review of the literature. CNS Oncol. 2012;1(1):29-37. doi:10.2217/cns.12.2
40. Comba A, Gülenç N, Çaltepe G, Dagçinar A, Yüce Ö, Kalayci AG, Ulus A. Ascites and abdominal pseudocyst: two uncommon ventriculoperitoneal shunt complications in two cases. The Turkish journal of pediatrics. 2013 Nov 1;55(6):655.
41. Woodfield J, Magdum S. Failure of peritoneal and gallbladder shunts in a child with craniopharyngioma. Journal of pediatric neurosciences. 2013 Sep;8(3):221.

42. Jamal H, Abrams G. A corny cause of cerebrospinal fluid ascites: A case report and review of literature. SAGE Open Medical Case Reports. 2016 Jul 26;4:2050313X16661961.
43. Siddiqi M, Kesavan A, Siddiqi M. Cerebrospinal fluid ascites as a late complication of ventriculoperitoneal shunt placement. Consultant. 2017;57(11):677-8.
44. Sachan D. Choroid Plexus Papilloma Causing CSF Shunt Ascites: A Rare Presentation. Ann Clin Case Rep. 2017; 2. 2017;1376.
45. Han H, Critelli K, Davis AW, Squires JE, Fox MD. Case 6: Ascites in a 20-year-old Man with Dandy-Walker Syndrome, Hydrocephalus, and Ventriculoperitoneal Shunt. Pediatr Rev. 2017;38(10):494-495. doi:10.1542/pir.2016-0140
46. Musa G, Gots A, Lungu MC, Mutumwa M. Cerebrospinal fluid ascites: a patient case report and literature review. Medical Journal of Zambia. 2018;45(4):230-3.
47. Khan AA, Gondal SS, Sharif MM, Yousaf M, Akhtar N. Outcome of Endoscopic Third Ventriculostomy. Journal of Rawalpindi Medical College. 2018 Mar 30;22(1):4-7.
48. Li DK, Platt JM, Shay JE, Yarze JC. Sterile cerebrospinal fluid ascites presenting as high SAAG ascites: a case report. BMC gastroenterology. 2019 Dec;19(1):1-4.
49. Suleiman SE, Tambovtseva A, Mejery E, Suleiman Z, Alaidy Z. Ventriculoperitoneal Shunt-Associated Ascites: A Case Report. Cureus. 2020 Jun 15;12(6).
50. Alexiou GA, Gavra MM, Ydreos J, Papadopoulos E, Boviatsis EJ. Ascites with elevated CSF protein levels after ventriculoperitoneal shunt surgery in an adult. Case report and systematic literature review. Clinical Neurology and Neurosurgery. 2021 Jan 27;202:106519-.
51. Mathew M, Chikani MC, Okpara SE, Uzoanya MU, Ezemba N, Mezue WC. Challenges in the management of cerebrospinal fluid ascites: a case report. Child's Nervous System. 2022 Feb 17:1-3.
52. Mehta N, Somani V, Shah S, Siddiqui A, Chauhan P. CSF ASCITES POST VP SHUNT AFTER 17 YEARS: CSF ASCITES-A RARE OCCURENCE. Bombay Hospital Journal. 2022 Feb 23;64(1).

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A comprehensive review on pituitary hydroscopy and the role of endoscopic diving techniques

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ABSTRACT

Pituitary hydroscopy is a new technique in skull base surgery that involves transnasal neuroendoscopy and gentle fluid distention of the sella turcica. Hydroscopy allows for a more thorough inspection of the sellar region and may make it easier to remove additional tumour cell foci. Endoscopic Diving Technique, on the other hand, uses a continuous water flow that is driven in front of the endoscope to aid explore the surgical cavity and improve image clarity. After tumour removal, a double-path aspirator is implanted inside the sella turcica and tumour cavity, providing a pressured flow with continuous irrigation in the Modified Endoscopic Diving Technique. Several groups' recent uses of diving techniques attest to the increased interest in these approaches. The development of dedicated surgical devices will improve the efficacy of diving procedures in the future. More research is needed right now to improve the effectiveness of diving techniques.

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INTRODUCTION

To understand the current renaissance of endonasal pituitary surgery, it's necessary to look back at the historical and anatomic progression of thought that has led to contemporary technical advancements and better patient care. Shorter operative times, decreased blood loss, improved differentiation between normal tissue and tumour, better visualisation of intrasellar and parasellar structures, shorter hospital stays, improved patient satisfaction, and decreased need for nasal packing have all been seen since the endoscope was married to the trans-sphenoidal approach. Furthermore, this union has brought the otolaryngologist and the neurosurgeon together as a true surgical team, allowing novel concepts like extracapsular tumour dissection, new approaches to investigate the tumour bed, improved tumour removal with angled views and hydroscopy.[6]

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Pituitary hydroscopy is a new technique in skull base surgery that involves transnasal neuroendoscopy and gentle fluid distention of the sella turcica. Hydroscopy provides for a more thorough inspection of the sellar region during minimally invasive pituitary surgery, as well as the excision of extra tumour cell foci. When compared to typical neuroendoscopic procedures, preliminary data suggests that hydroscopy may result in a lower rate of cerebrospinal fluid (CSF) leak and revision surgery. Hydroscopy is a safe and effective addition to traditional pituitary techniques, and endoscopic skull base surgeons should include it in their toolkit. Endoscopic resection of pituitary neoplasms appears to have the major benefit of a broader, potentially angled field of view, which may be especially advantageous for big tumours with extrasellar extension, according to the data. Endoscopic pituitary surgery has been linked to better rates of gross total resection, endocrinological cure, visual prognosis, shorter hospital stays, less postoperative discomfort, septal perforation, CSF leak, and a lower rate of diabetes insipidus as a result of its benefits.[16]

A constant water flow is propelled in front of the endoscope in Davide Locatelli's[9] Endoscopic Diving Technique (EDT). EDT is a flexible tool for exploring the surgical cavity and enhancing visibility. After tumour removal, a double-path aspirator is implanted inside the sella turcica and the tumour cavity in Marco Ceraudo's[3] Modified Endoscopic Diving Technique. This creates a pressured flow with continual irrigation, which aids in the removal of more minor tumour foci.

History

The creation of the cystoscope by Nitze in the 1800s provided the technological foundation for hydroscopy.[11] Herman Schloffer used a lateral rhinotomy to perform the first transsphenoidal approach to the pituitary in 1907. After an open approach via the nasal dorsum, Kocher described the first submucosal resection of the bony nasal septum and vomer to get access to the rostrum of the sphenoid in 1909.[8] Hirsh, a rhinologist, invented and championed the substantial breakthrough of the transnasal, transseptal technique in 1910. Hirsch tweaked the techniques he'd learned to access the sphenoid for infection therapy. The submucosal excision of the septum, developed by Kilian in 1904, was later added to his basic procedure. In 1914, Cushing described his sublabial, transseptal, transsphenoidal method using these techniques as well as those of Kanavel and Halstead. Following that, in the 1960s, the adoption of an operational microscope considerably increased visualisation of the sella.[13]

For vision of urological structures, early cystoscopes depended on air insufflation; later developments of this technology incorporated fluid distention, which enhanced patient comfort and surgeon visibility. The first attempts to apply endoscopic techniques to neurological pathology focused on the ventricles and other fluid-filled regions, with Victor L'Espinasse, a French urologist, examining the choroid plexus of two children with hydrocephalus using a cystoscope in 1910.[17] Jankowski performed the first purely endoscopic, endonasal pituitary excision in 1992, thanks to technological breakthroughs in endoscopes and cameras in the 1970s, and Jho and Carrau published the first extensive series of endoscopic pituitary surgery in 1997.[5] Endoscopic transsphenoidal methods to the pituitary have grown quite prominent in the last 25 years.

Anatomical considerations

The pituitary gland is a reddish-grey organ that rests in the sella turcica, a deep depression on the superior portion of the sphenoid bone's body, and measures around 1 cm in diameter. It's hidden behind the tuberculum sellae, which is itself hidden behind the optic chiasm. The dorsum sellae and the posterior clinoid processes define the sella's posterior boundary. The clivus is a bony extension of the dorsum sellae that slopes inferiorly and connects to the occipital bone. The anterior clinoid processes are formed by the tuberculum sellae's lateral expansions. The diaphragm, a dural fold spanned by the pituitary stalk, forms the roof of the fossa. The diaphragm and the pituitary capsule are separated by an arachnoid invagination. The roof of the cavernous sinus is formed by the diaphragm's lateral expansion. The optic chiasm and nerves, the carotid arteries, the third, fourth, fifth, and sixth cranial nerves in the cavernous sinus, as well as the basilar artery and brainstem posteriorly, are all within close proximity to the pituitary gland. As a result, proper anatomy knowledge is required during these approaches.[15]

The sphenoid sinus is pneumatized into the

sphenoid bone in a variety of ways, and three types of sphenoid pneumatization patterns are classified based on their relationship to the sella. A conchal type is one that has just slightly pneumatized and yet has thick bone across the sella's face. Sellar type denotes a sinus that has pneumatized to the sella's face, whereas post-sellar type describes a sinus that has pneumatized beyond the sella's face. The sellar and post-sellar types of sinuses make up the majority of adult sinuses.[15] The two sphenoid sinuses are separated by a septum that is off the midline in 60 to 70% of cases, resulting in asymmetry between the two cavities. Additionally, numerous septations may be present. The walls of the sphenoid sinuses have many structures running along them. The Vidian nerve's canal goes laterally along the floor. At approximately 5 and 7 o'clock, the carotid arteries flow along the lateral walls. At approximately 2 and 11 o'clock, the optic nerves run more superiorly along the lateral walls. Between the bulges of these two structures is the optico-carotid recess, which can extend into the anterior clinoid process. The sphenoid ostium runs along the anterior wall's superior aspect.[14]

Principles of endoscopic diving technique

The diving technique makes use of hydraulic concepts (flow and pressure) as well as visual approaches (lens effect given by liquid film). The procedure entails not only flushing the surgical cavity, but also the production of a saline solution lens: the first step is to determine the proper distance from the wall to be visualised in order to eliminate any turbulence induced by the liquid flow. The focus, which differs from that utilised in open-air surgery, is changed at this point. The surgeon must generate a field with a stationary flow, which means that the lines of flow must correspond with the lines of current, and the particles must follow trajectories that are not rectilinear but remain constant throughout time. The saline solution within the surgical cavity forms a fluid layer with a stationary flow that works as a concave-convex lens.[9]

Advantages of the technique

1. Removal of micro residues with final hydrodissection of the lesion.
2. As a result of the flushing pressure, structures, fistulas, and perforations of the cavernous sinus walls can be seen in the presence of bleeding.
3. Exploration of places buried by the cistern's fall as the saline solution flow re-expands the pseudocapsule through pressure and direction adjustments.
4. Hematic residues are removed, and bleeding is modest, preventing clear visibility.
5. Smaller visual field but greater visualisation due to the lens effect with amplification of vision.[9]

Limitations of the technique

1. A panoramic vision is not possible due to the short focal distance.
2. In a small field, there is no stereoscopic view.
3. Bleeding can make you feel disoriented.[9]

Preoperative considerations

Hydroscopy is recommended for patients undergoing transnasal, endoscopic pituitary and selected parasellar surgery. Certain diseases of the sella turcica less often require intraoperative hydroscopy: Rathke's cleft cysts can be easily marsupialized without it, while adamantinomatous craniopharyngiomas often have a fibrotic capsule that makes hydroscopy difficult. To continue with surgery, individuals with pituitary pathology must have a thorough preoperative evaluation and be recommended for transnasal, endoscopic surgical therapy. Multidisciplinary teamwork across neurosurgery, endocrinology, ophthalmology, and otolaryngology is the best way to make management suggestions. Surgical intervention is usually reserved for compressive symptoms, rapid development, or acute apoplexy in hormonally inert tumours. Size, type of hormone, and response to medical care are factors that affect surgery for a hormone-secreting tumor. Prolactinomas are treated with dopamine agonists at first, with surgical removal reserved for tumours that continue to grow. On the other hand, tumours that produce growth hormone or adrenocorticotropic hormone are frequently treated with surgery up front. Unless contraindicated, all patients have thin-cut computed tomography (CT) of the paranasal sinuses and magnetic resonance imaging (MRI).[2]

Surgical techniques:

On the operating table, the patient is positioned supine with a horseshoe headrest. The head is retained in a neutral position or slightly tilted to the right and elevated 10 to 30 degrees. The image

guidance and endoscopic monitors, as well as the nurse's table, are all placed at the patient's head, directly in front of the surgeons. The rigid endoscopes 0, 30, 45, and 70 degrees with diameters of 4 and 2.7 mm, 18 cm in length, and an external cover attached to the irrigation system are employed.[9] The procedure is performed with a standard 4-mm endoscope with various angulations; for the most part, the straight endoscope gives the best illumination and vision. After the sella is accessed and the tumour is removed, angled scopes are frequently utilised later in the surgery. The use of stereoscopic endoscopes to provide a three-dimensional vision has been described.[14]

The endotracheal tube is attached to the left lower lip to obtain general anaesthesia. The bed is turned 90 degrees counterclockwise, and preoperative CT and MRI images are combined before registration with a stereotactic image guidance system using facial surface matching. In the case that a fat graft is necessary for reconstruction, the abdomen is sterilely prepped. The availability of equipment and the strategy for surgical pathology specimens are evaluated, as well as key characteristics of the patient's anatomy.[16] Pledgets soaked in a solution of 0.05 percent oxymetazoline hydrochloride decongest the nasal canals. Greater palatine artery blocks, which are performed by injecting 1.5 mL of a 1 percent lidocaine solution with 1/100,000 epinephrine trans-orally into the greater palatine canal bilaterally, provide further hemostasis. Finally, a sphenopalatine artery block is achieved by injecting additional lidocaine with epinephrine endoscopically in the vicinity of the sphenopalatine foramen.[1] For better visualisation and subsequent hydroscopy, the endoscopic operation begins with the use of a 0-degree Hopkins rod equipped with a suction/irrigation system.[16]

The sphenoid ostia are recognised and the bilateral middle turbinates are lateralized. A nasoseptal flap may be lifted prior to performing a broad bilateral sphenoidotomy with removal of the rostrum and posterior septectomy, depending on the risk of CSF leak. Alternatively, the nasoseptal flap pedicle can be shifted inferiorly from the sphenoid face and posterior nasal septum without lifting the flap entirely, protecting the flap pedicle while permitting tissue regeneration if the flap is not required for reconstruction. After visual and imaging guidance, establish the position of the internal carotid arteries and optic nerves, the bony sellar face is removed with a 4-mm diamond drill bit and Kerrison rongeur. An inferiorly pedicled, U-shaped incision in the dura is produced, which is then reflected inferiorly and resected, with an otolaryngologist and neurosurgeon working in a two-surgeon, four-handed method. Standard microneurosurgical procedures are used to visualise and resect the tumour, taking care not to disturb the normal gland, cavernous sinus, or diaphragm. The 0-degree endoscope and irrigating sheath are inserted into the sella after gross total resection, and the sella is irrigated continuously with sterile saline. Suction or extra dissection may be used to identify and remove small particles of remaining tumour.[16] Hydroscopy uses regular saline irrigation with a water pressure of several cm linked to either straight or angled endoscopes. The saline flooding the field expands the sella's soft tissue borders, including the diaphragm, while also increasing visibility by washing away minute amounts of blood and clot. With increased visualisation, this approach allows for a thorough examination of the cavity and the removal of as much tumour tissue as feasible.[14]

After the surgeon has removed the majority of the lesion and visualised a new cavity, the surgeon can enter the space with the endoscope thanks to continual irrigation from the pump. Filling the dead space with saline solution allows the endoscope to be inserted into the tumour, allowing for a great "underwater" view of the remaining tumour, capsule, normal pituitary tissue, and cavernous sinus walls. The tumour is removed using this diving technique, which involves injecting saline solution into the hollow created following tumour resection and testing for residual tumour.[9] Hemostasis is achieved at the end of the procedure utilising a hemostatic substance such as microfibrillar collagen in thrombin. This is let to sit in the sella for a few minutes before being irrigated out. In the vast majority of cases, sella reconstruction is not required. In present practise, the only rationale for reconstruction is intraoperative suspicion of a CSF leak. If a leak is discovered, it is repaired with a little fat plug, sometimes augmented by a small resorbable microplate.[14]

The Endoscopic Diving Technique was introduced by Davide Locatelli. The irrigation pump is triggered and the endoscope is put into the surgical cavity according to the surgeon's desire (after full tumour

resection or anytime the amount of resection has to be evaluated). Continuous water flow is propelled in front of the endoscope, rapidly filling the cavity and allowing diving to begin. EDT is a versatile technique for exploring the surgical cavity and improving image clarity; it varies from Senior's "sellar hydroscopy"[14] in that it goes beyond simple observation of the surgical field, acting as an operative instrument all around. The irrigation stream's directed force may aid tumour hydro-dissection by washing out residuals. The intra-cavity pressure can contrast bleeding as blood is diluted and washed away inside the cavernous sinus.[9]

Marco Ceraudo introduced the Modified Endoscopic Diving Technique. The double-path aspirator is put inside the sella turcica and the tumour cavity after tumour removal in this procedure. The surgeon's assistant switches on the tap to flood the tumour cavity with a pressurised flow; if necessary, a nurse can maintain pumping the infusion pressure bag to provide continuous irrigation. The double-path technology lets you halt the suction while also increasing the hydrostatic pressure created by the saline infusion. The endoscope is inserted into the tumour cavity, which is filled with saline solution, allowing a clear view of the diaphragma sellae, cavernous sinus walls, and pituitary gland, as well as the detection of any tumour remnants inside the parapituitary recess that can be washed away from the sella. The optic system and the irrigation supply are divided into two distinct tools in the modified endoscopic diving technique, allowing surgeons to point the flow on a specific structure while the endoscope can be oriented in the same direction or not. Furthermore, the irrigation source and the optic system can be located at varying distances.[3]

There were some changes between Locatelli et al's endoscopic diving technique and Ceraudo et al's modified endoscopic diving approach. The irrigation system injects saline solution directly onto the endoscope's outer lens in the endoscopic diving technique. Second, the distance between the optic and the irrigation system is fixed in the endoscopic diving technique for the same reason. Third, a rotary pump produces constant irrigation in the surgical field in the endoscopic diving technique. Fourth, despite the fact that the irrigation system utilised during the treatment is included in a comprehensive endoscopic equipment package, it can become an expense in a department's budget. Furthermore, many irrigation systems (i.e., irrigation system and optic lens) supplied by different medical corporations are incompatible, which could drive up expenses even more.[3] Because dedicated instruments are not required, Ceraudo's process offers easy reproducibility and lower costs.[10]

Postoperative considerations

The patient is admitted to the ward for 48 hours after surgery to allow for routine neurologic monitoring. On the first postoperative day, an MRI is conducted to assess the extent of the resection. Antibiotics and hormonal replacement, if necessary, are usually given to patients before they are sent home. To avoid mucus being displaced into the open sellar cavity, patients are told not to blow their noses or sneeze through their noses. Sinonasal endoscopy is performed at the first postoperative visit, about 3 weeks later, to ensure proper healing; normally, the posterior sphenoidotomy is covered by a healthy mucosal layer.[14]

Complications

Meningitis, cerebral haemorrhage, ophthalmoplegia, carotid damage, and perioperative death are all rare consequences.[9] During the initial postoperative period, diabetes insipidus can be found in up to 60% of patients, but it is usually temporary, with only around 3% of patients requiring long-term care. CSF leak is the most prevalent significant consequence.[1]

Results of different studies

Senior et al[13] presented a series of more than 50 cases of pituitary hydroscopy employing the ClearESS irrigation system in 2005, noting that in about 25% of cases, the use of this approach resulted in an additional tumour diagnosis and removal.

Senior et al[14] described a case series of 176 individuals who underwent a total of 193 minimally invasive pituitary surgery procedures in 2008. The authors found that patients having hydroscopy had a decreased risk of CSF leak (24 vs 45 percent, p=0.005). These preliminary findings show that hydroscopy after pituitary surgery may enhance outcomes, but more prospective, controlled trials are needed.

Davide Locatelli[9] performed 410 surgical procedures in 2009 to remove lesions in the sellar, cavernous sinus, and clival regions using diving

surgery. They removed 379 pituitary adenomas (92%), 21 craniopharyngiomas, 5 meningiomas, 4 chordomas, and 1 epidermoid during the procedure. They were able to speed up and improve the surgical excision of numerous lesions in the sellar and parasellar regions using this surgical method.

In 2017, China's Hai-Bin Gao[7] performed Endoscopic Diving Technique on a total of 37 pituitary adenoma patients. The endoscopic diving approach, he claims, also allows the surgeon to view the undersea environment within the sella turcica.

Deyan Popov[12] performed intrasellar hydroscopy on 51 of his endoscopic group's cases in 2018. Overall, the endoscopic group had an 81.82 percent remission rate.

In 2019, Marco Ceraudo[3] performed 76 endoscopic surgical procedures using the modified endoscopic diving technique. Marco Ceraudo discovered that by combining the OLYMPUS InstaClear with a specific irrigation sheath (which is generally used to clean the endoscope lens during surgery), he was able to get a continuous water flow comparable to that generated by Locatelli et al[9]. Cleaner and sharper images can be obtained by combining EDT with Ultra High Definition or 4K systems to better understand minute anatomical details (especially in the presence of underwater vision during EDT), find tumour residuals or a clear cleavage plane, and differentiate pathological tissues from adherences or scar tissues.[3]

Conclusions

Pituitary hydroscopy is a safe, new addition to minimally invasive pituitary surgery that allows for a more complete inspection of the sella turcica using moderate saline irrigation. Hydroscopy after gross complete tumour excision frequently results in the elimination of extra, undetected tumour, potentially lowering the risk of recurrence and reducing the need for future surgery. Several groups' recent uses of diving techniques attest to the increased interest in these approaches. The development of dedicated surgical devices will improve the efficacy of diving procedures in the future. More research is needed right now to improve the effectiveness of diving techniques.

List of Abbreviations:
CSF: Cerebrospinal Fluid
EDT: Endoscopic Diving Technique
CT: Computed Tomography
MRI: Magnetic Resonance Imaging

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The authors have no conflicts of interest.

References

1. Bassim MK, Senior BA. Minimally invasive pituitary surgery. Operative Techniques in Otolaryngology-Head and Neck Surgery. 2006 Mar 1;17(1):31-6.
2. Bresson D, Herman P, Polivka M, Froelich S. Sellar lesions/pathology. Otolaryngologic Clinics of North America. 2016 Feb 1;49(1):63-93.
3. Ceraudo M, Anania P, Prior A, Rossi DC, Zona G. Modified endoscopic diving technique without the traditional irrigation system in endoscopic cranial base surgery. World Neurosurgery. 2019 Jul 1;127:146-9.
4. Ceraudo M, Anania P, Rossi DC. Letter to editor regarding “the endoscopic diving technique in endonasal transsphenoidal surgery: how I do it”. Acta Neurochirurgica. 2020 Sep;162(9):2115-6.
5. Doglietto F, Prevedello DM, Jane JA, Han J, Laws ER. A brief history of endoscopic transsphenoidal surgery—from Philipp Bozzini to the First World Congress of Endoscopic Skull Base Surgery. Neurosurgical focus. 2005 Dec 1;19(6):1-6.
6. Ebert C, Senior B. A review of minimally invasive pituitary surgery: the evolution from maximally to minimally invasive surgery. Otorinolaringologia. 2009;59:97-105.
7. Gao HB, Wang LQ, Zhou JY, Sun W. Investigating the application of diving endoscopic technique in determining the extent of pituitary adenoma resection via the trans-nasal-sphenoidal approach. Experimental and therapeutic medicine. 2018 Apr 1;15(4):3815-9.
8. Landolt AM, Vance ML, Reilly PR. History of pituitary surgery: Transsphenoidal approach. Pituitary Adenomas. New York: Churchill Livingstone. 1996;307314.
9. Locatelli D, Canevari FR, Acchiardi I, Castelnuovo P. The endoscopic diving technique in pituitary and cranial base surgery. Neurosurgery. 2010 Feb 1;66(2):E400-1.
10. Locatelli D, Veiceschi P, Castelnuovo P. Letter to the Editor Regarding "Modified Endoscopic Diving Technique without the Traditional Irrigation System in Endoscopic Cranial Base Surgery: Technical Note". World Neurosurg. 2019;128:634-635.
11. Mouton WG, Bessell JR, Maddern GJ. Looking back to the advent of modern endoscopy: 150th birthday of Maximilian Nitze. World journal of surgery. 1998 Dec 1;22(12):1256.
12. Popov D, Hadzhiyanev A, Bussarsky A, Ferdinandov D. Short-term outcome of endoscopic versus microscopic pituitary adenoma surgery in a single center. Biomed Res (Aligarh). 2018;29(14):2971-4.

13. Senior BA, Dubin MG, Sonnenburg RE, Melroy CT, Ewend MG. Increased role of the otolaryngologist in endoscopic pituitary surgery: endoscopic hydroscopy of the sella. American journal of rhinology. 2005 Mar;19(2):181-4.
14. Senior BA, Ebert CS, Bednarski KK, Bassim MK, Younes M, Sigounas D, Ewend MG. Minimally invasive pituitary surgery. The Laryngoscope. 2008 Oct;118(10):1842-55.
15. Sloan AE, Black KB, Becker DP. Lesions of the Sella Turcica. In: Donald PJ, ed. Surgery of the Skull Base. Philadelphia: Lippincott-Raven; 1998:555–582.
16. Theodore A. Schuman, Brent A. Senior. Hydroscopy: Application to Pituitary Surgery. In: Aldo C. Stamm, João Mangussi-Gomes, editors. Transnasal Endoscopic Skull Base and Brain Surgery: Surgical Anatomy and its Applications. 2nd ed. New York: Thieme; 2019. p. 362-366.
17. Walker ML. History of ventriculostomy. Neurosurgery Clinics of North America. 2001 Jan 1;12(1):101-10.

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Flail bone flap in decompressive craniotomy for infants. A case series of five patients

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Abstract

Background: Subdural hematoma in infants is a challenging condition. Acute subdural hematomas can cause intracranial hypertension and a midline shift, but decompressive craniotomies in young patients have shown promising results with specific complications in this age group. Hinge craniotomy is an old technique used in many neurosurgical procedures associated with elevated intracranial pressure. The objective of this study is to report the usage of flail bone flap in the management of acute subdural hematoma in infants, its outcome, advantages, disadvantages and related complications.

Methods: This is a review of the medical records of 5 infants younger than one-year-old who underwent decompressive craniotomy as management of acute subdural hematoma at Mansoura university hospital.

Results: In this series, five babies were included. Operative time for decompressive craniotomy (DC) ranged from 1 h and 40 min to 3 h. Four infants survived. Three infants recovered with good outcomes and one infant developed hemiparesis.

Conclusion: The use of flail bone flap technique in decompressive craniotomy is associated with a high success rate and low incidence of complications. Large-based studies are still required for a better assessment of the results.

Keywords
subdural hematoma,
flail bone flap,
decompressive craniotomy

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Introduction

Although acute subdural haematoma is considered uncommon in infants with an incidence of about 20-25 per 100000 cases but its management is a challenging condition. The most common cause in this age group is child abuse especially the shaken baby syndrome. [1].

Infantile subdural hematomas cause convulsive seizures, consciousness disorders, retinal haemorrhage, or apnea, which can progress to coma with hemiplegia or death [2]. If it is accompanied by intracranial hypertension, it will result in diffuse edoema, which will then lead to cerebral ischemia [3].

When treating infantile ASDH surgically, one must take into consideration how to best regulate intracranial pressure while minimising the risk of complications [4].

Decompressive craniectomy (DC) has been successfully used to alleviate (ICP) and massive brain swelling following infarction or

bleeding [5-7]. Improved cerebrovascular compliance, cerebral oxygenation, and cerebral perfusion can be achieved through reductions in ICP [8]. After a DC, a cranioplasty procedure is required [9] utilising either one's own autologous skull or more expensive synthetic materials [10].

Cranioplasty has been associated with some complications including surgical site infection (SSI) [11-13] and bone graft resorption (BGR) in pediatric populations [12-15].

During a decompressive craniotomy, a bone flap will be elevated followed by opening of the dura and evacuation of the hematoma. Finally, the bone flap will be repositioned loosely without fixation. The replacement of the bone flap eliminates the need of a second operation lead to avoidance of decompressive craniectomy and subsequent cranioplasty related complications. [16].

There is no clear guidelines for management of ASH using craniotomy, so we reported our experience with hinge craniotomy in 5 infants in our tertiary care centre.

Patients and methods

This retrospective case series that was conducted at Mansoura University Neurosurgery Department after obtaining approval from the local ethical committee and Institutional Review Board of Mansour Faculty of Medicine. We included five pediatric cases along one year duration.

All patients were subjected to standard history taking, general and detailed neurological examination. initial GCS and presence of other intracranial pathologies were also assessed. On admission, a CT scan of the patient's brain was analyzed to determine the hematoma's thickness as well as the amount of midline shift. The Glasgow Outcome Scale (GOS) was used to evaluate the results, and the follow-up period was increased to six months.

In addition, routine preoperative laboratory and radiological investigations were ordered. After deciding on surgical intervention, it was completely explained to the patients' guardians with its indications and complications and following that, informed written consent was obtained.

All of the procedures were carried out under general anesthesia. A large frontotemproparital question mark skin incision was done on the affected side followed by preservation of pericranial graft to be utilized in duroplasty.After that a small burrhole was done in the temporal region as fast as possible with small opening to the dura to help in relieve of the increase intracranial pressure followed by dissection of the dura from the skull bone. Due to very thin bone we used a scissor to complete the craniotomy with continuous dissection and separation of the dura from the bone flap. At the level of coronal suture, the dissection was difficult due to tight adhesion of the dura to the bone so we utilized this limb to hinge the bone flap without doing complete bone elevation. The squamous temporal bone was rongeured to the temporal fossa floor, ensuring that no edge of bone remained that could prevent the swollen temporal lobe from being displaced laterally. The dura was opened in cruciate shape manner followed by evacuation of the haematoma and ensuring haemostasis. Then the pericranial graft was used to do duroplasty and the craniotomy flap was left hinged without fixation followed by anatomical closure in layers.

All patients received standard post-operative care, with frequent assessment throughout the day. Any post-operative complications were noted and then recorded. Regular follow up visits were scheduled for these cases.

Early follow up C.T scan was done to all patients to document evacuation of the hematoma, improvement of the midline shift and to detect any complications that need further management. During the follow up serial follow up C.T scans was ordered to evaluate the brain and the fate of the bone flap.

Statistical analysis

Microsoft Excel was used to enter and analyse the data. This was followed by data being imported into the Statistical Package for Social Sciences (SPSS 27, IBM/SPSS Inc., Chicago, IL) for windows. According to Kolmogorov-Smirnov and Shapiro-tests, Wilk's the baseline characteristics of the study population were presented in the form of frequencies and percentages (percent) or mean values and standard deviations (SD) or median and range.

Results

The study included 5 infants, 3 boys (60%) and 2 girls (40%). Their age ranged from 25 days to 180 days with mean age of 81.5 days.

The cause of SDH was spontaneous in four cases (80%) and traumatic in one case only (20%). The hematoma located in the left side in 3 cases (60%) and on the right side in 2 cases (40%). The SDH was associated with ICH in one case only.

The lowest preoperative GCS was 5/15 (in one case) and the highest score was 11/15 (in two cases) while the other two cases had GCS of 8/15 and 10/15 respectively.

Coagulopathy was detected in 4 cases (80%). The mean operative time was 136 minutes with range between 100 minutes and 180 minutes. Regarding the outcome in our study, 3 cases (60%) showed favourable outcome in the form of full recovery while 1 case Survived with Rt. Sided weakness G 3. One case died thar represented 20% mortality rate.

Table 1. Detailed literature

Gender	Age	Diagnosis	Preop GCS	Coagulopathy	Operative time (min)	Outcome
Boy	25 days	Lt. acute SDH (spontaneous)	8/15	Yes	100	Fully recovered
Girl	2 months	Rt. Acute SDH (spontaneous)	10/15	Yes	130	Fully recovered
Boy	4 months	Lt. acute ICH + SDH (spontaneous)	11/15	Yes	180	Survived with Rt. Sided weakness G 3
Boy	3 months 14 days	Lt. acute SDH (spontaneous)	5/15	Yes	150	Died
Girl	6 months	Rt. Acute SDH (trauma, fall)	11/15	No	120	Fully recovered

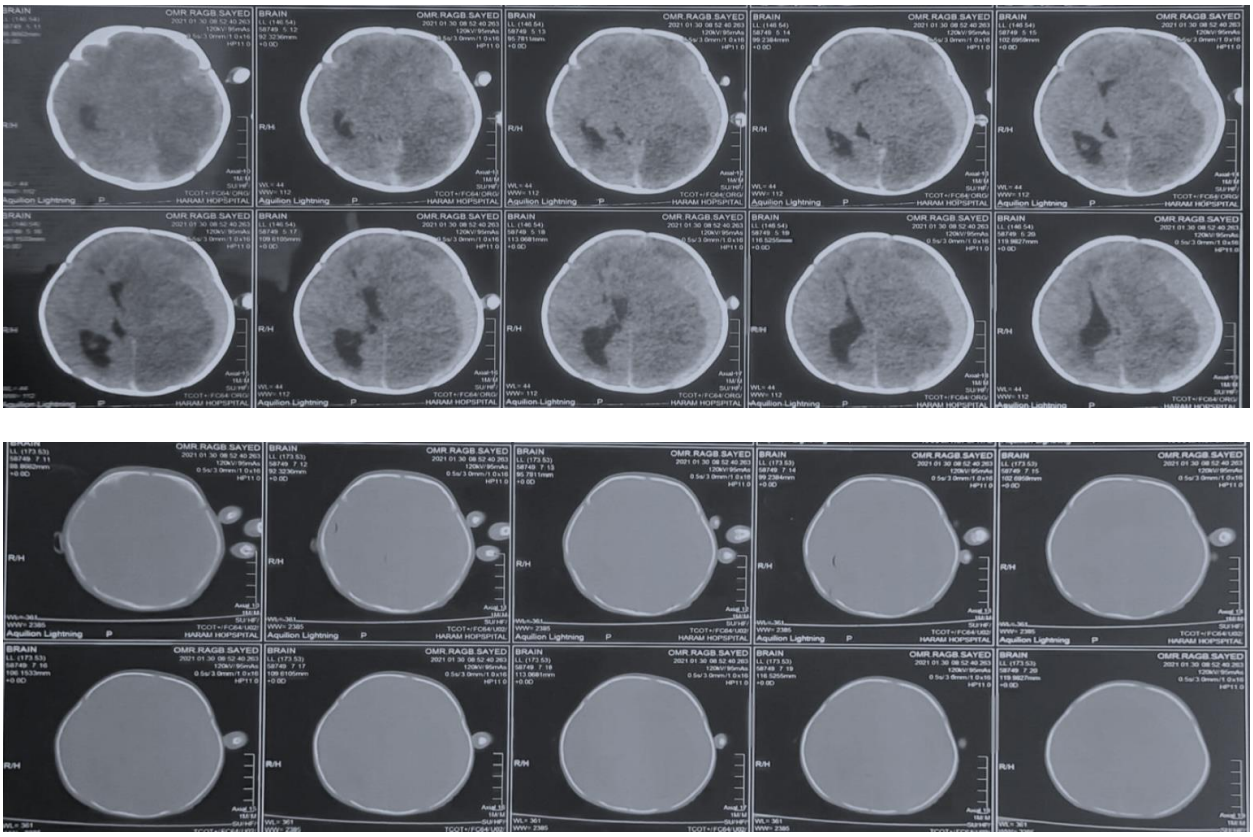

Figure 1. 25 days old male child with left acute SDH

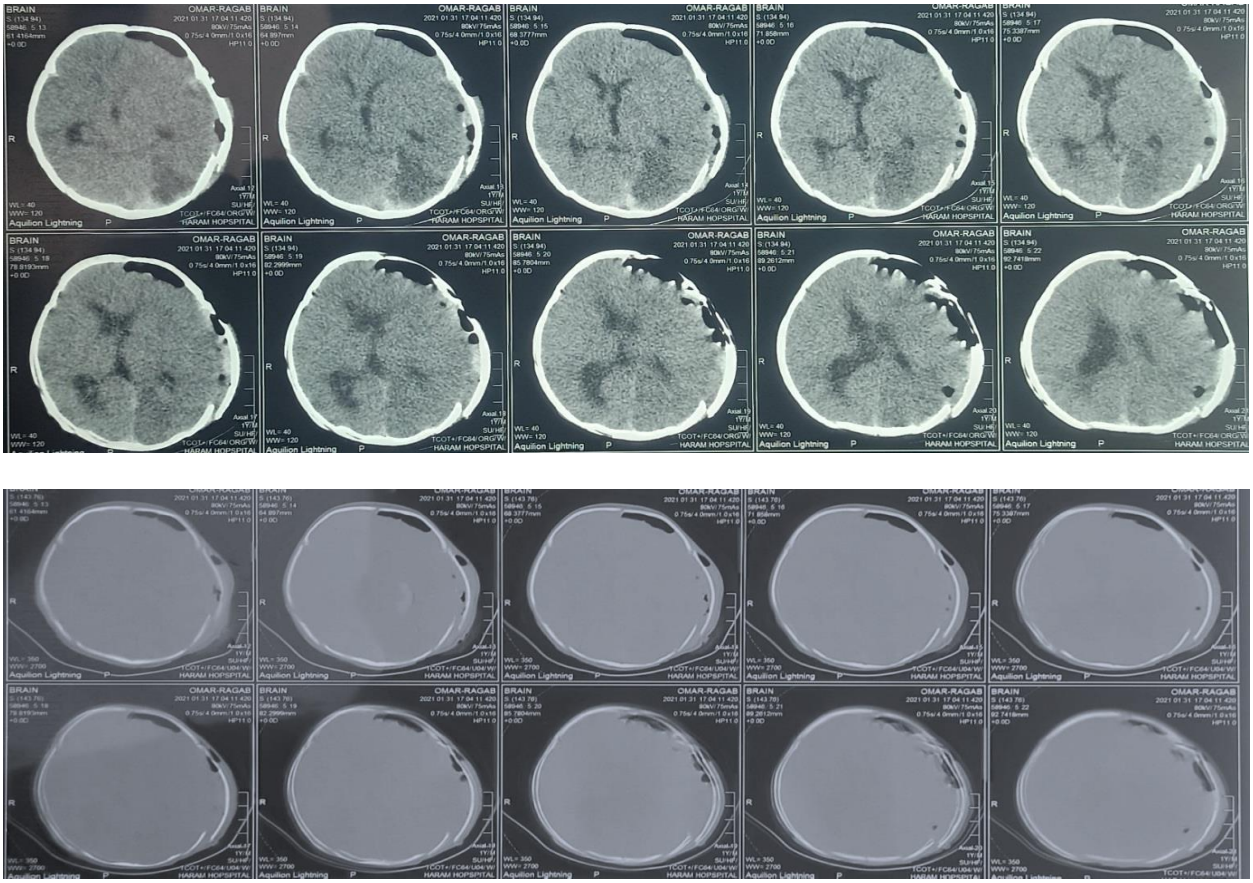

Figure 2. First day post operative after hematoma evacuation and flail bone flap position.

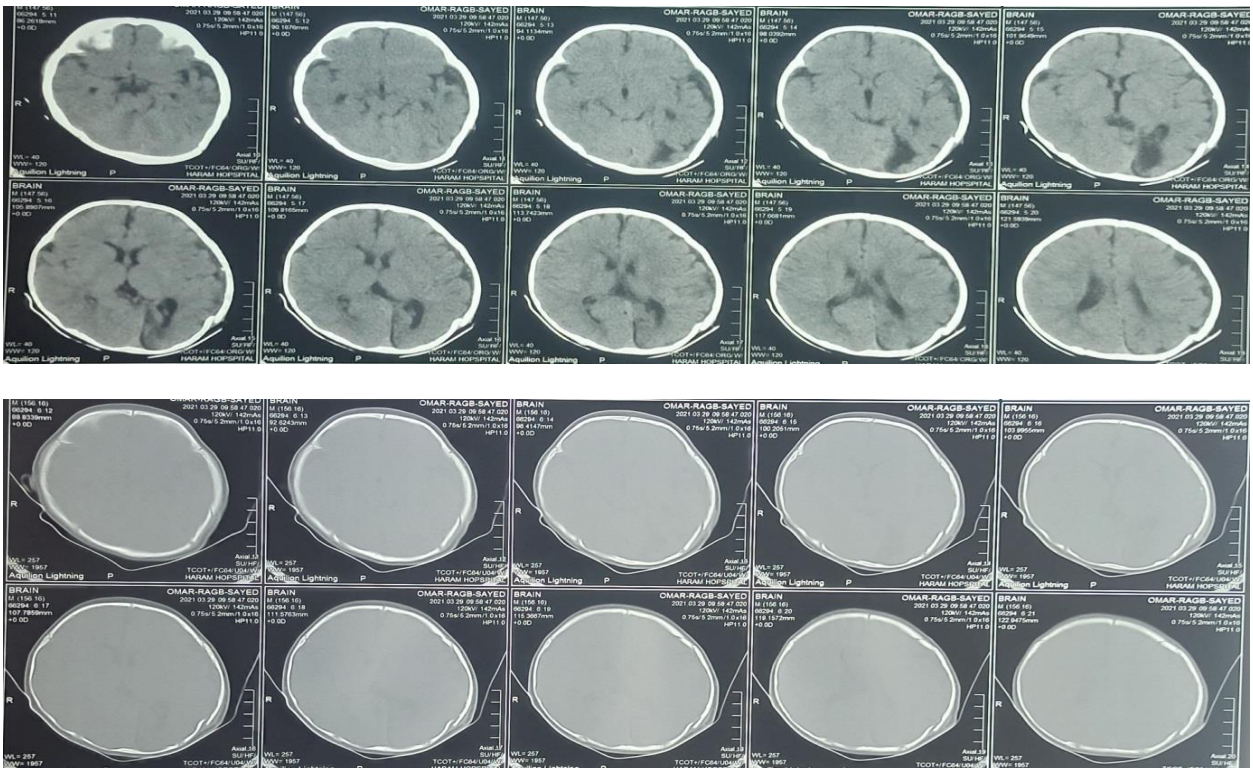

Figure 3. 2 months postoperative with disappearance of midline shift and bone flap return to normal position

Discussion

There are numerous surgical and non-surgical treatments for ASDHs, including burr holes, craniectomies, osteoplastic flaps, subtemporary decompressions, temporal lobectomy, dural openings, dural augmentation, and dural snips [17-20] . In spite of everyone's best efforts, the reported mortality rate has remained somewhere between 80 and 90 percent, and the morbidity rate among the population that has managed to survive has been extremely high [18, 19, 21, 22].

In addition to being less invasive surgically, the technique for hinged bone grafts leaves only one scar, eliminates the need for a second surgery to replace the bone graft, and is more anaesthetically preferred.

Our results showed full recovery in 3 cases (60%), 1 case died that represented 20% and 1 case survived with right sided weakness represented 20% morbidity.

In a study involving 30 adult patients diagnosed with ASDHs and undergoing craniectomy, subcutaneous placement of a hinged flail was used, according to the findings of Abd El-Wahed and Ahmed, 17 patients passed away while being treated at the hospital, accounting for 66.7 percent of the total; 13.3 percent of the patients who survived did so in a vegetative state, while 9 patients made a full recovery (30 percent) [23]. The variation could be explained due to different age groups.

The DC group had a worse preoperative GCS, younger age, more extracranial injuries, and a more severe CT, according to a study by Li et al., indicating that DC may be more effective than CR based on the actual outcomes, which were comparable in the two groups despite the predicted outcomes being worse for the DC group [24].

Tsermoulas et al. evaluated a total of 99 patients, 69 of whom had DC, 17 of whom had CR with a "riding flap," and 13 of whom had CR with a "fixed retained flap.". Despite the fact that patients in the DC group had worse outcomes, the baseline characteristics of the two groups were very different; those with DC had significantly more severe mechanisms, lower GCS, more extracranial injuries, and higher Rotterdam CT scores than those in the control group [25].

More herniation (pupillary changes) was found in the DC group, which was found by Woertgen et al., who looked at 180 patients (111 CR and 69 DC) and found a higher mortality rate in the DC group. There was no significant difference in the outcomes of CR and DC for patients who did not exhibit signs of herniation; however, there was a significant difference in the outcomes of CR and DC for patients who did exhibit signs of herniation [26].

Kwon et al. found that while patients with unfavourable features (age >70, anticoagulation or antiplatelet use, time to surgery > 4 hours, GCS < 8, nonreactive pupils, and major extracranial injury) had more poor outcomes those with less unfavourable features. [27].

The CR group and the DC group were compared by Kim and his colleagues in terms of age, gender, GCS score, hematoma volume, midline shift, ICH score, and the amount of time that passed between the ictus and the surgery. During the course of the study, CR was carried out on a total of 139 patients, while DC was carried out on 125 patients. The mortality rate at 30 days was the same for both the CR group and the DC group (13.7 percent vs. 15.2 percent, p = 0.729). On the other hand, the CR group had a functional survival rate of 46.0 percent after 12 months, which was significantly (p = 0.014) higher than the DC group's survival rate (32.0 percent) [28].

Our study has some limitations; it is a single-centre study that included a relatively small sample size. It also lacks long-term follow up for the included patients. These drawbacks must be handled in the upcoming studies.

Conclusion

Using a flail bone flap to perform a decompressive craniotomy may be beneficial, especially in infant cases, because of a high rate of complications associated with DC and subsequent cranioplasty in children and infants. The efficacy of this technique in terms of clinical outcomes and the reduction of complications necessitates further large-scale studies.

References

1. El Hadji Cheikh Ndiaye S, CISSE Y, NZISABIRA JM, DONZO A, NDIAYE PS, boubakar BADIANE S. Acute subdural hematoma post ventricular puncture in infants: A case report and review of the literature. International Journal of Surgery Case Reports. 2021:105913.
2. Elliott CA, Ramaswamy V, Jacob FD, Sankar T, Mehta V. Early diffusion restriction of white matter in infants with small subdural hematomas is associated with delayed atrophy. Child's Nervous System. 2017;33(2):289-95.

3. Karibe H, KaMeyaMa M, HayasHi T, Narisawa A, Tominaga T. Acute subdural hematoma in infants with abusive head trauma: a literature review. Neurologia medico-chirurgica. 2016:ra. 2015-0308.
4. Yokota H, Sugimoto T, Nishiguchi M, Hashimoto H. Greenstick fracture-hinge decompressive craniotomy in infants: illustrative case and literature review of techniques for decompressive craniotomy without bone removal. Child's Nervous System. 2019;35(9):1491-7.
5. Honeybul S, Ho K. The current role of decompressive craniectomy in the management of neurological emergencies. Brain injury. 2013;27(9):979-91.
6. Honeybul S, Ho K, Gillett G. Reconsidering the role of decompressive craniectomy for neurological emergencies. Journal of critical care. 2017;39:185-9.
7. Rahme R, Zuccarello M, Kleindorfer D, Adeoye OM, Ringer AJ. Decompressive hemicraniectomy for malignant middle cerebral artery territory infarction: is life worth living? Journal of neurosurgery. 2012;117(4):749-54.
8. Hossain-Ibrahim MK, Wasserberg J. Decompressive craniectomy--time for a change? British journal of neurosurgery. 2011;25(4):538-9.
9. Kolias AG, Kirkpatrick PJ, Hutchinson PJ. Decompressive craniectomy: past, present and future. Nature Reviews Neurology. 2013;9(7):405-15.
10. Shah AM, Jung H, Skirboll S. Materials used in cranioplasty: a history and analysis. Neurosurgical focus. 2014;36(4):E19.
11. Frassanito P, Fraschetti F, Bianchi F, Giovannenze F, Caldarelli M, Scoppettuolo G. Management and prevention of cranioplasty infections. Child's Nervous System. 2019;35(9):1499-506.
12. Rocque BG, Amancherla K, Lew SM, Lam S. Outcomes of cranioplasty following decompressive craniectomy in the pediatric population: A systematic review. Journal of Neurosurgery: Pediatrics. 2013;12(2):120-5.
13. Rocque BG, Agee BS, Thompson EM, Piedra M, Baird LC, Selden NR, et al. Complications following pediatric cranioplasty after decompressive craniectomy: a multicenter retrospective study. Journal of Neurosurgery: Pediatrics. 2018;22(3):225-32.
14. Bowers CA, Riva-Cambrin J, Hertzler DA, Walker ML. Risk factors and rates of bone flap resorption in pediatric patients after decompressive craniectomy for traumatic brain injury. Journal of Neurosurgery: Pediatrics. 2013;11(5):526-32.
15. Brommeland T, Rydning PN, Pripp AH, Helseth E. Cranioplasty complications and risk factors associated with bone flap resorption. Scandinavian journal of trauma, resuscitation and emergency medicine. 2015;23(1):1-7.
16. Phan K, Moore JM, Griessenauer C, Dmytriw AA, Scherman DB, Sheik-Ali S, et al. Craniotomy versus decompressive craniectomy for acute subdural hematoma: systematic review and meta-analysis. World neurosurgery. 2017;101:677-85. e2.
17. Aarabi B, Hesdorffer DC, Ahn ES, Aresco C, Scalea TM, Eisenberg HM. Outcome following decompressive craniectomy for malignant swelling due to severe head injury. Journal of neurosurgery. 2006;104(4):469-79.
18. Beck J, Raabe A, Lanfermann H, Berkefeld J, De Rochemont RDM, Zanella F, et al. Effects of balloon angioplasty on perfusion-and diffusion-weighted magnetic resonance imaging results and outcome in patients with cerebral vasospasm. Journal of neurosurgery. 2006;105(2):220-7.
19. Buschmann U, Yonekawa Y, Fortunati M, Cesnulis E, Keller E. Decompressive hemicraniectomy in patients with subarachnoid hemorrhage and intractable intracranial hypertension. Acta neurochirurgica. 2007;149(1):59-65.
20. Malliti M, Page P, Gury C, Chomette E, Nataf F, Roux F-X. Comparison of deep wound infection rates using a synthetic dural substitute (neuro-patch) or pericranium graft for dural closure: a clinical review of 1 year. Neurosurgery. 2004;54(3):599-604.
21. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW, et al. Surgical management of acute subdural hematomas. Neurosurgery. 2006;58(suppl_3):S2-16-S2-24.
22. Güresir E, Beck J, Vatter H, Setzer M, Gerlach R, Seifert V, et al. Subarachnoid hemorrhage and intracerebral hematoma: incidence, prognostic factors, and outcome. Neurosurgery. 2008;63(6):1088-94.
23. Abd El-Wahed M, Ahmed S. Comparative Study between Bone Flap Insertion in Abdominal Wall Versus Flail Replacement in Decompressive Craniectomy of Acute Subdural Hematoma. The Medical Journal of Cairo University. 2018;86(December):3825-32.
24. Li LM, Kolias AG, Guilfoyle MR, Timofeev I, Corteen EA, Pickard JD, et al. Outcome following evacuation of acute subdural haematomas: a comparison of craniotomy with decompressive craniectomy. Acta neurochirurgica. 2012;154(9):1555-61.
25. Tsermoulas G, Shah O, Wijesinghe HE, Silva AHD, Ramalingam SK, Belli A. Surgery for acute subdural hematoma: replace or remove the bone flap? World Neurosurgery. 2016;88:569-75.
26. Woertgen C, Rothoerl RD, Schebesch KM, Albert R. Comparison of craniotomy and craniectomy in patients with acute subdural haematoma. Journal of clinical neuroscience. 2006;13(7):718-21.
27. Kwon YS, Yang KH, Lee YH. Craniotomy or decompressive craniectomy for acute subdural hematomas: surgical selection and clinical outcome. Korean journal of neurotrauma. 2016;12(1):22-7.
28. Kim DB, Park SK, Moon BH, Cho BR, Jang DK, Jang KS. Comparison of craniotomy and decompressive craniectomy in large supratentorial intracerebral hemorrhage. Journal of Clinical Neuroscience. 2018;50:208-13.

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Diagnostic and prognostic role of magnetic resonance imaging in cases of moderate to severe traumatic brain injury

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diffusion axonal injury, haemorrhagic, magnetic resonance imaging, non-haemorrhagic, prognostication, traumatic brain injury

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ABSTRACT

Moderate to severe traumatic brain injury (TBI) remains a leading cause of death and disability worldwide. Timely diagnosis and accurate prognostication play a key role in informed clinical decision-making. Though magnetic resonance imaging (MRI) is a superior anatomical scan compared to computerized tomography (CT), the latter remains the current investigation of choice in the clinical setting of TBI due to some of the former's inherent deficiencies in imaging bone/blood, limited access, cost, etc. Nevertheless, the fact that MRI is a valuable adjunct in evaluating the TBI patients with clinical findings disproportionate to the CT scan substantiates its possible complementary/supplementary diagnostic and prognostic role in TBI. MRI scan is ideally placed on demonstrating the shear/diffuse axonal injury (DAI), non-haemorrhagic intraparenchymal lesions, and brain stem lesions poorly delineated by a CT scan. The currently available literature demonstrates that DAI and caudal brainstem lesions are indicators of poorer outcomes. However, the prognostic value of MRI, in addition to that of CT, remains an area of active investigation. We have tried to present the evidence-based use of MRI in moderate to severe TBI. Advances in newer MRI sequences like susceptibility-weighted imaging (SWI), diffusion tensor imaging (DTI), functional MRI (fMRI), and magnetic encephalography (MEG) have the potential to revolutionize the current role of MRI in TBI.

INTRODUCTION

Though computerized tomography (CT) scan of the head remains the investigation of choice for evaluation of a victim of acute traumatic

brain injury (TBI), magnetic resonance imaging (MRI) can play a valuable complementary diagnostic/ prognostic role in the same [1]. MRI is a superior anatomical scan to CT in all clinical settings, except in the acute moderate to severe TBI, due to its inherent deficiencies in imaging bone/blood. With ever-increasing accessibility seen to MRI scanners worldwide, there is an accompanying increase in the interest, among clinicians and radiologists alike, regarding the utility of MRI in diagnosing and prognosticating a variety of traumatic pathological conditions [2].

The role of MRI scanning in identifying and characterizing specific sequelae of TBI is well documented [3]. Particularly in evaluating patients whose clinical findings are disproportionate to the CT findings, MRI represents a valuable adjunct even in the acute phase. In such cases, MRI demonstrates the shear/diffuse axonal injury (DAI), non-hemorrhagic intraparenchymal lesions, and brain stem lesions poorly delineated by a CT scan. In subacute or chronic head injury, MRI is superior to CT and should be the primary imaging technique whenever possible [3]. Despite its unparalleled sensitiveness to deep intraparenchymal TBI lesions and shear injuries, the broad clinical adaptation of MRI in the trauma setting is limited, partly due to its higher costs, finite access, and more prolonged time consumption.

Early prognostication of moderate to severe TBI facilitates appropriate counseling of patients/families, aiding in sound clinical decisions. These informed clinical decisions are essential, as >50% of such patients end up with a permanent disability. Widely used CT prognostication scoring systems like Rotterdam/Marshall/Stockholm predict mortality better than TBIs' morbidity/permanent disability [1,4]. The 'centripetal model' of TBI, based on animal and postmortem studies, was proposed to better understand the role of shearing injury in clinical outcomes, and add to the existing CT prognostication [5]. It stated that the severity of grading of TBI should be directly proportional to the most caudal cerebral structure affected by the shearing injury. MRI is an ideal imaging modality to achieve the same. Nevertheless, the prognostic value of MRI, in addition to that of CT, remains an area of active investigation. We have tried to present the evidence-based use of MRI in moderate to severe TBI.

Protocol of MRI for TBI

The National Institute of Neurological Disorders and Stroke (NINDS) and several co-sponsoring Federal agencies have proposed common data elements (CDE) for developing data standards for clinical research. The following table shows the CDE for tier 1 evaluation of TBI using 1.5T MRI. Other advanced protocols are available at the NINDS website (**Table 1**).

Diagnostic Role of MRI in TBI

MRI appearance of traumatic lesions

Though CT is highly sensitive for detecting large intracranial hematomas, Gradient echo (GRE) and T2-weighted MRI are equally sensitive. T2 FLAIR (Fluid Attenuated Inversion Recovery) is more sensitive than CT to detect minor cerebral contusions. T2 FLAIR and GRE are as sensitive as CT for traumatic subarachnoid haemorrhage (SAH). T2 FLAIR and DWI (Diffusion-weighted Imaging) are more sensitive for non-hemorrhagic DAI, and GRE and SWI (Susceptibility weighted Imaging) for hemorrhagic DAI. Susceptibility weighted imaging (SWI) is a high-resolution three-dimensional imaging sequence. It is roughly six times more sensitive than the T2-weighted sequence for detecting traumatic microhemorrhages [6]. DWI is the sequence of choice for ischemia. It is essential to differentiate between hemorrhagic and non-hemorrhagic lesions as the hemorrhagic lesions are associated with a worse prognosis. The GRE and T2-weighted MRI sequences also detect signal dropout caused by iron-containing heme groups in slow-moving blood. Distributions of the microhemorrhages in areas associated with axonal injury such as the corpus callosum, brainstem, and other white matter tracts strongly suggest an imaging diagnosis of DAI. DAI microhemorrhages typically appear as punctate signal-free lesions in the white matter that 'bloom'.

Consequently, signal loss caused by punctate haemorrhages from DAI can be visualized years after injury though lesions fade over time. The density of T2-weighted lesions is associated with the severity of TBI in terms of admission Glasgow Coma Scale (GCS) and maximum intracranial pressure (ICP) during admission 3-month Glasgow Outcome Score. Another factor that needs consideration is the magnetic field strength used, as a 3 Tesla MRI demonstrates practically twice the sensitivity of a 1.5 Tesla device for microhemorrhages.

Table 1. Common data element (CDE) protocol for imaging parameters for MRI in TBI[1].

Sequence	3D T1W (MPRAGE, 3D IRFSPGR, 3D FFE)	T1W SE (opt if no 3D T1W)	T2W FSE	T2W FLAIR	DWI EPI	3D SWI†	2D GRE (FFE) (opt if no 3D SWI)
Orient	Sagittal	Sagittal	Axial*	Axial*	Axial*	Axial*	Axial*
TR (ms)	9-30	500-600	>3500	>9500	>5000	50	>500
TE(ms)	3-5	15-20	>90	>110	>100	40	>20
TI (ms)	1000			>2000			
FA (degrees)	8-10	90	90	150	90	15	15-20
Freq FOV mm (Phase FOV)	256(100%)	230(87.5%)	230(87.5%)	230(87.5%)	256(100%)	230(87.5%)	230(87.5%)
Matrix size	256x256	256x192	256x192	256x192	128x128	512x192	256x192
# Slices/ Thickness (mm)	120/2	32/4	32/4	32/4	32/4	94/2	32/4
Gap	0	0-20%	0-20%	0-20%	0-20%	0	0-20%
Voxel size(mm)	1x1x2	1x1x4	1x1x4	1x1x4	2x2x4	0.5x1x2	1x1x4
NEX	1	2	1-2	2	1-3	1	1-2
Phase Enc. Dir	A to P	A to P	R to L	R to L	A to P	R to L	R to L
Fat suppress	no	no	no	yes	yes	no	no
≅BW(Hz/Px)	160	120	130	200	≥1200	80	80-100
Flow Comp	no	slice	no	no	no	slice	slice
≅ETL			15-20	30	128		
b-values (sec/mm^2) (Directions)					0/1000** (3)		
≅Time* **	8:00	3:00	3:00	3:00	2:00	8:00	3:00

[1] Source-https://www.commondataelements.ninds.nih.gov/Traumatic%20Brain%20Injury#pane-162

*Recommend angle to AC-PC line; ** Use 800 sec/mm2 for infants <1 year old; ***To reduce acquisition time, use parallel imaging, if possible, AF/CL of 2/24-32; † Can use SWAN on GE systems.

Abbreviations: IR-FSPGR - Inversion recovery, fast spoiled gradient recalled echo; MPRAGE - Magnetization prepared-rapid gradient echo; FFE - Fast field echo; FSE – Fast spin echo; SE- Spin echo; FLAIR – Fluid attenuated inversion recovery; EPI - echo-planar imaging; SWI- Susceptibility-weighted imaging; GRE- Gradient echo; TE - echo delay time; TR - repetition time; TI- Inversion time; FA - fractional anisotropy; FOV - field of view; NEX - number of acquisitions; BW – bandwidth; ETL- Echo train length; A to P – Anterior to posterior; R to L – Right to left.

Classification of Severity of DAI

Grading of DAI has been described histologically according to the anatomic distribution of injury, which correlated with the clinical outcome. The classification was proposed first by Adams in 1989 and divided DAI into three grades [5]. This is the commonly applied grading system for classifying DAI lesions seen on MRI.

- Grade I: Involves grey-white matter interfaces (Figure 1).

Most commonly: Parasagittal regions of frontal lobes, periventricular temporal lobes, Parietal and occipital lobes, internal and external capsules, and cerebellum.

- Grade II: Involves corpus callosum in addition to grade I locations (Figure 2).

Most commonly: Posterior body and splenium but advance anteriorly with increasing injury severity. Most frequently seen unilateral. It may be seen on the SWI sequence.

- Grade III: Involves brainstem in addition to grade I and II locations (Figure 3).

Most commonly: Rostral midbrain, superior cerebellar peduncles, medial lemnisci, and corticospinal tracts.

Grading of brainstem lesions was proposed by Firsching et al. and has been validated by others [7–10]

- Grade I: No brainstem involvement; lesions of only hemispheres.
- Grade II: Unilateral brainstem lesions at any level with or without supratentorial lesions.
- Grade III: Bilateral lesions of the mesencephalon with or without supratentorial lesions.
- Grade IV: Bilateral lesions of the pons with or without lesions of lesser grades.

Brainstem injury can be categorized as anterior or posterior, hemorrhagic or non-hemorrhagic, and unilateral or bilateral [11]. Other alternative classification of brainstem injury is primary or secondary due to herniation. The primary injury can be due to a direct impact against the tentorial free edge or as a part of DAI [12,13]. The brainstem lesions are also classified as superficial or deep [13]. The grading assigned by both the systems is determined by the most caudal brain lesion present, though their definitions vary.

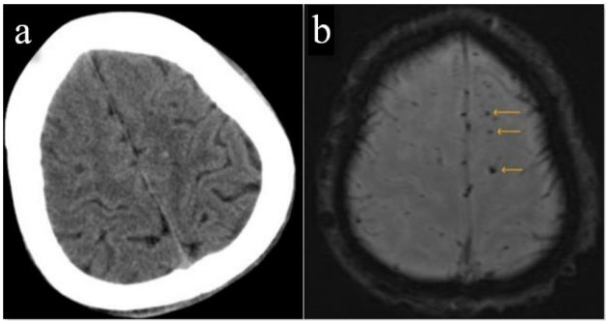

Figure 1. Computerized tomography (CT) scan (a) and magnetic resonance imaging (MRI) – susceptibility-weighted imaging (SWI) sequence (b) showing multiple haemorrhages in left parasagittal grey-white junction (yellow arrows). The presence of such lesions in absence of corpus callosal or brainstem involvement indicates grade 1 diffuse axonal injury (DAI).

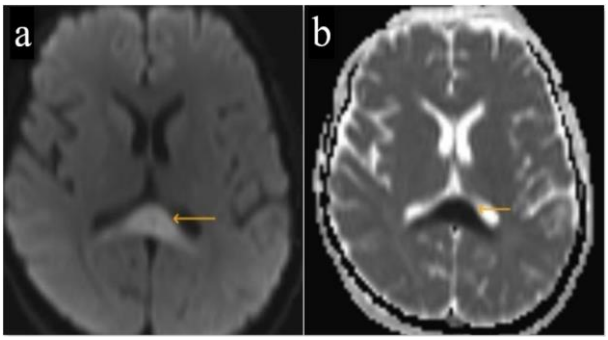

Figure 2. Magnetic resonance imaging (MRI) – diffusion-weighted imaging (DWI) sequence (a) and apparent diffusion coefficient (ADC) sequence (b) showing restricted diffusion (yellow arrows) in the splenium of corpus callosum indicating grade 2 diffuse axonal injury (DAI).

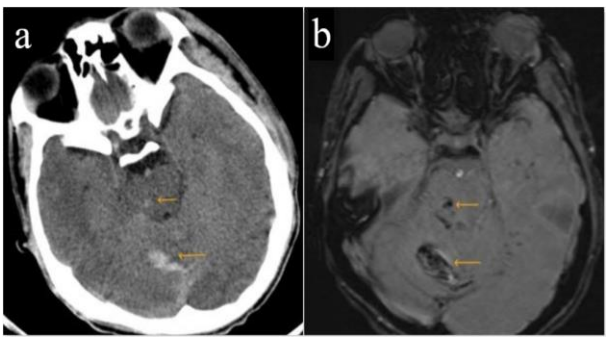

Figure 3. Computerized tomography (CT) scan (a) and magnetic resonance imaging (MRI) - susceptibility-weighted imaging (SWI) sequence (b) showing hemorrhages (yellow arrows) in right paramedian brainstem and cerebellum indicating grade 3 diffuse axonal injury (DAI).

Newer MRI sequences for TBI

Diffusion tensor imaging (DTI) is a newer MRI sequence increasingly used to diagnose DAI [14,15]. DTI is based on the principle of calculating the directional asymmetry of water diffusion, called anisotropy, in mapping white matter tracts. The injured axons in white matter tracts have lower anisotropy than normal ones. Some studies had found it extremely sensitive to axonal injuries following TBI of any severity, even when the CT and conventional MRI sequences showed no abnormalities [15,16]. DTI comes with its fair share of limitations, like its relative insensitivity to axonal injuries in complex white matter regions, due to the absence of one predominant direction of the axons and lack of spatial resolution to detect injuries in small white matter tracts. Other described unique MRI sequences for TBI include magnetic resonance spectroscopy (MRS), functional MRI (fMRI) and magnetic encephalography (MEG). MRS can map changes in the brain metabolic processes and resulting metabolite concentration changes after TBI [17]. fMRI can also reveal areas of either reduced or increased activation and altered connectivity via its BOLD (Blood Oxygenation Level-Dependent) imaging technique [18]. Some authors have reported the usefulness of MEG in detecting TBI induced abnormalities that were not identified with DTI or conventional MRI and correlated with clinical outcome [19].

Prognostic Role of MRI in TBI

There is no consensus about the optimal timing for MRI after TBI for predicting outcome. However, it should preferably be performed within the first-week post-injury for reliable prognostication [20]. The presence of brainstem involvement is correlated with outcome. Mortality increases gradually from 14% with grade I brainstem lesions to 100% with grade IV lesions [10]. Bilateral brainstem involvement is strongly associated with poor outcomes. Posterior location is associated with disability. The non-haemorrhagic, anterior lesions or unilateral injuries are associated with better outcome [11]. Superficial lesions are associated with better outcomes than deeper lesions [13]. SWI lesions in the midbrain corresponding to substantia nigra and tegmentum are independently related to poor outcomes [20].

The grading is also used as a prognostic indicator for recovery of consciousness. Park et al. reported that 14.3% of patients with cerebral white matter lesions (grade 1) did not recover their consciousness, and 50% of patients with corpus callosum lesions (grade 2), 51.6% of patients with brain stem lesion (grade 3) did not recover their consciousness [21]. The grading of DAI is well correlated with time to regain consciousness after TBI. Patients with grade 1 injury become conscious within a week after injury, while grade 2 take two weeks to recover, and patients with grade 3 take two months to regain consciousness [21]. Besides grading, the lesion volume also bears the outcome. The volume of visible DAI lesions in the corpus callosum, brainstem, and thalamus, in DWI and T2 FLAIR sequences, are independent prognostic factors in patients with severe TBI. An essential predictive MRI variable is DWI lesion volume in the corpus callosum. However, in moderate TBI cases, the number of cortical contusions is more critical for prognosis [22].

A systematic review published by Haghbayan et al. (2017), reviewing the prognostic value of MRI in moderate to severe TBI, concluded that the brainstem lesions were associated with higher mortality and unfavourable functional outcome (Glasgow Outcome Scale 1-3) at ≥ 6 months [23]. And that DAI patterns were associated with an increased risk of unfavourable functional outcomes, with depth-based MRI scores demonstrating an increased risk of unfavourable outcomes as more caudal structures were affected. Along the same lines, a recent meta-analysis by M. M. Van eijck et al. (2018), studying the prognostic value of DAI in TBI, reported that the presence of DAI resulted in three times higher risk of an unfavourable outcome, and this risk further increased three times with each increasing grade of DAI [24]. This meta-analysis reviewed data from 32 selected articles, deducing an overall unfavourable (Glasgow outcome score 1-3) functional outcome of 38% in patients with DAI in TBI.

Conclusion

MRI following TBI provides valuable assistance, either complementary or supplementary to CT scan, in determining diagnosis and prognosis in individual cases. The presence of DAI and caudal brainstem lesions lead to a poorer outcome. Advances in newer MRI sequences like SWI, DTI, fMRI, MEG. have the

potential to revolutionize the current role of MRI in TBI.

Abbreviations:

ADC - Apparent diffusion coefficient
CT - Computed tomography
DAI - Diffuse axonal injury
DWI – Diffusion-weighted imaging
GCS - Glasgow Coma Scale
GRE - Gradient recalled echo
ICP - Intracranial pressure
MRI - Magnetic resonance imaging
NINDS - National Institute of Neurological Disorders and Stroke
SAH - Subarachnoid hemorrhage
SDH - Subdural hematoma
SWI – Susceptibility-weighted imaging
T2 FLAIR - T2-weighted Fluid Attenuated Inversion Recovery
TBI - Traumatic brain injury
fMRI – Functional magnetic resonance imaging
BOLD – Blood oxygen level-dependent
MRS – Magnetic resonance spectroscopy
DTI – Diffusion tensor imaging
MEG - Magnetic encephalography

References

1 Schweitzer AD, Niogi SN, Whitlow CT, et al. Traumatic brain injury: Imaging patterns and complications. Radiographics 2019;39:1571–95. doi:10.1148/rg.2019190076

2 Blennow K, Brody DL, Kochanek PM, et al. Traumatic brain injuries. Nat Rev Dis Prim 2016;2:1–19. doi:10.1038/nrdp.2016.84

3 Kelly AB, Zimmerman RD, Snow RB, et al. Head trauma: comparison of MR and CT--experience in 100 patients. AJNR Am J Neuroradiol;9:699–708.http://www.ncbi.nlm.nih.gov/pubmed/3135716

4 Mata-Mbemba D, Mugikura S, Nakagawa A, et al. Early CT findings to predict early death in patients with traumatic brain injury: Marshall and Rotterdam CT scoring systems compared in the major academic tertiary care hospital in Northeastern Japan. Acad Radiol 2014;21:605–11. doi:10.1016/j.acra.2014.01.017

5 Adams JH, Doyle D, Ford I, et al. Diffuse axonal injury in head injury: Definition, diagnosis and grading. Histopathology 1989;15:49–59. doi:10.1111/j.1365-2559.1989.tb03040.x

6 Su E, Bell M. Diffuse axonal injury. In: Laskowitz D, Gran G, eds. Translation Research in Traumatic Brain Injury. Boca Raton (FL): CRC Press/Taylor and Francis Group 2016.

7 Wedekind C, Hesselmann V, Lippert-Grüner M, et al. Trauma to the pontomesencephalic brainstem--a major clue to the prognosis of severe traumatic brain injury. Br J Neurosurg 2002;16:256–60. doi:10.1080/02688690220148842

8 Kampfl A, Schmutzhard E, Franz G, et al. Prediction of recovery from post-traumatic vegetative state with cerebral magnetic-resonance imaging. Lancet 1998;351:1763–7. doi:10.1016/S0140-6736(97)10301-4

9 Weiss N, Galanaud D, Carpentier A, et al. Clinical review: Prognostic value of magnetic resonance imaging in acute brain injury and coma. Crit Care 2007;11:230. doi:10.1186/cc6107

10 Firsching R, Woischneck D, Klein S, et al. Classification of severe head injury based on magnetic resonance imaging. Acta Neurochir (Wien) 2001;143:263–71. doi:10.1007/s007010170106

11 Hilario A, Ramos A, Millan JM, et al. Severe Traumatic Head Injury: Prognostic Value of Brain Stem Injuries Detected at MRI. Am J Neuroradiol 2012;33:1925–31. doi:10.3174/ajnr.A3092

12 Shukla D, Mahadevan A, Sastry KVR, et al. Pathology of post traumatic brainstem and hypothalamic injuries. Clin Neuropathol 2007;26:197–209. doi:10.5414/NPP26197

13 Shibata Y, Matsumura A, Meguro K, et al. Differentiation of mechanism and prognosis of traumatic brain stem lesions detected by magnetic resonance imaging in the acute stage. Clin Neurol Neurosurg 2000;102:124–8. doi:10.1016/S0303-8467(00)00095-0

14 Niogi SN, Mukherjee P. Diffusion tensor imaging of mild traumatic brain injury. J Head Trauma Rehabil 2010;25:241–55. doi:10.1097/HTR.0b013e3181e52c2a

15 Hulkower MB, Poliak DB, Rosenbaum SB, et al. A decade of DTI in traumatic brain injury: 10 years and 100 articles later. Am J Neuroradiol 2013;34:2064–74. doi:10.3174/ajnr.A3395

16 Mac Donald CL, Johnson AM, Cooper D, et al. Detection of Blast-Related Traumatic Brain Injury in U.S. Military Personnel. N Engl J Med 2011;364:2091–100. doi:10.1056/nejmoa1008069

17 Maudsley AA, Govind V, Levin B, et al. Distributions of Magnetic Resonance Diffusion and Spectroscopy Measures with Traumatic Brain Injury. J Neurotrauma 2015;32:1056–63. doi:10.1089/neu.2014.3505

18 Irimia A, Van Horn JD. Functional neuroimaging of traumatic brain injury: Advances and clinical utility. Neuropsychiatr Dis Treat 2015;11:2355–65. doi:10.2147/NDT.S79174

19 Huang M-X, Theilmann RJ, Robb A, et al. Integrated Imaging Approach with MEG and DTI to Detect Mild Traumatic Brain Injury in Military and Civilian Patients. J Neurotrauma 2009;26:1213–26. doi:10.1089/neu.2008.0672

20 Abu Hamdeh S, Marklund N, Lannsjö M, et al. Extended Anatomical Grading in Diffuse Axonal Injury Using MRI: Hemorrhagic Lesions in the Substantia Nigra and Mesencephalic Tegmentum Indicate Poor Long-Term Outcome. J Neurotrauma 2017;34:341–52. doi:10.1089/neu.2016.4426

21 Park SJ, Hur JW, Kwon KY, et al. Time to Recover

Consciousness in Patients with Diffuse Axonal Injury : Assessment with Reference to Magnetic Resonance Grading. J Korean Neurosurg Soc 2009;46:205. doi:10.3340/jkns.2009.46.3.205

22 Moen KG, Brezova V, Skandsen T, et al. Traumatic Axonal Injury: The Prognostic Value of Lesion Load in Corpus Callosum, Brain Stem, and Thalamus in Different Magnetic Resonance Imaging Sequences. J Neurotrauma 2014;31:1486–96. doi:10.1089/neu.2013.3258

23 Haghbayan H, Boutin A, Laflamme M, et al. The prognostic value of MRI in moderate and severe traumatic brain injury: A systematic review and meta-analysis. Crit Care Med 2017;45:e1280–8. doi:10.1097/CCM.0000000000002731

24 van Eijck MM, Schoonman GG, van der Naalt J, et al. Diffuse axonal injury after traumatic brain injury is a prognostic factor for functional outcome: a systematic review and meta-analysis. Brain Inj 2018;32:395–402. doi:10.1080/02699052.2018.1429018

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Airway management in neurotrauma care. Basic considerations

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ABSTRACT

The predictability of the airway compromise affects the decision for tracheal intubation. Associated specific injuries, clinical presentation, and expected deterioration are the deciding factors regarding the need for securing the airway. Emergent or semi-urgent intubations are straightforward in the majority of patients. Airway management in trauma patients aims to improve tissue oxygenation, ensure ventilatory exchange, stabilize other injuries and prevent aspiration. Airway management in the trauma and emergency room is challenging as the emergency team has limited time for full airway assessment unlike pre-anaesthesia check-up clinic/operative room. The airway cart must be checked routinely in the emergency room for the working condition of the equipment and its availability. All trauma patients must be considered to have cervical spine injuries unless ruled out. The airway management for trauma patients is best done using a team approach including emergency medicine physicians, anaesthesiologists, surgeons, and trained paramedical staff. Regardless of the emergency room setting, airway management of a trauma patient requires effective communication and efficient teamwork.

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INTRODUCTION

Airway management in trauma patients aims to improve tissue oxygenation, ensure ventilatory exchange, stabilize other injury and prevent aspiration. Airway management in the trauma and emergency room is challenging as the emergency team has limited time for full

airway assessment unlike pre-anaesthesia check-up clinic/operative room. Trauma patients present a varied spectrum of injury from localized to multisystem involvement. The presence of hemodynamic instability, direct airway injury, thoracic injury, combative patient (Raised Intracranial pressure/intoxication/hypoxemia), etc. can lead to difficult airway situations. Availability of trained team, synchronized teamwork, and functional airway equipment are paramount for safe airway management. [1-3]

INDICATION FOR SECURING THE AIRWAY

Associated specific injuries, clinical presentation, and expected deterioration are the deciding factors regarding the need for securing the airway. Emergent or semi-urgent intubations are straightforward in the majority of patients. But in some patients, it may be less clear. The Eastern Association for the Surgery of Trauma (EAST) practice management guidelines and the Advanced Trauma Life Support (ATLS) program have given indications for intubation in trauma patients. [1, 4] In general, the indication for emergency tracheal intubation in trauma patients is the failure of oxygenation or ventilation, failure to maintain/protect the airway and anticipated deterioration of the airway. (**Table 1: Indication for tracheal intubation**). The trauma patients may have poor oxygenation and ventilation hypoxemia or hypoventilation due to multiple factors and may not respond to simple interventions e.g., oxygen supplementation. Adequacy of oxygenation and ventilation can be assessed clinically by pulse oximetry, respiratory effort, and associated injuries. Inability to protect the airway could be due to decreased level of consciousness secondary to traumatic brain injury or intoxication. In these cases, early intubation is typically indicated. Any patients with penetrating neck injury, inhalation injury (burns from closed space fire), hemorrhagic shock (due to complicated pelvic fracture, Liver laceration) may lose airway as natural clinical course, thus they will need intubation in anticipation. The predictability of the airway compromise affects the decision for tracheal intubation. [5, 6]

Table 1: Indication for tracheal intubation

Eastern Association for the Surgery of Trauma (EAST)
• Hypoventilation
• Persistent hypoxemia
• Decreased level of consciousness (GCS≤ 8)
• Cardiac arrest
• Hemorrhagic shock
• Airway obstruction
• Inhalation injury
• Facial injury
Advanced trauma life support (ATLS)
• Poor Respiratory efforts
• Hypoxia
• Hypercarbia
• Cyanosis
• Neurological deterioration (GCS≤ 8)
• Apnea
• Severe facial injury
• Direct airway injury
• Inhalational injury
• Unconscious patients

PREPAREDNESS

A preparedness and coordinated approach to airway management is the key step. [7, 8] The airway cart must be checked routinely in the emergency room for the working condition of equipment and its availability. The intuitional/local practice best determines the timing but checking after every shift is recommended. Standard airway equipment should be there in the airway cart. [9] The cart should have different sizes/types of facemasks, laryngoscopes, endotracheal tubes, oral airway, nasal airway, bougies, invasive airway equipment, etc. (**Table 2: Difficult airway cart**).

Table 2: Difficult airway cart

• Manual Resuscitator with oxygen reservoir
• Oral and nasal airways (various sizes)
• Rescue airways device: Combi tube, Laryngeal mask airway
• Endotracheal tube introducer (Gum elastic bougie)
• Semi-rigid stylet
• Endotracheal tubes (Range of sizes)
• Laryngoscope blades of shorted design and size
• Laryngoscope handle with battery (check for functionality)
• Syringes, Lubricant, Tube ties
• Video laryngoscope
• Cricothyrotomy kit

Always ensure that oxygen source and suction equipment are available in the functional stage. The emergency drug tray must have induction agents (e.g., etomidate, ketamine, propofol, etc.) and muscle relaxants (e.g., Succinylcholine, Rocuronium, etc.)

beside emergency drugs. [2, 3, 10] Regardless of the emergency room setting, airway management of a trauma patient requires effective communication and efficient teamwork. The airway management for trauma patients is best done using a team approach including emergency medicine physicians, anaesthesiologist's, surgeons, and trained paramedical staff. [11-13] Emergency intubation in the emergency room requires additional assistance to administer drugs, to ventilate the patient, to give cricoid pressure, and manual in-line stabilization (MILS) of the cervical spine if indicated. Even extra assistance is needed to control agitated patients due to head injury/intoxication.

Uncooperative/Agitated patients

The agitated patients can injure themselves. The trauma patients may be violent or agitated due to various reasons such as alcohol/drugs intoxication, hypoxia, hypercarbia, head injury, hypoglycemia, severe pain, etc. These factors should be addressed along with airway intervention. As per EAST guidelines, if the severity of agitation hinders assessment and resuscitation, intubation can be considered. [4]

Craniofacial trauma

A significant proportion of individuals with severe maxillofacial injury, more so with pan-facial involvement, have associated traumatic brain and spine injury; therefore, spine stabilization and preventing airway compromise are challenging in these patients. The mechanisms attributed to airway compromise in maxillo-facial trauma are primarily due to tongue fall secondary to bilateral mandible fracture, displacement of the fractured maxilla, hematoma, soft-tissue oedema, foreign body, or direct laryngeal trauma. The patient should be placed in a lateral position for mid-facial trauma with the potential risk of haemorrhage and the mandible pulled forward. This technique would help remove the blood and secretion, and the airway can be easily kept patient. Oropharyngeal airway and nasopharyngeal airway devices are used in these cases because traditional manoeuvres of jaw thrust, chin lift, and head tilt may not be possible due to associated oedema or C-spine injury. While intubating, a rigid high suction device may be kept alongside the laryngoscope to prevent soiling of the airway. [14] The available options are orotracheal intubation, nasotracheal intubation, cricothyroidotomy, and tracheostomy.

Direct airway trauma

In patients with direct trauma, the airway is a challenging situation for the emergency team. Direct trauma to the airway can be due to blunt or penetrating injury. Airway injury can occur at multiple levels and may be associated with a cervical spine injury, injury to the aerodigestive tract, etc. It can result in immediate or delayed airway obstruction. [5, 15, 16] General principles for the management of direct airway trauma include repeated clinical assessment because the airway can compromise due to tissue oedema or hematoma over time. Even if the patient appears clinically stable, airway management is required given anticipated deterioration. Swallowing of blood from a facial fracture can cause gastric distention and irritation thus it may increase the risk of regurgitation. The emergency team should assess the possibility of difficulty with bag-mask ventilation, endotracheal intubation, supraglottic device placement, and even with the surgical airway. A large-bore catheter suction should be used. If a difficult BMV is anticipated, an awake approach instead of RSII is safer. During bag-mask ventilation, airway obstruction can increase further due to pressure on the mandible and displacement of fractured segments. Airway disruption and bleeding make laryngoscopy and intubation challenging. Placement of supraglottic airways devices can be difficult due to distorted airway anatomy and limited mouth opening. If initial attempts to laryngoscopy fail, the surgical airway is indicated. In selected patients, the surgical airway may be the most appropriate initial approach to airway intervention.

Conclusion

All trauma patients must be considered to have cervical spine injury unless rules out. The selection of induction drugs should be based on the type/severity of the injury and the patient's hemodynamic status. A variety of effective rescue airway devices are available for use in trauma patients. Airway specialists should become familiar with and practice several of them to maximize the options available in case of a failed airway.

References

1 Trauma ACoSCo. Advanced Trauma Life Suport ATLS: Student Course Manual: American College of Surgeons, 2012.

2. Cranshaw J, Nolan J. Airway management after major trauma. Continuing Education in Anaesthesia, Critical Care & Pain 2006;6:124-127.
3. Louro J, Varon AJ. Airway management in trauma. International anesthesiology clinics 2021;59:10-16.
4. Mayglothling J, Duane TM, Gibbs M, et al. Emergency tracheal intubation immediately following traumatic injury: an Eastern Association for the Surgery of Trauma practice management guideline. The journal of trauma and acute care surgery 2012;73:S333-340.
5. Jain U, McCunn M, Smith CE, Pittet JF. Management of the Traumatized Airway. Anesthesiology 2016;124:199-206.
6. Rajandram RK, Syed Omar SN, Rashdi MF, Abdul Jabar MN. Maxillofacial injuries and traumatic brain injury--a pilot study. Dental traumatology : official publication of International Association for Dental Traumatology 2014;30:128-132.
7. Smith KA, High K, Collins SP, Self WH. A preprocedural checklist improves the safety of emergency department intubation of trauma patients. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine 2015;22:989-992.
8. Tsai AC, Krisciunas GP, Brook C, et al. Comprehensive Emergency Airway Response Team (EART) Training and Education: Impact on Team Effectiveness, Personnel Confidence, and Protocol Knowledge. The Annals of otology, rhinology, and laryngology 2016;125:457-463.
9. Bjurström MF, Bodelsson M, Sturesson LW. The Difficult Airway Trolley: A Narrative Review and Practical Guide. Anesthesiology research and practice 2019;2019:6780254.
10. Khan RM, Sharma PK, Kaul N. Airway management in trauma. Indian journal of anaesthesia 2011;55:463-469.
11. Kovacs G, Law JA, Ross J, et al. Acute airway management in the emergency department by non-anesthesiologists. Canadian journal of anaesthesia = Journal canadien d'anesthesie 2004;51:174-180.
12. Levitan RM, Rosenblatt B, Meiner EM, Reilly PM, Hollander JE. Alternating day emergency medicine and anesthesia resident responsibility for management of the trauma airway: a study of laryngoscopy performance and intubation success. Annals of emergency medicine 2004;43:48-53.
13. Mackersie RC. Pitfalls in the evaluation and resuscitation of the trauma patient. Emergency medicine clinics of North America 2010;28:1-27, vii.
14. DuCanto J, Serrano KD, Thompson RJ. Novel Airway Training Tool that Simulates Vomiting: Suction-Assisted Laryngoscopy Assisted Decontamination (SALAD) System. The western journal of emergency medicine 2017;18:117-120.
15. Barak M, Bahouth H, Leiser Y, Abu El-Naaj I. Airway Management of the Patient with Maxillofacial Trauma: Review of the Literature and Suggested Clinical Approach. BioMed research international 2015;2015:724032.
16. Saini S, Singhal S, Prakash S. Airway management in maxillofacial trauma. Journal of anaesthesiology, clinical pharmacology 2021;37:319-327.

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Post ventriculoperitoneal shunting S. Maltophilia Meningitis. An uncommon case

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ABSTRACT

Background: Leptomeningeal inflammation caused by S. Maltophilia is rare. It is inextricably linked with prior antimicrobial therapy; prolonged ICU stays and antecedent neurosurgical intervention.

Case description: We describe a case of a 5-year-old male child with posterior fossa medulloblastoma with obstructive hydrocephalus who underwent ventriculoperitoneal shunt followed by suboccipital midline craniotomy and later presented with S. Maltophilia meningitis.

Conclusion: The overall mortality in the cases reviewed was 17 per cent. Inherent resistance to a wide array of antimicrobial agents with a simultaneously increasing number of cases poses a therapeutic challenge. Trimethoprim/sulfamethoxazole is recommended as empirical and as a definitive treatment in patients with S. Maltophilia infection. The optimal duration of therapy for S. Maltophilia meningitis is similar to the treatment of gram-negative bacillary meningitis, which is usually 2 weeks after the culture has been negative.

Keywords
S. Maltophilia Meningitis, nosocomial meningitis, neurosurgery

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INTRODUCTION

After *P. Aeruginosa. Baumannii,S. Maltophilia* is the third most common isolated non-fermenting aerobic Gram-negative bacilli.[1]S. maltophilia rarely causes meningitis.[2]It is particularly common among critically ill / immunosuppressed patients and is inextricably linked with prior antimicrobial therapy, prolonged ICU stays, prematurity, intracranial hemorrhages, malignancies, and antecedent neurosurgical intervention. It has recently come into the limelight in the last two decades owing to its increased pathogenicity and also because of marked antibiotic resistance.[3]We describe a case of a 5-year-old male child with posterior fossa medulloblastoma with obstructive hydrocephalus who underwent ventriculoperitonealshunt followed by suboccipital midline craniotomy and later presented with S. maltophilia meningitis.

CASE REPORT

A 5-year-old male came to A&E with complaints of headache and vomiting (3-4) episodes since the last five days. There was no history of

fever, loss of consciousness, seizures, visual impairment, hearing loss, motor or sensory deficit. On presentation, neurological examination revealed Glasgow coma scale of E4V5M6, the pupil were equal and reactive, cranial nerve IX & X were involved (uvula was in the midline but gag reflex was impaired), and cerebellar signs (ataxia and dysdiadochokinesia) on the right side were positive. Non-contrast CT scan head showed posterior fossa hyperdense lesion arising from the floor of the fourth ventricle causing upstream dilatation of third and bilateral lateral ventricle causing obstructive hydrocephalus. MRI brain showed intra-ventricular solid cystic lesion arising from the floor of the fourth ventricle with no restriction on diffusion weighted sequence and elevated choline peak with reduced N-acetyl aspartate suggestive of medulloblastoma.The patient underwent right ventriculoperitoneal shunt via right keen's point under general anaesthesia in view of obstructive hydrocephalus, papilledema on direct fundoscopy (Frisen's grade II), and clinical signs of raised intra-cranial pressure. CSF analysis revealed no signs of meningitis and CSF for malignant cytology revealed no malignant cells. The patient was discharged thereafter.

Four weeks later, the patient presented to the A&E with complaints of altered sensorium, increased drowsiness, and recurrent episodes of vomiting. The Glasgow coma scale was E4V4M6, and pupils were equal and reactive. The shunt chamber was compressible and recoil was good. However, a repeat CT scan showed an increase in the tumour size with peri-lesional edema. The patient underwent suboccipital midline craniotomy with tumor excision under general anesthesia. Postoperatively, the patient was shifted on mechanical ventilation. An extubation trial was given but was not successful. Tracheostomy was done on post-operative day two in view of anticipated prolonged ventilator requirement, impaired gag reflex and pooling of chest secretions.

The Glasgow coma scale of the patient was E3VtM6. He developed fever 102.3°F and neck stiffness on post-operative day three. All routine investigations including blood, urine, tracheal, CSF cultures, and pro-calcitonin were sent for this patient. The patient's blood and urine cultures yielded no sign of bacteria. However, analysis of CSF revealed sugar 2.1mmol/L, protein 0.23g/L, WBC count 0.53 x 109 cells /L (78% neutrophils, 10% lymphocytes, 10% mononuclear). Pro-calcitonin was significantly positive for this patient (>10). CSF gram staining showed gram-negative bacilli. Antibiotics were upgraded to meropenem and vancomycin from ceftriaxone and amikacin. The patient fever and neck stiffness responded partially to the antibiotics.

However, the child later experienced an episode of the seizure (generalized tonic-clonic), and he was shifted on a continuous mode of mechanical ventilation in view of a dip in the Glasgow coma score (E2VtM5). Clinical examination showed that the shunt chamber was non-compressible and recoil was absent. Repeat CT scan revealed dilated ventricles with ventriculoperitoneal shunt in situ. The shunt was removed (in view of meningitis) followed by external ventricular drain insertion and the tip was sent for the culture. Tip culture yielded S. maltophilia; which showed sensitivity to trimethoprim/sulfamethoxazole, ciprofloxacin, and amikacin. Meropenem and vancomycin were discontinued. The minimum inhibitory concentration interpretive breakpoints of trimethoprim/ sulfamethoxazole were susceptible, ≤2/38 g/mL; and resistant, ≥4/76 g/mL for S. maltophilia. Trimethoprim/sulfamethoxazole, 8-12 mg/kg/day administered intravenously every 6 hours was added to the antibiotic regimen. The patient's fever abated 4 days later and her stiff neck resolved. The next sample analysis of CSF from the drainage fourteen days after starting trimethoprim/sulfamethoxazole revealed the following profile: sugar 3.0 mmol/L, protein 0.1g/L, WBC count 0.1 x 109 cells /L (30% neutrophils, 55% lymphocytes, 15% mononuclear). Repeat culture was consistent with S. maltophilia; ciprofloxacin (15 mg/kg q12hr) was added to the treatment regime. The external ventricular drain catheter was changed and after 7 days of the combination therapy, CSF culture was sterile. Antibiotics were continued for fourteen more days, which was followed by a right ventriculoperitoneal shunt insertion. However, the patient later developed bilateral basal pneumonia three weeks after recovering from meningitis, which led to acute respiratory failure. The patient could not be resuscitated and died thereafter.

Discussion

Leptomeningeal inflammation caused by S. maltophilia is rare. Medline search was conducted with the phrase "S. maltophilia" which revealed 1660

published articles. Of these, only twenty-nine cases including the present case were linked with a prior neurosurgical procedure, whereas the rest accompanied community-acquired meningitis.[4] The incidence of neurosurgery-related meningitis is less, complicating less than 1% of craniotomies.[5] S. maltophilia being a multi-resistant organism, meningitis due to it is often insidious and protracted in course when compared to spontaneously occurring Gram-negative meningitis.[6]

Fever was the most common presenting symptom in these cases. In patients with neurosurgery-related meningitis, the average CSF cell count was 0.434 x 109 cells/L (range, 0.014 – 1.77 x 109 cells/L), glucose was 32.94 mg/dl (range, 4.9 – 77 mg/dl) and protein was 916 mg/dl (range, 76 – 3400 mg/dl). The average age was 49.85 years (range, 28 – 73 years) in adults, 4.29 months in infants (range, 2-6 months), and 4.5 years in children (range, 4-5 years). Of all the 29 cases, six patients had an intracerebral haemorrhage, five patients had hydrocephalus (out of which two had congenital hydrocephalus), four were diagnosed with the intracranial-extra-axial lesion, four had intra-ventricular haemorrhage on the CT scan, three cases had extracranial lesion with brain metastasis, three patients had aneurysm as their initial diagnosis, and rest included recurring cholesteatoma, subdural hematoma, subarachnoid haemorrhage, and a posterior fossa tumor with hydrocephalus (current case). Out of 29 cases associated with neurosurgery-related meningitis, nearly 50 per cent of them were due to ventriculoperitoneal shunt and prior craniotomy respectively. In the remaining, nearly one-third (28 per cent) cases occurred in patients who underwent prior craniectomy and had external ventricular drain in situ. The remaining included three cases that had ommaya reservoir in situ, two were linked with prior endoscopic third ventriculostomy, and one with stereotactic aspiration.

Our patient also had a similar risk factor profile as reported earlier, i.e. neurosurgical procedures (ventriculoperitoneal shunt and craniotomy), ICU stays, exposure to broad-spectrum antimicrobial treatment (ceftriaxone, amikacin, meropenem, and vancomycin). The overall mortality rate in the cases reviewed was 17 per cent. Although up to 50 per cent of cases of shunt infections can be treated by using antibiotics alone, many authors recommend removal of the prosthetic device followed by immediate or delayed insertion at a later stage.[7] Clinical data are limited regarding optimal therapy for infections caused by S. maltophilia. Nicodemo et al. suggested trimethoprim/sulfamethoxazole as the empirical choice for clinically suspected S. maltophilia infections and as the treatment of choice for culture-proven infections by this agent.[3]

It has been found that S. maltophilia is generally resistant to quinolones, aminoglycosides, and third-generation cephalosporins. Inducible beta-lactamase activity (a zinc-containing penicillinase [L1] and a cephalosporinase [L2]), efflux mechanism, aminoglycoside-modifying enzyme activity, biofilm formation, and expression of an outer membrane protein (OMP54) are responsible for its resistance to multiple antibiotics. Contemporary literature shows that resistance to trimethoprim/sulfamethoxazoleis on the rise.[3] Tigecycline has demonstrated good in vitro activity against S. maltophilia strains.[3] New fluoroquinolones such as clinafloxacin, levofloxacin, moxifloxacin have shown superior in vitro activity compared to earlier quinolones. Gesu et al., in an in vitro study comparing levofloxacin and ciprofloxacin against S. maltophilia 124 strains, confirmed the susceptibility rates of 85.5 and 58.9%, respectively, to levofloxacin and ciprofloxacin.[8]Although, ticarcillin-clavulanic acid combination demonstrated susceptibility against S. maltophilia above 70%,[3] further in vitro studies showed incomplete growth suppression followed by regrowth, mandating the requirement of additional controlled studies to further establish the true potential of this combination in S.maltophilia infections.[9] As per Zelenitsky et al., combination therapy with ceftazidime, gentamicin, tobramycin, and ciprofloxacin showed a significant bactericidal effect when compared with the trimethoprim/sulfamethoxazole monotherapy alone.[10]

However, it is difficult to infer the treatment for S. maltophilia due to limitations in the number of strains tested, wide variety of antimicrobial combinations, and different method used in the in-vitro studies. Although the synergistic action between drug combinations is evident, it is difficult to achieve the synergism in clinical drug concentrations.[3]The median duration of antibiotic therapy was 13 days (range 10–28 days). The optimal duration of therapy for S. maltophilia meningitis is

not known but we believe it to be similar to the treatment of gram-negative bacillary meningitis, which is usually 2 weeks after culture have been negative.[11]

Conclusion

S. maltophilia is an evolving gram-negative bacilli with an armamentarium of antimicrobial resistance. Inherent resistance with a simultaneously increasing number of cases poses a therapeutic challenge.It is associated with prior neurosurgical procedures, long ICU stays, and previous exposure to antibiotic treatment. Empirical treatment should consist of vancomycin plus a third-generation cephalosporin (ceftazidime or cefepime) for 48-72 hours. Clinicians should be alerted for S. maltophilia in whom empirical therapy fails or in those with the risk factors mentioned earlier. Trimethoprim/ sulfamethoxazoleis the treatment of choice for culture-proven infections by this agent. Further in vivo studies are necessary to better delineate the efficacy of individual antimicrobial agents, combination therapy, and to establish the therapeutic outcomes for S. maltophilia meningitis.

References

1 Chang YT, Lin CY, Chen YH, Hsueh PR. Update on infections caused by Stenotrophomonas maltophilia with particular attention to resistance mechanisms and therapeutic options. Front Microbiol2015;6.

2. Yemisen M, Mete B, Tunali Y, Yentur E, Ozturk R. A meningitis case due to Stenotrophomonas maltophilia and review of the literature. Int J Infect Dis 2008;12.

3. Nicodemo AC, Paez JIG. Antimicrobial therapy for Stenotrophomonas maltophilia infections. Eur J Clin Microbiol Infect Dis2007;26:229–37.

4. Khanum I, Ilyas A, Ali F. Stenotrophomonas maltophilia Meningitis - A Case Series and Review of the Literature. Cureus 2020;12:e11221.

5. McClelland S, Hall WA. Postoperative central nervous system infection: Incidence and associated factors in 2111 neurosurgical procedures. Clin Infect Dis 2007;45:55–9.

6. Papadakis KA, Vartivarian SE, Vassilaki ME, Anaissie EJ. Stenotrophomonas maltophilia meningitis. J Neurosurg 2009;87:106–8.

7. James HE, Walsh JW, Wilson HD, Connor JD, Bean JR, Tibbs PA. Prospective randomized study of therapy in cerebrospinal fluid shunt infection. Neurosurgery 1980;7:459–63.

8. Gesu G Pietro, Marchetti F, Piccoli L, Cavallero A. Levofloxacin and ciprofloxacin in vitro activities against 4,003 clinical bacterial isolates collected in 24 Italian laboratories. Antimicrob Agents Chemother 2003;47:816–9.

9. Garrison MW, Anderson DE, Campbell DM, Carroll KC, Malone CL, Anderson JD, et al. Stenotrophomonas maltophilia: Emergence of multidrug-resistant strains during therapy and in an in vitro pharmacodynamic chamber model. Antimicrob Agents Chemother 1996;40:2859–64.

10. Zelenitsky SA, Iacovides H, Ariano RE, Harding GKM. Antibiotic combinations significantly more active than monotherapy in an in vitro infection model of Stenotrophomonas maltophilia. Diagn Microbiol Infect Dis 2005;51:39–43.

11. Briggs S, Ellis-Pegler R, Raymond N, Thomas M, Wilkinson L. Gram-negative bacillary meningitis after cranial surgery of trauma in adults. Scand J Infect Dis2004;36:165–73

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Traumatic brain contusions. Key things to know in the emergency room

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ABSTRACT

Traumatic brain injury is one of the most important causes of morbidity and mortality worldwide. One of its presentations includes traumatic brain contusions. Brain contusions are cortical lesions of necrotic tissue and multiple petechial haemorrhages, initially perivascular, that predominantly affect the crests of the convolutions, but that can extend through the cortex and reach the subcortical white matter. These result from a collision of the brain with the adjacent inner table of the skull, without proper treatment these can evolve and cause a rapid deterioration of clinical and neurological status. The classification includes mild, moderate, and severe TBI depending on the nature of the injury and the impact on the patient's clinical status. For the initial evaluation, computed tomography is usually used, although the magnetic resonance has greater sensitivity for the detection in these patients. Treatment is guided at preventing the progression of the lesion or the development of a secondary lesion, avoiding hypotension and hypoxia and maintaining adequate cerebral perfusion. Surgery is frequently needed in severe cases to remove intracranial hematomas, provide space for the brain to swell, or place monitors to track intracranial pressure and brain oxygenation. The aim of this article is to review the most important aspects to know about brain contusion.

INTRODUCTION

Traumatic brain injury (TBI) is a complex disease that should be understood as a public issue due to the high rates of mortality and

disability attributed to it; being part of the leading causes of death in developed countries [1]. This condition encompasses an interesting spectrum that should not only consider its immediate consequences, rather it is important to assess the long-term impact also, especially those of working age [2].

The classification of the severity of the TBI is based on the clinical status, using the Glasgow Coma Scale (GCS) [3,4], knowing that a patient with mild TBI is (GCS 13-15), moderate (GCS 9-12) or severe (GCS ≤8) [4]. Also, according to the radiological characteristics of the lesion in the computed tomography (CT) or magnetic resonance (MR), they can be classified into brain focal injuries or diffuse injury (affecting multiple brain regions); Different than diffuse injuries, the focal lesions are localized brain damage that may occur with the presence or absence of cranial opening and also present changes both intra and extra-axial [1,5]. Brain contusions are part of the focal injuries [5].

Brain contusions are one of the most common findings within the initial studies in patients with TBI, being present in up to 31% of the CT [1,6]. Contusions are found in 89% of the brains examined postmortem in patients with TBI [1]. These results from direct loading and often occurs in the absence of a generalized injury [1,7]. The most frequent locations of brain contusions are the brain regions where it collides with the irregular adjacent inner table of the skull [5], such as frontal and temporal poles, the orbitofrontal spin, the perisylvian cortex and temporal lobe cortex inferolaterally [1,8]. This injuries typically encountered with an hemorrhagic component eventually with the bleeding within a contusion which triggers local edema and ischemic changes, which leads to tissue destruction, neuronal necrosis, and ultimately cavitation and reactive gliosis around [3].

Epidemiology

Before discuss about specific numbers that allow us to discern the picture of this disease, we must remember that TBI is strongly related with traffic accidents and falls [4]; these are the most common causes of TBI of any severity which together account for over 50% of all cases [9,10]. Knowing this we could focus on prevention programs that reduce the incidence, mortality and cost. In the international frame, it has significant socio-economic implications, in the United States (US) over 1.7 million people suffer from TBI each year [1,2,4,5]. The incidence rate of hospitalizations due to TBI has been estimated in approximately 262 cases per 100,000 people derived from a meta-analysis of 16 European countries [7,9].

For contused brain injuries associated with sports, we have an incidence rate on emergency room visits in the US of 152 cases per 100,000 people, of whom at least two-thirds where children and adults under 19 years old [9,11]. Another visibly affected population are military, according to the Brain Injury Center, US defense and veterans, more than 22,000 service members had TBI in 2015 [9]. It is widely described in the literature that actually statistics are underestimated and it is believed that if population continue along this way in the future the numbers will be markedly higher than those of today.

Pathophysiology

Because of the complexity of this disease it can be seen that has a very diverse pathophysiology including from biomechanical forces to very specific cellular changes. However, although it has been heavily studied, main mechanism that underlies the brain contusion is not yet fully clarified [1]. When the individual receives an injury, energy transfer beyond the capacity of the brain tissue to absorb it (tensegrity) without develop consequences on the function, thereby an insult or traumatic injury is generated [12]. This insult commonly takes a short time and is known as a dynamic load including loads by direct impact and impulse without physical contact. It is essential to know the speed and the time elapsed for this insult given that these variables play an important role. It is known that an insult at high speed tends to cause more severe damage [1,7]. Accordingly, traumatic insult triggers a series of consequences directly related to the cerebral inflammatory response to, forming a contusion zone leading to brain suffering and death of the tissue [1].

Traumatic brain inflammation can be summarized in three related but different phases [3,13]. Firstly, lipids and proteins of the cell membrane are degraded into smaller molecules which prompt an osmotic gradient. In the central area of the contusion, cells as neurons and glia suffer disintegrative and homogenization processes. All this results in a disbalance in osmolality passing from normally 310 milliosmoles to 370-390 milliosmoles in

the contusion area [13]. Towards 24-48 hours after the insult the second phase predominates, which is mediated by the activation of thrombin as a result of the coagulation cascade [1]. Thrombin among other inflammatory mediators act accordingly to stop the cerebral blood flow, resulting in vasogenic edema. The start of the third phase is triggered by lysis of erythrocytes in the intracerebral clot, subsequently hemoglobin breakdown leads to the activation of the complement system, and cytokines and reactive oxygen species contribute to the inflammatory process [1,12,13].

This inflammatory process also has a vascular component that causes a hypoperfusion in the tissue. Mass effect in contusion processes results in decreased cerebral blood flow by various causes. The occurrence of increased intracranial pressure due to cerebral vascular failure self-regulatory mechanisms leads to a marked decrease of the perfusion pressure and the develop of secondary injuries [3,13].

Neuroimaging

Usually, for the initial evaluation of a patient with TBI, the imaging modality of choice is usually the CT, due to its availability, cost and sensitivity for acute intracranial hemorrhage and fractures [14]. However, in recent decades there has been increasing use of MR, because this offers improved soft tissue with increased sensitivity for the detection of a wide variety of traumatic pathologies such as diffuse axonal injury and brain contusions. This increased sensitivity for TBI is particularly useful in the context of a traumatic brain contusion where initial CT image may be negative [15]. However, images with CT tracking may become apparent, because these tend to enlarge and become more visible [16].

Contusions appear as mixed density lesions on brain CT, often surrounded by areas wedge-shaped, hypodense and are in close contact with the inner surface of the skull, this lack of homogeneity often confer an appearance of "salt and pepper" [1,17]. The MR is more sensitive (93% -98%) than the CT (18% -56%) in the location of hemorrhagic and non-hemorrhagic contusions, which are more explicitly distinguished in T2 weightings, therefore, MR better detects all types and stages of intracranial hemorrhage, including contusions [15,17]. The recovery sequence by fluid attenuated inversion (FLAIR) is superior to T1-weighted sequences and T2 weighted for detecting cerebral edema in the context of a CC [17]. Yuh et al. in RACK / TBI study (Clinical Research and Knowledge Transformation Traumatic Brain Injury) observed that 28% of patients with normal CT, MR showed abnormalities [18]. However, for primary evaluation of acute trauma not using MRI unless the patient continues with neurological signs and symptoms and CT proven no initial or follow-up is required no injury apparent recommended [1].

Treatment

Brain contusions become over time in space occupying lesions, as the inflammatory process and the secondary edema can elevate intracranial pressure (ICP), which may lead to deterioration of the patient's condition. In this sense, the treatment is guided to prevent progression of the lesion, reduce edema, ICP control and maintain good brain perfusion [1,19]. Some guidelines have recommended maintaining SBP at ≥ 100 mmHg for patients 50 to 69 years of age or ≥ 110 mmHg for patients aged 15 to 49 or more than 70 years [20,21], start treatment for ICP values above 22mmHg [20,21] and maintain cerebral perfusion pressure (CPP) between 60 and 70 mmHg to reduce mortality and improve outcomes [20–23].

Oxygenation

The guidelines recommend control ventilation and PaCO2 in patients with severe TBI [23], the PaCO2 should be maintained between 30 and 35mmHg and the PaO2 at 100%, since it optimizes the supply of O2 [13]. Hypocapnia induces cerebral vasoconstriction and cerebral ischemia [24].

Cerebrospinal fluid drainage

A method for reducing the ICP is the drainage of cerebrospinal fluid (CSF), with external ventricular drainage [13]. Brain Trauma Foundation's (BTF) recommends the use of CSF drainage to reduce ICP in patients with GCS <6 during the first 12 hours after injury [21].

Hyperosmolar therapy

Osmotherapy has been used for a long time for the management of intracranial hypertension (ICH) and still remains an important element for the management of TBI [20]. Hypertonic saline (HTS) and mannitol are commonly used effectively to reduce

ICP [25], these are able to establish an osmotic gradient between the brain and the cerebral vasculature, resulting in a net loss of water in brain tissue [26–28]. The HTS is administered in concentrations of 2% to 23.4% and usually of choice for patients requiring resuscitation volume, mannitol is administered at doses of 0.25 to 1g/kg every 4 to 6 hours [26,29]. Until recently the gold standard was considered mannitol, but is now controversial superiority of one agent over another [26], however, Rockswold et al showed that hypertonic saline had a more significant effect on ICP reduction, increased cerebral perfusion pressure, cardiac output and oxygen tension in the brain tissue that mannitol [30]. Consequently, the decision to choose one drug over the other may be based on factors such as drug availability, comfort physician to administer an unknown agent and side effects [26].

Anticonvulsant therapy

Patients with a GCS score ≤10, age <65 years, chronic alcoholism and cortical contusion increased risk of seizures, which can aggravate neurological deficit, therefore these patients should be considered anticonvulsant drugs [1]. BTF recommends the use of phenytoin for seizure prevention early posttraumatic (within 7 days after injury) when the overall benefit outweighs the complications associated with treatment, but not recommended for use late seizures posttraumatic [21].

Surgical management

Current indications for surgery for traumatic brain contusions include a lower score on the GCS, location of the contusion, presence of neurological deterioration, increase in the volume of the lesion, appearance of the lesion in CT (increase of the midline and/or compression of the basal cistern) and increase of the ICP [31].

Decompressive craniectomy

The aim of decompressive craniectomy (DC) is to suppress the relationship between pressure and volume of the closed cranial cavity, with a large bone flap is removed and the dura is expanded with the help of autologous or artificial tissue [13]. There is no evidence that DC improves the outcome compared to medical therapy [32]. The DECRA trial showed that in patients with severe TBI refractory diffuse and ICH, early bifrontotemporoparietal DC decreased ICP and length of stay in the ICU [33]. But, at six months of follow-up, 70% of patients in the craniectomy group had an unfavorable outcome compared to 51% of patients in the standard care group. In general, this trial has shown that DC reduces mortality but at the expense of a greater number of survivors with severe neurological disability and loss of independence [34].

Surgical evacuation

Surgical excision is best performed by brain contusions conservatively with minimal or absent trauma to the surrounding tissue, and ideally is performed through a limited incision and placed cortical optimally [1,13], but it is reported that conservative contusectomies are better combined with a decompressive craniectomy [13]. Sinha et al. A recent study showed that contusectomy or right lobectomy is useful in severe TBI with contusions [35]. The benefit of eliminating the contusion zone, include suppression and removal of necrotic and apoptotic process caused by degradation products of blood [13].

Outcome

A recent study observed that the frontal and temporal location is associated with a better surgical result than parietal and cerebellar contusions. In addition, they reported that age> 30 years, a severe GCS, and a median line displacement of more than 5 mm were the greatest predictors of mortality after surgery [36]. Laccarino et al, showed similar results to the previous study, but also observed that the clinical deterioration in the first hours after the trauma and the onset or increase of the midline change in the follow-up CT images were associated with unfavorable clinical results [37].

In this order of ideas, despite what has been described, there are many points that need to be reinforced from the volume and quality of evidence, such as epidemiology, diagnosis and specific treatment in areas where there are barriers to access high-cost technological tools, to contribute to the reduction of the burden of neurological diseases, in addition to reducing the risk of morbidity, mortality and disability [38-44]. It is necessary to carry out prospective multicenter studies that allow us to know the behavior, approach and outcomes of this disease in different contexts and to design a standardized prognostic tool that has an excellent

performance, accessible and understandable to all health professionals. In the current post-pandemic phase of COVID-19, many of the efforts in disciplines other than infectious diseases have waned, so it is necessary to resume research in other areas [45,46].

Conclusions

Brain contusions if not treated in time can have rapid and progressive in the clinical condition of the patient and neurologic effects, not only for their local ripple effects, but also the possible injury of hippocampal and brainstem. In this regard it is important to establish a proper, immediate and effective treatment because it has been shown that this improves clinical outcomes. Information about brain contusions is scarce and concepts need to be standardized to provide proper management of patients with TBI.

References

1 Alvis-Miranda H, Alcala-Cerra G, Moscote-Salazar LR. Traumatic cerebral contusion: pathobiology and critical aspects. Rom Neurosurg. 2013; 20(2):125–37.

2. Davanzo JR, Sieg EP, Timmons SD. Management of Traumatic Brain Injury. Surg Clin North Am. 2017; 97(6):1237–53.

3. McGinn MJ, Povlishock JT. Pathophysiology of Traumatic Brain Injury. Neurosurgery Clinics of North America. 2016; 27: 397–407.

4. Wells AJ, Hutchinson PJ. The management of traumatic brain injury. Surg (United Kingdom). 2018; 36(11):613–20.

5. Pervez M, Kitagawa RS, Chang TR. Definition of Traumatic Brain Injury, Neurosurgery, Trauma Orthopedics, Neuroimaging, Psychology, and Psychiatry in Mild Traumatic Brain Injury. Neuroimaging Clin N Am. 2018; 28(1):1–13.

6. Soustiel JF, Mahamid E, Goldsher D, Zaaroor M. Perfusion-CT for early assessment of traumatic cerebral contusions. Neuroradiology. 2008; 50(2):189–96.

7. Blyth BJ, Bazarian JJ. Traumatic Alterations in Consciousness: Traumatic Brain Injury. Emerg Med Clin North Am. 2010; 28(3):571–94.

8. Prins M, Greco T, Alexander D, Giza CC. The pathophysiology of traumatic brain injury at a glance. Dis Model Mech. 2013; 6(6):1307–15.

9. Blennow K, Brody DL, Kochanek PM, Levin H, McKee A, Ribbers GM, et al. Traumatic brain injuries. Nat Rev Dis Prim. 2016; 2:1–19.

10. Psota M, Theadom A, Taylor MS, Holkovic L, Buckova V, Synnot A, et al. Epidemiology of Traumatic Brain Injury in Europe: A Living Systematic Review. J Neurotrauma. 2015; 30:1–30.

11. Coronado VG, Haileyesus T, Cheng TA, Bell JM, Haarbauer-Krupa J, Lionbarger MR, et al. Trends in Sports- and Recreation-Related Traumatic Brain Injuries Treated in US Emergency Departments. J Head Trauma Rehabil. 2015; 30(3):185–97.

12. Dixon KJ. Pathophysiology of Traumatic Brain Injury. Phys Med Rehabil Clin N Am. 2017; 28(2):215–25.

13. Mathai K, Sengupta S, Shashivadhanan, Sudumbrekar S. Surgery for cerebral contusions: Rationale and practice. Indian J Neurotrauma. 2012; 6(1):17–20.

14. Agarwal R, Bergey M, Sonnad S, Butowsky H, Bhargavan M, Bleshman MH. Inpatient CT and MRI utilization: Trends in the academic hospital setting. J Am Coll Radiol. 2010; 7(12):949–55.

15. Altmeyer W, Steven A, Gutierrez J. Use of Magnetic Resonance in the Evaluation of Cranial Trauma. Magnetic Resonance Imaging Clinics of North America. 2016; 24:305–23.

16. Ratnaike TE, Hastie H, Gregson B, Mitchell P. The geometry of brain contusion: Relationship between site of contusion and direction of injury. Br J Neurosurg. 2011; 25(3):410–3.

17. Useche JN, Bermudez S. Conventional Computed Tomography and Magnetic Resonance in Brain Concussion. Neuroimaging Clinics of North America. 2018; 28:15–29.

18. Yuh EL, Mukherjee P, Lingsma HF, Yue JK, Ferguson AR, Gordon WA, et al. Magnetic resonance imaging improves 3-month outcome prediction in mild traumatic brain injury. Ann Neurol. 2013; 73(2):224–35.

19. Ahmad Helmy AK, Salmah Jalaluddin WM, Ab Rahman IG. Computed tomography perfusion imaging on traumatic cerebral contusion: a preliminary report. Malays J Med Sci. 2010; 17(4):51–6.

20. Dash HH, Chavali S. Management of traumatic brain injury patients. Korean J Anesthesiol. 2018; 71(1):12–21.

21. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GWJ, Bell MJ, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. Neurosurgery. 2016; 80(1):1.

22. Vanderkolk WE, Ott MM, Eriksson EA, Figueroa BE, Barletta JF, Bonnell BW, et al. Cerebral perfusion pressure and intracranial pressure are not surrogates for brain tissue oxygenation in traumatic brain injury. Clin Neurophysiol. 2011; 123(6):1255–60.

23. Geeraerts T, Velly L, Abdennour L, Asehnoune K, Audibert G, Bouzat P, et al. Management of severe traumatic brain injury (first 24 hours). Anaesth Crit Care Pain Med. 2018; 37(2):171–86.

24. Coles JP, Fryer TD, Coleman MR, Smielewski P, Gupta AK, Minhas PS, et al. Hyperventilation following head injury: Effect on ischemic burden and cerebral oxidative metabolism. Crit Care Med. 2007; 35(2):568–78.

25. Battison C, Andrews PJD, Graham C, Petty T. Randomized, controlled trial on the effect of a 20% mannitol solution and a 7.5% saline/6% dextran solution on increased intracranial pressure after brain injury. Crit Care Med. 2005; 33(1):196–202.

26. Jinadasa S, Boone MD. Controversies in the Management of Traumatic Brain Injury. Anesthesiol Clin. 2016; 34(3):557–75.
27. Vella MA, Crandall ML, Patel MB. Acute Management of Traumatic Brain Injury. Surg Clin North Am. 2017; 97(5):1015–30.
28. Tsang KKT, Whitfield PC. Traumatic brain injury: Review of current management strategies. Br J Oral Maxillofac Surg. 2012; 50(4):298–308.
29. Freeman N, Welbourne J. Osmotherapy: science and evidence-based practice. BJA Educ. 2018; 18(9):284–90.
30. Rockswold GL, Solid CA, Paredes-Andrade E, Rockswold SB, Jancik JT, Quickel RR. Hypertonic saline and its effect on intracranial pressure, cerebral perfusion pressure, and brain tissue oxygen. Neurosurgery. 2009; 65(6):1035–42.
31. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW, et al. Surgical management of traumatic parenchymal lesions. Neurosurgery. 2006; 58(S-3):S25-46.
32. Honeybul S, Ho KM. Decompressive Craniectomy - A narrative review and discussion. Aust Crit Care. 2014; 27(2):85–91.
33. Cooper DJ, Rosenfeld JV, Murray L, Arabi YM, Davies AR, D'Urso P, et al. Decompressive Craniectomy in Diffuse Traumatic Brain Injury. N Engl J Med. 2011; 364(16):1493–502.
34. Honeybul S, Ho KM, Lind CRP, Gillett GR. The current role of decompressive craniectomy for severe traumatic brain injury. J Clin Neurosci. 2017; 4.
35. Sinha S, Rathore YS, Mahapatra AK, Sharma BS. Surgical outcome of brain contusions treated by decompressive craniotomy with or without lobectomy at high volume tertiary care trauma centre. Indian J Neurotrauma. 2014; 11(1):5–9.
36. Akyam L, Gudla V, Jyothi S. Factors affecting the surgical outcome of patients with cerebral contusions. Int Surg J. 2015; 2(4):665–9.
37. Cerasti D, Goldoni M, Caspani M, Schiavi P, Iaccarino C, Picetti E, et al. Patients with brain contusions: predictors of outcome and relationship between radiological and clinical evolution. J Neurosurg. 2014; 120(April):908–18.
38. Lozada-Martínez I, Maiguel-Lapeira J, Torres-Llinás D, Moscote-Salazar L, Rahman MM, Pacheco-Hernández A. Letter: Need and Impact of the Development of Robotic Neurosurgery in Latin America. Neurosurgery. 2021; 88(6):E580-E581.
39. Herrera-Martinez MP, García-Ballestas E, Lozada-Martinez I, Torres-Llinás D, Moscote-Salazar L. Letter to the Editor. Creating the conditions for gender equality to end sexual harassment in neurosurgery. J Neurosurg. 2021 Feb 5:1-2.
40. Gaitan-Herrera G, Lozada-MartÍnez I, Acevedo-Aguilar L, Bohorquez-Caballero A, Moscote-Salazar L. Simulation as a tool to educate the patient about neurosurgical pathology. J Neurosurg Sci. 2021 Jan 22
41. Ortega-Sierra MG, Durán-Daza RM, Carrera-Patiño SA, Rojas-Nuñez AX, Charry-Caicedo JI, Lozada-Martínez ID. Neuroeducation and neurorehabilitation in the neurosurgical patient: programs to be developed in Latin America and the Caribbean. J Neurosurg Sci. 2021 Jun 10.
42. Blanco-Teherán C, Quintana-Pájaro L, Narvaez-Rojas A, Martínez-Pérez R, García-Ballestas E, Moscote Salazar L, et al. Evidence-based medicine in neurosurgery: why and how? J Neurosurg Sci. 2021 Aug 3.
43. Ortega-Sierra MG, Prado-Grajales V, Martinez-Imbett R, Unás-Perea K, Lozada Martinez ID. Research career in neurosurgery: a challenge for future neurosurgeons. J Neurosurg Sci. 2021 Aug 3.
44. Zuluaga-Ramírez P, Lozada-Martínez I, Moscote-Salazar L, Cabrera-Vargas L. Sexual harassment and racism in surgery: A latent problem. Int J Surg. 2021; 86:13-14.
45. González-Herazo MA, Silva-Muñoz DC, Guevara-Martínez PA, Lozada-Martinez ID. Post-COVID 19 Neurological Syndrome: a fresh challenge in neurological management. Neurol Neurochir Pol. 2021;55(4):413-414
46. Llamas-Nieves A, Maiguel-Lapeira J, Lozada-Martinez I, Torres Llinas D, Moscote-Salazar L. The desire to publish a scientific article and the difficulties of publishing it in a highquality neurosurgery scientific journal. J Neurosurg Sci. 2021 Mar 11

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Study of association of serum vitamin D and serum calcium with spontaneous aneurysmal subarachnoid haemorrhage in a tertiary care centre

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hypocalcaemia, hypovitaminosis, ASAH (aneurysmal subarachnoid haemorrhage), bleeding

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ABSTRACT

Background: Aneurysmal subarachnoid haemorrhage (aSAH) is a disease associated with high mortality and morbidity. Recent studies have postulated a correlation between Vitamin D deficiency and aSAH, however, the mechanism of which remains obscure. Vitamin D and Calcium in patients withaSAH has not been formally investigated. Therefore, the aim of this study was to evaluate the incidence of hypovitaminosis D and hypocalcemia in patients with aSAH.

Methods: An observational study was conducted at the Department of Neurosurgery at tertiary care centre, New Delhi, India. 40 patients with spontaneous aneurysmal SAH were enrolled during the period January 2019 to 15th April 2020. The standard protocol of care was given to all patients included in the study. Laboratory investigations including Vitamin D and Calcium levels; Clinical examination and grading were done for each patient. The data thus collected was used to see the clinic-demographic profile of patients of aSAH with an emphasis on Vitamin D and Calcium levels.

Results: The study reported mean vitamin D level of 17.4 ± 7 ng/ml; mean calcium level of 8.3 ± 0.9 mg/dl amongst the study participants. Out of 40 patients, 8 patients (20%) were severely deficient, 24 patients (60%) were mild to moderate deficient and 8 patients (20%) were having normal vitamin D levels. 50% of the patients (n=20) were hypocalcaemic and 50% were normocalcaemic.

Conclusion: A higher incidence of vitamin D deficiency was observed in our study along with an equal incidence of hypocalcemia vs normocalcemia. Further studies with a comparison group and a bigger sample size are needed to validate this evidence.

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INTRODUCTION

Subarachnoid haemorrhage (SAH) is the extravasation of blood into subarachnoid space of the CNS, which is normally filled with

cerebrospinal fluid (CSF). The prevalence of Subarachnoid Haemorrhage (SAH) is approximately 9 per 100,000 person per year[1]. There is a slight preponderance in women as compared to men, and this increases with age. Peak incidence has been observed in 5th and 6th decade of life[2]. The commonest cause of SAH overall is trauma, whereas commonest cause of spontaneous SAH is rupture of intracranial aneurysms[3]. About 80% of non-traumatic SAH happens due to aneurysms[4].

Most common symptom of SAH is headache, which is referred to by the patient as the worst headache he/she has ever experienced in his/her life. It can also be accompanied by nausea, vomiting, loss of consciousness.

Aneurysmal subarachnoid haemorrhage (aSAH) is a disease associated with a high mortality and morbidity. A study from Netherlands reported that the overall mortality rate of non-traumatic SAH has been found out to be 30%[5]. SAH because of the rupture of an intracranial aneurysm is a potentially fatal event .Altough it accounts for 5% of all strokes but its burden is relevant due to high mortality ,high disability and higher incidence in the young[6]. Even after good outcome of SAH, long term cognitive deficits (commonly in memory, language and executive functions) may happen to patients. Further, a study reported that approximately 40% of SAH survivors may not be able to return back to their previous jobs[7].Even after successful aneurysmal clipping in patients with aSAH, overall quality of life was found to be decreased as compared to controls in a study[8].

Recent studies have postulated a correlation between Vitamin D deficiency and aSAH, however the mechanism of which remains obscure[9,10,11]. Probable mechanisms that have been postulated are indirect variations in blood pressure[9], anti-proliferative and anti-inflammatory action of Vitamin D on smooth muscle of blood vessels[10]. These effects of vitamin D becomes more important as cerebral vasospasm has been implicated as a major causative factor for long term neurological deficits present in patients with SAH.

In the past decade, there has been a surge of interest in the impact of vitamin D levels on various conditions ranging from bony fractures to malignancy. A growing body of evidence also implicates hypovitaminosis D in cerebral small-vessel disease and stroke[12,13].Recent investigations, primarily in the cardiothoracic[14,15]and vascular surgeryliterature, have suggested a concordance of hypovitaminosis D and arterial disease, including aneurysmal dilation of the aorta[16].This relationship is believed to be mediated by a variety of mechanisms, including modulation of vessel wall inflammation, changes in vascular smooth muscle cell development, and numerous systemic effects such as changes in insulin resistance and lipid processing[17].

Hypocalcaemia has been significantly associated with extent of bleeding in patients with intracerebral haemorrhage because magnesium and calcium have roles in platelet function and coagulation cascade[18]. However, research regarding the association of intracranial aneurysm rupture risk in hypocalcaemia and hypomagnesemia are lacking. Vitamin D and Calcium in patients with cerebral aneurysms and aneurysmal SAH has not been formally investigated. Therefore, the aim of this study was to evaluate the incidence of hypovitaminosis D and hypocalcemia in patients with aSAH.

Methods

This was an observational study conducted at the Department of Neurosurgery at tertiary care centre New Delhi, India. 40 patients with spontaneous aneurysmal SAH were enrolled during the period January 2019 to 15th April 2020. All cases of spontaneous aneurysmal SAH admitted in the institute during the study period were included and patients who had a previous history of renal disease; history of liver dysfunction; history of chronic intestinal malabsorption; and those taking Vitamin D and Calcium supplementation for any reason were excluded from the study.

Informed written consent was taken from each eligible patient before his/her enrolment. The baseline evaluation included Personal and family history including any comorbidities or prior surgical intervention; General physical examination and thorough neurological evaluation; Laboratory tests including complete blood count (CBC), Liver function tests (LFTs), Renal function tests (RFTs); Non-contrast enhanced CT (NCCT) head; CT Angiography/ MR Angiography/DSA; Serum Calcium levels; and Vitamin D (25-hydroxyvitamin D) levels using radioimmunoassay method.

Standard protocol of care was given across to all patients included in the study. Grading was done by

the World Federation of Neurological Societies (WFNS) Grading of SAH, Modified Fisher grade, Hunt and Hess grade and Glasgow Coma Scale (GCS).

Mayo Medical laboratories reference ranges for Total serum 25-hydroxyvitamin D were adhered to for classifying the patients in terms of Vitamin D levels which are - Severe deficiency - <10ng/ml; Mild to moderate deficiency – 10-24.9 ng/ml; Optimal – 25-80 ng/ml; Possible toxicity - >80 ng/ml; Calcium reference levels used at our institute areNormal total calcium level 8.5 mg/dl – 10.5 mg/dl; Normal ionized calcium level 4.5-5.6 mg/dl.

Data collection

All enrolled patients of spontaneous aneurysmal SAH had these tests as part of their routine investigations during their treatment (conservative management or operative management).

Statistical analysis

All statistical calculations were conducted with standard statistical programs (IBM SPSS version 26) . Shapiro wilk test was applied to check the normality of variables that were included in the study. Parametric data was assessed with help of Student's T-test, one way ANOVA test. Non- Parametric data was analyzed with help of Chi Square, Mann Whitney U test, Kruskalwallistest. P-value of <0.05 was considered to be of statistical significance in the study.

Results

Out of 40 patients with aSAH, 18 were males (45%). 15 patients (37.5%) were in age group of 25-45 years, 16 (40%) were in age group of 46-60 years, 9 (22.5%) were in the age group of 61 -75 years. The mean age of patients was 51 years.

In our study 10 patients were current smokers (25%); 22 patients (55%) were hypertensive;and 14 patients (35%) were diabetic. The most common site of aneurysm was found to be anterior communicating artery (47.5%) and the least common was cerebellar artery (2.5%).

The study reported mean vitamin D level of 17.4 ± 7 ng/ml; mean calcium level 8.3 ± 0.9 mg/dl.

The study reported that out of 40 patients, 8 patients (20%) were severely deficient, 24 patients (60%) were mild to moderate deficient and 8 patients (20%) were having normal vitamin D levels. Amongst males, 61.1% were Vitamin D deficient whereas amongst females, 77.3% were deficient and this difference was found to be statistically insignificant (p-value=0.2).

Mean Vitamin D levels in males and females were 19.4 ± 6.7 ng/ml and 15.7 ± 7.0 ng/ml respectively. As Vitamin D levels in the study participants were found to be not normally distributed, therefore independent sample Mann-Whitney-U test was applied to check the mean difference of Vitamin D among gender and it was found to have no significant difference in the two groups (p-value = 0.106) (**Figure 1**).

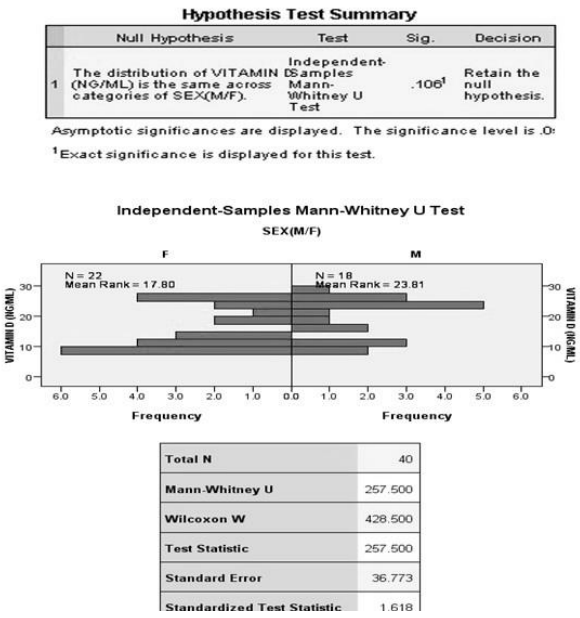

Figure 1. Independent sample Mann Whitney U test showing the mean difference of Vitamin D among gender.

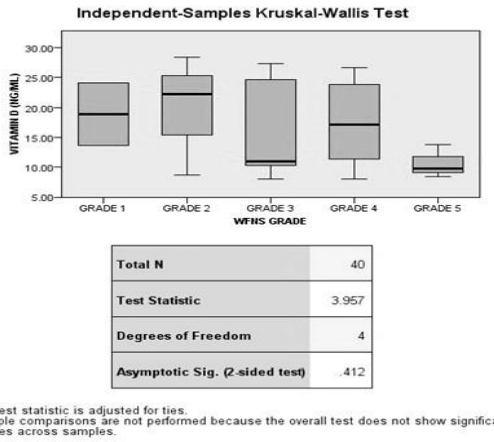

Figure 2. Kruskal Wallis test showing the mean difference of Vitamin D among WFNS Grade.

Mean Vitamin D level in smokers and non-smokers were 18.9 ± 7.1 ng/ml and 16.9 ± 7.0 ng/ml respectively and this difference was found to be non-significant, (p value - 0.45). Similarly, mean Vitamin D levels in Diabetics and Non-Diabetics; and Hypertensives and Non-hypertensives patient were 17.2 ± 6.6 ng/ml and 17.4 ± 7.4 ng/ml; and 17.3 ± 6.6 ng/ml and 17.4 ± 7.7 ng/ml respectively and these differences were found to be statisticallynon-significant (p value – 1 and 0.757 respectively) (**Table 1**).

Table 1. Mean Vitamin D levels in smokers - non-smokers, diabetics –non diabetics and hypertensive and normotensive patients.

Gender	No of patients	Mean (vitamin D)	SD	P value
Female	22	15.7	7.0	0.106
Male	18	19.4	6.7	
Smoking	No of patients	Mean (vitamin D)	SD	P value
No	30	16.9	7.0	0.45
Yes	10	18.9	7.1	
Diabetes mellitus	No of patients	Mean (vitamin D)	SD	P value
No	26	17.4	7.4	1.00
Yes	14	17.2	6.6	
Hypertension	No of patients	Mean (vitamin D)	SD	P value
No	18	17.4	7.7	0.757
Yes	22	17.3	6.6	

The mean vitamin D levels in the various WFNS grades (**Figure 2**), Modified Fischer grades and Hunt and Hess gradesof patients were found to be statistically non-significant using the Kruskal-Wallis test (p value =0.412, 0.568, 0.529 respectively) (**Table 2**).

Table 2. Vitamin D levels across WFNS grades, Modified Fischer grades and Hunt & Hess grades.

WFNS grades	**Mean (Vitamin D)**	**SD**	**P value**
I	18.9	7.4	0.412
II	20.4	7.0	
III	16.9	8.6	
IV	17.3	6.7	
V	10.7	2.8	
Modified FISCHER grades	Mean (vitamin D)	SD	P value
I	19.2	6.9	0.568
II	16.8	9.7	
III	15.7	6.0	
IV	17.7	7.1	
HUNT & HESS grades	Mean (vitamin D)	SD	P value
I	13.7	0	0.529
II	20.6	7.0	
III	19.7	8.0	
IV	15.5	8.0	
V	16.6	5.8	

The present study reported that half of the patients (n=20) were hypocalcaemic and the other half were normocalcaemic. Mean calcium levels in males and females were 8.5 ± 1.0 mg/dl and 8.2± 1.0 mg/dl respectively and this difference was not statistically significant (p value=0.3)

Similarly, the mean calcium levels in smokers and non-smokers; diabetics and non-diabetics; Hypertensives and Non-hypertensives were 8.4 ± 0.9 mg/dl and 8.3 ± 1.0 mg/dl;8.0 ± 0.9 mg/dl and 8.5 ± 1.0 mg/dl; 8.3 ± 0.9 mg/dl and 8.4 ± 1.0 mg/dl respectively and these differences were not statistically significant (p value=0.8, 0.07, 0.65) (**Table 3**).

Table 3. Mean serum calcium levels across gender, smokers - non-smokers, diabetics –non diabetics and hypertensive and normotensive patients.

Gender	**No of patients**	**Mean(calcium)**	**SD**	**P value**
Female	22	8.2	1.0	0.3
Male	18	8.5	1.0	
Smoking	No of patients	Mean(calcium)	SD	P value
No	30	8.3	1.0	0.8
Yes	10	8.4	0.9	

Diabetes mellitus	No of patients	Mean(calcium)	SD	P value
No	26	8.5	1.0	0.07
Yes	14	8.0	0.9	
Hypertension	No of patients	Mean(calcium)	SD	P value
No	18	8.4	1.0	0.65
Yes	22	8.3	0.9	

The mean serum calcium amongst the different WFNS grades did not differ statistically significantly (p value = 0.07) whereas the mean serum calcium levels were found to differ statistically significantly amongst the various Modified Fischer grades Hunt & Hess grades with p values 0.002 and 0.04 respectively (**Table 4**).

Table 4. Serum Calcium levels across WFNS grades, Modified Fischer grades and Hunt & Hess grades.

WFNS grades	**Mean(calcium)**	**SD**	**P value**
I	8.6	0.14	0.07
II	9.0	0.87	
III	8.3	1.3	
IV	8.2	0.83	
V	7.3	0.4	
Modified FISCHER grades	Mean(calcium)	SD	P value
I	9.0	0.8	0.002
II	8.9	0.4	
III	7.8	0.9	
IV	7.9	0. 9	
HUNT & HESS grading	Mean (calcium)	SD	P value
I	8.7	0	0.04
II	8.4	0.3	
III	8.8	1.4	
IV	8.6	0.7	
V	7.7	0.8	

Discussion

Despite recent advances in thediagnostic modalities, management and availability of plenty of literature, a substantial mortality as well as morbidity rate is attributable to unfavourable overall outcomes in patients following aSAH. Various factors have been implicated in occurrence and poor outcome in aSAH patients. However only handful of those have been found to reliably predict the incidence of aSAH . This study was designed to identify the mean serum Vitamin D and serum Calcium levels and its any association in aSAH patients.

The mean age of patients was 51 years. Weir et al[19]studied 945 patients of cerebral aneurysm and they found mean age of patients was 46 years. Aarhus et al[20]studied 444 patients of cerebral aneurysm and the median age of patients was 56 years . In our study out of 40 patients, 18 were males (45%) and 22 patients were females (55%) , which is comparable to the available literature suggesting that cerebral aneurysm is more common in females.

In our study 10 patients were chronic smoker (25%) and 30 patients (75%) were non smoker. 22 patients (55%) were hypertensive and 18 patients (45%) were non hypertensive. 14 patients (35%) were diabetic and 26 patients (65%) were non diabetic. Tuenissen et al[21]reviewed 9 longitudinal and 11 case control studies to identify the risk factors for aSAH and they found smoking ,hypertension and alcohol consumption were significantly related to the risk of spontaneous SAH .

We observed that the mean Vitamin D levels in males and females were 19.4±6.7 ng/ml and 15.7±7.0 ng/ml respectively and this difference was not statistically significant (p value=0.106). In our study in males, 61.1% were Vitamin D deficient whereas in females, 77.3% were deficient and however this difference was not statistically significant (p value=0.2). Guan J et al[10]in a retrospective study found the mean serum vitamin D level in patients with aneurysm was 23.3± 12.3 ng/ml whereas control group had mean level of 28.7± 14.1 ng/ml which was statistically significant .They used multivariable poisson regression and backward elimination to identify the risk factors .They found patients in the aneurysm group were older ,mostly females ,tobacco users ,hypertensive and had hypovitaminosis D but race ,body mass index and diabetes were not significantly different.

There was no statistically significant difference in mean vitamin D levels across WFNS grading (p value = 0.412) , Modified Fischer grading (p value = 0.568) and HUNT & HESS grading (pvalue-0.529).

We noted that the mean serum calcium level in males and females was 8.5 ± 1.0 mg/dl and 8.2 ± 1.0

mg/dl respectively and this difference was not statistically significant (p value=0.3).In our study 9 male patients and 11 female patients had calcium deficiency and it was not statistically significant (p value =1.0). Anil Can et al[22]did a multivariate analysis of serum calcium and magnesium levels to see the association with the ruptured aneurysm and they found hypomagnesemia and hypocalcemia were significantly associated with ruptured aneurysms.

In our study there was no significant difference in mean calcium levels across WFNS grades (p value = 0.07) (**Figure 3**). However, we found significant difference in mean calcium levels across Modified Fischer grades (p value = 0.002) and HUNT & HESS grades (p value=0.04) (**Figure 4**) which means low serum calcium level was associated with the higher grades.

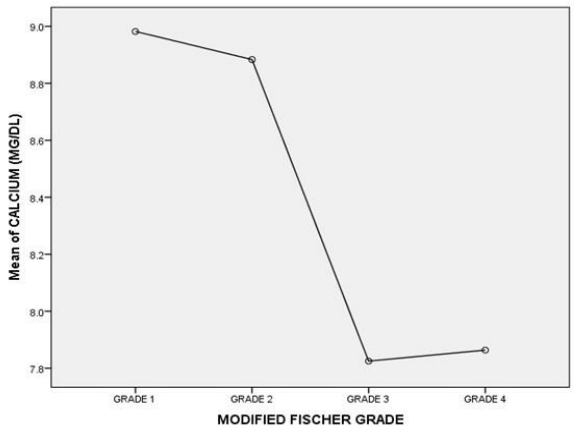

Figure 3. One-way Anova test showing the mean difference of calcium among WFNS Grade.

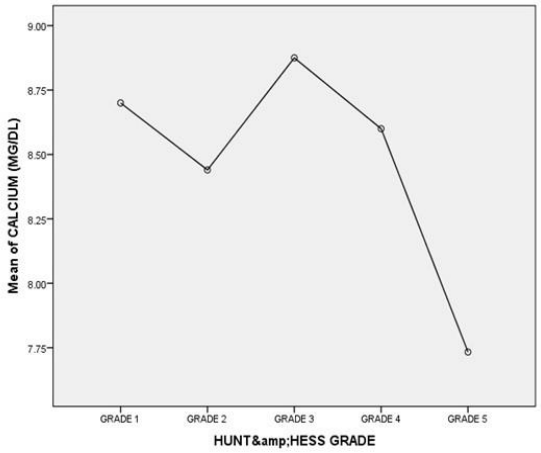

Figure 4. One-way Anova test showing the mean difference of calcium among HUNT & HESS Grading.

Van Heuven et al[23]in a retrospective study validated the prognostic value of WFNS grading on admission in determination of the outcome . Lindvall et al[24]found a significant correlation of Fischer scale and Hunt & Hess scale with the outcome of patient although the predictive value of limited due to low sensitivity and specificity of these scales .

We observed that the serum calcium has moderate positive correlation with Vitamin D and GCS . This correlation was statistically significant with a p value of 0.006 which explains the direct effect of serum vitamin D level in calcium absorption and its metabolism.

Conclusion

Aneurysmal subarachnoid hemorrhage is associated with high mortality and morbidity. We observed higher incidence of serum Vitamin D and serum Calciumdeficiencyin aSAHpatients .We found statistically significant difference in mean calcium levels across Modified Fischer grades (p value = 0.002) and HUNT & HESS grades (p value=0.04) .However further studies need to be undertaken to evaluate the role of Vitamin D and serum Calcium in aSAH. Also studies with a control group could help further validate this data.

Conflict of Interest

The authors have no conflict of interest to declare.

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References

1 De Rooij, N.K., Linn, F.H.H., van der Plas, J.A., Algra, A., Rinkel, G.J.E. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. J NeurolNeurosurg Psychiatry. 2007;78:1365–1372.

2 Ingall T, Asplund K, Mahonen M, Bonita R. A Multinational Comparison of Subarachnoid Hemorrhage Epidemiology in the WHO MONICA Stroke Study. Stroke. 2000;31:1054-1061.

3 Van Gijn J. Subarachnoid haemorrhage: diagnosis, causes and management. Brain. 2001;124:249-278.

4 Suarez J, Tarr R, Selman W. Aneurysmal Subarachnoid Hemorrhage. New England Journal of Medicine. 2006;354:387-396.

5 Risselada R, de Vries L, Dippel D, van Kooten F, van der Lugt A, Niessen W et al. Incidence, treatment, and case-

fatality of non-traumatic subarachnoid haemorrhage in the Netherlands. Clinical Neurology and Neurosurgery. 2011;113:483-487.

6 Bansal M , Mittal R S .Clinical Demographic Association and Outcome in Patients with Aneurysmal Subarachnoid Hemorrhage.Indian J Neurosurg2015;4:63–68.

7 Timour Al-Khindi, R Loch Macdonald, Tom A. Schweizer. Cognitive and Functional Outcome After Aneurysmal Subarachnoid Hemorrhage. Stroke. 2010;41:519-536.

8 Preiss M, Netuka D, Koblihova J, Bernadova L. Quality of life 1 year after aneurysmal subarachnoid hemorrhage in good outcome patients treated by clipping or coiling. Journal of neurological surgery, Central European neurosurgery. 2012;73:217-23.

9 Lai PM, Dasenbrock H, Du R. The Association between Meteorological Parameters and Aneurysmal Subarachnoid Hemorrhage: A Nationwide Analysis. PLoS One. 2014;9:112961.

10 Guan J, Karsy M, Eli I, Bisson EF, McNally S, Taussky P, Park MS. Increased Incidence of Hypovitaminosis D Among Patients Requiring Treatment for Cerebral Aneurysms. World Neurosurgery. 2016;88:15-20.

11 Alvarado Y, Perez A. Effects of Vitamin D deficiency in aneurysmal subarachnoid hemorrhage. Critical Care Medicine. 2015;43:138 .

12 Chung PW, Park KY, Kim JM, Shin DW, Park MS, Chung YJ, et al. 25- hydroxyvitamin D status is associated with chronic cerebral small vessel disease. Stroke. 2015;46:248-251.

13 Poole KE, Loveridge N, Barker PJ, Halsall DJ, Rose C, Reeve J, et al. Reduced vitamin D in acute stroke. Stroke. 2006;37:243-245.

14 Giovannucci E, Liu Y, Hollis BW, Rimm EB. 25-hydroxyvitamin D and risk of myocardial infarction in men: a prospective study. Arch Intern Med. 2008;168:1174- 1180.

15 Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation. 2008;117:503-511.

16 Wong YY, Flicker L, Yeap BB, McCaul KA, Hankey GJ, Norman PE. Is hypovitaminosis D associated with abdominal aortic aneurysm, and is there a dose-response relationship? Eur J VascEndovasc Surg. 2013;45:657-664.

17 Kassi E, Adamopoulos C, Basdra EK, Papavassiliou AG. Role of vitamin D in atherosclerosis. Circulation. 2013;128:2517-2531.

18 Inoue Y, Miyashita F, Toyoda K, Minematsu K. Low serum calcium levels contribute to larger hematoma volume in acute intracerebral hemorrhage. Stroke. 2013;44:2004–2006. doi: 10.1161/STROKEAHA.113.001187.

19 Weir B. Unruptured intracranial aneurysms: a review. J Neurosurg. 2002;96:3–42.

20 Aarhus, M., Helland, C.A. & Wester, K. Differences in anatomical distribution, gender, and sidedness between ruptured and unruptured intracranial aneurysms in a defined patient population. ActaNeurochir 151, 1569 (2009).

21 Teunissen LL, Rinkel GJ, Algra A, van Gijn J. Risk factors for subarachnoid hemorrhage: a systematic review. Stroke1996; 27: 544–9.

22 Can A, Rudy RF, Castro VM, Dligach D, Finan S, Yu S, Gainer V, Shadick NA, Savova G, Murphy S, Cai T, Weiss ST, Du R. Low Serum Calcium and Magnesium Levels and Rupture of Intracranial Aneurysms. Stroke. 2018 Jul;49(7):1747-1750. doi: 10.1161/STROKEAHA.118.020963.

23 Van Heuven A, DorhoutMees S, Algra A, Rinkel G. Validation of a Prognostic Subarachnoid Hemorrhage Grading Scale Derived Directly From the Glasgow Coma Scale. Stroke. 2008;39(4):1347-13.

24 Lindvall P, Runnerstam M, Birgander R, Koskinen L. The Fisher grading correlated to outcome in patients with subarachnoid haemorrhage. British Journal of Neurosurgery. 2009;23(2):188-192

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Risk factors for preoperative seizures in meningiomas - base versus non-bases of supratentorial. Single centre retrospective study in a series of 244 cases

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Keywords
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oedema

ABSTRACT

Background: Meningiomas are the most frequent benign intracranial lesions. The literature review reported that 19-63% of the patients with meningioma suffer from preoperative seizures, and 35% experience epileptic seizures as the initial symptom. The present study attempted to establish the risk factors for seizures before surgery of supratentorial meningiomas.

Objective: To compare predictive factors for preoperative seizures for skull base meningiomas (SBMs), with non-skull base meningiomas (NSBMs).

Materials and methods: The clinical data of 244 patients with supratentorial meningiomas treated microsurgically between 2007 and 2018 were analyzed retrospectively. There were two groups; Group "A" with (NSBMs) and Group "B" with (SBMs). Demographic, clinical, imaging, histopathological, and electroencephalographic data were assessed. Univariate statistical analyses were performed among factors that might correlate with preoperative seizures.

Results: A total of 244 patients with a diagnosis of intracranial meningioma were retrospectively evaluated. The mean age was 54.34 years (range 16- 84), females 165, meals 79. Of these 154 patients for the non-skull base, seizures in 65 (42.2%), whereas, 90 patients for skull base, with 32 (35.5%) patients with seizures. The groups had similar preoperative seizure occurrence in relation to age (p=0.154, p=0.819), gender (p=0.396, p=0.445) tumor size (p=0.318, p=0.244), tumor side (p0.836, p=0.702) for Group A and B respectively. The pre-op seizure was the third presentation in both groups after non-focal symptoms and (FND) respectively. For Group "A" seizure as the initial symptom was in 49.2% of patients versus 50.8% for others, while in Group "B" was in 37.5% vs 62.5%.

The both groups had statistically significance between PTBE and pre op seizure, for Group "A", PTBE was in 93(60.4%) patients, (seizure in 51patients 78.5%) vs (42 patients 47.2% for non-seizure), (?2=15.356, p=0.000). For Group "B", PTBE was in 43(47.8%) patients, (seizure in 25 patients 78.1%) vs(18 patients 31% for non-seizure),(?2=18.328, p=0.000).

The most frequently seizure for Group "B" was in OGM (seizure 25% vs 13.8 without seizure) and SWM (seizure 71.8% vs 65.5% non-seizure), while lesser overall in planum/tuberculum (seizure3.2% vs 20.7% non-seizure). There was a statistically

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significant relationship between tumour location and preoperative seizure for (SBM), ($?^2$=5.985, p=0.050) while absent in Group "A". (?2=1.373, p=0.503). There were no differences between the two groups with WHO grade and pre-op seizure. The unexpected finding in this study is that the presence of preoperative neurologic deficits has been less frequently associated with preoperative seizures in both groups. Careful analysis and further investigation are needed.

Conclusion: We identified that the major risk factor for pre-op seizure in both group studies is PTBE, and location for skull base meningiomas, where the planum/tuberculum lesser overall risk for pre-op seizure. While other radiological and histopathological factors are statistically non-significant. Interestingly, the factors associated with preoperative seizures were the absence of preoperative neurologic deficits for both groups.

Introduction

Meningioma is the most common benign intracranial tumor, accounting for approximately one-third of all CNS tumors [32]. In the literature review; it was reported that 19-63% of the patients with meningioma are suffered from preoperative seizures, and 35% of them experience epileptic seizures as the initial symptom [19]. Interestingly, patients with meningioma experience seizures even more frequently than patients with primary glioblastoma or brain metastasis. This is in particular a high rate taking into account that meningiomas are extra-axial tumors [31].

Recurrent seizures in patients with brain tumors lead to significant morbidity, cognitive problems, inability to drive, and diminished quality of life [11,25,29]. For patients with meningioma, surgery is the main treatment modality and offers the possibility of a cure. However, complications and morbidity from meningioma surgery are common [3, 23, 26,27]. The mechanisms of tumor-induced seizures are poorly understood. The causative neoplasm may act as a generator to produce an epileptogenic focus in the peri-tumoral brain. The mechanisms of epileptogenesis pre and postoperative are not sufficiently known. Distortion of the cortical structures may be the generator areas for focal seizure [6,12,17,30,34]

The following retrospective study summarizes the most important identified risk factors for preoperative seizure in a series of 244patients who underwent surgery for supratentorial meningioma, and subsequently, compares between the skull base and non-skull base.

Materials and methods

General information. Between 2007 and 2018, a total 244 of patients with supratentorial meningiomas were treated in Uzhhorod Neurosurgical Center. Pediatric(<16 years), recurrent and multiple meningioma patients, also posterior fossa meningiomas included; (clival,petro clival, foramen magnum, tentorial and cerebellopontine angle) were excluded from statistical analysis in this study. They were 244 patients divided into two groups: Group "A" (NSBMs) included 154 patients with preoperative seizure (65 patients) versus non-seizure (89 patients), and Group "B" (SBMs) included 90 patients, with preoperative seizure (32 patients) versus non-seizure (58 patients).

Clinical data collection. The medical records of all the patients were checked for history and initially preoperative seizures. All the patients had been diagnosed by head contrast-enhanced magnetic resonance imaging and/or computed tomography scans, and the maximum tumor size, tumor site and any peritumoral brain edema (PTBE), by employing high signal intensity changes on T2-weighted images, were preliminarily determined. We classified tumor size into 4 categories according to MRI findings; small (3cm and less), medium (3cm and less- 5cm), large (5cm-6cm), and giant (more 6 cm). All patients with preoperative seizures had been diagnosed by interictal 19 channel scalp electroencephalography (EEG). Craniotomy for meningioma resection was performed microscopically for all 244 patients.

After the resection of the tumor histopathological and immune histochemical analysis, were performed, according to WHO classification of tumors of the central nervous system,

We have analyzed the articles and summarized all risk factors investigated and subdivided risk factors for preoperative seizures into NSBMs and SBMs.

Results are summarized in (Table 1) NSBMs Group "A" and in (Table 2) for SBMs. Group "B"

Statistical analysis; Statistical analysis was performed using Chi-square test, t-test, and Fisher's Exact test. P <0.05 was considered statistically significant. Comparison between the two groups in relation to age, sex, tumor location, tumor site, tumor side, tumor size, histopathology, and clinical presentation was performed to identify predictive factors for preoperative seizure. Pearson Chi-square

statistics were used to examine the association between categorical variables (seizure and PTBE). There is a significant association at 5% significance level between seizure and PTBE of respondents (x2 =15.356, df=1, p=0.000) for Group "A", and (χ2=,18.328, df=1, p=0.000) for Group B.(seizure and location- for skull Base). There was a significant association at 5% significance level between seizure and location of tumor of respondents (x2 = 5.985, df = 2, p = 0.050).

Results

Demographic data

This study showed that meningioma in females had a higher tendency of 96 as compared to male 58, the ratio F/M was 1.6:1, and mean age 54.29 in Group "A". Like that in Group "B", the ratio F/M was 3.2:1.(female 69 vs 21 male), with a mean age of 54.49.

The patients' age ranged from 16 to 84 years old, the mean age for patients with seizures was 53.01 years (range 22 to 75), and 55.68 years (range 16-84) for non-seizure (χ2=3.737, p=0.154).

The seizure vs non-seizure for Group "A" female 58.4% vs 65.1%, while in male was 41.5% vs 34.8%. (χ2=0.720, p=0.396). There is a weak association was found between the male gender and pre-op seizure, however, the difference not reached statistically significant.

For Group "B", the seizure vs non-seizure in females was 81.5% vs 74.1% while in males was 18.5% vs 25.9%. (χ2=0.583, p=0.445). There is a weak association was found between female gender and pre-op seizure in Group "B". However, there was no statistically significant relationship between age or gender and preoperative seizure in both Groups.

Table 1. Factors associated with pre-op seizures in patients with NSBM Group "A"

Factor	No of cases n=154 (%)	Seizure n=65	No seizure n=89	P value
Sex Female Male	 96 (62.4%) 58 (37.6%)	 38 (58.4%) 27 (41.5%)	 58 (65.1%) 31 (34.8%)	0.396
Age/years < 40 40-60 >60	 20(13%) 76(49.4 %) 58(37.6 %)	 7 (10.7%) 38 (58.4%) 20 (30.7%)	 13 (14.6%) 38 (42.7%) 38 (42.7%)	0.154
Tumor size/ cm Small <3 medium >3- <5 large 5-6 giant >6	 37(24%) 59(38.3 %) 28(18.2 %) 30(19.5 %)	 17 (26.2%) 28(43%) 8 (12.3%) 12 (18.5%)	 20 (22.5%) 31 (34.8%) 20 (22.4%) 18 (20.3%)	0.318
Side LT RT Both/median	 74(48%) 73(47.4 %) 7(4.6%)	 33(50.8 %) 29(44.7 %) 3(4.5%)	 41(46%) 44 (49.4%) 4 (4.6%)	0.836
Location Convex Parasaital/Parafalx Intraventricular Site Frontal Fronto temporal Fronto parietal Temporal Tempo paraital Parietal Paraito occipital Occipital	 98(63.6 %) 51(33.1 %) 5(3.3%) 49(31.8) 17(11) 47(30.5) 7(4.5) 9(5.8) 12(7.8) 10(6.5) 3 (2)	 39(60%) 25(38.5 %) 1 (1.5%) 23(35.4 %) 6 (9.3%) 19 (29.2%) 4 (6.2%) 3 (4.6%) 6 (9.3%) 3 (4.6%) 1(1.5%)	 59(66.3 %) 26 (29.2%) 4 (4.5%) 26 (29.2%) 11 (12.3%) 28 (31.4%) 3 (3.3%) 6 (6.7%) 6 (6.7%) 7 (7.9%) 2 (2.3%)	0.503 0.683
PTBE Present Absent	 93(60.4 %) 61(39.6 %)	 51 (78.5%) 14 (21.5%)	 42 (47.2%) 47 (52.8%)	0.000

Imaging finding

Relation to location

In Group "A"; convex in 63.6% patients (seizure 60% vs 66.3% non-seizure), parasaital/ parafalx 33.1% patients (seizure 38.5% vs 29.2% non-seizure) and intraventricular 3.3% patients (seizure 1.5% vs 4.5% non-seizure), Parasagittal/ parafalcine location had higher occurrence of seizure in this group, however, there was no statistically significant relation between

tumor location and preoperative epilepsy, (χ2=1.373, p=0.503).

In Group "B" (Table 3.a, b); SWM in 67.8% patients (71.9% seizure vs 65.5% non-seizure), OGM in 17.8% patients, (25% seizure vs 13.8% non-seizure), and planum/tubeerculum in14.4% patients (3.1% seizure vs 20.7% non-seizure). Preoperative seizure was more incidence in OGM and SWM, respectively, while, lesser in planum and tuberculum meningiomas, (χ^2=5.985, p=0.05). There was statistically significant relation between tumor location and preoperative seizure for (SBM) Group"B", while absent in Group "A".

Table 2. Factors associated with pre op seizures in patients with SBM Group" B" 90

Factor	No of cases n=90 / %	Seizure n=32 (35.6%)	No seizure n=58 (64.4%)	p
Sex Female Male	69(76.7 %) 21(23.3 %)	26 (81.2%) 6 (18.8%)	43(74.1 %) 15 (25.9%)	0.44 5
Age/years < 40 40-60 >60	11(12.2 %) 58(64.4 %) 21(23.4 %)	3(9.3%) 21(65.6 %) 8(25%)	8(13.8%) 37(63.8 %) 13(22.4 %)	0.81 9
Tumor size/ cm Small 3 and <3 medium >3- <5 large 5-6 giant >6	27(30%) 28(31.1 %) 29(32.2 %) 6(6.7%)	12(37.5 %) 12(37.5 %) 7(21.9%) 1(3.2%)	15(25.8 %) 16(27.6 %) 22(38%) 5(8.6%)	0.24 4
Side LT RT Both/median	29(32.2 %) 32(35.6 %) 29(32.2 %)	12(37.5 %) 11(34.4 %) 9(28.1%)	17(29.3 %) 21(36.2 %) 20(34.5 %)	0.70 2
Location SWM/CS OGM Planum/Tubercul um	61(67.8 %) 16(17.8 %)	23(71.9 %) 8 (25%) 1 (3.1%)	38 (65.5%) 8 (13.8%)	0.05 0
	13(14.4 %)		12 (20.7%)	
PTBE Present Absent	43(47.8 %) 47(52.2 %)	25 (78.1%) 7 (21.9%)	18 (31%) 40 (69%)	0.00 0

Relation to Brain Lobes and Tumour Side

Preoperative seizure for (NSBM) occurred in all sites of brain lobes, moreover, there was a higher incidence of frontal (seizure 35.4% vs 29.1% non-seizure). However, There was no statistically significant relation between brain lobes lesion and preoperative seizure. (χ2=,0.288, p=0.687). According, to side of meningioma location in Group "A", right in 47.4% patients, (seizure 44.7% vs 49.4% non-seizure), left side in 48% patients (seizure 50.8% vs 46% non-seizure), and Medline both side in 6.4% patients, (seizure 4.5% vs 4.6 non seizure). There was no statistically significant relationship between the side of the lesion and preoperative seizure. (χ2=,0.358, p=0.836). While in Group "B" left side in 35.6% patients, (seizure 37.5% vs 29.3 non seizure), right side in 48% patients, (seizure 34.4% vs 36.2 non seizure), and Medline both side in 32.2% patients, (seizure 28.1% vs 34.5% non-seizure). Despite the weak relationship was found between the left side and pre-op seizure, however, there was no statistically significant relationship between the side of the lesion and preoperative seizure. (χ2=,0.707, p=0.702).

Table 3a. Location * Seizure. Cross tabulation for Group B

			SEIZURE		Total
			No	Yes	
LOCATION	SWM	Count	38	23	61
		Expected Count	39.3	21.7	61.0
		% within LOCATION	62.3 %	37.7 %	100. 0%
		% within SEIZURE	65.5 %	71.9 %	67.8 %
	OGM	Count	8	8	16
		Expected Count	10.3	5.7	16.0
		% within LOCATION	50.0 %	50.0 %	100. 0%
		% within SEIZURE	13.8 %	25.0 %	17.8 %
		Count	12	1	13

	PLA/TUBERCULUM	Expected Count	8.4	4.6	13.0
		% within LOCATION	92.3%	7.7%	100.0%
		% within SEIZURE	20.7%	3.1%	14.4%
Total		Count	58	32	90
		Expected Count	58.0	32.0	90.0
		% within LOCATION	64.4%	35.6%	100.0%
		% within SEIZURE	100.0%	100.0%	100.0%

Table 3b. Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	5.985[a]	2	.050
Likelihood Ratio	7.078	2	.029
Linear-by-Linear Association	2.170	1	.141
N of Valid Cases	90		

Chi-square statistics were used to examine the association between categorical variables (Seizure and Location- Skull Base). There is a significant association at 5% significance level between seizure and location of tumor of respondents (x2 = 5.985, df = 2, p = 0.050).

Relation to Tumor Size

Preoperative seizure was occurs in all different tumor size, for Group "A" small size was in 24% patients,(seizure 26.2% vs 22.5% non-seizure), medium 38.2% patients (seizure 43%vs 34.8% non-seizure), and large/giant in 37.7% patients (seizure 30.8% vs 42.7% non-seizure).The difference is statistically insignificant, ($\chi2=3.073$, p=0.381). While for Group" B", small size 30% patients,(seizure 37.5% vs 25.8%), medium 31.1% patients (seizure 37.5% vs 27.6%) and large/giant 38.8% patients (seizure 25% vs 46.5%). The difference is statistically insignificant($\chi2=4.167$, p=0.244).Despite the weak relation was found between small/medium size and pre op seizure, however, distribution of tumor size in both groups showed that there was no statistically significant relation between tumor size and occurrence of pre-op seizure.

Relation to PTBE

There was a higher incidence of peri-tumoral edema in seizure in both groups; for Group "A" (Table 4.a,b), PTBE was in 93(60.4%) patients,(seizure in 51patients 78.5%) vs (42 patients 47.2% for non-seizure). There was a statistically significant relation between peri-tumoral edema and pre-op seizure, ($\chi2=15.356$, p=0.000).For Group "B",(Table5.a,b) PTBE was in 43(47.8%) patients,(seizure in 25 patients 78.1%) vs(18 patients 31% for non-seizure). There was a statistically significant relation between peri-tumoral edema and pre-op seizure, ($\chi2=18.328$, p=0.000).The incidence of PTBE was higher in NSBM, however, distribution of PTBE in both groups showed that there was statistically significant relation between PTBE and occurrence of pre-op seizure .

Table 4a. Seizure * PTBE cross tabulation for group a

			PTBE		Total
			No	Yes	
SEIZURE	No	Count	47	42	89
		Expected Count	35.3	53.7	89.0
		% within SEIZURE	52.8%	47.2%	100.0%
		% within PTBE	77.0%	45.2%	57.8%
	Yes	Count	14	51	65
		Expected Count	25.7	39.3	65.0
		% within SEIZURE	21.5%	78.5%	100.0%
		% within PTBE	23.0%	54.8%	42.2%
Total		Count	61	93	154
		Expected Count	61.0	93.0	154.0
		% within SEIZURE	39.6%	60.4%	100.0%
		% within PTBE	100.0%	100.0%	100.0%

Table 4b. Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	15.356[a]	1	.000		
Continuity Correction[b]	14.077	1	.000		
Likelihood Ratio	15.962	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	15.256	1	.000		
N of Valid Cases	154				

Chi-square statistics were used to examine association between categorical variables (Seizure and PTBE). There is a significant association at 5% significance level between seizure and PTBE of respondents (x^2 =15.356, df=1, p=0.000).

Table 5a. PTBE * Seizure crosstabulation for Group B

			SEIZURE		Total
			No	Yes	
PTBE	0	Count	40	7	47
		Expected Count	30.3	16.7	47.0
		% within PTBE	85.1%	14.9%	100.0%
		% within SEIZURE	69.0%	21.9%	52.2%
	1	Count	18	25	43
		Expected Count	27.7	15.3	43.0
		% within PTBE	41.9%	58.1%	100.0%
		% within SEIZURE	31.0%	78.1%	47.8%
Total		Count	58	32	90
		Expected Count	58.0	32.0	90.0
		% within PTBE	64.4%	35.6%	100.0%
		% within SEIZURE	100.0%	100.0%	100.0%

Table 5b. Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	18.328[a]	1	.000		
Continuity Correction[b]	16.489	1	.000		
Likelihood Ratio	19.120	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	18.125	1	.000		
N of Valid Cases	90				

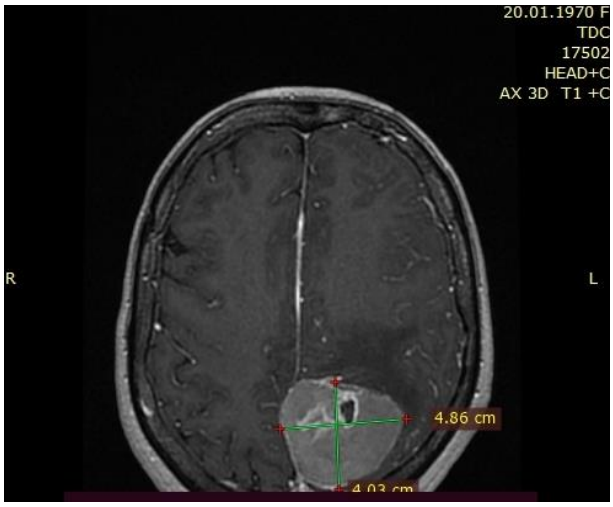
Chi-square statistics were used to examine association between categorical variables (Seizure and PTBE). There is a significant association at 5% significance level between seizure and PTBE of respondents (χ2=,18.328, df=1, p=0.000).

Clinical data

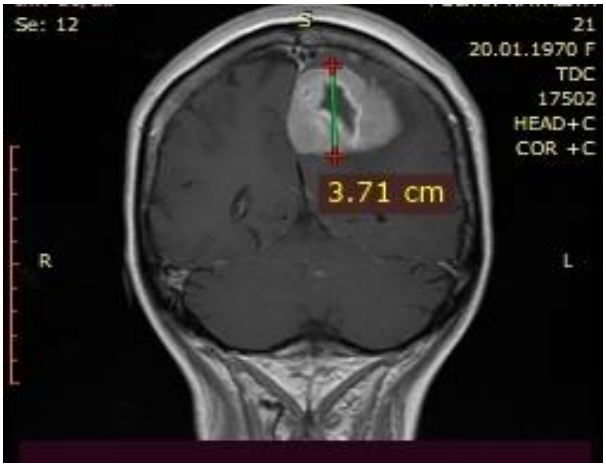
The preoperative clinical symptoms and signs (non-focal) like;, headache, vomiting, mental change, memory disorder and cognitive decline, were found in most cases 92(59.7%) patients for Group A", While second presentation was focal neurological deficit (FND), include; motor weakness, sensory , cranial nerves dysfunction, aphasia, were found in 78(50.6%). In this study, pre op seizure was the third presentation 65(42.2%), of these 32 patients were seizure was single presentation.

For Group B", non-focal was first presentation and occurs in 59(65.5%) patients, followed; focal symptoms 36(40%) patients, then seizure was the third presentation 32(35.5%) patients of these 12(37.5%) patients were seizure was single presentation. Clinical types of seizure in both groups was; complex partial in (158 patient, 64.8%), generalized tonic clonic (43 patients, 17.6%). Simple partial (23 patients, 9.5%) and combined (20 patients, 8.1%). (Figure1,2).

Focal neurological deficit were associated with reduced incidence of pre-op seizure, in both groups for Group A,16 (24,6%) patients with seizure compared to 62(69.7%) patients without seizure, and Group B, (7patients, 21.8% seizure vs, 29 patients, 50% without seizure). moreover, pre-op seizure was in 49.2% as a first presentation of disease compared to 50.2% for others in Group A, and 37.5% vs 62.5 for Group B".



A.



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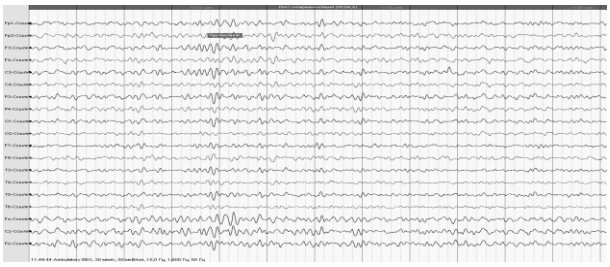
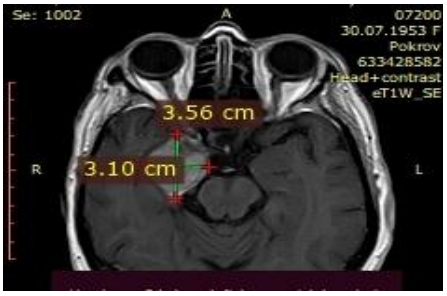
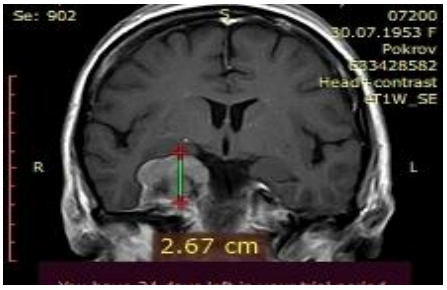


C.

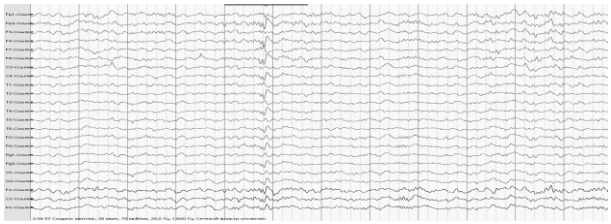
Figure 1. A female patient aged 48 years, presented with fits, mental changes, and headache. (a) Axial and (b) coronal T1 with contrast showing left middle falx meningioma type I, hemispheroid tumor invagination deeply into one hemisphere. (c) Preoperative electroencephalography showing focal epileptiform activity in left parietal lobe.



A.



B.



C.

Figure 2. (a) A female patient aged 65 years, presented with fits, headache, and vision impairment on right side (a) axial and (b) coronal T1 with contrast showing right medial sphenoid wing meningioma. (c) Preoperative electroencephalography showingfocal epileptiform activity in right hemisphere.

Histopathological finding

In our groups study (Table 6), pathological finding was found; Grade I were included 121 (78.6%) cases,(seizure 80% vs 77.5% non-seizure), Grade II in 24(15.6%) cases, (seizure 13.8% vs 16.8% non-seizure) and Grade III in 9(5.8%) cases, (seizure 6.2% vs 5.7%% non-seizure) for Group A. While for Group B", Gr.I in 75(83.3%)cases, (seizure 87.5% vs 81% non-seizure), GradeII in 13(14.4%) cases, (seizure 12.5% vs15.5% non-seizure), Grade III in 2(2.3%) cases ,(seizure 0% vs 3.6% non-seizure).

For both groups, meningothelial meningioma was the most common histopathological type, and angiomatous subtype had slightly higher occurrence of seizure 10(15.4%) cases compared to 5(5.6%) cases without seizure four Group A.

Table 6.

WHO Grade	**Grou pA**			**Group B**		
	No of Case s 154	Seiz ure 65	Non Seizu re89	No of Case s90	Seizu re 32	Non Seiz ure 58
WHO I meningi othelial	121 (78.6 %) 53	52(8 0%) 21	69(77 .5%) 32	75(83 .3%) 44	28(87 .5%) 15	47(8 1%) 29
fibroblas t	33	14	19	11	3	8
transitio nal	10	3	7	6	3	3
angioma tous	15	10	5	8	4	4
psammo matous	9	3	6	5	3	2

microcyst	1	1	-	1	-	1
WHO II	24(15.6%)	9(13.8%)	15(16.8%)	13(14.4%)	4(12.5%)	9(15.5%)
WHO III	9(5.8%)	4(6.2%)	5 (5.7%)	2(2.3%)	-	2(3.6%)

Discussion

Seizures are one of the three most common clinical symptoms besides (and after) headache and focal neurological deficit of patients with meningioma [33]. In the present study, we report the risk factors associated with preoperative seizures in different locations of supratentorial meningiomas.

The occurrence of preop seizure for (NSBM) Group "A" was slightly higher (42.2% patients) as compared to (SBM) Group "B" (35.5% patients). Gender distribution in our study in both groups showed that was no statistically significant relationship between gender and preoperative seizure. p=0.396 and p=0.445 respectively. Similar results were reported by Islim Al et al [14] and Chozick et al. [9].

The epileptic patients in Group "A" have their tumor location mostly in frontal and temporal regions, however, there was no statistically significant relation between tumor related to brain lobes (site) and occurrence of a seizure, p=0638, also we could not find the difference between convexity and parasagittal/parafalcine for the occurrence of a seizure, p=0.503. While we observed an increase of seizure in SWM and OGM compared to planum/tuberclum meningiomas and the relation was significant p=0.050

According to most studies addressing this question were reported different results,Lieu et al. and Das et al. [10,17] identified temporal. Islimet al. [14] identified parietal meningiomas to be significantly associated with preoperative seizures. Skardelly et al. [28] further identified parafalcine meningiomas to be significantly associated with preoperative seizures. Kawaguchi et al.[15] who studied convexity meningioma found that there was a significant relationship between the seizure occurrence and tumor location. However, our result corresponds with other studies that were reported lacking significant relation between the seizure occurrence and tumor location and site. Liigant et al.[18] found that a higher incidence of seizures was in tumors involving the frontoparietal (58%), frontotemporal (44%), and temporal (40%) regions but no significant association with tumor location. Riva [24] and Hess K, et al., [13] found no statistically significant relation between tumor site and occurrence of seizure.

In our study, the distribution of tumor side in both groups showed that the left side was slightly higher than the right side, however, there was no statistically significant relationship between the side of the lesion and preoperative seizure, for both groups, (Gr. "A", p=0.836 and Gr." B", p=0.702. Our results were similar to what was reported by, Lieu and Howng [17]. Moreover, tumor side and a number of lesions had no significant influence on preoperative seizure rate [9,14].

The distribution of tumor size in both groups showed that there was no statistically significant relation between tumor size and the occurrence of seizures. Similar results were reported in three studies. [6,14,18]. In contrary to what was reported by other studies, were shown a positive correlation between tumor size and preoperative seizure rate [7,15,20,33].

Here, we showed that PTBE may be the factor most strongly related to preoperative seizures for both groups: A" and" B". ($\chi 2$=,15.356, p=0.000) and ($\chi 2$=,18.328, p=0.000), respectively. Various studies in the past have reported a correlation between vasogenic edema and seizure occurrences. [6,11,15,33]. Furthermore, Lieu and Howng[17], and Kawaguchiet al.[15]reported that most patients with evident or severe edema, had preoperative and postoperative epilepsy with a significant correlation.

Despite primarily extra-axial locations, slow progression rates, and usually benign histological characteristics, meningiomas frequently are associated with PTBE [4]. PTBE, as assessed on CT scan, has been found to be associated with more than half of the cases [16]. Though the exact mechanism involved in the development of PTBE is not known, several factors have been previously studied like tumour location and tumour volume, interleukin-6, sex hormone receptors and several others [1,2,21]. Moreover, peritumoral edema fluid contains a high concentration of glutamate, which may trigger hyperexcitability and epileptogenesis [34].

The preoperative seizure was the third clinical symptom after non-focal and focal symptoms in both groups of patients respectively. Moreover, the

pre-op seizure was in 49.2% as the first presentation of disease compared to 50.2% for focal and non-focal symptoms for the non-skull base, and 37.5% vs 62.5 for skull base meningiomas. In the literature review; it was reported that 19-63% of the patients with meningioma are suffered from preoperative seizures, and 35% of them experience epileptic seizures as the initial symptom [19].

In our data presence of preoperative neurologic deficits has been less frequently associated with preoperative seizures in both groups: Group "A" patients,(seizure in 16 cases 24.6% vs 62 cases 69.7% non-seizure), Group "B" patients, (seizure 7 cases, 21.8% vs 29 cases 50% without seizure). This is an unexpected finding. However, considering the increase in meningioma detection and widespread availability of neuroimaging [22], this may be explained by the diagnosis of the tumor prior to the occurrence of neurological deficits or just after a seizure attack. Furthermore, by Riva study (among seizure in intrinsic brain tumors), he reported that patients with seizures showed a significantly lower incidence of neurological deficit, headache, and mental disturbances compared with nonepileptic patients [24]. Otherwise, Careful analysis and further investigation are needed.

The distribution of tumor histopathology in both groups showed that meningothelial meningioma was the most common histopathological type. While high grade (GrII-III) was higher in non-skull base (21.4%) than skull base (16.7%). Despite the increased occurrence of pre-op seizure among angiomatous type, however, there was no relation between the different histopathological types and occurrence of seizure. Kawaguchiet al. [15] believed that fibroblastic meningiomas were significantly correlated with preoperative seizures. Skardelly et al. demonstrated an increase of preoperative seizures from WHO Gr. II and Gr.III [28] Chowet al.[8]showed that the histologic types were not significantly correlated with preoperative seizure. Moreover, in other studies did not have a significant influence on pre-or postoperative seizure rate [5,9].

Conclusion

We identified that the major risk factor for pre-op seizure in both groups study is PTBE, and location for skull base meningiomas, where the planum/tuberculum lesser overall risk for pre-op seizure. There was a trend for the occurrence of preoperative seizure among (male gender in skull base and female gender in non-skull base), frontal, temporal, left side, and size <5 cm and angiomatous subtype, however, these predictors were statistically insignificant. The factor associated with preoperative seizures were the absence of preoperative neurologic deficit for both groups. Careful analysis and further investigation are needed.

Abbreviations

SWM: Sphenoid Wing Meningiomas;
OGM: Olfactory Groove Meningioma;
CT: Computer Tomography;
MRI: Magnetic Resonance Imaging;
PTBE: Peritumoral Brain Oedema;
FND: Focal Neurological Deficit;
WHO: World Health Organization;
CNS: Central Nervous System;
SBM: Skull Base Meningioma;
NSBM: Non-Skull Base Meningioma;
EEG: Electro Encephalo Graphy;
CS: Cavernous Sinus.

References

1. Benzel EC, Gelder FB. Correlation between sex hormone binding and peritumoral edema in intracranial meningiomas. Neurosurgy. 1988; 23:169–74.
2. Bitzer M, Opitz H, Popp J, Morgalla M, Gruber A, Heiss E, Voigt K. Angiogenesis and brain oedema in intracranial meningiomas: influence of vascular endothelial growth factor. Acta Neurochir (Wien).1998;140:333–40.
3. Black PM (1993) Meningiomas. Neurosurgery 32:643–657
4. Bradac GB, Ferszt R, Bender A, Schorner W. Peritumoral edema in meningiomas : A radiological and histological study. Neuroradiology.1986; 28: 304-312.
5. Brennan CW, Verhaak RGW, McKenna A, Campos B, Noushmehr H, Salama SR, et al. The somatic genomic landscape of glioblastoma. Cell 2013;155:462–77. https://doi.
6. Chaichana KL, Pendleton C, Zaidi H, Olivi A, Weingart JD, Gallia GL, *et al.* Seizure control for patients undergoing meningioma surgery. World Neurosurg 2013;79:515-524.
7. Chen WC, Magill ST, Englot DJ, Baal JD, Wagle S, Rick JW, et al. Factors associated with pre- and postoperative seizures in 1033 patients undergoing supratentorial meningioma resection. Neurosurgery 2017;81:297–306. https://doi.org/10.1093/ neuros/nyx001.
8. Chow SY, Hsi MS, Tang LM, Fong VH. Epilepsy and intracranial meningiomas. Zhonghua Yi Xue Za Zhi (Taipei) 1995;55:151-5.
9. Chozick BS, Reinert SE, Greenblatt SH. Incidence of seizures after surgery for supratentorial meningiomas: a

modern analysis. J Neurosurg 1996;84:382–6.https://doi.org/10.3171/jns.1996.84.3.0382.
10. Das RR, Artsy E, Hurwitz S, Wen PY, Black P, Golby A, et al. Outcomes after discontinuation of antiepileptic drugs after surgery in patients with low grade brain tumors and meningiomas. J Neurooncol 2012;107:565–70.
11. Englot DJ, Berger MS, Chang EF, Garcia PA: Characteristics and treatment of seizures in patients with high-grade glioma: a review. Neurosurg Clin N Am 23:227–235, vii–viii, 2012
12. Fang S, Zhan Y, Xie YF, Shi Q, Dan W. Predictive value of electrocorticography for postoperative epilepsy in patients with supratentorial meningioma. J Clin Neurosci 2013; 20:112-6.
13. Hess K, Spille DC, Adeli A, Sporns PB, Brokinkel C, Grauer O, et al. Brain invasion and the risk of seizures in patients with meningioma. J Neurosurg 2018:1–8.https://doi.org/10.3171/2017.11.JNS172265.
14. Islim Al, Ali A, Bagchi A, Ahmad MU, Mills SJ, Chavredakis E, et al. Postoperative seizures in meningioma patients: improving patient selection for antiepileptic drug therapy. J Neurooncol 2018;0:0. https://doi.org/10.1007/s11060-018-2941-2.
15. Kawaguchi T, Kameyama S, Tanaka R. Peritumoral edema and seizure in patients with cerebral convexity and parasagittal meningiomas. Neurol Med Chir (Tokyo) 1995;36:564–8.
16. Kim IS, Kim HD, Kim KU, Shin HC, Choin HJ, Kim KH. Factors influencing the development of peritumoral brain edema in menigiomas. J Korean Neurosurg Soc.1997;26:940-5.
17. Lieu AS, Howng SL. Intracranial meningiomas and epilepsy: Incidence, prognosis and influencing factors. Epilepsy Res 2000;38:45-52.
18. Liigant A, Haldre S, Oun A, Linnamägi U, Saar A, Asser T, *et al.* Seizure disorders in patients with brain tumors. Eur Neurol 2001;45:46-51.
19. Longstreth WT Jr, Dennis LK, McGuire VM, Drangsholt MT, Koepsell TD. Epidemiology of intracranial meningioma. Cancer1993;72(3):639-48.
20. Odebode TO, Akang EE, Shokunbi MT, Malamo AO, Ogunseyinde AO. Factors influencing visual and clinical outcome in Nigerian patients with cranial meningioma. J ClinNeurosci2006;13:649–54. https://doi.org/10.1016/j.jocn.2005.07.023org/10.1016/j.cell.2013.09.034.
21. Park KJ, Kang SH, Chae YS, Yu MO, Cho TH, Suh JK, et al. Influence of interleukin-6 on the development of peritumoral brain edema in meningiomas. J Neurosurg. 2010;112:73–80.
22. Porter KR, McCarthy BJ, Freels S, et al: Prevalence estimates for primary brain tumors in the United States by age, gender, behavior, and histology. Neuro Oncol 12:520-7, 2010
23. Reinert M, Babey M, Curschmann J, Vajtai I, Seiler RW, Mariani L. Morbidity in 201 patients with small sized meningioma treated by microsurgery. Acta Neurochir. 2006;148(12):1257–1265; discussion 1266.
24. Riva M. Brain tumoral epilepsy: A review. Neurol Sci 2005;26 Suppl 1:S40-2.
25. Rudà R, Trevisan E, Soffietti R: Epilepsy and brain tumors. Curr Opin Oncol 22 :611–620, 2010
26. Sanai N, Polley MY, Berger MS. Insular glioma resection: assessment of patient morbidity, survival, and tumor progression. J Neurosurg. 2010;112(1):1–9.
27. Sanai N, Sughrue ME, Shangari G, Chung K, Berger MS, McDermott MW. Risk profile associated with convexity meningioma resection in the modern neurosurgical era. J Neurosurg. 2010;112(5): 913–919.
28. Skardelly M, Rother C, Noell S, Behling F, Wuttke TV, Schittenhelm J, et al. Risk factors of preoperative and early postoperative seizures in patients with meningioma: a retrospective single-center cohort study. World Neurosurg 2017;97:538–46. https://doi.org/10.1016/j.wneu.2016.10.062.
29. Taphoorn MJ, Klein M: Cognitive deficits in adult patients with brain tumours. Lancet Neurol 3:159–168, 2004
30. Tomasello F. Meningiomas and postoperative epilepsy: It is time for a randomized controlled clinical trial. World Neurosurg 2013;79:431-2.
31. VanBreemen MSM,Wilms EB, Vecht CJ. Epilepsy in patients with brain tumours: epidemiology, mechanisms, and management. Lancet Neurol 2007;6:421–30. https://
32. Wiemels J, Wrensch M, Claus EB: Epidemiology and etiology of meningioma. J Neurooncol 99**:**307–314, 2010
33. Xue H, Sveinsson O, Bartek J, Förander P, Skyrman S, Kihlström L, et al. Long-term control and predictors of seizures in intracranial meningioma surgery: a population-based study. Acta Neurochir 2018;160:589–96. https://doi.org/10.1007/s00701-017-3434-3.
34. Zheng Z, Chen P, Fu W, Zhu J, Zhang H, Shi J, *et al.* Early and late postoperative seizure outcome in 97 patients with supratentorial meningioma and preoperative seizures:A retrospective study. J Neurooncol 2013;114:101-9

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Letter to the Editor: A new enthusiastic generation of Romanian neurosurgery

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ABSTRACT
At the beginning of every spring, Cluj becomes for 3 days the main topic of discussion among students passionate about neurosurgery throughout Romania. The "Neurosurgical Masterclass" is the catalyst for young and enthusiastic students to learn the mysteries of the human brain and this year was organized the 10th edition of this interesting congress. The event succeeded in joining together 185 neurosurgery enthusiasts and 36 renowned speakers.

Keywords
Romanian, neurosurgery, new generation

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Image 1. Prof. Ioan-Stefan Florian M.D. PhD. with attendees of the event.

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Since neurosurgery is a practical medical specialty, the first day began with unique workshops, from viewing a live operation that familiarized students with some anatomical landmarks, to the dissection of the white substance of the brain. The participants also had a demonstration of correct and complete neurological examination, so that the young students were initiated into the basic neurosurgical terminology. Overall, 7 hands-on workshops were organized.

In a festive spirit, the guest of honor was the distinguished Prof. Dr. Madjiid Samii from the International Neuroscience Institute (Hannover, Germany) who opened the proceedings of the congress with the presentation "What I could develop in Neurosurgery", offering an auspicious energy and an encouraging word for the students.

Image 2. Stud. Dragos Font and Prof. Ioan-Stefan Florian M.D. PhD. presiding over the student session.

Prof. Madjid Samii's presentation was followed by the work of our resident colleague at the Institute of Neurology and Neurovascular Diseases Bucharest, Dr. Andrei Alexandru Marinescu, who delighted us with the secrets of cerebral vascularization, presenting in detail the Willis' Circle.

After two sessions of presentations, at the end of the first day, the students had the opportunity to participate in the Neuroquiz anatomy competition, having as the prize neurosurgical study materials of the highest quality.

The second day of works was very special being marked by renowned European neurosurgeons such as Prof. Dr. Lukas Rasulic, Prof. Dr. Stefano Ferarresi (Italy) or Prof. Dr. Ishan Soraloglu (Turkey) who offered more gravitas to this event.

The founder of the congress, Prof. Dr. Ioan Ștefan Florian has impressed as always with the novelty of his works, addressing the students in an accessible and friendly speech.

At the same time, student Dragoș Font, co-president of the congress and leader of the Student Circle of Neurosurgery in Cluj-Napoca, presented ''An operative perspective of the posterior fossa'', in an impeccable manner.

The last day was dedicated exclusively to student presentations. The delegation of Serbian students, Stud. Stefan Radojevic and Stud. Aleksa Micic (coordinated by Prof. Lukas Rasulic) impressed with detailed presentation of peripheral neuroanatomy. The delegation of students from the "Walter E. Dandy" Neurosurgical Club in Bucharest distinguished itself through Stud. Mădalina Popescu, Stud. Max Blega (winner of the Neuroquiz contest) and Stud. Firas Al-Krayem (winner of the contest for presentations of clinical cases).

At the end of the 3 days of congress, each participant left with new interesting and “up-to-date” knowledge, and with new memories to share with other neurosurgery enthusiasts.

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included inside the text, and the author's name. The label will be placed on the top of the picture. The drawings may be sent on vellum paper, tracing paper or transparent paper. The use of pictures belonging to other publications is accepted, only if mentioning the original source. Further, the partial use of any previously published text is accepted with the approval of its author and editor. All pages should be consecutively numbered, starting with the title page.

7. Abbreviations

Abbreviations should be consistently used throughout the text and established in a fixed form from the beginning.

8. Submission

Manuscripts should be sent to the Editor:
Dr St.M. Iencean,
Romanian Neurosurgery
"Gr.T. Popa" University of Medicine and Pharmacy
Universitatii Street, No. 16, 700115, Iasi, Romania
or by e-mail to ***mirceasteffan@yahoo.com***.

9. Disclaimer

The editors disclaim any responsibility for opinions expressed in the papers.

10. The review process

After the manuscript submission, the peer review process is broken down into the following steps:
1. The Editor assigns Reviewers to the manuscript.
2. The Reviewers review the manuscript.
3. The Editor drafts a decision to be sent to the author/authors.

The review process takes between three weeks and two months.