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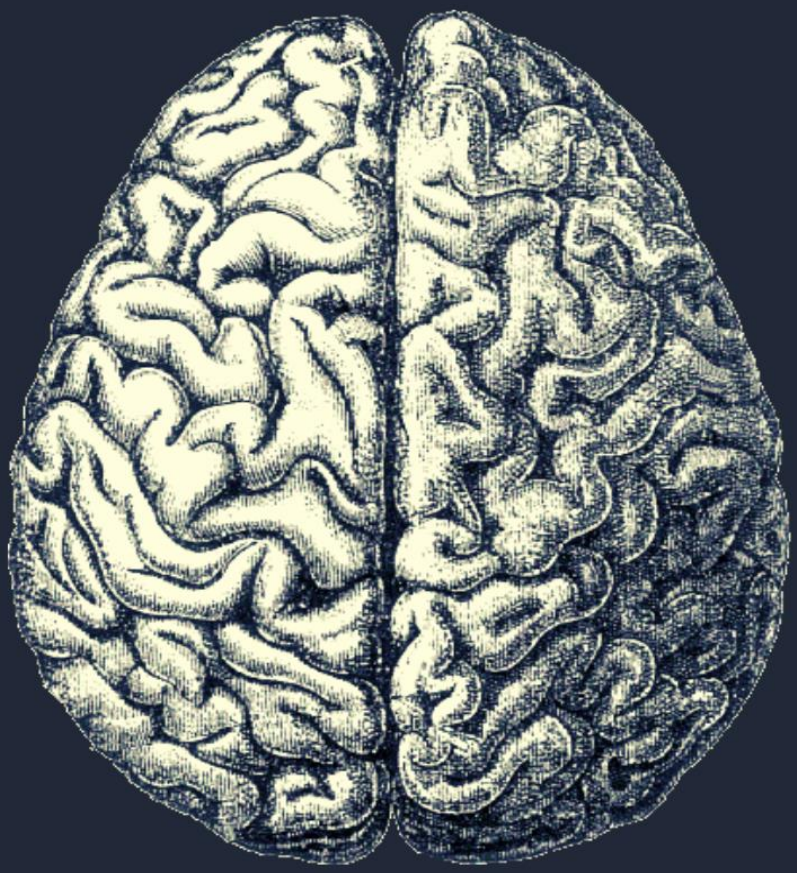

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The T2FLAIR mismatch novel radiogenomic marker in the newly suspected low-grade gliomas. Implications for grading and neurosurgical management in light of the 2021 WHO Classification of Tumours of the Central Nervous System (WHOCNS5)

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Keywords
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low-grade gliomas,
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ABSTRACT

Background. The T2-FLAIR (fluid-attenuated inversion recovery) mismatch sign has been defined over the last few years as an important novel radiogenomic marker highly suggestive of isocitrate dehydrogenase mutated (IDH-mut) 1p19q non-codeleted gliomas (astrocytomas). Existing studies have demonstrated that this has good specificity but limited sensitivity for IDH-mut astrocytomas. The new 2021 WHO Classification of Tumors of the Central Nervous System (WHO CNS5) has introduced a layered grading system in which all IDH mutant diffuse astrocytic tumours are considered a single type (Astrocytoma, IDH-mutant) and are graded as CNS WHO grade 2, 3, or 4. Because of the growing importance of molecular information in CNS tumour classification, diagnoses and diagnostic reports need to combine different data types into a single diagnosis. Whether the T2FLAIR mismatch sign is of clinical relevance for the management of low-grade gliomas still needs to be further determined.

Methods. We included histologically verified supratentorial low-grade gliomas (LGG) WHO grade 2-3 retrospectively during the period 2013–2018 (n=18). For the period 2019–2023 (n=27), patients with a radiological presumptive diagnosis of low-grade glioma were prospectively included, and we took into consideration the fact that in this group we could encounter other diagnoses than glioma. Clinical, radiological and histology data were collected. We aimed to examine the association of the T2-FLAIR mismatch sign (where identified) with clinical factors and outcomes. We evaluated the diagnostic reliability of the mismatch sign and its

relation to the definitive histological diagnosis, the co-existence of an MR spectroscopy signature; we have also tried to determine whether the identification of the radiogenomic marker had any impact on the clinical outcome through the decision-making in neurosurgical management.

Results. Out of 45 patients with radiological suspected glioma, 30 had a definitive diagnosis of diffuse astrocytoma grade 2 and 3 (Astrocytoma, IDH-mutant according to WHOCNS5). 6 patients had a diagnosis of glioblastoma (Glioblastoma, IDH-wildtype according to WHOCNS5). 8 patients have been diagnosed with oligodendroglioma (Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted according to WHOCNS5) and 1 case had a definitive histology of cerebral abscess. Out of the 30 patients with IDH-mut astrocytoma, 6 (20.0%) showed a mismatch sign. The sensitivity and specificity of the mismatch sign for IDH-mut astrocytoma detection were 20% and 98.6%, respectively. There were no differences between patients with an IDH-mut astrocytoma with or without T2FLAIR mismatch sign when grouped according to this with related to baseline characteristics, clinical outcome and presenting symptoms. MR spectroscopy sequences were analyzed where available for the retrospective and prospective cohort. There were 7 cases where MR spectroscopy was performed and, for the IDH-mut astrocytoma cases (n=4) it showed a persistent high Cho/NAA ratio without any difference between the patients with or without the T2FLAIR mismatch sign.

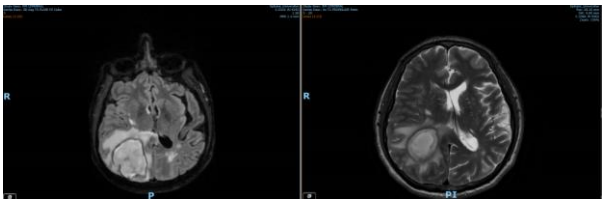

Figure 1 (Left)**.** Axial T2FLAIR images of 50M with final histology brain abscess.

Figure 2 (Right)**.** Axial T2W images of 50M with final histology brain abscess.

Conclusion. In our relatively small retrospective and prospective cohorts, the T2-FLAIR mismatch sign, where identified, was not correlated with clinical features at presentation, prognosis or outcome. Until recently, the grading of CNS tumours has been focusing mainly on histology characteristics, but specific molecular markers can now be used for valuable prognostic information. For this reason, molecular-specific information has been added as an essential feature in grading and it is considered very useful for further estimation of prognosis within variable tumor types. We could not determine if the IDH-mut astrocytomas with mismatch sign represent a specific subgroup. Our study has confirmed that the T2-FLAIR mismatch sign is a reliable and specific marker of IDH-mut astrocytomas.

Background

The T2-FLAIR (fluid attenuated inversion recovery) mismatch sign has been defined over the last few years as an important novel radiogenomic marker highly suggestive of isocitrate dehydrogenase mutated (IDH-mut) 1p19q non-codeleted gliomas (astrocytomas)[7]. Existing studies have demonstrated that this has a good specificity but limited sensitivity for IDH-mut astrocytomas. The new 2021 WHO Classification of Tumors of the Central Nervous System (WHO CNS5) has introduced a layered grading system in which all IDH mutant diffuse astrocytic tumors are considered a single type (Astrocytoma, IDH-mutant) and are graded as CNS WHO grade 2, 3, or 4 [10]. Because of the growing importance of molecular information in CNS tumor classification, diagnoses and diagnostic reports need to combine different data types into a single diagnosis.

Whether the T2FLAIR mismatch sign is of clinical relevance for the management of low-grade gliomas still needs to be further determined [11].

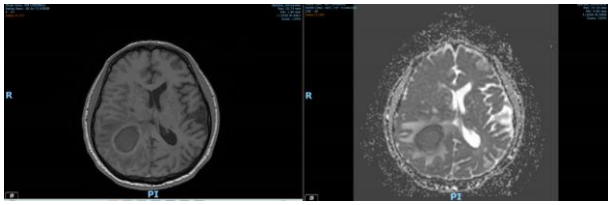

Figure 3 (Left)**.** Axial T1W non-contrast images of 50M with final histology brain abscess.

Figure 4 (Right)**.** ADC map images of 50M with final histology brain abscess.

Several recent studies have recently demonstrated that the IDH mutation and 1p/19q non co- deletion status can be predicted by conventional and advanced MRI [13].

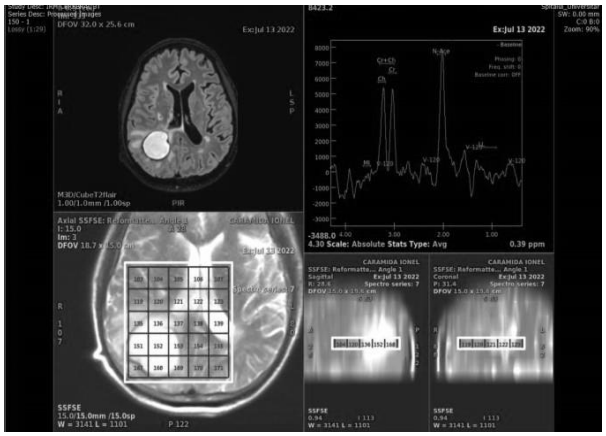

Figure 5. Brain MRI Spectroscopy images of 50M with final histology brain abscess.

MRI with gadolinium contrast is the main imaging investigation of election for diagnosis and management [11]. Diffuse astrocytoma IDH-mut involves the white matter and causes expansion of the surrounding cortex. On conventional MRI, the T2-FLAIR mismatch sign is an easily identifiable imaging finding that has been studied in extensor recently [11, 12, 13]. Few studies in the last couple of years have validated the idea that this radiogenomic marker plays a relevant role in making preoperative diagnosis and treatment planning [6, 7, 8].

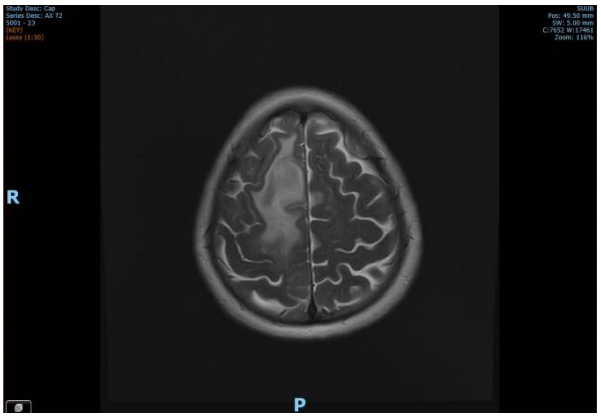

Figure 6. AxialT2W images of 61F with final histology WHO grade 3 astrocytoma.

The T2-FLAIR mismatch sign is defined by a homogenously hyperintense signal on T2Weighted Imaging and a central hypointensity with peripheral hyperintensity on FLAIR. This constitutes a radiogenomic marker regarded as highly specific for IDH-mutant and 1p/19q non-co-deleted gliomas (astrocytomas). There is a strong possibility that it reflects microcystic changes in IDH- mutant astrocytomas [14].

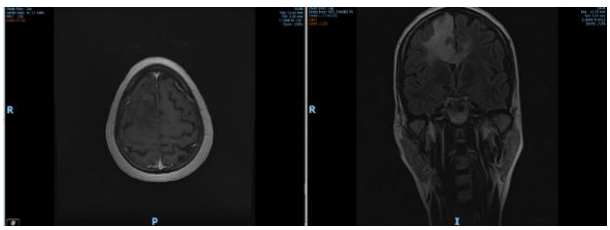

Figure 7 (Left)**.** Axial non-contrast T1W images of 61F with final histology WHO grade 3 astrocytoma.
Figure 8 (Right)**.** Coronal FLAIR images of 61F with final histology WHO grade 3 astrocytoma.

Biomarkers are the essential elements of patient-specific management strategies, but the commonly analyzed histological biomarkers are available only after the surgical procedure [Correll et all. (2020)]. Therefore, in the neurosurgical management and decision making, radiogenomic biomarkers are of great interest to help identify relevant subgroup of patients. The newly described imaging feature of T2-FLAIR (fluid attenuation inversion recovery) mismatch sign has attracted increased interest, since it is a widely available and simple potential imaging marker to predict IDH- mutated (IDH-mut) 1p19q non-codeleted (non-codel) gliomas (astrocytoma) with high specificity [16].

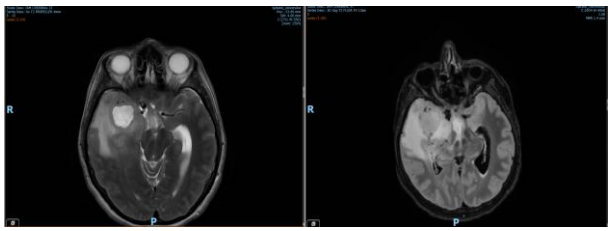

Figure 9 (Left)**.** Axial non-contrast T1W images of 61F with final histology WHO grade 3 astrocytoma.
Figure 10 (Right)**.** Coronal FLAIR images of 61F with final histology WHO grade 3 astrocytoma.

The tumors showing a T2FLAIR mismatch sign on MRI are different radiologically from gliomas without the mismatch sign with their distinct features. This raises questions regarding underlying biology. Until recently existing studies have not indicated that this radiogenomic marker is reflected by a specific biological feature [17].

We aimed to evaluate demographic, clinical, radiological and histological parameters with regard to mismatch sign and we have tried to redefine the diagnosis in conformity with the new 2021 WHOCNS5 classification of CNS tumors. In addition, we analyzed if IDH-mut astrocytomas with mismatch sign had similar MR spectroscopy features compared to samples without the mismatch sign.

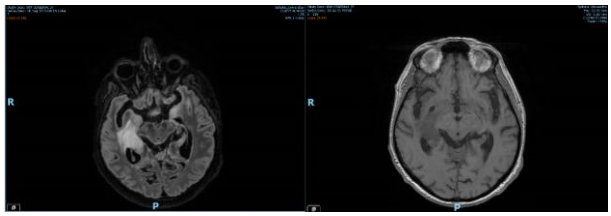

Figure 11 (Left)**.** Axial T2FLAIR images of 61M with final histology WHO grade 3 astrocytoma.
Figure 12 (Right)**.** Axial T1W non contrast images of 61M with final histology WHO grade 3 astrocytoma.

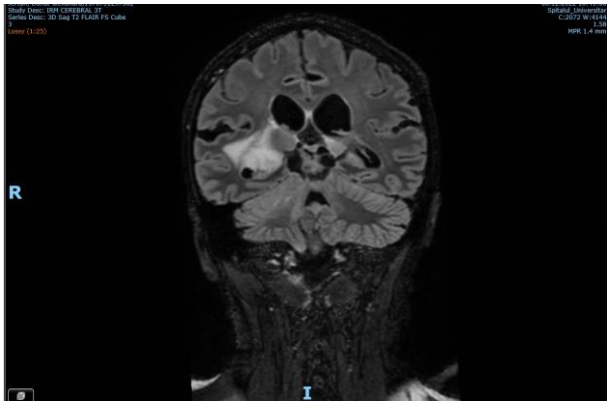

Figure 13. Coronal T2FLAIR images of 61M with final histology WHO grade 3 astrocytoma.

Methods

We included histological verified supratentorial low-grade gliomas (LGG) WHO grade 2-3 retrospectively during the period 2013–2018 (n=18). For the period 2019–2023 (n=27), patients with a radiological presumptive diagnosis of low grade glioma were prospectively included, and we took into consideration the fact that in this group we could encounter other diagnoses than glioma. Clinical, radiological and histology data were collected.

We centralized and redefined the perspective on the histological diagnosis of all the patients in both the prospective and retrospective cohorts in line with new 2021 WHO Classification of Tumors of the Central Nervous System (**WHO CNS5**).

We aimed to examine the association of the T2-FLAIR mismatch sign (where identified) with clinical factors and outcomes. We evaluated the diagnostic reliability of the mismatch sign and its relation to the definitive histological diagnosis, the co-existence of an MR spectroscopy signature; we have also tried to determine whether the identification of the radiogenomic marker had any impact on the clinical outcome through the decision making in the neurosurgical management.

The Neurosurgical department at the Emergency University Hospital in Bucharest covers the population of approximately 1 million inhabitants.

The patients in the Bucharest region in Romania with newly diagnosed primary intracranial intra- axial tumors are referred either through the GP (General Practitioner) service or by direct presentation in the Accident and Emergency Department. From the moment of clinical and radiological presumptive diagnosis of CNS tumor they enter a clinical pathway involving Neurosurgery, Neuroradiology, Oncology, being managed in a multidisciplinary team (MDT) with weekly meetings ("Tumor Board") at the Emergency University Hospital Bucharest.

Our patients groups consisted of two components; one retrospective group (2013-2018) and one prospective (2019-2023).

We performed a retrospective analysis of clinical and imaging data between 2013 and 2018, including surgical procedure logs, patients clinical notes and histology results, including all patients with a histology result diagnosis of a supratentorial infiltrating WHO grade 2 or 3 glioma with available magnetic resonance imaging (MRI) (n=18).

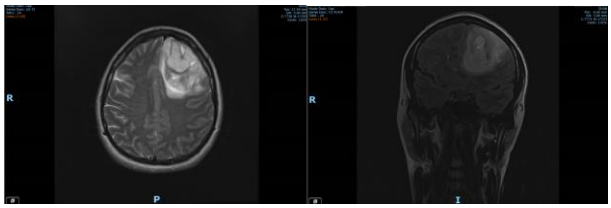

Figure 14 (Left)**.** Axial T2W images of 37F with final histology WHO grade 3 oligodendroglioma.

Figure 15 (Right)**.** Coronal FLAIR images of 37F with final histology WHO grade 3 oligodendroglioma.

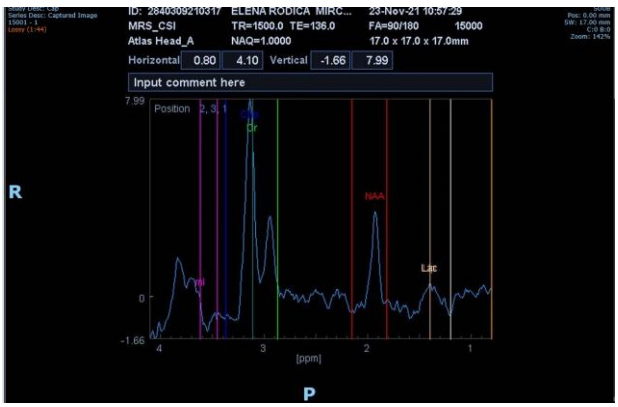

Figure 16. MR Spectroscopy of 37F with final histology WHO grade 3 oligodendroglioma.

Between 2019 and 2023, we worked prospectively on a cohort including patients with a suspected diagnosis of diffuse low grade glioma, referred either through the GP or presenting directly to our Emergency Department (n=27).

This prospective group of patients consisted of intraaxial space-occupying lesions suggestive of primary brain tumor with a hyperintense signal in T2W images, with or without significant contrast enhancement. We took into consideration the fact

that we might encounter other histopathological diagnoses (e.g. cerebral abscess or other tumors). The main reason for including these patients was to enable the evaluation of the mismatch sign in a group with mostly similar MRI appearance, but also potential different diagnoses than low grade glioma, as opposed to previous studies that used tissue diagnosis as inclusion criteria [7, 17].

We used MRI images from all patients in the both retro- and prospective groups to identify the T2-FLAIR mismatch sign (N = 45).

We included parameters such as patient age, gender, presenting symptom, localisation of the lesion, eloquence. We separated further the patients with IDH-mut astrocytomas (n=30) divided into two subgroups, with and without mismatch sign.

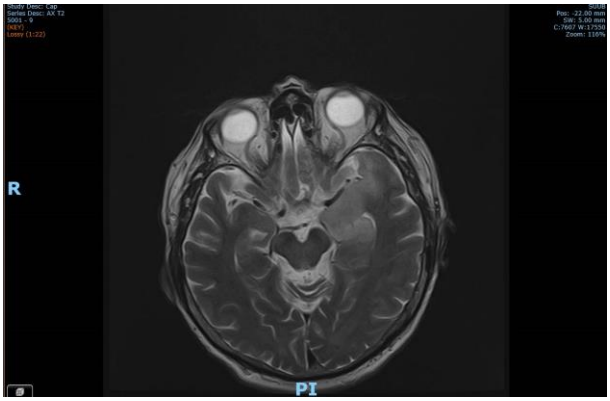

Figure 17. Axial T2W images of 69M with final histology WHO grade 2 diffuse astrocytoma.

MRI examinations reviewed in this study were performed in the Radiology Department of the Emergency University Hospital Bucharest as part of the pre-operative work-up investigation. MRI images were analyzed for: main part of the brain involved (frontal, temporal, parietal, occipital, insula), side (right, left, bilateral), eloquence [14], T2-FLAIR mismatch (yes/no) and MR spectroscopy sequences characteristic features (Cho/NAA high ratio) correlated with the presence or absence of the T2FLAIR mismatch sign.

Evaluation was performed independently by a neurosurgical specialist, a neurosurgical resident, a senior neurosurgeon and a neuroradiologist [14, 16, 17].

Results

Out of 45 patients with radiological suspected glioma, 30 had a definitive diagnosis of diffuse astrocytoma grade 2 and 3 (Astrocytoma, IDH-mutant according to WHOCNS5). 6 patients had a diagnosis of glioblastoma (Glioblastoma, IDH-wildtype according to WHOCNS5). 8 patients have been diagnosed with oligodendroglioma (Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted according to WHOCNS5) and 1 case had a definitive histology of cerebral abscess.

Out of the 30 patients with IDH-mut astrocytoma, 6 (20.0%) showed a mismatch sign. The sensitivity and specificity of the mismatch sign for IDH-mut astrocytoma detection were 20% and 98.6%, respectively. There were no differences between patients with an IDH-mut astrocytoma with or without T2FLAIR mismatch sign when grouped according to this with related to baseline characteristics, clinical outcome and presenting symptoms. MR spectroscopy sequences were analyzed where available for the retrospective and prospective cohort; a number of n=4 MRI spectroscopy images were available for the IDH-mut astrocytoma group (n=30). In all the cases of MR spectroscopy from the IDH-mut astrocytoma group, this showed a persistent high Cho/NAA ratio without any difference between the patients with or without the T2FLAIR mismatch sign.

Table 1. Demographic, clinical and radiological characteristics of patients diagnosed between 2013 and 2023 with low grade glioma (N = 30), analyzed comparing the T2-FLAIR mismatch sign presence or absence and the MR spectroscopy high Cho/NAA ratio.

	T2 FLAIR mismatch sign present n=6	T2 FLAIR mismatch sign absent n=24	High Cho/NAA ratio on MR spectroscopy n=4
Age (median)	51	52	51.5
Gender (F) n	4 (66.6%)	16 (67%)	3
Location of the tumor (lobe) n			
Frontal	3 (50%)	16 (67%)	2
Temporal	0	1 (4%)	0
Parietal	2 (33%)	6 (25%)	2
Insular	1 (16%)	1 (4.6%)	0
Lateralisation and eloquence n			
Right side	2 (33.3%)	13 (54.16%)	3
Left side	3 (50%)	8 (33.3%)	1
Bilateral	1 (16%)	3 (12.5%)	0
Functional area	4 (75%)	11 (45.83%)	1
Presenting symptoms n			
Asymptomatic	0	3 (12.5%)	0
Motor deficits	3 (50%)	12 (50%)	2
Dysphasia	3 (50%)	7 (29.17%)	1

Visual disturbance	0	2 (8.33%)	0
Cognitive impairment	1 (16%)	5 (20.83%)	0
Seizures	3 (50%)	14 (58.33%)	3
Intracranial hypertension	1 (16%)	3 (12.5%)	0
Surgical procedure			
Biopsy only	1 (16%)	4 (16.67%)	1
Resection	5 (84%)	20 (83.3%)	3
WHOCNS5 grade			
2	2 (33.3%)	11 (45.83%)	1
3	4 (66.6%)	13 (54.17%)	3

Our patient cohort included retro- and prospectively 45 patients with available MRI images. The retrospective part of the cohort included 18 patients with mean age of 47 years and 11 patients (61%) were females. The majority of this group underwent biopsy followed by resection, as opposed to biopsy only (n=15, 83.33%).

In the prospective part, we evaluated 27 patients with a suspected diffuse IDH-mut astrocytoma. This included both tumor and non-tumor diagnoses, such as an atypical cerebral abscess. In this cohort, 18 patients were female (66.6%) and the mean age was 49.2 years.

The most common surgical procedure was resection (83.3%). Out of the 45 patients, the majority were diagnosed with WHO grade 2 or 3diffuse astrocytoma (N = 30), oligodendroglioma (N = 8) and glioblastoma (N = 6). Other diagnoses included non-neoplastic lesions such as cerebral abscess (N=1). The mismatch sign was not present in the non-tumor diagnosis.

In total there were 30 patients with IDH-mut diffuse astrocytoma. These were separated based upon the presence of T2- FLAIR mismatch sign (N = 6) or absence (N = 24). In Table 1 we elaborate on comparison between these groups in regards to clinical features, imaging variables (including MR spectroscopy) and clinical aspects.

There were no differences regarding lobe involvement, presenting symptoms or surgical procedure employed. There was no difference between groups with respect to the extent of resection, with mismatch sign and without mismatch sign) [14].

In six patients (20%) from both groups the T2FLAIR mismatch sign was identified and all of them had IDH-mutated diffuse astrocytomas. We have not identified any patient with positive T2FLAIR mismatch sign in the IDH-wild type group (glioblastoma).

From the retrospective and prospective groups, 7 cases had available MR spectroscopy images. From the total number of MR spectroscopy performed (n=7), 4 patients were diagnosed with IDH- mut diffuse astrocytoma, 1 patient was diagnosed with IDH-mut 1p19q co-deleted glioma (oligodendroglioma), 1 patient was diagnosed with IDH-wild type glioblastoma and 1 with cerebral abscess. In all of the cases of MR spectroscopy and IDH-mut astrocyoma, a persistent high Cho/ NAA ratio, without any difference between the patients with or without the T2FLAIR mismatch sign was present.

Discussion

Until recently, the grading of CNS tumors has been focusing mainly on histology characteristics, but specific molecular markers can now be used for valuable prognostic information. For this reason, molecular specific information has been added as an essential feature in grading and it is considered very useful for further estimation of prognosis within variable tumor types. See tables 2-4 [10]

Table 2. World Health Organisation Classification of Tumors of the Central Nervous System, fifth edition (WHO CNS5) [10].

2021 WHO Classification of Tumors of the Central Nervous System
Gliomas • Adult-type diffuse gliomas; • Astrocytoma, IDH-mutant; • Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted; • Glioblastoma, IDH-wildtype.

In this relatively small study we found no difference between diffuse IDH-mut astrocytomas with or without the mismatch sign with regards to extent of resection or any other clinical variable. We reconfirmed that the T2- FLAIR mismatch sign has a good specificity for diffuse IDH-mut astrocytomas.

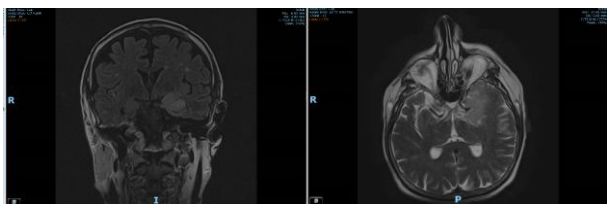

Figure 18 (Left)**.** COR FLAIR images of 69M with final histology WHO grade 2 diffuse astrocytoma.
Figure 19 (Right)**.** MR Spectroscopy images of 69M with final histology WHO grade 2 diffuse astrocytoma.

As reiterated in many previous studies, it is well known that gliomas may vary in consistency and their macroscopic aspect, and with the radiological image of homogenous signal on T2-weighted sequences and infiltrative tumor border, the question was raised whether the extent of the resection is related to the mismatch sign. This may be of particular importance, since the IDH-mut astrocytoma group seems to be the one where extensive surgery is of definite benefit [11, 12, 14].

Table 3. Key Diagnostic Genes, Molecules, Pathways, and/or Combinations in Major Primary CNS Tumors (WHO CNS5) [10]

Tumor Type	Genes/Molecular Profiles Characteristically Altered
Astrocytoma, IDH-mutant	IDH1, IDH2, ATRX, TP53, CDKN2A/B
Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted	IDH1, IDH2, 1p/19q, TERT promoter, CIC, FUBP1, NOTCH1
Glioblastoma, IDH-wildtype	IDH-wildtype, TERT promoter, chromosomes 7/10, EGFR

In our study, the extent of resection was not different between groups, therefore the T2FLAIR mismatch sign should probably not be considered a factor influencing the extent of resection in diffuse IDH-mut astrocytomas. Patel et all. had evaluated the association between survival and the mismatch sign, with a median follow-up of 65.7 months, and found no differences in overall survival between groups [17].

Table 4. CNS WHO Grades of Selected Types, Covering Entities for Which There Is a New Approach to Grading, an Updated Grade, or a Newly Recognised Tumor That Has an Accepted Grade (WHO CNS5) [10]

CNS WHO Grades of Selected Types	
Astrocytoma, IDH-mutant	2, 3, 4
Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted	2, 3
Glioblastoma, IDH-wildtype	4

Broen et al and Patel et al have reported a 100% specificity for IDH-mut astrocytomas [6, 17]. More recent studies have found overall specificity in the range of 96.0–100.0% [6, 17, 18]. The T2 FLAIR mismatch sign has been found rarely in IDH-mut codel gliomas (oligodendrogliomas), but also in pediatric low-grade brain tumors. Until now, the mismatch sign has been reported in pilomyxoid astrocytoma, low grade glioma with MYB rearrangement, oligodendroglioma (IDH- mut co-del) [11].

One previous study (Correll et all.) has reported a patient with T2-FLAIR mismatch sign had a diagnosis of IDH-mut glioblastoma, suggesting that the mismatch sign is not grade specific [11]. Importantly, there were no other differential diagnoses beyond diffuse gliomas that presented with the mismatch sign. Although of low sensitivity (27.1–51.0%), the specificity for IDH-mut astrocytomas makes the evaluation of mismatch sign useful in a clinical setting for individual cases [6, 11, 17, 18]. Adding advanced imaging characteristic sequences like apparent diffusion coefficient (ADC) and cerebral blood volume (CBV) to the mismatch sign may further improve the diagnostic capabilities of IDH-mut astrocytomas[11].

Foltyn et all. (2022) have hypothesised that the higher ADC value in IDH-mutant gliomas with a T2/FLAIR-mismatch sign (as compared to those without) translate into a measurable prognostic effect, although this requires investigation in future studies. The same study affirms that spatial differences in ADC values between the core and rim of tumors with a T2/FLAIR-mismatch sign potentially reflect specific distinctions in tumor cellularity and microenvironment [12].

Conclusion

In our relatively small retrospective and prospective cohorts, the T2-FLAIR mismatch sign, where identified, was not correlated with clinical features at presentation, prognosis or outcome. We could not determine if the IDH-mut astrocytomas with mismatch sign represent a specific subgroup. Our study has confirmed that the T2-FLAIR mismatch sign is a reliable and specific marker of IDH-mut astrocytomas. MR spectroscopy, where available, has proven a very useful imaging investigation with a high value for management of these CNS neoplastic tumors.

Fast progress in identification of more pre-operative non-invasive tumor markers represents the way forward in the context of rapid evolution of the complexity and transformation of the whole concept of cancer treatment; advanced imaging characteristic sequences like apparent diffusion coefficient (ADC), cerebral blood volume (CBV) and identification of the T2FLAIR mismatch will improve the pre-operative diagnostic possibilities [11].

It is also of crucial importance that the new WHOCNS5 grading system will be integrated into our standard clinical practice, with the main purpose being a more adaptable and reliable, also more practical diagnosis and management tool.

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Endoscopic endonasal transsphenoidal surgery for pituitary adenomas. A single-centre initial experience

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ABSTRACT

Endoscopic endonasal transsphenoidal surgery (EETS) is a widely accepted technique for the surgical resection of pituitary tumours. In this report, we present our single-centre experience with EETS for pituitary adenomas, mainly focusing on its efficacy and postoperative complications. Among 100 patients who underwent EETS, 57 (57%) were female and 43 were (43%) male. The mean age of the patients was 51.55 ± 13.51 years. Nonfunctional adenoma was found in 61 (61%) patients, acromegaly was found in 29 (29%) patients, Cushing's disease in six (6%), and prolactinoma was found in four (4%) patients. On average, a 75.8% decrease in the postoperative tumour volume was observed in nonfunctional adenomas. Surgical cure was achieved in 51.7% of patients with acromegaly, 50% of those with Cushing's disease, and 25% of those with prolactinoma. The most common postoperative complication was found to be cerebrospinal fluid fistula.

Keywords
adenoma,
endoscopy,
pituitary,
transsphenoidal

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INTRODUCTION

Pituitary adenomas, accounting for 10%–15% of all primary intracranial tumors, develop from the adenohypophysis and are considered benign neoplasms.[1] The prevalence of pituitary adenoma was reported to be between 1/865 and 1/2688 persons in different clinical studies.[2-4] Despite their benign nature, pituitary adenomas may cause significant morbidity and mortality because of their endocrine activity and mass effect.[5] The diagnosis, treatment, and follow-up of pituitary adenomas require a multidisciplinary approach, including neurosurgery, endocrinology, and radiosurgery.

The primary aim in the surgical treatment of pituitary adenomas is to excise the tumor without damaging the surrounding anatomical structures. Initially, the transcranial surgical approach was adopted in treating pituitary adenomas. However, less invasive methods have been developed later on because of the high morbidity and mortality rates associated with this method.[6] Recently, the endonasal approach for the surgical excision of pituitary adenomas has gained great popularity and has been considered the "gold standard."[7] Currently, the endoscopic endonasal transsphenoidal surgery (EETS) technique,

which provides a wide panoramic view of the surgical field and anatomical structures, has become a preferred surgical method.[8,9]

In this study, we report our initial experience with EETS in patients with pituitary adenoma, mainly focusing on its efficacy and postoperative complications.

Materials and Methods

Study Population

In this study, 100 patients diagnosed with pituitary adenoma who underwent EETS at our clinic between February 2014 and December 2020 were included. Patients with missing data, pediatric cases, and those operated with the transcranial route were excluded from the study.

The records of the patients included in this study were retrospectively reviewed, and their clinical, radiological, and biochemical findings were recorded.

Microadenomas were defined as adenomas that have a maximum diameter of 10 mm, and macroadenomas were defined as those with a diameter of at least 10 mm. Tumor volumes were calculated by measuring the largest tumor diameters in the axial, sagittal, and coronal axes in the cranial magnetic resonance imaging (MRI), as described previously in macroadenomas.[10] All patients with nonfunctional adenoma underwent cranial MRI within the first 3 months after surgery, and the postoperative volumetric decrease was calculated. The Knosp grade of the tumor was determined using preoperative MRI.[11]

The efficacy of surgical treatment in functional adenomas was evaluated according to the Pituitary Diseases Diagnosis, Treatment and Follow-up Guideline published by the Society of Endocrinology and Metabolism of Turkey.[12] Accordingly, in patients with acromegaly, a serum growth hormone level of <0.4 μg/L at the third month after surgery was accepted as a marker of surgical remission and a value of <1 μg/L was accepted as a marker of surgical control of the disease. In patients with Cushing's disease, a morning serum cortisol level of <2 μg/dL within the first week after the operation was accepted as surgical remission. Initial remission was defined as a measured prolactin level that had returned to normal.[13]

The study protocol was approved by the local Ethics Committee (2021/3019), and written informed consent was obtained from all participants or their legal successors.

Surgical Procedure

All patients underwent EETS under general anesthesia by the same surgical team. Neuroradiological images of the patients were analyzed before the procedure. Computed tomography of the paranasal sinuses was examined to evaluate the sellar access route and to detect pathologies related to this pathway. Anatomical relationships between the internal carotid arteries (ICAs) and pituitary adenomas were evaluated. Any suprasellar and intrasellar vascular pathologies were excluded.

In the operating room, the patients were placed in the supine position, and their head was fixed using a skull clamp. Image guidance was used in all patients using the Medtronic ®StealthStation (Medtronic, MN, USA) surgical navigation system. Subsequently, the patient's face, both nasal cavities, and abdominal region were cleaned with povidone-iodine solution. The vasoconstrictor agent, adrenaline, was applied to the nasal mucosa. The surgical procedures were performed through the binostril approach with a diameter of 4 mm, length of 18 cm, and rigid scopes of 0° and 30° (Karl Storz GmbH & Co. KG, Tuttlingen, Germany), and related endoscopic skull base instruments were used.

Initially, the middle nasal turbinate was accessed by passing the lower turbinate and choanae. The middle nasal turbinate was dissected laterally using a dissector, and the surgical corridor was established. Then, the superior turbinate was accessed by moving posteriorly between the middle turbinate and the septum. The natural ostium of the sphenoid sinus was identified between the superior turbinate and the septum. Then, the vomer was opened, and a binostril corridor was achieved.

The anterior wall of the sphenoid sinus was opened following clear identification of the sphenoid ostium. Using a Kerrison rongeur or micro-drill, the anterior wall of the sphenoid sinus was opened laterally. The mucosa covering the sellar floor was excised. Then, the base of the sella and neighboring structures were revealed. Then, the base of the sella was opened and widened using a micro-drill and Kerrison rongeur, and the dura mater was exposed. To not damage the ICAs, intraoperative doppler ultrasonography was performed, as necessary. After

that, the dura mater was incised and opened using scalpel blades and micro-scissors. The tumor was identified and evacuated using an aspirator, ring curettes, and micro-forceps (Fig. 1). If cerebrospinal fluid (CSF) leakage was observed during the procedure, fat and fascia grafts taken from the abdomen were placed on the field. Additional nasoseptal flaps, which were prepared in early stages of the operation, were engrafted in some cases (particularly those with large macroadenomas). Multilayer closure was achieved, and the operation was terminated.

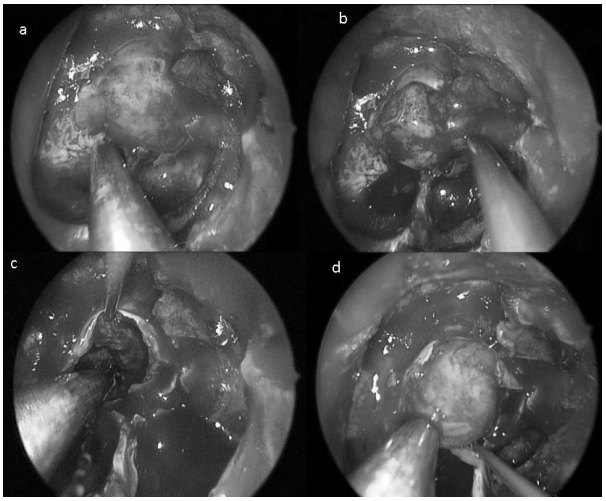

Figure 3 Different stages of the endoscopic endonasal approach in a case of macroadenoma. **a**: Revealing the osseous structures belonging to the base of the sella. **b**: Opening of the dura and excision of the tumor. **c**: Control of the residual tumor. **d**: Sagging of the diaphragm sella toward the surgical field after radical resection.

Statistical Analysis

Statistical Package for the Social Sciences, version 22.0, was used for data analysis. Categorical data are expressed as numbers and percentages, while continuous data are presented as means ± standard deviations.

Results

Among the 100 patients who underwent EETS, 57 (57%) were female, and 43 (43%) were male, and the mean age of the patients was 51.55 ± 13.51 years. Macroadenoma was detected in 84 (84%) patients, and microadenoma was found in 16 (16%) patients.

Nonfunctional adenoma was found in 61 (61%) of the operated patients, acromegaly in 29 (29%), Cushing's disease in six (6%), and prolactinoma in four (4%). When the patients were classified according to their sex, among female patients, 34 (59.6%) had nonfunctional adenoma, 16 (28.1%) had acromegaly, five (8.8%) had Cushing's disease, and two (3.5%) had prolactinoma. Meanwhile, among male patients, nonfunctional adenoma was found in 27 (62.8%), acromegaly in 13 (30.2%), Cushing's disease in one (2.3%), and prolactinoma in two (4.7%).

Of all patients, 25 (25%) had Knosp stage 0 lesions, 23 (23%) had Knosp stage 1 lesions, 16 (16%) had Knosp stage 2 lesions, seven (7%) had Knosp stage 3a lesions, nine (% 9) had Knosp stage 3b lesions, and 20 (20%) had Knosp stage 4 lesions.

Patients with nonfunctional adenomas

The mean preoperative volume of nonfunctional adenomas was 9.84 ± 9.79 cm^3, which decreased to 2.35 ± 3.79 cm^3 within the first 3 postoperative months. When the preoperative and postoperative volumes were compared, on average, there was a 75.8% decrease in the tumor volume postoperatively.

Patients with acromegaly

Surgical remission was achieved in six (20.7%) of the 29 patients with acromegaly, and surgical control was achieved in 15 (51.7%) patients. Of the patients with surgical remission, four had microadenomas and two had macroadenomas. Again, of the 15 patients with surgical control, eight had microadenomas and seven had macroadenomas.

Patients with Cushing's disease and prolactinoma

According to the criteria stated in the methods section, remission was achieved in three (50%) of the six patients with Cushing's disease, and all cured patients had microadenomas.

Surgical remission was achieved in only one (25%) of the four patients with prolactinoma who underwent surgery. All patients with prolactinoma were found to have macroadenomas, which were resistant to medical therapy.

Postoperative complications

Permanent DI occurred in one patient with acromegaly and one patient with Cushing's disease, who all had microadenomas. These patients received desmopressin treatment, which was adjusted after endocrinology consultation.

Postoperative rhinorrhea was observed in eight (8%) patients within the first month after surgery. CSF leakage was ceased with external lumbar drainage in three patients. Two patients underwent reoperation, and the remaining three patients underwent both external lumbar drainage and endoscopic reoperation. All CSF leaks were treated successfully using these methods. Meningitis occurred in two patients and was treated with appropriate antibiotics.

Discussion

In this study, we presented our single-center experience with EEST, a widely used technique for the surgical resection of pituitary adenomas. In our series of 100 patients with pituitary adenomas, we observed a reasonable remission rate, low incidence of postoperative complications, and no mortality. This study contributes to the current literature regarding the safety and efficacy of EETS.

The demographic characteristics of our study population revealed a mean patient age of 51.55±13.51 years and female preponderance. These findings were comparable with the data reported in previous surgical series for pituitary adenomas.[9,14,15] Furthermore, our findings demonstrated that 84% of the study group had macroadenomas and 61% had nonfunctional adenomas. In a previous surgical series, Eseonu et al. have reported that 71.6% of their patients had macroadenomas and 63.6% had nonfunctional adenomas.[14] In another series, Singh et al. have reported that 86% of their patients had macroadenomas and 79% had nonfunctional adenomas.[9] All these data show that our patient group had similar demographic and clinicopathological features with those in previous surgical series in the literature.

Transsphenoidal surgery is the primary therapeutic option for pituitary adenomas, except for prolactinomas, and is associated with high remission rates, particularly in patients with microadenomas (80%–90%).[5,16] We evaluated the preoperative and postoperative tumor volumes in patients with nonfunctional adenomas and found a 75.8% decrease in tumor volume postoperatively. Similarly, Eseonu et al. have reported a 85.1% decrease in tumor volume postoperatively using the EETS technique in a previous study.[14]

In our patient group, surgical control was achieved in 51.7% of patients with acromegaly. In a similar series, including patients with acromegaly, Yildirim et al. have reported that biochemical remission was achieved in 80.0% of patients with microadenomas and 64.7% of patients with macroadenomas. The total remission rate was found to be 66.1%.[17] In another series, Hazer et al. have revealed that biochemical cure was achieved in 62.6% of patients with acromegaly following EETS.[18] All these data suggest that EETS is associated with a reasonable remission rate in patients with acromegaly and that there are minor differences between different series regarding its efficacy.

In addition to its efficacy, EETS has also shown to be associated with low complication rates following the surgical removal of pituitary tumors.[19,20,21] CSF leakage, DI, vascular complications, hypopituitarism, meningitis, and visual complications were most commonly reported complications in other series.[5,19] In our patient group, we detected rhinorrhea because of CSF leakage in 8% of the patients. All these patients were successfully managed with endoscopic repair and/or external lumbar drainage. In previous reports, CSF leakage following EETS was reported in 2.4%–24% of patients.[20,22] Death is a rare complication of EETS and usually occurs because of carotid artery injury and meningitis.[5,19] No carotid injury was observed in our series.

This report has some limitations. First, this was a single-center study and has a retrospective nature, lacking prospective follow-up data. This situation restricts the generalization of the results of this study. Second, there was no control group of patients operated with another surgical technique, such as microscopic endonasal transsphenoidal surgery, to compare perioperative outcomes of EETS. However, we suggested that EETS is a safe and efficient method for treating pituitary adenomas. Although learning is relatively steep, augmented experience and throughout knowledge of the neurosurgical anatomy make significant differences.

Conclusions

EETS is an effective technique frequently used for resecting pituitary tumors. This report revealed that EETS is associated with a good remission rate, low incidence of postoperative complications, and low mortality rates. These findings support the previous

data regarding the safety and efficacy of EETS for the surgical treatment of pituitary adenomas.

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Penetrating thoracic spine injury causing haemothorax. A case report

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Keywords
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ABSTRACT

Background. Penetrating spine injuries can cause catastrophic complications to the patient, and it demands immense medical care to minimize the insult. Mainly, it occurs in the military field; however, it has become more prevalent among civilians due to gun availability. The thoracic spine is the most affected part, followed by the cervical and lumbar spine.

Case report. A 15-year-old teenage boy had a penetrating injury to the thoracic (T10) vertebrae due to a missile bullet that resulted in bilateral lower limb weakness and required him to undergo decompressive laminectomy. During surgery, a missed hemothorax was discovered incidentally.

Conclusion. To the best of the author's knowledge, this case of penetrating thoracic spine injury due to a missile bullet associated with missed hemothorax has not been previously reported. This paper discusses the importance of early detection and treatment of injuries associated with penetrating spine trauma to improve patient survival and disability.

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INTRODUCTION

Penetrating spine injuries can lead to devastating effects on the patient, representing a significant challenge to the patient and the treating surgeon. Although most penetrating spine injuries occur in the military field, the ubiquity of guns in our society makes them more prevalent among the civilian population. These injuries can be due to any cause, such as a knife, nail, or sharp object but missile bullet injuries due to gunshots represent an important cause. It accounts for about 17-21% of all traumatic spine injuries. It is regarded as the third most common

cause of spine injuries in the civilian population after falls from height and motor vehicle accidents [4].

The thoracic spine represents the most affected part, followed by the cervical and lumbar spine [9]. The complications due to penetrating thoracic spine injuries can extend beyond the trauma to involve neural elements, supporting structures, and other organs, such as neurological compromise, vascular damage, spine instability, and cerebrospinal fluid (CSF) leakage [6]. Hemothorax is also a significant complication associated with spine injuries and may occur due to damage to pulmonary parenchyma, heart, intercostal vessels, and major intrathoracic vessels [3].

However, associated missed hemothorax due to penetrating spine injury has rarely been reported. In this paper, the authors report a case of a teenage boy who was presented with a missile bullet injury to the back and then discovered to have a missed hemothorax intraoperatively that required further surgical care and postoperative management.

CASE REPORT

A 15-year-old teenage male presented to the emergency department with a missile injury to his back; during the physical examination, he was conscious and alert, and there was bilateral lower limb weakness with grade 1 power. Moreover, there were two entry points in the mid-back region at the thoracic 10 (T10) vertebrae level but without an exit site. After the appropriate management and stabilization, a spine X-ray was ordered (Fig.1), which revealed two large foreign bodies (metallic fragments) about 2.5-3 cm in size located at the level of T10.

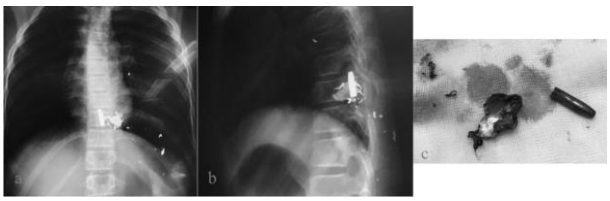

Figure 1. Spine x-ray of both anteroposterior (**a**) and lateral (**b**) views showing two metallic fragments at the level of T10. Also, (**c**) shows the extracted foreign bodies.

Computed Tomography (CT) scan (Fig.2) has been done and revealed two fragments of foreign bodies at the level of T10 that cross the transverse process and extend to the left pleural cavity. The patient had incomplete spinal cord injury and CSF leakage, which renders in performing decompressive laminectomy surgery with foreign bodies (bullet) extraction.

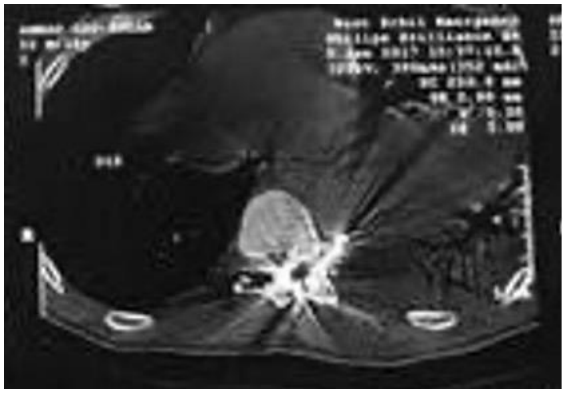

Figure 2. A plain axial CT scan of the spine showing foreign bodies that crosses the transverse process and extends to the left pleural space.

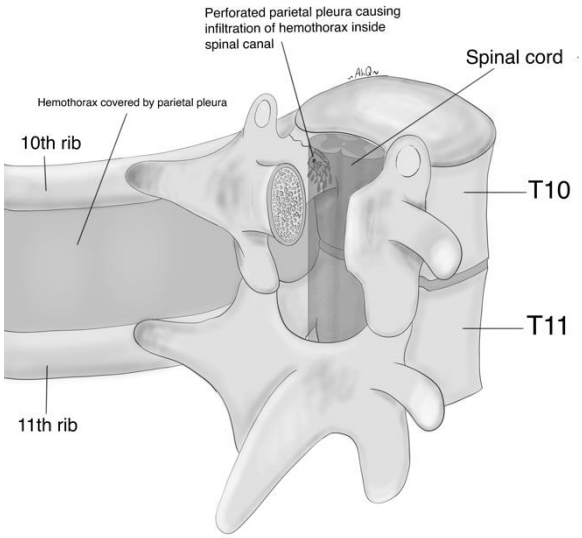

Figure 3. Artistic depiction shows the site of the penetrating bullet to the spinal cord and extending to the parietal pleura.

During surgery, total T10 laminectomy and partial T11 laminectomy were done with midline bullet extraction, then removal of stacked shell from pedicle area. After extraction, a gush of dark-tinged bleeding swung with each ventilation. In the beginning, the source of blood was suspected to be from the fractured bone in the lateral part of the vertebral ring, which stopped using bone wax and

direct compression. However, the gush of blood still came with each ventilation, so there was also a suspicion of associated missed hemothorax that required further cardiovascular care. After chest tube insertion, the collecting system is filled with blood, and the suspicion of hemothorax is confirmed (Fig.3). A few days after the laminectomy surgery, the patient underwent another surgery for partial lobectomy due to a collapsed left lung. On the follow-up, the patient was stable, had normal respiration, and the chest tube was removed. Upon discharge, his paraparesis improved to grade 4.

Discussion

Penetrating spine injuries represent a significant cause of morbidity and mortality in the military field; however, nowadays, it has also become more prevalent among the general population due to the availability of firearms. Male victims are disproportionately affected higher (78-91%) than females, with high incidence during the third decade of life [4,8]. However, in this case, the victim was a male in a child age group who had a penetrating spine injury due to a missile bullet.

Thoracic spine penetrating injuries cause complications such as myelopathy, central nervous system infections, CSF leak following dural tear, spinal instability, and delayed neurological deficits [6,7]. Of these complications, our patient had CSF leakage with partial neurological compromise. Furthermore, according to Manzone et al., early removal of a foreign body in penetrating spinal injury may reduce myelopathy, infection, and delayed neurological deficits. Hence, the patient underwent laminectomy surgery for correction and bullet and shell extraction [5].

Thoracic spine fractures are associated with pleural collection; for example, in a study of 72 patients with thoracic spine fractures, 24% were found to have hemothorax [1]. Usually, the hemothorax results from bleeding from the edge of the bone at the unstable fracture site; hence the stabilization of the thoracic spine controls the bleeding [2]. However, in this patient, a gush of blood after extraction of the foreign bodies fluctuated with each ventilation, even after stabilizing the fractured bone with bone wax and direct compression. The bleeding did not stop; therefore, a suspicion of missed hemothorax was confirmed after tube thoracotomy insertion, which resulted in patient stabilization. This hemothorax occurs due to the bullet's penetration of the parietal pleura.

Hemothorax is usually detected and treated at admission during advanced trauma life support (ATLS) protocol due to the significant risk of late complications [10]. However, this patient had no signs of respiratory compromise before surgery, and the imaging did not show any signs of pleural effusion, so the diagnosis was missed and firstly present during surgery.

To the best of the authors' knowledge, this presentation of penetrating thoracic spine injury due to a missile bullet associated with missed hemothorax has not been previously reported. This paper refers to the importance of early detection and treatment of injuries associated with penetrating spine trauma, especially hemothorax, as it can raise the mortality and morbidity of the patient.

Conclusion

Penetrating spine injuries due to missile bullets are increasing nowadays. It can lead to many complications that increase mortality and morbidity. In this case, we present a patient who had missed hemothorax that was discovered and treated intraoperatively.

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Bobble Head Doll Syndrome. A series of 3 clinical cases managed at the Yalgado Ouédraogo University Hospital and review of the literature

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ABSTRACT

Introduction. Bobble head doll syndrome is a neurological syndrome characterized by abnormal involuntary movements of the head combining repetitive or episodic movements of 2 to 3 Hz back and forth in the anterior-posterior direction that can be assimilated to approval movements (yes-yes) and occasionally lateral rotations that can be assimilated to disapproval signs (no-no). It is a rare entity first described by Benton[1]. We describe three cases managed at the Yalgado Ouédraogo University Hospital in Burkina Faso.

Observations. Three children, one girl and two boys, aged respectively 5, 9 and 14 years were seen for involuntary abnormal head movements associating lateral rotations assimilated to signs of disapproval (no-no) in two cases, and back and forth movements of the head in one case. In the 14-year-old adolescent, there was also a picture of intracranial hypertension. Clinical examination revealed ataxia and macrocrania in both cases and a syndrome in 1 case. Imaging revealed triventricular hydrocephalus on aqueductal stenosis in all cases with an associated supra sellar cyst in 2 cases. The treatment consisted of endoscopic treatment in 2 cases and ventriculoperitoneal shunt in 1 case. Surgery allowed a considerable regression of involuntary movements of the head in the immediate postoperative period and a complete recovery in the long term.

Conclusion. The bobble head doll syndrome is a rare entity related to the consequences of chronic hydrocephalus responsible for abnormal movements whose management done well and early leads to favourable results.

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INTRODUCTION

Bobble head doll syndrome is a rare pediatric neurological syndrome characterized by abnormal involuntary head movements with repetitive or episodic 2-3Hz back-and-forth movements in the anterior-posterior direction that can be assimilated to approval movements (yes-yes) and occasional lateral rotations that can be assimilated to

disapproval signs (no-no). This condition was first described in 1966 by Benton[1]. It is a complication of chronic hydrocephalus. The intracranial anomalies that are commonly observed are: non-communicating hydrocephalus, supra sellar arachnoid cyst, septum pellucidum cyst, choroid plexus papilloma, stenosis of the mesencephale aqueduct[5,7,8,10]. We report 03 cases observed and managed at the Yalgado Ouédraogo University Hospital of Burkina Faso with review of the literature.

Clinical aspects

Case report No. 1

A 9-year-old child, attending school, was admitted for abnormal lateral head movements and recent blindness associated with walking disorders evolving since the age of 3 years. The abnormal movements were initially intermittent and later on permanent, causing, with the onset of blindness, an enormous hindrance to the good progress of schooling. Moreover, this child had a history of two congenital cataract surgeries without favorable results. The physical examination noted normal consciousness, a cranial perimeter of 56 cm, bilateral blindness, microphthalmia, and permanent lateral movements of the head in the form of lateral rotation, which could be assimilated to signs of disapproval (no-no).

Encephalic computed tomography (CT) showed triventricular hydrocephalus by stenosis of the mesencephalic aqueduct with major lamination of the cerebral cortex (Figure 1), and diffuse parenchymal and subarachnoid calcifications.

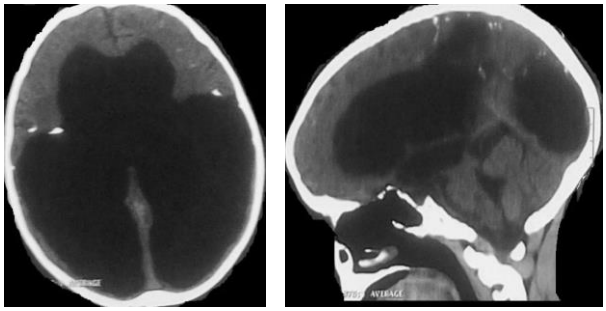

Figure 1. Preoperative CT images of case N° 1. **a**): axial section, **b**): sagittal reconstruction showing triventricular hydrocephalus with cortical lamination predominating in the parietal and occipital lobes, and intra parenchymal calcifications.

An indication for ventriculocisternostomy was given and performed.

The postoperative course was initially favorable with considerable regression of the abnormal movements but 4 weeks later, there was a resumption of lateral movements associated with spasms described as electrical discharges and generalized hyperesthesia treated as sensory epilepsy.

Magnetic resonance imaging (MRI) of the brain revealed persistent triventricular hydrocephalus (Figure 2). Therefore, a new ventriculocisternostomy was performed.

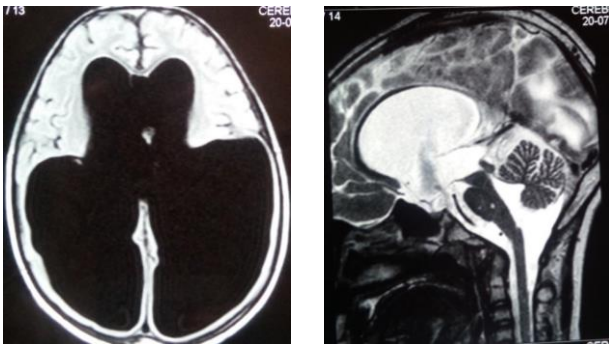

Figure 2. MRI images of case N° 1 performed 4 weeks after the first ventriculocisternostomy at the resumption of abnormal movements. **a**): T1 axial slice; **b**): T2 sagittal slice showing the persistence of a significant triventricular hydrocephalus.

The clinical evolution was marked by a total regression of the abnormal movements.

Two months later he was readmitted for a left hemiparesis of progressive onset, associated with moderate headaches. A follow-up CT scan revealed a chronic right hemispheric subdural hematoma with a mass effect on the medial structures. The hematoma was evacuated and drained, and the postoperative course was favorable, marked by a complete recovery of the hemiparesis.

Three months later he was readmitted again for a resumption of involuntary head movements; after a cranioencephalic CT scan which showed no other abnormality apart from hydrocephalus, we concluded that the ventriculocisternostomy had failed and indicated a ventriculoperitoneal shunt with a medium pressure valve, which was immediately performed. After this bypass, the abnormal movements disappeared completely and definitively.

Case report No. 2

A 14-year-old boy suffering from chronic headaches

was admitted for involuntary head movements associated with a recent worsening of the headaches with the occurrence of vomiting in an intracranial hypertension picture. The history also revealed episodes of generalized seizures and a notion of running away.

On physical examination, we noted a psychomotor slowing down, a head circumference of 58 cm, permanent lateral movements of the head with lateral rotation that could be assimilated to signs of disapproval (no-no). These movements were aggravated by arousal, diminished during voluntary movements and disappeared during sleep. These movements could also be suspended for a few seconds to a few minutes on demand. There was also a spastic right hemiparesis with a motor strength rated at 4/5, a static and locomotor ataxia. Brain MRI (Figure 3) showed tri-ventricular hydrocephalus, a supra sellar cyst exerting a mass effect on V3 and a left temporo-parietal arachnoid cyst. There was also a ptosis of the cerebellar tonsils suggestive of an Arnold Chiari type I malformation.

A ventriculoperitoneal shunt was performed with a medium pressure valve.

The immediate postoperative course was favorable, with improvement of the intracranial hypertension syndrome and significant regression of involuntary head movements. At three months post-op, the abnormal head movements had completely disappeared.

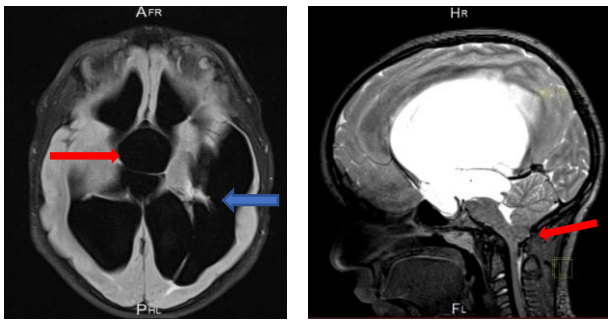

Figure 3. Brain MRI of case N° 2. **a**): T1 axial slice; **b**): T2 sagittal slice showing triventricular hydrocephalus with supra sellar cyst (red arrow on axial slice), left temporo-parietal arachnoid cyst (blue arrow on axial slice) and Arnold Chiari I malformation (arrow on sagittal slice).

Case report No. 3

A 4-year-old girl operated at the age of 2 years for triventricular hydrocephalus (ventriculoperitoneal shunt) with placement of a medium-pressure valve was admitted for abnormal head movements in the form of "yes-yes" head movements. Clinical examination was normal.

Craniocerebral CT scan noted triventricular hydrocephalus and a cyst extending from the pineal region to the third ventricle, exerting a mass effect on the cerebellum (Figure 4).

We indicated endoscopic treatment, which consisted of a cysto-ventriculostomy.

The postoperative course was favorable, marked by an improvement of the abnormal movements from the first postoperative days. The control made 6 months later noted a complete amendment of the abnormal movements.

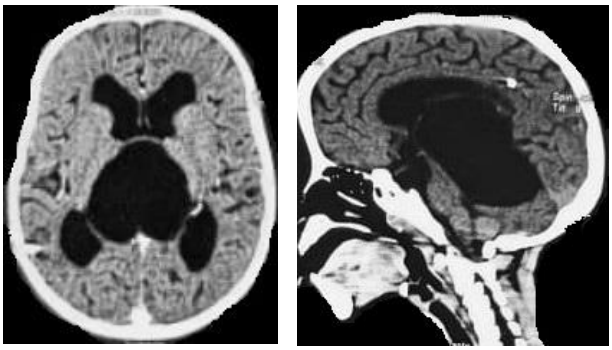

Figure 4. CT images of case N°3 **a**): axial section, **b**): sagittal reconstruction showing triventricular hydrocephalus and a cyst of the septum pelucidum extending from the pineal region to the third ventricle and compressing the cerebellum.

Discussion

Bobble head doll syndrome is a disorder of children under 10 years of age, rarely seen in adults. It is characterized by a stereotypy of back-and-forth movements of the head of 2-3Hz and inconstantly of laterality movements. In some cases the movements may extend to the shoulders, all upper limbs and trunk [9]. These movements are rhythmic, may intensify during stress, but are partially controllable by the patient and disappear during sleep [11]. At least 81 other cases have already been described before our cases [2,3,5,8,14,15,17,20] which have a particular clinical character due to the predominance of "non-non laterality movements". Since the first description in 1966[1], the consistency of intracerebral cystic abnormalities has been noticed but the direct causal link remains for the moment subject to controversies. The intracranial anomalies commonly observed are non-communicating hydrocephalus, supra sellar arachnoid cyst, septum

pellucidum cyst, choroid plexus papilloma, midbrain aqueduct stenosis and by extension all lesions of topography likely to lead to chronic obstructive hydrocephalus. These cystic lesions constitute valves that close the midbrain aqueduct[11,19,23].

The precise physiopathology remains unknown until now but many authors recognize the involvement of dysfunctions of the interconnections between the frontal lobes, the corpus callosum and the basal ganglia[16,17]. On this subject, several hypotheses have been formulated.

In the case of supra sellar cysts, some authors stipulate that the movements of the head would aim at tilting the cyst making the valve backwards in order to allow the opening of the mesencephalic aqueduct. Thus, the movements are interpreted as adaptation mechanisms serving to promote the restoration of normal cerebral spinal fluid (CSF) circulation in order to lower the intracranial pressure[19,23].

For other authors, the perpetual and rhythmic movements of the intracystic fluid or CSF on the diencephalon, the dorso-medial red nucleus and the motor pathways in the upper part of the midbrain would lead to dysfunctions of the extrapyramidal motor pathway[11,17,23]. The patient's ability to control movements and their disappearance during sleep would be arguments that support this hypothesis.

In our series we noted 2 cases of supra sellar cysts interfering with the circulation of the CSF; in addition we noted diffuse intracerebral calcifications which suggest sequelae of TORCH (Toxoplasmosis, Other Agents, Rubella, Cytomegalovirus, and Herpes Simplex) infection including cytomegalovirus infection[6,18,22] in the pediatric age. These same infections could also lead to meningitis and hydrocephalus as well as ocular manifestations including cataracts [12,18,21,22]. The symptomatology may be enriched by other signs related to intracranial hypertension.

The development of CT and MRI scans has improved the diagnostic time. Early diagnosis allows to avoid the permanent installation of the consequences of intracranial hypertension[9] such as blindness and endocrine disorders. Surgical management combines several techniques depending on the causal lesion: ventriculocisternostomy, cysto-ventriculoperitoneal shunt, cystectomy, endoscopic or open marsupialization [10,11,13]. In our case the indicated techniques were ventriculocistrenostomy, cysto-ventriculostomy and ventriculo-peritoneal shunt.

The postoperative results are generally marked by a significant clinical improvement[10,20]. On the other hand, there is still a residual risk of the usual complications linked to the type of operation and the approach. Recurrences are rare[20], estimated at 11%, and may be the consequence of obstruction of the ventriculocisternostomy orifices, dysfunction of the ventriculoperitoneal shunt system or postoperative ectasia of the fourth ventricle[11,4]. In one of the cases in our series (case N° 1) early clinical improvement was observed but shortened due to the probable closure of the ventriculocisternostomy orifices. The occurrence of the chronic subdural hematoma would result from a possible hyper draining following the second ventriculocisternostomy.

Conclusion

Bobble head doll syndrome is a rare pediatric clinical entity, responsible for abnormal movements. It is a manifestation of the consequences of chronic hydrocephalus, which, if managed well and early, leads to favorable results. The quality of the clinical improvement depends on the diagnostic delay and the success of the etiological procedure. Our series of cases are typical examples that have been effectively managed with favorable results.

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Management of brain aneurysm neck-avulsion during clipping surgery. Illustrative case and literature review

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Keywords
aneurysmal neck tear, aneurysmal neck avulsion, intraoperative aneurysmal rupture

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ABSTRACT

Background. Intra-operative rupture (IOR) of intracranial aneurysms is a critical event affecting the operation course and the patient's outcome. However, A rupture induced by an avulsion in the aneurysmal neck is exceedingly challenging, as sealing the neck tear by clip application might result in ischemic injury due to parent vessel occlusion. Here we reviewed the literature regarding the intraoperative avulsion of the aneurysmal neck with an illustrative case to provide explanations of its surgical management intricacies.

Methods. A Midline PubMed literature review was performed using the following keywords; (Aneurysm) AND (neck) AND (surgery or clipping) AND (tear OR avulsion). Fifty-three results were found initially. After excluding non-human subject studies, and non-English studies, two independent researchers examined the title and the abstract for the cases of neck tear or avulsion with its management.

Results. Fourteen articles were found to be included in this study. The average age of the cases is around 57 years. The percentages of females in the review were 62% (8/13), and among the males, 38% (5/13). Regarding the locations, PcomA and AcomA were both 23% (3/13) of the cases; other locations include ACA, 15%, and MCA, 15%. The surgical techniques that opted from the literature include the cotton clip method, clip wrapping, parallel clipping and micro-suturing

Conclusion. IOR due to aneurysmal neck avulsion is a devastating surgical complication, and its management may differ according to the extent of the rupture. Choosing the most convenient technique depends on the surgeon's knowledge and experience.

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INTRODUCTION

Intra-operative rupture (IOR) of intracranial aneurysms is a catastrophic event that can adversely affect the course of the operation and the patient's outcome (3). Although there is a continuous decrease in the IOR due to microscope introduction in the neurosurgical field, the

incidence of aneurysmal IOR has reached approximately 20%, ranging from 5.5 to 40 % (7, 9, 16). It is commonly encountered in anterior communicating artery (AcomA) aneurysms which are estimated by 40 % of all IOR (20), and the risk is significantly increased in ruptured versus unruptured AcomA aneurysms (8). The dome of an aneurysm is the most common site for IOR, reaching up to 29% of the cases (20). In Surgery, a clip application to the neck of the aneurysm may cease the IOR of an aneurysmal dome origin (1). However, A rupture induced by a tear in the aneurysmal neck is far more challenging (10), as sealing the neck tear by clip application might result in ischemic injury due to parent vessel occlusion. IOR due to aneurysmal neck tear has been well stated in the literature, yet, there is scarcity regarding its operative management (1,4,10,11). Here we reviewed the literature regarding the intraoperative avulsion of the aneurysmal neck with an illustrative case, to provide explanations of its surgical management intricacies.

Case Scenario

A 44-year-old female presented with behavioral changes, aphasia, headache, and right-sided weakness of grade 3 on the Medical Research Council of Canada (MRC) scale. Preoperative computed tomography (CT) scan (Figure.1) findings included left Sylvian subarachnoid hemorrhage (SAH) along with interhemispheric hemorrhage. Pre-operative CT Angiography (CTA) (Figure. 2) showed a right saccular superiorly-directing anterior communicating artery (AcomA) aneurysm.

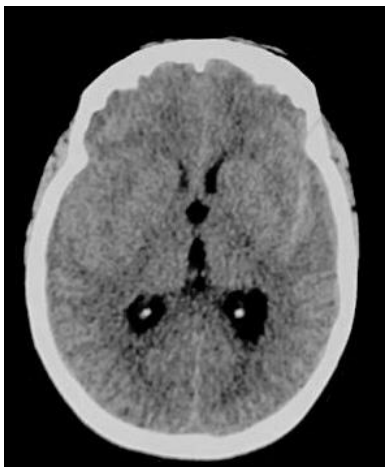

Figure 1. Pre-operative CT scan, axial section revealing the left Sylvain SAH along with interhemispheric haemorrhage.

Intraoperatively, the right lateral supraorbital approach was performed following the typical steps of surgery. After meticulous dissection, IOR was encountered during the initial clip application. It is caused by a tear (avulsion) in the aneurysmal neck; two suction devices were applied in the surgical field alongside attempts for micro-suturing of the rupture site were carried out but weren't successful as the neck tear was extending to the AcomA.

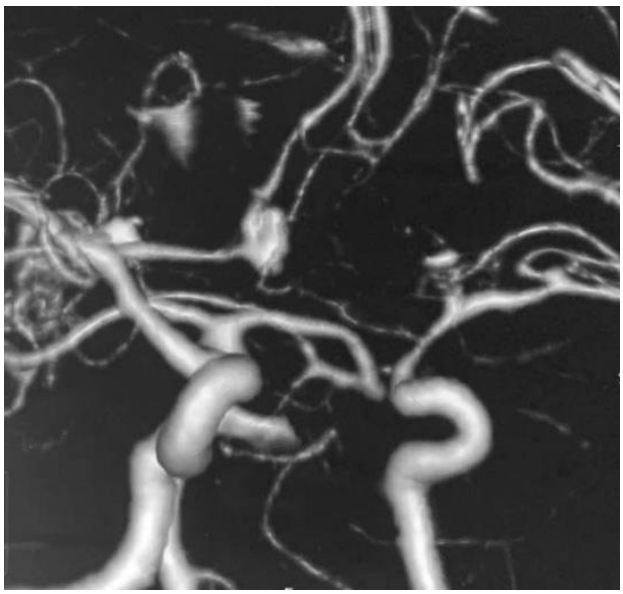

Figure 2. Pre-operative CTA showing a superiorly directed saccular aneurysm from the AcomA.

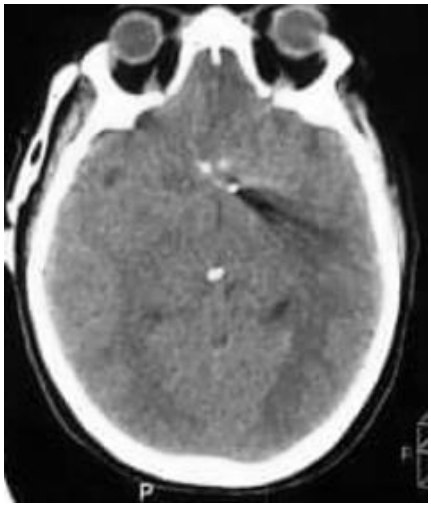

Figure 3. Post-operative CT scan, axial section, showing the location of AcomA clips as a metallic artifact.

Temporary clips were placed to regain haemostasis. Intra-operative neurophysiological monitoring (IONM), including somatosensory evoked potential (SEP) and motor evoked potential (MEP), revealed intact motor function in the right lower limbs and no findings of paresis that can be induced by the expected ischemia caused by the temporary clips. A final decision for permanently clipping the AcomA

aneurysm was made. A postoperative CT scan (Figure. 3) showed no complication of SAH or interventricular haemorrhage (IVH). Postoperatively, the patient's Glasgow Coma Scale (GCS) was 13 with the same preoperative weakness. The GCS improved over the next two weeks with the resolution of the right-sided weakness.

Discussion

IOR is considered one of the most challenging complications of the surgical management of cerebral aneurysms, with a major influence on patient morbidity and mortality (2,3). Similar to other surgical complications, numerous measures are taken to prevent the occurrence of IOR; this includes sufficient exposure to the aneurysm, sharp dissection, and the use of temporary clips (1, 6). Despite the advances in neurosurgical approaches, techniques, and instruments, aneurysmal IOR is still a well-known surgical complication that can impact the surgical procedure and the patient's prognosis (12).

The classification of IOR depends on the specific times within the surgery, which include: pre-dissection, initial microdissection, definitive microdissection, clipping, and post-clipping. (12) Pre-dissection IOR happens between induction of anesthesia and opening of the dura mater. IOR during initial microdissection is an aneurysmal rupture that happens while the parent vessels or branches are being defined. IOR during definitive microdissection is a rupture happening during exploration of the base or wall of the aneurysm or while the attempt to detach a branch vessel away from the aneurysm. IOR during clipping was an aneurysm rupture when the clip was applied to the neck, or it may occur when the clip is manipulated. Any change of the clip after its initial application is considered a "clip manipulation" (12). If bleeding occurs after the reopening, moving, or reapplying to the initial clip, the IOR is defined as occurring during a clip manipulation. Post-clipping IOR is defined as any IOR that occurs after placement of a permanent aneurysm clip (such as IOR caused by intentional puncture of an aneurysm that was incompletely clipped or placement of an additional permanent clip on the aneurysm) (12). In our case, IOR happened while the clip was being applied and caused a tear in the neck of the aneurysm, even though the tear extended to the parent artery.

There are generally two main obstacles surgeons encounter in the presence of IOR; the first is the continuous hemorrhage, which results in a limited field of vision, and the second is difficulty in localizing the aneurysm for clipping, which might endanger the parent vessel (20). Several variables might contribute to aneurysmal ruptures intraoperatively; this includes; The aneurysmal site, size, and configuration. Fundal adherence to the surrounding structures is also an essential factor associated with IOR (2).

In previous studies for analyzing the IOR rates according to the aneurysmal location, rupture rates in AcomA aneurysms reached approximately (48%) which was the highest rate among different aneurysmal sites. The surgical outcome of IOR is significantly affected by the bleeding position; Although the neck is the least common site constituting approximately 16% of all aneurysmal ruptures (20), IOR of the neck is one of the most severe and challenging complications encountered (1).

Multiple methods have been suggested and applied in managing different types of IOR. If the technique is accurately executed, the surgical outcome will mostly improve (20). Large-bore suction over the site of aneurysmal rupture (one in the surgeon's non-dominant hand and the other controlled by an assistant) helps reduce the bleeding and clear the visual field. Temporary clipping of the parent vessel is another form of proximal control to prevent blood loss but can be associated with ischemic complications (1,4). Clipping of the distal sac of the aneurysm can be applied in cases of IOR without neck involvement (3); the cotton-clip method is a widely suggested technique that can be useful for neck avulsion induced IOR, it is performed by a cotton placement over the bleeding site to prevent further blood extravasation, and after clearing the field, the neck of the aneurysm can be clipped. When performing this technique, it is considered that the clip and cotton must not compromise and affect the parent vessel (1, 10, 15). Numerous other practices and methods are reporting good results in neck tear IOR, such as micro-suturing of the ruptured neck, which has variable results, wrapping options, encircling clips placement, bypass, and endovascular trapping techniques (1, 17).

Although there are many methods for managing IOR, they cannot be considered standard

management of all types of aneurysmal neck tears. The cotton-clip method reported good outcomes in many cases of neck tear IOR when the tear is deemed to be minor and can be controlled by adding pressure and cotton placement (1,10, 15). However, this method is not always applicable for a neck tear that extends to the parent vessel, as there cannot be enough pressure applied over the avulsed segment and the bleeding is more profuse than in slight neck tears (20). Unconditional neck tears, larger avulsions arising at the aneurysmal neck with an extension to the parent vessel, are far more complex to manage. This is highly dependent on the neck tear degree, as well as the size, location, and shape of the aneurysm. Such as the longitudinal finger-like appearance of aneurysms can make them more liable for neck avulsions. The cotton-clip method can be applied successfully for partial neck tear ruptures (10).

In our case, initial clip placement over the aneurysmal neck induced IOR. Further dissection revealed a tear in the neck of the aneurysm extending to the AcomA. The modification of surgical steps while repairing the IOR due to an aneurysmal neck tear with extension to the parent vessel can be summarized in two points, 1) micro-suturing of the aneurysmal neck to seal the tear, which eventually didn't work in our case, 2) temporary clip placement over the AcomA to reestablish hemostasis with IONM which did not reveal any changes indicating hypoperfusion. As a result, a 3) final decision for permanently clipping the AcomA was made. The choice not to use the cottonoid clip is that the tear was extending to the parent artery, and there was no space to put the cottonoid patty around the parent artery. The forced decision to clipping the AcomA was the only choice left to cease the hemorrhage encountered intraoperatively.

A Midline PubMed literature review was conducted using the combinations of the following keywords; (Aneurysm) AND (neck) AND (surgery or clipping) AND (tear OR avulsion). Fifty-three results were found initially. After excluding non-human subject studies, and non-English studies, two independent researchers examined the title and the abstract for the cases of neck tear or avulsion with its management. Fourteen articles were found to be included in this study. The average age of the cases is around 57 years. The percentages of females in the review were 62% (8/13) and among the males 38% (5/13). Regarding the locations, PcomA and AcomA were both 23% (3/13) of the cases, other locations include ACA 15%, and MCA 15%.

The primary aim of our review is to deliver a comparative synopsis of the reported management techniques and outcomes for aneurysmal neck avulsions. The first case was reported in 1997 by Yasui et al. (19), who described two cases of intraoperative complications due to neck tears, both managed by the parallel clipping method. Since then, several similar cases have been identified in the literature. In 2002, Yanaka et al. (18) reported a thin-walled aneurysm on the C1 segment of the right ICA, which ruptured at the neck tear during dissection and was further fully separated from the parent vessel. This was managed by temporarily clipping the ICA proximally and distally to the avulsion, micro suturing the tear in the arterial wall, and then using an encircling clip on the rupture site. Despite postoperative hemiparesis, the outcome and recovery of the patient were good upon follow-up. In 2003, Lanzio et al. (10) reported using the clip wrapping method, which consisted of neck clipping preceded by wrapping a cotton swath around the avulsed aneurysmal neck in an AcomA aneurysm. The outcome was good during 1-year postoperative follow-up. The cotton-clip method was reported in 2011 by Barrow et al. (1) in three different cases of intracranial aneurysms in which clip placement induced a slight tear in the aneurysmal neck managed by the cotton clip method, which was preceded by temporary clipping in the second case (Table 1).

Although it is difficult to draw conclusions from this small number of cases, a few observations can be made. First, the scarcity of cases reported can be partially attributed to the inconsistency and different management methods of intraoperative neck tears, which are not always suitable due to multiple variables. The second observation is the lack of the post-operative outcome for a few of the management methods reported.

The main focus of neurosurgeons during microsurgical procedures should be the prevention of intraoperative complications. Various measurements for the management of IOR are reported; they differ according to the rupture site and the extent of the tear. Provisional knowledge of the suggested strategies with awareness of the convenience of each type of IOR can drastically improve the surgical procedure and outcome.

Table 1. The reviewed cases of aneurysmal neck tear

N	Authors	Age (years), Gender	Aneurysm location	Surgical Technique	Outcome
1	Yasui *et al.* 1997 (9)	50, Female	ACA (A1)	Parallel clipping	-
	Yasui *et al.* 1997 (9)	57, Female	IC-PC	Parallel clipping	-
2	Yanaka *et al.* 2002 (16)	46, Female	ICA	Suturing and encircling clip	Good
3	Lanzio *et al.* 2003 (10)	60, Female	AcomA	Clip wrapping	Good
4	Vashu R *et al.* (17)	14, Female	PcomA	Micro-suturing	Good
5	Park J et al 2009 (14)	73, Female	ACA pericallosal	Occlusion of pericallosal artery along with A4-A5 in situ bypass with micro-suturing.	Good
6	Barrow *et al.* 2011 (71)	51, Male	AcomA	Cotton-clip method	-
7	Barrow *et al.* 2011 (1)	62, Female	MCA	Cotton-clip method	-
8	Barrow *et al.* 2011 (1)	52, Female	PcomA	Cotton-clip method	-
9	Feng YG et al 2013 (5)	40, Male	PcomA	Dural Wrapping with clipping	Good
10	Feng YG *et al.* 2013 (5)	43, Female	Anteromedial wall of ICA	Dural Wrapping with clipping	Good
11	Feng YG *et al.* 2013 (5)	41, Male	Anteromedial wall of ICA	Dural Wrapping with clipping	Good
12	Safavi-Abbasi S *et al.* 2015 (15)	-	-	Cotton-clip method	-
13	Jiangang Liu *et al.* 2019 (13)	52, Male	Ophthalmic artery	Cotton-clip method	Good
14	Jiangang Liu *et al.* 2019 (13)	45, Male	MCA	Cotton-clip method	Good
15	Al Ageely *et al.* 2022	44, Female	AcomA	Parent artery clipping	Good.

*All the patients are presented with SAH

Conclusion

IOR due to aneurysmal neck tears is a devastating surgical complication requiring prevention and management approaches, which can be unique to each case. Its management may differ according to the extent of the rupture. Several methods have been suggested to treat such cases and the choice of the most convenient technique depends on the surgeon's knowledge and experience for the best outcome possible.

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Chiari 1 malformation with Platybasia. A case report

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ABSTRACT

Background. The incidence of CM-I is estimated to be 1/1,000 births. In rare cases, CM-I is complicated by associations with other malformations of the craniocervical junction, including mainly Basilar invagination (BI). Chiari malformation (CM) is characterized by a congenital malformation of the posterior cranial fossa with cerebellar tonsils herniation through the foramen magnum, probably due to the underdevelopment of the posterior bony skeleton (exo-occipital and supraoccipital bones). CM may be complicated by a variety of other malformations, including platybasia, basilar invagination and occipitalization, although syringomyelia (SM) is the most commonly observed

Case Report. A girl, 14 years old came with a chief complaint of headache, which is exacerbated whenever the patient coughed or sneezed. The patient also complained about neck pain and a tingling sensation in her hand. A history of vomiting or seizure has not been found. A history of muscle weakness was not found. On physical examination, the patient has a GCS score of 15 on admission, with normal muscle tone and normal reflexes. The patient has a sensory deficit, on the level below C4. The patient underwent CT Scan and MRI whole spine, Chiari 1 malformation and platybasia were diagnosed. The patient underwent posterior fossa decompression, and postoperatively symptoms of Chiari and sensory deficit gradually improved.

Discussion. As an association with this syndrome, there is also basilar invagination as shown by flat basioccipt (platybasia) and upward odontoid projection. hydrocephalus [3].

Virchow coined the term 'platybasia' to describe an abnormal flattening of the skull base, a defect which he attributed to abnormal bone development. In addition to the flattening of the base of the skull, there was upward displacement (impression) of the basilar and condylar portions of the occipital bone, which caused infolding, or impression of the foramen magnum, reduction of the posterior fossa, and consequent protrusion of the upper cervical spine into the anterior brainstem, with neurological signs. The symptomatology presented by CM-1 patients is diverse, and its severity does not correlate with the degree of TH, with some asymptomatic cases presenting with prominent TH. The onset of symptoms generally develops gradually, however, trauma, coughing/sneezing or pregnancy can also precipitate the event. The most common treatment for these patients is surgical PCF decompression (alone or with duraplasty), although cerebellar tonsillectomy, cervical laminectomy, and suboccipital cranioplasty are also applied. The goal of these surgical procedures is to decompress the foramen magnum and increase the subarachnoid space in order to avoid the impaction of the cerebellar tonsils, reestablish the CSF flow and reverse the symptoms

Keywords
Chiari malformation,
Platybasia,
posterior fossa surgery

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Conclusion. This patient was diagnosed with Chiari 1 malformation and platybasia, as suggested in the literature, posterior fossa decompression was done and the patient improved clinically.

Background

According to estimates, 1 in 1,000 newborns will result in CM-I. In a small percentage of instances, CM-I is complicated by relationships with other craniocervical junction abnormalities, primarily Basilar invagination (BI).[1]A cerebellar tonsil herniation through the foramen magnum is a characteristic of the Chiari malformation (CM), which is most likely caused by the posterior bony skeleton's incomplete development (exo-occipital and supraoccipital bones).[2] The cerebellar tonsils and the medial sections of the lower cerebellar lobes were pushed >5 mm past the craniospinal transition and into the upper spinal canal, resulting in the disease known as Chiari malformation type I. (CM-I).[1]

Syringomyelia (SM) is the most frequently reported abnormality, but CM may be worsened by a number of other deformities, such as platybasia, basilar invagination, and occipitalization.[3] Basilar invagination, basilar impression, and platybasia are examples of congenital and acquired abnormalities of the craniovertebral junction (CVJ), which can manifest as either abrupt or slowly advancing neurologic impairment.[4] While basilar invagination refers to the projection of the odontoid process toward the posterior fossa, platybasia refers to flattening of the skull base. Basilar impression, platybasia, brainstem kinking, and retroflexed odontoid deformities were present in 7.7% of our Chiari malformation type I patients.[6]

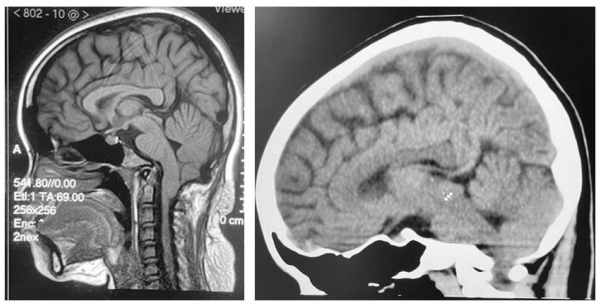

Figure 1. CT and MRI of patient, Chiari I was found.

In addition to a reduction in the size of the posterior cerebral fossa (PCF), CM is usually linked to a number of disorders including platybasia, basilar invagination, and clivus concavity. In roughly 20–72% of instances involving CSF problem, the cerebrospinal fluid (CFS) flow dynamics can deteriorate in CMI, and syringomyelia can develop most frequently in the cervical area. Nearly 20–30% of people will experience cranial-vertebral junction anomalies include basilar invagination, platybasia, a small posterior fossa, concavity of the clivus, occipitalization of the atlas, and spina bifida in the upper cervical area.[7]

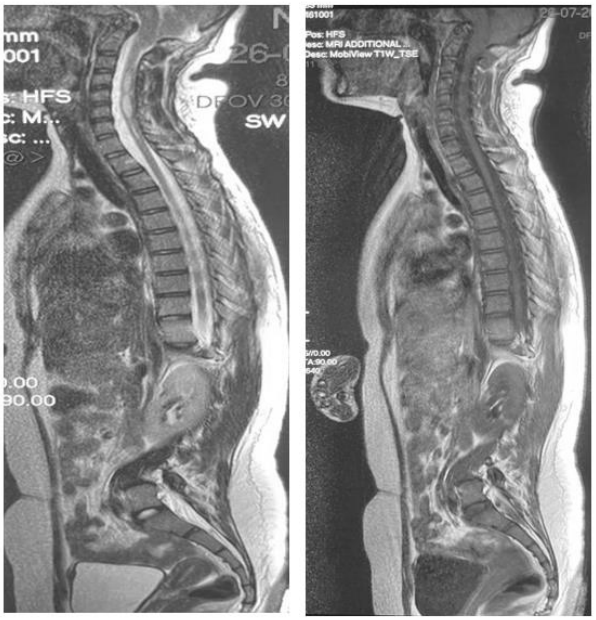

Figure 2. MRI of spine.

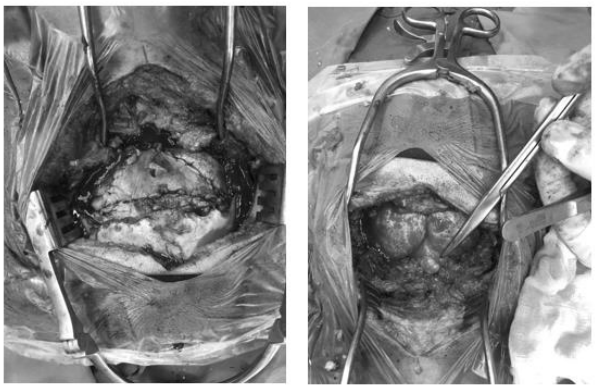

Figure 3. Posterior fossa decompression surgery done on patient.

Case report

A girl, 14 years old came with a chief complaint of headache, which is exacerbated whenever patient

coughed or sneezed. Patient also complain about the neck pain and tingling sensation on hand. History of vomiting or seizure has not been found on patient. History of muscle weakness was not found. On physical examination, patient has GCS score of 15 on admission, with normal muscle tone and normal reflex. Patient has sensory deficit, on level below C4. Patient underwent CT Scan and MRI whole spine, Chiari 1 malformation and platybasia was diagnosed. Patient underwent posterior fossa decompression, and postoperatively symptom of chiari and sensory deficit gradually improving.

Discussions

The most common kind of "Chiari malformations," known as Chiari malformation type 1 (CM-1), is characterized by a downward herniation of the caudal section of the cerebellum into the upper cervical area through the foramen magnum.[8] Syringomyelia and a downward tonsillar herniation make up the Chiari I malformation. Additionally, basilar invagination, as evidenced by a flat basioccipt (platybasia) and an upward odontoid projection, is associated with this disease. The dens should typically extend up to 3 mm above the Chamberlain line and 5 mm above the McGregor line.[9] According to Bao et al., problems related to Chiari I malformation (CMI) included hydrocephalus in 17 patients, 51 patients with basilar impressions, 38 patients with platybasia, 32 patients with occipitalization, 67 patients with scoliosis, and 16 patients with neuropathic arthropathy.[3]

To characterize an abnormal flattening of the skull base, a deformity he linked to aberrant bone growth, Virchow developed the name "platybasia." The occipital bone's basilar and condylar portions were displaced upward, flattening the base of the skull in addition. This upward displacement resulted in reduction of the posterior fossa, infolding of the foramen magnum, and protrusion of the upper cervical spine into the anterior brainstem, along with neurological symptoms.[10] It is commonly recognized that platybasia and basilar invagination are related. In his initial investigation, Chamberlain referred to both of these things as being the same thing. Later, a number of scholars questioned platybasia's clinical value and claimed that it solely had anthropological significance. The more horizontal angulation and shortening of the clivus were related to the superior position of the odontoid process. Klaus observed that the tip of the odontoid process almost never reaches the Wackenheim clival line in basilar invagination associated with platybasia, whereas in a steeply shelving or normal clivus, the line from the dens frequently reaches or even overshadows it. The presence of platybasia suggests that it played a similar role to odontoid process invagination in producing the front concavity of the brainstem and decreasing the size of the posterior fossa.[11]

The current diagnosis of Chiari malformation type 1 relies on imaging evidence of cerebellar tonsil herniation (TH) that extends at least 3-5 mm below the foramen magnum. In other words, the resulting decreased cranial space causes overcrowding in the brain processes and causes the cerebellum to herniate through the foramen magnum. This directly compresses the neural tissue at the craniovertebral junction and frequently causes disruptions in the cerebrospinal fluid (CSF) (decreased velocity and increased impedance), which can lead to various related diseases. The symptoms displayed by CM-1 patients are varied, and the severity of the symptoms does not always correspond to the degree of TH, with some asymptomatic instances exhibiting substantial TH. The onset of symptoms often happens gradually, although it's possible for trauma, coughing/sneezing, or pregnancy to trigger it.[8] For more than a century, basilar invagination has been associated with physical characteristics such a short neck, low hairline, web-shaped neck muscles, torticollis, a reduction in the range of neck movements, and several other morphological abnormalities. There have also been reports of other bone fusion abnormalities and platybasia. It is common to experience neck pain, muscle spasms, and restricted neck movement, all of which point to localized instability.[11]

The most effective diagnostic approach for identifying Chiari malformation is MRI. MRI can reveal precise anatomical details on the structures in the cranial basement. The diameter of the foramen magnum, the volume of the PCF, and the condition of the platybasia were measured using cranial distance and angle measurements. Measurements of PCF development and platybasia were made using the slope of the Tentorium Cerebelli. The patient group showed a considerable reduction in distances measured for the evaluation of platybasia, such as the distance between the Chamberlain line and the tip of the dens axis, the Klaus index, the clivus length,

and the distance between the internal occipital protuberance and the opisthion. The measurement of head basis angles reveals a platybasia tendency.[7]

Although cerebellar tonsillectomy, cervical laminectomy, and suboccipital cranioplasty are also used, surgical PCF decompression (either alone or in conjunction with duraplasty) is the most often used treatment for these patients. In order to prevent the impaction of the cerebellar tonsils, restore the CSF flow, and treat the symptoms, these surgical treatments aim to widen the foramen magnum and enhance the subarachnoid space.[8] To choose the best care and compare surgical results, it is becoming increasingly important to divide all other cases into particular subgroups. Chiari malformation type I is the general term for the results of CMI patients who have a platybasia or a hypoplasic posterior cerebral fossa. Actually, the same surgical procedure, posterior fossa decompression, with or without dural expansion, might result in a further hindbrain descent in the first case or in "ascent" of the cerebellar tonsils in the second case.[12] Marin-Padilla concluded from their study that the Chiari-like deformities reflect the effects of clival and occipital molding, which act mainly anteriorly. Platybasia did not directly result in any neurological symptoms, but it participated with basilar invagination in critically reducing the posterior cranial fossa volume.[11]

Conclusion

Chiari malformation is generally related to occipital bone dysplasia and it is frequently associated with various conditions such as platybasia, basillar invagination and clivus concavity in addition to decrement in posterior cranial fossa (PCF) size. Chiari malformation type 1 results in a direct compression of the neural tissue at the craniovertebral junction and, often, cerebrospinal fluid (CSF) disturbances (decreased velocity and elevated impedance), that can cause other related conditions and bone fusion deformities such as platybasia. MRI method is the best diagnostic tool for detecting Chiari malformation. MRI provides detailed anatomical information regarding the structures located at the cranial basement. The most common treatment for these patients is surgical PCF decompression (alone or with duraplasty), although cerebellar tonsillectomy, cervical laminectomy, suboccipital cranioplasty are also applied. The goal of these surgical procedures is to decompress the foramen magnum and increase the subarachnoid space in order to avoid the impaction of the cerebellar tonsils, reestablish the CSF flow and reverse the symptoms.

List of Abbreviation

CM: Chiari Malformation
CSF: Cerebrospinal fluid
CT: Computed Tomography
CVJ: Craniovertebral Junction
GCS: Glasgow Coma Scale
MRI: Magnetic Resonance Imagin
PCF: Posterior Cranial Fossa
SM: syringomyelia
TH: Tonsillar herniation

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West syndrome and multiple sclerosis association. About a case

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ABSTRACT

Introduction. West syndrome is a rare and severe infantile epileptic encephalopathy, beginning around the age of six months, characterized by a classic electro-clinical triad. This is a pathology totally different from multiple sclerosis (MS) which is a demyelinating disease of the central nervous system caused, affecting young adults, especially females. The association of these two pathologies has never been described.

Observation. We report here an exceptional presentation of MS in a 14-year-old girl with a history of West syndrome. She had normal development until the age of six months, when she began to have flexion spasms. The diagnosis of West syndrome was made with a normal MRI. The infantile spasms disappeared after treatment with vigabatrin and adrenocorticotropic hormone (ACTH). It had generally progressed to Lennox Gastaut encephalopathy, with delayed psychomotor development and epileptic sequelae. At 14, she presented with left hemiparesis within a few days. A cerebral MRI showed multiple nodular hyperintensities of the supra and infratentorial white matter, with the presence of an active lesion, fulfilling the diagnostic criteria for multiple sclerosis. CSF analysis was normal. Anti-AQP4, anti-MOG, anti-NMDA and anti-GABA (AB) antibodies were absent in the blood. Antibodies against HIV and viral hepatitis were. Biotinidase activity and autoimmunity tests were correct. The patient received high doses of methylprednisolone IV (1g/day) for three days with remarkable clinical improvement after 15 days.

Discussion. MS is a complex and heterogeneous central nervous system (CNS) demyelinating disease. It is not uncommon for epilepsy to be the first symptom of multiple sclerosis. Seizures, on the other hand, are more common after disease progression. Although the disease is characterized by inflammatory lesions of the white matter, various neuropathological and radiological studies have shown that the disease also affects the grey matter. Several studies have shown that seizures are three to six times more common in MS patients than in the general population. Even though MS can start with epilepsy and a seizure may be the only symptom of a relapse of MS, it is still not known whether the two diseases coexist or whether MS predisposes to seizures.

Conclusion. The association of these two totally different pathologies can lead us to say that the mechanism of multiple sclerosis may begin in childhood and that the clinical signs appear in adulthood.

Keywords
West syndrome, multiple sclerosis, inflammation

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INTRODUCTION

West syndrome is a rare and severe age-related epileptic encephalopathy of infancy comprising a triad of infantile spasms, hypsarrhythmia and psychomotor delay. 50% to 90% of patient evolve

to other syndromes mostly Lennox Gastaut syndrome, whereas multiple sclerosis (MS) is a central nervous system demyelinating disease caused by an autoimmune process. It is highly prevalence among young female adults. Their presence with a single patient has never been described.

We herein report an exceptional presentation of MS in a 14-year-old girl child with a childhood history of West syndrome.

Observation

A 14-year-old_female child presented with rapidly onset left hemiparesis. Concerning her past medical history, she was born into a second-degree consanguineous marriage. She had a history of intrauterine growth restriction (IUGR) and low birthweight in a normal delivery. Nevertheless, she had normal development until the age of six months, when she started having flexion and extension spasms occurring in clusters, usually shortly after waking up.

The diagnosis of West syndrome was established. The infantile spasms disappeared after three years of treatment with vigabatrin and adrenocorticotropic hormone (ACTH). It had typically progressed to Lennox Gastaut encephalopathy, with psychomotor developmental delay and epileptic sequelae.

At the age of four, she presented stereotyped behaviours, most commonly involving hands. Therefore, the diagnosis of Rett syndrome has been suspected, and it was ruled out by a negative genetic study. A brain MRI at this age was without abnormalities.

Her epilepsy was relatively stable under lamotrigine and sodium valproate with motor and cognitive sequelae. Interestingly, she was able to walk at the age of 8 years after intensive motor rehabilitation and was relatively autonomous in day-to-day tasks.

At the age of 14, she presented a left hemiparesis worsening over few days. On examination, we found a conscious, very agitated and irritable child with incessant cries and tears, retrognathism, microcrania, low hair implantation, stereotyped hand rubbing movements, generalized hypotonia and left hemiparesis. A brain MRI showed multiple nodular and bilateral T2/FLAIR hyper signals and T1 hyposignals in the supra and subtentorial white matter, with the presence of one active lesion in the left oval centre (Figure 1).

CSF analysis with iso-electro-focalisation showed a proteinorachia at 0.33mg/l with the absence of the oligoclonal band (OCB). The anti AQP4, anti-MOG, anti NMDA, and anti-GABA antibodies (AB) were absent in the blood. Antibodies to HIV and viral hepatitis were negative. The biotinidase activity and autoimmunity tests were correct.

The patient received high doses of IV methylprednisolone (1g/day) for three days with a remarkable clinical improvement after 15 days.

Five months later, her motor symptoms had worsened with the recurrence of her left hemiparesis. A brain and spinal cord MRI showed a significant increase in lesion load with the presence of at least eight active lesions as well as multiple spinal cord lesions (figure 2). Consequently, treatment was initiated, including an IV infusion of methylprednisolone (1 g/d for five days), followed by an IV Ig course (25mg/d for three days) with a favourable response. Another IV Ig course was given after one month, and the girl was remarkably stable.

Six months after that, the patient had another relapse, which was made of left arm weakness with an exacerbation of her seizures. A brain MRI was performed, showing the presence of multiple active lesions (figure 3). She was then admitted for an IV infusion of methylprednisolone (1g/d for three days) followed by monthly repeated courses of IV Ig as the diagnosis of MOGopathy was highly suspected.

Under this treatment, the patient's evolution was favourable, and he has been free of relapses ever since.

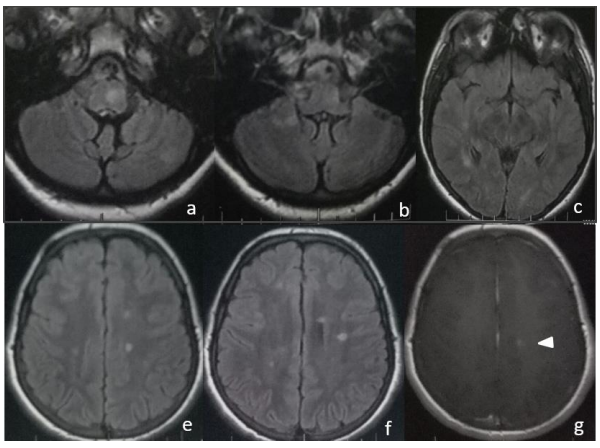

Figure 1. Brain MRI showing multiple FLAIR hypersignals in sub and supra tentorial white matter.

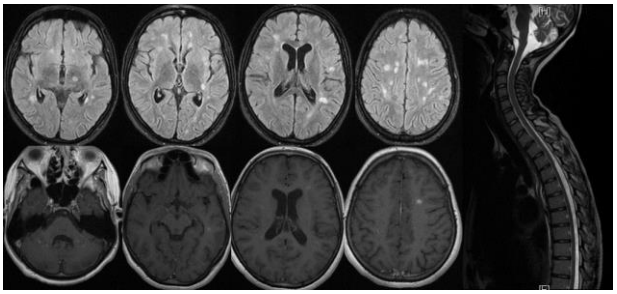

Figure 2. Brain and spinal cord MRI after 2 months, showing an increase in the number and volume of the lesions.

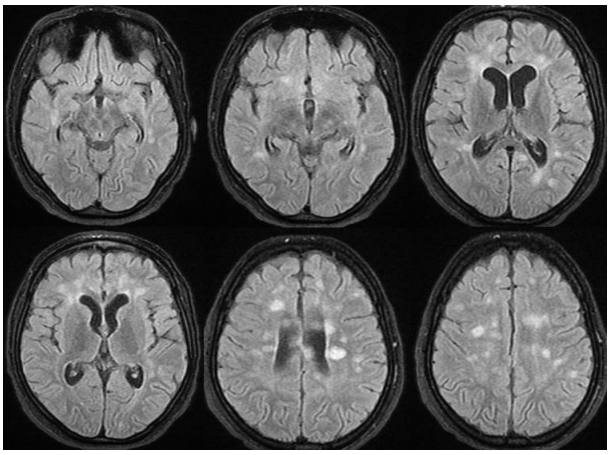

Figure 3. Brain MRI after 11 months from the first relapse.

Discussion

Multiple sclerosis (MS) is a central nervous system (CNS) demyelinating disease that is both complex and heterogeneous.

It is not rare for epilepsy to be the first symptom of multiple sclerosis. Seizures, on the other hand, are more common after the start of the condition (1). Although the disease is characterized by inflammatory lesions in the white matter, various neuropathological and radiological studies have shown that the disease also affects the grey matter. Several studies have showed that seizures are three to six times more common among MS patients than in the general population (2) (3). Even though MS can start with epilepsy (4) and that a seizure may be the only symptom of an MS relapse (5), it's still unclear whether the two diseases coexist or whether MS predisposes to seizures (6).

On the other hand, infantile spasms initially discovered by William James West in his own son in 1841.

The term Infantile spasms syndrome (ISs) now refers to an epileptic syndrome that affects children under the age of one year (rarely older than two years), with clinical spasms that usually occur in clusters, with hypsarrhythmia as the most common EEG finding. The spasms that are frequently associated with developmental arrest or regression. The name West syndrome (WS) refers to a subset of ISs marked by clustered spasms and hypsarrhythmia on an EEG, as well as delayed brain development or regression.

The pathophysiology of infantile spasms isn't completely understood. It is well-known that partial seizures can progress to spasms, as evidenced by invasive and surface EEG recordings, as well as the peculiar PET (positron emission tomography) finding of hypometabolism of deep grey structures and the brain stem in children with spasms, all support the cortical-subcortical interaction hypothesis (7). The therapeutic response to hormonal therapy, on the other hand, has shown a role for the hypothalamic-pituitary axis and immunological systems. The Developmental - desynchronization model better explains the narrow age of onset as well as the developmental effects (7).

Conclusion

The association of West syndrome and multiple sclerosis has never been described, and the common point is neuroinflammation, which can open perspectives on the understanding of the physiopathological mechanisms of these two pathologies, and can be an argument that the substance gray is not spared from multiple sclerosis.

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The first and foremost unilateral pallidothalamic tractotomy done in India for Parkinson's Disease. An interesting case report

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ABSTRACT

Background. Pallidothalamic tractotomy" can be effective in Parkinson's disease by exhibiting anti-parkinsonian effects.

Case presentation. The patient was a 53 years old gentleman, having Parkinson's disease for the last 14 years. The disease onset was on the left side and slowly moved to the right side. He had tremors, slowness of body movements and stiffness of the movements. The first right Pallidotomy was done in January 2019. There was a noticeable improvement in a few weeks. He continued to have symptoms on the right side. The preoperative Unified Parkinson Disease Rating Scale (UPDRS) part 3 score in 2019 was 53 while the postoperative score was only 26 showing drastic improvement after right Pallidotomy. After 2 years of the first surgery, a new technique called Pallido Thalamic Tractotomy (PTT), an MRI-guided stereotactic surgery was done on the left side. Tremors reduced gradually by 99% in 3 weeks after surgery. This is the first case of PTT performed on a patient with Parkinson's disease in India.

Conclusion. PTT is an effective procedure in PD that acts by disconnecting the pallidothalamic tract. Unilateral pallidothalamic tractotomy done on the left side improved contralateral side rigidity, tremors and bradykinesia.

Keywords
pallidothalamic tractotomy,
pallidotomy,
Parkinson's Disease,
tremor,
unilateral

✉

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INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder primarily affecting the body's movements [1]. It is characterized by global slowing of body movements, known as bradykinesia, and other symptoms such as resting tremors and rigidity. James Parkinson first described Parkinson's disease in 1817 [2,3]. Initially, the term shaking palsy was used by medical writers like Parkinson for Parkinson's disease [2]. It was further refined, characterized, and expanded by Jean-Martin Charcot in the mid-1800s [3]. It affects, on average, one to two people per 1000 population at any time.

PD is a multifactorial disease [4]. The etiology is unknown in the majority of the cases, with genetic and environmental risk factors also playing a role [4,5]. The prevalence increases with age affecting about

1% of the population aged more than 60 years [6]. The prevalence of PD generally increases with an increase in age [7,8]. The incidence is higher in males in all age groups, with a significant difference in incidence between 60-69 and 70-79 years [8]. According to "The Parkinson's Foundation Prevalence Project," it was estimated that around 930,000 people in the United States would have PD by the year 2020, and it is expected to rise to 1.2 million by 2030 [9]. Symptoms start gradually, sometimes starting with a barely noticeable tremor in just one hand. Tremors are typical, but the disorder mainly causes stiffness or slowing of movement [1,4,10]. Postural instability occurs with the progression of the disease. But, the detailed clinical course has not yet been elucidated [10].

The primary pathophysiology appears to be due to the accumulation of alpha-synuclein in various parts of the brain, primarily the substantia nigra, leading to degeneration and subsequent loss of dopamine in the basal ganglia that control muscle tone and movement [4,11].

Parkinson's disease is typically treated with medication. The medication usually works very well in the first few years of treatment, but it becomes less effective after some time. The best management then usually involves placing a pacemaker inside the brain by inserting electrodes and modulating the pacemaker's frequency. It produces a result for the patient for the symptoms of the disease. It is known as Deep brain stimulation surgery (DBS) [12]. But it is costly, especially considering the cost of the pacemaker. As known, there is no cure for Parkinson's Disease at all. Parkinson's is a progressive degenerative disease that can only be treated by medicines to curb rapid growth or sustain tremors. It progresses faster in some and slow in some patients. All Parkinson's patients do not benefit from surgery.

The Pallidothalamic tract is a part of the basal ganglia. It connects the internal globus pallidus and thalamus (a ventrolateral portion of the thalamus). It is comprised of ANSA lenticularis and fasciculus lenticularis [13]. Both of them take their origin from the internal part of the pallidum. These tracts merge into the fasciculus thalamicus before entering the thalamus [13]. Pallidothalamic fires of the Ansa reticularis and fasciculus lenticularis are funneled into the thalamic fasciculus (H1 forel field) before reaching the thalamus. They join two to three millimeters below the intercommissural plane (H2 forel field). Hence interruption of the Pallidothalamic tract at the H1 level amounts to Pallidotomy functionally because the major pallidal outputs go through it and can be achieved with smaller lesion size. PTT can be compared to a pallidotomy that is optimized, as it is capable of extensive liberation of the dynamics of the thalamocortical system by leaving intact thalamus using a very restricted ablation of the tissue. Neurosurgical ablation of the pallidothalamic tract is called Pallidothalamic Tractotomy (PTT). It has been reported as an effective treatment for PD in a few studies by exhibiting anti-parkinsonian effects [14,15]. But there is a lack of literature in India regarding PTT.

CASE PRESENTATION

Case description

The patient was a 53 yrs old gentleman, having Parkinson's disease for the last 14 yrs. It started with mild tremors in his left hand and progressed to some stiffness and difficulty moving the hand. He had tremors, slowness of body movements, and stiffness. Over the next few years, it involved his entire body, with the left side more affected than the right side to the extent of losing his confidence in even walking or performing his daily activities. With this situation, he was unable to do his tailoring, which was his sole source of revenue for him and his family. He approached doctors, took treatment, and was put on regular medications. They were given since the disease started. An increase in the dosage of drugs did not alter the symptoms. It was started with two doses of Levodopa and carbidopa and increased gradually. The medication included tablet levodopa and carbidopa 100/25 mg used four times a day, T.Ropinorole 6mg per day, and T.Trihexyphendyl 4mg per day. The patient was intolerant to drugs for further enhancement. His tremors would subside when he took medicines and aggravate once their effect was over, the medicines' so-called on and off period. He was suggested to undergo Deep brain stimulation surgery (DBS). But it was not affordable for him. Medical treatment was started at various places for nearly 12 years without full benefit. The patient had developed a side effect called Drug-induced dyskinesia (Levodopa). He presented in 2018 – 2019 to a tertiary care institute with symptoms despite medications. Levodopa (400 mg/day) was required to maintain daily activities. The

timeline of the clinical presentation and management is shown in Figure 1.

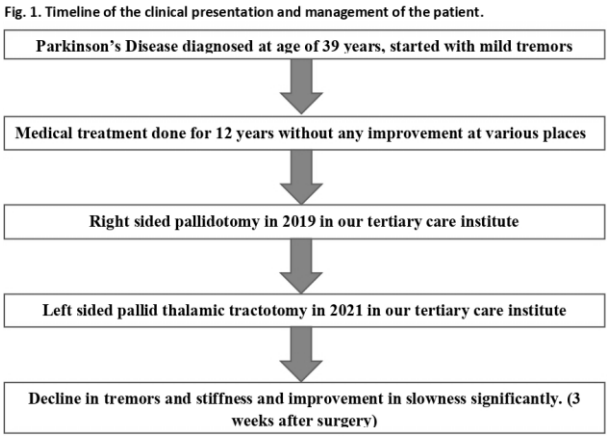

Figure 1. T1 axial MRI of the brain showing the first operation pallidotomy scar on the right side.

First surgery (2019)

The first right pallidotomy was done in January 2019. It was an MRI-guided macro stem controlled, stereotactic right pallidotomy [16,17]. It was done on 2 Postero Ventral Pallidum (PVP) tracks with 3 lesions each, using a 1x4 electrode at 70 degrees centigrade for 40 seconds. There was a noticeable improvement in a few weeks. Tremors, stiffness, and slowness improved significantly on the left side. He continued to have symptoms on the right side. The preoperative Unified Parkinson Disease Rating Scale (UPRDS) part 3 score in 2019 was 53, while the postoperative score was only 26 showing drastic improvement after right Pallidotomy. The old pallidotomy scar on the right side can be seen in Figure 2.

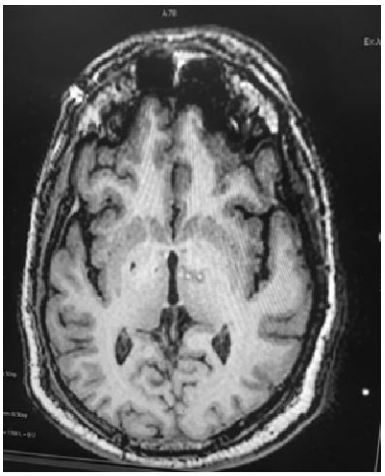

Figure 2. Surgiplan software post-op MRI, showing the precision of targeting with pre-op planned targets in Green and the post-op lesion. Green indicates Pallidothalamotomy lesion in PTT lesion area.

Second surgery (2021)

After 2 years of the first surgery, a new technique called Pallido Thalamic Tractotomy (PTT), an MRI-guided stereotactic surgery was done on the left side [14,15,18,19]. On 7th July 2021, he underwent PTT surgery. There is a risk of dysphagia and dysarthria with bilateral Pallidotomy, even if it is a staged pallidotomy. Hence, we decided to use a white matter target - the PTT or the Pallido Thalamic Tract. This tract is just lateral to the mamillothalamic tract. It covers the cZI/ PSA area (including the fields of Forel H1 & H2) [13]. These 2 references were based on the Schaltenbrand-Wahren atlas [20], and studies reported by Aufenberg C et al. (2005) [19], and Magara A et al. (2014) [21]. This is located just above the superior border of the STN, seen as low-intensity areas on T2 MRI and the location where we usually get the best results in STN DBS. MRI-guided, stereotactic, macro stem-controlled lesioning in PTT-1 and PTT-2. One lesion each using 1x4 electrode, at 70 degrees centigrade for 40 secs. The pre-op targets fixed for PTT can be seen in Figure 3.

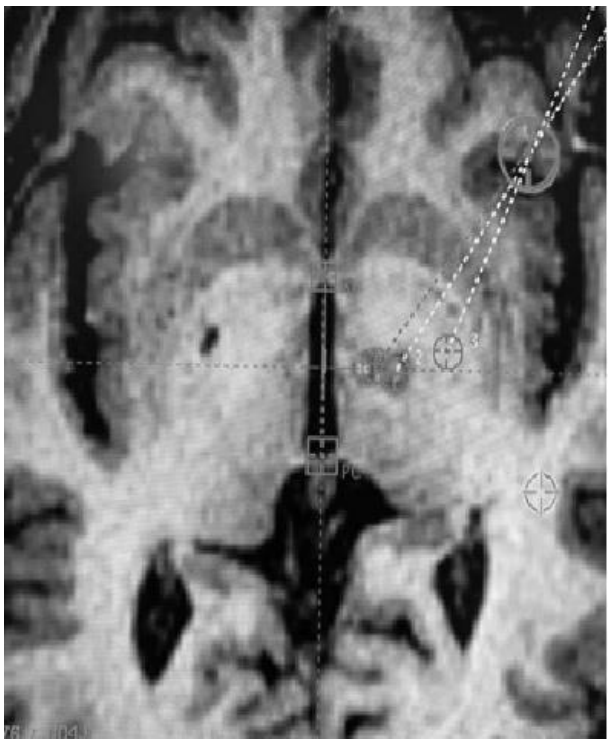

Figure 3. Surgiplan software post-op MRI, showing the precision of targeting with pre-op planned targets in Green and the post-op lesion.

Stereotactic MRI is taken to mark the exact location with the help of special software to locate the target

circuit to be burnt. Stereotaxic surgery or stereotactic surgery is a three-dimensional surgery technique [13,18,22]. It enables the detection of deep lesions in the tissues to be located and then treated using heat or cold, or chemicals. The procedure itself is so complicated. It is a procedure that involves fixing a particular frame called a stereotactic frame on the skull by drilling 4 screws [23].

A 14 mm hole is made in the skull. An electrode is inserted inside the brain. The correct location is tested by giving a mild current and burning the circuit at 70 degrees for 40 seconds with a Radio Frequency Lesion generator. This procedure is called an MRI-guided stereotactic Pallidotomy, which goes 9 to 11 cm deep inside the brain [16]. As soon as the lesioning was done, Tremors came down gradually, and the hand became loose. Rigidity, stiffness of their body - both in his hand and leg improved gradually.

Within a few weeks, there was a decline in tremors, stiffness, and improvement in slowness significantly. Tremors reduced gradually and significantly within 3 weeks after surgery as measured by the UPDRS scale. He had no memory or other intellectual brain issues. He can carry out day-to-day activities without any difficulties. PTT surgery on the left side resulted in a significant fall in the Right side UPDRS off phase score from 25 in the preoperative period to 4 in the postoperative period. Unilateral Pallidothalamic Tractotomy on the left side improved contralateral side rigidity, tremors, and bradykinesia.

Table 1. Comparative table for total score of part 3 UPDRS (Unified Parkinson Disease Rating Scale)

Year	Surgery done	Pre-operative (or) Post-operative	UPDRS Score
2019	Right Pallidotomy	Pre op	53
		Post op	26
2021	Left Pallidothalamic tractotomy	Pre op - off phase	30
		Post op - off phase	10

Table 1 describes the UPDRS (Unified Parkinson Disease Rating Scale) scores preoperatively and postoperatively after right Pallidotomy in 2019 and left Pallidothalamic tractotomy in 2021, respectively. The preoperative UPRDS part 3 score in 2019 was 53, while the postoperative score was only 26 showing drastic improvement after right Pallidotomy. The preoperative UPRDS part 3 score in 2021 was 30, while the postoperative score was 10, thereby demonstrating significant clinical improvement after left pallidotomy tractotomy. There was no alteration in cognitive function before and after surgery.

Table 2 describes the comparison of right and left UPDRS scores preoperatively and postoperatively after left Pallidothalamic tractotomy in 2021, respectively, in the off phase. The preoperative UPRDS score was 25 in the off phase in the right, while the postoperative score was only 4 showing drastic improvement after right pallidothalamic tractotomy in 2021.

Table 2. Comparative table for right and left UPDRS scores before and after left Pallidothalamic tractotomy done in 2021

Pre-operative (or) Post-operative	Right	Left
Pre op - 2021 off phase	Off- 25 (On- 11)	Off-5 (On-4)
Post op – 2021 off phase	Off- 4	Off-6

Discussion

The present case report describes a staged lesioning surgery with Pallidotomy and PTT for treating Parkinson's Diseases symptoms. It is the first time in India Pallidothalamic tractotomy has been done to cure Parkinson's or any other Movement Related Disorder. In other countries like the U.S. and Japan, PTT has been used to manage Parkinson's Disease and other Movement Disorders. Stereotactic surgery has become popular in treating Parkinson's disease (PD) due to the long-term complications of levodopa therapy, causing significant disability.[24] Surgery for Parkinson's disease has evolved from ablation with careful lesion placement in various brain structures to stimulating particular brain targets in the basal ganglia.[25] There has been a better understanding of the physiology and the circuit of basal ganglia in recent decades with the improvement of neuroimaging and surgical techniques.

The first surgery we did in 2019 is called the Pallidotomy, and the surgery done in the area of the brain is called GPi – Globus Pallidus interna. The second surgery is called the Pallidothalamic tractotomy (PTT), where the surgery was an MRI-guided stereotactic surgery.

PTT is a part of the brain circuit that connects two nucleus - Globus pallidus and the thalamus deep inside the brain, which plays a vital role in the symptoms of Parkinson's disease. Lesioning or burning a circuit inside the brain has been a standard of care treatment and has been there for around several decades [13,26,27]. Burning this circuit can alleviate Parkinson's symptoms. The brain circuit connects two prominent nucleus in the brain. Alteration of the activity due to the disease process causes Parkinson's symptoms on the opposite side. By burning this circuit - pallido-thalamic tract (PTT), the symptoms of Parkinson's disease. This is the first case of PTT performed in a patient with Parkinson's disease in India. It has been reported as an effective treatment for PD in a few descriptive studies worldwide by exhibiting anti-parkinsonian effects [14,15]. Our current approach, i.e., targeting the pallidal efferent fibers in the subthalamus as shown in Figure 3, was proposed by Meyers R [28]. Then, Pallidothalamic tractotomy was explicitly done for PD by Aufenberg C et al.[19], Godinho F and Magnin M et al.[29]

There was a drastic improvement in postoperative score after right Pallidotomy in the present case. After 2 years of the first surgery, PTT surgery was done. The UPRDS off-phase preoperative score (in 2021) was 30, while the postoperative score was only 10 after PTT surgery. There was no alteration in cognitive function before and after surgery. PTT surgery is done on the left side, resulting in a significant fall in the right side UPDRS off phase score from 25 in the preoperative period to 4 in the postoperative period. Horisawa S et al.[14] in 2019 presented the first single case report of PTT performed in a patient with Parkinson's disease, with a follow-up of one year. Their patient was a 68-year-old woman who had a similar presentation of PD in comparison with the present case. She started to experience the "wearing-off" phenomenon after 14 years of medical management. She also required Levodopa (300 mg/day) to maintain daily activities similar to the present case. During the preoperative, She underwent PTT on the left side without any perioperative complications.

On follow-up after 1 year, she had daily maintenance levodopa (200 mg) without an "off" condition all day. The 1-year UPDRS scores showed significant improvement, similar to the present case. They concluded that PTT might be useful in PD subjects who don't desire device implantation. Horisawa Set al.[15] in 2021 studied Unilateral pallidothalamic tractotomy for akinetic-rigid Parkinson's disease in 14 patients. They observed that the total MDS-UPDRS Part III score significantly improved from 45 ± 4.6 at baseline to 32.9 ± 4.8 at 12 months postoperatively ($p = 0.005$) in the 10 patients available for follow-up. They also observed, similar to our case, that contralateral side rigidity and bradykinesia significantly improved. They also observed no severe permanent neurological deficits similar to our study.

Horisawa S et al. [14] in 2019 presented the first single case report of PTT performed on a 68-year-old female patient with Parkinson's disease, with a follow-up of one year on Levodopa (300 mg/day) for maintaining daily activities. Her preoperative Unified Dyskinesia Rating Scale (UDysRS) and Parkinson's Disease Questionnaire-39 (PDQ-39) scores were 102 and 46, respectively. She underwent left-sided PTT, and no perioperative complications were observed. Her UDysRS and PDQ-39 scores after one year of surgery were 20 and 20, respectively. PTT might be useful in patients who do not desire device implantation. Gallay MN et al.[18] in 2021 did Bilateral MR-Guided Focused Ultrasound PTT for 10 patients suffering from chronic and therapy-resistant PD. They were followed up for 1 year after the operation of the second side. They observed a reduction in total UPDRS score off-medication similar to the present case at 1 year after the second PTT by 52% compared to baseline on-medication ($p < 0.007$). They concluded that bilateral PTT effectively controls PD symptoms compared to medical management at its best.

Conclusions

Preliminary case reports across the globe have shown reasonably good outcomes. The present case report, the first of its kind in India, reports this procedure's effectiveness and safety. It was the first time in India, Pallidothalamic tractotomy had been done to treat motor symptoms of Parkinson's or any other Movement Related Disorder. It is also the first time in India, Bi-Lateral Lesioning surgery for treating Parkinson's Diseases symptoms has been done. This surgery will be a boon for patients with PD as it will improve their quality of life. The cost associated with this surgery is much less than the cost of pacemaker

implantation in the brain. This case report gives substantial evidence to support the need for future studies. Larger scale interventional studies with randomization are required to make evidence-based recommendations.

Limitations

Being a single case report, the reliability of the present study findings is poor. There was also no control to compare the results. The data available from this study is not enough to advocate the use of PTT and it's relatively low risk profile.

Lessons

PTT is an effective procedure in PD that acts by disconnecting the pallidothalamic tract. Unilateral pallidothalamic tractotomy on the left side improved contralateral side rigidity, tremors, and bradykinesia. It is the first time in India that PTT has been done for treating symptoms of Parkinson's Disease. It will enable them to carry out their day-to-day activities without support. The cost associated with this surgery is much less than the cost of pacemaker implantation in the brain.

Abbreviations

PTT – PallidoThalamic Tractotomy,
PD - Parkinson's disease,
UPDRS - Unified Parkinson Disease Rating Scale,
DBS - Deep Brain Stimulation Surgery

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Similarities and differences between two coincidently gravitational bullet cases. A case report from Iraq

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Keywords
traumatic brain injury, craniocerebral falling bullet, aerial firing, advanced trauma life support

ABSTRACT
Many cases of gravitational bullets are reported in developed and non-developed countries. However, few papers highlighted these cases in the literature. In our study, we present two cases of gravitational bullets that have an unusual coincidence in the injury characteristics through their ages, and gender, the site of the inlet.

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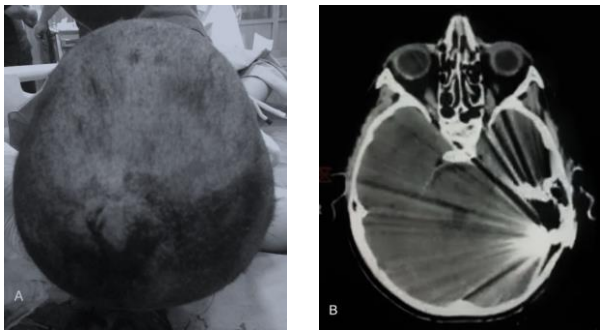
INTRODUCTION

Traumatic brain injury (TBI) is young people's most common cause of death and disability. Represented by disruption of the brain function when physical force is applied to the brain, in case an object hits the head violently and suddenly or when an item pierces the skull and enters the brain (1). The annual incidence of TBI is estimated at 50 million cases worldwide; this means that half of the international population has occasion of TBI in their life (2). Higher mortality and morbidity rates in TBI were found in low- and middle-income countries, making this a global health problem (2). A concussion is among the most common form of TBI; the other types might be in the form of a bullet. In aerial firing or celebratory firing, when the bullets are shot into the sky for celebration or anger expression in some countries, the bullet will firstly move under the effect of explosive acceleration, this velocity will decrease according to the gravity force, and finally, its velocity will reach zero, at this moment the bullet will move downward. Its velocity will be increased by the gravity force until reaching the final steady velocity when the air resistance drag equalizes the effect of gravity. The bullets injury caused by this mechanism is called gravitational bullets or

falling bullets (3). As the minor victims do not go for medical care and death at the scene is not recorded in the hospital, the incidence and outcome of the gravitational bullet are complex and challenging. However, high numbers of falling bullets are announced in the news media, and this number is increasing as firearms are more accessible and available (4). In this paper, we present two cases of randomly gravitational bullets with the characteristic of coincidence in their names, age, site of the inlet, and most site of the bullet inside the brain; no previous study highlighted such discussion about this issue.

THE CASES SCENARIOS

The two incidental cases were urgently admitted to the Neurosurgical emergency department on the same day, complaining that an unknown object had struck their child's head, resulting in minor bleeding (figure 1A) (figure 2A); both families and children were not sure of what had hit the dome. Both patients had the same name and gender, and both were in six years old; the site of inlet injury was in the midline parietal area (figure 1C) (figure 2C).



A. **B.**

C.

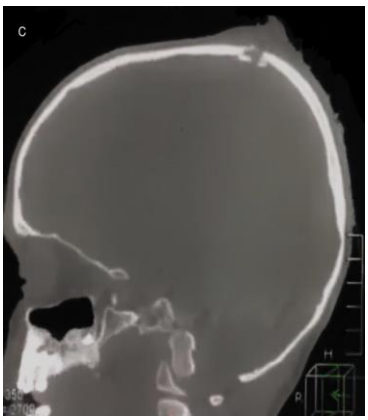
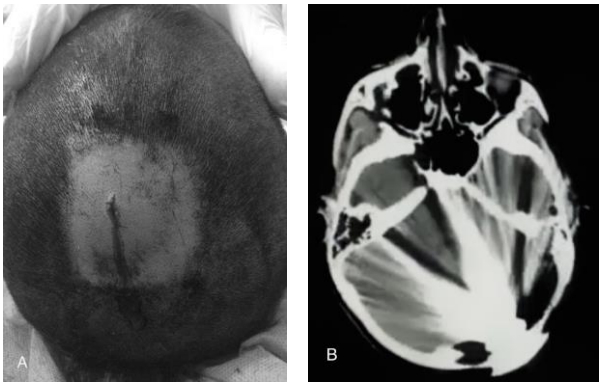


Figure 1. (**A**) superior view of scalp showing site of wound, (**B**) Computed tomography (CT) scan of the brain showing an axial view in which a metallic artefact is seen near left petrous bone, (**C**) CT scan bone window sagittal view showing site of bullet entrance of the first patient.

A complete neurological examination revealed that both patients were unconscious, Glasgow coma scale (GCS) was 11, 12, with right-sided weakness grade 4 in both. A skull x-ray was ordered, surprisingly revealing a bullet inside the skull. A non-contrast brain computed tomography (CT) scan revealed no significant hemorrhage or soft tissue edema and the location of the bullet was confirmed to be near the left petrous bone in the first patient (figure 1B) and left cerebellar hemisphere in the second patient (figure 2B). In the emergency room, the wound was cleaned and redressed; after that, both of them were given amoxicillin and carbamazepine for protection against infection and convulsions. Conservative treatment was chosen, and the parietals were neurologically intact on a 6-month follow-up.



A. **B.**

C.

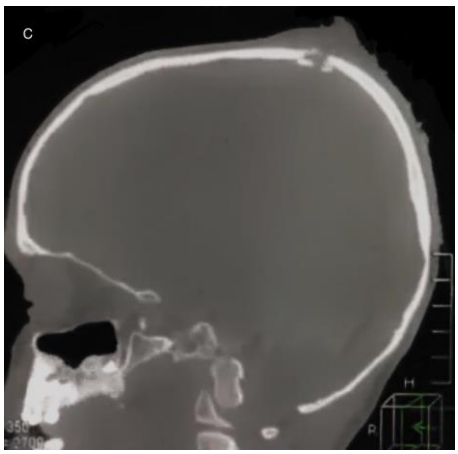


Figure 2. (**A**) superior view of scalp showing site of wound, (**B**) Computed tomography (CT) scan of the brain showing an axial view in which a metallic artefact is seen in left cerebellar hemisphere, (**C**) CT scan bone window sagittal view showing site of bullet location of the second patient.

Discussion

TBI is an important cause of morbidity and mortality in developed and industrialized countries. The estimated incidence of hospitalized patients with one or more TBIs is 57 million cases worldwide (5). In the United States, the annual average of patients with TBI is 1.4 million, 1.1 million recorded from emergency department visits, 235,000 were hospitalized, and 50,000 were dead. Regarding gender and age variability, the occurrence of TBI in males is twice as females. For emergency visits, hospitalizations, and deaths combined, children aged 0-4 years and 15-19 years are more likely to suffer from TBI than other ages; for hospitalizations the adults aged 75 years and older have the highest incidence (6). The important causes of TBI are falls, vehicle crashes, blasts, and bullets; sports and recreation activities are also important causes of TBI, including concussions (6). Of patients who die from TBI, 90% of them die within 48 hours of injury, frequently because of uncontrolled raised intracranial pressure that leads to brain stem herniation and death (7).

Craniocerebral gunshot wounds by areal firing are one of the TBI categories that involve bullets injury falling vertically onto the head after being shot into the sky; the primary cause of this situation is the gravity force that pulls the bullet downward when its muzzle force decreases until reaching the zero. This situation mostly occurs in celebrating events, military and civilian conflicts, or in cases of anger expression in some regions like North Africa, South America, the Middle East, and the middle of Asia. Iraq has been involved in many conventional and unconventional wars in the last three decades, becoming one of the most heavily armed nations. These injuries are frequently non-intentional, and the bullet escapes the sociodemographic space or perimeter customarily organized by the circumstances surrounding the firing. So, the source of firing is apart from the scene of injury (9).

Although the terminal velocity of the bullet is lower than its muzzle, the bullet shot upward may not come back downward. However, it may still cause severe brain injury with a high mortality rate (10). Only bullets that travel at 150 feet/second (46 m/s) to 170 feet/sec (52 m/s) can pierce the skin, while at less than 200 feet/sec (60 m/sec) can pierce the human skull and get entrance to the brain (11,12). In general, the mortality rate of falling bullets, about 32%, is more significant than non-falling bullets, with a 2-6% mortality rate.

The death cases of falling bullets may sometimes mimic the sudden death without apparent cause, specifically in those with prior medical history (3). Managing patients with acute life-threatening traumatic injuries are sometimes challenging and anxious, even for experienced clinicians. To provide an effective and easy approach to management, the American College of Surgeons developed the advanced trauma life support (ATLS) program for initial assessment, stabilization, and management of such injuries starting from brief history. Then assessment of (airway, breathing, circulation, disability, and exposure) focused history with a physical exam to the injured area (such as GCS, scalp laceration, avulsions, and open skull fractures) after that recognize the specific problem, for such injury should refer to radiology including CT scan and finally start with the specific treatment (12).

For craniocerebral wounds, the management may be just conservative. At the same time, if there is any serious indication, the surgery should be done urgently through bullet ablation, debridement of injured tissue, and evacuation of the hematoma. The outcome of patients with falling bullets is based mainly on the age, GCS of admission, pupil reactivity, the course of bullet through the brain, presence of injured structures, and patency of basal cisterns (13). It is important to highlight the relation between psychological reaction toward the gravitational bullet and its prognosis; the magnitude of psychological trauma is frequently disproportionate to the prognosis, which means that whenever the traumatic reaction is strong, the prognostic management outcome will be more than better.

The gravitational bullet is completely different from the cases of homicidal or suicide because the occurrence of the first one is always unexpected, and its prognosis or outcome is better than the other two cases. Regarding traumatic psychological reaction of the family and patients, there is also a difference between them; in the event of a gravitational bullet, they react fearfully more than in other situations because the occurrence is unexpected and unknown. Many cases of gravitational bullets are reported in developed and non-developed countries. However, few papers highlighted these cases in the literature. In our study, we present two cases of gravitational bullets that have an unusual

coincidence in the injury characteristics through their ages, and gender, the site of the inlet was in the midline parietal area. Patients were unconscious on their examination, the Glasgow coma scale (GCS) was 11, 12, with right sided weakness grade of 4.

The location of the bullet inside the brain was confirmed by non-contrast CT scan, which was revealed to be near the left petrous bone and left cerebellar hemisphere for the first and second case, respectively; there was no significant hemorrhage or soft tissue edema. The initial management for both cases in the emergency room was cleaning, redressing, and drug coverage by amoxicillin to prevent wound complication by infection and carbamazepine to prevent epileptic attacks. Conservative treatment was chosen and the parietal were neurologically intact on 6-month follow-up. the similarities and differences of both patients were recorded and documented in Table 1.

Table 1. Similarities and differences between two gravitational bullet cases

Similarities	Differences
Name	Site of inlet: midline parietal area
Age: both were 6 years old.	The GCS: was 11 in the first case and 12 in the second one.
Gender: both were male.	Location of bullet inside the brain: was near left petrous bone in the first case while left cerebellar hemisphere in the second one.
Time of admission: same day	
Knowledge about the injury: patients and families of both cases were unknown about their child's cause of injury.	
Neurological deficit: both had right side grade 4 weakness.	
Pathology in brain CT scan: both patients had not significant hemorrhage or soft tissue edema.	
Initial management in the emergency room by giving amoxicillin and carbamazepine to prevent wound complication and epileptic attacks.	

The occurrence of same injury at different location in different patients with same age, gender, site of inlet and time of admission was incredible that may base on scientific cause or not. Such situation was challenging to be resuscitated and managed at the same time and this circumstance had occurred once till now in our center. In Iraq, there is unstable security situation and huge numbers of traumatic cases can be seen, at the same time the Neurosurgical Teaching Hospital is considered to be one from three centers in Baghdad that receive and manage such urgent cases which represent a further challenge to the health care professionals. So, well-trained team with the appropriate skills for the particular cases are needed to prevent the occurrence of complication in such urgent admission. The problem caused by this coincidence should be addressed from training perspective and there is no previous study highlighted such discussion about this issue before.

Conclusions

The prevalence of aerial firing that result in gravitational bullet injuries is alarming on rise especially in countries of unstable security, the occurrence of this injury may happen in more than one patient at the same time coincidently. So, this issue should be addressed for any department treating such urgent injuries to be trained and prepared in order to prevent or decrease the occurrence of complication and death.

Abbreviations

TBI - Traumatic brain injury,
GCS - Glasgow coma scale,
CT - Computed tomography,
ATLS - Advanced trauma life support.

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Role of extent of resection on the survival of glioblastoma multiforme. A monocentric retrospective study

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Abstract

Background. Glioblastoma Multiforme (GBM) is the most prevalent form of brain cancer. The effect of Extent of Resection (EOR) on GBM survival is controversial. EOR degree, pre- and postoperative tumour volume estimation, and significance to residual tumour volume are still challenged. GBM has a 14-month Overall Survival (OS) rate. There is no evidence of a link between EOR and OS survival. We wish to determine whether GBM tumour removal increases survival.

Methods. At the Regional Center for Neurosurgery and Neurology in Uzhhorod, Ukraine, we conducted a retrospective evaluation of 86 consecutive patients diagnosed with glioblastoma who underwent surgery between January 1, 2010, and December 31, 2020, and who are being followed until January 1, 2022. Patients were selected if they met the following criteria: they were at least 18 years old, they had a diagnosis of glioblastoma (primary, secondary, or recurrent), they were either IDH mutants or wild types, they had an MRI within 2 weeks before surgery, and they had another MRI within 72 hours after surgery. Before and after surgery, we did a volumetric analysis of gadolinium-enhanced T1 MRI scans of the tumour to figure out EOR. Partial resection (PR) is <70%, sub-total resection (STR) is 70-90%, near-total resection (NTR) is 91-99%, and gross total resection (GTR) is >99%. By comparing pre- and post-operative volumes with the EOR, the Kaplan-Meier survival curve and Cox's regression analysis determined the impact of the EOR on survival rates. Many researchers considered a p value of 0.05 or below to be significant.

Results. A total of 86 patients were included in the analysis after being subjected to the criteria used to narrow the pool of potential participants. The average length of time people lived was 15 months. For PR patients, the median survival time was 3 months, for STR patients it was 10 months, and for NTR patients it was 16 months. Patients receiving GTR, on the other hand, had a considerably better outcome, with a median survival time of 36 months. This data demonstrate a direct correlation between EOR and survival rates. It was discovered that EOR improvement affected post-op survival. High EOR patients have a better prognosis for survival. Adjuvant therapy, pre- and post-operative KPS score, pre- and post-operative tumour volume, and gender also contributed significantly to enhanced survival.

Conclusion. Patients with glioblastoma appear to benefit from a more aggressive treatment strategy that combines maximal safe resection with the use of salvage adjuvant therapy. There was a correlation between complete resection (gross total resection) of intracranial GBM and improved survival. Whenever feasible, complete surgical removal of the tumour is recommended.

Keywords
glioma,
GBM,
extent of resection,
glioblastoma multiforme

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Introduction

Glioblastoma multiforme (GBM) is the most common malignant primary brain tumor in adults [1]. There is currently no agreed-upon drug, surgery, or radiation therapy regimen for treating GBM [2]. The surgical component of treatment may consist of anything from a craniotomy to a minimally invasive biopsy (GTR).

However, not all patients have a radical resection [3], despite improvements in 5-aminolevulinic acid-guided intraoperative procedures that increase the EOR that can be achieved during surgery. Large retrospective cohort studies in the field of neuro-oncology have shown better survival with greater EOR in patients with a newly diagnosed GBM, and mathematical modeling of retrospective data implies incremental gains in survival with EORs ranging from 78% to 98% [4,5].

The current set of known predictive markers for glioblastoma includes age, preoperative health performance status, tumor resection, and postoperative adjuvant therapy [6-9]. It is challenging to achieve entire excision of tumors despite evidence that it can improve overall survival (OS) [10,11,12] because to the risk of neurologic function deficiencies such as paralysis, aphasia, and others, which can reduce quality of life and finally limit longevity.

However, reaching this goal of GTR can be challenging due to the peculiarities of brain anatomy and the fear of damaging expressive structures, lowering life quality. Pathologic and radiologic investigations show that GBM often invades multiple lobes and both hemispheres at diagnosis [13-16].

Age, [17] preoperative performance status according to the KPS,[18] tumor location,[19] and preoperative MR imaging characteristics of the tumor,[20] and whether radiation therapy or chemotherapy is delivered affect a patient's prognosis after being diagnosed with GBM. Due to the interconnectedness of these characteristics, a multivariate analysis is required to identify the influence of surgical resection on survival and the subset of patients for whom extensive resection is most advantageous. We wanted to establish if surgical resection, as assessed by preoperative and postoperative tumor volumes, has predictive significance and to examine survival durations in defined patient subpopulations in relation to tumor resection. Finding out what aspects of life are connected to EOR was the driving force behind this research. Time-to-event analysis is a useful tool for studying GBM patients, but it should only be used when the confounders have been properly addressed.

Patients and methods

Materials and methods:

The Uzhhorod Regional Center of Neurosurgery and Neurology cared for 120 patients diagnosed with GBM between 2010 and 2020. For this statistical analysis, we did not include 86 individuals who had been lost to follow-up, had insufficient information, or were younger than 18 years old. Eighty-six patients' medical records were examined in retrospect. The patients who participated in our study broke down as follows: 55 men (63.95 percent), with a mean age of 52.76, and 31 women (36.05 percent), with a mean age of 50.32. Our inclusion criteria meant that these patients' records met our minimum standards for inclusion, thus we used them in our analysis. We performed surgery on adults diagnosed with GBM (astrocytoma, grade IV, as determined by histopathology). Results were tracked until January 2022. Patients were enrolled if a full clinical dossier was available, including information about the patient's background, current condition, previous medical history, radiographic results, surgical specifics, tumor features, and pathology reports.

Diagnosis and follow-up

All patients were judged to have the potential for headache and other regional neurological abnormalities. All patients who met these criteria underwent a preoperative MRI with and without gadolinium. No surgical patient was allowed to wait longer than 72 hours before undergoing an MRI scan. Patients were followed for a median of 36 months (range: 2-144 months) after hospital discharge. All patients were followed up with serial MRI scans. Moreover, data on postoperative quality of life and recurrence was gathered via telephone interviews, clinical examinations, and imaging. The aberrant mass was initially revealed by a T1-weighted magnetic resonance imaging scan, and a resection biopsy was used to confirm the diagnosis, as previously described in the medical literature. Independent neuroradiologists evaluated preoperative T1 contrast-enhanced MRI sequences

to quantify tumor volume. Using T1 contrast-enhanced images in the axial (A), sagittal (B), and coronal planes, the tumor's maximum diameters were measured, and the tumor's volume was then computed using the volumetric approach, as V = (AxBxC/2) cm3. Within 72 hours of the procedure, we took a second MRI scan (post-operative) and used the same volumetric method as before to determine the post-operative volume. Patients who underwent follow-up MRI were monitored for recurrence, clinical symptoms, and mortality through January 2022. Family members, phone calls, and messages were used to verify all deaths.

Data management and analysis

The size of the tumor before surgery (X) was divided into four groups: 1) less than 20 cm3, 2) between 20 and 50 cm3, 3) between 51 and 100 cm3, and 4) greater than 100 cm3, while the size of the tumor after surgery (Y) was divided into groups ranging from 1 to 10 cm3, 20 to 50 cm3, and 51 to 100 cm3. The EOR was calculated using the volume before and after surgery (X-Y/X*100%). After obtaining EOR% once more, we categorized our data as follows: 1) Gross total resection (GTR), 2) Near complete resection (NTR), 3) Sub-total resection (STR), 4) Partial resection (PR), and 5) Biopsy for outcomes with EOR% of 70% or lower. Our study focused primarily on how long patients lived after surgery. The data allowed us to conduct a Kaplan-Meier analysis of survival for GBM patients, with survival time measured in months post-op and separated into groups based on the percentage of endotracheal intubation used (EOR). We used a log-rank test to determine the effect of EOR percentage on survival, and we used COX regression analysis models to determine the effect of pre- and post-op volumes on median survival time.

Results

When strict inclusion criteria were applied, only 86 patients were considered for further study. For the population as a whole, the median survival time was 15 months. Those diagnosed with PR lived an average of 3 months longer than those diagnosed with STR or NTR, while those diagnosed with NTR lived 16 months longer than those diagnosed with PR. But patients who had GTR had a much better outcome, with a median survival time of 36 months. It reveals that there is a linear link between survival and EOR. Longevity post-operation was observed to be affected by an increase in EOR. High EOR predicts a higher life expectancy for patients.

Survival outcomes

Kaplan-Meier Analysis with EOR

The Kaplan-Meier test was used to compare the median post-operative survival times of patients in each EOR group. The significance level for the log rank test was high (X^2 (4) = 118.03, p .001). (Table 1). It demonstrates that there is a statistically significant variation in death rates among EOR categories. Patients who had BIOPSY had a median survival time of 12 months after surgery. Patients with an EOR of 70% or lower had a median survival duration of 3 months. With an EOR of 70-90%, patients had a median survival period of 10 months after surgery. Patients with 91-99% EOR levels have a median survival time of 16 months following surgery. However, for those with an EOR of >99%, the median time to death is 36 months (Table 2). It shows that there is a linear relationship between survival and EOR. Increase in EOR was found to have an influence on the time of survival since operation (Fig 1). Patients with high EOR are more likely to survive longer.

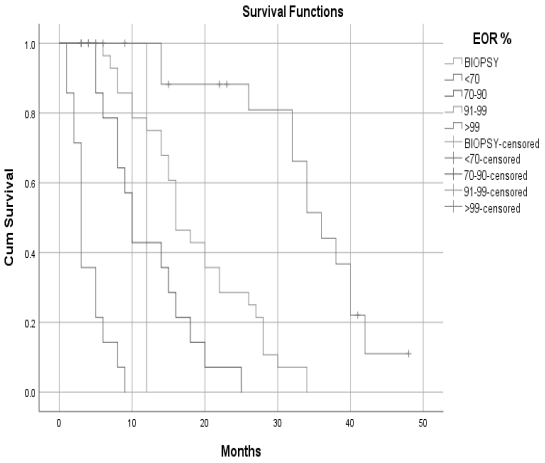

Figure 1. Kaplan-Meier Survival Graph with EOR as Factor Variable for GBM

Table 1. Log Rank Test for EOR and Survival for GBM

Overall Comparisons			
	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	118.032	4	.000
Test of equality of survival distributions for the different levels of EOR %.			

Table 2. Median Survival Time Based on EOR Levels for GBM

EOR %	Median			
	Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
BIOPSY	12.000	.	.	.
<70	3.000	.359	2.297	3.703
70-90	10.000	.926	8.185	11.815
91-99	16.000	1.583	12.897	19.103
>99	36.000	2.416	31.265	40.735
Overall	15.000	1.274	12.503	17.497

Cox Regression with Pre-Op Tumour

Cox regression indicated that there is a significant impact of pre-op tumor volume on survival time of patients as Omnibus test was significant ($\chi 2$ (3) = 20.444, $p < .001$) (Table 3). The results also indicated that patients with pre-op tumor volume of >100 were approximately 7.7 times more likely to die compared to those having pre-op tumor volume of <20 (*B* = 2.041, *SE* = .536, Wald (1) = 14.502, *Odds Ratio* = 7.699, $p < .001$) (Table 4) (Fig 2-3).

Table 3. Omnibus Test for Pre-Op Volume and Survival for GBM

Omnibus Tests of Model Coefficients[b]										
Step	-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
		Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
1[a]	479.921	20.444	3	.000	10.861	3	.013	10.861	3	.013
a. Variable(s) Entered at Step Number 1: PRE-OP VOLUME										
b. Beginning Block Number 1. Method = Forward Stepwise (Conditional LR)										

Table 4. Coefficients for Pre-Op Volume and Survival for GBM Sheet

Variables in the Equation									
		B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
								Lower	Upper
Step 1	Pre-op volume			15.522	3	.001			
	Pre-op volume(1)	.081	.300	.073	1	.787	1.084	.602	1.954
	Pre-op volume(2)	.330	.316	1.088	1	.297	1.391	.748	2.584
	Pre-op volume(3)	2.041	.536	14.502	1	.000	7.699	2.693	22.012

Cox Regression with Post-Op Tumor

The results indicated that there is a significant impact of post-op tumor volume on survival of patients as Omnibus test was significant ($\chi 2$ (3) = 41.181, $p < .001$) (Table 5). Patients with post-op tumor volume of 10.1-50 are 6.7 times more likely to die than those with post-op tumor volume of 0 (*B* = 1.908, *SE* = .564, *Wald* (1) = 11.456, *Odds Ratio* = 6.737, $p < .001$) (Table 6). Similarly, patients with post-op tumor volume of 50.1-100 are approximately 36 times more likely to die compared to those who had 0 post-op tumor (*B* = 3.579, *SE* = .926, *Wald* (1) = 14.946, *Odds Ratio* = 35.841, $p < .001$) (Fig 4-5).

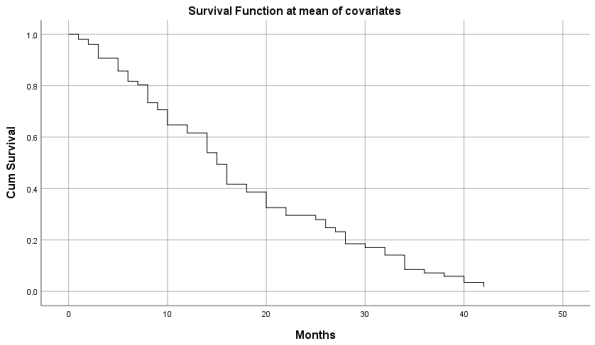

Figure 2. Survival Graph for Pre-Op Volume for GBM

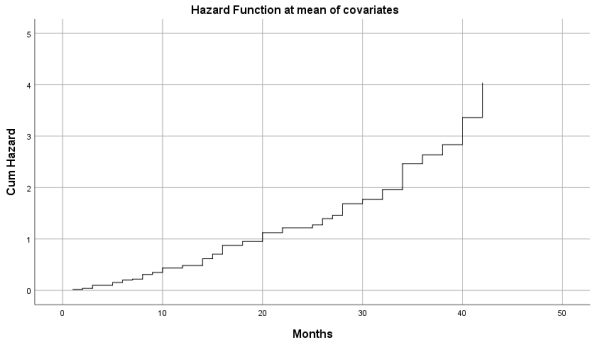

Figure 3. Hazard Graph for Pre-Op Volume for GBM

Table 5. Omnibus Test for Post-Op Volume and Survival for GBM

Omnibus Tests of Model Coefficients[b]										
Step	-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
		Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
1[a]	470.384	41.181	3	.000	20.398	3	.000	20.398	3	.000
a. Variable(s) Entered at Step Number 1: POST-OP VOLUME										
b. Beginning Block Number 1. Method = Forward Stepwise (Conditional LR)										

Table 6. Coefficients for Post-Op Volume and Survival for GBM

Variables in the Equation									
		B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
								Lower	Upper
Step 1	Post-op volume			27.508	3	.000			
	Post-op volume(1)	.521	.470	1.229	1	.268	1.684	.670	4.232

	Post-op volume(2)	1.908	.564	11.456	1	.001	6.737	2.232	20.332
	Post-op volume(3)	3.579	.926	14.946	1	.000	35.841	5.839	220.003

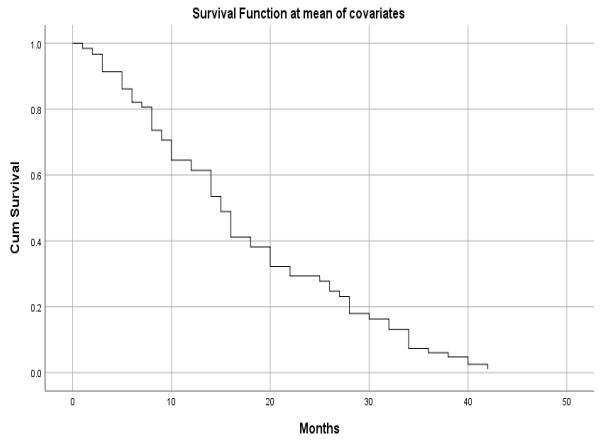

Figure 4. Survival Graph for Post-Op Volume for GBM

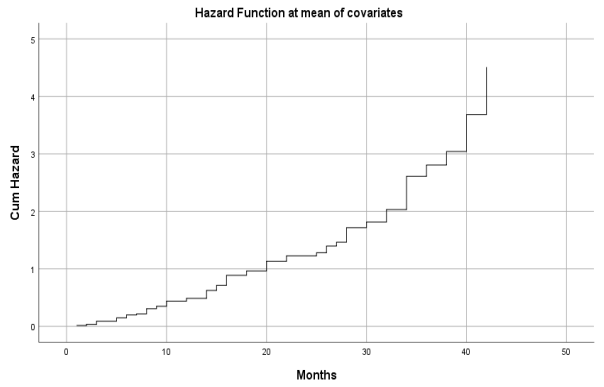

Figure 5. Hazard Graph for Post-Op Volume for GBM)

Discussion

In our study, we reported the median survival time following excision of a glioblastoma multiforme. Our analysis also shows that the size of the surgical resection affects post-operative survival rates. Surprisingly, both the pre- and post-tumor volume were linked to the median survival time following surgery.

The EOR has been demonstrated to be a significant survival predictor [23-27]. Total tumor resection rates for GBM, an infiltrative tumor, have been reported to be between 17.4% and 40% [27, 28]. Multiple variables affect EOR in practice, although no proof has been documented in the literature. Most studies relying on volumetric evaluation conclude that extensive surgical resection is linked to increased survival rates for high-grade gliomas [28,29].

Total resection was also substantially correlated with a tumor volume of 30 mL in GBM. Tumors that are less massive are easier to operate on [29,30]. Brain edema and midline displacement were found to be substantially linked with the size of the GBM, and both adversely affected the extent to which the tumor could be removed. In addition, the prognostic factor most strongly linked to complete resection in GBM was a tumor volume of 30 mL or less. Surgery is easier to do on smaller tumors than on larger ones [31,32]. Brain edema and midline displacement were found to be strongly linked with the size of the GBM and to have a direct impact on the extent to which the tumor could be resected in this investigation [33]. In our data, we found that patients with post-op tumor volume of 10.1-50 cm3 are 6.7 times more likely to die than those with post-op tumor volume of 0 cm3. Similarly, patients with post-op tumor volume of 50.1-100 cm3 are approximately 36 times more likely to die compared to those who had 0 cm3 post-op tumor

We discovered that a substantially higher likelihood of survival was associated with an EOR of 98%. This agrees with the findings of a comprehensive study on the volumetric tumor assessment of 416 GBM patients, conducted by Lacroix et al. at MD Anderson Cancer Center in 2001 [34]. In a study of 92 patients with GBM, Keles et al. [35] analyzed how EOR affected survival. Among the 5 "percent of resection" groups studied, those with a 100% EOR had a median survival time of 93 weeks, whereas those with a 75%-99% EOR had a median survival time of 88.5 weeks. The median survival time is just 62.9 weeks, based on an EOR of 50-74%.

In a review of the literature, Sanai and Berger (2008) contrasted studies that did and did not measure tumor volume (high- and low-grade gliomas). A total of 25 trials supported the idea of maximum EOR, while 13 did not show a clear preference for either resection group [36].

McGirt et al. [37] did a retrospective analysis with a large group of 1215 patients who had malignant glioma. In this study, resections were put into one of three groups based on MRIs taken soon after surgery: near-total resection (NTR), subtotal resection (STR), or gross-total resection (GTR). After a GBM primary tumor was removed, the average survival time was 11 months for GTR, 9 months for NTR, and 5 months for STR. This was linked to GTR vs. NTR and NTR vs. STR. But in our data, 86 patients

were considered for further study. For the population as a whole, the median survival time was 15 months. Those diagnosed with PR lived an average of 3 months longer than those diagnosed with STR or NTR, while those diagnosed with NTR lived 16 months longer than those diagnosed with PR. But patients who had GTR had a much better outcome, with a median survival time of 36 months. It reveals that there is a linear link between survival and EOR.

Adjuvant therapies, such as chemotherapy and radiation, have a significant impact on patient survival, progression-free survival, and overall survival [38-41], and should be included in the standard of care for GBM patients alongside surgical treatment modalities. With a focus on the SVZ and high-dose proton beam treatment, Matsuda et al. [42] found that patients with newly diagnosed GBM who had GTR had a median overall survival of 36.9 months, compared to 26.2 months for patients who got standard radiation therapy.

Kaplan-Meier estimates from our sample agree with those from the literature that link EOR and survival. According to Sanai et al. [43], we saw survival improve linearly with EOR. Full resection should be pursued whenever possible because of the survival data reported here and the evidence supporting the need of optimizing EOR to prolong survival in glioblastoma patients. These promising findings highlight the need to maximize resection with cutting-edge techniques; Future study should focus on GBM microenvironment and, if needed, surgery and despite the difficulty of treating GBM, the latter should not be ignored.

Conclusions

Removing 99% or more of a glioblastoma multiforme (GBM) tumor is associated with improved survival, according to volumetric analyses. We advise a gross-total resection for these patients whenever possible, but never at the expense of their ability to think and move normally. The primary objective of surgical treatment for GBM should be GTR with an emphasis on cerebral function preservation, as an EOR 99% has been found to greatly enhance patient survival. Small pre- and post-operative tumor volume considerably increases survival, as does an EOR of 99%. Patients with glioblastomas now use EOR as a prediction of survival, therefore it's important to learn what factors influence surgical success.

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Delayed intraoperative rupture of clipped aneurysm during the awaking from anaesthesia

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Keywords
microsurgical clipping, intraoperative rupture, inadequate anaesthesia

ABSTRACT

Introduction. Intraoperative rupture (IOR) of an aneurysm is a frightful complication that causes significant morbidity and mortality worldwide. IOR can be attributed to various parameters, including hypertension, increased intracranial pressure (ICP), fragility of the vessels, and inadequate anaesthesia. IOR due to insufficient anaesthesia is scarcely reported in the literature. Here, we describe a re-ruptured anterior communicating artery (ACoA) after incomplete clipping of the neck during craniotomy closure due to unintended early wake-up from anaesthesia with a discussion about the management.

Case description. A 38-year-old male suddenly developed a severe headache, a brief loss of consciousness, and vomiting. Computed tomography (CT) scan showed a subarachnoid haemorrhage in the basal cistern. CT angiography showed a bilobed right ACoA aneurysm with a wide neck and Murphy's teat. The patient was considered for surgery. Clipping of the aneurysm neck was done through two curved clips. During craniotomy closure, the patient started coughing and gagging then a huge IOR was encountered. These events can be mainly attributed to unintended inadequate anaesthesia, particularly muscle relaxants. The bleeding ceased after two suction catheters were inserted, temporary clips were applied, and the readjustment of permanent clips. After surgery, the patient showed a left-sided weakness. His postoperative CT scan showed a right distal anterior cerebral artery (ACA) territory infarction. The weakness improved in the follow-up period.

Conclusion. Delayed IOR due to early awaking from anaesthesia should be considered a potential source of complications and bad outcomes in aneurysm surgery.

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Introduction

Intraoperative rupture (IOR) of aneurysm is a dreadful complication that causes significant morbidity and mortality worldwide [2]. The overall incidences of IOR are 6.7 percent per aneurysm and 7.9 percent per surgery [10]. IOR can be classified according to specific times within the surgery into pre-dissecting, dissecting, clipping, and post-clipping [10]. Regarding its causes, IOR can be attributed to a variety of parameters, including hypertension, increased intracranial pressure (ICP), the fragility of the vessels due to comorbidities, procedural related, and inadequate anesthesia [4,5]. In surgery, re-rupture of the aneurysm intraoperatively due to insufficient anesthesia is scarcely reported. Here, we described a case of a re-ruptured anterior communicating artery (ACoA) aneurysm after incomplete clipping of the aneurysmal neck during craniotomy closure due to unintended early wake-up from anesthesia.

Case description

An otherwise healthy 38-year-old male suddenly developed a severe headache, brief loss of consciousness, and vomiting. The patient presented no weakness and uncontrollable hypertension, and he is a heavy smoker. His initial computed tomography (CT) scan showed subarachnoid hemorrhage (SAH) in the basal cistern. CT angiography exhibiting a bilobed right inferiorly directed ACoA aneurysm (9 mm) with a wide neck and Murphy's teat. The patient was considered for surgery. The endovascular option is usually not applicable in Iraq due to its high cost and absence of proper health insurance.

Following the typical operative steps of the right supra-orbital approach, the aneurysm was identified. The application of a temporary clip was performed on the ipsilateral A1 for proximal control. Clipping of the aneurysm neck was done through two curved clips. However, Severe arachnoid adhesions due to SAH renders the confirmation of complete clipping, which is not feasible. Next, muscle wrapping is applied around the aneurysmal neck to enforce the clipping construct, followed by hemostasis.

During the closure, the patient suddenly moved his head and started coughing (resisting the endotracheal tube). Concretely, a huge IOR has been encountered, and bleeding fills the operative field. These events can be mainly attributed to unintended inadequate anesthesia, particularly muscle relaxants. Here, two suction catheters were used to control the bleeding with the application of temporary clips under a microscope. To be noticed, the permanent clips were moved after the IOR. Eventually, the clips were adjusted to include the whole aneurysmal neck, and the IOR stopped. This takes around seventeen minutes from the moment of rupture. Postoperatively, the patient showed a left-sided weakness grade of 0 on The Medical Research Council of Canada (MRC) scale. His postoperative CT scan showed a right distal anterior cerebral artery (ACA) territory infarction (Figure 1). The weakness improved to grade 4 over the next three weeks. At a 3-month follow-up, the patient was neurologically intact with the imaging showed no aneurysm.

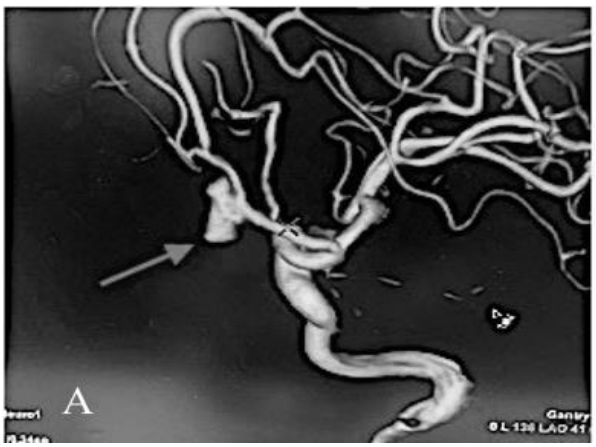
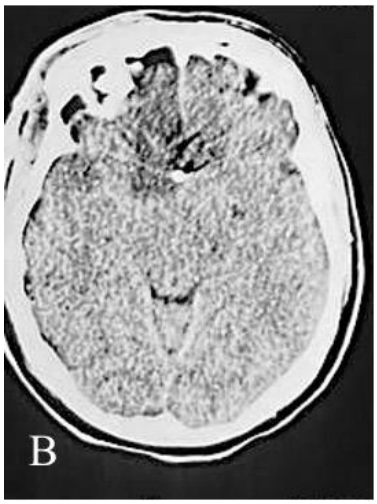


Figure 1. (**A**) (Pre-Operative) 3D constructed imaging of cerebral catheter angiography showing a right bilobed inferiorly directing anterior communicating artery aneurysm (Red arrow) with a superiorly directing Murphy's teat.



(**B**) (Post-Operative) CT scan (axial view) showing ipsilateral anterior communicating artery (ACA) distal territory infarction.

Discussion

The incidence of overall IOR has recently varied between 15 and 50 % [7]. Leipzig TJ et al, reported that the ruptured aneurysms rate is significantly higher than the unruptured (10.7 versus 1.2 %, P <0.0001). Among the 970 ruptured aneurysms treated surgically, 104 of the cases have IORs, and its rate in the ruptured aneurysms constitutes 92 % of all IORs [10]. They also reported that IOR in the ruptured aneurysms during clipping occurred in 49 cases (47.1%) while occurred in 42 cases (40.4%) during the dissection [10]. However, pinpointing the exact cause of IOR is quite challenging.

The location of the aneurysm is a major risk factor for IOR. The ACoA and posterior communicating artery aneurysms and the posteroinferior cerebellar artery aneurysm were more likely to rupture intraoperatively [4,10]. However, Sundt et al, discovered no association between aneurysm site and IOR [13]. Aneurysms originating from the ACoA and anterior cerebral artery had a greater incidence of IOR, with a rate of 36.9%, according to Schramm and Cedzich [12]. In contrast, neither Giannotta et al nor Houkin et al found evidence that ACoA aneurysms had greater IOR rates [7,9]. Middle cerebral artery aneurysms were found to have lower IOR rates in various studies [7]. In our report, the site was inferiorly directed ACoA aneurysm.

Other factors predisposing to IOR can be categorized into preprocedural and intraprocedural [4]. Preprocedural rupture of cerebral aneurysms, though uncommon, can result in devastating consequences with a high fatality rate. This phase of IOR is influenced by factors associated with anesthesia. There is a delicate balance Between mean arterial pressure, ICP, and transmural pressure (TMP). Acute changes in hemodynamics during the induction, surgical incision, and skull pin fixation may raise transmural pressure and may predispose IOR [8]. Sudden coughing or gagging at this stage can cause an abrupt increase in blood pressure and ICP, resulting in a premature rupture [15]. On the other hand, intraprocedural-related factors are primarily determined by arterial wall fragility, which can be influenced by various comorbidities such as a history of coronary artery disease, hyperlipidemia, COPD, and race [6]. IOR can be encountered during different phases of surgery, such as in the pre-dissection phase, dural and arachnoid opening, clipping, hematoma evacuation, or during brain retraction [4,6].

On the other hand, brain swelling is a significant factor for IOR during the dissection phase [9]. During the clipping phase, IOR may occur due to 1) increased turgor in the aneurysm's dome due to pressure transmitted from the neck while applying the clip, 2) detachment of an adherent dome as the clip closure slightly moves the aneurysm, 3) tearing of the neck due to clip misapplication, or 4) shearing of the aneurysmal neck from the parent arterial wall [10]. In our case, the IOR occurred during craniotomy closure (post clipping) which is a very rare phenomenon and an equally challenging situation. The main factor that contributed to the IOR during the closure, in this case, is the unintended inadequate anesthesia resulting in the patient awakening during the craniotomy closure, where he experiences recurrent coughing and gagging.

This was attributed to insufficient muscle relaxant dosing or quality that resulted in a sudden increase in the ICP and eventually the IOR. Despite the patient history of heavy smoking and uncontrollable hypertension, these risk factors may lead to early rupture rather than delayed (post clipping) rupture.

The confirmation of complete clipping is usually difficult due to the challenging anatomy of the ACoA complex and thick adhesions from the SAH, which led to constructing the clipping with muscle wrapping. This step is usually sufficient to protect the aneurysm from rupture. However, in our case, the early waking from anesthesia made the clipping construct fails and resulted in IOR.

The management of IOR has surgical and non-surgical aspects. Surgery-wise, the use of temporary clipping aid in accurate aneurysm clipping and reduce the risk of IOR [1,3,14]. Factors that influence the success of temporary clipping may include aneurysm location, duration of application, and age [11]. The non-surgical aspects of IOR management may consist of cerebral protection, temperature regulation (hypothermia), hemodynamic set points adjustment, and neurophysiological monitoring. These treatment options may all have an impact on temporary occlusion results. However, the current evidence on the usage and benefit of each option is debatable [16]. The prevention of IOR will depend on identifying all potential factors and treating them accordingly. Thus, ensuring IOR-related complication

avoidance and improving the overall patient outcome.

The current literature is mixed regarding the outcome of IOR and its long-term neurological outcomes in the form of stroke. Some studies have found that intraoperative rupture has a negative impact on the outcome; however, these findings should be interpreted in light of a variety of parameters, including size, location, treatment (clipping vs. coiling), age, management strategies, and the surgeon expertise. The outcome of IOR with its re-rupture in our case is an ischemic stroke in the distal circulation territory of ipsilateral (right) ACA due to prolong application of the temporary clip after re-rupture. However, our patient is fortunate enough that the deficit is eventually resolved with rehabilitation.

In summary, patients with delayed IOR during the post-clipping phase can be managed with the typical steps of treating Intraoperative bleeding with a relatively higher risk of complications. Prevention of the delayed IOR can be achieved with adequate anesthesia toward the end of surgery. When construction of the clipping is not straightforward, it may become vulnerable to external circumstances.

Conclusions

Intraoperative rupture during aneurysm surgery closure due to early wakeup from anesthesia should be highlighted as a potential source of complications and poor outcomes. Sufficient anesthesia is necessary to prevent delayed intraoperative rupture.

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Prospective study of selective intra-arterial cerebral infusion and intra-operative local application of carboplatin for recurrent glioblastoma multiformis

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Keywords
GBM, carboplatin, intra-arterial injection, tumoricidal, DSA

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ABSTRACT

Background. High-grade glioma is the commonest primary malignant brain tumour in adults. Intra-arterially selectively infused chemotherapeutic agents into the tumour bulk is being widely trialled recently with promising results.

Methods. This is a prospective study designed between November 2015 and November 2019. Thirty patients were diagnosed with recurrent histo-pathologically proven GBM after one surgery at least and followed by standard radiotherapy and temodal. Patients aged between 37-76 years, 18 males and 12 females were subdivided into group A of 21 patients who underwent intra-arterial delivery of carboplatinand group B of 9 patients who underwent re-surgical resection and local application of carboplatin.

Results. The mean age of the included cases was 55.4 years (range, 37-76 years). Selective intra-arterial injection was performed in 21 cases (70%), while the remaining 9 cases (30%) had local application of carboplatin in the tumour bed. Post-treatment vomiting was reported in 7 cases (23.3%). Significant and partial responses were achieved in 2 cases for each (6.7%). Time to tumour progression had a mean of 19.03 weeks (range, 3 – 30 weeks). After receiving carboplatin, the study cases had a mean survival of 26.5 weeks (range, 6 – 70 weeks). Intra-arterial injection had significantly better results compared to local tumour bed infiltration (p = 0.01).

Conclusion. Although recurrent glioblastoma multiformis has poor survival, intra-arterial delivery of carboplatin may have a slight positive impact on patient survival. The procedure however is relatively safe with manageable complications.

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Introduction

High grade glioma is the commonest primary malignant brain tumor in adults with an incidence of approximately 5 per 100,000[1].

A published phase III randomized trial showed only 9.8% 5-year survival rate for patients with high grade glioma treated by standard protocol of surgery plus radiation and temozolomide. Intra-arterially selectively infused chemotherapeutic agents into the tumor bulk is being widely trialed recently. Some of the trails showed promising results and point to more investment in the field of selective intra-arterial infusion of tumoricidal agents for treatment of malignant glioma[2].Glioblastoma multiformis which is the high-grade glioma targeted in our study like most malignant carcinoma, its cells possess replicative immortality. Normal cells that undergo DNA damage and telomere shortening have the ends of their DNA strands bind together to stop replication and apoptosis commences. Loss of P53 gene results in over expression of telomerase enzyme that is responsible in maintaining DNA strand length, repairing damage and protecting the ends of chromosomes allowing cells to continuously proliferate [3].

The protocol of maximum safe surgery of GBM followed by adjuvant chemo-radiotherapy and adjuvant chemotherapy is established as usual standard management[9]. But local recurrence is expected, with the majority of cases within 6–9 months of 1ry treatment due to resistant stem cells of GBM [10, 11].

Molecular factors such as mutation of P53, methylation of O-6-methylguanine-DNA methyltransferase (MGMT) and MIB-1 labeling index are associated with GBM recurrence [16]. Controversy exists regarding diagnosing recurrence, with histo - pathological examination of tissue as the ultimate diagnosis .On the other hand, the majority of cases having imaging finding indicative of progression could be unfit for a surgery, hindering diagnosis of recurrence difficult [12,13,17,18].

Surgery is still a significant important strategy in management of GBM. On the other hand, only few cases are recognized appropriate for a complete resection. Re-irradiation (ReRT) has improved in the last years [19]. Chemotherapy is utilized by variable groups to improve survival. Despite this , however , patients of rGBM and GBM still remain fated for poor outcomes[15].The blood–brain barrier (BBB) prevents the deliverance of the majority of the chemotherapeutic drugs [20]. On the other hand, the majority of the regimens of management surfaced via single institute retrospective analysis of phase II clinical trials, thus, there is no standard treatment for those patients non responsive to TMZ [21].

Carboplatin is the drug chosen to target recurrent glioblastoma in our study, it is an analogue of cisplatin containing a platinum atom. Once inside tumorous cells carboplatin becomes activated to produce reactive platinum complexes that form inter-strand and intra-strand cross linking of DNA molecules inhibiting DNA synthesis and replication resulting in cellular death. Its action can occur during any phase of the cell cycle (cycle non-specific). In the brain only malignant cells will be affected and normal cells are spared because they are normally non dividing stable cells [4].

Adverse effects of systemic IV Carboplatin use includes**;** Bone marrow depression usually reversible within 30days resulting in anemia 71%, febrile neutropenia18%, thrombocytopenia 25% [5].

Nausea (15%) and vomiting (64%)starts within 6-12 hours after carboplatin injection but can be limited by prior anti-emetics**[5].**Hepatotoxicity may also occur in the form of elevated alkaline phosphatase (24%), elevated AST (15%), elevated bilirubin (5%) [6].

Selective Intra-arterial Cerebral Infusion of Carboplatin involves its delivery to tumor site via balloon assisted endovascular techniques and prior focal disruption of the blood brain barrier by injecting 10cc of mannitol 20% over 2 mins[7].

Pre-infusion studies and post-infusion studies including magnetic resonance imaging with and without gadolinium to detect the effect on tumor size and magnetic resonance spectroscopy to detect the metabolic response are carried out for candidate patients [8]. IA infusion of chemotherapy refers to the regional delivery of chemotherapy to the CNS, that results in a major rise in plasma peak concentration and in the AUC associated with the 1stpass effect. This leads to a 3– 5.5-fold factor major rise in the concentration of intra-tumoral chemotherapy as theses lesions are vascular in nature[27].

The Fischer animal model [29], found that accumulation of platinum in the tumor cells nuclei was elevated by a 20-fold factor (9 ng platinum/g tissue) when infused via an IA route, when put side by side with the IV route (0.5 ng platinum/g tissue) [30].

Clinical trials incorporating patients with GBM who received cisplatin monotherapy or combined with others chemotherapeutic drugs as etoposideor TMZ documented only modest outcomes [27,28].

PATIENTS AND METHODS

This is a prospective study designed for patients have recurrent GBM between November 2015 and Novemeber2019 in Neurosurgery department, Mansoura university Hospitals, Egypt.

This study aims to evaluate the efficacy of single dose selective intra-arterial cerebral infusion and tumor bed application of carboplatin for such patients.is.

Study subject

Thirty patients were diagnosed with recurrent histo pathologically proven GBM after a one surgery at least and followed by standard radiotherapy and temodal. They were all referred from the outpatient neurosurgery clinic. Patients aged between 37-76 years , 18 males and 12 females were subdivided into two groups: Group A(21 patients who underwent intra-arterial delivery of carboplatin), Group B(9 patients who underwent re-surgical resection and local application of carboplatin).

Inclusion criteria

- Age above18 years old
- Patients with recurrent glioblastoma multiforme
- Karnofsky performance status scale 40 or above

Primary outcome measures

Evaluating response to both ways of chemotherapy delivery using imaging techniques.

Secondary outcome measure

1. Post-treatment complications.
2. Survival.

Patients consent

A written informed consent was obtained from all patients before the operation after describing and explaining the details and complications of each approach.

Procedure

Patients were admitted for a variable period of time ranging between 3-7 days. All patients were investigated by a baseline pre and post enhanced MRI and routine lab most notably serum creatinine and a baseline blood picture (CBC). History taking and baseline neurological examination was established as well for all patients. The patients were then grouped into two groups after assessment of the following:

- whether or not they require surgical decompression because of significant radiological mass effect and weather the recurrence is surgically accessible or not
- history of complications (CSF wound leakage, poor wound healing, poor scalp texture after radiotherapy, deep venous thrombosis, pulmonary embolism severe chest infection) related to prior surgery or adjuvant chemo-radiotherapy rendering surgery high risk.

Carboplatin dosage was calculated based upon body surface area calculated using the Mostellar Formula BSA (m2) = SQRT ([height (cm) * weight (kg)] / 3600) Body surface area ($m^{2)}$ = square root ([Height (cm) * weight (kg)] divided by 3600.

The first group (Group A)

Selective Intra-Arterial Cerebral Infusion of Carboplatin was performed at a dose of 400 mg/m^2 BSA. On table, digital subtraction angiography (DSA) was done to identify the tumor vascular bed then endovascular techniques are employed to reach the vascular bed, followed by injection of 10cc mannitol 20% over to 2 minutes, DSA was redone to detect focal hyperemia indicating successful BBB disruption, after that Carboplatin infusion was commenced through a Marathon flow directed micro-catheter usually within the middle cerebral artery(MCA) or anterior cerebral artery(ACA) or one of their branches as well as a small dosage at the carotid bifurcation. Mostly, this was carried out under local anesthetic with the patient instructed to either report increasing headache, nausea, blurring of vision or increasing tingling or numbness or heaviness of an extremity.

The second group (group B)

Local application of Carboplatin during re-surgery at a dose 400mg/m2 BS. After sufficient tumor debulking a cotton pack soaked in Carboplatin solution is placed in the tumor cavity before coagulation of the walls of the cavity for 10mins; the pack is then removed and final hemostasis is

achieved and lastly the cavity is filled with the rest of Carboplatin solution.

Post-procedural follow up MRI with CE was carried out at 2 weeks and at one or two months later. Response to treatment was then determined as a significant response (SR) if CE tumor size was reduced in any of the following MRIs. A partial response PR was considered if the tumor exhibited less mass effect and edema without reduction in the size of CE tumor. A stable disease SD if no changes regarding size or mass effect occurred. A progressive disease PD was established if size or mass effect and edema were increased post procedurally.

Data Analysis

Statistical analysis of the data in this study was performed using SPSS software, version 20 (Chicago, IL). Descriptive data was expressed as means with standard deviation or medians with ranges according to data distribution.

RESULTS

The mean age of the included cases was 55.4 years (range, 37-76 years). We included a total of 18 males (60%) as well as 12 females (Figure 1).

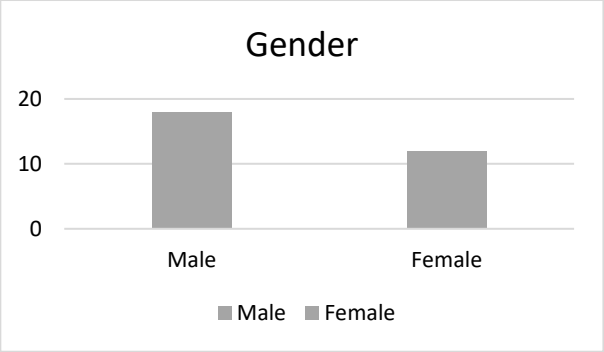

Figure 1. Gender distribution in the study cases.

The Karnofsky Performance Score (KPS) had a mean of 71.33 in the study cases (range, 50-80) (Table1).

Table 1. Analysis of KPS in the study cases

Items		*Study cases n=30*
KPS	Mean ± SD	71.33 ± 8.99
	Median (min-max)	70 (50-80)

Continuous data expressed as mean ±SD and median (range)

All study cases had been commenced on chemo radiotherapy after the first surgery. Evidence of mass effect was present in all study cases (Table2).

Table 2 Analysis of the history of the disease in the study cases.

ID	Hx of radiotherapy	Hx of chemotherapy	Previous surgery	Pre-ttt evidence of mass effect
1	Yes	Temodal	yes	yes
2	Yes	Temodal	yes	yes
3	Yes	Temodal	yes	yes
4	Yes	Temodal	yes	yes
5	Yes	Temodal	yes	yes
6	Yes	Temodal	yes	yes
7	Yes	Temodal	yes	yes
8	Yes	Temodal	yes	yes
9	Yes	Temodal	yes	yes
10	Yes	Temodal	yes	yes
11	Yes	Temodal	yes	yes
12	Yes	Temodal	yes	yes
13	Yes	Temodal	yes	yes
14	Yes	Temodal	yes	yes
15	Yes	Temodal	yes	yes
16	Yes	Temodal	yes	yes
17	Yes	Temodal	yes	yes
18	Yes	Temodal	yes	yes
19	Yes	Temodal	yes	yes
20	Yes	Temodal	yes	yes
21	Yes	Temodal	yes	yes
22	Yes	Temodal	yes	yes
23	Yes	Temodal	yes	yes
24	Yes	Temodal	yes	yes
25	Yes	Temodal	yes	yes
26	Yes	Temodal	yes	yes
27	Yes	Temodal	yes	yes
28	Yes	Temodal	yes	yes
29	Yes	Temodal	yes	yes
30	Yes	Temodal	yes	yes

Regarding the method of carboplatin delivery, selective intra arterial injection was performed in 21 cases (70%), while the remaining 9 cases (30%) had local application of carboplatin in the tumour bed (Figure2).

Post-treatment vomiting was reported in 7 cases (23.3%), whereas epilepsy was present in 8 cases

(26.7%). Additionally, hemiparesis was diagnosed only in 2 cases (6.7%) (Figure3).

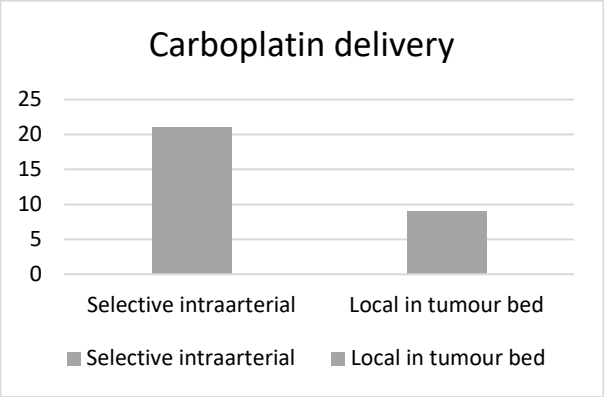

Figure 2. Method of carboplatin delivery in the study cases.

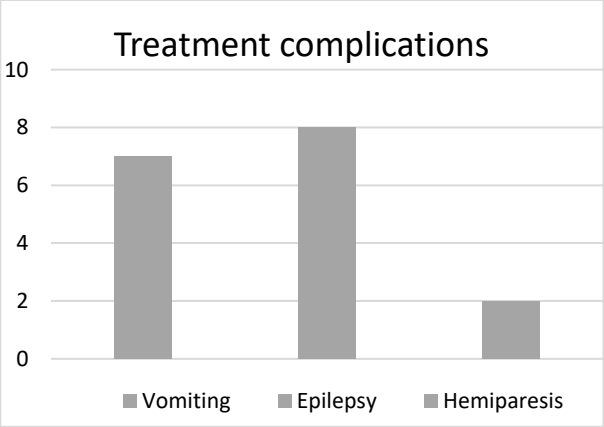

Figure 3. Treatment complications in the study cases.

More than half of the study cases had progressive disease (16 cases – 53.3%), followed by stable disease (10 cases – 33.3%). Significant and partial responses were achieved in 2 cases for each (6.7%)

Time to tumour progression had a mean of 19.03 weeks (range, 3 – 30 weeks).After receiving carboplatin, the study cases had a mean survival of 26.5 weeks (range, 6 – 70 weeks).

On dividing our study cases according to the method of carboplatin delivery, no significant difference was detected between the two groups regarding treatment complications ($p > 0.05$) (Figure 4).

Regarding treatment response, it was evident that intra arterial injection had significantly better results compared to local tumor bed infiltration ($p = 0.01$). All cases in local bed infiltration had progressive disease after treatment, while 2 cases in the other group had significant response (Table3).

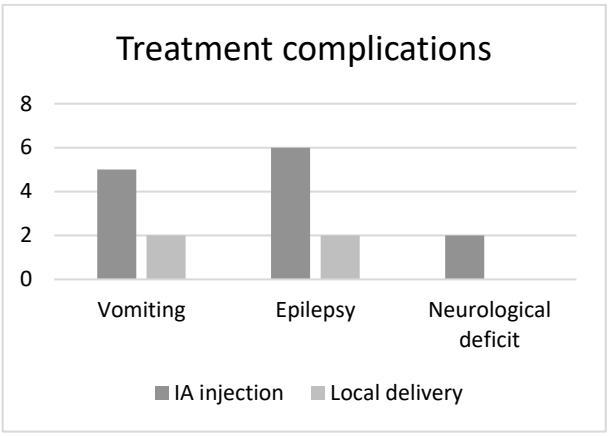

Figure 4. Treatment complications in both study groups.

Table 3. Analysis of response in the two study groups

	Groups		Test of significance
	Group 1 [Selective IA] (N=21)	Group 2 [Local in tumor bed] (N=9)	
Significant response	2 (9.5%)	0 (0%)	$\chi 2$= 11.250 P= 0.010*
Stable disease	10 (47.6%)	0 (0%)	
Progressive disease	7 (33.3%)	9 (100%)	
Partial response	2 (9.5%)	0 (0%)	

P: probability.
Categorical data expressed as Number (%)
x2= Chi-square test

Table 4. Analysis of TTP in the two study groups.

	Groups		Test of significance
	Group 1 [Selective IA] (N=21)	Group 2 [Local in tumor bed] (N=9)	
TTP (weeks)	19 (6.5 -34)	8 (7.5 -11)	t= -1.383 P = 0.178

P: probability. Continuous data expressed as median (IQR).
z= Mann Whitney U-test

There was no significant difference between the two groups regarding time to disease progression (p = 0.178) although the mean TTP was shorter in the tumor bed infiltration group (8 vs. 19 weeks in the IA group) (Table4).

Survival was significantly longer in the IA drug group (35 vs. 14 weeks in the local tumour bed group – p = 0.028) (Figure5).

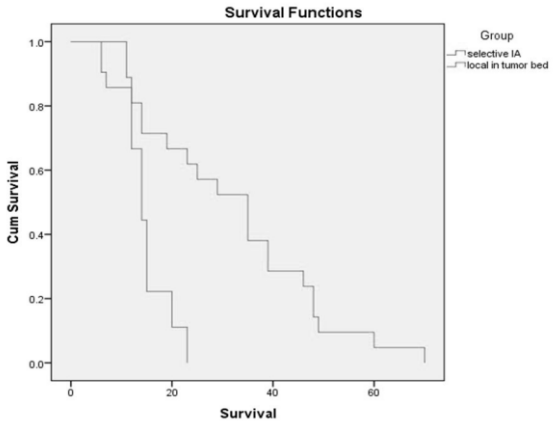

Figure 3. Survival in the study groups.

Discussion

Even with respect to all advances in aspects of treatment, patients with GBM still remain of poor prognosis[33].

During progression, salvage treatments provide highly modest efficiency. Several agents have been tested concerning this topic, providing low rates of response varying from 5 to 20% and median total survival between 5 and 7.5 months [34].

We included an overall of 30 patients in the current study, having a mean age of 55.4 (range, 37 – 76 years). We included a total of 18 males (60%) as well as 12 females.

Another study conducting similar perspective included 24 patients with recurrent GBM. The mean age of the included cases was 44.5 years (range, 26 – 67 years). Investigators comprised 13 males and 11 females in that study [25].

Another study included an overall of 25 patients whose mean age was 37.8 years (range, 22 – 68). A total of 13 males and 12 females were included in that study [26].

In our study, Karnofsky Performance Score (KPS) had a mean of 71.33 in the study cases (range, 50-80). In a similar study, at the time of initiation of therapy, median KPS was eighty. At the time of disease progression, the median KPS was sixty [35].

Another study reported that the mean KPS score was 66.8 (range, 40 – 90) [26].

In the current study, time to tumor progression had a mean of 19.03 weeks (range, 3 – 30 weeks).

Newton and his associates reported that the overall median TTP was 24.2 weeks, while for responders the median TTP was 32 weeks (range 10–174 weeks) [26].

In the current study, more than half of the study cases had progressive disease (16 cases – 53.3%), followed by stable disease (10 cases – 33.3%). Significant and partial responses were achieved in 2 cases for each (6.7%). It was evident that intra-arterial injection had significantly better results compared to local tumor bed infiltration (p = 0.01). All cases in local bed infiltration had progressive disease after treatment, while 2 cases in the other group had significant response.

IA injections depend on drug provision throughout capillary networks and finally to the perfused tissue. The tissue concentrations reached by utilizing a selective IA route are significantly greater than those reached following IV administration [36].It is assessed that above 2000 cases were managed with IA chemotherapy for GBM, most of which are parts of Phases I and II trials. There has been small evidence of considerably better results throughout the course of these trials. Numerous series state increased survival by only some weeks, with neurotoxicity or ocular toxicity appearing in 7-50% of the patients [22].In another study, volumetric analysis of serial MRIs revealed decrease in tumor mass in three out of ten cases. A rise in tumor mass in the range of 23% to 230% was detected in the other 7 cases in time extending from 2.3 to 37.7 months after starting of therapy by carboplatin [25].

Additionally, 68.29% of cases had tumor progression while the remaining cases had stable disease in another study [24].

In another study, that utilized criteria of Macdonald in order to categorize tumor responses radio logically, authors detected three full responses, twenty-two partial responses, fourteen stable disorders and twelve progressions [28].

Follézou et al. showed that carboplatin had a partial response in high grade glioma patients using a dose of 400 mg/m2[31, Clocchlatti et al. achieved a

74% response rate after 250 mg/m2 IA carboplatin infusion[32], and Cloughesy et al. increased carboplatin dose up to 1400 mg/ hemisphere in a dose-escalation study based on cerebral blood flow[37]. Other authors reported that 45 out of 57 patients evaluated with GBM (79%) experienced SD or better. Authors concluded that along with the use of standard treatment guidelines and protocols, intra-arterial chemotherapy with or without osmotic disruption of the BBB is feasible across several centers with a low incidence of catheter-related complications[23].

After receiving carboplatin, our study cases had a mean survival of 26.5 weeks (range, 6 – 70 weeks). Survival was significantly longer in the IA drug group (35 vs. 14 weeks in the local tumor bed group – p = 0.028).In another study, twenty-three patients (out of 46 cases) died after an average of 205 days; 18 were surviving at an average of 324 days from the start of intra-arterial chemotherapy [24].

Stewart et al. reported the results of intra-carotid infusion of carboplatin (200–400 mg/m^2) in 15 patients with either glioblastoma or metastatic tumors. Median survival was 9 weeks [191]. In another study, more than one year survival subsequent to start of IA therapy by carboplatin has been observed in twelve out of the twenty-three cases [25].

Furthermore, in another study, the median total survival from time of diagnosis was twenty-three months with a median survival of eleven months from start of study was detected. The progression-free survival subsequent to therapy was 6.1 months, while a free survival progression of 4.3 months was detected subsequent to the IA therapy [38].

Surgery in case of recurrent GBM may involve either biopsy (for diagnostic purposes) or repeat debulking of tumor. Only approximately 20 to 30 percent of patients with recurrent glioblastoma are candidates for a second surgery [39].

In a patient with recurrent GBM, the indications for a debulking reoperation are still to be definitely recognized. The median survival for cases submitted to operation for recurrent glioblastoma ranges from 8 to 12 months in most series [40.41] and varies from 12 to 18 months for patients with anaplastic astrocytoma [42,43,44]. There is no evidence to suggest that the results of re-surgery are more useful than could be expected with radiation and/or chemotherapy alone. However, selected patients could benefit from reoperation (eg, those with a bulky tumor exerting symptomatic mass effect). Favorable prognostic variables include patients whose age is young, a greater interval from the original operation, and the size of the recurrence as well as extent of the 2nd surgical resection [45,46].

In the current study, post-treatment vomiting was reported in 7 cases (23.3%), whereas epilepsy was present in 8 cases (26.7%). Additionally, hemiparesis was diagnosed only in 2 cases (6.7%). On dividing our study cases according to the method of carboplatin delivery, there was no major difference observed among the 2 groups regarding treatment complications (p > 0.05).Bone marrow suppression (BMS) in the form of thrombocytopenia or leucopenia was not observed in cases in this study and this can be most probably be attributed to the fact that the patients received only a single non incremented dose of carboplatin that the body eliminated too soon before BMS sets in.

In the study conducted by Stewart and his associates, three of four patients who received 400 mg/m2 of carboplatin developed retinal toxicity. Three of 9 patients who received 300 mg/m2 had decreased ipsilateral vision and one other developed worsening of a preexisting hemiparesis. Focal seizures and transient aphasia occurred in one patient each [38].

Follezou et al. described 23 patients with malignant glioma who were treated with an intra-arterial infusion of 400 mg/m2 of carboplatin every 4 weeks. One patient developed central neurotoxicity and another developed a reversible decrease in visual acuity [31].

Cloughesy et al. reported the use of escalating doses of carboplatin (up to 1400 mg/hemisphere) infused either in the supra clinoid internal carotid artery or basilar artery above the anterior inferior cerebellar artery in 21 patients with recurrent glioma. One patient had permanent neuromotor decline. The predominant complication was hemopoietic toxicity. The median survival was 39 weeks [37].

In another series of 51 cases, authors detected one grade III anemia, three grades IV and five grade III thrombocytopenia and three grade III neutropenia according to criteria of the National Cancer Institute common toxicity. These toxicities were all manageable easily. 3 cases of carotid spasms were detected and there was a asymptotic. These spasms were elicited by positioning of the catheter, and all

resolved spontaneously. No cases of neurotoxicity had been detected in this work [28].

Conclusion

Although recurrent glioblastoma multiformis has a poor survival, intra-arterial delivery of carboplatin may have a slight positive impact on patient survival. The procedure however is relatively safe with manageable complications.

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Sellar hematoma as a new potential radiological clue for superior hypophyseal artery aneurysm rupture. A case report

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sellar hematoma, superior hypophyseal artery aneurysm, multiple intracranial aneurysms

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ABSTRACT

Background. In cases of spontaneous subarachnoid haemorrhage (SAH) with multiple intracranial aneurysms (MIAs) detected on angiography, some radiological clues assist in determining the site of a ruptured aneurysm which is bleeding is quite beneficial for the selection of the best treatment strategy.

Case description. We report a case of a 60 years old patient who presented with spontaneous SAH, sellar hematoma, and three different aneurysms detected in angiography. Although the right Posterior communicating artery (PcomA) aneurysms showed Murphy's teat on angiography intraoperatively, we discovered that the right superior hypophyseal aneurysm (SHA) was the source of the index bleeding. Both aneurysms were clipped successfully.

Conclusion. From the preoperative radiological and intraoperative surgical findings, we propose that sellar hematoma on a non-contrast CT scan is a new potential sign to be correlated with superior hypophyseal artery aneurysm rupture.

INTRODUCTION

Cranial computed tomography (CT) scan without contrast is the most sensitive imaging choice for the diagnosis of aneurysmal subarachnoid hemorrhage (SAH), with a sensitivity of 93% within the first 24 hours of onset [14]. However, the CT scan value for determining the primary source of the hemorrhage (i.e., the site of a ruptured aneurysm) has not been demonstrated with some exceptions. Examples of such exceptions include unilateral pure Sylvian SAH and gyrus rectus hematoma as potential clues for Middle cerebral artery (MCA) and Anterior communicating artery (AcomA) aneurysms, respectively [4], propped by an accuracy ratio up to 78% of all cases with challenging multiple intracranial aneurysms (MIAs) [8]. In cases of spontaneous SAH

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with MIAs detected on angiography, these clues are paramount to direct the most appropriate management strategy. In literature, we are the first paper demonstrating the presence of sellar hematoma associated with the typical basal SAH on an initial CT scan as a new potential clue for superior hypophyseal artery (SHA) aneurysm rupture in a case of MIAs.

Case scenario

A previously healthy, 60-year-old female was admitted with the complaint of a sudden severe headache, photophobia, and drowsy associated with meningismus, with no weakness. A brain CT scan disclosed acute SAH with no specific clue except for an apparent sellar hematoma (Figure 1 and 2). The cerebral catheter angiography showed three intracranial aneurysms distributed to (right PcomA, SHA, and left PcomA aneurysms) (Figure 3).

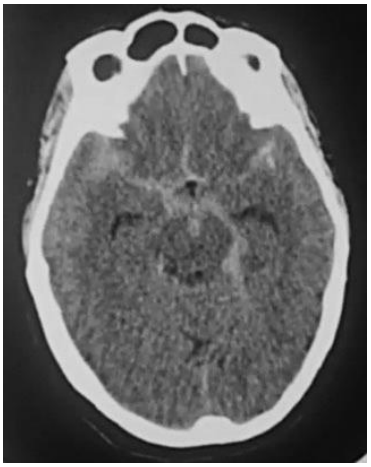

Figure 1. Non-contrast cranial CT scan axial section showed basal subarachnoid hemorrhage with no predominant clue for the location of the ruptured aneurysm.

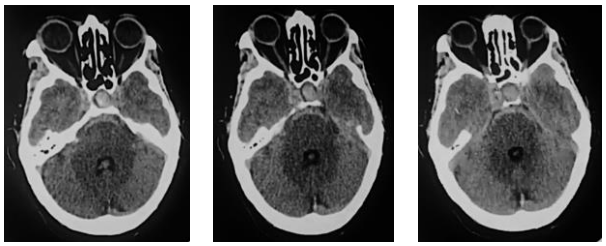

Figure 2. Non-contrast cranial CT scan axial sections (the same CT in figure 1) showing a hematoma in the sella turcica.

According to the angiography, the right PcomA aneurysm was the most probable site of rupture due to having murphy's teat (daughter cyst). Notably, because our country lacked an endovascular facility, the decision was made to manage the case surgically, using the right pterional approach. The patient was in a supine position with the head tilted to the left side, inverted curvilinear skin incision 1 cm posterior to the hairline, and the craniotomy, osteoplastic bone flap, and durotomy were then performed. Following the dissection of the Sylvian fissure, the supraclinoid internal carotid artery (ICA) and the neck of the right PcomA aneurysm were dissected and clipped. Then, intra-operatively, we encountered a huge intraoperative rupture from the right SHA aneurysm after dissection of the clipped right PcomA aneurysm. Eventually, both aneurysms were clipped with no intraoperative or postoperative complications.

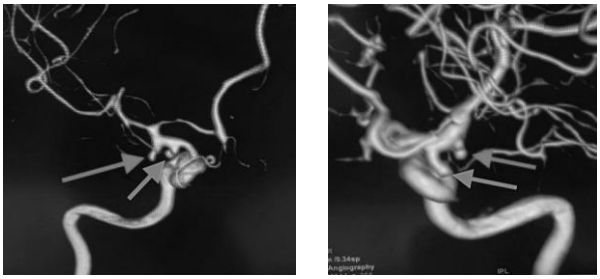

Figure 3. 3D Cerebral catheter angiography. (A and B) Right ICA anterior and left oblique views respectively, showing PcomA (red arrow) and SHA (yellow arrow) aneurysms. The PcomA aneurysm has a daughter cyst.

The postoperative course was uneventful. We decided to follow the left PcomA aneurysm due to its size and configuration (small, shallow, and wide neck). At a 6-moth follow-up, the patient is conscious without any neurological deficit, and the Left PcomA aneurysm is stable.

Discussion

Non-contrast brain CT scan is the most sensitive imaging study in cases with SAH. The CT scan has 100% sensitivity and specificity when a CT is performed within 6 hours of headache onset; sensitivity is about 93% during 24 hours of onset, 80% at three days, and 50% in the first week [1,4]. Ruptured aneurysms constitute the most common etiology for 80% of nontraumatic (spontaneous) SAH, with a 0.4-6% prevalence of intracranial aneurysms in the general population [9,13]. Multiple intracranial aneurysms (MIAs) are evident for 15-33.5% of all patients with aneurysms [5]. Detecting the primary source of aneurysmal SAH is relatively not straightforward and not without difficulty, and this increases the likelihood of re-bleeding in patients

with MIAs. An observational study reported mortality rates for an aneurysmal SAH of 10% to 32% within the first day, 27% to 43% during the first week, and 49% to 56% in the first month after onset [9]. Most deaths occur due to re-bleeding from the same aneurysm; if untreated, re-bleeding occurs in 15% of patients on the first day and in 40% of people by one month after SAH [9].

In cases with MIAs, the definite indication of a ruptured aneurysm is the angiographic dye extravasation (smoking gun) sign [10]. However, this is an uncommon sign that denotes a grim prognosis [5]. Other high-resolution angiographic findings include the area of focal spasm, irregularity in aneurysm shape (Murphy's teat), focal mass effect, and shifts in aneurysm shape upon repeat imaging. If none of the above help, the suspected ruptured one is the largest aneurysm [4,10]. While these signs have a large predictive value for bleeding sources, they are relatively rare [10].

CT scanning can provide suggestions about where the rupture is through potential pivotal clues based on the pattern of a SAH that has been proven effective in 78% of all cases with MIAs, especially for MCA and AcomA aneurysms [4,8,12]. The most evident clue is the thickness of the clot located within the subarachnoid space. Occasionally, an apparent focus clot within the SAH area represents the aneurysm responsible for hemorrhage [12]. Another clue is the hemorrhage distribution pattern, including SAH concentrated in the anterior interhemispheric fissure with or without blood in lateral ventricles or within the gyrus rectus suggests AcomA aneurysm rupture [8,12]. While blood mainly concentrated in unilateral Sylvian fissures is compatible with PcomA or MCA aneurysm on that side [12]. Likewise, SAH predominantly within the prepontine or peduncular cistern suggests a basilar apex or superior cerebellar artery (SCA) aneurysms [8]. Also, patterns of blood primarily in the fourth and third ventricle indicate lower posterior fossa source, such as posterior inferior cerebellar artery (PICA) aneurysm or Vertebral artery (VA) dissection [8,12]. Then, blood primarily within the third ventricle suggests a basilar apex aneurysm [8]. These potential clues are of critical importance for the surgeon to prevent re-bleeding by determining which aneurysm needs urgent surgery and to assist in deciding optimal surgical strategies and procedures. It has been lucid that the most prevalent cause of late re-bleeding is the ruptured aneurysm misidentified at the time of initial surgery [11].

In our case, The aneurysm suspected of being ruptured was the right PcomA aneurysm, as it contained a murphy's teat. A cerebral CT scan showed acute SAH with none of those mentioned above CT clues. CT revealed a concentrated blood pattern within the sella turcica (sellar hematoma) (Figure 1 and 2). Patients with SHA aneurysms are vulnerable to developing MIAs, as in our case [7]. These aneurysms are uncommon entities and more likely to be ruptured at a relatively smaller size than other intracranial aneurysms [7]. SHA aneurysm originates from the supraclinoid segment, where SHAs that supply the hypophysis and optic chiasm consistently arise from the ICA near the lateral aspect of the sella.

Mostly SHA aneurysms fall into two classifications that are divided into sellar and supraclinoid variants. The sellar variant is directed medially over the diaphragma sellae, while the paraclinoid variant projects inferomedially. These projections are directed by the size of the supraclinoid ICA segment and the height of the lateral sellar wall [1,8]. The second classification falls within the sellar variant itself, which has two different varieties: suprasellar or parasellar [6]. The rupture of a parasellar aneurysm typically presents with SAH [1]. In our patient, the SHA aneurysm was a parasellar variant lying over the sellar area, which was the source of sellar hematoma in the initial CT scan. The sudden massive intraoperative rupture of the right SHA aneurysm affirmed that the initial ruptured aneurysm was the same aneurysm, which we did not take seriously despite the clear sign of sellar hematoma.

In literature, here, we are the first to report the concentrated blood pattern within the sella turcica (sellar hematoma) in non-contrast brain CT scan, as a new potential radiological clue to be correlated in cases with SHA aneurysm rupture.

To our knowledge, Cranial CT scanning can show sellar hematoma, and SAH from an SHA aneurysm rupture appears as high-density blood concentrated within the sellar area and suprasellar subarachnoid spaces. With or without typical star shape SAH through major cerebral fissures [8,10]. In contrast, pituitary apoplexy (PA) is a rare and potentially severe clinical condition caused by neurologic deterioration as a result of a sudden expansion of a mass within the sella turcica, usually due to an acute

ischemic infarction or hemorrhage of the pituitary gland [2,10]. On CT scan, it appears an intrasellar mass with hemorrhagic components, seen in 80% of pituitary apoplexy cases as a patchy or hyperdensity in CT scan within a pituitary lesion, leading to sellar enlargement in up to 94 % of cases [2,3]. So these radiological signs of PA, including heterogeneous pituitary mass, are utterly different from clear sellar hematoma with typical basal SAH, as in our case. So the PA can be excluded from the differential diagnosis list for patients with SHA aneurysms and MIAs.

In summary, the sellar hematoma on the initial CT imaging is a possible milestone sign that hands over a significant indication for SHA aneurysm rupture to answer the question of which aneurysm rupture is responsible for this SAH in cases with MIAs.

Conclusion

In cases of spontaneous subarachnoid hemorrhage with imaging showing multiple intracranial aneurysms, the presence of a radiological clue for the source of bleeding in an initial CT scan is quite beneficial for the selection of the best treatment strategy. Sellar hematoma on a non-contrast CT scan is a new potential sign to be correlated with superior hypophyseal artery aneurysm rupture.

Abbreviations

CT; computed tomography,
SAH; subarachnoid hemorrhage,
MCA; Middle cerebral artery,
AcomA; Anterior communicating artery,
MIAs; multiple intracranial aneurysms,
PcomA; posterior communicating artery,
ICA; internal carotid artery,
SCA; superior cerebellar artery,
PICA; posterior inferior cerebellar artery,
VA; vertebral artery,
PA; pituitary apoplexy.

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Intracranial lipoma associated with a subcutaneous lipoma. A rare entity

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ABSTRACT
Intracranial lipomas are rare, frequently asymptomatic, congenital malformations. They are most commonly located in the pericallosal region and are often detected incidentally during neuroimaging studies or postmortem examinations. While other associated brain malformations, most notably callosal agenesis, are frequently reported, association with a subcutaneous scalp lipoma is extremely rare. We present a case of pericallosal lipoma associated with callosal agenesis and subcutaneous lipoma over the anterior fontanelle in a 6-month-old female infant who had excision of only the extracranial mass and has remained asymptomatic from the intracranial mass for the 3 years of follow up.

Keywords
intracranial,
lipoma,
subcutaneous

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INTRODUCTION

Intracranial lipomas are rare benign congenital lesions[1]. They are most commonly located in the deep interhemispheric fissure especially in the pericallosal region[2]. Intracranial lipomas are frequently asymptomatic and are therefore usually detected incidentally during neuroimaging studies or postmortem examinations[3, 4]. They are often managed conservatively because the surgical risks outweigh the benefits[1, 5, 6, 7]. They are frequently associated with other brain malformations, agenesis or dysgenesis of corpus callosum being the most common[7]. Extremely rare however is the association of intracranial lipoma with a subcutaneous lipoma[8, 9]. We present a case of an asymptomatic giant intracranial lipoma associated with corpus callosal agenesis and a midline frontoparietal subcutaneous lipoma.

CASE PRESENTATION

A 6-month old female infant was referred to us with a midline frontoparietal subcutaneous mass. The mass was noticed at birth and was increasing in size progressively. The child was otherwise well; the developmental milestones were within normal limits. The neurological examination findings were also essentially normal. The mass measured

8cm by 6cm by 5cm with the anterior half over the anterior fontanelle (Fig. 1). Other systemic examination findings were normal. Brain MRI showed a large inter-hemispheric pericallosal and a fronto-parietal subcutaneous mass, hyper intense on T1 (Fig. 2) and T2 weighted images but hypointense on T2* and fat suppression sequences (Fig 3) consistent with lipoma. There was no connection between the intra and extra-cranial masses. The extracranial mass was excised completely. No cranial defect was found at surgery, confirming no connection between the extra-cranial and intra-cranial masses. The excised subcutaneous mass was confirmed to be a lipoma on histology. She is currently being followed up at the outpatient clinic. She remains asymptomatic 3 years after surgery and her developmental milestones are within normal limits.

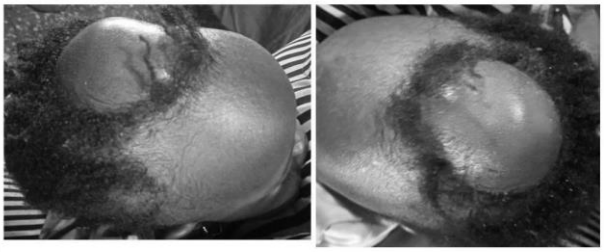

Figure 1. Clinical photograph showing the frontoparietal subcutaneous lipoma.

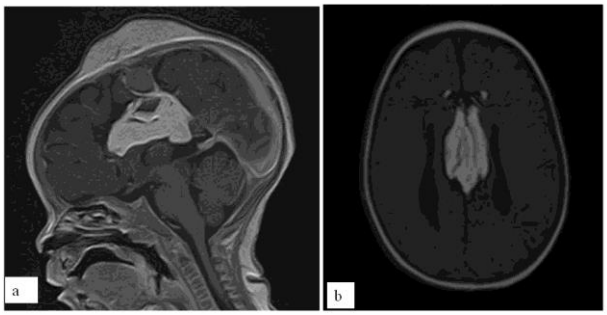

Figure 2. A sagittal (a) and axial (b) T1weighted MRI showing hyperintense frontoparietal subcutaneous and an interhemispheric pericallosal masses.

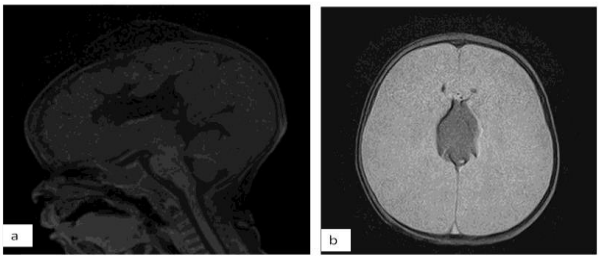

Figure 3. Sagittal T1 fat suppressed (a) and axial T2* weighted MRI images showing hpyointense lesion consistent with lipoma.

Discussion

Intracranial lipomas are rare benign congenital lesions accounting for 0.06% to 0.46% of all intracranial tumours[1]. They result from abnormal persistence and mal-differentiation of the meninx primitive during the development of the subarachnoid cisterns and hence are congenital anomalies rather than true neoplasms[10]. About 45% of cases occur in the pericallosal region, 25% in the quadrigerminal cistern and 15% in the suprasellar cistern. Other locations include cerebellopontine angle cisten (9%), Sylvian cistern (5%) and rarely on the surface of the cerebral hemispheres[8, 11, 12, 13]. The callosal lipomas can be divided into two types: a bulky tubulonodular anterior variety which is associated with forebrain and rostral callosal anomalies and a ribbon-like curvilinear posterior lipoma with a normal or nearly normal corpus callosum[14].

More than half of intracranial lipomas are associated with other malformations of the central nervous system including callosal agenesis or hypogenesis (the most common), encephalocele, spinal bifida, vermian hypoplasia, absent septum pellucidum and cortical malformation[1, 13]. Interhemispheric lipoma associated with a subcutaneous lipoma as in our patient is however extremely rare[8]. In these cases, the intra and extracranial masses may have no connection with each other, may be connected by a fibrous lipomatous stalk or may be continuous with each other through cranium bifidum[6, 15, 16, 17].

Intracranial lipomas are usually asymptomatic, often discovered only incidentally on neuroimaging[3, 4]. When symptomatic, symptoms depend on the location of the lipoma and may include epilepsy, persistent headache, ataxia, psychomotor retardation and cranial nerves deficits[7, 18, 19, 20]. The imaging findings in intracranial lipomas are characteristic. On cranial CT scan, lipomas are markedly hypodense (density of -50 to -100 HU) with frequent areas of calcifications, the latter being more common in the pericallosal lipomas[4, 7]. On MRI, they have high intensity on T1 and T2 weighted images and low intensity on T2* weighted and fat suppression images without contrast enhancement[21, 22].

Radical surgical excision is usually contraindicated because of attendant high morbidity and mortality due to high vascularity and strong adherence to surrounding tissues[6, 7]. Stable or asymptomatic lesions are managed conservatively[1, 5]. In patients with epileptic seizures, anticonvulsant therapy is the treatment of choice[23]. Our patient had excision of only the subcutaneous fat and is being followed up at the outpatient clinic.

Conclusion

Intracranial lipomas are rare congenital malformations and are often asymptomatic. Intracranial lipoma associated with subcutaneous lipoma is extremely rare. Children with subcutaneous scalp lipoma should have brain imaging to look for possible associated intracranial lipoma and other associated anomalies.

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A giant A4-A5 distal anterior cerebral artery aneurysm treated with microsurgical clip reconstruction

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Keywords
distal anterior cerebral artery aneurysms, giant cerebral aneurysms, microsurgical clip reconstruction

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ABSTRACT

Background. Aneurysms of the distal anterior cerebral artery (DACA) are uncommon; they often form near the pericallosal-callosomarginal junction and are typically small. To our knowledge, giant DACA aneurysms developing from the more distant parts of the anterior cerebral artery (ACA), A4-5, have been described only once in the literature.

Case description. A 66-year-old gentleman reported with a brief loss of consciousness followed by weakness in his right lower leg. The patient was admitted with a Glasgow Coma Score (GCS) of 15. A computed tomography (CT) scan of the head revealed a left hyperdense mass in the frontal parasagittal supracallosal region. Contrast MRI revealed a heterogeneously enhancing mass measuring 35x30x25 mm. CT angiography (CTA) revealed a small saccular aneurysm on the posteromedial aspect of the mass, perpendicular to the vertical plane of the coronal suture, corresponding to the A4-A5 junction of the left ACA. Through a left paramedian craniotomy, a modified anterior interhemispheric approach that was more posterior than the conventional projection was performed. A giant partially thrombosed was found. The aneurysm was resected, and the neck was reconstructed using four clips placed on top of them to enhance the clipping force over any remaining thrombus. The patient recovered as expected and was neurologically intact three months later.

Conclusion. Giant distal anterior cerebral artery (DACA) aneurysms found in the A4-A5 segment represent a pathologically uncommon phenomenon. Due to the rarity of giant aneurysms at this location, their reporting is important to inform meticulous pre-operative planning.

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Introduction

The distal anterior cerebral artery (DACA) represents all segments of the anterior cerebral artery (ACA) distal to the anterior communicating artery. DACA aneurysms constitute up to 6% of all intracranial aneurysms (7, 10, 12, 13, 16, 17, 19, 21, 23, 29, 30, 31). Most of these aneurysms arise from relatively "proximal" segments of the ACA; mainly the pericallosal-callosomarginal junction (69-82%). DACA aneurysms arising from the more distal A4 and A5 segments of ACA are very rare; representing less than 0.6% of all intracranial aneurysms (7, 13).

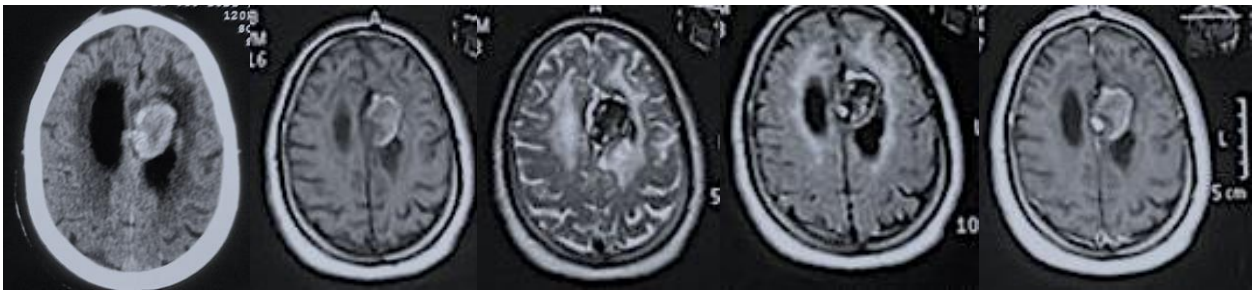

Figure 1. Pre-operative imaging. Axial sections of non-contrast head CT scan **(A)** as well as T1 (**B**), T2 (**C**), FLAIR (**D**), and gadolinium-enhanced T1 (**E**) MRI show a left frontal parasagittal (supracallosal) mass that appears hyperdense on CT and heterogenous on MRI, with contrast enhancement of the posteromedial part of the lesion.

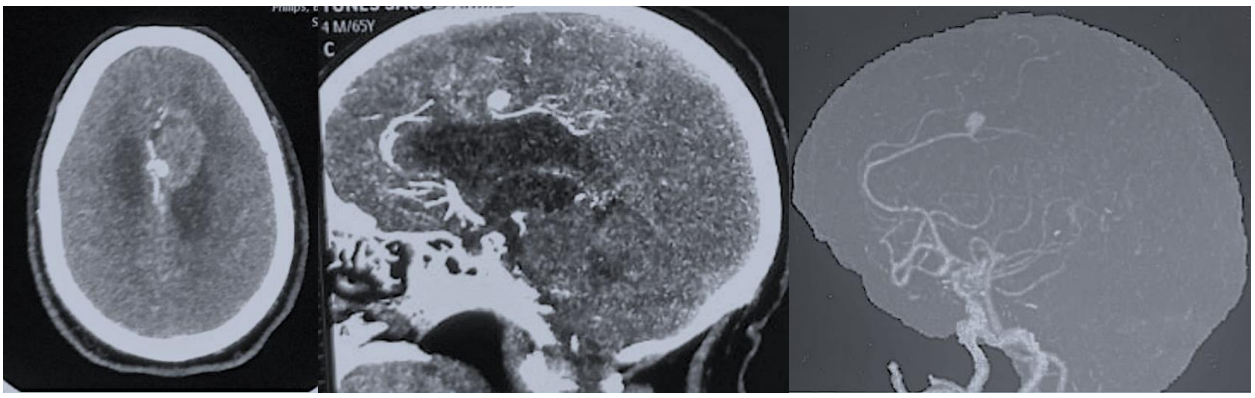

Figure 2. Pre-operative CT angiography with **(A)** Axial section, (**B**) sagittal section, and (**C**) 3D reconstruction. A superiorly-directing aneurysm (8x4 mm) can be seen at the A4-A5 junction, with 2 distal A5 branches arising from the neck of the aneurysm. The location of this aneurysm corresponds to the posteromedial enhancement of the mass on MRI.

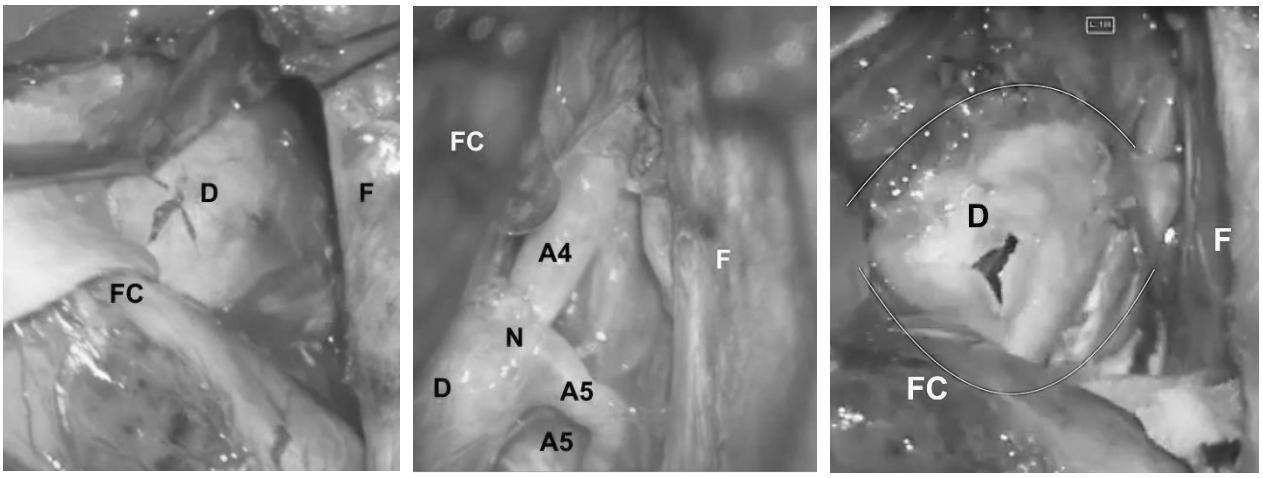

Figure 2. Intraoperative images for a pericoronal anterior interhemispheric approach. A: Initial exposure showing the large dome of the aneurysm (D), which is opened for internal decompression and thrombectomy. B: The borders of the giant dome of the

aneurysm are outlined in yellow with an incision in the center for internal decompression and thrombectomy. C: Following internal decompression of the thrombosed aneurysmal dome, the pericallosal artery (A4) and the distal branches (A5) can be seen, as well as the neck (N) and dome (D) of the intraluminal portion of the aneurysm, prior to the application of clips. Hemosiderin staining can be seen deep within the interhemispheric fissure, denoting old hemorrhage from the aneurysm.
FC; frontal cortex, D; aneurysmal dome, F; falx cerebri, N; aneurysmal neck, A4, A5; segments of pericallosal artery.

Giant DACA aneurysms (those measuring more than 25 mm in their greatest diameter) are extremely rare and mostly fusiform in nature. To the best of our knowledge, saccular aneurysms of the A4-A5 segments have only been reported once in the literature (4). Giant partially thrombosed aneurysms usually have been proposed to result from accumulative intramural bleeding, enlargement, and thrombosis (11). Therefore, endovascular treatment can often be ineffective, as it only eliminates the intraluminal portion of the aneurysm, leaving the mural portion liable to more bleeding, enlargement, and even rupture (2). This makes microsurgical management of giant partially thrombosed A4-A5 aneurysms more appealing, and raises several surgical challenges owing to their location posteriorly within the anterior interhemispheric fissure, the configuration of their domes, involvement of proximal and distal vessels within their base, and the mass effect which can significantly alter the anatomy of this region (11-13).

All of the aforementioned highlights the importance of this paper, in which we report the second case of an idiopathic, giant, saccular, partially thrombosed A4-A5 DACA aneurysm, discussing the treatment nuances of such extremely rare lesions.

Case description

A 66-year-old male with a history of a prior ischemic stroke and infrequent seizures on treatment presented with sudden temporary loss of consciousness, followed by right lower limb weakness. He had complained of a poorly localized headache for the past few months with no other symptoms. On admission, the patient had a Glasgow Coma Score (GCS) of 15 and his neurological examination was normal apart from weakness of the right lower limb, medical research council (MRC) grade 4.

Head computed tomography (CT) scan revealed a left frontal parasagittal supracallosal hyperdense mass with relative ventriculomegaly (figure 1A). Magnetic resonance imaging (MRI) of the brain showed a left extra-axial heterogenous lesion measuring 35x30x25 mm, with contrast enhancement of its postero-medial part (figure 1B-1E). CT angiography (CTA) showed a small (8x4 mm) saccular aneurysm perpendicular to the vertical plane of the coronal suture, corresponding to the A4-A5 junction of the left ACA (figure 2). Digital subtraction angiography was not performed as modalities were not available. This aneurysm corresponds to the contrast-enhancing part of the lesion. A pre-operative list of differentials for the mass was made to help with planning for the procedure, and included cavernous malformation, hematoma, neoplasm, and lastly, or a thrombosed part of an aneurysm.

The patient was operated via a left paramedian craniotomy bisected by the coronal suture, and a modified anterior interhemispheric approach that was more posterior than the classic projection, to target the more posterior A4-A5 junction. Splitting of the fissure revealed a yellowish, solid wall of a thrombosed part of the aneurysm, corresponding to the giant mass on preoperative imaging (figure 3A). A rupture site on the lateral surface of the dome (the part of the dome facing the cerebral hemisphere). The fissure also showed thick adhesions and hemosiderin staining, indicating previous rupture of the aneurysm. The thrombosed part was opened, the thrombus evacuated and the mass internally decompressed to allow easier exposure of the active part of the aneurysm and identification of proximal and distal vessels (figure 3B). Proximal control of the ipsilateral A4 was gained, and the aneurysm was resected, followed by reconstruction of the neck with 2 opposing tandem clips and 2 additional clips stacked over them to reinforce the clipping force over any residual thrombus. Patency of proximal and distal vessels was visually confirmed by micro-doppler. No intraoperative angiography was available in the facility.

Postoperatively, the patient was fully conscious with no new neurological deficits. A post-operative CTA showed complete occlusion of the aneurysm, with preservation of the distal branches of the ACA. The patient was put on antiepileptic medications and discharged 7 days post-operatively, One- and 3-month follow-up appointments revealed a

neurologically intact patient, with complete resolution of the headache and no seizure activity.

Discussion

The ACA is anatomically divided into 5 segments; A1 through A5. The first "pre-communicating" segment arises at the bifurcation of the internal carotid artery, and ends at the anterior communicating artery. The second segment extends to the region between the rostrum and genu of corpus callosum, and its continuation curving anterior to the genu is the A3 segment, which ends at the rostral part of the body of corpus callosum. A4 and A5 segments comprise the horizontal portion of the ACA, and are demarcated by the virtual plane of the coronal suture. A2 to A5 segments are collectively referred to as DACA (12, 13).

The majority of DACA aneurysms (69-82%) are located within the A3 segment, usually around the callosomarginal-pericallosal junction. DACA aneurysms of the A4-A5 segments are rare, representing 5-20% of DACA aneurysms, and less than 0.6% of all intracranial aneurysms (7, 10, 13, 16, 17, 19, 21, 23, 29, 30, 31). A4-A5 aneurysms arise anywhere along the horizontal portion of the ACA back towards the spleneum of the corpus callosum, and the distal cortical branches that arise from the termination of that segment (12).

On the other hand, giant cerebral aneurysms are in themselves a rare occurrence, representing about 5-8% percent of all intracranial aneurysms (13). With a predilection for the posterior circulation, they tend to arise in large vessels, such as the basilar tip, and are usually partially or completely thrombosed (15, 27). A possible explanation for this predilection is the increased flow rate at these locations, which increases the shear forces acting on the vessel wall, increasing the risk of damage and microdissection (32). Such vascular injuries accumulate damage on the vasa vasorum of the vessel, causing repeated intramural bleeding and progressive swelling of the aneurysm into giant sizes (2). Additional factors such as trauma or infection also play a role in the pathogenesis of these giant aneurysms (13). There are less than 40 cases of giant DACA aneurysms reported in the literature. The majority of those are fusiform in nature, and none are located at the A4-A5 segments (5, 12, 14, 15, 20, 25). A possible explanation of this scarcity would be the decreased flow rate at the distal cerebral circulation, reducing the wall shear stress on the arterial walls and making damage, dissection, and formation of giant aneurysms less likely (8, 18, 32). As such, the finding of an idiopathic, giant saccular aneurysm at this location is surprising, counter-intuitive, and raises questions regarding the possible underlying pathomechanisms of these lesions.

The natural history of giant thrombosed aneurysms tends to differ from that of intracranial aneurysms in general. In many cases, they present due to their size as mass lesions compressing adjacent structures and causing subsequent neurological deficits, as was the case in our patient (11, 13). However, according to the International Study of Unruptured Intracranial Aneurysms (ISUIA) trial, 50% of giant intracranial aneurysms tend to rupture within 5 years of presentation (28). It is worthwhile to mention that the ISUIA does not report on the presence of intramural thrombosis within these giant aneurysms, which might be an important determinant of the risk of rupture (11).

The pathomechanism responsible for the formation of giant partially thrombosed aneurysms implies that bleeding from those lesions is often extraluminal (2). This entails that endovascular management of giant partially thrombosed aneurysms can be ineffective (14, 27). Endovascular coiling can obliterate the lumen of the aneurysm, but the aneurysm continues to grow despite a patent lumen as their growth is related to intramural hemorrhage from the vasa vasorum (2, 14). Moreover, coiling DACA aneurysms in general poses a challenge compared to other aneurysms, given the distal location of these lesions (12). As such, resection of these lesions with neck reconstruction or trapping with bypass may provide the best outcomes (15, 22, 31).

The scarcity of giant saccular DACA aneurysms in general, all the more so of giant A4-A5 aneurysms, makes for little experience in the surgical management of such complex lesions. DACA aneurysms are treated via an anterior interhemispheric approach (12). The interhemispheric fissure presents a very narrow and challenging surgical corridor, leaving little room for instrument manipulation and limiting the possible angles for application of clips (12, 13). To complicate things, A4-A5 aneurysms, laying way posterior to the genu of corpus, are difficult to identify in the fissure due to lack of any reliable landmarks at this location

(12). This posterior location also means that the classic anterior interhemispheric approach needs to be modified, to project more posteriorly and reach the lesion.

We recommend creating a paramedian craniotomy centered around the coronal suture, to ensure direct access to the A4-A5 junction. Additional factors also affect the anatomy of the fissure, such as the presence of a large intracerebral hematoma displacing the structures, subarachnoid hemorrhage causing thick adhesions within the fissure, and the variation in the anatomy of A4-A5 segments and their branches (12, 13, 26). Fortunately, internal thrombectomy and decompression of the giant thrombosed part in our case was used reliably to reach the active part of the aneurysm and identify proximal and distal vessels. An alternative would be the use of neuronavigation to help guide the surgeon into the lesion (15).

Resection of the thrombosed part of the aneurysm ensures the arterial dissection and potential intramural space is treated (2, 11). Simple clipping is sometimes difficult in these cases, due to their wide-base and the presence of atherosclerotic plaques at the neck, preventing full closure of the clip (9). This can be overcome with multiclipping techniques like booster clips and tandem clipping, as well as techniques like clip compression and microendarterectomy (3, 9, 24). In our case, clip reconstruction of the neck was possible, due to thorough evacuation of the thrombosis, absence of calcification at the base of the aneurysm, and favorable configuration of the pericallosal artery, which allowed for the application of the clips without impinging proximal and distal vessels. When neck reconstruction is difficult, microsurgical trapping of the parent vessel with intracranial-intracranial bypass can be attempted. This technique ensures cessation of blood flow both into the wall and the lumen of the aneurysm while maintaining blood flow to distal vessels.

Many bypass techniques for the reconstruction of the ACA and its branches have been studied (30). However, these intracranial-intracranial bypass techniques require a high level of surgical dexterity, practice, and experience, and carry a possibility of failure and complications, particularly when dealing with small-caliber vessels such as those of the distal ACA (1, 6, 12, 13).

Giant partially thrombosed aneurysms of the A4-A5 segments of the ACA are extremely rare lesions. We report the second such case in the literature. The intramural -rather than intraluminal- nature of these lesions makes them poor candidates for endovascular therapy. The anatomical disruption they cause within the anterior interhemispheric fissure makes the already difficult task of locating them more daunting. Excluding these lesions from the circulation without compromising proximal and distal branches of the pericallosal artery is challenging, and requires a comprehensive knowledge of the pertinent anatomy, as well as experience in microvascular procedures like neck reconstruction and intracranial-intracranial bypass techniques.

Conclusions

Giant partially thrombosed A4-A5 aneurysms are an extremely rare disease entity. Their pathological mechanisms are likely to be different from small saccular aneurysms, and their location poses unique surgical challenges. Surgical management must be adjusted to deal with these challenges and ensure the best outcome.

Abbreviations

DACA: Distal anterior cerebral artery.
CT: Computed tomography.
MRI: Magnetic resonance imaging.
CTA: CT angiography.
GCS: Glasgow Coma score. MRC: Medical research council.

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Total intracranial migration of ventriculoperitoneal shunt. A case report with literature review

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ABSTRACT

Background. The ventriculoperitoneal shunt is a common treatment for hydrocephalus. There are several complications associated with it. Shunt failure is one of the most frequent complications, but total intracranial shunt migration is quite uncommon. The exact cause of shunt migration is unknown, but several factors are thought to play a role.

Case presentation. A 10-month-old boy was diagnosed with total intracranial migration of a ventriculoperitoneal shunt (Chhabra type). We used neuroendoscopy to remove this intracranially migrated shunt and implanted a new ventriculoperitoneal shunt (Medtronic type) on the opposite side. He had a favourable clinical outcome.

Conclusion. Total intracranial shunt migration is an uncommon complication which is most likely caused by increased intraperitoneal pressure, strong head movements, and insufficient shunt fixation. Better patient handling combined with appropriate operative technique would be the best way to prevent shunt migration.

Keywords
ventriculoperitoneal shunt, intracranial migration, shunt complications

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INTRODUCTION

The ventriculoperitoneal (VP) shunt is one of the most commonly performed procedures in neurosurgery. It is frequently used to treat various types of hydrocephalus, namely obstructive, non-obstructive and normal pressure hydrocephalus. Kausch performed the first VP shunt surgery for the treatment of hydrocephalus in 1908.[1] Shunt failure is the most common complication in 40-70% of cases. Shunt blockage, infection, overdrainage, underdrainage, and visual field defects are all possible complications associated with the VP shunt. Shunt migration is another complication and it can migrate to various parts of the body such as the thorax, stomach, liver, gallbladder, umbilicus, colon, and urinary bladder but complete intracranial migration of the VP shunt has rarely been reported.[2]

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anterior cerebral artery (DACA) represents all segments of the anterior cerebral artery (ACA) distal , saccular aneurysms of the A4-A5 segments have only been reported once in the literature (4). Giant partially thrombosed aneurysms usually have been proposed to result from accumulative intramural bleeding, enlargement, and thrombosis (11). Therefore, endovascular treatment can often be ineffective, as it only eliminates the intraluminal portion of the aneurysm, leaving the mural portion liable to more bleeding, enlargement, and even rupture (2). This makes microsurgical management of giant partially thrombosed A4-A5 aneurysms more appealing, and raises several surgical challenges owing to their location posteriorly within the anterior interhemispheric fissure, the configuration of their domes, involvement of proximal and distal vessels within their base, and the mass effect which can significantly alter the anatomy of this region (11-13).

All of the aforementioned highlights the importance of this paper, in which we report the second case of an idiopathic, giant, saccular, partially thrombosed A4-A5 DACA aneurysm, discussing the treatment nuances of such extremely rare lesions.

Case description

A 10-month-old boy came in with a history of progressive head enlargement, multiple episodes of vomiting, and decreased oral intake for the last three days. He had congenital hydrocephalus and received a medium pressure VP shunt (Chhabra type) surgery at another hospital when he was one month old. He recovered well from his VP Shunt surgery. On clinical examination, he had an enlarged head, as well as a tense and bulging anterior fontanelle. Engorged scalp veins were prominent and there was a sunset sign present. The shunt chamber could not be felt. Routine investigations became the norm. An X-ray shunt series revealed abnormal cranially migrated VP shunt assembly (Figure. 1, A&B). Computed Tomography (CT) brain plain revealed grossly dilated ventricles, subdural hygroma, and the assembly of VP shunt within the ventricles (Figure. 2 A&B). The previous burrhole site was explored during surgery. The burrhole was approximately 1x1 cm in size. Through the burrhole, a rigid paediatric neuro endoscope was inserted, and the entire shunt was seen coiled up within the lateral ventricle. An endoscopic grasper was used to remove it. On the opposite side, a new VP shunt (Medtronic type) was implanted. He recovered well postoperatively, improved clinically, and was discharged in the next three days.

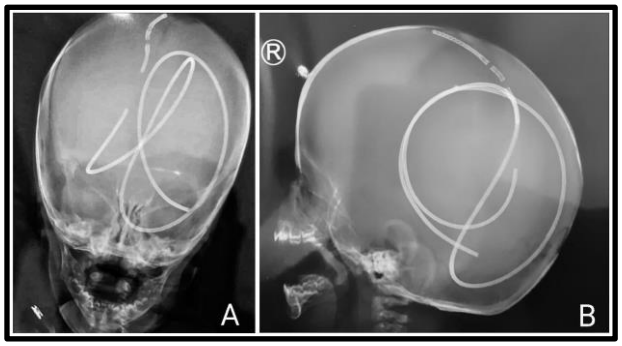

Figure 1. A&B: X-rays skull AP and lateral views showing total intracranial migration of ventriculoperitoneal shunt.

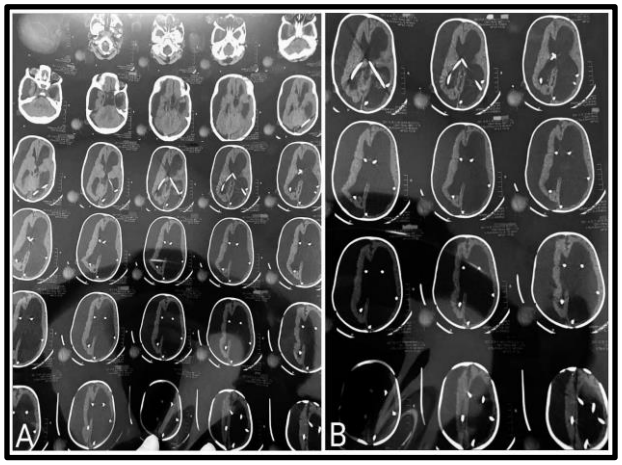

Figure 2. A&B: CT scan brain plain axial views showing gross hydrocephalus, subdural hygroma and intracranial migration of ventriculoperitoneal shunt.

Discussion

VP shunts may be simple to perform but they are associated with intracranial and intra-abdominal complications. Meningitis, ventriculitis, sepsis, and subcutaneous infection are intracranial complications, whereas pseudocyst formation, intestinal volvulus, and spontaneous bowel perforation are intra-abdominal complications. One of the complications of VP shunt is the migration of the shunt. This migration typically occurs distally, into the thorax, diaphragm, heart, pleural cavity, breast, stomach, gallbladder, liver, umbilicus, inguinal canal, hernia sac, scrotum, urinary bladder, urethra, vagina, colon, and rectum, among other places.[3] On the other hand, proximally total

intracranial migration of the VP shunt is a very uncommon complication.

Total upward intracranial migration of VP is estimated to be between 0.1 and 0.5 percent.[4] We discovered twenty-eight cases of total intracranial VP shunt migration to date after conducting a thorough literature review (Table.1). Although the precise cause of this unusual complication is unknown, a number of factors are thought to play a role in proximal shunt migration. Paediatric patients are particularly vulnerable to shunt migration due to the shorter distance between the peritoneum and the cranium. This short distance, combined with violent, uncontrolled head movements, could result in mechanical shunt displacement.[5] Another possibility for proximal shunt migration is insufficient distal shunt fixation or detachment due to rapid growth in the early stages of life.[6,7] Furthermore, the thin cortical mantle, large ventricles, and wide fontanelles produce intracranial pressure close to atmospheric pressure, whereas abdominal pressure remains positive in comparison to atmospheric pressure. This produces a pressure gradient, which can cause the shunt to suction towards the cranium. This drastic complication can be avoided by tightly securing connector sites of the shunt to the periosteum and by avoiding large dural openings and burrholes.[5] It is interesting to note that numerous additional case reports list comparable patient-related characteristics, such as malnutrition, younger age, a thin cortical layer, and severe hydrocephalus, all of which may be connected to upward shunt migration.[4,5,6,7] In most VP shunt insertions, a burrhole is made in the occiput to provide a straight path up from the peritoneum because it is the simplest mode of insertion, but as the path is straightforward, it may contribute to cranial shunt migration.[8]

Due to their affordability, Chhabra shunt systems are commonly used in our area. This type of shunt system contains a valve and a reservoir, but the valve is cylinder-shaped and it has a diameter that is just a little bit larger than the shunt tube. It appears that this type of shunt system is more vulnerable to migration. In our case, we used a neuro endoscope to remove the shunt assembly through a burrhole to avoid craniotomy-related morbidity. The safe removal of the shunt tube and prevention of unintentional pulling, which could result in choroid plexus bleeding, are additional benefits of using a neuro endoscope. In the future, as an alternative to shunting techniques, the use of endoscopic third ventriculostomy and choroid plexus cauterization should be acknowledged and encouraged in suitable patients.

Table 1. Twenty-eight previously reported cases of intracranial migration of ventriculoperitoneal shunt in literature.

S. no.	Authors' Name	Year reported	No. of cases reported
1	Mori K et al.[6]	1975	1
2	Gariejo JA[9]	1979	1
3	Villarejo F et al.[10]	1979	1
4	Drigo P et al.[11]	1983	2
5	Young HA et al.[7]	1983	2
6	Eljamel MS et al.[12]	1995	1
7	Ammar A and Nasser M[8]	1995	1
8	Abou el Nasr HT[13]	1998	1
9	Gupta PK et al.[14]	1999	1
10	Dominguez CJ et al.[15]	2000	1
11	Acharya R et al.[16]	2002	1
12	Shimzu et al.[17]	2002	1
13	Umberto Pereira C et al.[18]	2004	1
14	Nadkarni TD et al.[5]	2007	1
15	Oluwole KE and Abiodun AA[19]	2007	1
16	Ali MN et al.[20]	2008	1
17	Agarwal A and Kakani A[21]	2011	1
18	Shahsavaran S et al.[2]	2012	2
19	Naik V et al.[22]	2013	1
20	Malhotra A and Malhotra M[23]	2015	1
21	Sharma R et al.[4]	2015	1

22	Gundogdu EB et al.[24]	2017	1
23	Shrestha R et al.[3]	2018	1
24	Mehtab H et al.[25]	2021	1
25	Deo RC et al.[26]	2022	1

Conclusions

Total intracranial migration of the VP shunt in individuals with severe hydrocephalus is an uncommon but significant event. The optimum strategy for limiting shunt migration would involve better shunt attachment to the pericranium and peritoneum, a frontal burrhole instead of an occipital burrhole, and a smaller burrhole opening. Additionally, parents should be informed about warning signs and shunt related issues and should receive continuous follow-up. A nationwide analysis of the prevalence as well as incidence of risk variables for VP shunt migration is advised to direct future therapeutic practises.

Abbreviations

VP: Ventriculoperitoneal
CT: Computed Tomography

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Electroencephalographic findings in autistic non-epileptic children

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ABSTRACT

Despite the well-acknowledged link between autism spectrum disorders (ASDs) and epilepsy, the prevalence and significance of electroencephalogram (EEG) changes in epileptic children in the absence of clinical seizures remains underdetermined.

Aim. The primary goal of this study is to report the prevalence of EEG abnormalities in non-epileptic or pre-epileptic autistic children, investigate their association with a set of pre-determined risk factors, speculate on their significance, and direct future research efforts.

Methods. A case-based sampling for children diagnosed with autism was done. Only patients without a history of epilepsy and those under the age of 15 were included. All patients underwent an EEG study. Children with abnormal EEG findings (case group) were compared to age-matched controls with normal EEG findings using a set of pre-determined factors.

Results. A total of 38 patients were enrolled in our study, of whom 31.6% (n=12) had abnormal EEG readings. Of those, the presence of the following EEG abnormalities were noted – each being present in two patients: frontal sharp waves, frontal slowing, temporal slowing, bitemporal slowing, frontal sharp waves, and generalized sharp waves, Frontal intermittent rhythmic delta activity (FIRDA). Patients with abnormal EEG findings were more likely to have a positive family history of epilepsy and/or autism, with odd ratios of 28.05, and 12.62, accordingly.

Conclusion. Aberrant brain connectivity patterns have been observed in non-epileptic ASD patients, and our findings support these findings. Furthermore, we believe that gender, mother's age, mode of delivery, and speech abnormalities could all have an impact on the EEG results. However, more research is needed to expand on these findings.

Keywords
autism spectrum disorders, EEG

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INTRODUCTION

Autism spectrum disorders (ASDs) are a broad category of complex neurodevelopmental disorders. ASDs are distinguished by impaired social interaction, deterioration of language skills, and a limited

repertoire of interests. Individuals appear to differ in terms of cognitive function decline, the presence of intellectual disability, behavioral changes, and symptom severity and onset. Despite extensive research, the biological factors that govern autism development remain unknown.

The first report on the possible neuronal links of ASD was published in 1943; Kanner examined 11 children with ASD in this report; three of them had seizures, three were mute, and five were macrocephalic (5). However, it was not until 1970 when Gubbay et al. published the first report on EEG abnormalities in children with ASD (3). Since then, there has been extensive research into the evidence of neurological involvement in ASD subjects.

Despite the fact that epilepsy is associated with an increased morbidity rates, the clinical significance of EEG abnormalities in the absence of seizures has not been established. Nonetheless, the majority of the evidence points to the presence of hyperexcitable brain regions, which may contribute to aberrant connectivity within the brain, resulting in faulty functioning of neural circuits in the brain responsible for basic information processing (1,4).

As a result, the primary goal of this study is to report the prevalence of EEG abnormalities in non-epileptic or pre-epileptic autistic children, investigate their association with a set of pre-determined risk factors, speculate on their significance, and direct future research efforts.

Methods

Setting

The study was conducted at Baghdad Teaching Hospital (BTH), Medical City, spanning the period September 2018 to March 2019.

Patient sampling

A case-based sampling for children diagnosed with autism was done. Only patients without a history of epilepsy and those under the age of 15 were included. Patients with medications that might affect EEG readings were excluded. All patients underwent an EEG study. Written informed consent was obtained from the parents for participation in the study. EEG findings were interpreted by two consultant neurophysiologists. The study was approved by the ethics committee of Baghdad Medical City.

Study design

This is a case-control study. Children with abnormal EEG findings (case group) were compared to age-matched controls with normal EEG findings. Both groups had a definite diagnosis of autism and no clinical history of epilepsy.

Study aim

The study was conducted to examine the association between the patient's age, gender, mode of delivery, maternal age at delivery, family history of epilepsy or autism, socioeconomic status, and speech difficulties.

Statistical methods

The odds ratio (OR) was calculated to determine the association of each of the abovementioned factors with the presence of abnormal EEG findings. Fisher exact test was used to determine the significance of association. The significance level was set at a p-value of < 0.05.

Results

A total of 38 patients were enrolled in our study, of whom 31.6% (n=12) had abnormal EEG readings. Of those, the presence of the following EEG abnormalities were noted – each being present in two patients - : frontal sharp waves, frontal slowing, temporal slowing, bitemporal slowing, frontal sharp waves, and generalized sharp waves, Frontal intermittent rhythmic delta activity (FIRDA).

The age range was (3-10) years with a mean of 6.1 years. The male-to-female ratio was 32.6. As for the mother age, 26.3% (n=10) were 35 years or older. The percentage of patients that were delivered by cesarean section was 47.4% (n=18). A family history of epilepsy and autism was documented for 10.5% (n=4), and 5.3% (n=2) of the patients, respectively. Speech difficulty was present in 47.4 (n=18) of the participants, and 10.5% (n=4) of them belonged to high socioeconomic group. (Table 1). Patients with abnormal EEG findings were more likely to have a positive family history of epilepsy and/or autism, with odd ratios of 28.05, and 12.62, accordingly. The other parameters understudy, including patient and mother age, gender, mode of delivery, socioeconomic status, and the presence of speech difficulties failed to achieve statistical significance in this study. (Table 2).

Table 1. Patients' characteristics.

Characteristic	% (n)
Age range	3-10 yrs
Age mean	6.1 yrs
M:F	32:6
Mother age of 35 +	26.30% (10)
C/S delivery	47.40% (18)
FHX epilepsy	10.50% (4)
FHX autism	5.30% (2)
High SES	10.50% (4)
Speech difficulty	47.40% (18)
EEG +	31.60% (12)

Table 2. Odds ratios, 95% confidence intervals, and P-values for the association of abnormal EEG readings with the parameters understudy.

	OR	95% CI	P-value
Gender (M)	0.9	0.14 - 5.81	1
Maternal age (35+ years)	0.45	0.08 - 2.5	0.5
Delivery (CS)	3.2	0.76 - 13.5	0.2
FHX of epilepsy	28.05	1.37 - 576.2	0.002
FHX of autism	12.62	0.56 - 285.6	0.03
SES (high)	0.2	0.01 - 4.03	0.3
Speech difficulties	1.4	0.35 – 5.4	0.73

Discussion

The high rate of co-existence of epilepsy and ASD is well recognized, pointing to a possible shared pathophysiology. However, the prevalence, nature, and clinical implications of abnormal EEG findings in the absence of clinical seizure activity in ASD children have received less attention. The existence and potential value of such abnormalities are indicated by data from scattered reports, but their exact nature and clinical significance remain unknown.

In our cohort of 38 non-epileptic ASD patients, 31.6 percent (n=12) had abnormal EEG findings, which is consistent with the published literature. Having a positive family history of epilepsy and/or autism showed a significant association with the presence of abnormal EEG findings among the factors studied. The non-significance of the other factors may be due to the fact that the study is underpowered, and expanding the scope of the study to include more participants or a control group such as children with ASD and epilepsy may reveal statistically significant associations. Follow-up is also required to determine the persistence or absence of the observed EEG abnormalities.

Aside from the abovementioned, well-designed longitudinal studies are also required to determine the role, if any, of these bioelectrical abnormalities in the development and natural course of autistic symptoms, language, and cognitive decline. The presence of epileptic discharges in patients with non-epileptic ASD may represent an endophenotype with treatment and prognostic implications, and it aids in the precise characterization of study samples.

The results of this study as well as the available literature over the span of the previous four decades highlights a set of key questions to be addressed. First, is the cost-effectiveness of extensive initial EEG, and/or follow-up EEG in non-epileptic ASD patients justified? Currently, there is no data on the cost-effectiveness of EEG testing in children exhibiting ASD symptoms. However, if early intervention can prevent or ameliorate a life-long disorder, even a low yield may be justified not only economically, but also in terms of avoided suffering for patients and their families.

The second question is whether the lack of an epileptic discharge detected by EEG or magnetoencephalography (MEG) technology indicates the absence of such an abnormality. According to data published by Small (6) and Frye et al. (2) different study designs that used alternate detection protocols, such as EEG monitoring units, will result in higher yield. Furthermore, comparing electroencephalography (EEG) and magnetoencephalography (MEG) readings reveals that the latter is superior, with detection rates of 68 percent and 82 percent, respectively. This means that while an EEG test may produce "negative results," this does not imply that there is no abnormality, and it also highlights the significant false negative problem, which is especially common in EEG studies.

Another unanswered question is whether the nature of EEG abnormalities influences the course of clinical symptomatology and whether the location of the EEG abnormality is causal. Hashimoto et al. found that the coexistence of frontal and temporal lobe abnormalities had a significant impact on the rate of emergence of autistic features in their study.

Unraveling the clinical significance of these findings in terms of how they might inform treatment decisions is critical, and it is the starting point for answering the questions raised above.

Conclusion

Aberrant brain connectivity patterns have been observed in non-epileptic ASD patients, and our findings support these findings. Furthermore, we believe that gender, mother age, mode of delivery, and speech abnormalities could all have an impact on the EEG results. However, more research is needed to expand on these findings.

Abbreviations

ASDs: autism spectrum disorders;
EEG: electroencephalogram;
FIRDA: frontal intermittent rhythmic delta activity;
MEG: magnetoencephalography.

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Cerebellopontine angle tumours: clinico-radiological features and surgical outcome. Single institutional experience

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ABSTRACT

Object. Our aim is to demonstrate the various aspects of clinical-Radiological presentation and surgical Outcome with association to the tumour size concerning cerebellopontine angle (CPA) tumours.

Materials and method. This is a prospective study of 40 patients at the Department of Neurosurgery, Jayarogya Group of Hospitals, GRMC Gwalior, M.P. India. All of the patients were pre-operatively evaluated with either non-enhanced and enhanced computerized tomography (CT) or Magnetic-resonance (MR) imaging or both.CPA tumours (predominantly acoustic neuroma) that underwent surgical removal using a suboccipital retro sigmoid approach over a 2-year period (June 2019 to May 2021).

Results. There was a female preponderance. The most common presentation was Sensorineural hearing loss (90%) followed by Headache (67.5%). The majority of cases of Vestibular Schwannoma have heterogenous enhancement with cystic component.65% of patients have large (26-40mm) size tumours and facial nerve preservation is 86.4% in medium size tumours (10-25 mm).and Incidence of post-postoperative of facial nerve palsy is more in Giant size tumour (> 40mm) so Positive association between size of lesion and Incidence of Post-operative facial nerve palsy. CSF leak occurs in 6 patients and postoperative Hydrocephalus occur in 2 patients and Mortality occurs in 3 patients.

Conclusion. CP angle Tumor was common in middle age group, with the incidence in females slightly more than in males. The majority of lesions were of large size (26-40mm). Most of the patients on admission had a non-serviceable hearing. Heterogeneous enhancement with cystic components was found in most of the lesions. Gross-total excision was one in the majority of cases and vestibular schwannoma was the most common histopathological lesion obtained. Facial nerve palsy was the most complication and as the size of the lesion increased, the possibility of facial nerve palsy also increased post-operatively. Overall mortality is 7.5%.

Keywords
cerebellopontine angle tumours,
tumour size,
facial nerve,
surgical outcome

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INTRODUCTION

CP Angle tumors account for 5-10% of intracranial tumors. [1, 2] Most Cerebello-pontine Angle tumors are benign, with over 85% being vestibular schwannomas (acoustic neuromas). Primary malignancies or metastatic lesions accounting less than 2% of neoplasm in the CPA.

CT and MRI are widely used radiological methods for cerebello-pontine angle imaging. The main radiological diagnostic goal is the description of the relation of the tumor to IAM, the brainstem and cerebellar hemispheres. The second line basic information is if the lesion is extra-or intracerebral.

The options available for management includes Observation, Surgery, Stereotactic Radiosurgery, Fractionated radiotherapy. Some patients might also be candidates for a combination of these therapies. The ideal treatment is total excision of tumor. Several approaches and techniques are available for the resection of CPA tumors, including trans labyrinthine, retro sigmoid, suboccipital, retro labyrinthine, trans cochlear, transotic and middle fossa approaches. Surgery improves quality of life in patients but each approach is associated with postoperative complications like mortality, hematoma, pneumocephalus, cranial neuropathies, cerebellar dysfunction, brainstem complications, infections, CSF leaks etc.

The Suboccipital retro sigmoid approach is a popular method of excising CPA tumors. Advantages of this approach include a low complication rate, particularly with regard to facial nerve function, and total tumor removal in the vast majority of cases. Moreover, the technique is safe and effective, even with the largest of tumors.

Technical advances in surgery and anesthesia have revolutionized the results of surgery in cerebellopontine angle lesions with reduced mortality and morbidity. Use of intra-operative nerve stimulators and intraoperative evoked potentials have made the resection of the lesions possible along with preservation of cranial nerves.

Material and methods

This is a prospective study of 40 patients at the Department of Neurosurgery Jayarogya group of Hospitals , G.R.M.C. Gwalior, M.P. were carried out and undergoing surgical removal using the suboccipital retro sigmoid approach. All of the patients were pre operatively evaluated with either non-enhanced and enhanced computerized tomography (CT) or Magnetic-resonance (MR) imaging or both. Computed tomography characteristics reviewed included tumor density and homogeneity, presence and type of contrast enhancement and calcifications. MRI examination was performed on different imaging units, using a field strength ranging between 0.5 and 1.5 tesla. The magnetic resonance (MR) image parameters used for this study included signal homogeneity and intensity (T1-,and T2-weighted images), presence and type of contrast enhancement, calcifications, and lesion margins, characteristic of the tumor on Diffusion weighted (DWI) and Absoluted diffusion coefficient(ADC)sequences. Hearing assessment was done with the help of Puretone audiometry (PTA) analysis pre-operatively in all patients and were divided into serviceable and non-serviceable category. Gardner Robertson hearing classification scale was used. Speech discriminations coreless than 50% and PTA value>50dB were defined as non-serviceable hearing. Fundoscopy was done in all patients with the help of direct ophthalmoscope to assess the papilledema pre-operatively and was graded according to modified Frisen scale. In all patients, radical excision was attempted. Operating microscope was used in every case. The patients were maintained peri-and postoperatively on steroids. Operative data, including surgical approach, extent of removal, morbidity, and mortality, were evaluated. The completeness of tumor removal was assessed intraoperatively and with postoperative CT and MR imaging. Extent of removal was divided into gross total removal, near-total removal and sub-total removal.

Discussion

In general CPA tumors are divided in to acoustic and non-acoustic tumors. The main factor under scoring the importance of accurate preoperative diagnosis is the different surgical approach for vestibular schwannomas and the other tumors. There is general agreement that completeness of tumor resection and preservation of the facial nerve are the major neurosurgical goals. An appreciation of the vascular and cranial nerve micro anatomy and the relationships between neurovascular structures and the tumor are essential for achieving optimal surgical results.

In our study majority of patients 21-30yr, 32.5% [Table-1] Females in our study were 57.5% whereas the males were 42.5%. Arismendi G, et al. showed a 2:1 female to male ratio with a median age was 48+/-12. 7years. Faramarz Memari, et al. [3]. showed that the mean age was 49 years and there was a slight male predominance of 55%.Joarder MA,etal. [4] showed the maximum incidence between 30-50yrs

with female predominance of 55%. Maheswararao Y.V.N, et al. [5] showed that the highest incidence of extra axial Cerebo-pontine angle tumors' were found in 51- 60 years age group with 70% being females.

Table 1. Distribution of case according to age

Age (yrs)	Total patients	Percentage
0-20	2	5
21-30	4	10
31-40	13	32.5
41-50	11	27.5
51-60	8	20
61-70	2	5

Table 2. Distribution of cases according to clinical presentation

Clinical Findings	Vestibular Schwanoma	Meningioma	Epidermoid cyst	Abscess	Total patients	Percentage
Sensorineural Hearing loss	30	3	2	1	36	90
Cerebellar signs	20	2	1	0	23	57.5
Headache	22	3	1	1	27	67.5
Trigeminal dysfunction	15	2	0	0	18	45
Facial Dysfunction	17	2	1	0	19	47.5
Papilloedema	7	3	0	0	11	27.5
Tinnitus	14	2	0	0	16	40
Pyramidal signs	9	1	0	0	10	25
9,10,11 nerve Dysfunction	5	1	0	0	6	15

In our study sensorineural hearing loss was observed in 90% cases, cerebellar signs were present in 57.5% cases, headache was present in 67.5%,trigeminal dysfunction was present in 45%, facial nerve dysfunction was present in 47.5%, papilledema was present in 27.5%, tinnitus was present in 40%,pyramidal signs was present in 25%, 9,10,11 nerve dysfunction was present in 15% [table-2] .Our Pure tone audiometry results of serviceable hearing were in 22.5% cases and non-serviceable hearing in 77.5% cases[table-3]. Faramarz Memari, et al,& Joarder MA, et al [3,4] showed same results of clinical presentation.

Table 3. Distribution of cases according to pure tone audiometry

Class	Vestibular Schwanoma	Meningioma	Epidermoid cyst	Abscess	Total patients	Percentage
I &II (Serviceable)	3	3	2	1	9	22.5
III & IV (Non Serviceable)	28	2	1	0	31	77.5

Table 4. Distribution of cases according to size of lesion & anatomical preservation of facial nerve

Size	Total patients	Patients with anatomically preserved facial nerve
Medium (10-25mm)	6	6 (100%)
Large(26-40mm)	26	22 (84.6%)
Giant (>40 mm)	8	4 (50%)

Our study depicted medium size (10-25mm) tumors in 15%, large size (26-40 mm) in 65%, giant (>40mm) in 20% [table-4]. Faramarz Memari, etal [3] showed the mean tumor size was 24mm, ranging from 35 mm. Joarder MA, et al [4] showed medium size, tumors in 15%, large size in 58%, giant (>40mm) in 27%.

Anatomical preservation of facial nerve was achieved in the present study for large size tumors in 84.6% of the cases and for giant size tumors in 50% . Joarder MA ,et al.[4]showed that preservation of facial nerve was achieved in 75% for large size tumors and in 55% for giant size tumors. In our study anatomical preservation of facial nerve was achieved in 80.6% of vestibular schwannoma cases overall. In a study on VS by Samii and Matthias preservation rate was reported to be 93%, independent of tumour size. In a study on VS by Vijendra K.Jain, et al [6].the preservation of facial nerve was 84.3%.

In our study it is observed that there is a positive association between size of tumor and incidence of

post-operative facial nerve palsy. Post operatively 1 patient developed facial palsy in medium tumors (16.6%), 14 patients developed facial palsy in large tumors (53.8%) and 7 patients developed facial palsy in giant tumors (87.5%) [Table-5]. As the size increases, possibility of facial nerve palsy also increases post-operatively. Joarder MA, et al [3] and Faramarz Memari,et al [3] also depicted a significant correlation between tumor size and facial nerve outcome, with larger tumors yielding worse outcomes.

Table 5. Distribution of cases according to size of lesion & incidence of post -operative facial nerve palsy

Size	Total Patients	Facial nerve palsy
Medium (10-25mm)	6	1 (16.6%)
Large (26-40 mm)	26	14 (53.8%)
Giant (>40mm)	8	7 (87.5%)

Table 6. Distribution of cases according to facial nerve Functional grading (post- operative) in already involved facial nerve on admission)

Grade	Pre-op (19)	Post-op (19)			Follow -up (6 month) (16)		
		2	3 & 4	5 & 6	2	3 & 4	5 & 6
2	16	8	6	2	7	4	2
3 & 4	3	0	0	3	0	1	2
5 & 6	0	0	0	0	0	0	0

Our study showed 19 patients have pre-operative facial palsy in which16 have grade 2,and 3 have grade 3 & 4.Out of 16 patients of grade 2, 6 patients increase to grade 3& 4and 2 patient increase to grade 5 & 6.Out of 3 patients of grade 3&4 , 3patient increase to grade 5 & 6 [Table-6]. Samii M,etal. [8] showed postoperative grade1 & 2 facial nerve function in 64% cases, grade 3 & 4 in 21% cases and grade 5 & 6 in15%cases.

Our study on radiological examinations in vestibular schwannoma showed homogenous enhancement in 2 cases, heterogenous enhancement in 29 cases, cystic component in 29 cases, hyperostosis not found in any radiologiacal imaging. In meningioma,5 cases had homogenous enhancement and 2 cases had hyperostosis, none had cystic component. In epidermoid cyst, none case had heterogenous enhancement and one case had cystic component, where as in abscess the only case had heterogenous enhancement with cystic component [Table-7]. In the study of Maheswara raoY.V.N,etal [5] .

Table 7. Distribution of cases according to finding on imaging

Imaging finding (MRI)	Vestibular Schwannoma (31)	Meningioma (5)	Epidermoid cyst (3)	Abscess (1)
Homogenous enhancement	2	5	0	0
Heterogenous enhancme nt	29	0	1	1
Cystic Component	29	0	1	1
Centered of IAM	27	1	0	0
Broad base dural tail	0	5	0	0

Table 8. Distribution of cases according to resectability

Tumor	Gross Total Excision	Near-Total Excision	Sub-Total Excision
Vestibular Schwannoma (31)	26 (84%)	3 (10%)	2 (6%)
Meningioma (5)	4 (80%)	1 (20%)	0 (0%)
Epidermoid (3)	2 (67%)	1 (33%)	0 (0%)
Abscess (1)	1 (100%)	0 (0%)	0 (0%)

We performed VP-shunt followed by definite surgery in 25% cases and direct tumor surgery in 75% cases.

In our study, in vestibular schwannoma we did gross total excision in 84% cases, near-total in 10% and sub-total in 6%cases. In meningiomas we had gross total excision in 80%, near-total in 20%. In epidermoid we had 67% gross-total excision and 33% near total excision. Where as in abscess we had gross total excision in 100% of cases [Table-8]. Overall gross total resection done in 33 patients (82.5%) and near-total resection in 5 patients (12.5%) and sub-total resection in 2 patients (5%).

In all the 40 cases, operation was done by sub-occipital retro-mastoid approach in semi-sitting position and in none of the cases we found any position related clinically apparent complication

(intra-operative and postoperative). IAC drilling was done in all cases of VS (31cases). Faramarz Memari,et al. [3] in a study on CP-angle lesions, achieved complete gross tumor removal in 92% of patients. In study done by Sourabh Dixit, et al [10] on VS, the gross total resection was done in 84.61% cases and subtotal done in 15.38% cases.

In our study, in histopathology, vestibular schwannoma accounted for 77.5% cases, meningioma for12.5%, epidermoid cyst for 7.5% and abscess for 2.5%.

Our study showed CSF leak in15% cases over all. All were initially managed conservatively with lumbar drain and medication. Meningitis occurred in10% cases in which two patients recovered with appropriate antibiotics whereas rest of the two patients who also had simultaneous CSF leak, deteriorated and expired. Faramarz Memari, et al [3].in CP-angle cases had rates of CSF leakage for retro-sigmoid approach around 18% and meningitisin10% cases.

In our study lower cranial nerves palsy was seen in 20% cases (6 deteriorated cases+2 new onset cases) and they were managed with nasogastric tube feeding. At 6 months follow up 2 patients showed incomplete recovery of lower cranial nerves palsy. We observed, in VS subgroup, facial nerve palsy in 47.5% cases and lower cranial nerve palsy in 22.5% cases. Vijendra K.Jain,et al [6] in their study on VS had the incidence of lower cranial nerve paresis of 6.8%.Sourabh Dixit, et al [10] in their study on VS had transient lower cranial nerve paresis in 46.15% patients which gradually improved. The reported incidence of lower cranial nerve paresis in the rest of literature ranges from1.5%to 5.5%.

In our study pre-operatively, 77.5% of cerebello-pontine angle tumor patients had no useful hearing(>50decibels).Out of the 9 patients (3 Vestibular Schwannomas, 3 meningiomas, 2 epidermoid cyst,1 abscess) who had useful hearing preoperatively, 3 patients (2 epidermoid cyst and1 abscess patient) retained it postoperatively also making our over all hearing preservation upto 33.3%.InVS sub-group hearing preservation was 0%.Hearing status of all the patients at 6 months follow up remained same as that of post-operative period. Samii, et al [8].in their study on VS, reported hearing preservation in 23.6% with large tumors.VijendraK.Jain,et al[6]. in their study on VS, reported hearing preservation in 29.6% of their patients who had useful pre-operative hearing.

In our study, follow up of 37 patients showed recurrence in two patients (5%) (one vestibular schwannoma and one meningioma) and were managed conservatively as both the patients were not ready for re-operation or SRS referral. Faramarz Memari, etal. [3] in their study on CP angle lesions, had residual tumor in 7% for retro sigmoid approach. In our study, in VS subgroup we had 3.22% recurrence. Gormley and Sekhar, et al [7] in their study on VS, reported complete tumor resection was accomplished in 99% of the patients, and there was no evidence of recurrence in this group. Vijendra K. Jain,etal.[6] in their study on VS, had achieved complete tumor excision in 96.5%.

In our study overall mortality was seen in 7.5% cases mainly attributable to post-operative CSF leak and meningitis. Faramarz Memari, et al [3] in their study on CP angle lesions, had mortality of 2% for retro-sigmoid approach. mortality in their series of VS.

Conclusion

CP angle SOL was common in middle age group, with incidence in females slightly more than males. Decreased hearing and cerebellar symptoms were the most common complaints. Majority of lesions were of large size(26-40mm). Most of the patients on admission had non-serviceable hearing. Heterogenous enhancement with cystic component was found in most of the lesions. Gross-total excision was done in majority of cases and vestibular schwannoma was the most common histopathological lesion obtained. Facial nerve palsy was the most complication and as the size of lesion increased, possibility of facial nerve palsy also increased post-operatively. Overall mortality was in 7.5% cases, mainly due to post-operative meningitis and CSF leak.

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