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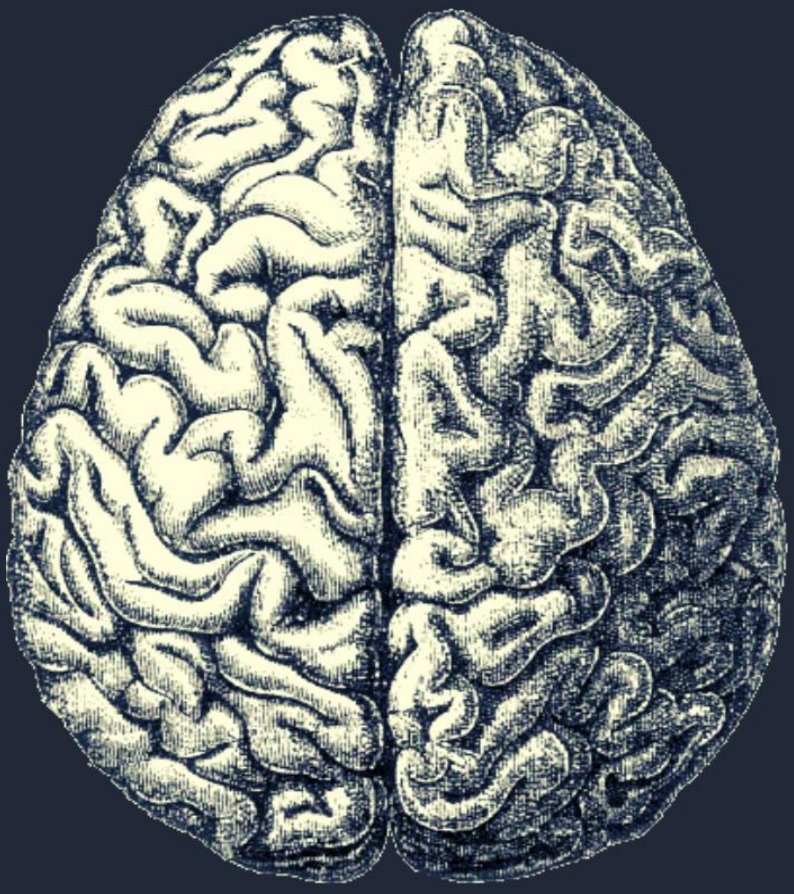

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Pitfalls in the diagnosis of glioblastoma

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ABSTRACT
Glioblastoma (GBM) is one of the most dreadful human cancers having a literature-reported median of life of 14 months with maximal treatment. The correct diagnosis is of crucial importance for the best chances of treatment. Misdiagnosis is uncommon, but seen in daily practice, and leads to important delays for patients. This paper will discuss the delays found in glioblastoma diagnosis in a series of 60 newly diagnosed patients. Four out of 60 patients had a delay of more than 6 weeks of treatment initiation, as at first imaging, GBM was not suspected as a diagnosis.

Keywords
glioblastoma misdiagnosis, glioblastoma diagnosis pitfalls, glioblastoma treatment delay

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INTRODUCTION

Glioblastoma is one of the most dreadful human cancers having a literature reported median of life of 14 months with maximal treatment[6]. The natural history of the disease is a median of two to three months from diagnosis. Hence the correct diagnosis is of crucial importance so that these patients have the best chances to treatment. The clinical manifestations of glioblastoma vary from headaches to neurological deficits, epilepsy or, in some instances, psychiatric manifestations are seen[21]. Imaging is normally done for neurological manifestations or persistent symptomatology, starting with MRI or CT scan. Resection surgery or biopsy is usually the next step in diagnosing and treating a glioblastoma patient. At surgery tumour tissue is taken and analysed in the pathology laboratory. During all these steps, from first symptoms to diagnosis, due to the complexity of cases, difficulties can arise, and these could lead sometimes to misdiagnosis. This paper will discuss the delays found in glioblastoma diagnosis in a series of 60 newly diagnosed patients.

CLINICAL MATERIAL AND METHODS

From January 2015 to October 2022, 60 newly diagnosed patients with glioblastoma have been operated by the first author either by resection or stereotactic biopsy. Of these patients we have analysed the cases in which the time from first imaging to surgery was more than six weeks. Six weeks is an arbitrary number chosen to sort out only the patients where an important delay has been observed. Usually, in our clinic it takes a maximum of ten days to schedule a patient with

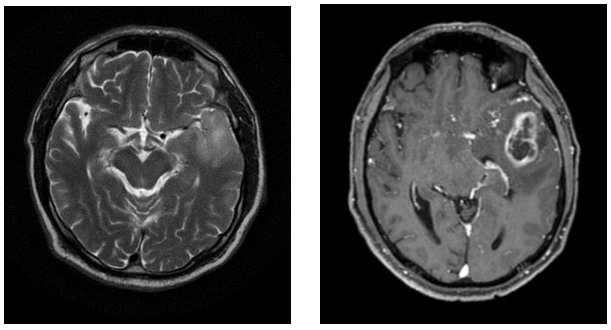
glioblastoma for surgery, so definitely six weeks sorts out only a patient where GBM was missed as diagnosis. In our standard procedure follow up is not an option when GBM is a suspicion.

Medical records were reviewed, including all imaging. Patient data included age, gender, diagnosis, symptoms, past medical history, Karnofsky score, imaging, time from first to secondary imaging, symptoms that led to secondary imaging and then to surgery.

Results

We found five patients out of 60 that had surgery more than 6 weeks after first cerebral imaging was done. Of these five patients 1 had an initial image highly suggesting GBM, but the patient refused any form of treatment for 3 months. She showed up to the hospital eventually with a state of confusion and hemiplegia and surgery was done. This patient is excluded from the discussions as the diagnosis was suspected from the first imaging.

The other four patients had initial imaging 7, 6, 4 and 2 months respectively after first imaging to surgery for GBM and the considered diagnosis was ischaemia for two patients, haemorrhage, and low-grade glioma respectively for the other two (Table 1). The first patient is a 61-year-old male who presents an episode of intermittent paraesthesia on the right side of the body followed by slurred speech, and simple motor Jackson contractions on the right side. A non-contrast MRI scanning is done showing left temporal pole T1 hypointensity, and T2 hyperintensity (Fig. 1).

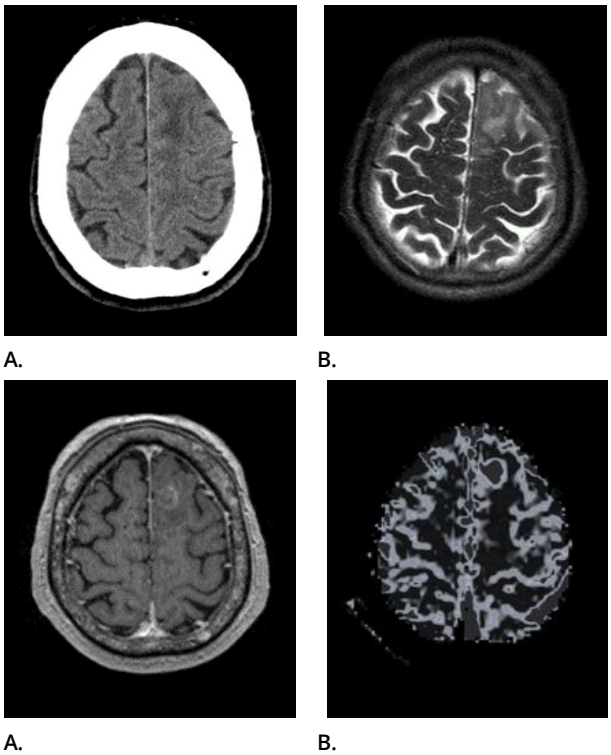


A. B.

Figure 1. (Case No. 1): **A.** MRI T2 hyperintensity at first imaging; **B.** Contrast enhancing T1 MRI showing tumour 7 months later.

The past medical history shows hypertension and dyslipidaemia. Ischaemia is considered as diagnosis and the patient is sent home with antiepileptics and follow up indication. Seven months later the patient presents to hospital with fatigue, headaches and a follow up MRI shows a contrast enhancing lesion. Stereotactic biopsy is done in the first instance in another clinic confirming the diagnosis of GBM, followed by resection surgery in our clinic one month later.

The second patient is a 69-year-old male who presents to the emergency room with an episode of confusion and memory disturbances. An initial CT scan is done, and the patient is considered to have had a stroke. Low resolution MRI is done during the same hospitalisation, and it does not raise the suspicion of tumour. Initial evolution is favourable, and the patient is discharged home. Few months later progressive confusion is observed, situation which culminates with a grand-mal convulsion. He is referred to the emergency room where new scanning is done including enhanced MRI that shows left frontal enhancing intra axial tumour (Fig. 2). The patient is referred to surgery and the glioblastoma diagnosis is confirmed. Six months have passed between first head scan and surgery.



A. B.

A. B.

Figure 2. (Case No. 2): **A, B.** CT scan and MRI scan at first symptoms; **C, D.** Contrast enhanced MRI and perfusion MRI 6 months later.

The third patient is a 47-year-old lady that is referred to our clinic with confusion, aphasia, right side

hemiparesis, having hypertension and epilepsy as past medical history. Four months in advance the patient presents to the emergency room with right side hemiplegia. A CT enhanced and non-enhanced scanning shows a left frontoparietal profound ICH (Fig 3). She is considered to have haemorrhage after hypertensive bleed, and she is discharged to rehabilitation. There is initial good evolution but 3 months later the patient slowly deteriorates presenting again to the emergency room with confusion, aphasia and deteriorated right sided hemiparesis. MRI shows a contrast enhancing tumour. The patient is referred to surgery and GBM is confirmed by the pathology report.

Table 1. Medical record details of patients. LGG – low grade glioma

No	Gender	Age	Initial imaging	Initial diagnosis	Time to surgery	Initial symptoms	Karnofsky score before surgery
1	Male	61	MRI	ischemia	8 months	epilepsy	90
2	Male	69	CT/MRI	ischemia	6 months	confusion	70
3	Female	47	CT	hemorrhage	4 months	hemiplegia	40
4	Female	61	MRI	LGG	2 months	slurred speech	90

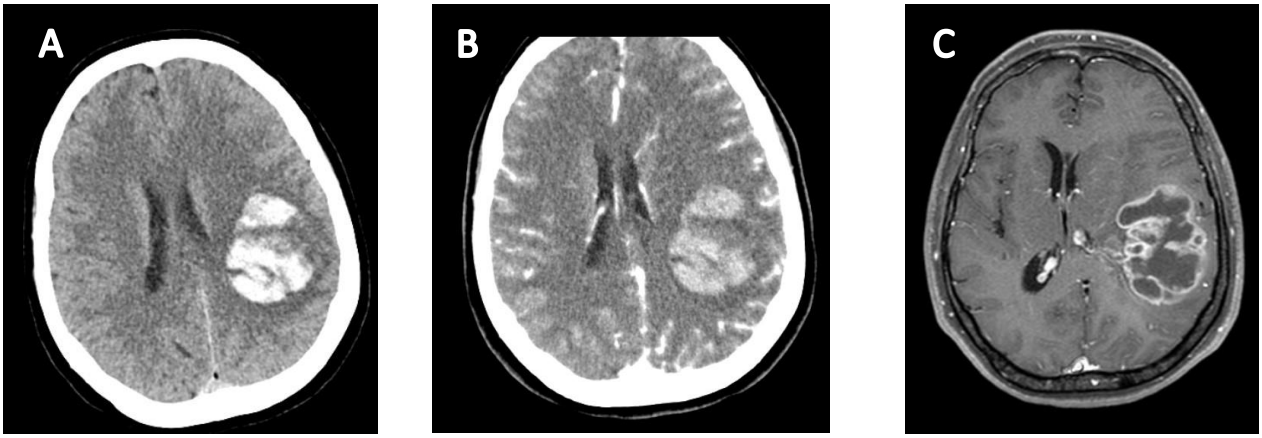


Figure 3. (Case No. 3): **A.** Non enhanced CT scan showing ICH at first symptoms; **B.** Contrast enhanced CT scan with no obvious tumour; **C.** Contrast enhanced MRI 3 months later showing tumor, highly suggestive for GBM.

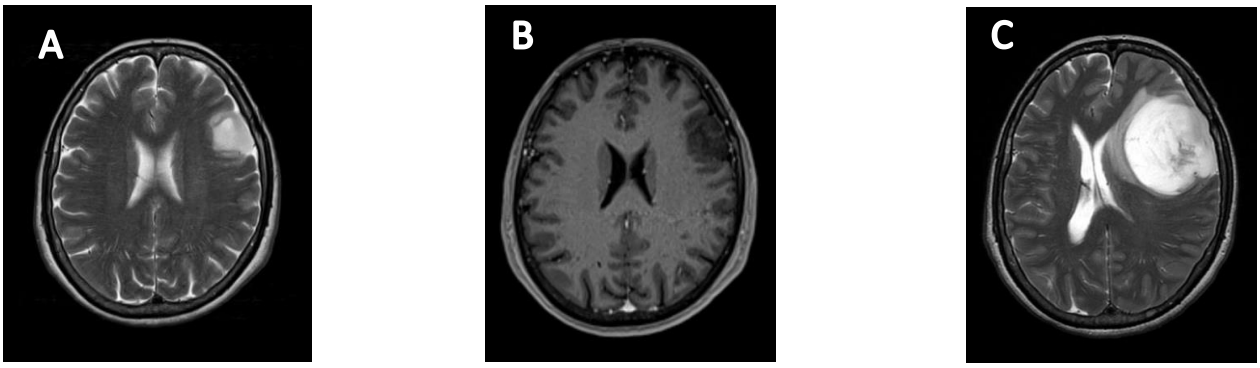


Figure 4. (Case No. 4): **A.** T2 hyperintensity 1 at first symptoms; **B.** Contrast enhanced T1 at first symptoms; **C.** T2 hyperintensity 6 weeks later. Very fast growing is to be observed.

The fourth patient is a 61-year-old lady that is referred to the neurology department for slurred speech. Initial contrast enhanced MRI is done showing a left frontal tumour in the vicinity of Broca area which is considered as low-grade glioma (Fig 4). Initial evolution is favourable under corticosteroids and the patient is sent home with MRI follow up indication. Six weeks later after initial good clinical evolution the slurred speech reappears, and the patient complains also of headaches and fatigue.

Imaging studies show an important augmentation of the tumour which is highly suggestive for glioblastoma at this point. The patient is referred to surgery confirming diagnosis.

Discussions

Misdiagnosis can be seen in different phases of the GBM diagnosis. Misdiagnosis can be of different sources: symptomatic/clinical origin[12,13, 14, 19], of radiological origin, of surgical origin or of pathology origin [5, 9]. When considering the radiological origin of misdiagnosis in glioblastomas, the initial image can be interpreted as other diagnostics like lymphoma[4], metastasis, meningioma[10], ischemia[7,17], haemorrhage[11], parasites[23], abscess[1], inflammatory diseases and degenerative processes[13]. It can even be misdiagnosed as contusion[15]. Other sources of errors can be seen but the discussion is beyond the scope of this article.

In this cohort of patients three of the 60 patients have been considered on initial scanning of having other diagnosis than tumour. A fourth one has been diagnosed with tumour, but it has been considered to be a lower grade, whose treatment implied only follow up if the diagnosis were to be correct.

The survival of patients with glioblastoma is dismal. With treatment, most of the teams report a 14 months median survival. Without treatment the median survival is two to three months[6]. Sometimes patients present as emergency cases and surgical treatment needs to be instituted immediately. This is usually the case of high-volume tumours that have mass effect. In such cases the survival of the patient can be even of days without surgery[14]. Very fast evolution can be seen[23] confirming in vitro studies[8]. In our current practice we have all met patients, in whom despite maximal treatment with surgery, very fast recurrence of tumour is observed. Case number four in this article seems to have such an evolution (Fig 4).

The importance of a correct diagnosis is crucial for patients with glioblastoma because of the speed of evolution of this disease. The longer the delay to diagnosis, the more difficult the surgery. The delay allows the spread of the tumour, by infiltrating farther into the brain. There are several prognostic factors for patients with GBM and one of them is the extent of resection. There are multiple studies showing that the extent of resection is important on the survival of these patients[16]. The sooner the diagnosis, the better for the patient in terms of surgery complexity and initiation of treatment. The delay makes surgery more complex, resection complexity usually being proportional with the size and location of the tumour. An important part of GBM patients is sent directly to palliative care, in part probably due to the operability of the tumour[18], meaning that a late diagnosis can even prevent any initiation of active treatment.

Two of our patients were considered to have an ischemic stroke. They were discharged home with prophylactic antithrombotic therapy, but with no clear follow up indication of MRI, as tumour was not considered as differential diagnosis. There are other case reports in literature with an almost identical trajectory with a percentage of misdiagnosis up to 10% in different series[3]. In our patients, presentation at the hospital did not imply thrombolysis or thrombectomy, but should they have arrived at the hospital inside the thrombolysis window, the stroke treatment could have harmed them as thrombolytic therapy should not be given to patients with brain tumours[17]. For the third patient, hypertensive bleed was the diagnosis on the initial enhanced CT scan. The diagnosis of tumour was not suspected. Hence, the patient presented three months later with deteriorated symptomatology. A contrast enhanced MRI showed tumour (Fig 3). Other teams report delay of diagnosis in case of haemorrhage[20].

In the case of the fourth patient, on the initial MRI the diagnosis was low grade glioma.

Four out of 60 patients, 6,66% of patients, in this cohort of GBM patients, have been misdiagnosed in a way or another. As this is a devastating disease time is crucial for these patients. Certain teams relate that in the case of misdiagnosis, only initial CT scanning was done[3]. In our cohort three of the patients had initial MRI scanning, situation that could suggest that standard MRI scanning or low-resolution MRI is not always enough in depicting differential diagnosis between ischemic stroke and GBM or between LGG and GBM. Diffusion MRI, including DWI and ADC, should be standard procedure for every brain pathology.

New advanced MRI techniques like spectroscopy, perfusion MRI, DTI should be used in diagnosing and making the differential diagnosis between other brain diseases and GBM[22]. Obviously, advanced MRI techniques cannot be made for every ischemic stroke even in highly developed societies because of

cost-effectiveness issues[11], as for developing societies advanced MRI techniques for every patient is prohibitive. In difficult cases where there is doubt over the diagnosis SPECT[1] and PET CT[2] have been proposed as imaging techniques to be able to sort out the diagnosis.

There are several possible reasons for fallacies in our cases, as retrospectively, few things could have been done better: better communication between clinician and radiologist, closer follow up, better communication with the rehabilitation clinic, advanced MRI techniques when in doubt. These cases leave the impression that the scanning was done at the very beginning of the developing of the tumor. Unfortunately, no genetic profile of the tumor has been done to further understand the evolution of these cases.

GBM could be misdiagnosed as other pathologies like lymphoma, metastasis, or abscess. In these cases, immediate surgery is the standard treatment so at least there is no harm done by any delay. The correct diagnosis is the target for every single case, the diagnosing methods should be properly used, but this discussion is beyond the aim of this study.

Conclusions

Literature suggests that a non-negligible percentage of patients with 'stroke' are actually misdiagnosis for an even more devastating disease. Other brain pathologies have been rarely considered instead of GBM, so it should be kept in mind that GBM is part of the differential diagnosis in other types of diseases of the brain. The conclusion of our study is in concordance with the reports of other teams. There are permanently updated guidelines for the diagnosis of GBM, but the pattern observed in all our cases is that the diagnosis has not been considered in the first instance. Yet, the multitude of teams reporting misdiagnosis shows that this problem is not yet solved. Improvements can be done in decreasing the number of misdiagnoses in GBM patients, but the diagnosis is not always straight forward, nor advanced technology is readily available.

List of Abbreviations

ICH: intracerebral haematoma;
GBM: glioblastoma;
MRI: magnetic resonance imaging;
CT: computed tomography;
LGG: low grade glioma.

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The challenges and opportunities of patient safety culture in neurosurgical departments from the Republic of Moldova

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Abstract

Neurosurgery is a high-risk speciality, so the Patient Safety Culture should become a priority to improve patient safety and the quality of medical care. The purpose of the study was to explore the perception of Patient Safety Culture (PSC) among the staff in the neurosurgical departments of the Republic of Moldova.

A cross-sectional study was conducted in neurosurgical departments using the Hospital Survey on Patient Safety Culture (HSOPSC). Descriptive statistics were carried out, comprising the Cronbach "α" coefficient, frequency of positive answers (PPRs), and level of minimum and maximum of 95% confidential interval. PPRs by question and dimension were analysed overall and classified according to the Harrington scale.

Medical staff from five hospitals voluntarily participated in the study. Most of the respondents rated the patient's safety grade as excellent and very good. The value of the frequency of positive responses to the dimensions of the survey varies between 37.3% (nonpunitive response to error) and 85.0% (teamwork within units). The dimensions with the highest score of the PPRs stand out: „teamwork within units", „organizational learning- continuous improvement" and „supervisor/manager expectations and actions promoting patient safety". The dimension with a high score of PPRs was „feedback and communication about error". The dimensions with a satisfactory score of the PPRs were „handoffs and transitions", „frequency of events reported", „management support for patient safety", „teamwork across units", „communication openness", „overall perceptions on patient safety", „non-punitive response to errors" and „staffing".

For the first time in the Republic of Moldova, the perception of patient safety culture in neurosurgery departments was studied. The results reflect the positive attitude of the staff towards most dimensions of the patient safety culture. The study made it possible to highlight the strong and vulnerable points of the patient safety culture in neurosurgical departments from Moldova.

Keywords
patient safety culture,
neurosurgery,
patient safety

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Introduction

Patient safety is a strategic priority for modern health care and is central to countries' efforts in working towards universal health coverage (1).

Developing a culture of safety is cardinal to any sustainable efforts towards patient safety improvement (1).

According World Health Organization patient safety is a framework of organized activities that creates cultures, processes and procedures, behaviours, technologies, and environments in health care that consistently and sustainably: lower risks, reduce the occurrence of avoidable harm, make error less likely and reduce its impact when it does occur (2).Incident: any deviation from usual medical care that either causes an injury to the patient or poses a risk of harm, including errors, preventable adverse events and hazards (2).Adverse event: an incident that results in preventable harm to a patient (2)

Every year, large number of patients are harmed or die because of unsafe health care, creating a high burden of death and disability worldwide, especially in low- and middle-income countries. On average, an estimated one in 10 patients is subject to an adverse event while receiving hospital care in high-income countries. Available evidence suggests that 134 million adverse events due to unsafe care occur in hospitals in low- and middle-income countries, contributing to around 2.6 million deaths every year. The social cost of patient harm can be valued at US$ 1 trillion to 2 trillion a year (1).

In neurosurgery, little is known about the frequency of adverse events and the contribution of human error (3)According Hanno S. Meyer (2021) one in four patients treated at an academic neurosurgical tertiary care centre experiences at least one adverse event. Most adverse events occurred during (19.6%) or after (76.3%) surgery (3). More than one in four of the cases with adverse events were associated with human error (25.9%). The most frequent class of human performance deficiency (HPD) was execution (18.3%). Another relevant HPD was planning or problem solving (5.6%). Rules violation accounted for 1.7% of adverse events cases. (3)

Mardon RE(2010) explored the relationships between Hospital Patient Safety Culture and Adverse Events and found that hospitals with a more positive patient safety culture scores had lower rates of in-hospital complications or adverse events (4). The study supports the idea that a more positive patient safety culture is associated with fewer adverse events in hospitals (4).

The Global Patient Safety Action Plan strives to eliminate avoidable harm in health care with the vision of "a world in which no one is harmed in health care, and every patient receives safe and respectful care, every time, everywhere" (1).

According to AHRQ patient safety culture is the extent to which an organization's culture supports and promotes patient safety. It refers to the values, beliefs, and norms that are shared by healthcare practitioners and other staff throughout the organization that influence their actions and behaviours. Patient safety culture can be measured by determining the values, beliefs, norms, and behaviours related to patient safety that are rewarded, supported, expected, and accepted in an organization (5). It is believed that in order to reduce the number of adverse events, hospitals have to stimulate a more open culture and reflective attitude towards errors and patient safety (6). A strong safety culture is not only core to reducing patient harm, it is also critical for providing a safe working environment for health workers. This includes creating a psychologically safe work environment, whereby health workers can speak up regarding patient safety and other concerns without fear of negative consequences (1).

"Changing our culture to advance patient safety" served as the theme of the 81st Annual Meeting of the American Association of Neurological Surgeons (7). The neurosurgeon of the future has to embrace the ideals of individualism and innovation while never giving up the art of medicine, prioritizing the doctor-patient relationship, and changing our culture to practice the science of medicine within systems that help us to understand and prevent errors from occurring (7). Leaders should be educated in the importance of safety culture, and they need tools to help create this culture (8). In addition, many organizations now use standard surveys to measure culture, although many struggle with how to improve in low-scoring areas (8). The AHRQ Surveys on Patient Safety Culture™ (SOPS®) are surveys of providers and staff that assess the extent to which their organizational culture supports patient safety and safe practices (9). The areas of patient safety culture assessed by the AHRQ SOPS surveys include: Communication About Error, Communication Openness, Organizational Learning—Continuous Improvement, Overall Rating on Patient Safety, Response to Error, Staffing,

Supervisor and Management Support for Patient Safety, Teamwork, Work Pressure and Pace (9).

As of September 2022, there are 107 known countries where the AHRQ Surveys on Patient Safety Culture™ (SOPS®) have been administered (10). As of September 2022, there are 56 known translations for the AHRQ Surveys on Patient Safety Culture™ (SOPS®) (11). The European Network for Patient Safety (EUNetPas) has been an important promoter of this tool in Europe. One of the aims of the EUNetPaS project was "Promoting a Culture of Patient Safety" (12).

The original US Hospital Survey on Patient Safety Culture (HSOPS), designed by the American Agency for Healthcare Research and Quality (AHRQ) in 2004 was translated in Romanian and experimented in Romania. The study explored the psychometric properties of the Romanian version of the US HSOPS and found that Psychometric properties of the Romanian version of the HSOPS tested in Romania was acceptable for nine composites with 31 items (13). Then a cross-sectional study which measured the patient safety culture was carried out in six hospitals, located in four Romanian regions by Tereanu C et all (2017)(14).The study shows that staff perceptions of most areas of patient safety were positive although reporting of adverse events was low(14).Later a cross-sectional study was conducted in Moldovan healthcare settings, using the Romanian translation of the US Hospital Survey on Patient Safety Culture HSOPSC (15). The results of the study suggested that staff avoid to openly report adverse events and/or discuss errors, likely because a poor understanding of the potential of these events for learning and because of fear of blame or punitive actions (15). Also, the phenomenon of underreporting of adverse events was mentioned in the study by Turcanu T. et all in 2010 regarding patient safety, medical errors, and event reporting in Moldova (16).

Currently, the Republic of Moldova does not have in use any tool to assess patient safety culture in hospital settings (15).Therefore, the actuality of the problem was associated with the lack of research on the Patient safety Culture of neurosurgical patients during hospitalization and the high risks of medical care for patients with neurosurgical diseases.

The purpose of the study was to explore the perception of patient safety culture among the staff in neurosurgical departments from Republic of Moldova.

METHODS

A cross sectional study was conducted in neurosurgical departments from Moldova using the Hospital Survey on Patient Safety Culture (HSOPSC) Romanian version, developed by the US Agency for Healthcare Research and Quality, created by Sorra J, Yount N, Famolaro T, et al. (17). The research project was approved by the Research Ethics Committee of State University of Medicine and Pharmacy "Nicolae Testemitanu", Republic of Moldova on 19.06.2018.

The survey was distributed from January till September 2019 in neurosurgical departments in five hospitals from Republic of Moldova. There was voluntary involved in the survey 345 doctors, residents, and nurses. We distributed paper form questioners to 400 members of medical staff. The questionnaire was anonymously completed. The surveys that did not meet the requirements for completion of the AHRQ guide were excluded. Overall, 345 completed questioners were returned, which constituted the 86% response rate. Completed surveys were collected and digitized. Statistical analyses were performed using IBM SPSS Statistics 26. The matrix of results was created. The survey contains forty-two questions and two output indicators: one question asks the respondents to appreciate the patient safety grade and another question asks about the number of events reported during the last 12 months.

The survey questions used Likert scale of 5-point response options of degree of agreement: 1 point mean strongly disagree, 5 points -strongly agree, and the frequency 1 point mean never, and 5 points mean always. For negatively worded items, percentage of positive responses is the percentage of respondents who answered "Strongly disagree" or "Disagree," or "Never" or "Rarely," because a negative answer on a negatively worded item indicates a positive response (17). We recoded negatively worded items to calculate an item percent positive score. We averaged the percent of positive scores for each item included in the composite measure, to calculate score on a particular safety culture composite measure as described the AHRQ guide (17). Descriptive statistics were carried out, comprised the Cronbach "α" coefficient, frequency of positive answers PPRs, variance, standard error, level

of minimum and maximum of 95% confidential interval. PPRs by question and dimension were analysed overall and classified according to Harrington scale (18).

RESULTS

For the first time we explored the staff perception about patient safety culture in neurosurgical departments from five hospitals providing in-patient hospital care. 345 persons voluntarily participated in the study. From 345 respondents there were: doctors - 124- 36.0%, nurses- 172- 49.8%, residents- 49-14.2%. All of respondents were in direct interaction or contact with patients. Most of respondents 173 (50,1%; ÎI 95% [44,6-55,1]) were worked in neurosurgery units and 172 (49,9%; ÎI 95% [44,9-55,4]) were worked in anaesthesiology and intensive care units where neurosurgical patients received medical care. The distribution of respondents by intervals of years of work experience in the hospital showed that a third of them have a work experience in the hospital 1-5 years-109 people (31,6%; ÎI 95% [27,0-36,5]), and another third had 21 and more years of work experience - 122 people (35,4%; ÎI 95% [30,1-40,6]). The distribution of respondents by intervals of years of work experience in the unit showed that: 1-5 years -38.6 % respondents, 6-10 years-18.6% respondents, 11-15 years -10.7% respondents, 16-20 years -9% respondents, > 20 years -23.2 % respondents. The results showed that a half of respondents worked 40-49 hours per week Figure 1.

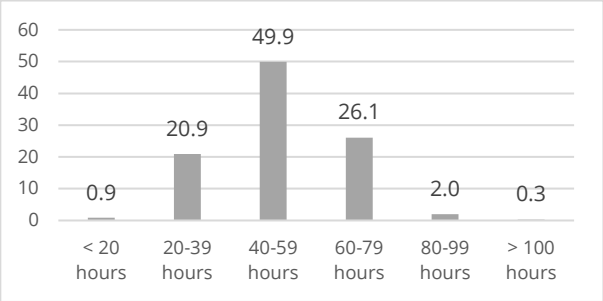

Figure 1. Distribution of respondents according to working hours per week, %.

The output indicator -frequency of adverse events reported in the last 12 months by respondents reflects that the most part of staff did not report any adverse events during last year of activity Figure 2.

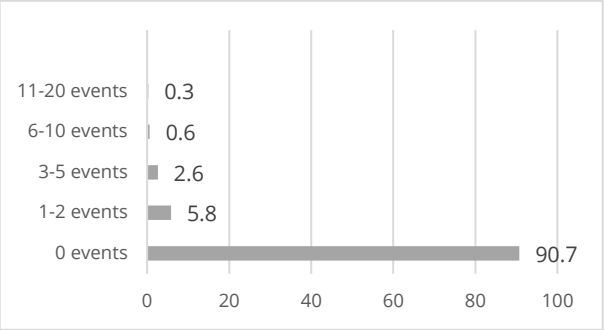

Figure 2. Frequency of adverse event reported in the last 12 months, %.

Most of the employees rated the patient's safety grade as excellent- 39,1 % and very good 43,8%. Table 1 reflects the staff perception of patient safety grade.

Table 1. Patient Safety Grade -output indicator.

Patient Safety Grade -points	Frequency of responses			Patient Safety Grade
	Abs.	%	95% CI	
9-10	135	39,1	33,9-44,1	Excelent
7-8	151	43,8	38,6-48,0	Very good
5-6	44	12,8	9,3-16,5	Acceptable
3-4	11	3,2	1,4-5,2	Poor
1-2	4	1,2	0,3-2,3	Failing

Table 2 express the item and composite positive scores for the patient safety culture with 95% confidence intervals.

Table 2. Item and Composite Percent Positive Scores for the Patient safety culture with 95 % confidence intervals.

Code	Composites and items	Abs.	%	95% CI
D I Teamwork within units		***1173***	***85,0***	***83,1-86,9***
A1	People support one another in this unit	301	87,2	83,8-90,7
A3	When a lot of work needs to be done quickly, we work together as a team to get the work done	310	89,9	86,7-92,8
A4	In this unit, people treat each other with respect	292	84,6	80,9-88,1
A11	When one area in this unit gets really busy, others help out	270	78,3	73,6-82,9

D II Supervisor/manager Expectations and Actions Promoting Patient Safety		***1117***	***80,9***	***78,9-83,0***
B1	My supervisor/manager says a good word when he/she sees a job done according to established patient safety procedures	311	90,1	87,0-93,0
B2	My supervisor/manager seriously considers staff suggestions for improving patient safety	285	82,6	78,8-86,7
B3r	Whenever pressure builds up, my supervisor/manager wants us to work faster, even if it means taking shortcuts	220	63,8	58,8-68,7
B4r	My supervisor/manager overlooks patient safety problems that happen over and over	301	87,2	83,8-90,7
D III Organizational Learning-Continuous Improvement		***839***	***81,1***	***78,7-83,4***
A6	We are actively doing things to improve patient safety	276	80,0	75,7-84,3
A9	Mistakes have led to positive changes here	288	83,5	79,4-87,2
A13	After we make changes to improve patient safety, we evaluate their effectiveness	275	79,7	75,7-83,8
D IV Management Support for Patient Safety		***613***	***59,2***	***56,2-62,2***
F1	Hospital management provides a work climate that promotes patient safety	228	66,1	60,9-71,3
F8	The actions of hospital management show that patient safety is a top priority	228	66,1	60,9-71,3
F9r	Hospital management seems interested in patient safety only after an adverse event happens	157	45,5	40,3-50,8
D V Overall perceptions on Patient Safety		***611***	***44,3***	***41,7-46,9***
A10r	It is just by chance that more serious mistakes don't happen around here	105	30,4	25,8-35,1
A15	Patient safety is never sacrificed to get more work done	96	27,8	22,9-32,8
A17r	We have patient safety problems in this unit	178	51,6	46,4-56,8
A18	Our procedures and systems are good at preventing errors from happening	232	67,2	62,0-72,2
D VI Feedback and Communication About Error		***792***	***76,5***	***73,9-79,1***
C1	We are given feedback about changes put into place based on event reports	300	87,0	83,2-90,1
C3	We are informed about errors that happen in this unit	220	63,8	58,6-68,7
C5	In this unit, we discuss ways to prevent errors from happening again	272	78,8	74,2-82,9
D VII Communication openness		***491***	***47,4***	***44,4-50,5***
C2	Staff will freely speak up if they see something that may negatively affect patient care	225	65,2	60,3-70,4
C4	Staff feel free to question the decisions or actions of those with more authority	144	41,7	36,5-47,0
C6r	Staff are afraid to ask questions when something does not seem right	122	35,4	30,7-40,3
D VIII Frequency of Events Reported		***621***	***60,0***	***57,0-63,0***
D1	When a mistake is made, but is *caught and corrected before affecting the patient*, how often is this reported?	215	62,3	57,1-67,2
D2	When a mistake is made, but has *no potential to harm the patient*, how often is this reported?	210	60,9	55,9-66,1
D3	When a mistake is made that *could harm the patient*, but does not, how often is this reported?	196	56,8	51,3-62,0

D IX Teamwork Across Units		***719***	***52,1***	***49,5-54,7***
F2r	Hospital units do not coordinate well with each other	122	35,4	30,4-40,9
F4	There is good cooperation among hospital units that need to work together	212	61,4	56,2-66,9
F6r	It is often unpleasant to work with staff from other hospital units	140	40,6	35,1-46,1
F10	Hospital units work well together to provide the best care for patients	245	71,0	66,1-75,9
D X Staffing		***515***	***37,3***	***34,8-39,9***
A2	We have enough staff to handle the workload	135	39,1	33,9-44,6
A5r	Staff in this unit work longer hours than is best for patient care	103	29,9	25,5-35,1
A7r	We use more agency/temporary staff than is best for patient care	147	42,6	37,1-47,8
A14r	We work in "crisis mode" trying to do too much, too quickly	130	37,7	32,5-42,9
D XI Handoffs and transitions		***854***	***61,9***	***59,3-64,4***
F3r	Things "fall between the cracks" when transferring patients from one unit to another	202	58,6	53,3-63,2
F5r	Important patient care information is often lost during shift changes	238	69,0	63,5-73,9
F7r	Problems often occur in the exchange of information across hospital units	192	55,7	50,4-60,9
F11r	Shift changes are problematic for patients in this hospital	222	64,3	59,4-69,3
D XII Non punitive Response to Errors		***447***	***43,2***	***40,2-46,2***
A8r	Staff feel like their mistakes are held against them	207	60,0	54,8-65,5
A12r	When an event is reported, it feels like the person is being written up, not the problem	150	43,5	38,0-48,7
A16r	Staff worry that mistakes they make are kept in their personnel file	90	26,1	21,7-30,7

Table 3. Classification of the results of patient safety culture dimensions according to the Harrington scale.

Grade	Frequency of positive responses %	Level of Harrington scale	Dimension	The total value of dimension %
I.	80-100%	Very good (excellent)	Teamwork within units	85,0
			Organizational Learning-Continuous Improvement	81,1
			Supervisor/manager Expectations and Actions Promoting Patient Safety	80,9
II.	63-79%	Good	Feedback and Communication About Error	76,5
III.	37-62%	Satisfactory	Handoffs and transitions	61,9
			Frequency of Events Reported	60,0
			Management support for patient safety	59,2
			Teamwork Across Units	52,1
			Communication openness	47,4
			Overall perceptions on Patient Safety	44,3
			Non punitive Response to Errors	43,2
			Staffing	37,3
IV.	20-36%	Bad	not identified	-
V.	0-19%	Very bad (critical)	not identified	-

DISCUSSIONS

The ultimate goal of the Global Patient Safety Action Plan is to achieve the maximum possible reduction in unavoidable harm due to unsafe health care globally (1). One from Seven guiding principles establish underpinning values to shape the development and implementation of the action plan is instill a safety culture in the design and delivery of health care (1). Because of its high level of complexity, neurosurgery is a high-risk specialty, and improving patient outcomes has remained central in its spectrum of academic pursuits (19). For the first time was explored the perception on patient safety culture of staff in neurosurgical departments from Republic of Moldova. The staff demonstrates openness to participate in this study and the participation rate was high. The results of the study

express the positive attitude of the staff from the neurosurgery departments towards the culture of patient safety. The study reflects the particularities of patient safety culture in neurosurgical departments from Republic of Moldova with strength and weaknesses. The value of the frequency of positive responses to the dimensions of the survey varies between 37.3% (nonpunitive response to error) and 85.0% (teamwork within units). Russell E. Mardon et all (2010) reflected similar results in their study where the mean HSOPS scores ranged from 42% positive response (nonpunitive response to error) to 79% positive response (teamwork within units) (20).

The mean value of patient safety grade was 7.8 points (CI 95% [7,6-8,0]) from 10 that correspond to very good level of patient safety grade. 39.1% of respondents appreciated as a "excellent" the grade of patient safety, 43.8% - "very good", 12.8%- "acceptable", 3.2%- "poor" and 1.2%- "failing". The results of the study showed that the assessment of patient safety in neurosurgical departments is higher compared to previous studies carried out in the Republic of Moldova and Romania (13) (15). The explanations can be that neurosurgery clinicians have always taken pride in being providers who carry a strong sense of personal responsibility for their patients (19).

Neurosurgery is far from immune to the errors. The complexity of neurosurgical patients and the interdisciplinary teams required to manage their conditions expose these patients to the same errors found in other medical and surgical specialties, along with errors unique to neurosurgery (21). Our study reflects the phenomenon of underreporting of adverse events -about 90 % of respondents did not report any adverse event during the last year. Tereanu C. et all find the same phenomenon in their study in Moldova- 68% of respondents did not report any adverse event in the last 12 months (15) and 73 % in Romania (14). In comparison with Japan "No event reports" was in 34,9 %, Taiwan 48.8% and United States 50.8% (22). Understanding the frequency and danger posed by medical errors, and offering strategies to prevent them, forms the basis of the modern patient safety movement (21). Although voluntary event reporting is often described as an inadequate method to detect patient safety events and is marked by underreporting rates (23). In Moldova, there is no centralized system for mandatory anonymous reporting of adverse events. The high level of underreporting of adverse events can be explained by the voluntary reporting system. Russell E. Mardon mentioned in 2010 that there tends to be considerable underreporting of events in hospitals, which is problematic because potential safety problems may not be recognized or identified and therefore may not be addressed (20).Maureen L. Falcone mentioned in his study 4 factors accounted for 67.5% of the variance in barriers to reporting medication errors: fear, cultural barriers, lack of knowledge/feedback, and practical barriers. Other barriers include workload, interruptions, and lack of knowledge. Also, an important barrier is providers not prioritizing problems as reportable if they are easily resolved (24).

The Item and Composite Percent Positive Scores with 95 % confidence intervals represented in table 2 highlight the strengths and the weaknesses of the patient safety culture in neurosurgery departments from Republic of Moldova. Their classification was carried out using the Harrington verbal-numerical universal scale, which is used in cases when the answers have a subjective character (18).

Among the dimensions with the highest score of the frequency of positive answers according to Harrington scale, the following dimensions stand out: „teamwork within units", „organizational learning -continuous improvement" and „supervisor/manager expectations and actions promoting patient safety". The dimension with a high score of the frequency of positive answers according Harrington scale was „feedback and communication about error". The dimensions with a satisfactory score according Harington scale of the frequency of positive answers were „handoffs and transitions", „frequency of events reported", „management support for patient safety", „teamwork across units", „communication openness", „overall perceptions on patient safety", „non punitive response to errors" and „staffing". In our study, no dimensions with a "bad" or "critical" score according to the Harrington scale were identified.

The results of our study reflected that the composite "Staffing" was rated with the lowest score of the frequency of positive responses. The same results reflected in the AHRQ database where this composite was rated with the lowest score of the frequency of positive answers (25). C Tartaglia Reis explain that the staff felt overloaded by the unsuitability of personnel to their work activities,

which can prejudice the quality of care provided (26). Another reason of low score in Moldova could be the insufficient staff of both doctors and nurses, which is why they work more intensively and more hours per week. Lower frequency of adverse event reporting, „Non punitive response to errors" and "Communication Openness" are another weakness points of patient safety culture in neurosurgical departments in Moldova. Maureen L. Falcone et all remarked in their study that fear of blame and retaliation are common reasons nurses and physicians do not report errors (24). The item "Staff worry that mistakes they make are kept in the personnel file" had the lowest level of positive responses and it influenced the composite score. The results suggest the existence of a so-called blame culture in neurosurgical departments,

Conclusions

For the first time in the Republic of Moldova, the perception of patient safety culture in neurosurgery departments was studied, using an international instrument. The results reflect the positive attitude of the staff from the neurosurgery departments towards most dimensions of the patient safety culture. The study made it possible to highlight the strong and vulnerable points of the patient safety culture in neurosurgical departments, which require prompt intervention to be improved.

The study outlined that the most vulnerable aspect of the patient safety culture is staffing. A particular problem in neurosurgical departments from Republic of Moldova remains the shortage of personnel and the large number of hours worked per week, which negatively influence patient safety, highlighting the necessity to develop policies and implement measures to motivate and influence health specialists to stay working in the medical system.

Another weakness points of patient safety culture in neurosurgical departments which need a prompt intervention for improvement are the Lower frequency of adverse event reporting, along with „Non punitive response to errors" and "Communication Openness". To change the situation in this sensitive but very important field, it is necessary to develop and to implement a system for reporting of adverse events associated with the medical care, to encourage and to stimulate the adverse event reporting and to develop the culture of learning from errors. It is important to exclude blaming or punishing those who report or commit errors. To achieve this, it is necessary to organize training courses and constructive discussions to analyse the reported adverse events, so that the staff understand that the goal of this process is to increase patient safety and the quality of medical care.

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Autologous versus synthetic cranioplasty. Single centre study and literature review

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Abstract

Background. Cranioplasty has been described in history as far back as the 16th century. The use of autologous cranioplasty has been published since 1821 and is still under practice today worldwide. Recent evidence however has suggested increased complication and revision rates with the use of autologous bone. We compared our results of autologous cranioplasty versus synthetic material.

Methods. A retrospective study was carried out of cranioplasty procedures at our unit between August 2009 and March 2018. Bone flaps were placed in a sterile sealed plastic container and stored at -81 degrees. Swabs and bone chips were used for cultures and bone flap disposed if positive. On re-implantation, the bone was thawed at room temperature and soaked in gentamicin. Synthetic cranioplasties were constructed using thin-slice CT to design a custom flap for each patient.

Results. 144 cranioplasties were studied. 51 own bone and 93 synthetic. The average delay in cranioplasty was 286 days (Range 16 – 1264 days). The overall complication rate for all 144 cranioplasties was 20.8%; Autologous 31.4% and synthetic 15.1%; p 0.031. Bone flap infection rate overall for all 144 cases was 9.7% - Autologous 11.8% and Synthetic 8.6%; p 0.565. The revision rate was found to be 13.2% overall; 23.5% for autologous and 7.5% for synthetic. The difference in revision rate was found to be statistically significant (p 0.01).

Conclusion. Revision rate and overall complication rate were higher in the own bone group with P<0.05. There was no difference in infection. Our results mirror recent publications and should be considered when undertaking a cranioplasty.

Keywords
cranioplasty,
autologous cranioplasty,
synthetic cranioplasty,
bone flap

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Introduction

The practice of cranioplasty is well documented in history and records date back to the 16th century when gold plates were used in reconstruction. There is also evidence of the practice of trephination and cranioplasty from as early as 3000 BC. The first reported use of bone for reconstruction was in 1668 when a canine bone was described to have been used to repair a cranial defect in a Russian male. Walther in 1821 was reported to be the first to practice autograft cranioplasty. This technique was subsequently popularised by Macewen in 1885 who began routinely replacing trephined bone plugs back into the defects. Wagner in 1889 took this one step further by describing the osteoplastic

craniotomy in which bone was left attached to underlying muscle[1,2].

The practice of successful delayed cranioplasty in its earliest form was described by Sedel in 1889 who used pieces of tibia to repair a parietal defect and later Axhausen used this technique successfully for multiple cases[1]. This technique became popular in early 1900s with multiple authors reporting good results. Muller and Konig in 1890[3] described their technique of split local graft of skin, periosteum and outer table to reconstruct defects, and later Hacker modified this to include only periosteum and outer table[4].

Subsequent to this, various anatomical sites have been used for autografts including ribs, scapula, ilium and sternum with varying popularity[5]. Cadaver allografts have also been used in the past but were noted to be susceptible to infection and resorption[1].

Aluminium was the first metal in the development of modern cranioplasty but was found to be locally irritant and epileptogenic[6]. Silver and gold[7] were also used with good results being reported with gold cranioplasties however this practice was not considered cost efficient. Lead has also been used but abandoned due to the obvious risk of toxicity. Platinum revealed very little reaction but again abandoned due to cost. Use of alloys showed promising results and Vitallium (cobalt, chromium and molybdenum)[8] and Ticonium (cobalt, chromium, nickel, molybdenum)[9] became popular prior to the second world war. Tantalum, an inert metal with good results in animal models, became popular and used widely to treat combat injuries in the second world war[10] but due to the difficulties in acquiring and purifying this, it remained an expensive metal. Zirconium was also shown to have minimal tissue reaction in studies[11].

The use of titanium was first described by Simpson in 1965[12]. The author reported that although the material was not perfect and less malleable than tantalum, it was radiolucent when used in an appropriate thickness and cheaper as a material in his experience of 7 cases.

Non-metallic compounds have also been long explored in a bid to find an ideal cranioplasty material. Celluloid was first used in 1890 and subsequently gained popularity due to its elasticity and resilience[13]. This material lost favour as there was noted to be considerable tissue reaction sometimes causing fistula formation. Acrylic gained increasing popularity around 1940 when its use in dental implants was recognised to show no tissue reaction. Methyl methacrylate (also known as Lucite, Vitacrylic, Plexiglass, Crystallite, Craniolast and Perspex) was felt to be considerably malleable and radiolucent and could be easily used to reconstruct large defects[14]. Use of other inert compounds such as Polyethylene[15] and silicon rubber[16] have been considered but did not gain popularity due to their soft structure.

[1] Abhay S, Haines SJ. Repairing holes in the head: a history of cranioplasty. Neurosurgery. 1997 Mar 1;40(3):588-603.

[2] Feroze AH, Walmsley GG, Choudhri O, Lorenz HP, Grant GA, Edwards MS. Evolution of cranioplasty techniques in neurosurgery: historical review, pediatric considerations, and current trends. Journal of neurosurgery. 2015 Oct;123(4):1098-107.

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[7] Mitchell AB. Repair of injuries to the skull by perforated plates. British Journal of Surgery. 1917;5(17):40-1

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[14] Gurdjian ES, Webster JE, Brown JC. Impression technique for reconstruction of large skull defects. Surgery. 1943 Dec 1;14(6):876-81.

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[16] Courtemanche AD, Thompson GB. Silastic cranioplasty following cranio-facial injuries. Plastic and reconstructive surgery. 1968 Feb 1;41(2):165-72.

It was however noted that the acrylic plates could be prone to fracture and therefore Galicich and Hovind in 1967 described stainless steel mesh reinforced acrylic cranioplasty[17]. This was later modified by Malis to use a titanium mesh instead of stainless steel due to multiple reasons including the artefact produced on CT and compatibility issues with MRI[18].

Hydroxyapatite is a more recent development in cranioplasty materials and is a calcium phosphate compound. This is a natural mineral found in bone but can be synthesised as a hexagonal structure creating a ceramic. The material has shown minimal tissue reaction. It has also shown increased bone repair and osteointegration to its advantage. However if used alone it can be very brittle and prone to fracture. It has been used in oral and maxillofacial surgery for many years[19],[20] and Pompili et al published one of the first series in use of this material for cranioplasty[21]. A total of 11 cases underwent cranioplasty with a material composed of hydroxyapatite, combined with a gel, and laid on titanium mesh or micronets. Post operatively the patients were reported to have good outcomes with impressive levels of osteo-integration according to the authors.

Polyetheretherketone (PEEK) is another organic compound which has gained popularity as it is inert and radiolucent. It is a semicrystalline thermoplastic which has been shown to have similar strength to bone and can be used to print accurate 3D reconstructions of the required implant. One main disadvantage is the cost involved as PEEK implants can often be expensive[22].

The debate between autologous versus synthetic cranioplasty has been ongoing with various publications and authors arguing advantages and risks of both. In our unit we practice both autologous and synthetic cranioplasty and historically this has been done with surgeon preference in cases where both options were available. We chose to look at our outcomes for these groups.

Method

A retrospective study was carried out of all cranioplasty procedures at our unit between June 2009 and March 2018. The patients were identified from a combination of electronic theatre records for a cranioplasty coded procedure and from our bone bank register. Once patients were identified, information was collected via their electronic patient records, theatre notes and all available imaging.

Bone flaps sent to the bank were placed in sterile saline solution during the period of operation until a decision was made regarding replacement. Once a decision was made, swabs and bone chips were taken prior to the bone being placed in a double sterile sealed plastic container (one sealed container within another). Swabs and bone chips were used for cultures and sensitivity. If any positive cultures were found, the bone was disposed. The plastic containers were wrapped in a further plastic bag before being stored in a deep freezer at -81 degrees. Prior to re-implantation, the bone was thawed at room temperature and soaked in either gentamicin in sterile saline or aqueous betadine based on surgeon preference and/or patient allergies. This was undertaken while incision and exposure were taking place.

Decision for material used for synthetic cranioplasty was based on surgeon preference. There are no established protocols within our department for choice of material however in general if a bone flap can be salvaged (i.e. It is not deemed immediately infected or fragmented due to trauma), then an autologous cranioplasty is usually undertaken in the future. There are however exceptions in even these cases whereby a consultant may choose to select synthetic materials out of personal preference or experience.

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[22] Shah AM, Jung H, Skirboll S. Materials used in cranioplasty: a history and analysis. Neurosurgical focus. 2014 Apr;36(4):E19.

Each cranioplasty was custom manufactured using thin slice CT. A combination of Titanium, Ceramic, Acrylic and hydroxyapatite plates were used, all pre-manufactured and delivered in a sterile pack which was opened just prior to surgery. These too were placed in either gentamicin in sterile saline or aqueous betadine prior to placement. All cranioplasties were fixed with 5mm self-tapping titanium screws with mini plates. Figure 1 demonstrates the common synthetic materials used within our department.

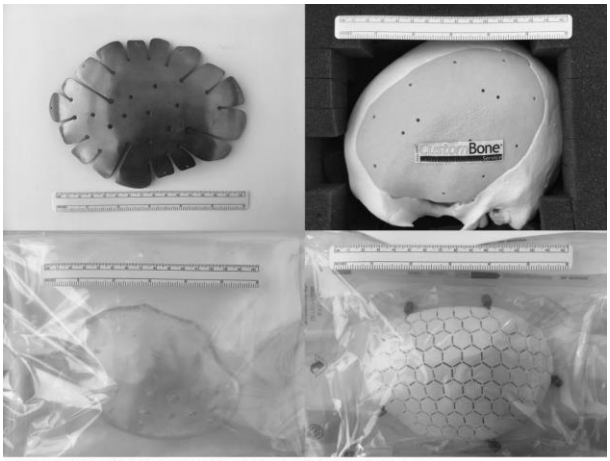

Figure 1: Examples of cranioplasty materials. Titanium *(top left)*, Ceramic *(top right)*, Acrylic *(bottom left)*, Hydroxyapatite *(bottom right)*

Primary outcome was need for revision. Information was also collected for other complications including infection, timing of cranioplasty and original diagnosis. Fisher 2 tailed tests were conducted at 5% significance level to confirm statistical significance for revision rates and multiple factors. Odds ratios were calculated for various factors.

Results

145 patients were identified. 1 patient with synthetic cranioplasty was exclude as the implant had to be removed due to failure of a complex advancement skin flap

One patient had own bone cranioplasty which was complicated by resorption of the bone flap. This complication was included under autologous group. The defect was then repaired using a synthetic implant which was placed overlying the partially absorbed autologous flap. However, this was further complicated by infection and necessitated removal of the partially resorbed bone and synthetic implant. As it was not clear as to what caused the infection, this was excluded from infection rate of both groups.

81 males and 63 females were included in the study with an average age of 51.6 years (Range 18.1 – 85.3 years). Overall 51 cranioplasties were performed using own bone and 93 synthetic. Table 1 details the synthetic cranioplasty materials used. Average delay in cranioplasty was 268 days (Range 16 – 1264 days). The most common reason for craniectomy was Acute Subdural Haemorrhage (23.6%), post operative infection (19.4%) and intracranial haemorrhage (15.3%). Table 2 illustrates patient characteristics for those undergoing cranioplasty.

Cranioplasty Material	No. of Patients
Titanium	52
Acrylic	18
Ceramic	14
Hydroxyapetite	9

Table 1: Synthetic cranioplasty materials

		Bone	Synthetic
Age *(Years)*	Range	20.5 - 74.8	18.1 - 85.3
	Average	49	53.1
Male		32	49
Female		19	44
Reason for Craniectomy *(No. of Patients)*	Non-Traumatic		
	Post op infection	N/A	28
	ICH	9	13
	MCA infarct	10	4
	Intra-osseous tumour	N/A	10
	Post op haematoma	1	2
	Post op subdural empyema	0	3
	Post op swelling	1	1
	SAH Haematoma	2	0
	Spontaneous subdural empyema	0	2
	Post SAH infarct	1	0
	SAH	1	0
	Traumatic		
	ASDH	20	14
	TBI	2	6
	Extradural	3	4
	Large Contusion	1	5
	Depressed skull Fracture	0	1
Time from Craniectomy to Cranioplasty *(Days)*		194.6	325.3

Table 2: Patient characteristics

Overall complication rate was 20.8% (30 cases) with 16 cases in the own bone group (31.4%) and 14 cases in the synthetic group (15.1%). There were significantly more complications in the autologous group as compared to the synthetic group (p 0.031). Bone flap infection rate for all 144 cases was 9.7% (14 cases) with 6 cases in the autologous group (11.8%) and 8 cases in the synthetic group (8.6%). Difference

in Infection rate was not found to be statistically significant (p 0.542). Other complications are shown in Table 3. The only significant difference was found to be in post operative extra-dural haematoma (EDH) with 3 cases (5.9%) in autologous group and none in synthetic group (p 0.043). Resorption was not included as a comparative complication risk for analysis as this would not apply to synthetic cranioplasty and therefor was analysed as part of revision rates.

	Overall	%	Autologous	%	Synthetic	%	P-Value
Infections	14	*9.72*	6	*11.76*	8	*8.60*	0.5654
Hydrocephalus	4	*2.78*	3	*5.88*	1	*1.08*	0.1273
Pseudomeningocele	4	*2.78*	3	*5.88*	1	*1.08*	0.1273
Extradural Haematoma	3	*2.08*	3	*5.88*	0	*0.00*	0.0427
Wound breakdown	2	*1.39*	0	*0.00*	2	*2.15*	0.5393
DVT	1	*0.69*	1	*1.96*	0	*0.00*	0.3542
CSF Leak	1	*0.69*	0	*0.00*	1	*1.08*	1
Chronic pain	1	*0.69*	0	*0.00*	1	*1.08*	1
Superficial Wound infection	1	*0.69*	0	*0.00*	1	*1.08*	1

Table 3: Complications of cranioplasty

Overall resorption rate for autologous cranioplasty was 27.5%. Of these 14 cases, 6 required revision due to significant resorption of the bone flap, however 8 cases only had partial resorption, hence did not need revision. Resorption was deemed significant if it resulted in either gross anatomical or aesthetic defect necessitating revision. Partial resorption included those patients with evidence of radiological bone resorption without a substantial anatomical deficiency or concerns from the patient. If bone resorption is included in the complication, the complication rate in autologous group becomes 31.4% if only revised flaps were included. The total complication rate for autologous group was 54.9% including all bone flaps which showed any resorption (either partial or near total).

Revision rate was found to be 13.2% overall with 12 revisions in the autologous group (23.5%) and 7 in the synthetic group (7.5%). All revisions in the synthetic group took place due to infection, including 1 case of subdural empyema. 6 cases within the autologous group were revised due to infection and the remaining 6 cases due to resorption. Difference in revision rate was found to be statistically significant (p 0.01). The significant increase in revision rate was found to be due to bone resorption in the autologous group. Risk of requiring revision of cranioplasty in autologous group was 3.5 times (Range1.5 – 8.1) that of synthetic group.

Discussion

Autologous cranioplasty remains practiced across the world but is losing popularity due to growing belief in increased complication rates and the inherent risk of resorption. One study of 125 patients undergoing autologous cranioplasty estimated complication rate at 9.2% and resorption rate at 19.7%[23]. There has also been some dispute as to the best solution for storing autologous cranioplasties and some have argued that different techniques can contribute to complication risks.

In one study, the infection rate following re-implantation of cranioplasty stored subcutaneously was 5.6% and 2 further bone flaps (2.2%) were removed for resorption. 2 haematomas were noted, one extradural and one within the abdominal pocket. The remaining results were deemed to be acceptable however follow up was only for 1 year at the time of publication[24]. The authors felt the subcutaneous storage was a viable and acceptable means of storage.

Another study of 53 patients undergoing cranioplasty following subcutaneous storage reported 3 bone flap infections (6%). One was noted to be infected in the subcutaneous space where it was stored and had to be discarded. Two were infected post cranioplasty and needed removal[25]. The paper does however report that 8 of the cranioplasties (15%) required immediate augmentation with synthetic material but do not specify whether this was for resorption or other reasons. They also do not specify whether infections occurred within the augmented cranioplasties or entirely autologous grafts. Morina et al reported only 2 revisions needed out of 75 cases for infection for bone stored in an abdominal subcutaneous pocket[26]. Again, 9 of their cases required

[23] Brommeland T, Rydning PN, Pripp AH, Helseth E. Cranioplasty complications and risk factors associated with bone flap resorption. Scandinavian journal of trauma, resuscitation and emergency medicine. 2015 Dec;23(1):75.

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[26] Morina A, Kelmendi F, Morina Q, Dragusha S, Ahmeti F, Morina D, Gashi K. Cranioplasty with subcutaneously preserved autologous bone grafts in abdominal wall—Experience with 75 cases in a post-war country Kosova. Surgical neurology international. 2011;2.

augmentation with synthetic material and the authors do not comment on whether the infection was in autologous alone or combined cranioplasties.

Hauptli and Segantini report their change in practice after observing frequent osteolysis in their cryopreserved bone flaps, particular at edges, in up to 60%. Following changing their method of preservation to subcutaneous pocket, they reported improved bone resorption rates with only 2 bone flaps showing signs of resorption following implantation and one removed for infection[27]. The paper however does only quote a 2 year follow up.

Cryopreservation is another method widely employed of storing bone flaps. In a large retrospective study, Fan et al reported their experience of cryopreserved bone flaps over a 12-year period[28]. A total of 946 cases of cranioplasties were assessed and re-implantation took place between 67 – 641 days (average 194 days). Bone flaps were stored after gentile irrigation with sterile saline, wrapped in 2 layers of sterile plastic and then placed in a storage medium (including dimethyl sulfoxide, DMSO) and slowly cooled by various methods to a final temperature of -196 degrees in liquid nitrogen. Swabs were sent prior to storage and if any positive growth found, the flaps were discarded. Through their storage process the authors reported that microscopically the bone retained features of normal bone including good osteocyte activity as compared to fast freezing or autoclaving. Overall infection rate was 4.06% (39 flaps) and resorption rate was 4.28% (42 flaps). All infected bone flaps were removed however the authors do not report their outcomes with resorbed flaps. The use of bioactive materials such as those used by Fan et al have been argued to improve bone flap viability during cryopreservation and in a laboratory study of mice femoral tissue, storing in DMSO solution was shown to have improved cell proliferation as compared to a control solution[29].

Hng et al discussed their results of 187 patients with cryopreserved cranioplasty over a 10-year period[30]. Bone was wrapped in a sterile plastic sheath and stored at -30 degrees. Prior to re-implantation the bone was thawed at room temperature and soaked in betadine. The authors also recommend against autoclaving due to the higher risk of bone resorption. 64.7% of cranioplasties were undertaken within 90 days (range 10 – 390 days) and overall complication rate was 34.2% (64 cases). Bone flap infection requiring removal was noted in 11.2% and revision of bone flap due to resorption occurred in 5.34%. Other complications included superficial wound infection (3.21%), hydrocephalus 3(.21%) and seizures (2.67%)

Iwama et al also reported good outcomes with their experience of cryopreserved bone flaps in 49 patients[31]. They stored bone in 3 sterile vinyl plastic bags at either -35 or -84 degrees and flaps were washed in sterile saline and Tobramycin prior to re-implantation (4 – 168 days, average 50.6 days). Only 2 complications were noted (4%), one case of infection and one case of revision needed for bone resorption. Grossman et al reported no complications in their 12 cases of cryopreserved cranioplasties[32]. In their series the bone was irrigated with saline and neomycin antibiotic, wrapped in 2 sterile plastic wraps and stored at -80 degrees. An extended point in this series was the average re-implantation duration was 9.25 months (0.25 to 27 months) however despite this duration, no complications were reported in this, albeit small sample.

Lu et al published their experience with 16 cases of cryopreserved bone flaps at -80 degrees[33]. The bone flaps were wrapped in 2 sheets of sterile plastic

[27] Häuptli J, Segantini P. New tissue preservation method for bone flaps following decompressive craniotomy. Helvetica chirurgica acta. 1980 Jun;47(1-2):121-4.

[28] Fan MC, Wang QL, Sun P, Zhan SH, Guo P, Deng WS, Dong Q. Cryopreservation of Autologous Cranial Bone Flaps for Cranioplasty: A Large Sample Retrospective Study. World neurosurgery. 2018 Jan 1;109:e853-9.

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[33] Lu Y, Hui G, Liu F, Wang Z, Tang Y, Gao S. Survival and regeneration of deep-freeze preserved autologous cranial bones after cranioplasty. British journal of neurosurgery. 2012 Apr 1;26(2):216-21.

before being placed into an "ultra low freezer" at -80 degrees. Prior to replacement, they were soaked in providone-iodine for 30 minutes and average delay in cranioplasty was 117 days (Range 63 – 289 days). They reported no infection or other complication with their re-implanted bone and conducted post operative SPECT imaging which the authors reported showing equal radioactive uptake in re-implanted bone as compared to native bone.

This is in contrast to some studies that have suggested that bone flap viability becomes limited following a period of storage. A laboratory study by Bhaskar et al revealed no cell growth in bone flaps stored at -30 degrees for over 6 months rendering the bone flaps non-viable[34]. Another study however, revealed no effect on the biomechanical properties of human skull bone when comparing fracture loading, tested by bending forces until the sample fractured. The bones were tested following storage at -20 degrees for up to 3 months[35].

In a paper comparing subcutaneously stored (SC) bone versus cryopreservation (CP) at -70 degrees following betadine soaking, there was no statistical difference in infection rates between the groups. Of the 39 cranioplasty stored in subcutaneous pocket and 31 cryopreserved, there were 2 (5.1%) and 5 (16.1%) infections respectively. In the SC group, one infection occurred in the abdomen and one on re-implantation. On infection within the CP group was considered superficial only and treated with intravenous antibiotics. A subgroup analysis however revealed significantly higher infection in cryopreserved bone for those undergoing craniectomy for traumatic brain injury (TBI)[36].

Cheng et al also compared subcutaneous versus cryopreservation of bone flaps of patients undergoing decompression over a 10-year period[37]. 290 patients were included with 110 preserved subcutaneously and 180 cryopreserved. The bones were immersed in betadine for 30 mins and then vancomycin for another 30 mins prior to being stored. Microbiology swabs were sent. Overall infection rate was 13.8% with 20 cases of infection in each group (11.11% SC, 18.18 CP) with no statistically significant difference. In the subcutaneous pocket group, 12 of these were as a result of cranioplasty and the remainder were within the stored pocket requiring disposal of bone flap. The authors also studied bone resorption by comparing frontal bone thickness and found that there was statistically significant decreased thickness in the CP group, but they do not comment on whether any revisions were needed as a result.

Another method of bone flap preservation used by some surgeons is subgaleal storage on the opposite side of the craniectomy. Goel and Deogaonkar reported their outcome of subgaleal bone flap preservation[38]. 8 cases were included however only 4 of the bone flaps were replaced with very unclear indication within the paper as to the reason for this. The authors concluded that within the replaced bone flaps, there were no complications with bone flaps being stored for anywhere between 3-16 months.

Krishnan et al described 55 cases of subgaleal preserved bone flap and reported only 2 complications related to wound or skin breakdown from pressure[39]. Korfali and Aksoy reported no complication following 27 cases of replacement of bone flaps stored under the galea. Both papers felt subgaleal storage was an easy and cost-effective method of storage.

A review paper comparing multiple techniques of bone flap storage concluded that there was no statistically significant difference between technique of bone flap preservation and post operative

[34] Bhaskar IP, Yusheng L, Zheng M, Lee GY. Autogenous skull flaps stored frozen for more than 6 months: do they remain viable?. Journal of Clinical Neuroscience. 2011 Dec 1;18(12):1690-3.

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[38] Goel A, Deogaonkar M. Subgaleal preservation of calvarial flaps. Surgical neurology. 1995 Aug 1;44(2):181-3.

[39] Krishnan P, Bhattacharyya AK, Sil K, De R. Bone flap preservation after decompressive craniectomy-Experience with 55 cases. Neurology India. 2006 Jul 1;54(3):291.

outcome[40]. This was however not a systematic review. Yadla et al conducted a systemic review on subcutaneous storage versus extracorporeal and found no statistical difference[41].

Many papers have also attempted to compare autologous bone flaps with synthetic materials. Piitulainen et al studied their results over a 10-year period with 100 cranioplasties[42]. 20 were performed using autologous bone and the remainder with various synthetic material. Bone flaps were stored at -80 degrees and swabs were taken to ensure no growth prior to re-implantation. Overall complication rates were 60% for autografts and 25% for synthetic material. Revision rates were 40% for autografts and 14% for synthetic materials. The paper reports there was no significant difference between autologous cranioplasty and synthetic subgroups but do not undertake an overall comparison. From their data a chi squared test reveals a p value of 0.02. Serious infection rate was 25% in autologous and 5% in synthetic group with a resorption rate of 15%. There were no specific risk factors shown to be significant including time of implantation.

Klinger et al also published their experience of 258 cranioplasties over a 10-year period[43]. Autologous bone was stored between -40 to -80 degrees following swabs being undertaken to ensure no growth. Synthetic cranioplasty was undertaken with acrylic flaps. A total of 138 (53%) procedures were with autologous bone and 120 (47%) with acrylic. The authors reported an overall 10.9% complication rate and reported no significant difference between the two groups. In their series, only 2 (1.4%) bone flaps underwent significant bone resorption.

A systemic review looking at impact of cranioplasty material on infection rates concluded that there was no significant difference between autologous and synthetic flaps[41]. Another systemic review and meta-analysis comparing PEEK cranioplasty to other materials including autologous again did not find any significant difference in complication rates[44]. However, they analysis only included 2 studies in their review.

Time of cranioplasty has long been debated as an independent risk factor for revision. A large retrospective study reported that cranioplasty undertaken between 15 to 30 days post craniectomy were associated with a lower infection, seizure and resorption rate[45]. Cranioplasty after 90 days was associated with lower hydrocephalus rates but higher risk of seizures.

A recent systemic review found that although early cranioplasty (<90 days) was associated with higher incidence of hydrocephalus, there was no statistical difference between any other complication[46]. Overall infection rate was reported between 0 to 24% with an average of 7.4%. This systemic review echoed a previous study which concluded the same results with no significant difference between early and late groups but a significantly higher hydrocephalus rate in the early group[47]. Although the several systemic reviews have concluded that there is no increase in complication rates, evidence has suggested neurological outcome may be improved with early cranioplasty[48]. A

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Cochrane registered article by a German team concluded in their abstract that ultra-early (within 6 weeks) cranioplasty improved neurological outcome[49]. However, the remaining article is in German and therefore we could not critique their methods.

Another Cochrane registered prospective multinational trial concluded that there was no increase in risks by early cranioplasty (under 12 weeks) but did not establish a significant benefit[50]. The authors admit that they only recruited 70 patients into their study and potentially was underpowered to obtain statistically significant results.

In our study the average delay in cranioplasty was 268 days with a range of 16 to 1264 days with a median of 224 days. There are no specific established protocols within our department to specify the timing of cranioplasty however most surgeons' preference is to undertake this procedure after 3 to 6 months to judge clinical recovery. With cases of infection, the surgery is usually undertaken after a period of observation on completion of antibiotic therapy, which is usually continued for a minimum of 6 weeks. 31.3% of cranioplasties occurred within 6 months and 69.4% within 1 year. Some cases had an unusually long delay mainly due to patient factors with regards to clinical recovery however due to the retrospective nature of our study, in some cases the delay was unclear.

In view of paucity of data, a recent randomised control trial has been published comparing autologous flaps with titanium cranioplasty[51]. 64 patients were recruited and outcomes assessed at 1 year. Bone flaps were preserved at -80 degrees in double layer of sterile plastic and on the day of procedure, were thawed in warm saline solution. All patients underwent post operative CT on day 1. The authors reported no infection of primary cranioplasty however 1 case of infection in a patient requiring titanium cranioplasty following own bone resorption. Complete resorption was reported in 7 (22%) of cases but only 5 of these patients agreed to a revision cranioplasty as the other 2 were still satisfied with overall cosmesis. Resorption was observed more commonly in younger patients (32 vs 45, p 0.013 and a further 12 cases were noted to have some degree of resorption. There was no difference between complication rates including post op haematoma requiring surgery which was reported as 5% in own bone and 6% in titanium group. The authors also conducted a cost analysis and found no statistical difference and thus concluded that primary titanium cranioplasty should be considered in all patients, especially young to improve cosmesis and reduce need for revision.

A follow up article by this author looking at 24 months outcome reported that the 2 patients who chose for conservative management of their resorbed bone flaps changed their minds due to increasing postural headaches and another patient progressed from moderate to severe resorption needing revision. Therefore, over the 24-month period, 25% of own bone cranioplasty required revision versus none in the titanium group (p 0.001)[52]. A recent systematic review and meta-analysis also reported similar finding of significantly increased revision rate with autologous cranioplasty primarily due to resorption, which was reported as 20% overall[53]. The article reported no significant difference in other complications including infection.

Our series reflects the findings of the randomised control trial and recent systematic review in that significantly greater revisions were needed with own bone cranioplasties. There were also greater number of complications overall as compared to the

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synthetic group. This raises the question of continuation of own bone cranioplasties and whether all patients should receive synthetic flaps.

In our series the only statistically significant complication was extradural haematoma however the significance of this is uncertain. No previous study has highlighted a significant increase in post operative EDH and this may be purely artefactual. No factors could be clearly identified in relation to this complication, including placement of drain which is routinely practiced regardless of cranioplasty material.

One consideration for choice is cost of cranioplasty. In our unit, the storage cost of bone flaps are negligible and cost of theatre and ward stay are the same regardless of the choice of material. Therefore there is a significant cost disparity between the groups and use of synthetic cranioplasty in all patients would increase costs for the unit. A formal cost analysis was not undertaken and when accounting for increased complication rates with autologous cranioplasty, the difference may not be significant.

Conclusions

Our study reflects results from previous publications showing increased revision rates with autologous cranioplasty as compared to synthetic materials. Although there may be a cost implication, the increased risks should be strongly considered when deciding the best method of cranioplasty for any patient. In keeping with other recent publications, we would recommend synthetic cranioplasty should be favoured over autologous unless patient factors, cost implications or local resources influence otherwise.

Abbreviations

3D - Three-dimensional
CP - Cryopreservation
CT - Computed Tomography
DMSO - Dimethyl sulfoxide
EDH – Extra-dural Haematoma
MRI - Magnetic Resonance Imaging
PEEK - Polyetheretherketone
SC - Subcutaneously stored
SPECT - Single-photon emission computed tomography
TBI - Traumatic Brain Injury

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Preliminary results of minimally invasive stereotaxic surgery of intraparenchymal hematomas at the Hospital of Mali (23 cases)

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ABSTRACT

Introduction: Spontaneous intracerebral haemorrhage (ICH) is a rupture of blood vessels in the brain parenchyma, in the absence of any underlying structural vascular lesion. It's destructive and associated with a high mortality rate. There is a specific threshold of hematoma evacuation to impact mortality or functional outcome in ICH even the curative effect of minimally invasive hematoma removal for cerebral haemorrhage has not been fully recognized worldwide. We aim to evaluate surgical performance on hematoma volume and functional outcomes of patients.

Methods: This study is a retrospective and observational clinical study. A total of 30 ICH patients were treated in the Department of neurosurgery at the Hospital of Mali from December 2019 to November 2020. Minimal invasive puncture hematoma removal was performed in all the patients. The modified Rankin scale (mRS) was used to assess functional outcomes at 6 months and one year of surgery. Was considered poor functional outcome mRS >3. The percentages (%) of the count data were assessed by Fisher's exact test by SPSS 23.0 software was used.

Results: A total of 23 ICH patients met the inclusion criteria, the mean was 47,78 years. Among the risk factors, the HTA is present in 91,3% of patients. The evacuation was satisfactory in 91.30% of cases.

Conclusion: This first study of minimally invasive stereotaxic for ICH evacuation must be followed up and encouraged. Even if the results are satisfactory, a double-blind study is required in the largest sample.

INTRODUCTION

Spontaneous intracerebral hemorrhage (ICH) or primary intracerebral hemorrhage (ICH) is a rupture of blood vessels in the brain parenchyma, in the absence of any underlying structural vascular

lesion, can lead to the accumulation of the blood within the brain substance (7). ICH is the second most severe type of stroke; it is destructive and associated with a high mortality rate. The current treatment methods are limited, and only a few surviving patients can recover their self-care ability, leading to a heavy economic burden on families and society (12). It is urgent that new therapeutic methods for cerebral hemorrhage are developed. A brain injury caused by cerebral hemorrhage can be considered either a primary brain injury or a secondary brain injury, and the treatment of cerebral hemorrhage focuses on the following two concepts: on the one hand, a mechanical injury, on the other hand, reducing the risk for deterioration of neurological function after cerebral hemorrhage (10). There is a specific thresholds of hematoma evacuation to impact mortality or functional outcome in ICH (5) even the curative effect of minimally invasive hematoma removal for cerebral hemorrhage has not been fully recognized worldwide (4,7). In Mali there is no study on the intracerebral hemorrhage evacuation, nor in west Africa and with the development of minimally invasive techniques we initiated the stereotactic evacuation of ICH. We aim to evaluate surgical performance on hematoma volume and functional outcome of patients.

Methods

Subject

This study is a retrospective and observational clinical study. A total of 30 ICH patients treated in the Department of neurosurgery at the Hospital of Mali from December 2019 to November 2020. Were included in this study 23 patients with complete clinical and radiological data. The inclusion criteria were: Age ≥18 with ICH whose surgical volume was location function.

Lobar≥ 30cc, Thalamic and basal ganglia≥ 15cc, brainstem≥5cc, cerebelum≥10cc with blood presure≤160/90 mmhg.

Glasgow score≥8pts and/or motor deficit≤3/5, presence of symptoms≤72h

Exclusion criteria were: secondary ICH, patient on anticoagulation or antiaggregating or plaletet≤100000.

The stereotaxic frame was attached to the patient's head under local anesthesia (Lidocaine 2%). All patients were operated on under general anesthesia,10cc plastic syringes were used for hematoma aspiration. Evacuation was considered satisfactory for a volume evacuated ≥ 80% of the volume of the hematoma.

The cavity was rinsed with isotonic serum, the temperature of which oscillated between 2 and 4 degrees.

All patients were awakened in intensive care unit, a brain CT scan at 24h-48h postoperatively was performed.

Minimally invasive puncture hematoma removal method: Surgical procedures

Brain CT scan was performed after frame fixation. The center of the largest plane of the scanned hematoma was selected as the target point and we used the axial plan for the planification and calculation of coordinates. In the operating room the patient position depended of hematoma location and all coordinates were calculated by manual way as ANKE formula (11).

We disinfected the surgical area with a conventional way and the patient is champed (figure1). A 3cm skin incision is made at the enter point and we drilled through the skull a 5mm hole. After opening the dura, we make a puncture with 4mm canula and the gently aspiration was made a 10cc sterile syringe (Figure 2). Finally, the hematoma cavity was cleaned with 2–4-degree Nacl 0,9%.

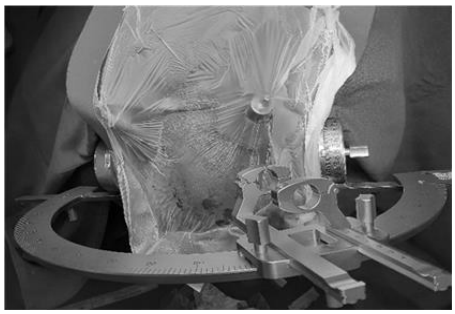

Figure 1. Patient Champed

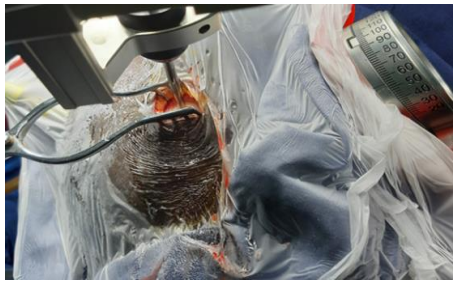

Figure 2. Puncture of hematoma

Clinical data collection

In this study the variables analyzed were demographic (sex, age), history (hypertension, diabetes mellites,), toxic habits (smoking, alcoholism) mode of transport to hospital (ambulance, personal vehicle, taxi), Glasgow scale at admission, the volume of the hematoma was measured by the ABC/2 method, presence or absence of intraventricular blood. The time points for minimal invasive surgery were divided into three groups: ≥6h ≤24 h group Ⅰ, >24h≤48h group Ⅱ and >48h≤72h group Ⅲ. Modified Rankin scale (mRS) was used to assess functional outcome at 6 months and one year of surgery. Was considered poor functional outcome mRS >3. The percentages (%) of the count data were assessed by Fisher's exact test. Univariate analysis with chi-square test and Mann-Whitney test by SPSS 23.0 software was used.

Results

A total of 23 ICH patients met the inclusion criteria, including 12 males and 11 females who were aged mean 47,78years. According to the time from onset to minimally invasive surgery, they were divided into three groups: group Ⅰ (34,8%), group Ⅱ (26,1%), and group Ⅲ (39,1%). Among the risk factors, the HTA is present in 91,3% cases with 100% in the group Ⅱ. All patients were transported by personal vehicle. The majority of patient operated were GSC between 9 and 13pts as showed in table 1. 65.14% of patients had deep localization versus 30.43% lobar localization. The less volume operated is 6cc in the brainstem and 70cc in lobar hematoma as maximum volume (Figure 3). The evacuation was satisfactory by 91.30% of patients. There was no intraventricular blood in 95.7% of cases. There was no difference between the 6 months and 12 months mortality.

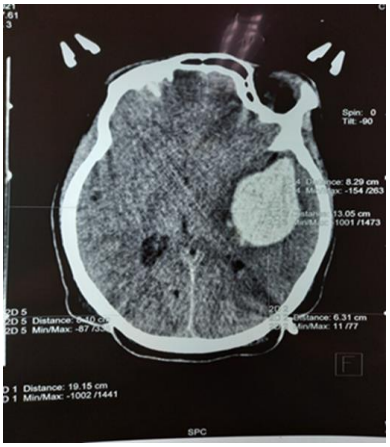

Figure 3. Preoperatory CT scan after frame fixation.

Discussion

The evacuation of intraparenchymal hematomas is a holy grail in management, however, no previous study has correlated the success of the procedure with the residual volume of ICH (8,9). The conclusions in an explanatory trial, with rigorous monitoring of the process and results of the surgical intervention, demonstrated that there is a threshold (of ≤15ml EOT ICH or ≥70% hematoma evacuated) associated with the favorable functional result, after the control of the gravity variables of the disease (5). In this first study of hematoma evacuation in Mali, we didn't used the thrombolytic drogue and for hemostatic effect we used isotonic salt serum from 2-4 degree to clean the hematoma cavity, the relationship between temperature and adrenergic response seems to be one of the pivots of the cold-induced vasospasm process (3). We considered EOT if the was absolutely clear. Our satisfaction threshold was an evacuation ≥80% of hematoma and it was 91.30% of patient. The mean residual volume was 6,95cc.

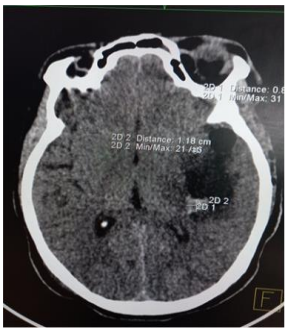

Figure 4. Postoperative CT scan

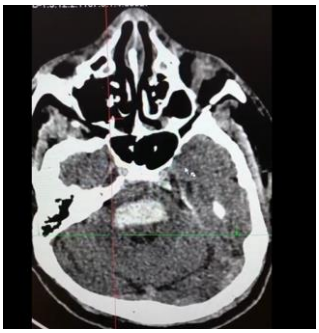

Figure 5. Preoperatory CT scan of brainstem hematoma

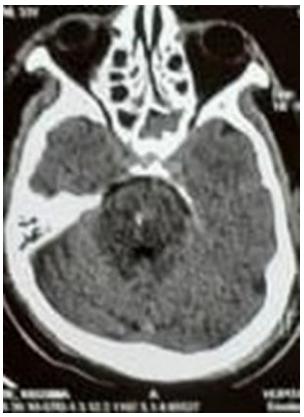

Figure 6. Control CT scan

There is no consensus on the appropriate timing of minimally invasive surgery. The time at which the surgery is performed may affect the curative effect,

Table 1. Data analysis of the three groups

Variables	Group Ⅰ (n=8)	Group Ⅱ (n= 6)	Group Ⅲ (n= 9)	P value
Sex(M/F)	(5/3)	(4/2)	(3/6)	
Mean Age	39,12	50,16	53,89	
HTA	87,5%	100%	88,89%	
DM	0%	16,67%	11,11%	
Smoke	12,5%	50%	0%	
Alcoholism	0%	33,33%	0%	
Mode of transport				
• Ambulance	0%	0%	0%	
• Personal vehicle	100%	100%	100%	
• Taxi	0%	0%	0%	
Hematoma Location				
• Lobar	25%	33,33%	33,33%	
• Thalamic and BG	62,5%	66,67%	66,67%	
• Brainstem	12,5%	0%	0%	
• Cerebellum	0%	0%	0%	
Glasgow scale				
• 8pts	12,5%	33,33%	0%	
• 9-13pts	75%	50%	100%	
• 14=15pts	12,5%	16,66%	0%	
Mean Vol of Hematoma	40,5cc	44,7cc	51,5cc	
Mean Residual vol	4,4cc	4,33cc	11cc	
mRS at 6 months				0.01
• ≤3	75%	83,33%	55,56%	
• >3	25%	16,67%	44,44%	
mRS at 1year				0.01
• ≤3	75%	83,33%	55,56%	
• >3	25%	16,67%	44,44%	

thus affecting the selection range of patients for this treatment (12). The choice to divided the time point was motived by:

The time for hematoma stabilization generally 6 hours after bleeding and 72 hours after ICH, delayed perihematomal oedema (PHE) is associated with the destruction of the blood–brain barrier (angioedema), massive lysis of red blood cells and neurotoxicity induced by hemoglobin decomposition products (6). About 39% of the patients were in group Ⅲ because of the blood pressure which was very high and which had to be checked first. None of our patients has benefited from a pre-hospital resuscitation because all of them came to the hospital in personal vehicle, which is perhaps a worsening factor.

The deep location was most frequent in all three groups with a total of 65,13% of patients. The threshold associated we favorable functional outcome maybe applicable to lobar, thalamic and basal ganglia hematoma but not to brainstem hematoma (figure 4 and figure 5) in which despite zero cc EOT the patient was mRS at 6 in the first month.

One month mortality rates associated with this devastating illness range from 35% to 52%, with half of those deaths occurring in the first 2 days (1,2) and in our sample it was 21,73%. Theoretically, removal of hematoma and reduction of cerebral oedema through surgical treatments can reduce intracranial pressure, relieve symptoms of cerebral tissue compression, and reduce inflammatory response and neurotoxic effects. However, the benefits of clinical surgical treatment for deep cerebral hemorrhage are unclear at present. The risks of surgery itself and the damage to brain tissue during the process of entering the hematoma limit the therapeutic effect (13).

There was no statistical difference at 6 mouths and one-year functional outcome and mortality between the three groups (p value 0.01).

Limitations: This is a single department study with limited means. The sample is small and the inclusion criteria are not accepted by many neurosurgeons.

Conclusion

This first study of minimally invasive stereotaxic for ICH evacuation must be followed up and encouraged. Even if the results are satisfactory, a double-blind study is required in largest sample. The result on the hematoma volume was good.

Abbreviations:
ICH: intracerebral hemorrhage
CT: computed tomography
mRS: modified Rankin Scale
CC: centimeter cubic
EOT: end of treatment
PHE: Perihematomal oedema
BG: Basal ganglia
M: Male.
F: Female.
HBP: High Blood Pressure
DM: Diabetes Mellitus
SPSS: statistical package for the social sciences.
ANKE: Name of company.
FMOS: Faculty of Medicine and Odontostomatology
USTTB: University of Sciences, Technics and Technologies of Bamako

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Anterior approach arthrodesis - ALIF with use of a titanium cage for treatment of postoperative spondylodiscitis after lumbar microdiscectomy

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Keywords
arthrodesis,
discitis,
discectomy,
postoperative period

ABSTRACT

Introduction. Infectious spondylodiscitis has an incidence of 0.21-3.6%. The best intervention should be individualized, using antibiotics only or combining them with stabilizing surgeries.

Case presentation. A 38-year-old man presented with lumbosciatalgia, severe pain and inability to ambulate. Magnetic resonance imaging (MRI) of the lumbar spine showed L5-S1 extruded disc herniation and the patient underwent endoscopic microdiscectomy with complete remission of symptoms. After two weeks, he reported severe low back pain and a return of difficulty to walk. Laboratory tests showed an increase in CRP and ESR. MRI showed signs of lumbar spondylodiscitis. The patient started on broad-spectrum intravenous antibiotic therapy. He evolved with improvement in laboratory parameters and maintenance of low back pain. Due to the failure of conservative treatment, anterior approach arthrodesis (ALIF) was chosen, with the complete improvement of the low back pain and the return of the ability to walk.

Discussion. Postoperative spondylodiscitis' frequency depends on the invasiveness of the operation and the type of surgery performed. The most likely source of infection is direct inoculation by virulent pathogens during surgery. A diagnosis delay of more than two months is considered a risk factor for generating adverse results. A Conservative approach is indicated for the patient who is neurologically intact and with minimal bone destruction. Surgical indications are the presence of neurological deficits, intraspinal abscesses, extensive bone destruction, and failure of conservative management. ALIF is supported in the literature because it allows wide exposure of the entire disc space through efficient access to the spine with the complete evacuation of the disc, avoiding dissection of perineural scar tissue and preserving the articular facets.

Conclusion. Early diagnosis and treatment are crucial, although there is still no consensus about the best treatment approach. The use of a titanium cage with a bioglass graft had a good response in pain and infection control in our case.

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Introduction

Infectious spondylodiscitis is an infection of the intervertebral disc and adjacent vertebral bodies, with an postoperative incidence of 0.21-3.6%[1]. The most recommended diagnostic method is Magnetic Resonance Imaging (MRI), due to the early identification of the disease made by this exam[2,3]. The appropriate intervention should be individualized, using either conservative methods alone, such as antibiotic therapy, or combined with stabilizing surgery [2,4]. The purpose of this paper is to report and discuss the case of a patient who underwent an anterior approach arthrodesis (ALIF) using a titanium cage after presenting postoperative spondylodiscitis from a lumbar microdiscectomy.

Case presentation

Male patient, 38 years old, attended the first medical appointment with lumbosciatalgia on the right side. He reported severe pain with progressive worsening and inability to ambulate. Neurological examination revealed distal paresis of the right lower limb with achilles hyporeflexia and pain in S1 root territory. Magnetic resonance imaging (MRI) of the lumbar spine showed L5-S1 extruded disc herniation with radicular compression on the right side. Patient underwent endoscopic microdiscectomy with complete remission of symptoms.

After two weeks, the patient reported severe mechanical low back pain, unresponsive to the use of opioids. Moreover, there was a return of difficulty in walking and the need for intravenous analgesia for pain control. Laboratory tests showed an increase in C-reactive protein (CRP) and erythrocyte sedimentation rate. Control MRI showed signs of contrast-enhanced L5-S1 lumbar spondylodiscitis, such as diffuse hyposignal on T1 between the L5 and S1 vertebral bodies, with irregularity and loss of definition of the terminal plateaus and compression of the ventral surface of the dural sac and nerve roots (Figure 1).

In view of the diagnosis, the patient was hospitalized and started on broad-spectrum intravenous antibiotic therapy with Vancomycin Hydrochloride and Meropenem for eight weeks. He evolved with improvement in laboratory parameters, but there was maintenance of intense low back pain. Due to the failure of conservative treatment, anterior approach arthrodesis (ALIF) using a titanium cage and bioglass graft was chosen (Figure 2).

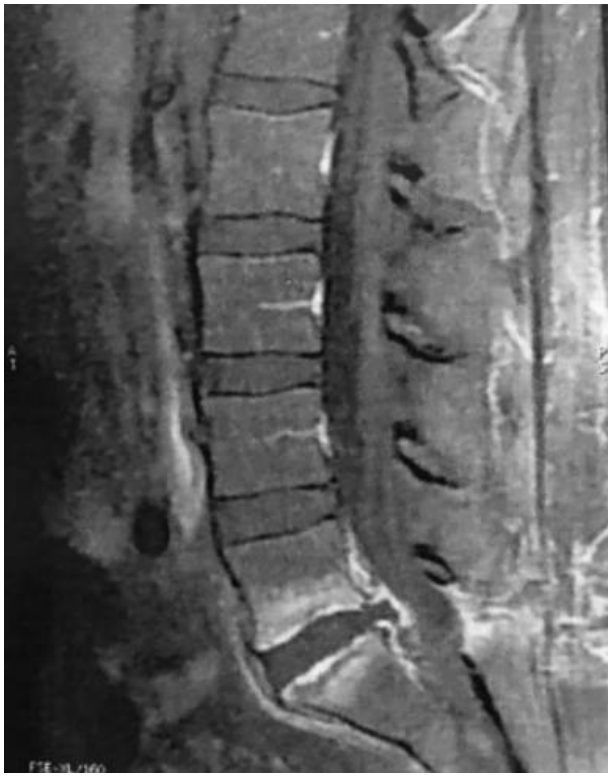

Figure 1. MRI with contrast uptake exposing spondylodiscitis of the L5 and S1 vertebral bodies.

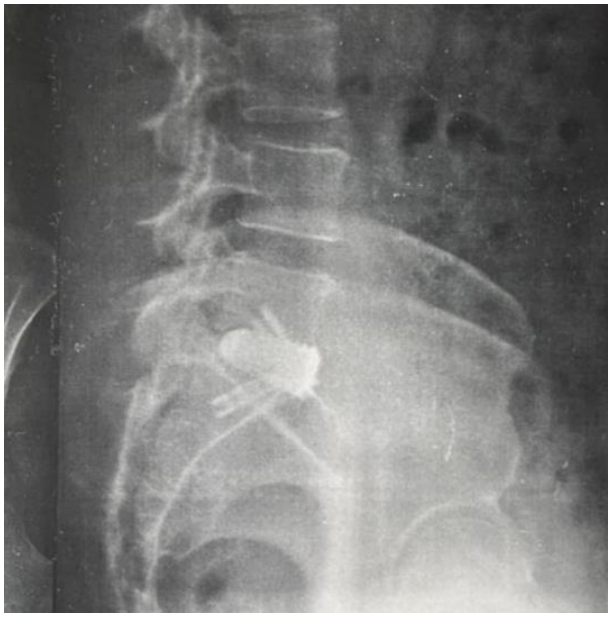

Figure 2. Postoperative X-ray presence of the titanium cage and graft.

Three months after the procedure, the patient presented complete improvement of the low back pain, return of the ability to walk, and undergoing rehabilitation for muscle strengthening.

Discussion

Spinal infections are relatively uncommon, but the incidence is significantly increasing due to the growing number of spinal interventions, which often require long operation times and deployment of significant amounts of instrumentation [3,5]. Postoperative spondylodiscitis is a rare primary infection of the nucleus pulposus, with secondary involvement of the cartilaginous endplate and vertebral bone, mainly affecting single segments in the lumbar region [1,6]. The frequency depends on the invasiveness of the operation and is between 0.1% and 0.6% for microsurgical operations, as in the reported case, and between 1.4% and 3% for macrosurgical operations [7]. The incidence also varies with the type of surgery performed, and usually occurs after minimally invasive spinal procedures, including laminectomy, discectomy, discography, myelography, paravertebral injection, lumbar puncture, and spinal fusion, with or without instrumentation [1, 6, 8]. In the presented case, the patient had spondylodiscitis after a microdiscectomy to treat a herniated disc. The most likely source of infection for postoperative spondylodiscitis is direct inoculation by virulent pathogens during surgery, the most common being Staphylococcus aureus and Streptococcus epidermidis bacteria, but hematogenous contamination, although uncommon, is also a possible cause [6].

Among the risk factors, malnutrition, neoplasms, obesity, alcoholism, smoking, chemotherapy, immunosuppression, advanced age, diabetes mellitus, and spinal trauma have been reported in the literature to predispose patients to postsurgical discitis [1, 6]. In addition, several studies report a bimodal age distribution among patients with spondylodiscitis, with peaks in the under 20 age group and the 50 to 70-year-old group, although all ages can be affected [9]. Spondylodiscitis also has a male preponderance, with a female/male ratio of 1.5-2:1.9 [9].

The main symptom is low back pain [2, 10, 11]. The pain is not always severe, but tends to be persistent, often preceded by a febrile episode [10, 11]. In the patient, the febrile episode was not reported, but there was intense low back pain. Among the diagnostic procedures described in the literature, MRI, in particular, is able to show the expansion of inflammatory processes into the spinal canal and soft tissues. ESR, CRP and the white blood cell count are key parameters for monitoring disease activity and the suspicion of associated infection [2, 11, 12]. Early diagnosis including assessment of the extent of infection is crucial [2, 3]. A delay of more than two months is considered a risk factor for generating adverse results [9].

The treatment possibilities consist of conservative or surgical management. A conservative approach is indicated for the patient who is neurologically intact and with minimal bone destruction. Therapeutic options are based on the culture and use of antibiotics, immobilization, analgesics and orthoses [3]. Despite having a good outcome in most cases, the prolonged period of immobilization and the long duration of antibiotic regimens in the conservative approach can lead to medical - such as renal failure and allergic reactions - and psychosocial consequences [2].

Surgical indications are the presence of neurological deficits, intraspinal abscesses, extensive bone destruction, and failure of conservative management [3, 9, 13, 14]. The objectives of surgical treatment are root decompression, debridement, eradication of the focus of infection, identification of pathogens, correction of deformity, and restoration of the physiologic profile of the spine [3, 14]. Based on the treatment of 75 Postoperative Discitis, Ahsan et al. reported that the success rate of surgical treatment was 90% and, compared to conservative treatment, required a shorter hospital stay, shorter immobilization period and administration of antibiotics and greater symptom relief with lower complication rates, similar to other studies [2]. However, there is still no consensus about the decision between proceeding conservatively or surgically and, like the procedure of choice, these are topics still under discussion [3].

The technique chosen in this case was anterior lumbar (interbody) fusion (ALIF), which is supported in the literature because it allows wide exposure of the entire disc space through efficient access to the spine with complete evacuation of the disc, avoiding dissection of perineural scar tissue and preserving the articular facets. This facilitates the insertion of the cage -correcting the overload of the structure and relieving pain - and the restoration of the disc height, which increases the foraminal volume, indirectly decompressing the nerve roots and relieving radicular symptoms [9, 15, 16, 17]. However, the longer surgery time and the

consequent increased risk of infection were also exposed as negative points of ALIF [17]. Jägersberg et al. reported, in a German retrospective study in which 83 patients with post-discectomy lumbar complications between 2005 and 2011 were analyzed, that from 2008, due to the previously mentioned advantages, the ALIF technique was applied in preference to the others - except in patients with risk factors that complicated the previous approach, such as extreme overweight and men who spoke out against this approach due to the risk, although low, of retrograde ejaculation [17].

The recorded mortality of spondylodiscitis is less than 5% [11]. Although uncommon, postoperative spondylodiscitis can be associated with severe long-term sequelae, such as neurological deficit and severe pain resulting in disability, which occurs in about 30% of cases [1, 5, 9]. In addition, it has complex diagnosis and treatment, usually resulting in prolonged hospital stays and recovery time [14]. However, most cases reported in the literature, especially those undergoing surgical treatment and without delay in diagnosis, had good outcomes with significant - but partial - reduction of symptoms, especially low back pain. The studies by Chang et al., Ahsan et al. and Jägersberg et. al. reported positive results in 80%, 90% and 76% of patients, respectively [2, 8, 17]. For conservative treatments, on the other hand, the overall prognosis is successful in about 70-83% of cases [2].

Finally, in the literature, the only factor found to prevent infection was pre- and intraoperative antibiotic prophylaxis. Brown et al. recommend first or second generation cephalosporin. Vancomycin associated with Gentamicin is advised in patients allergic to cephalosporins or colonized by methicillin-resistant Staphylococcus aureus and in long operative procedures, and for this last group, the use of frequent saline irrigation, with or without povidone-iodine to reduce wound contamination, is also recommended [1].

Conclusion

In our report, a patient who underwent an arthrodesis for the treatment of postoperative spondylodiscitis was presented. Early diagnosis and treatment are crucial, although there is still no consensus about the best treatment approach. The use of titanium cage with bioglass graft had a good response in pain and infection control in our case.

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Influence of clinical and neurophysiological parameters on the function outcome of the facial nerve after vestibular schwannoma surgery

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Keywords
facial nerve,
nerve palsy,
paralysis,
vestibular schwannoma

ABSTRACT

Introduction: Vestibular schwannomas are benign neoplasms of the nerve seath, and they represent the third most common endocranial tumour, following the meningioma and the pituitary adenomas. The primary symptoms of vestibular schwannomas are hearing loss, tinnitus as well as a balance disorder. The therapy of vestibular schwannoma consists of observation, surgery and radiosurgery. The majority of patients who are good candidates for surgery are already affected by significant hearing impairment, thus one of the primary goals of the surgery is the preservation of facial nerve function.

Aim: To analyze the outcome of facial nerve function one-year post-surgery using clinical and neuropsychological parameters.

Material and methods: This study analyzed the patient's clinical status on admission along with the neuroradiological characteristics of tumours and the neurophysiological intraoperative parameters and their effect on the facial nerve function in the early postoperative period as well as one year after the surgery using the House–Brackmann scale.

Results: A total of 30 patients who underwent surgery from January 1st 2015 to December 31st 2018 at the Clinical Centre of Serbia, Neurosurgery Clinic for vestibular schwannomas were examined. The median age of the patients was 51 years. Hearing loss was present in all patients. Sensitivity drop in the innervation region of n. trigeminus was present in 7 (23.3%) patients, as was tinnitus. Cerebellar symptomatology (76%) was present in the highest percentage of patients.

Conclusion: We can conclude that the most important aspects of the facial nerve function are the preoperative state of the facial nerve and the electrophysiological parameters. Although the radical procedure of surgery led to an immediate postoperative outcome, it was not significant for the ultimate outcome of treatment. Thus, radical surgery may be considered to carry the same risk of definitive impairment of the facial nerve function, just like a combination treatment with subtotal resection and stereotaxic radiosurgery.

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INTRODUCTION

Vestibular schwannomas, also called acoustic neuromas, are benign intracranial tumors arising from Schwann cells of the vestibular portion of the eight cranial nerve. The cause of vestibular schwannomas is usually unknown; however there are evidences that sporadic defects in tumor suppressor genes, including familial and sporadic vestibular schwannomas, have been linked to a mutation in a single gene, the neurofibromin 2 (NF2). The gene is located on the long arm of chromosome 22, band q11-13.1 [1].

Vestibular schwannomas represent 85% of intracranial growths arising at the cerebellopontine angle [2]. The size of the tumor is commonly classified via the Koos grading scale with respect to extrameatal extension and brainstem compression (Table 1) [3].

Table 1. Koos grading system for vestibular schwannoma

Koos grade	Description
I	Intracanalicular
II	Extension into cerebellopontine angle, <2cm
III	Occupies cerebellopontine angle, no brainstem displacement, < 3cm
IV	Brainstem displacement, > 3cm

Vestibular schwannomas represent a risk to varius intracranial structures due to mass effect. Symptoms include progressive hearing loss and tinnitus which are reported in over 60% of patients. Larger tumor manifestations can cause hydrocephalus and brainstem compression which are followed with symptoms such as facial paraesthesia, vertigo, and headache [4].

Approximately around 8% of all intracranial tumors are vestibular schwannomas with an incidence of 10.4 per million per year [5]. In the population at a median age of 50 years, vestibular schwannomas are presented. They are predominantly unilateral in >90% of patients, with an equal incidence on the left and right. Patients are more often presented with chronic asymmetric sensorineural hearing loss than tinnitus or unsteadiness. Via audiometry and brain stem-evoked response audiometry, sensorineural hearing loss can be confirmed in >90%-95% of patients with vestibular schwannomas [6]. From the pathological aspect of the tumor behavior, more than half of all vestibular schwannomas grow at an average of 2-4mm/year, whereas <10% regress [7].

One study has revealed that extrameatal tumors (28.9%) show a tendency to grow progressively compared with intrameatal tumors (17%), and a larger percentage of tumors grew early on after detection [8]. Some studies have also revealed that vestibular schwannomas of >2cm are more likely to grow compared with a smaller size [9], [10]. Decreased rates of hearing preservation have been associated with growth rates of>2mm/year, compared with slower growth rates [11].

Surgical Approaches

Surgical techniques which are used to approach the tumor are the translabyrinthine approach (TL), retrosigmoid approach (RS), or middle fossa (MF) craniotomy. At the Clinical Centre of Serbia, Neurosurgery Clinic, the prefered surgical approach is the retrosigmoid approach (RS).

The retrosigmoid approach is a posterior approach that which allows the neurosurgeon a panoramic view of the cerebellopontine angle (CPA). This approach also allows the neurosurgeon to have a better view on the facial and vestibulocochlear nerve; hence the facial nerve and hearing preservation has a higher rate. Following a suboccipital craniotomy posterior to the sigmoid sinus, the cerebellum is then retracted medially, that allows the exposure of the cerebellopontine angle (CPA) mass and neurovascular structures. The facial nerve can be identified, and the cerebellopontine angle (CPA) component is dissected. With the use of the neurosurgical drill on the posterior meatal lip, the intrameatal component can then be accessed and removed. Vestibular schwannoma infiltration of the cochlear nerve, poor preoperative hearing, and larger tumor size, decrease the likelihood of hearing preservation [12].

With the retrosigmoid approach (RS) the neurosurgeon can resect large extrameatal and small medial intrameatal tumors while allowing hearing preservation [13], [14], [15].

The retrosigmoid approach to intrameatal vestibular schwannomas can be limited by a high-riding jugular bulb or obstructed by the labyrinth [15]. When the cerebellum is retracted the consequence can be a parenchymal injury. Also included are early postoperative headaches which

are more often in the retrosigmoid approach (RS) than in the translabyrinthine approach (TL) [16].

Electrophysiological monitoring

Electrophysiological monitoring is a standard procedure in modern neurosurgery of the vestibular schwannoma. The main goal of the intraoperative monitoring process is the preservation of the facial nerve. In cases with large tumors it is necessary to monitor the brain stem function that includes monitoring the long motor nerve pathways and other cranial nerves. Beside the neuromonitoring, the electrophysiological methods can give us also the location of the cranial nerves, which by the presence of the vestibular schwannoma can be dislocated and deformed [17].

MATERIALS AND METHODS

A retrospective analysis of 30 patients with histologically confirmed vestibular schwannoma was performed. The cohort consisted of adult patinets operated on between January 2015. and December 2018. by a surgical team of neurosurgeons at the Department of Neuro-oncology of the Clinical Senter of Serbia. This study analyzed the patients clinical status on admission along with the neuroradiological characteristics of tumors and the neurophysiological intraoperative parameters and their effect on the facial nerve function in the early postoperative period as well as one year after the surgery using the House–Brackmann scale. This study also analyzed the intraoperative neurophysiological parameters and their influence on the facial nerve function in the early postoperative period, likewise one year after the surgery using the House-Brackmann scale (HB scale) (Table 2). Patient demographics, clinical preoperative features, extent of resection, postoperative treatment modalities, date of progression, or reoperation, salvage chemotherapy, and date of latest follow-up or death were retrieved from an electronic database.

Table 2. House-Brackmann scale

Grade	Description	Measurement	Function %	Estimated function%
I	Normal	8/8	100	100
II	Slight	7/8	76-99	80
III	Moderate	5/8 – 6/8	51-75	60
IV	Moderately severe	3/8 – 4/8	26-50	40
V	Severe	1/8 – 2/8	1-25	20
VI	Total	0/8	0	0

Statistical analysis

From statistical methods, frequency estimation and relative numbers were used as methods of descriptive statistics. In the analysis of the results, depending on the nature of the variables themselves, the Pearson-ov x2 was used in the form of stacking tests and contigency tables to compare the frequency difference in nonparametric features respectively. Fisher0s exact probability test was applied twice to the numerical constraints of the table. In the statistical analysis, the p-value <0,005 was taken as a statistically significant. The data are presented in tables and graphs. Data were prcoessed using the easy-R system (EZR, version 1.41. 64-bit).

RESULTS

Our study consisted of 30 patients with histologically confirmed vestibular schwannoma from the period 01.01.2015. till 31.12.2018 at the Department of Neuro-oncology of the Clinical Senter of Serbia, where 18 patients were female (60%), and 12 patients were male (40%) (Figure 1). Mean age was 51 years, the youngest patient was 30 years of age, and the oldest was 76 years old (Figure 2).

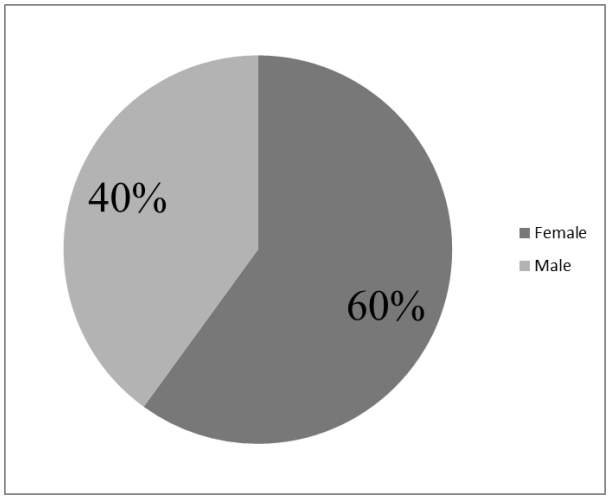

Figure 1. Gender distribution.

The symptoms lasted 3,3±2,1 years at avreage, with maximum od 10 years, and minimum of 2 months. The loss of sensation in the trigeminal nerve region and tinitus was reported in 7 (23,3%) patients. Most

of the patients had cerebelar simptomatology (76%). Preoperative facial nerve palsy was reported in 23,3% patients (Figure 3.).

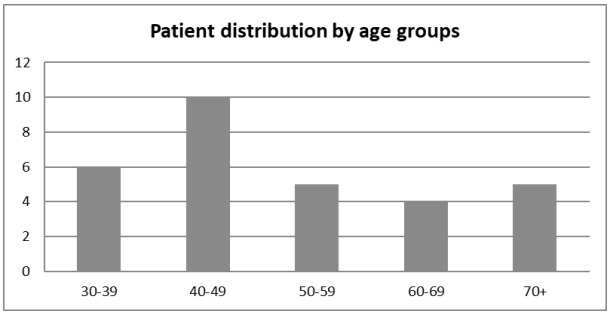

Figure 2. Distribution by age groups.

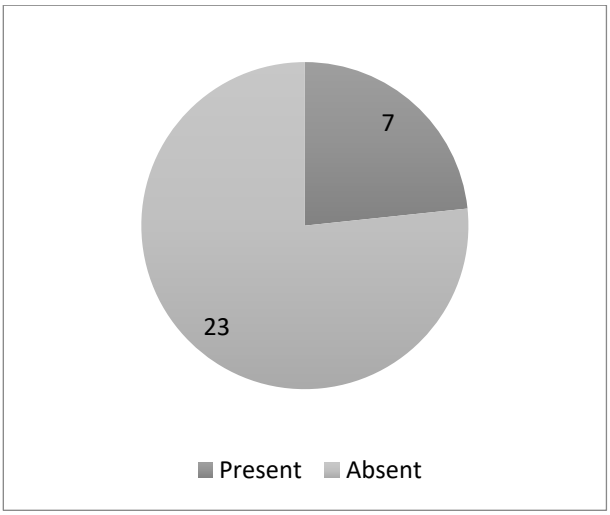

Figure 3. Frequency of the preoperative facial nerve lesion.

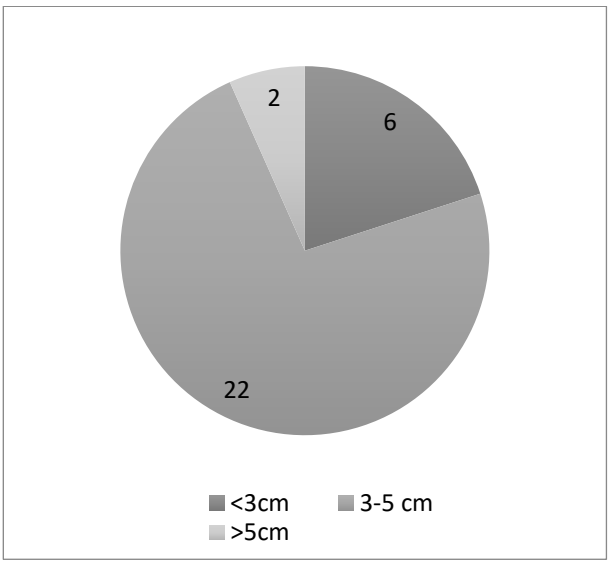

Figure 4. Patient distribution by tumour size.

The largest number of patients 22 (73,4%) had tumors in size between 3 to 5cm, in 6 (20%) patients the tumor size was less then 3cm, and in 2 patients (6,6%) a giant tumor, whose dimensions are >5cm in size. The average tumor size was 38±9,4mm. The distribution of patients according to tumor size iz shown in Figure 4.

The tumor was localized with approximately the same frequency in the left and right internal auditory canal (meatus acusticus internus – MAE) (56,7% on the left, and 43,3% on the right).

Hydrocephalus was noted in 16 patients (53,3%) and a VP shunt was placed in all patients before surgery. Optic nerve papillary edema was present in 3 patients (10%).

Half of the patients, 15 (50%), underwent radical surgery when the MAE was opend and part of the tumor was removed, while in the other half of the patients, a smaller part of the tumor was left in the porus of the mantle of the tumor towards the brainstem and the facial nerve. On this occasion, more than 90% of the tumors were removed. Patients who had a residual tumor were treated with stereotactic radiosurgery. None of the patients progressed during the follow-up period.

Postoperative complications occured in 2 patients (6,7%) – hematoma located in the field which required surgical evacuation. Also, in 2 patients (6,7%) there were general complications – pneumonia and systemic infection. No postoperative local infection, and CSF infection, nor infection of the central nervous system was present.

Examination of electrophysiological parameters proved the connection of the baseline function of the facial nerve with a clinical presentation, and in 7 patients (23,3%) in whom preoperative facial nerve paresis was reported, neurophysiological damage to the nerve function was detectetd preoperatively.

Table 3. Postoperative facial nerve function

House Brackman	n (%)
I	5 (16,7)
II	8 (26,7)
III	8 (26,7)
IV	8 (26,7)
V	1 (3,3)

The facial nerve was located in the region of the brainstem, and in the porus region, as well as in relation to the localization of the tumor via the direct nerve stimulation. In 3 patients (10%) there was a decrease in the facial nerve potential reported during tumor removal, but the potentials were not completly extinguished in any patient. Posteperatively, in most patients there was a deterioration in facial nerve function (Table 3.).

Postoperative physical therapy measures were implemented, and the House Brackman scale (HB) was tested at subsequent controls. After a follow-up period of 2 years, the results of the recovery of the facial nerve function were recorded (Table 4.). Satisfactory results were achieved in 17 patients (56%), their facial nerve function can be considered perserved (HB gradus 1 and 2). In 4 (13%) patients the results were unsatisfactory, there still was severe impairment of the facial nerve function present (HB grade 4 and 5).

Table 4. Facial nerve function 2 years after surgery.

House Brackman	(%)
I	12 (40)
II	5 (16)
III	9 (30)
IV	3 (10)
V	1 (4)

In the further course, predictor factors – clinical, and electrophysiological parameters of postoperative facial nerve function were examined, immediately postoperatively, and 2 years after surgery.

In relation to the immediate postoperative function of the facial nerve, (Table 5) were examined, where no statistical sigificance was detected (p> 0,05).

The degree of tumor resection (p=0,025) proved to be a statistically significant parameter, which indicates that in patients who underwent radical surgery, statistically significantly more patients had worse results on the HB scale. The existene of preoperative neurophysiological impairment of the facial nerve function also stood out as a predictor of poor outcome (p=0,015).

In relation to the facial nerve function, 2 years after surgery, the factors (Table 6) were examined, where the existence of statistical significance was not reported (p>0,05).

Preoperative facial nerve function (p=0,012) was singled out as a predictor of the facial nerve function after 2 years of surgery, with a worse outcome in patients who had preoperative loss of facial nerve function. Preoperative neurophysiological impairment of the facial nerve function (p=0,022) as well as a decrease in potentials during surgery (p=0,018) were also singled out as negative predictors.

Table 5. Presentation of predictor factors for immediate postoperative function of the facial nerve in which the existence of statistigal significance was not detected.

Examined predictive factor	p-value
Years of age	0,072
Gender	0,631
Lesion of the trigeminal nerve	0,176
Tinitus	0,173
Cerebellar symptomatology	0,839
Comorbidities	0,092
Facial nerve function preoperative	0,247
Tumor size	0,336
The side on which the tumor is located	0,855
Hydrocephalus	0,360
Intraoperative drop of nerve potential of the facial nerve	0,055

Table 6. Predictive factors for the facial nerve function 2 years after surgery in which the existence of statistical significance was not detected.

Examined predictive factor	p-value
Years of age	0,620
Gender	0,586
Lesion of the trigeminal nerve	0,497

Tinitus	0,497
Cerebellar symptomatology	0,942
Comorbidities	0,333
Tumor size	0,736
The side on which the tumor is located	0,847
Hydrocephalus	0,333
Degree of tumor resection	0,547

Discussion

Vestibular schwannomas, although they make up a third of all endocranial tumors, still represent an insufficiently researched topic. In most patients who are candidates for surgical treatment, there is already significant hearing impairment, so one of the main goals of surgery is to perserve the facial nerve function.

The average age of patients with vestibular schwannoma is 50 years of age and it is unilateral in more than 90% of patients, with equal incidence of left and right side.

In the cohort stury of I.Taha et al., in 2020. [18], the function of the facial nerve and the function of the sense of hearing after microsurgical removal of sporadic vestibular schwannoma were analyzed. The average age of the patients was 54 years of age. The study consisted of 95 subjects, 37 males, 58 females, compared to our study which contains 30 subjects, 12 males, 18 females.

After 1 year of surgery in a study by I. Taha et al., 67% of patients had a good outcome (HB 1-2), no intraoperative facial nerve damage, no hydrocephalus, and a 30mm tumor. 16% of patients had a moderate outcome (HB 3-4), while 17% of patients had a poor outcome (HB 5-6). Tumor size varied within groups ($p<0,05$). Patients were divided into 3 groups based on the House-Brackmann scale, where the third group had the largest tumor diameter 32±15mm, the second group 33±10mm, and the first group 24±12mm.

Based on the HB scale, the symptomatology was also divided into thre groups, where the most pronounced hydrocephalus (33,3%) was in the third group, as well as facial nerve paresis (20%) and headache (15,3%) in the first group together with dizziness (59,3%), impaired hearing (86,4%), tinnitus (32,2%), loss of trigeminal sensigility (25,4%), and cerebellar symptomatology (8,5%). [18]

In the study Lawani et al. [19] the data has shown that HB grade 1 or 2 facial nerve function was 100% for tumors ≤30mm but 79% for tumors larger than 30mm in 1 or more years after surgery. The predictive function was further studied by Fenton et al. [20], and demonstrated that the long-term facial nerve function was strongly correlated with tumor size by a correlation factor of 0.47. In another study by Samii M. et al. [21], a comparsion was made of facial nerve function between tumors larger than 4cm (giant) and tumors smaller than 3.9cm (2.6cm in average). The result indicated that patients with giant tumors were less likely to achieve facial nerve function of HB grade 1. No significant difference was found between two groups with grade 2 to 6.

For large vestibular schwannoma resection, one of the primary goals is to maintain facial neve integrity, which is thought to be the key aspect of good facial nerve function [20]. In this study, the facial nerve functions of 98,1% patients were intact after tumor removal. Acceptable facial nerve function was achieved in 37,8% of total cases 3–7 days after surgery and 78% remained good facial nerve function after 2 years. The adventage of intraoperative neruomonitoring (INOM) is to lessen intraopeative facial nerve damage and to get a higher total resection rate.

One INOM parameter as prognostic factor for postoperative facial nerve function is A-train activity, which is a distinct EMG waveform classified as a sinusoidal symmetric sequence of high-freqzency and low-amplitude signal during intraoperative EMG monitoring [22]. The overall appearance of its pattern might vary in different cases. In a study Prell et al [23], the time exceeding 10s was correlated with deterioration of post-surfical facial nerve function by two or more grades immediately after surgery. In this study, long train time predicted poor facial function.

Another key factor for the prediction of the facial nerve function is the facial motor evoked potential (FMEP), which was documented to be correlated with postoperative facial nerve function [24, 25]. Because of its adventage of less invasivity, FMEP monitoring can be performed before and after operation do tedect nerve integrity without direct visualization and its thought to be a useful supplement for facial nerve monitoring [24]. In a study by Fakuda et al. [20, 26] and Acioly et al. [24], it has been found that a start-

to-final baseline FMEP amplitude ratio of 50% was a predictive threshold for a poor facial nerve outcome (HB grade 3–6) both in short and long-term follow-up.

Tringali et al. observed a good correlation between caloric weakness and tumour size when they tested the preoperative response of 629 tumour patients. In the group of patients with UW > 70%, who had a larger tumour size, postoperative facial palsy was more frequent. Postoperative hearing preservation was more frequently observed in the "normal group" with a UW < 20%. They concluded that a normal caloric response can be a good predictive factor for hearing preservation and normal postoperative facial function [27].

In our study the tumor size were between 3 and 5cm in 22 patients (73,4%), <3cm in 6 patients (20%), and >5cm in 2 patients (6,6%). Based on th HB slace, preoperative facial nerve lesion was reported in 7 patients (23,3%), hearing loss was present in all patients. Sensitivity drop in the innervation region of n. trigeminus was present in 7 (23,3%) patients, as was tinnitus. Cerebellar symptomatology (76%) was present in the highest percentage of patients.

Conclusion

In the examined series of 30 patients who underwent surgery in the Clinic for Neurosurgery, the function of the facial nerve after vestibular schwannoma surgery was monitored. The degree of tumor resection as well as the existence of preoperative neurophysiological impairment of the facial nerve function stood out as significant predictors of function immediately after surgery. The preoperative neurophysiological impairment of the facial nerve function as well as nerve potential decrease during surgery were singled out as negative predictors.

Based on the results we can conclude that for the final outcome of the facial nerve function and the most important aspects for the facial nerve function are the preoperative state of the facial nerve and the electrophysiological parameters. Although the radical procedure of surgery led to immediate postoperative outcome, it was not significant for the ultimate outcome of treatment. Thus, radical surgery may be considered to carry the same risk of definitive impairment of the facial nerve function, just like a combination treatment with subtotal resection and stereotaxic radiosurgery.

In interpreting these results, it should be borne in mind that this is a relatively small series of patients, and the study should be expanded to include a larger number of subjects. It is also clear that for the successful treatment of these patients it is necessary to diagnose the tumor early as possible, so there would be a significant improvement in outcomes. These outcomes are also in correlation with education of the physicians in primary care, as well as education of the general population, so that hearing loss can be understood as a significant symptom of the vestibular schwannoma. With a better education the diagnostic procedures could be carried out early on, and the result would be a more successful treatment.

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Black cumin 0.3 gram and 0.4 gram on apoptotic levels in Cerebral Contusions Rattus Norvegicus Wistar

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ABSTRACT

Background. Apoptosis is one of the indicators to check for following brain damage. Along with this trend, treatment in the form of herbal and phytopharmaca therapy is required more frequently to treat brain injury complications. Black cumin possesses a function that opposes the apoptotic mechanism.

Objectives. This study sought to determine the effect of black seed on an animal model of brain damage using apoptotic measures.

Methods. Four treatment groups were created from the experimental animals as follows: Group BC1: For 7 days following the brain contusion, they were given [0.3 gram] g/kg bw of black cumin extract daily. Group BC2: For 7 days following the brain contusion, they were given [0.4 gram] g/kg bw of black cumin extract daily. Following the brain contusion, Group K received 3 ml of Nacl 0.9% daily for 7 days. The TUNEL DNA fragmentation method was used to count the amount of apoptotic cells and analysis was conducted using ANOVA with F-test and Tukey HSD.

Results. The control group had the greatest amount of apoptosis at 30.4. Apoptosis averages for BC1 (0.3 g), and BC2 (0.4 g) groups of rats were 25.0, and 18.8, respectively. Black cumin anova test with apoptosis was present while a higher dose of black cumin will minimize the amount of apoptosis.

Conclusions. Injecting black cumin extracts into rats with head injuries reduced apoptosis, albeit not significantly. In rats with experimental head injuries, black cumin extract induces a connection through the apoptosis mechanism.

INTRODUCTION

The progression of a brain injury is not random, but rather a continuous process between primary and secondary brain injuries[1]. Consequently, the initial diagnosis, treatment, and prognosis of brain injury are not

simple, despite the fact that methods of diagnosis and management of brain injury are constantly evolving[2]. Numerous research have demonstrated the advantages of black cumin seeds, which include analgesic, antibacterial, anti-inflammatory, anti-microbial, antioxidant, anti-pyretic, anti-tumor, immunomodulatory, and neuroprotective activities [3–5]. Experimental animals receiving black cumin seed extract for cerebral ischemia have lower levels of MDA (malondialdehyde)[6]. Black cumin prevents formaldehyde from causing neuronal apoptosis when administered to animals[7].

It is believed that black cumin inhibits calcium channel blockers, hence decreasing calcium flow[8]. Black cumin research as a neuroprotectant in non-traumatic settings has been validated. Black cumin has not yet been investigated as a neuroprotectant in models of head injury (cerebral contusion) or trauma. This study aimed to examine the effect of black cumin on Apoptotic neuron cells following head damage in Rattus norvegicus wistar rats.

Methods

In this laboratory investigation, mice were utilized as the experimental animals, and the experiment was designed to be entirely randomized. The Ethical Clearance No. 351/KEPKVII/2012 Commission for Health Research Ethics granted permission for this line of investigation. Dr Saiful Anwar General Hospital Malang Indonesia. Four treatment groups were created from the experimental animals as follows: Group BC1: For 7 days following the brain contusion, they were given [0.3 gram] g/kg bw of black cumin extract daily. Group BC2: For 7 days following the brain contusion, they were given [0.4 gram] g/kg bw of black cumin extract daily. Following the brain contusion, Group K received 3 ml of Nacl 0.9% daily for 7 days. The Rattus norvegicus wistar strain was used in this experiment, and the average age and weight of the animals used were 12-14 weeks and 200-250 grams, respectively. The male experimental animal was in good health and was freely moving around. Supplies needed to sustain experimental animals for 10 days. Black cumin extract is manufactured by. Salinity of Seawater, typical of normal (0.9% Saline) (Otsuka).

Apoptosis examination material: mouse brain tissue, Apoptec (Proteinase-K Enzyme, Apoptag, DAB liqud), Assay diluent A, Assay diluents B, Tetramethyl benzidine (TMB) One Step Substrate Reagent, Stop Solution.

Cerebral contusion model: Cerebral contusion was done on experimental animals [9], which has been modified. A load of 0.2 kg was dropped through a cylindrical tube from a height of 0.8 m (impact energy of 1.6 Joules) over the head of a stereotactic frame-mounted experimental animal. Previously, 1 mg/Kg of body weight (i.m.) of ketamine was administered intramuscularly to sedate the test animals [10].

The TUNEL DNA fragmentation method was used to count the amount of apoptotic cells and the results are as follows: Slides were cleaned in PBS pH 7.4 and then treated with proteinase K (20 ug/mL) for 15 minutes at 37 °C. Three times, each for five minutes, wash with PBS pH 7.4. 15 minutes of 3% H2O2 incubation. Three times, each for five minutes, wash with PBS pH 7.4. Typical commercially available black cumin extract formulations contain 100 mg/cc of a suspension prepared by dissolving 600 mg of black cumin extract from capsules in 6 cc of 0.9% NaCl. Group BC1 0.3 grams (g), and group BC2 0.4 grams (g) via nasogastric tube. Following the administration of black cumin extract, specimen collection (harvesting) was performed on the seventh day for each group (n=5) in the study. Infusions of ketamine at a dose of 1 mg/kg body weight were used to induce anesthesia. After performing a decapitation on the animal model, a ventriculostomy procedure with a spinal needle placed 27.3 mm in front of the central sulcus and 3 mm lateral to the fissure was used to withdraw cerebrospinal fluid from the animal model. Half of the right and left brains were removed sterilely and placed in a petri dish with 10% formalin.

The computation method utilizes *SPSS™* software tools. A statistical analysis was conducted: Examine the difference between Black Cumin extract treatments. In each group, analysis was conducted using ANOVA with F-test and Tukey HSD for multiple comparisons.

Results

Four treatment groups present data. The BC1 group fed black cumin at 0.3 g/kgbw, the BC2 group fed 0.4 g/kgbw, and the control group fed 0.9% 3cc NS.

Brain tissue on a macroscopic level from rats who had head trauma

A head injury model was used for the experimental

group BC1, BC2, as well as the control, and it had an energy of 1.6 joules. A macroscopic examination of the animal model's brain tissue did not reveal any signs of cranial fracture, subdural hemorrhage, subarachnoid or intracerebral bleeding. On a macroscopic scale, there was no discernible difference between the treatments; more specifically, the structural characteristics of the brain parenchyma were identical across all treatment groups (Figure 1).

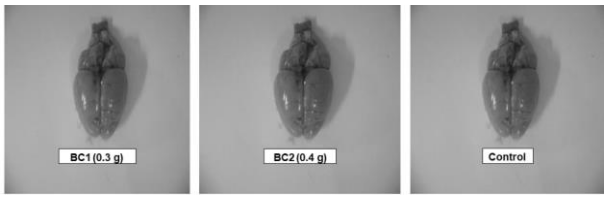

Figure 1. shows a macro view of the parenchyma of rat brain tissue. After seven days of treatment with either black cumin (BC), the macroscopic picture of the rat brain parenchyma did not reveal any differences between the two groups.

Table 1. Average and One Way ANOVA test for apoptosis

Treatment	Average	Standart deviation	F value	p
BC1 (0.3 g)	25,00	7,91		
BC2 (0.4 g)	18,80	5,67		
Control	30,40	7,77	2,761	0,076
Total	25,35	6,42		

Table description; From the table above, it was found that the control group had the highest degree of apoptosis (mean 30.40) BC1 (mean 25.00) and BC2 (mean 18.80). The results of the ANOVA test with p=0.076 are not significant.

The correlation between black cumin and the death of neurons (apoptosis)

The analysis of TUNNEL apoptosis revealed that there were differences between the treatment groups, with the amount of apoptosis decreasing with increasing the dose of black cumin.

The table shows that the quantity of apoptosis decreases with increasing doses of black cumin. Comparing all of the groups of rats administered black cumin, the control group had the greatest amount of apoptosis at 30.4. Apoptosis averages for BC1 (0.3 g), and BC2 (0.4 g) groups of rats were 25.0, and 18.8, respectively. The table below displays the outcomes of the black cumin anova test with apoptosis, even though descriptively it was discovered that the higher the dose of black cumin will minimize the amount of apoptosis.

Table 2 shows that no significant differences between treatments were found at the 0.05 level or lower, although descriptively, the control group and feeding normal saline caused the most apoptosis (average 30.4), the group BC1 with black cumin feeding 0.3 g/kg body weight per day for 7 days (average 25), and the group BC2 with (average 18.8). The difference between the means of apoptosis in each treatment group was not statistically significant, but p = 0.076 indicates that the risk of failure of 7 treatments in 100 clinical trials is extremely high.

Table 2. Tukey HSD Apoptosis test results

Treatment	N	subset alpha=0.05
		1
BC1	5	18,8000
BC2	5	25,0000
control	5	30,4000
Sig		,058

Note: from the Tukey HSD test, it appears that the three treatments have no significant difference even though they have different mean values.

Discussion

In this experiment, a male Rat Rattus Norvegicus weighing between 250 and 300 grams was employed. The choice of these experimental animals was made in accordance with Kanter[7] research. The low mortality rate of rats, cost-effectiveness, and simplicity of the brain contusion model all contribute to the usage of this experimental rodent[11]. In this particular experiment, only male experimental animals were utilized. When there is a difference between the sexes, the results will be different. XIAP production was more in female rats than in male rats, resulting in reduced apoptosis in female rats compared to male rats. It is believed that increased estrogen levels in female rats contribute to higher XIAP levels protein[12]

The head injury model was executed by impacting the head of the experimental animal with an energy of 1.6 Joules, specifically by lowering a 200-gram weight through a 0.80-meter-tall cylindrical pipe. This agrees with model of brain contusion of previous study[10], which assumes an impact of 1.62–1.89 Joules. There is bleeding inside the skull (either subdural, subarachnoid, or intracerebral) but no visible fractures of the skull. Increased permeability of the cerebral vasculature, decreased cerebral blood flow, and raised intracranial pressure are all

possible outcomes of the contusion model. Mild bleeding will start after 48 hours of impact. These animal models are reproducible and can be used to simulate mild or moderate head trauma in humans, depending on the weight of the load, the height of the fall, and the weight of the experimental animal. This study employs 1.6 Joules of energy, hence the brain contusion model in this study is consistent with the usual cerebral contusion model[10].

Using a probe, black cumin (BC) was administered orally using the following dosages: BC1 0.3 g/kgBW, BC2 0.4 g/kgBW, and a control with 3 cc Normal saline. The 0.4 g/kg bw dosage is based on research conducted by Kanter[7].

However, a dose of 0.3 grams per kilogram of body weight is a dose that falls between a low dose and a high dose[7]. Since black cumin's use is predicated on the idea that scavengers need to be present before free radicals appear or are generated, it is administered as soon as possible after injury. After 4 hours post-traumatically, cerebrovascular leakage and iNOS/NO expression both began to rise [11,13].

When a person suffers a head injury, the intracranial pressure rises, which can alter the physiology of the brain. Blood flow in the brain is interrupted, which can lead to ischemic processes and brain metabolic diseases. Brain edema will result from secondary brain injury caused by this mechanism up to 48–72 hours after the incident. The load inside the skull will rise as a result. The process through which black cumin extract increases the quantities of endogenous proteins that has been researched focuses on its anti-oxidant properties. Black cumin, which acts as a chelating agent against free radicals, boosts the activity of the acetylcholinesterase enzyme in the central nervous system[14]. In experimental chicken erythrocytes, black cumin administration dramatically decreased MDA levels (p0.002) and increased GSH levels (p0.005)[15]. Additionally, black cumin suppresses inflammation by inhibiting the 5-lipoxygenase enzyme, hence inhibiting different inflammatory leukotrienes. LPS-induced iNOS (inducible nitric oxide synthase) expression is suppressed, resulting in decreased NO generation by macrophages, which improves the inflammatory response and reduces cell damage due to fewer free radicals[16]. Black cumin's anti-apoptotic effects were observed in this investigation; however, they were not statistically significant (p 0.076). The mechanism through which black cumin extract reduces neuronal cell death is currently unknown. The treatment of black cumin extract to rats with brain injuries was observed to reduce the levels of MDA (malondialdehyde) p0.001, an end product of lipid membrane peroxidation, possibly through its anti-oxidant activity[7]. A dose of 0.4 g/kgbb black cumin extract was proven to dramatically reduce apoptosis (p0.0001) in a non-trauma model (formaldehyde induced neuronal damage).

The TUNEL technique revealed brown apoptotic entities, which included condensed cytoplasm, degeneration of cell nuclei, and dark, picnotic nuclei. The mechanism of prevention of neuronal cell apoptosis inhibitory pathways has not been thoroughly disclosed in a study on the effect of black cumin extract as an anti-apoptotic neuron cell model of non-trauma. Degenerative changes in neurons are typically accompanied by elevated oxidative stress. High oxidative metabolic ability, a high concentration of polyunsaturated fatty acids, and a low antioxidant capacity make the brain, and particularly the cortex and hippocampus, particularly vulnerable to oxidative stress[13]. Thymoquinone (2-Isopropyl-5-methylbenzo-1,4-quinone), which makes about 30% of black cumin's composition, has been shown to promote apoptosis in colon carcinoma cells by upregulating the activation of the MAPK pathway and ERK and JNK signaling (mitogen). active protein kinases)[17]. Thymoquinone can also initiate apoptosis by p53-dependent and p53-independent pathways in addition to these methods. Thymoquinone is a double-edged blade that acts as both a pro- and an anti-oxidant due to its two potentials. Thymoquinone may be reduced to semiquinone (1 electron) or thymohydroquinone, depending on the structure of the thymoquinone molecule (2 electrons). Thymohydroquinone has anti-oxidant properties, whereas semiquinone has pro-oxidant properties[17]. This study found that giving black cumin extract to experimental rats with head traumas raised neuronal apoptotic levels. In experimental rats with head injuries, injection of black cumin extracts reduced apoptosis, albeit not significantly. In experimental rats with head injuries, treatment of black cumin extract causes a connection through apoptosis mechanism. It is necessary to do pharmacological study on the various methods of extracting black cumin in order to increase levels of

understanding regarding thymohydroquinone. To learn more about thymohydroquinone, pharmacological research on black cumin extraction methods is needed.

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Conservative management of intraventricular migrating intracranial bullet. A case report

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Keywords
gravitational bullet injury, conservative management, migrating intracranial bullet injury

ABSTRACT

Background. The high mortality rate of a cranial bullet injury, the catastrophic damage of vital tissue, and the frequency of gunshot accidents made managing such cases highly effortful in neurosurgical trauma centres. One category of these injuries is the gravitational bullet injury, in which the bullet's movement depends on gravity after losing its kinetic energy. This paper aims to describe the conservative treatment plan we applied for a patient who suffered an intracranial gravitational bullet injury.

Case description. The patient presented with a cranial bullet injury that migrated caudally to his lateral ventricle. This unapproachable location of the bullet made the surgical intervention undoable. Therefore, after the implication of resuscitative management, the patient went under heavy observation with a suitable follow-up plan. The patient's short-term outcome was excellent, and his Glasgow coma scale was 15 at the discharge.

Conclusion. Conservative management in a gravitational bullet is one of the possible methods to reach the best outcome in non-operable patients. Such measures are highlighted in this case, even when a complication like a bullet migration may occur.

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INTRODUCTION

Cranial bullet injuries constitute a frequent clinical challenge for neurosurgeons in trauma centers. The impact of such injury includes damage to vital tissue and subsequent complications. A missile bullet injury is considered to have a high mortality rate that ranges from 51% to 84% (10). On the other hand, gravitational bullet injury, also known

as falling bullet injury, occurs when the bullet loses its acceleration and kinetic energy; therefore, its movement will depend only on gravity. In this situation, the bullet does not have a cavitary effect, and the damage will be less dramatic than the missile bullet injury (2). It is noteworthy that there is inadequate mention of the indications of conservative management regarding gravitational bullet injury in the literature, especially the rare phenomena of bullet migration.

The aim of this article is to discuss the conservative management steps of gravitational bullet injury and the remarkable outcome of the patient despite the critical location of the bullet and its consequent craniocaudal migration.

CASE DESCRIPTION

Thirty-three years old male with unremarkable past medical history was admitted to the neurosurgical emergency department due to a bullet head injury. His transfer to the hospital was delayed more than one hour because he lives in a rural area. The initial assessment revealed that one entry wound was positioned on the upper part of the frontal bone, slightly right to the Bregma area; neither an exit wound nor other concomitant injury has been found. GCS was 14 (E4M5V5) at the admission. He presented with a severe headache with no motor deficit. His vitals were stable, and pupils were equally round and reactive to the light and accommodation. Initial skull X-ray was performed, which documented an intracranial bullet (Fig 1, 2). Computed tomography (CT) scan was done, which revealed a foreign body with moderate volume subarachnoid hemorrhage (SAH) (Fig 3. E).

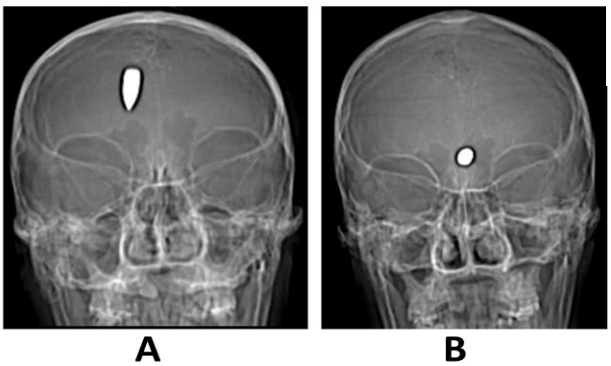

Figure 1. Head x-ray in coronal view, **A**: before bullet migration, **B**: after bullet migration.

Resuscitative measures were performed with conservative management, including wound debridement with intravenous effusion of antibiotics, including Ampicillin-sulbactam, Metronidazole, and Cefotaxime for one week in addition to Paracetamol, anticonvulsant (Phenytoin) and Ranitidine. The next day's follow-up CT revealed the migration of the bullet to the occipital horn of the right lateral ventricle (Fig 4. H). No surgery was done for him, and he went under heavy observation. The patient was discharged from the hospital after one week of observation.

The patient's GCS was 15 at the discharge, with Blood pressure 150/65. The follow-up strategy includes repeated imaging that will be conducted every three months to monitor the site of the bullet and the subsequent complications.

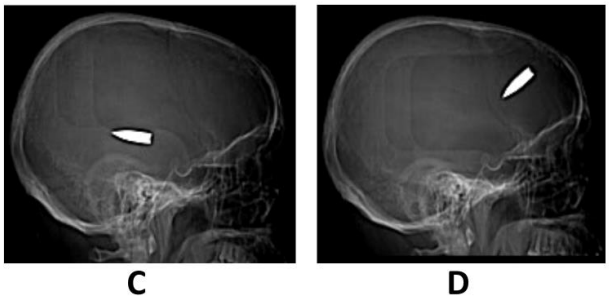

Figure 2. Head x-ray in sagittal view, **D**: before bullet migration, **C**: after bullet migration.

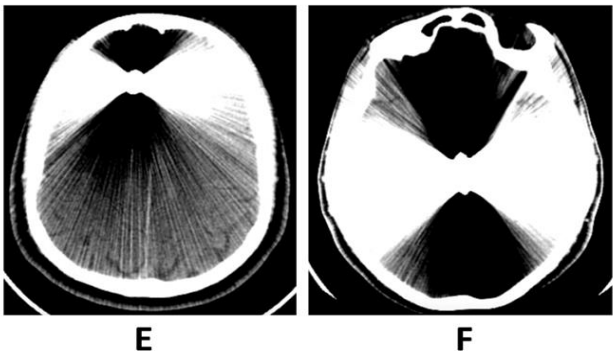

Figure 3. Head CT in cross-sectional view, **E**: before bullet migration, **F**: after bullet migration.

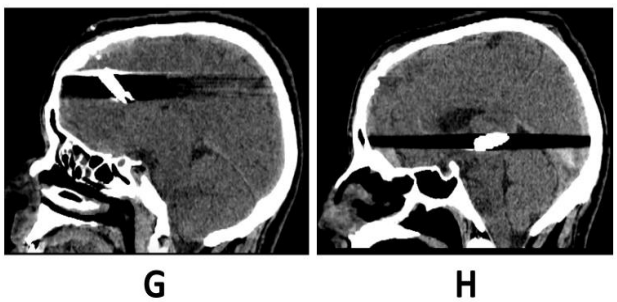

Figure 4. Head CT in sagittal view, G: before bullet migration, H: after bullet migration.

Discussion

Avoiding invasive measures through a conservative management strategy to preserve vital anatomical structures constitutes a relatively infrequent approach in cranial bullet injuries. One of the compelling situations in which a neurosurgeon will implement conservative management is when a migrating intracranial bullet is positioned in an inaccessible site. Bullet fragment migration has been reported in 0.06-4.2% of bullet injury cases (13). Since the additional neurological deficit could result from the removal of the bullet, managing such cases is challenging (2,10). Additionally, several studies revealed no remarkable association between retained bullet fragments and infection and no associated seizure occurrence (9,14), favoring conservative management for such critical cases.

This paper aims to observe the effectiveness of conservative management regarding inaccessible cranial bullets and the patient's short-term outcome.

Regarding the gravitational bullet effect mechanism, there are three velocity phases (2). The first one is the explosive acceleration after the gun's firing, the second phase represents the velocity's deceleration due to gravity's effect, and the third phase starts when the bullet movement changes in a downward direction with accelerated velocity. After these phases, the bullet reaches the terminal velocity, which depends on multiple factors, including the bullet material, angle of firing, and flight characteristics (7,11). The action of gravitational force on the bullet, the flow of cerebrospinal fluid (CSF), the vessels pulsation, and finally, the local tissue damage and the consequent edema with tissue softening are all considered factors that would enable the bullet's movement inside the cranial cavity. The migration will stop by gliosis and the formation of fibrotic scar tissue in a healing process that can take several weeks to years to be completed (3,6). The availability of firearms and the rise of terrorist-related aggressiveness have increased the incidence of missile injuries. Indeed, one of the frequent events in which there is a traditional aerial firing is the marriage ceremony which led to an increased incidence of gravitational bullet injuries (3).

The ventricular system is one of the most vulnerable sites in craniocerebral bullet injuries. The main reasons for this are the fragility of its structures and its critical site with proximity to vital vascular and neural structures as for the circle of Willis, which are located below the frontal horn and the body of the lateral ventricles. Moreover, the choroidal arteries have a close correlation with the lateral ventricles. Another crucial relation to the ventricles represents the course of the venous channels that drain the deep white and gray matter surrounding the lateral and third ventricles and the basal cisterns into the brain's deep venous system, which include the internal cerebral vein, basal vein, and great vein of Galen. These channels pass subependymally through the walls of the lateral ventricles (5).

Regarding the conventional management of head bullet injury, resuscitative stabilization must be done according to international trauma life support guidelines. Then, accurate identification of wound entry sites, monitoring the intracranial pressure, and administering prophylactic anticonvulsants and tetanus toxoids (1,15). It is essential to mention that the leading cause of mortality in falling bullet injuries is a cerebral hernia resulting from increased intracranial pressure (12). After that, individual-based assessment must be applied before making surgical decisions. To illustrate the previous statement, many studies advocated removing the bullet if it is accessible and the removal procedure will not cause severe morbidity. These studies include Özkan study (16) and the study of Kumar et al. (8). In contrast, there were two reported cases by Zafonte et al. (16) Of spontaneous migration that caused a neurological collapse in which the two conditions were improved after applying surgical management.

The severity of complications associated with the migration of intracranial projectiles often contributes to poor prognostic consequences (8). These complications are divided into two categories; the first one will include bullet lethality with the entering of shattered bone fragments and bleeding. The second category represents the development of seizure foci, neural tissue necrosis, pressure effect of the foreign body, and different types of intracranial infections. This category also includes hydrocephalus, a predicted complication of an intraventricular bullet (13).

In our case, after adequate resuscitation of the patient according to advanced trauma life support (ATLS) protocol by the well-trained neurosurgical team in the emergency department, he was admitted to the operating room for meticulous wound debridement. CT imaging demonstrated that

bullet removal is more dangerous than leaving it inside the ventricle. Thus, surgical intervention was not considered an option.

The initial GCS of the patient is One of the most important predictors of outcome (12). As for our case, GCS was 14 (E4M5V5). The patient received an intravenous fluid and antibiotics, including Ampicillin-sulbactam, Metronidazole, and Cefotaxime. Palliative measures were performed to relieve his pain using analgesia. Anticonvulsant drugs, including Phenytoin, were given to avoid the Complication of the development of seizure foci in addition to Ranitidine. The next day, a follow-up CT was performed to guide further management, revealing the bullet's migration to the occipital horn of the right lateral ventricle. The migration of the bullet made it even more unapproachable; hence, no operation was conducted, and he went under heavy observation. The patient was discharged from the hospital after one week of careful surveillance.

At the discharge, the patient's GCS was 15. His blood pressure was 150/65. His follow-up strategy involves repeated imaging every three months to monitor the site of the bullet in addition to regular neurological examination to manage the predicted complications.

The follow-up plan has further significance because the bullet might migrate again and give rise to more damage. For instance, in 2010, Castillo-Rangel et al. reported the case of a 9-year-old female who had an intracranial bullet injury. No surgical intervention had been performed, and she was discharged after being conservatively managed by a healthcare team. Later and after twenty-seven years, she suffered several symptoms, including thoracic pain, bladder/bowel habitus changes, and bilateral lower extremity weakness. The imaging revealed that the bullet had migrated and is now at the T4 level. Thus, it was surgically removed (4).

To sum up, everything has been stated so far, removing deep-seated bullets could raise the potential for morbidity and mortality. Nevertheless, leaving the bullet inside the brain tissue may result in its migration, and a correspondingly significant neurological deficit will occur. This fact decided whether to apply surgical treatment or convey conservative management, a severe challenge in neurosurgical departments. Finally, implementing efficient guidelines and the documentation of similar cases would ensure better patient care in such compelling circumstances.

Conclusion

It is essential to acknowledge that gravitational bullet injury cases need more documentation in the literature to be oriented with manageable complications like bullet migration and individualized treatment plans. Regarding our case, the bullet settled in the lateral ventricle, which made it inaccessible. The excellent recovery of the patient and the critical location of the bullet encouraged to go with conservative management.

Abbreviations

Glasco coma scale = GCS;
Computed tomography = CT;
Subarachnoid hemorrhage = SAH.

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Wandering intracranial bullet. A case report with review of the literature

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ABSTRACT

Multidirectional migration of bullets has been reported infrequently in the literature. The Surgical retrieval of an intracranial migrating bullet is suggested because of its capacity to produce an additional neurological deficit. Intraoperative image guidance using the C arm is indicated in all intracranial migrating metallic foreign bodies following gunshot injury. A rare case of migrating bullet fragment in its trajectory with the migration of metallic fragment in both cerebral hemispheres is reported, and relevant literature is reviewed.

Keywords
migrating bullet, intracranial

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INTRODUCTION

A bullet generally travels in a straight line after entering the body and following the dissipation of its energy, either exits or lodges. The initial movement of the bullet fragment follows the physical principles and power of moving pieces; the subsequent migrating of the bullet fragment in the intracranial compartment depends upon gravity, pulsatile force, coughing, sneezing and movement of the patient's head1. We report a case of a bullet injury in which the metallic fragment was moving freely from its initial site in the left parietal to the opposite side and then traversing back to the original position, probably in the initial trajectory created by the force of a bullet. The bullet fragment in the present case migrated along the path of least resistance created at the initial impact. This differs from the other reported case where the fragment moved according to gravity and dependent position.

CASE REPORT

A 30-year-old male becomes unconscious after a gunshot injury to the head. Glasgow's coma scale on admission was E2V2M5 with left-side hemiparesis. His pupils were equally reactive, and his vitals were stable. The entry wound was situated on the right parietal bone; the exit wound could not be found. Cranial Non-contrast computerised tomography (NCCT) revealed a gunshot wound through the right parietal bone and underlying right parietal lobe, with underlying contusions, intraventricular bleed, and corpus callosum contusions. The single metallic foreign body was found over the left parietal lobe **(Figure 1)**. Initially, the patient was managed conservatively with debridement and

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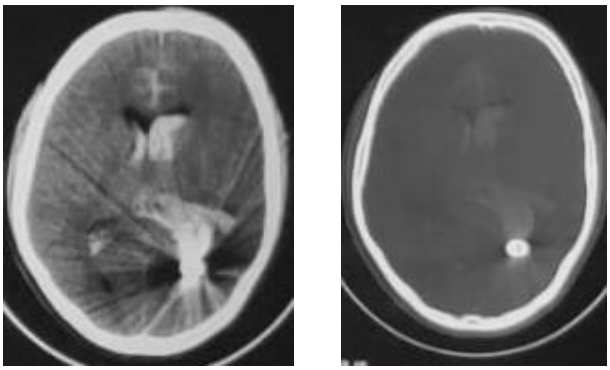
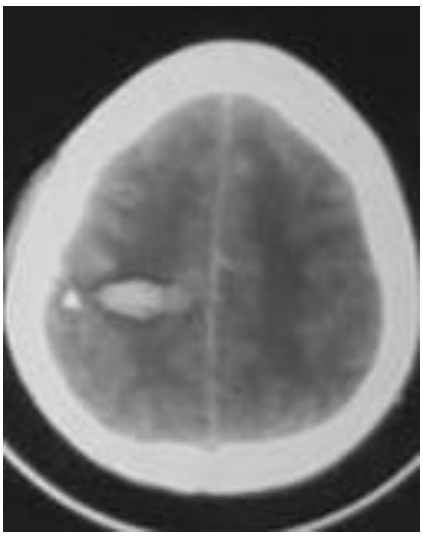
primary closure of the cranial wound. Repeat NCCT head was done after two days to find the status of contusions, brain oedema, and location of metallic foreign body. Repeat NCCT head revealed resolving contusion. However, the single foreign metallic body was shifted to the right parietal lobe near the entry wound **(Figure 2)**, thereby confirming the migration of the bullet fragment in the trajectory. Considering the bullet location and the entry wound, the patient was planned for bullet retrieval with wound debridement under image guidance. A fresh CT scan was done before shifting the patient to the operation theatre, and a repeat NCCT revealed the remigration of the bullet towards the left parietal lobe **(Figure 3)**. Right parietal craniotomy was done with wound debridement and primary closure of dura matter using the pericranial patch. Intraoperatively bullet position was re-confirmed with the c-arm, and a left-side parietal craniotomy was done with the removal of the bullet. Post-operative CT showed resolving intraparenchymal contusion and intraventricular haemorrhage with no foreign body **(Figure 4)**.



A. **B.**



C

Figure 1. Day 1: Initial NCCT head showing **A**) Metallic foreign body over left parietal lobe; **B**) bone widow with foreign body; **C**) Entry wound over right parietal bone.

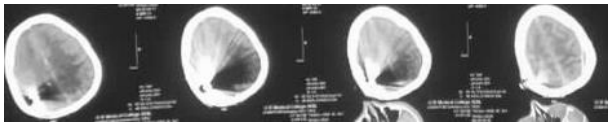
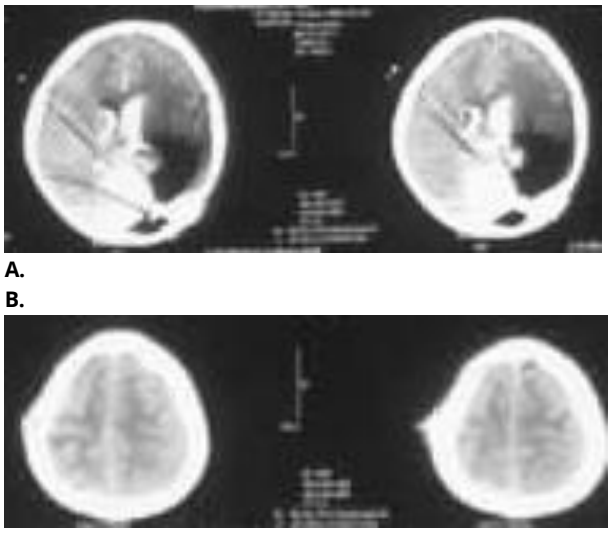


Figure 2. Day 3: NCCT head revealed entry wound over right parietal bone with metallic fragment over right parietal lobe, suggesting migration of bullet towards entry wound.



A.
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Figure 3. Day 4: NCCT head revealed remigration of bullet towards left parietal lobe.

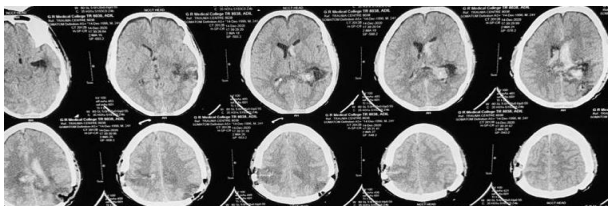

Figure 4. Postoperative NCCT head revealed post-operative changes with no foreign body with resolving contusions.

Discussion

The bullet migration in the intracranial cavity has been reported previously by several authors. The metallic fragments following gunshot injuries have been reported to migrate in different cranial compartments depending upon the brain's and cerebrospinal fluid's gravity and pulsatile forces. Extensive migration of bullet fragments from the intracranial compartment to the spinal subarachnoid space has been reported in the literature 2,3. However, in the present case, the movement of the fragment across the cerebral hemisphere crossing the midline was noted in the direction of the initial trajectory, as pointed out in the first CT scan. The bullet initially impacted the right parietal region,

causing a fracture of the right parietal bone and lodging in the left parietal lobe involving injury to the ventricle system, causing an intraventricular bleed. The subsequent CT scan showed the bullet fragment shifted to the right parietal lobe at the original point of impact.

At the time of surgery, the bullet fragment was again turned to the left parietal lobe following the same trajectory. This is very clear that the metallic foreign body was moving freely to and fro in the same course. The hemispheric migration of bullet has been earlier reported by Umredkar et al. 4Yadav yr. et al. have reported supratentorial to infratentorial migration of bullet5. According to Rapp, at all. 4.2% of bullet fragments migrate6; other authors have found that less than 0.1% to 10% of bullets migrate inside the head.

The mechanism of migration of intra cerebral bullet is influenced by the following Factors: 1. cerebral softening, 2. the specific gravity of the bullet compared with brain tissue, 3. pulsatile force of the brain and the cerebral spinal fluid pulsatile waves, 4. the sink function of the cerebral ventricles. Hence, it is not only the firearm injury but also any foreign body with a different density than the brain and cerebrospinal fluid that will migrate intracerebrally. (4,7) Repeated bullet movement in the same injury tract is rare and makes our case unique. After reviewing the available English literature in detail, we have not found any similar issues. The least resistance can explain the movement of the bullet offered to the bullet fragment in the preformed trajectory.

CT is the imaging procedure of choice for evaluating these injuries; however, the migrating fragments require intraoperative image guidance to know the position of the bullet fragment in the operating theatre. The retained bullet complications include infection, haematoma formation, seizures, and abscess formation. Spontaneous bullet migration causing additional parenchymal damage because of migrating nature makes surgery difficult.

Surgical treatment of bullet injury is controversial and represents a dilemma for the neurosurgeon. Where feasible, the missile and bone fragments must be removed, but without enhancing the pre-existing neurological deficit. Kumar at all. Reported that removal of bullet should be done in the patients undergoing surgery for the vacation of haematoma if it is easily accessible and removal does not lead to further deterioration of neurological structures8. Zofonte et al. reported two cases with neurological deterioration from spontaneous migration of bullet; postoperatively, the patient demonstrated significant functional recovery9; considering the potential of neurological deterioration due to migration of bullet in several compartments, including spinal subarachnoid, the surgery of retrieval of the bullet fragment is advisable, we have removed the bullet. However, few cases reports favour conservative treatment in which the bullet is lodged in safe areas without evidence of migration and additional neurological damage.

Conclusion

Spontaneous intratragectory migration of bullet represents a rare complication and makes treatment more challenging. The Surgical retrieval of the intracranial migrating bullet is suggested because of its capacity to produce an additional neurological deficit. Intraoperative image guidance using the C arm is suggested in all intracranial migrating metallic foreign bodies following gunshot injury.

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Intramedullary cavernoma. A case report

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ABSTRACT

The cavernoma is a vascular malformation made of well-circumscribed agglomeration of pseudo-capillaries. Bone marrow localization is rare and accounts for about 5% of spinal cord vascular lesions. Clinical symptomatology is marked by progressive bone marrow compression syndrome. The diagnosis is strongly evoked in magnetic resonance imaging and confirmed by histology. The management is essentially surgical.

We report a case of bone marrow cavernoma in a 38-year-old man seen in consultation, paraplegic for 2 weeks. The spinal cord MRI revealed a lesion opposite D11, evoking a cavernoma. The patient was operated on with total removal of the lesion; histology confirmed the diagnosis of cavernoma. The immediate post-operative follow-up was marked by the partial recovery of the deficit. We discuss, through this clinical case, the clinical, radiological and especially therapeutic aspects of the medullary cavernoma.

Keywords
cavernoma,
microsurgery,
spinal cord

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INTRODUCTION

Cavernomas are benign vascular abnormalities consisting of cavities into which blood circulates at low flow and low pressure. Intramedullary localization is unusual, represents about 5 to 12% of spinal vascular malformations and 3% of intramural vascular malformations (5% of spinal vascular malformations) (1). Unlike cerebral cavernomas, intramedullary cavernomas often have a more aggressive clinical course due to acute or rapidly progressive alteration of spinal cord functions. Asymptomatic forms are common. The diagnosis is strongly evoked by imaging, in particular by magnetic resonance, and confirmed by the anatomo-pathological study. Surgery is essential especially in symptomatic forms.

We report a case of dorsal intramedullary cavernoma and analyses in the light of literature, the clinical, radiological and surgical aspects of the spinal cavernoma.

CASE REPORT

This is a 38-year-old man patient with no significant medical history and who had a low back pain for 1 year. One year after back pain, it showed

a total functional impotence of the lower limbs of rapidly progressive installation. We received him in consultation, coming from a neighbouring country, two weeks after the establishment of the deficit. The clinical examination found a conscious patient, a urinary tube in place (because of urine retention), paraplegic at 0/5, hypoaesthesia under umbilical region, a positive Babinski sign, sharp osteotendinous reflexes. Magnetic resonance imaging showed an irregular intramedullary lesion (previous reverse) opposite D11, in hyper signal in both T2 and T1 and surrounded by a hypo signal halo and myelopathy extended up to L1. The set evoked recent bleeding and the diagnosis of cavernoma was mentioned.

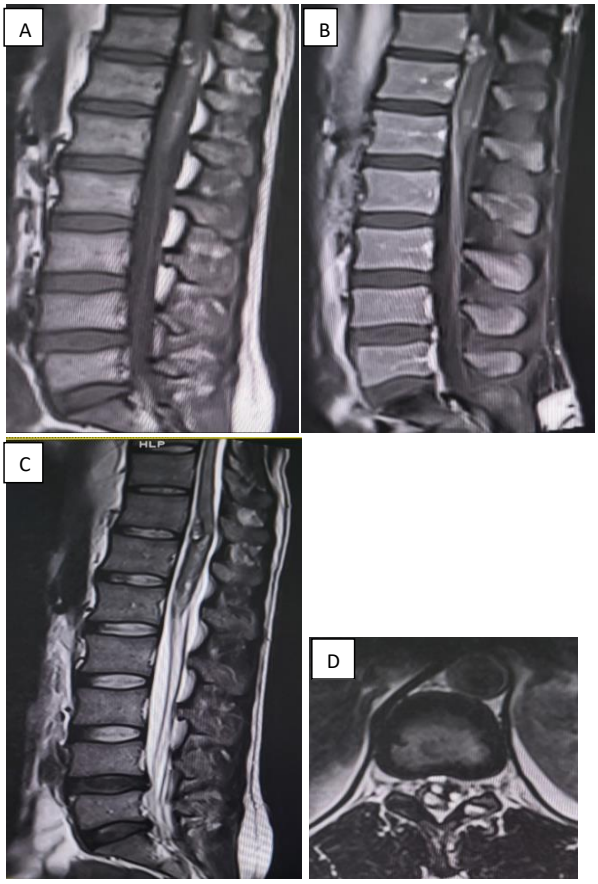
The patient was operated on, a laminectomy D11 and D12 was performed. After opening the hard mother, we discovered intramedullary in depth a globular, reddish and little hemorrhagic lesion. We realized a complete single-block removal.

The immediate postoperative follow-up at 24 hours were simple and marked by a clear improvement in neurological deficit, in particular, the removal of the urinary catheter and correct urination without retention, the improvement in the motor deficit whose rating increased to 1/5 in proximal (quadriceps) and 3/5 in distal (toes). Three months after the surgery, the patient presents an improvement, 4/5 in extension and 3/5 in flexion of the lower limbs.

The anatomopathological study confirmed the diagnosis of cavernoma

Discussion

The definition of cavernoma is histological, it is a vascular malformation made of dystrophic and ectasic blood vessels without interposition of tissue between the vessels (2). It is an unusual vascular malformation of the central nervous system. It occurs sporadically or hereditaryly. Cavernomas are generally not associated with other pathological entities. However, one case of cavernoma associated with oligodendroglioma, two cases associated with an NF1 and one case, with Klippel-Trenaumay syndrome, have been reported (3, 4). Medullary cavernomas are considered rare (5) and thoracic localisation is the most common (2, 6). The origin of these malformations is poorly known, they are said to be more common in women with a peak frequency between 30 and 60 years (6). The risk of bleeding is on average 2 to 3% each year (7). The rate of re-bleeding increases to 9 to 10% each year in case of cavernoma larger than 1cm, symptomatic patients and those with a history of haemorrhage (8).



Picture A: T1 sequence in the sagittal plane: intradural intramedullary lesion, in projection of D11-D12, in spontaneous T1 hypersignal associated with intramedullary haemorrhagic changes.

Picture B: T1 FS sequence after injection of gadolinium in the sagittal plane: absence of notable enhancement of the intramedullary intradural lesion.

Picture C: T2 sequence in the sagittal plane: the intradural intramedullary lesion 2cm in height is of heterogeneous signal with alternating zones in hypo and hypersignal T2 realizing the appearance of salt and pepper; it is associated with a range of edema in T2 hypersignal.

Picture D: SE T2 sequence in the axial plane: the intradural intramedullary lesion is lateralized to the left, pushing the marrow to the right, of heterogeneous signal with zones in hypo/hypersignal T2 in pepper and salt.

The clinic for intramedullary cavernomas is not pathognomonic. They can remain asymptomatic for a very long time or be responsible for a slowly progressing alteration of neurological functions or reveal themselves abruptly (9). Acute forms occur in

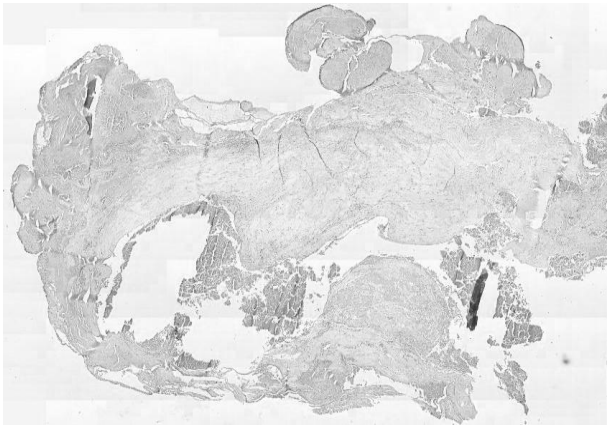
order of a hemorrhagic context while progressive forms (60%), can be reversible during the first month or be accompanied by a progressive pseudotumour worsening (10). Classical symptomatology is made of moderate spinal pain followed by muscle weakness in the lower limbs of progressive worsening, responsible for walking disorders (1, 3). In children, the clinical picture is most often acute in the form of a very rapid neurological deficit (3).

Radiological diagnosis is essentially based on magnetic resonance imaging (11). MRI currently represents the most efficient imagery for both dignostic and evolutionary monitoring (12, 13, 11). Technically, we must emphasize the interest of T2 in gradient echo (T2*). The typical aspect is that of a heterogeneous hyper signal lesion on the T1 and T2 sequences, surrounded by a hypointense peripheral area in T1 and T2 (12). Bone angiography is most often normal but retains its place in differential diagnosis especially with arteriovenous malformations (13, 14) or haemorrhagic spinal cord tumors (15). Computed tomography is less in demand and rarely poses diagnostic (13, 16).

The treatment of medullary cavernoma is neurosurgical with complete microsurgical resection of the malformation. Surgery improves the functional prognosis and very often allows a permanent cure without major sequelae (14, 5). The removal of the lesion must be done in operational theatre by bipolar coagulation of the surface, which decreases its volume and makes removal easier (17). Our case consisted of block removal without much coagulation. The basic principle is to avoid bleeding of the lesion during its removal to operate in a clean field so as not to lose sight of the border with the marrow (9). In the absence of surgical treatment, the evolution can be chronic myelopathy (14, 11). It is indeed essential in case of surgical indication to know the exact situation of the cavernoma, schematically near or in contact with the ventral surface, the lateral surface, or the dorsal surface of the marrow (18). Topography is therefore one of the determining criteria for the surgical indication and the expected clinical results (19). The superficial posterior forms make it possible to consider complete removal, most often without long-term neurological worsening. Centromedullary localisations are accessible through a classic median commissural myeloma with a transient probability of posterior cord damage. An anterior or anterolateral distribution is often respected in paucisymptomatic forms, in the case of a surgical approach (severe or recurrent deficit), a previous approach may be considered (10). This last localisation corresponds to that of our case but a later approach was enough for a complete excision.

Unanimity seems to be around abstention in asymptomatic forms while symptomatic forms hardly lend for discussion (18). However, a distinction must be made between haemorrhagic, deficit forms and only painful forms. The disappointing post-surgical results observed in painful forms make surgical indications cautious in this context (20).

Post-operative results are variable. A multicentre series (10) of 19 operated patients obtained 47% improvement, 42% aggravated and 5% unchanged. Another series (9) of 24 operated patients, did not get any improvement, however, notes 2 patients aggravated while 22 patients kept a condition similar to that observed before surgery. She recommends rapid surgery for any cavernoma associated with neurological disorders consistent with the localisation of the lesion.



Picture E: Histological appearance of a cavernous hemangioma. Hematoxylin and eosin coloring. Low magnification (x20).

Conclusion

The bone marrow localization of the cavernoma is unusual. The thoracic site is the most common. The origin of these vascular malformations is poorly known. The clinic is not pathognomonic, it is that of a rapidly progressive installation medullary compression. MRI is the most efficient examination for the diagnosis, topographical assessment and monitoring of cavernoma. The diagnosis of certainty

is histological. The management of symptomatic spinal cavernomas is surgical with complete resection of malformation followed by quality physiotherapy.

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Common peroneal neuroma in continuity with complete foot drop secondary to a bullet fragment injury. A case report demonstrating end-to-end nerve repair

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ABSTRACT

Background. Common peroneal nerve (CPN) injuries are generally common but they are uncommon due to gunshot injuries and are associated with poor motor outcomes. Managing neuroma-in-continuity is still challenging because there are currently no accepted standards for deciding on the most effective course of treatment or estimating the time needed for repair. Treatment options for a neuroma-in-continuity include neurolysis, neuroma resection with interposition, end-to-side nerve grafting, and bypass grafting.

Case presentation. A 40-year-old man presented with findings of complete right foot drop due to an 8-month-old firearm injury to his right distal thigh. Following baseline investigations, imaging, and anaesthesia fitness, he underwent surgical exploration under general anaesthesia. A neuroma-in-continuity was found in the CPN, resected, and an end-to-end nerve repair was performed. Along with the neuroma-in-continuity, a bullet fragment was also removed. The neurological status remained unchanged postoperatively.

Conclusion. Regardless of the cause of the lesion, patients should be urged to seek surgical therapy if there is no spontaneous recovery within four months after the CPN injury. Sharp injuries and knee dislocations have a better chance of recovery than crush injuries and gunshot wounds.

Keywords
peripheral nerves,
peripheral nerve injuries,
peroneal neuropathies,
neuroma,
foot drop,
firearms

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INTRODUCTION

Sciatic nerve splits into common peroneal nerve (CPN) and tibial nerve in the mid to distal third of the thigh. From the apex of the popliteal fossa to the lateral popliteal fossa, the CPN descends obliquely across the plantaris muscle and curves around the proximal peroneus longus muscle. It then makes its way to the anterior lower leg, where it splits into deep and superficial branches.[1] CPN injuries are generally common but they are uncommon due to gunshot injuries and they are associated with poor motor outcomes. So far, it is believed that nerve reconstruction is a reasonable option and it is recommended up to 6 months after the primary injury.[2]

Managing neuroma-in-continuity is still challenging because there

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are currently no accepted standards for deciding on the most effective course of treatment or estimating the time needed for repair. Neurolysis, neuroma resection with interposition, end-to-side nerve grafting, and bypass grafting are all treatment options for a neuroma-in-continuity. The issue with complete neuroma resection is that it separates and sections not only the disorganised fibro-neural tissue mass that forms the neuroma, but also all potentially still viable nerve fibers passing through the damaged nerve part, removing the possibility of spontaneous recovery. Simultaneously, there is a limited time frame for axonal regrowth before motor endplates degenerate and muscles are irreversibly paralyzed. It is possible that with a neuroma-in-continuity, enough trophic factors have been transported to the motor endplates to preserve some mechanisms, such as enhanced synchronization of motor unit actuating, muscle fiber hypertrophy, and distal motor fiber sprouting, resulting in doubly innervated muscle fibers and allowing functional recovery. This may allow recovery to extend beyond the traditional one year limit after injury.[2] The following case report demonstrates neuroma-in-continuity resection and end-to-end nerve repair in a patient with a CPN neuroma-in-continuity secondary to a bullet fragment injury.

Case presentation

A 40-year-old man presented to us as an outpatient with findings of complete right foot drop due to an 8-month-old firearm injury to his right distal thigh. On examination, he had plegia of the ankle dorsiflexors and extensors of the great toe, as well as hypesthesia in the right peroneal nerve supply area. He underwent surgical exploration under general anaesthesia after baseline investigations, imaging, and anaesthesia fitness. Nerve conduction study was not performed because the patient was very poor and non-affording. Anteroposterior (AP) and lateral X-rays of his right distal thigh and knee revealed a bullet fragment (Figure. 1). The patient was positioned prone, with padding beneath the knee and ankle. A vertical S-shaped incision was made in the lower thigh, medial to the short head of the biceps femoris muscle, after cleaning and draping. Dissection was carried out. The sciatic nerve bifurcation, the tibial nerve, and the common peroneal nerve were discovered (Figure. 2A). A neuroma-in-continuity of the CPN was identified, resected, and an end-to-end nerve repair was performed using Ethicon Prolene 10.0 suture (Figure. 2B). Exploration also turned up the bullet fragment, which was also removed along with the neuroma-in-continuity (Figure. 3A&B). The surgical wound was thoroughly washed with saline before being closed. The postoperative neurological status remained unchanged. Hematoxylin and Eosin (HE) stains revealed a random and convoluted arrangement of nerve bundles within a fibrous connective tissue stroma (Figure. 4).

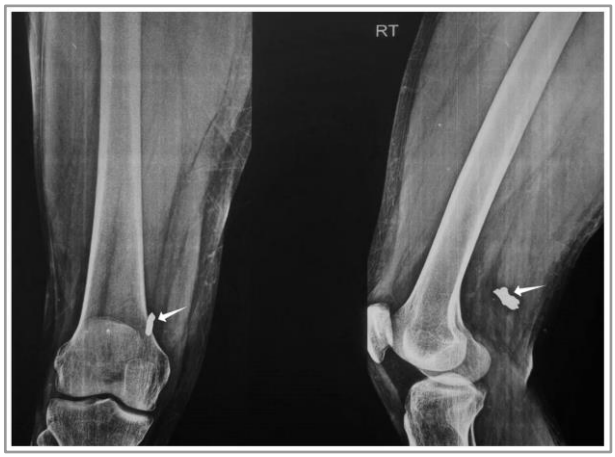

Figure 1. X-rays right distal thigh and knee AP and lateral views showing a bullet fragment (marked by white arrows).

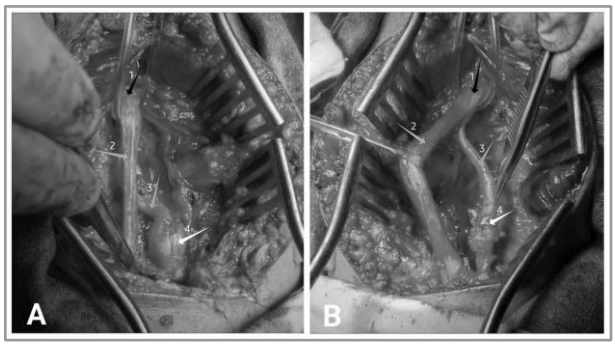

Figure 2. A; 1 (black arrow) Sciatic nerve bifurcation, 2 (yellow arrow) Tibial nerve, 3 (blue arrow) Common peroneal nerve, 4 (white arrow) Neuroma-in-continuity. **B**; 1 (black arrow) Sciatic nerve bifurcation, 2 (yellow arrow) Tibial nerve, 3 (blue arrow) Common peroneal nerve, 4 (white arrow) End-to-end nerve repair after neuroma in-continuity resection.

Discussion

The CPN has been shown to be the most vulnerable and frequently injured nerve of the lower extremity[3] due to its superficial anatomical location[1,4] and

fixation at the sciatic notch and the peroneus longus muscle, as opposed to the less vulnerable location of the tibial nerve.[1,2,4,5] At the same time, CPN injuries have a poorer recovery rate when compared to other lower extremity nerve injuries. The reasons for this are a poorer neural blood supply, a "lower force-absorbing fascicle or connective tissue count," and a greater demand for innervation of peroneal nerve supplied muscles.[2,4]

Aside from the injured nerve, factors influencing the outcome after nerve reconstruction include the trauma mechanism such as laceration, compression, traction, and focal ischemia, the graft length, and the time between grafting and intervention. Sharp trauma, shorter grafts, and early reconstruction or neurolysis have all been linked to a better prognosis.[6,7] The main limiting factor in the optimal treatment of peroneal nerve lesions associated with foot drop is time. It is well known that nerve regeneration occurs at a rate of 1 mm per day,[7,8] that motor endplates die 12-16 months after denervation,[7] and that innervated muscles remain viable 18-24 months after the injury.[9] When the rate of regeneration and the distance to cover are disproportionate, it leads to irreversible degeneration and fibrosis, as well as permanent paralysis of the denervated muscles.[10]

The CPN nerve transfer or reconstruction has been said to be reasonable for motor recovery up to 6 months, by no means later than 12 months after denervation, and denervation longer than 12 months has been said to be an absolute contraindication.[8,11,12] On the other hand, in patients grafted 13 and 18 months after the injury, simultaneous CPN reconstruction and tibialis posterior tendon transfer results in satisfactory functional recovery, indicating the importance of rebalancing ankle movement forces to enhance neural regeneration.[13]

Neurolysis has been shown to be an effective method for improving nerve function in the context of neuroma-in-continuity,[4,14,15] for up to 8 months after the injury.[6] However, this method has been linked to microvascular damage and the formation of intraneural scars.[16] A few months after the injury, intraoperative nerve action potentials have been proposed as a crucial tool for reevaluating the reason for resection and nerve grafting against neurolysis in the CPN lesions.[1] CPN injuries in open wounds should undergo exploration in an emergency room. Patients should be urged to seek surgical treatment if a close injury fails to recover on its own within four months of the damage, regardless of the cause of the lesion. Sharp injuries and knee dislocations have got a good recovery compared to crush injuries and gunshot wounds which have a poor recovery.

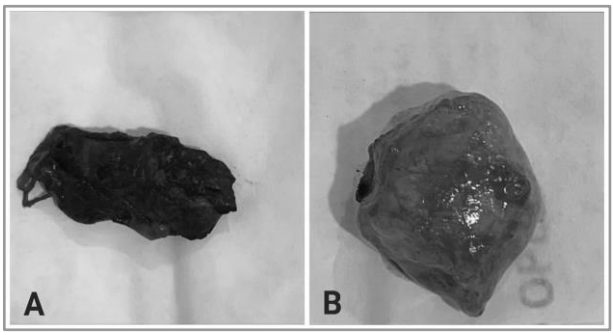

Figure 3. A: Removed bullet fragment. **B**: Resected neuroma.

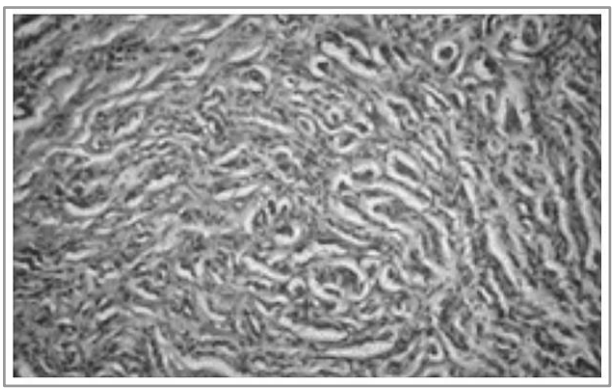

Figure 4. Hematoxylin and Eosin (HE) stains reveal a random and convoluted arrangement of nerve bundles inside a fibrous connective tissue stroma.

Conclusion

CPN is the most vulnerable and frequently injured nerve in the lower extremity but gunshot injuries are a less common cause. Time is the most important limiting factor in the optimal treatment of peroneal nerve lesions associated with foot drop. CPN injuries in open wounds should be explored in the emergency room. Patients should be advised to seek surgical treatment if there is no spontaneous recovery within four months of the injury, regardless of the causative mechanism of the lesion. Sharp injuries and knee dislocations have a better chance of recovery than crush injuries and gunshot wounds.

List of Abbreviations

CPN: Common Peroneal Nerve
AP: Anteroposterior

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Bilateral clinoidal Rosai Dorfman disease mimicking meningioma – a rare cause of bilateral blindness

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ABSTRACT

Rosai Dorfman disease is a self-limiting disease usually affecting the lymph nodes. Intracranial lesions are seen in less than 5% of cases. Isolated intracranial RDD without nodal involvement is rare, only 70 cases have been reported to date. Skull base lesions are seen in only 7 cases, petro clival RDD. Clionoidal lesions of RDD have not been reported in the literature, we report a rare case of bilateral clionoidal lesions of RDD presenting with bilateral blindness in a young male.

Keywords
bilateral,
clionoidal,
Rosai Dorfman disease,
blindness

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INTRODUCTION

Rosai Dorfman disease was first described in 1969 by Juan Rosai and Ronald Dorfman as sinus histiocytosis with lymphadenopathy in young male. It commonly presents as painless massive cervical lymphadenopathy and symptoms of fever, malaise and / or anemia. Although all age groups have been effected with the disease, Rosai Dorfman disease commonly effects young males, usually less than 20 years of age group. The disease is extra nodal in up to 43% of patients with or without lymphadenopathy at any point of time in disease. Common extra nodal sites being skin, nose & paranasal sinus, eyelid, orbit & Central nervous system. Intracranial involvement in Rosai Dorfman disease is seen in <5 % of cases of extra nodal disease & in most of these cases leptomeninges are affected.

Isolated cranial involvement without nodal involvement is rare and only 70 such cases are reported in literature till date. To our knowledge bilateral lesions involving the clionoid are not reported in literature, so we report first such case of Rosai Dorfman disease involving bilateral clionoid process.

CASE REPORT

A 21 Year male patient presented to us with complaints of decreased vision in both eyes since 1-month, intermittent headache since 15 days more in morning hours. Patient had one episode of generalized tonic

clonic seizure 2 days back and then he was referred to our hospital. On neurological examination patient only had visual deficits, his vision was 6/12(snellen chart) on right side and only perception of hand movements on left side. Patient was investigated further with radilogical examination. MRI brain with contrast (Fig 2-4) was done which showed two large well circumscribed lobulated extra axial mass lesion seen along both planum sphenoidale region extending upto both anterior clinoid processes of size 5.2 X 3.2 X 1.2 cm on left side and 1.4 x 2.7 X 3 cm on right side with extension to bilateral anterior temporal lobe and inferior frontal lobe. The lesion was isointense on T1 image and hypointense on T2 image with intense post contrast enhancement. The mass was abutting the cavernous sinus bilaterally without any obvious infiltration. And the lesions were compressing optic chiasma from both sides. Patient was planned for staged surgery for both sideds considering the lesions as meningioma. Left sided lesion was approached in first stage as he was developing optic atrophy on that side.

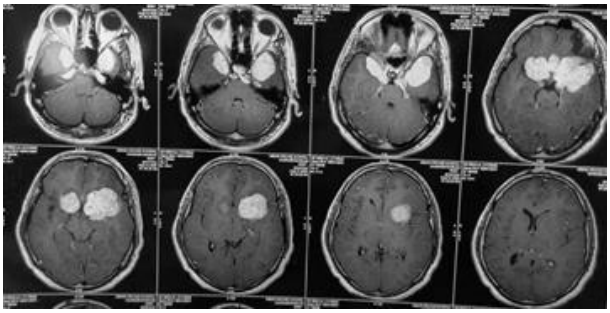

Figure 1. Preoperative MRI Brain with contrast showing bilateral clinoidal lesion (Axial images).

Intraoperatively lesion was reddish grey in color, firm and moderately vascular. Complete excision was achieved. To our surprise Histopathological examination was showing fibro-collagenous tissue with dense chronic inflammatory infiltrate comprising plasma cells, lymphocytes at places showed large histiocytes with phagocytosis of intact lymphocytes and plasma cells (emperipolesis). Russell bodies also noted. CD1a marker was absent suggestive of Rosai Dorfman disease. (Fig 5)

As the disease is self limiting with good prognosis after complete excision, patient underwent second stage surgery immediately after 15 days on right side. Complete excision was achieved, patient was discharged with minimal improvement in vision on right side. Histopathology of the lesion on right side was also suggestive of Rosai Dorfman disease. Post operative MRI brain with contrast after 1 month was suggestive of complete removal of both lesions, no residual lesion. patient was planned for radiotherapy.

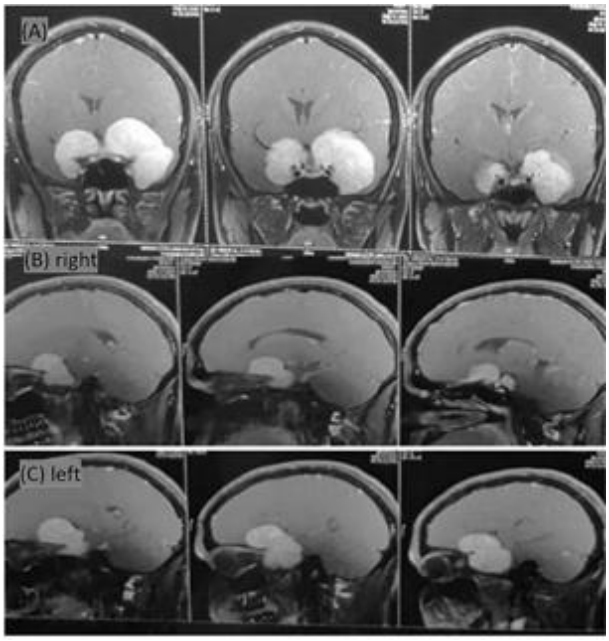

Figure 2. Preoperative MRI Brain with contrast showing bilateral clinoidal lesion (Saggital & Coronal images).

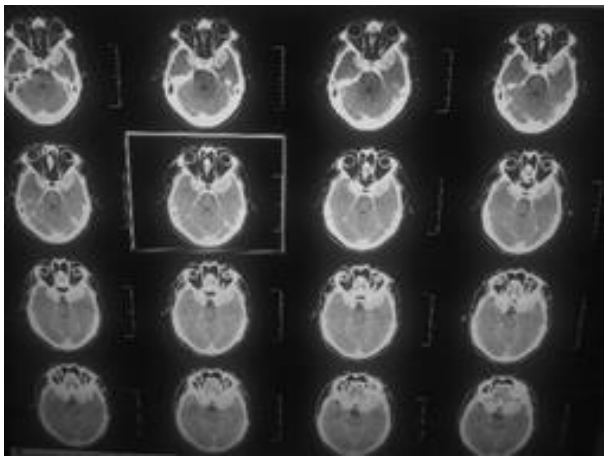

Figure 3. Preoperative CT Brain with contrast showing bilateral clinoidal lesion.

DISCUSSION

RDD is a benign, self-limiting histiocytic disease with

poorly understood etiopathogenesis. Intracranial manifestations are seen n only 5% of cases. There is no age preponderance, th male predomiance seen. The clinical symptoms depend on the location of the lesion, and includes headache, nausea and vomiting, seizures, cranial nerve deficits, and weakness.

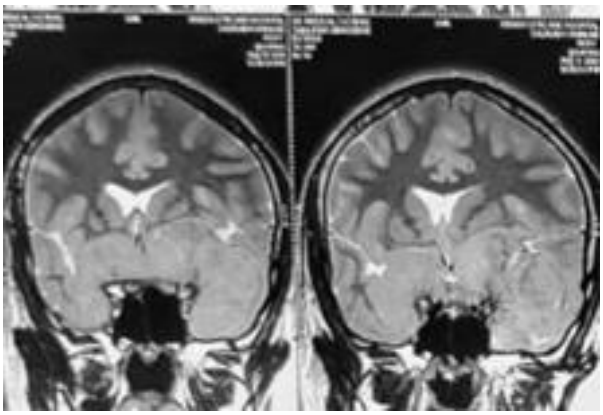

Figure 4. Preoperative MRI Brain with contrast showing bilateral clinoidal lesion (Coronal images, T2 weighted images).

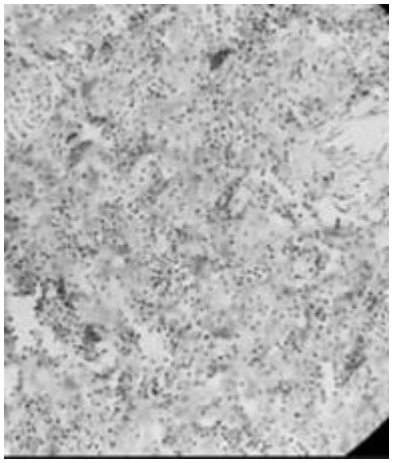

Figure 5. Histopathological slide.

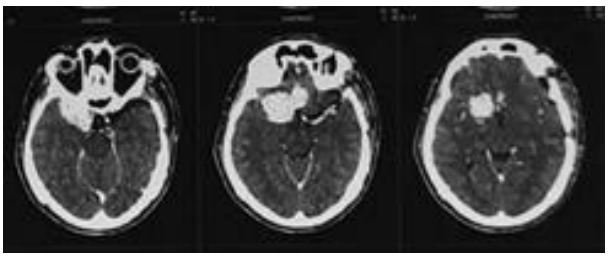

Figure 6. Preoperative images CT brain with contrast before second stage surgery.

In literature only 70 cases have been reported of isolated cranial manifestations in RDD. no case is been reported of clinoidal RDD. So this first case so far presenting with bilateral lesions of RDD involving the clinoid process on both sides. 7 cases of petroclival lesions have been reported in literature.

A previous study found intracranial lesions re growth or recurrence of symptoms in 14% of 29 patients with a mean follow-up period of 10.1 years.

Radio logically lesions are typically dural based, extra-axial, well-circumscribed mimicking meningioma.[16–19] On CT, they are homogeneous hyperdense or isodense masses. MRI is gold standard investigation for evaluating lesions of intracranial RDD. On T1-weighted images, the lesions appear as iso to hyperintense masses with clear margins. On T2-weighted images, the lesions usually appear as isointense masses. On contrast images, the lesions demonstrate homogeneously enhancement, and the dural tail can commonly be seen.

In our case, CT demonstrated bilateral well-defined, homogenous, hyperdense masses bed clionoid process; MRI showed dural based well-defined, homogenous lesions based on clinoid process left more than right with cavernous sinus extension on both sides. The lesions were isointense on T1 weighted images, hypointense on T2-weighted images, and homogeneously enhanced. So our working diagnosis was meningioma preoperatively.[12,20] Preoperative radiological findings using the current MRI sequences are difficult to distinguish RDD from meningiomas, but the absence of hyperostosis, bony erosion, or calcification should suggest RDD as a differential diagnosis of meningiomas.[17] Radiologically the lesions in RDD are similar to meningioma on T1 post contrast enhancement, but they have low signal intensity in T2 weighted images, which is very unlikely with meningioma. Other intracranial lesions with T2 image low signal are melanoma, malignant lymphoma, markedly fibrous or calcified meningioma. The reason of low signal in T2 weighted image in this disease is presence of free radicals released by macrophages during phagocytosis. N-isopropyl P-[123I] iodoamphetamine ([123I]IMP) single-photon emission computerized tomography (SPECT) reveals a hot lesion on early and delayed images which is unlikely in cases of meningioma. Final diagnosis of RDD can only be confirmed by histopathological and immunohistochemical examinations.

On histopathology Rosai Dorfman disease shows

fibrosis, histiocytes and lymphoplasmacytic cells. Russell bodies also seen. Histopathological examination is definitive for diagnosis of RDD, especially visualization of emperipolesis and s100, and absence of CD1a (a marker of Langhens cell histiocytosis) . Histopathological differential diagnosis includes lymphoplasmacytic meningioma,Langerhans histiocytosis, lymphoma, plasmacytoma and sarcoidosis.

Lymphoplasmacytic meningioma can be differentiated by presence of typical meningioma picture with epithelial membrane antigen positivity. Langerhans histiocytosis can be differentiated by presence of eosinophils, both s100 and CD1a.Lymphoma can be differentiated by presence of CD15 and CD30 along with Reed Stenberg cells. Plasmacytoma also gives similar picture but the lineage of plasma cells is not polyclonal as in Rosai Dorfman disease. Sarcoidosis can be ruled out by presence of granulomatous inflammation.

In cases of chronic inflammatory back ground in histology with prominent histiocytes and an absence of infectious agent should alert to proceed with immunohistochemistry staining for s-100. S-100 positivity suggests either Rosai Dorfman disease or Langerhans cell histiocytosis. LCH the histiocytes typically show reniform or indented nucleus, contain birbeck granules and CD1a positivity which differentiated it from Rosai Dorfman disease.

Surgery with complete resection of the lesion is the goal. Use of steroids has shown some promising results in some cases. The lesion is radiosensitive and radiotherapy is a good option for residual or recurrent lesions.

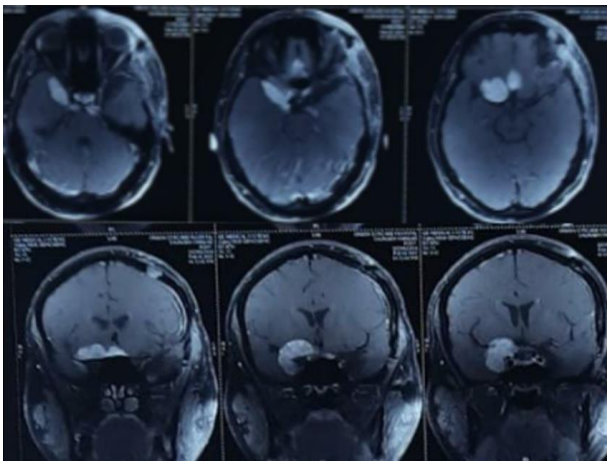

Figure 7. Preoperative images MRI brain with contrast before second stage surgery.

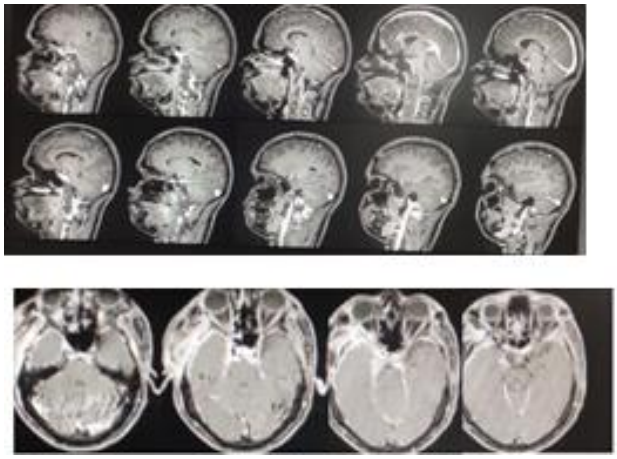

Figure 8. Post operative MRI Brain with contrast after second surgery at 1 month follow up.

Conclusion

Rosai Dorfman disease mimics intracranial dural based lesions causing mass effect. It may or may not be associated with extranodal disease. It should be included in differential diagnosis in cases with low intensity T2 image lesion and histologically fibrotic chronic inflammatory lesions of CNS with predominant histiocytic component. Resection of the intracranial lesion is the most effective treatment. In case of subtotal resection, the application of adjunctive radiotherapy and/or steroid agents should be advised.

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Secondary optic neuropathy due to sphenoid-ethmoidal sinus mucocele

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ABSTRACT

Secondary visual impairment induced by sinusitis is a rare condition that cannot be recognized in all cases. A steady decline in visual acuity and visual field together or alone is the main symptom patients may complain of on admission. This might be hard for general practitioners in Uzbekistan, as possible causes are either intracranial or ophthalmic abnormalities. Hence, it is frequently misdiagnosed or leads to late diagnosis once visual impairment becomes severe. In this paper, we discuss the case of a 9-year-old boy with impaired vision on the left side that was detected almost too late and could have led to complete vision loss. Ineffective conservative therapy was provided for four months. CT and MRI confirmed a lesion in the left sphenoethmoidal sinus. The patient then underwent endoscopic sphenoiethmodotomy with drainage of the left sphenoethmoidal sinus. In the early postoperative phase, as early as the next day after the surgical procedure, the patient experienced visual improvement. Forty days following surgery, in combination with postoperative conservative care in an eye hospital, there was a noticeable improvement in vision. In conclusion, it is crucial for ophthalmologists, neurologists, and ENT surgeons to focus on inflammation in the sphenoethmoidal sinus in children even with mild vision impairment.

Keywords
optic neuropathy
endonasal surgery,
sphenoid sinus mucocele

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INTRODUCTION

Visual disturbances in optic neuropathies may be produced by numerous etiologic events such as toxic, nutritional, and other ophthalmological as well as intracranial disorders[1,2]. The most prevalent intracranial pathologies that can lead to optic neuropathies are lesions in the sellar and parasellar areas such as pituitary tumors, meningiomas, craniopharyngiomas, and intracerebral lesions affecting the visual pathways, as well as primary or secondary hydrocephalus. In addition to numerous main ophthalmologic illnesses [3], rhinogenic optic neuritis may also be induced by sphenoid sinus mucocele with sinusitis, ethmoiditis, and onodi cell inflammation [4-7].

In some selected circumstances, it is difficult to make a differential diagnosis. When children with good musculoskeletal development

show evidence of gigantism and complain of vision difficulties, they contact multiple physicians such as endocrinologists, neurologists, and even neurosurgeons for probable pituitary tumors. In such particular conditions, MRI and CT can be valuable diagnostic tools to detect lesions in the pituitary region that compress the optic nerve and produce vision abnormalities. MRI is the best choice to evaluate optic nerves except for its intraocular portion and it is fairly difficult to visualize the retina with high-resolution MR imaging. If a lesion is diagnosed in the sphenoidal and ethmoidal sinuses, notably inflammation of the Onodi cells, the physician should think of secondary optic neuritis resulting from this inflammatory process.

CASE REPORT

A 9-year-old kid first visited the outpatient clinic of the Republican Specialized Scientific Practical Medical Center of Neurosurgery in Tashkent, Uzbekistan. His major complaints were acute progressive headache and moderate visual problems when his mother initially consulted his brother, a young neurosurgeon. The patient was tall and had strong musculoskeletal development. He complained of headache and slight visual disruption in the left eye that had continued for a week.

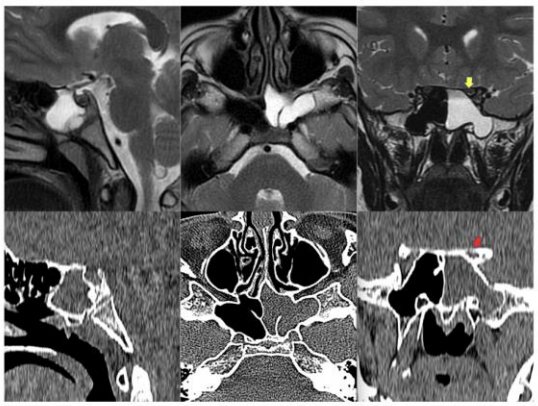

Figure 1. Preoperative MRI and CT show a lesion within the left sphenoethmoidal sinus. On CT, there is no bone erosion around the optic canal. Yellow arrow optic nerve, Red arrow- optic canal.

The patient had no fever or other symptoms; yet, he experienced rhinogenous sinusitis and tonsillitis multiple times in early childhood. In addition, the boy's family history was negative for neurologic or autoimmune disorders. Because of his appearance, which was suggestive of a pituitary lesion, he was advised for an MRI scan. An ophthalmologic examination yielded normal results, but MRI showed a lesion in the left sphenoethmoidal sinus but did not discover any abnormalities in the sellar region (Figure 1). On visual evoked potential (VEP) (table 1), there was extending latency of the P100mc component by 104,2 mc on the left eye and 100,1 mc on the right eye. Ophthalmological examination: visual field: OD-mild stage of myopia and OS-myopic astigmatism, left temporal hemianopsia, visual acuity was as follows: OD-0.9; 0S-0,1. The patient was then advised to consult an ophthalmologist and an otolaryngologist (ear, nose, and throat specialist) in the region where he lived for additional assessment and treatment. After 4 months of conservative outpatient treatment by an ophthalmologist and an otolaryngologist with antibiotics and steroids, the patient's mother called his brother, who was a neurosurgeon, complaining of his son's progressive worsening of visual acuity in his left eye. Ophthalmologic and fundus investigations revealed alterations in the vascular anatomy and optic nerve. CT indicated a left sphenoethmoidal lesion (sinusitis) with no mass effect on the left optic canal; no bone erosion was seen with an inferior-medial wall of the left optic canal (figure 1). Collegial consultation with experts in endoscopic neurosurgery, and several ENT Surgeons and ophthalmologists, as well as literature searches, led to the conclusion that optic neuropathy was diagnosed to be induced by sphenoethmoidal sinusitis.

Table 1. Neuroophthalmological examination

	Visual acuity		Visual field		Visual evoked potential P100mc component	
	Right	Left	Right	Left	Right	Left
Preoperative	O,9	0,1	normal	Hemianopsia	100,1	104,2
Postoperative	1,0	0.9	normal	normal	100,1	101,7

As a result, in case of probable bone involvement and any intraoperative intracranial findings, along with neurosurgeons, endoscopic sphenoethmoidotomy with the excision of the lesion and draining of the left sphenoid sinus and ethmoidal sinus was performed. During surgery, no direct intracranial invasion and no direct

compression of the optic nerve were identified. In the early postoperative phase, as early as the next day after the surgical treatment, the patient reported visual improvement. Then the patient was taken to the Eye hospital where he got postoperative conservative outpatient treatment with antibiotics and steroids. Forty days after surgical therapy in combination with postoperative conservative treatment in an eye hospital, there was a considerable improvement in vision. 40 days follow-up ophthalmologic examination (table 1) showed significant positive changes such as P100mc component latency decreased and was almost similar in both eyes and, On CT (Figure 2) near total removal of mucocele in the left sphenoid sinus and there was a small residual one within the left ethmoidal sinus respectively.

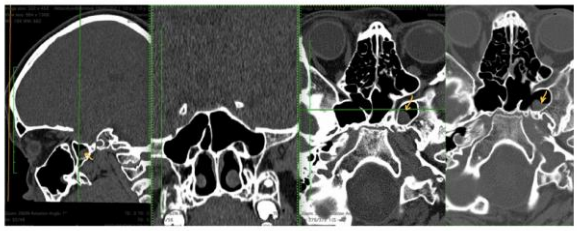

Figure 2. postoperative CT. 40 days post-operative CT shows near total drainage of the left sphenoethmoidal sinus with small remaining mucocele (arrow) within the left ethmoidal sinus.

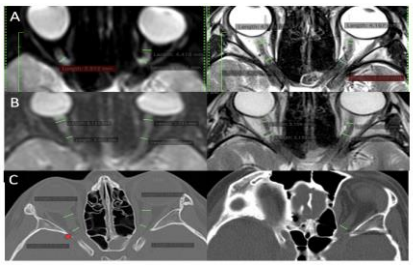

Figure 3
MRI images of a 9-year-old boy: thickness is 3 mm.
A. MRI imaging 4 months before surgery shows the diameter of 3,86 mm retrobulbar left optic nerve and 3,92 mm right optic nerve. On the T2 axial cut MRI image, the diameters of left and right optic nerves on retrobulbar space are 3,6mm and 4,2mm respectively. And on this T2 axial cut image, we can see a lesion that is very close to the left optic nerve and the optic chiazm.
B. Follow UP MRI just 5 days before surgery. On axial cut diffuse MRI shows diameters of left and right optic nerves on the retrobulbar space are 3,4mm and 4,01mm respectively. On the T2 axial cut MR image, the diameter of retrobulbar left and right optic nerves are 4,4mm and 5,1mm respectively.
C. Preoperative CT (left to right): diameters of right and left optic nerves on retrobulbar space are 4,9mm and 5,6mm respectively. Postoperative 40 days follow-up CT shows 5,4 mm diameter of left optic nerve on retrobulbar space.

Discussion

Mucoceles are encapsulated fluid-filled lesions, that can represent in paranasal sinus cavities and there is rarely involvement of sphenoid sinus (up to 3% of all cases) as they are often present in individuals aged over 40 [7]. Since the optic canal and the optic nerve have a closer relationship with the posterior part of the sphenoethmoidal sinus, the Onodi cells which are usually found in that part can cause serious retrobulbar optic neuropathy and in association with cholesterol granuloma, it causes bone destruction and compression [8,10,11]. The most typical symptoms are headache or facial pain, and occasionally, even if this happens seldom, there are the optic and other III, IV, and VI cranial nerves become involved. Cheng et al. described the case in the pediatric population, where they documented a big sphenoid sinus mucocele of a 10-year-old boy who exhibited right eyelid droop and double vision. Even though there was compression and cerebral involvement, following surgery, the patient reported full clearance of mucocele and excellent visual outcome and they argue that the literature reveals cranial neuropathy due to sphenoid sinus mucocele is highly unusual. Prompt diagnosis and care may lead to improved clinical results and the avoidance of permanent neuropathy.

However, postoperative care also plays a significant role as there is usually secondary optic neuritis that needs to be handled carefully. Otsuka et.al. [9] concur with their perspective on the importance of preoperative visual acuity as the prognostic factor for postoperative vision in patients with rhinogenic optic nerve neuropathy, however, poor preoperative vision may be improved by surgical therapy. In addition to this, younger patients are likely to have comparably better results than older people. Steroid pulse treatment occasionally might be utilized for visual acuity improvement following surgery. Even in their research, there was not any significant difference in the prognosis of vision based on the presence or absence of steroid pulse therapy, in our experience, we consider that both preventative preoperative and postoperative use of steroids may enhance surgical results.

Numbers of studies have shown that the origin of visual impairment related to mucoceles involves direct mechanical compression, local ischemia, and inflammation. They indicate distinct prognoses. While the slow manifestation of clinical symptoms and a better prognosis typically occur in mechanic compression, the latter two, ischemia and inflammation generate an early start of symptoms that may have a bad prognosis [12-15]. Carefully preoperative screening may indicate various causes of optic neuropathy. However, it is difficult to identify a normal optic nerve and an optic nerve lesion. The disc component may be analyzed by utilizing fundoscopy and high-resolution optical coherence tomography, whereas the other three parts are less accessible and require imaging procedures like MR imaging, sonography, and CT. MR imaging is preferred to the other tests described above thanks to several features such as exceptional soft tissue resolution, the absence of ionizing radiation, and high diagnostic accuracy. MR imaging has a

sensitivity of 60-75% and a specificity of up to 90% for identifying abnormalities in the optic nerve [16,17]. In typical circumstances, the intraorbital portion of the optic nerve has a mean diameter ranging from 2.2 to 5.2 mm. The diameter of the optic nerves normally grows throughout the first two years of life. However, for children aged 6 to 12, whereas the diameter of the optic nerves on axial cut MR images on the retrobulbar level is 2.26 0.38 mm, it is 2.27 0.41 mm on coronal plane MRI on the retrobulbar space. As a consequence, on both axial and coronal incisions, the midaspect part of the optic nerve should be thinner than the retrobulbar region [18].

In our case, we assume that the visual impairment that the patient experienced was secondary owing to inflammation of the sphenoethmoidal sinus, specifically the posterior region which normally has a tighter relationship with intracanalicular optic nerves. Even though there is no direct compression on the optic nerves, this inflammation and toxins are thought to irritate the optic nerve creating a circulatory disturbance and nerve trophic dysfunction. As a consequence, this might lead to a deterioration in vision. Our findings on radiological exams such as MRI (figure 3A and 3B) and CT (Figure 3C), measuring diameters of the optic nerves in retrobulbar space might identify probable alterations in circulation and optic nerves ` an or/and hypotrophy that commonly leads in visual difficulties.

In early observation days, when the patient first came to admission because of headache and mild impaired vision, an early MRI showed a mass lesion within the left sphenoid and ethmoidal sinus. We measured the diameters of both optic nerve and it was almost similar in distal part of the retrobulbar optic nerve in both eyes (Figure 3A), however, in its proximal part, close to mass lesion there was a gap between the diameters of the retrobulbar left and right optic nerves on a T2 axial cut MR scan(3.6 mm and 4.2 mm, respectively). The diameters of both optic nerves should be almost the same in principle, but in the present patient, there was a gap between the diameters of the right and left optic nerves as seen on T2 MRI images, and the difference was around 1.2mm, suggesting hypotrophy of the left optic nerve. The diameters of the right and left optic nerves, as well as their difference, remained stable in early preoperative computed tomography (figure 3C right); however, due to the resolution of CT compared to MR imaging, those numbers were slightly different; 4,9mm and 3,6mm in retrobulbar space, respectively. The gap between the right and left optic nerves was about 1.3mm. Even after 4 months of conservative therapy by otolaryngologists and ophthalmologists, the patient's visual acuity had deteriorated, and they have referred to us again. Because of these alterations and decreasing visual acuity, conservative therapy was proven ineffective, and the patient needed surgical intervention. The patient was checked again 40 days following endonasal surgery and postoperative conservative therapy with antibiotics and steroids. His vision dramatically improved, and he recovered rapidly. There was also no headache. The diameter of the left optic nerve was 5,4 mm on CT, which was approximately identical to the diameters of the right optic nerve we measured before the surgery. As a consequence, the diameter of the left optic nerve expanded from 3,6mm to 5,4mm (figure 3C left). However, owing to a lack of precision and resolution quality, CT may not be a viable technique for assessing the diameter of the optic nerve, which we feel is a drawback of our research.

Conclusion

Secondary optic neuropathy, due to sphenoid sinus mucocele is common in the pediatric population. Pricey exams such as MRI and CT are required for a correct diagnosis and treatment selection. Minimally invasive surgical therapy is the major therapeutic objective to conquer even such basic and infrequent instances. If inflammatory illnesses become chronic in youngsters. Rhinogen sinusitis may occasionally produce visual difficulties since sinusitis is prevalent in both children and adults.

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The efficacy of endoscopic endonasal duraplasty compared to transcranial duraplasty for post-traumatic CSF rhinorrhea in terms of CSF rhinorrhea recurrence and other complications. A prospective cohort study from a low-middle-income country

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Keywords
traumatic brain injury,
CSF rhinorrhoea,
dura mater,
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craniotomy,
developing countries

ABSTRACT

Objectives. To determine the efficacy of endoscopic endonasal dura repair versus transcranial dura repair for post-traumatic CSF rhinorrhoea in terms of CSF rhinorrhea recurrence and other complications.

Materials and methods. A total of 92 patients (age 15-50 years, both genders) with an established diagnosis of CSF rhinorrhea following traumatic brain injury were enrolled in this prospective cohort study. Group A and Group B were formed from the patients. Group A received endoscopic endonasal duraplasty, while Group B received transcranial duraplasty. Recurrence of CSF rhinorrhea, as well as any other complications (meningitis, anosmia, hydrocephalus, and abscess), were noted and compared between the two groups one week, two weeks, and four weeks after the procedure.

Results. In Group A, the mean age was 28.6 ± 9.9 SD years and in Group B it was 29.9 ± 8.6 SD years. In group A, there were 63% (n=29/46) patients who had age between 15-30 years and 37% (n=17/46) had age between 31-50 years. In group B, 52.2% (n=24/46) patients had age between 15-30 years and 47.8% (n=22/46) had age between 31-50 years. In group A, there were 82.6% (n=38/46) males and 17.4% (n=8/46) were females and in group B there were 87% (n=40/46) males and 13% (n=6/46) females. At one month follow-up, overall recurrence of rhinorrhea was observed in 17.4% (n=8/46) patients in Group A, while it was 41.3% (n=19/46) patients in Group B (P=0.012). On the other hand, overall complications were 8.7% (n=21/46) in Group A patients, while they were 45.7% (n=21/46) in Group B patients (P=0.001).

Conclusions. During a one-month follow-up, patients who received endoscopic repair experienced fewer recurrences and other complications overall than patients who underwent transcranial duraplasty, and the difference was statistically significant. We advise conducting studies with a larger sample size and longer follow-up periods.

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Introduction

Cerebrospinal fluid (CSF) rhinorrhea is defined as the leakage of CSF from the nose as a result of communication with the subarachnoid space.[1] It entails removing all of the barriers that separate the subarachnoid space from the upper aerodigestive tract, including the nasal cavity or paranasal sinus mucosa, skull base (i.e., bone), dura mater, and subarachnoid membrane.[2] Accidental trauma is responsible for 70-80% of CSF rhinorrhea.[3] More than half of the leaks are discovered within the first two days, 70% within the first week, and nearly all within the first three months.[4] The most commonly presenting sign is unilateral watery nasal discharge following skull base trauma.[5] Patients may also present with altered mental status, seizures, or meningitis, necessitating a high level of suspicion for an accurate diagnosis.[6]

The treatment can be either conservative or surgical. Early surgical repair is critical to avoid the risk of ascending infection.[7] Early surgical repair (within 7 days) appears to reduce the risk of meningitis.[8] Neurosurgeons have traditionally repaired these lesions via a transcranial approach.[1] According to reports, the endoscopic endonasal approach is much safer than the transcranial approach and is well tolerated.[4] It has gained widespread acceptance as the preferred technique due to its superior visualisation, exact graft placement, minimal harm to the surrounding tissue, preservation of olfactory function in the event of a fistula leak through the cribriform plate, shortened operating time, and quicker recovery time.[1]

According to published data, the endoscopic endonasal approach results in significantly less recurrence of CSF rhinorrhea. Given the high morbidity rate associated with open craniotomy, such as brain retraction, olfactory nerve injury, anosmia, abscess/wound infection, sepsis, and recurrence, an endoscopic endonasal approach is preferable. Furthermore, the shorter hospital stay and return of functional independence associated with endoscopic endonasal surgery have made it the method of choice for CSF rhinorrhea repair. In our study, patients who had endoscopic repair had fewer overall recurrences and other complications than patients who underwent transcranial duraplasty during a one-month follow-up.

Materials and methods

Study design: A prospective cohort study

Setting: Department of Neurosurgery, Pakistan Institute of Medical Sciences, Islamabad, Pakistan.

Study duration: 3 years (30-07-2017 to 29-07-2020)

Sample size: It was calculated by World Health Organization (WHO) sample size calculator while keeping the parameters as: 5% level of significance and 80% power of test. The sample size turned out to be 46 patients in each group and a total of 92 patients were included in the study.

Sampling technique: Non-probability based consecutive sampling technique.

Sample selection

a) Inclusion criteria

- CSF rhinorrhea following traumatic brain injury
- Age: 15-50 years

b) Exclusion criteria

- CSF rhinorrhea with concomitant otorrhea
- Redo surgeries
- Acute infections
- Severe deviated nasal septum (DNS)
- Pregnant woman

Data collection procedure

Following approval from the hospital's ethical committee, the study was launched. The study included patients admitted to the Neurosurgery ward who had CSF rhinorrhea as a result of traumatic brain injury as evidenced by clinical examination, Computed Tomography (CT) scan skull with 3D reconstruction, and Magnetic Resonance Imaging (MRI) brain T2 weighted images with coronal cuts. Each study participant provided written informed consent. On pre-designed performa, initial data such as age, gender, contact number, and date of admission were recorded. Group A and Group B were formed from the patients. Group A received endoscopic endonasal duraplasty, while Group B received transcranial duraplasty. Any complications with any of the procedures were documented.

Surgical technique for endoscopic duraplasty

After baseline investigations, imaging, necessary blood products, and pre-anaesthetic evaluation, the patient was shifted to the operating room with informed written consent. Preoperative nasal

preparation was performed to clean the nasal cavity and prevent perioperative nasal bleeding. Eight hours before surgery, cotton gauze soaked in a 2% adrenaline/lignocaine/antibiotic mixture was placed inside each nostril. The surgical field was cleaned and draped after the patient was put under general anaesthesia. The procedure began with locating the source of the leak. A partial middle turbinectomy was performed to widen the surgical corridor and to use the bone as a graft in multilayer repair. To prepare the area for grafting, the mucoperiosteum around the defect was removed. Depending on the size, location, and aetiology of the defect, a multilayer (sandwich grafting) reconstruction was performed using some or all of the following 5 layers. The first layer is a fat plug harvested from the anterior aspect of the thigh, the second layer is a fascia layer with fascia lata tucked beneath the bony edge, the third layer is bone harvested from the middle turbinate or nasal septum, the fourth layer is fascia lata overlay graft over defect, and the fifth layer is free mucoperiosteal fat or vascularized nasoseptal flap or middle turbinate flap. The nose was then packed with a water-filled catheter and left for 3-4 days after surgery. At one week, two weeks, and four weeks, CSF rhinorrhea was noted if it occurred at all.

Surgical technique for transcranial duraplasty

Bicoronal or unilateral subfrontal approaches were used to accomplish transcranial intradural repairs. All patients underwent preoperative standard investigations to get them ready for surgery, and their general anaesthesia readiness was assessed. The patient was moved to the operating room and placed in the supine position. After making the appropriate hairline incisions, the patients who required a wide exposure underwent a bicoronal approach, while the remaining patients underwent a unilateral approach. Both techniques used the same remaining steps, which included drilling burr holes and elevating the bone flap bilaterally or unilaterally depending on the situation. If necessary, frontal sinuses were cranialized. A linear dural incision was made, the brain was retracted, the CSF was sucked, a cribriform plate defect was found, and a fascia lata graft was applied to cover the defect. Dura was sealed up watertight. The dural hitch stitches were applied, and the bone flap was replaced and secured. Skin was closed in the usual manner and an antiseptic dressing was applied.

Data analysis procedure

Statistical Package for Social Sciences (SPSS) version 23.0 was used to enter and analyse the collected data. For numerical variables such as age, mean and standard deviation were calculated. For categorical variables such as gender and complications, frequency and percentages were presented in both groups. The Chi-square test was used to compare the complication rate between the two groups. P-values of 0.05 were deemed significant.

RESULTS

1. Demography of the selected population

A total of 92 patients (age 15-50 years, both genders) with an established diagnosis of CSF rhinorrhea following traumatic brain injury were enrolled in the study. Group A and Group B were formed from the patients. Group A received endoscopic endonasal duraplasty, while Group B received transcranial duraplasty. Recurrence of CSF rhinorrhea, as well as any other complications, was recorded and compared in both groups one week, two weeks, and four weeks after the procedure. There were 82.6% (n=38/46) males and 14.4% (n=8/46) females in group A, and 87% (n=40/46) males and 13% (n=6/46) females in group B. (Figure. 1 & Table. 1). The mean age in Group A was 28.6 (± 9.9 SD) years, while it was 29.9 (± 8.6 SD) years in Group B (Table. 1). In group A, 63% (n=29/46) of the patients were between the ages of 15 and 30, while 37% (n=17/46) were between the ages of 31 and 50. In group B, 52.2% (n=24/46) of the patients were between the ages of 15 and 30, and 47.8% (n=22/46) were between the ages of 31 and 50 (Figure. 2 & Table. 1).

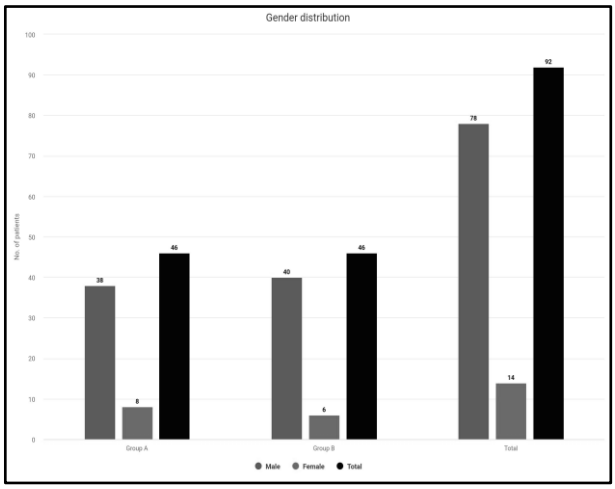

Figure 1. Gender distribution in both the study groups

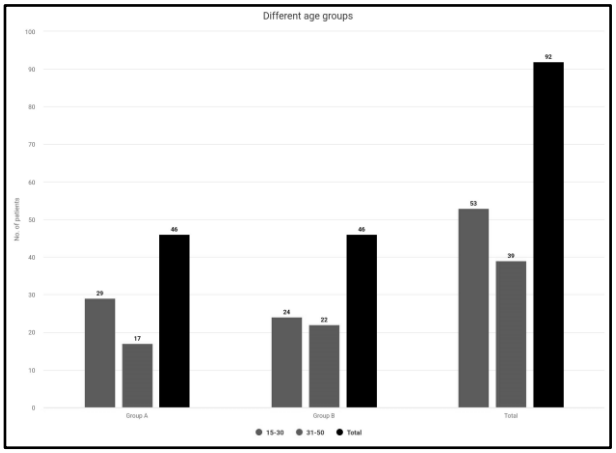

Figure 2. Different age groups in both the study groups

2. Outcomes of therapy:

a. At one week

Recurrence of rhinorrhea was observed in 10.9% (n=5/46) patients in Group A, while it was 19.6% (n=9/46) in Group B patients. Although the recurrence rate was lower in patients who underwent endoscopic repair, yet the difference was not statistically significant (P=0.246) (Table. 2). Overall complications were observed in 6.5% % (n=3/46) patients in Group A, while they were observed in 32.6% (n=15/46) patients in Group B. The complication rate was lower in patients who underwent endoscopic repair and the difference was statistically significant (P=0.006). The most frequent complication was hydrocephalus (4.3%) followed by meningitis (2.2%) in group A, while the most frequent one in group B was anosmia (8.7%) followed by meningitis (6.5%) (Table. 2).

b. At two weeks

Recurrence of rhinorrhea was observed in 13% (n=6/46) patients in Group A, while it was 6.5% (n=3/46) in Group B patients (P=0.292) (Table. 3). Overall complications were observed in 2.2% (n=1/46) patients in Group A, while they were observed in 6.5% (n=3/46) patients in Group B. Although the complication rate was lower in patients who underwent endoscopic repair, yet the difference was not statistically significant (P=0.360). The most frequent complication was meningitis (2.2%) in group A, while in group B it was hydrocephalus (4.3%) and meningitis (2.2%) (Table. 3).

c. At four weeks

Recurrence of rhinorrhea was observed in 0% (n=0/46) patients in Group A, while it was 4.5% (n=4/46) in Group B (P=0.041) (Table. 4). Overall complications were 0% (n=0/46) in Group A, while they were 6.5% (n=3/46) in Group B (P=0.060) (Table. 4). The most frequent complication was abscess (6.5%) in group B at four weeks.

d. Overall recurrence and other complications rate during one-month follow-up

During one month follow-up, recurrence of rhinorrhea was observed in 17.4% (n=8/46) patients in Group A, while it was observed in 41.3% (n=19/46) patients in Group B. The recurrence rate was lower in patients who underwent endoscopic repair and the difference was statistically significant (P=0.012) (Table. 5). During one month of follow-up, complications were observed in 8.7% (n=4/46) patients in Group A, while they were observed in 45.7% (n=21/46) patients in Group B. The complication rate was lower in patients who underwent endoscopic repair and the difference was statistically significant (P=0.001) (Table. 5). Stratification results with reference to gender and age groups for overall recurrence and other complications during one-month follow-up are given in Table. 6 and Table. 7, respectively.

Discussion

CSF leaks can be injurious to brain blood supply and function, as well as increase the risk of direct trauma to the brain parenchyma due to fluid cushion loss. Furthermore, the presence of CSF leak indicates the need for additional evaluation and management to find out the cause. The open communication of the subarachnoid space with CSF leak presents a path for life-threatening central nervous system (CNS) infection, including meningitis. Both intracranial and endoscopic transnasal approaches have been used to treat CSF rhinorrhea with high success rates of 70-100%. When compared to the endoscopic transnasal approach, the morbidity associated with the intracranial approach has been reported to be significantly higher.[8,9,10] We intended to compare the efficacy of endoscopic endonasal dural repair versus transcranial dural repair in this study. A total of 92 adult patients (age 15-50 years, both genders) with a confirmed diagnosis of CSF rhinorrhea after traumatic brain injury were included. The recurrence of CSF rhinorrhea, as well as any other complications, was recorded at one, two, and four weeks after the

procedure and compared between the two groups.

According to published data, the endoscopic endonasal approach results in significantly less recurrence of CSF rhinorrhea. Given the high morbidity rate associated with open craniotomy, such as brain retraction, olfactory nerve injury, anosmia, abscess/wound infection, sepsis, and recurrence, an endonasal endoscopic approach is preferable. Moreover, decreased time of hospital stay, return of functional independence associated with endoscopic endonasal surgery has established itself as the procedure of choice for CSF rhinorrhea repair.[8,9,10] We found similar findings in our study. During one month follow-up, the recurrence (17.4% versus 41.3%, P=0.012) and other complications rate (8.7% versus 45.7%, P=0.001) was significantly lower in patients who underwent endoscopic duraplasty compared to those who underwent transcranial duraplasty. Bhatti SN et al.[9] examined the outcomes of transnasal endoscopic repair for CSF rhinorrhea in a previous study. Twenty-one patients with CSF rhinorrhea who had failed to respond to conservative treatment were included in the study and were operated on transnasally with a rigid endoscope. Over a 9-month follow-up period, the overall success rate was 95% (n=20/21 cases). One patient died as a result of CSF leak and meningitis one month after surgery. The authors concluded that transnasal endoscopic treatment of CSF rhinorrhea was highly effective and safe. Tahir MZ et al.[10] presented 11-year data on the management of CSF rhinorrhea at a tertiary care hospital in Karachi in another study from the local population. The medical records of 43 patients were scrutinised. Eleven of the 43 patients were treated conservatively, 22 had intracranial repairs, and 10 had transnasal endoscopic repairs. They found that the transnasal endoscopic approach has comparable success rates to the intracranial approach while causing significantly less morbidity. Furthermore, a summary of different studies performed in Pakistan regarding the surgical management of CSF rhinorrhea is given in Table. 8. A total of 460 patients including 273 with traumatic cause for CSF rhinorrhoea had been operated on. Endoscopic repair was performed in 223 (49.6%) patients compared to transcranial repair performed in other 232 (50.4%) patients. Recurrence was 7% in the endoscopic cases compared to 7.8% for the transcranial ones. Other complications were 0.44% in the endoscopic cases compared to 20.3% for the transcranial cases.

Christoforidou et al.[11] conducted a prospective study on 18 consecutive patients with CSF leaks who underwent endonasal repair and compared outcomes to a previous cohort of 25 patients who had CSF leaks treated with a craniotomy. The endoscopic group had similar success rates with a significantly lower rate of complications and a shorter length of hospital stay than the craniotomy group. Endoscopic technique was also associated with significantly lower costs and higher patient satisfaction. The authors concluded that an endoscopic approach is the best way to treat CSF leaks in the anterior and middle skull base that are not associated with complex intracranial pathology. However, we did not use cost or patient satisfaction as outcome variables in our study. Komotar RJ et al.[12] assessed the role of endoscopy in the management of CSF rhinorrhea due to traumatic injury in a large systematic review that included 71 studies and 1178 patients. Their combined findings showed that the rate of successful repair was comparable (90%) between the open and endoscopic cohorts. However, when compared to open approaches, the endoscopic group had a significantly lower rate of complications. Meningitis (3.9% versus 1.1%, P=0.034), abscess/wound infection (6.8% versus 0.7%, P=0.001), and sepsis (3.8% versus 0%, P=0.003) were observed as complications.

In summary, the current study's findings and evidence from the literature suggest that an endoscopic endonasal approach is a safe and effective treatment for CSF rhinorrhea caused by traumatic injury. Endoscopic endonasal approach has a success rate comparable to transcranial duraplasty, but with significantly lower recurrence and complication rates. Due to the difficulty of randomization and ethical concerns, there are not many studies comparing the two techniques in the literature. The current study's main strength is its prospective design. There are several limitations to the current study. Firstly, we feel the sample size was relatively smaller yet sufficient to draw the inference. Secondly, the follow-up period (four weeks) was relatively shorter as several studies reported recurrence of CSF rhinorrhea even a year after the surgery. Furthermore, we did not account for other variables such as procedure duration and hospital stay duration in both groups. The other variables that we did not investigate in this study were patient

satisfaction and the overall cost of both procedures. We recommend larger sample size studies with longer follow-up periods. We also propose future studies that take into account other variables such as procedure duration, length of hospital stay, overall cost incurred, and patient satisfaction. Several studies have been conducted using various graft materials for endoscopic repair; we believe this is an area for future research.

Conclusions

During a one-month follow-up, patients who underwent endoscopic repair had a lower recurrence and other complications rate than those who underwent transcranial duraplasty, and the difference was statistically significant. We recommend studies with larger sample sizes and longer follow-up periods. We also propose future studies that take into account other variables such as procedure duration, length of hospital stay, overall cost incurred, and patient satisfaction.

Table. 1. Different parameters in both the study groups

Parameters		Groups		Total
		A	B	
Gender	Male	38 (82.6%)	40 (87%)	78 (84.8%)
	Female	8 (14.4%)	6 (13%)	14 (15.2%)
Total no. of patients		46 (100%)	46 (100%)	92 (100%)
Mean age ± SD (years)		28.6 ± 9.9	29.9 ± 8.6	-
Age groups (years)	15-30	29 (63%)	24 (52.2%)	53 (57.6%)
	31-50	17 (37%)	22 (47.8%)	39 (42.4%)

Table. 2. Recurrence and complications at one week in both the study groups

At one week		Groups		Total	P-value Chi-square
		A	B		
Recurrence	Present	5 (10.9%)	9 (19.6%)	14 (15.2%)	0.246
	Absent	41 (89.1%)	37 (80.4%)	78 (84.8%)	
	Total	46 (100%)	46 (100%)	92 (100%)	
Complications	Meningitis	1 (2.2%)	5 (10.9%)	6 (6.5%)	0.006
	Anosmia	0 (0%)	8 (17.4%)	8 (8.7%)	
	Hydrocephalus	2 (4.3%)	2 (4.3%)	4 (4.4%)	
	None	43 (93.5%)	31 (67.4%)	74 (80.4%)	
	Total	46 (100%)	46 (100%)	92 (100%)	

Table. 3. Recurrence and complications at two weeks in both the study groups

At two weeks		Groups		Total	P-value Chi-square
		A	B		
Recurrence	Present	3 (6.5%)	6 (13%)	9 (9.8%)	0.292
	Absent	43 (93.5)	40 (87%)	83 (90.2%)	
	Total	46 (100%)	46 (100%)	92 (100%)	
Complications	Meningitis	1 (2.2%)	1 (2.2%)	2 (2.2%)	0.360
	Hydrocephalus	0 (0%)	2 (4.3%)	2 (2.2%)	
	None	45 (97.8%)	43 (93.5%)	88 (95.6%)	
	Total	46 (100%)	46 (100%)	92 (100%)	

Table. 4. Recurrence and complications at four weeks in both the study groups

At four weeks		Groups		Total	P-value Chi-square
		A	B		
Recurrence	Present	0 (0%)	4 (8.7%)	4 (4.3%)	0.041
	Absent	46 (100%)	42 (91.3%)	88 (95.7%)	
	Total	46 (100%)	46 (100%)	92 (100%)	
Complications	Abscess	0 (0%)	3 (6.5%)	3 (3.3%)	0.06
	None	46 (100%)	43 (93.5%)	89 (96.7%)	
	Total	46 (100%)	46 (100%)	92 (100%)	

Table. 5. Overall recurrence and complications during one month follow-up

During one month follow-up		Groups		Total	P-value Chi-square
		A	B		
Overall recurrence	Present	8 (17.4%)	19 (41.3%)	27 (29.3%)	0.012
	Absent	38 (82.6%)	27 (58.7%)	65 (70.7%)	
	Total	46 (100%)	46 (100%)	92 (100%)	
Overall complications	Present	4 (8.7%)	21 (45.7%)	25 (27.2%)	0.001
	Absent	42 (91.3%)	25 (54.3%)	67 (72.8%)	
	Total	46 (100%)	46 (100%)	92 (100%)	

Table. 6. Overall recurrence rate during one month follow-up (stratification with reference to gender and age groups)

Variables	Overall recurrence during one month follow-up	Groups		Total	P-value Chi-square
		A	B		
Male	Present	6 (15.8%)	15 (37.5%)	21 (26.9%)	0.031
	Absent	32 (84.2%)	25 (62.5%)	57 (73.1%)	
Female	Present	2 (25%)	4 (66.7%)	6 (42.9%)	0.119
	Absent	6 (75%)	2 (33.3%)	8 (57.1%)	
15-30 years	Present	5 (17.2%)	9 (37.5%)	14 (26.4%)	0.096
	Absent	24 (82.8%)	15 (62.5%)	39 (73.6%)	
31-50 years	Present	3 (17.6%)	10 (45.5%)	13 (33.3%)	0.041
	Absent	14 (82.4%)	12 (54.5%)	26 (66.7%)	

Table. 7. Overall complication rate during one month follow-up (stratification with reference to gender and age groups)

Variables	Overall complications during one month follow-up	Groups		Total	P-value Chi-square
		A	B		
Male	Present	4 (10.5%)	21 (52.5%)	25 (32.1%)	0.001
	Absent	34 (89.5%)	19 (47.5%)	53 (67.9)	
Female	Present	0 (0%)	0 (0%)	0 (0%)	1.0
	Absent	8 (100%)	6 (100%)	14 (100%)	
15-30 years	Present	3 (10.3%)	11 (45.8%)	14 (26.4%)	0.004
	Absent	26 (89.7%)	13 (54.2%)	39 (73.6%)	
31-50 years	Present	1 (5.9%)	10 (45.5%)	11 (28.2%)	0.006
	Absent	16 (94.1%)	12 (54.5%)	28 (71.8%)	

Table. 8. Summary of different studies performed in Pakistan regarding surgical management of CSF rhinorrhea

S. no.	Authors	Year	Total no. of patients	Trauma	Endoscopic duraplasty A	Transcranial duraplasty B	Recurrence		Complications	
							A	B	A	B
1	Amin MU and Ghaffar A[13]	2006	1	1	-	1	-	0	-	0

2	**Bhatti SN et al.**[9]	2011	21	16	21	-	2	-	0	-
3	**Tahir MZ et al.**[10]	2011	32	11	10	22	3	3	NA	NA
4	**Farooq MU and Ansar MA**[14]	2011	23	17	23	-	1	-	0	-
5	**Akhter S et al.**[15]	2012	5	1	5	-	0	-	0	-
6	**Aurangzeb A et al.**[16]	2012	27	23	-	27	-	1	-	5
7	**Khaleeq S et al.**[17]	2015	48	48	-	48	-	5	-	10
8	**Sheikh F et al.**[18]	2015	20	4	20	-	2	-	0	-
9	**Amir S et al.**[19]	2017	30	30	-	30	-	3	-	10
10	**Rahman ZU and Khan MM**[20]	2018	60	60	-	60	-	6	-	20
11	**Abbas T et al.**[21]	2019	40	27	40	-	4	-	0	-
12	**Satti SA et al.**[22]	2021	14	14	-	14	NA	NA	NA	NA
13	**Saleem S et al.**[23]	2021	27	11	27	-	2	-	0	-
14	**Mahmood K et al.**[24]	2021	62	NA	62	-	NA	-	NA	-
15	**Simair IA et al.**[25]	2021	40	NA	20	20	2	0	1	1
16	**Samija S et al.**[26]	2022	10	10	-	10	-	NA	-	1
Total			460	273	228 (49.6%)	232 (50.4%)	16 (7.0%)	18 (7.8%)	1 (0.44%)	47 (20.3%)

*NA: not available

List of Abbreviations
CSF: Cerebrospinal fluid
DNS: Deviated nasal septum
CT: Computed Tomography
MRI: Magnetic Resonance Imaging
WHO: World Health Organization
SPSS: Statistical Package for Social Sciences

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Combined endoscopic-microscopic trans-nasal trans-sphenoidal approach for pituitary adenomas. An institutional experience

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ABSTRACT

Objective. To obtain evidence that the use of endoscopy along with a microscope in the surgical management of pituitary tumours improves intraoperative visualization and significantly impacts operative outcomes in the trans-nasal approach.

Material and methods. Each patient underwent endonasal transsphenoidal microscopic tumour resection. The procedure was modified by the use of intrasellar endoscopy as an adjunctive imaging modality. Following complete microscopic resection of tumour, rigid 0° and 30° 4.0-mm endoscopes were used to conduct a final survey of the sellar and parasellar spaces. Residual tumour fragments identified during this endoscopic examination were removed.

Results. In 50 patients with pituitary macroadenomas, the rigid 30 ° angled rigid endoscope was found to be highly beneficial. Hidden areas could be visualized and tumour residues were detected. In the majority of the patients with detected tumour residues, adenomatous remnants were safely removed by meticulous endoscopic dissection under optimum visual control after the main part of the tumour had been removed with the operating microscope.

Conclusions. Endoscopy provides distinct advantages over microscopy in imaging intrasellar and parasellar structures during pituitary tumour resection which are often missed by microscopy alone.

Keywords
pituitary macroadenomas, micro-endoscopy, trans-nasal surgery, endoscopy

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INTRODUCTION

Since Sir Victor Horsley[1] performed the first surgery for pituitary tumor, different approaches have been described for it. The transnasal-trans-sphenoidal route by Schloffer [2] and Cushing[3] sublabial trans-septal route had been widely used. This surgery was further improved with the introduction of the microscope by Hardy[4] and the use of endoscope in management the first time for such lesions, by Jankowski[5]. With the evolution in the technology of endoscope, it's use has become much more frequent[6].

The endoscopic transsphenoidal approach requires different surgical skills from those needed for microsurgery. Surgeons need to handle surgical instruments in a relatively narrow working space with a two−dimensional view. Added to this, an unfamiliarity of neurosurgeons with sino-nasal surgery is also an obstacle to widespread use of the endoscopic transsphenoidal approach for pituitary lesions. In this study we have applied microscopic endonasal septal pushover technique described by Griffith and Veerapen[7]. Since this approach consists of relatively simple surgical procedures, access to the sphenoid sinus is quick and causes minimum disruption of normal tissue in the nasal cavity. We, later convert this microsurgical technique into endoscopic method by using a rigid endoscope after reaching the sellar floor. In this study, we describe our experience using this technique in 50 patients.

PATIENTS AND METHODS

This is a retrospective review of case records of patients who had undergone endonasal transsphenoidal surgery for pituitary tumors from January 2018 to December 2021. A total of 50 patients with pituitary tumors underwent endoscope-assisted endonasal trans-sphenoidal microsurgery in our institute. All patients underwent a complete endocrinological, neurological, neuro-ophthalmological and neuro-radiological work-up prior to surgery.

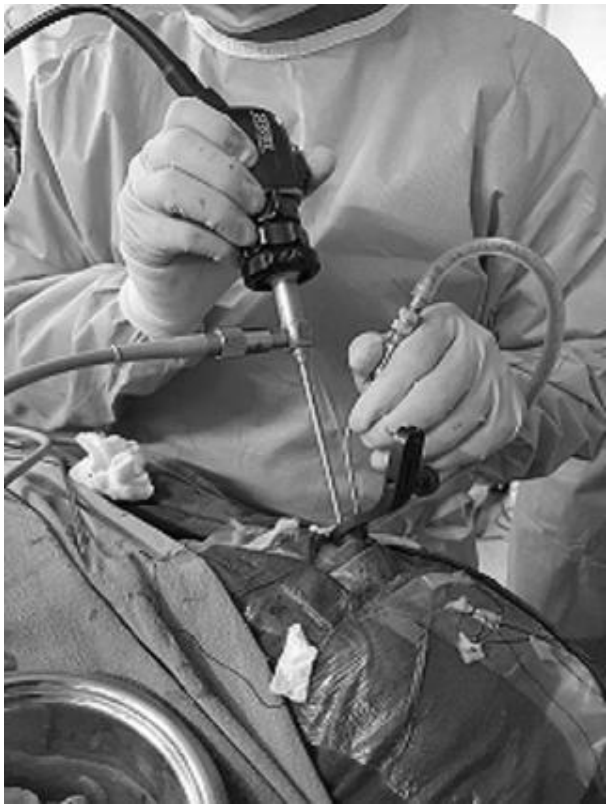

Figure 1. (A & B) show intra-op use of microscope and endoscope during resection of pituitary adenoma.

OPERATIVE TECHNIQUE

Our endonasal trans-sphenoidal surgery for pituitary tumors is performed using combined microscope and endoscope in order to exploit the advantages of each modality. Primarily, we perform the surgeries with an operating microscope. The endoscope is used in later stage to inspect and excise the residual tumor.

The surgical procedure is performed under general endotracheal anesthesia with the patient supine. The oropharyngeal cavity is packed with 3-in moist gauze. The head is cradled in a horseshoe head-holder and tilted toward the surgeon. A navigation system is used for providing intraoperative guidance in the sphenoid sinus and the sella turcica. The lateral side of the thigh is prepared to harvest fat and fascia graft. The procedure in the nasal cavity is primarily performed with a microscope, and later assisted by an endoscope to observe lateral anatomy including carotid prominences, especially in the sphenoid sinus with complicated structure.

A nasal speculum is used to inspect the nasal cavity and identify the middle turbinate. An incision

is made in the nasal septum just opposite to the middle turbinate at the junction of the bony and cartilaginous nasal septum. The mucosa of the intact contralateral nasal cavity is also elevated off the septum laterally. The nasal mucosa is elevated to expose the sphenoid sinus ostia bilaterally, in order to achieve the classical an "Owl's eye" view. A Hardy nasal speculum is placed to achieve a wider surgical field. The perpendicular plate of the vomer is fractured with the blade of the Hardy speculum and dislocated toward the contralateral side. Then, the keel bone of the vomer and the sphenoid rostrum are exposed, which are the distinct landmarks of the midline. It is essential to have the midline orientated to the sella at this point of the surgery. Neuronavigation is used as for assessing the real time location of the surgical exposure. The anterior wall of the sphenoid sinus is removed with alligator forceps and Kerrison rongeurs. The intra-sinus septa are also removed and the floor of the sella turcica is exposed and removed subsequently. The dura is coagulated and incised in a cruciate manner. A high-speed drill is sometimes used on the thick bone or incomplete pneumatization of the sphenoid sinus and the sellar floor to achieve adequate exposure.

The sella is entered and the tumor is debulked using curettes, forceps, and suction. During or after removal of the tumor, an endoscope is used to inspect the tumor cavity, especially in the blind spot of the microscope. The residual tumor is often extirpated under an endoscope (2.7 mm and 4 mm in diameter with viewing angles of 0 and 30 degrees, Olympus, Tokyo, Japan). At the end of surgery, the tumor bed is packed with Surgicel (Ethicon, Somerville, NJ, USA) and fibrin glue. In case of relatively significant cerebrospinal fluid (CSF) leakage, a fascia lata and fat graft harvested from the patient's thigh is also packed with fibrin glue. The speculum is withdrawn and the residual nasal septum and nasal mucosa is returned to the midline. Nasal packing done to prevent formation of the posterior synechiae.

Table 1. Summary of pituitary adenoma

Tumor Characteristics	No. of Patients
Sellar Only	20
Microadenoma	10
Suprasellar Extension	30
Parasellar Extension	12
Non-Secretory Tumor	30
Secretory Tumor	11

Table 2. Post-complications of procedure

Complications	No. of Patients	Treatment
CSF Leak	4	Thigh fat graft placement
Diabetes Insipidus ***Temporary*** ***Permanent***	 8 2	 Temporary Use of Desmopressin Desmopressin
Worsening of Anterior Pituitary Function	6	Hormone replacement
Asymptomatic Synechia of Nasal Mucosa	2	None
Chronic Sphenoidal Sinusitis	3	5- Day oral antibiotic course
Meningitis	2	Injectable antibiotic

OBSERVATIONS

From a total of 50 pituitary adenomas, 11 (22%) were hormonally active, while 39(78%) were non-functioning. Mean follow-up period was 9 months. The average length of hospital stay was 4 days. The most common indications for longer hospitalization included temporary diabetes insipidus and prior co-morbid conditions which required extended monitoring or rehabilitation. All patients had postoperative MRI/CT studies to assess residual or recurrent disease; all patients with hormonally active tumors had additional postoperative hormonal studies. Remission, being defined as no hormonal or radiological evidence of recurrence within the time-frame of the follow-up. Remission was demonstrated in 45/50 (90%) of adenomas. There were 26 males (52%) and 24 females (48%). The age ranged from 18 years to 56 years, with a mean of 26.4 years. Other than hormonal symptoms, the most common presenting complaints includes visual symptoms, changes in visual acuity or visual field deficits (44) (88%) headache (38) (76%) menstrual cycle disturbance or impotence (18) (36%), and acromegalic features (6) (12%). Forty patients had

macroadenoma (80%) and 10 had microadenomas (20%). Thirty patients out of 40 macroadenoma had suprasellar extensions (60%). Only 10 patients (20%) had lumbar drain inserted prior to commencement of the surgery and the majority of these were macroadenomas.

All cases were performed under general anesthesia. Postoperatively all of our patients who underwent this procedure, recovered well with normal and unobstructed nasal airways. Postoperative pain was reported to be minimal and the patients often did not require analgesic medication beyond second day post-operatively. Because of the potential occurrence of diabetes insipidus, every patient was kept in the hospital at least 3 days. Among the 50 endonasal procedures performed, 37 operations were completed with the patients needing to stay 4 days in the hospital. Thirteen procedures were accomplished with the patients requiring a 7 days hospitalization.

The mean follow-up duration for these patients was 9 months. The common complications encountered were diabetes insipidus (8) (16%), cerebrospinal fluid leak (4) (8%), meningitis (2) (4%), epistaxis (2), septal perforation or synechia (2) (4%), and anterior pituitary insufficiency (6) (12%). Mean operative time was 90 min.

Our study reveals that Hybrid transsphenoidal approach is a safe and effective method of management of pituitary adenomas. Patient outcomes were determined from post-operative assessment of tumor resection, postoperative hormonal levels. MR imaging studies were performed for all patients during the early postoperative period, to be repeated after 6–12 months and then annually for the rest of their follow-up period. This combined Microscopic and endoscopic transnasal technique demonstrated remission (being defined as no hormonal or radiological evidence of recurrence within the time-frame of follow-up) in 40/50 (80%) patients. Five of the patients demonstrating recurrent tumor had a mass ranging from 5 to 8 mm on an MRI scan performed postoperatively, 6 of them underwent revision surgery and 3 of them having recurrence located in the cavernous sinus were referred for radiosurgery. There was no mortality in our series.

Discussion

The surgery for pituitary tumors has evolved significantly in the past few decades from trans-cranial approach to Microscopic trans-nasal approach and then to Endoscopic Trans-nasal approach. Gerard Guiot[8] popularized the use of endoscope in the trans-sphenoidal approach. Apuzzo et al.[9] used an endoscope as an adjunct in the microscopic resection of pituitary lesions with extrasellar extension. Axel Perneczky[10] has been credited to describe the micro-anatomy not apparent with the microscope, by endoscope, and introduced the concept of minimally-invasive neurosurgery.

Both, microscope and endoscope have some advantages and disadvantages. The microscope offers a single, unobstructed and continuous three-dimensional field of vision where depth perception is more accurate. However, field of view is relatively narrow as compared to that of endoscope. Most of the Neurosurgeons are familiar and more comfortable with microscope.

On the other hand, endoscope provides panoramic view with better illumination. Angled scope can enhance vision and provide better view at lateral part of tumors and cavernous sinus which helps surgeons to work more efficiently. However, field of view in endoscope is two dimensional and often obstructed by surgical debris and since nasal speculum is not used, maneuvering in nasal cavity is difficult.

In this study we have expressed our experience of combined use of microscope and endoscope where surgery is started with microscope and endoscope is used to excise the residual tumor which is not accessible with microscope.

In present study, we found that residual tumor after microscopic excision could be easily identified with endoscope. Similar findings have also been reported in separate studies of endoscope assisted microscopic surgery, in which after microscopic tumor resection endoscope was introduced into the Sella to look for the residual tumour.[11] In this series, an average of 40% of patients were found to have after microscopic resection and were discovered and resected during the endoscopic surveys. Thus, microscope alone was successful only in 60% of cases for complete tumor removal[12].

In our hybrid technique the surgical procedure is started with microscope. Here, an incision is made at nasal septum mucosa at the junction of bony and cartilaginous part, opposite to middle turbinate and

this junction is fractured. The septal mucosa on opposite side is dissected off the bony septum to expose the keel of vomer. A Hardy nasal speculum is then inserted for adequate retraction and proper visualization of both sphenoid ostia as classical Owl's eye appearance. It also provides an appropriate surgical corridor through which surgical instruments can be taken in and out without hindrance.

Our experience with 50 patients, operated through hybrid technique, shows that it is accurate, convenient and time efficient approach for complete resection of sellar tumours. In majority of the cases, sellar floor was reached within 10-15 minutes of starting the procedure. The most crucial step is to reach sphenoid ostium for which most of the neurosurgeons are unaccustomed, especially during early stage of their practice. In purely endoscopic technique, nasal speculum is not used to achieve sphenoidotomy and thus it needs several other surgical steps to achieve adequate corridor to reach sphenoid ostia. Maneuvering endoscope in nasal cavity is often cumbersome due to limited space, especially for those who are naïve in endoscopic surgery. In microscopy the approach to sphenoid ostia is direct and most of the Sino nasal procedures performed in endoscopy are omitted.

A potential advantage of the purely endoscopic approach over the microscopic direct endonasal approach remains to be discussed since these two techniques adopt the same surgical route to the sella. It is accepted that the microscopic direct endonasal approach has the advantage of a simpler and less time consuming sphenoidotomy with fewer postoperative rhinological complications[13]. The microscopic approach also has the drawback in that it does not provides access to the lateral margins of the sellar cavity and the surgical trajectory is deviated from the midline[14]. Surgical microscopes also need the retraction of superficial structures (i.e., the nostrils), which otherwise hinder the entry of the light beam.

The nasal speculum used in the microscopic approach has a wider opening of its blade which can cause excessive stretch force on the nostril, and at time needs a relaxing alar incision. This incision was reported in a 20% of the patients by was Zada et al.[15] in his study of 100 patients. In contrast, endoscopes can provide a more panoramic view without any need of such incision. In our series of 50 patients, we needed alar release incision in only 5 cases that is less than 10% of patients.

Our technique exploits a more simplistic and familiar approach to Pituitary tumors with added advantage of endoscopic visualization of the residual tumor in the lateral part of the sella as well as those trapped in the arachnoid folds. Despite a limited number of cases, the present study also suggests that this simplified hybrid technique is a safe and time efficient technique where judicious use of microscope and endoscope can reduce the operative time and post-op rhinological complication with comparable surgical outcome.

Conclusions

We consider that the endoscope, which allows visualization of areas not seen with the operating microscope, should be used actively in conjunction with the operating microscope that provides three-dimensional visualization and is timesaving. Our surgical method for pituitary tumors provides good results with minimal invasion, by exploiting the advantages of a microscope and an endoscope at the same time.

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Spontaneous complete resolution of a giant cavernous carotid aneurysm in the setting of ipsilateral ICA occlusion

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Keywords
cavernous carotid aneurysm, internal carotid artery, spontaneous resolution

ABSTRACT

Background. Cavernous carotid aneurysms (CCA) are rare aneurysms with a relatively benign natural history. The association between CCA aneurysm and ipsilateral Internal carotid artery (ICA) thrombosis or occlusion has not been described previously. The management of patients with these dual lesions is a challenging problem.

Case description. In this report, we describe an 18-year-old man who presented with left abducent nerve palsy of 3 weeks duration, and imaging revealed left CCA with left ICA occlusion. The patient was managed conservatively with clinical and imaging follow-up. The patient recovered well with complete resolution of clinical symptoms and disappearance of left CCA.

Conclusions. The association of giant CCA and ICA occlusion on the same side is a rare phenomenon with no current consensus on the appropriate follow-up and management strategy. In this report, we described the first case of spontaneous complete disappearance of a giant CCA in the setting of ipsilateral ICA occlusion with complete resolution of symptoms at nine months of follow-up.

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INTRODUCTION

Cavernous carotid aneurysms (CCA) are rare with a relatively benign natural history and a lower risk of morbidity and mortality compared to size-matched equivalent aneurysms at other locations [6]. When CCAs are asymptomatic or have mild tolerable symptoms, then conservative treatment can be justified with long-term clinic-radiological follow-up. Other forms of presentations may require a multidisciplinary team of neuroendovascular and micro-neurosurgeons with catheter-based therapy as the treatment of choice [10].

Although partial thrombosis of intracranial aneurysms is reported in

large and giant aneurysms, a complete thrombosis is a rare phenomenon [2]. An interesting association is reported between large CCA thrombosis and parent vessel occlusion with many suggested theories [2]. With extreme rarity, a decrease in the size of the thrombosed aneurysm represents a regression in the hemodynamic pressure and indicates a better prognosis [3]. Here we describe the first report on the spontaneous total disappearance of a giant CCA in the setting of ipsilateral internal carotid artery (ICA) occlusion with complete resolution of symptoms.

Case scenario

An 18-year-old male patient presented to us with left abducent nerve palsy and recurrent attacks of a severe headache of nonspecific localization and character. Apart from the palsy, the patient was neurologically intact and had no remarkable medical history. Brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) at presentation showed a giant (28mm x 24mm x 21mm) left cavernous ICA aneurysm with mass effect on the left temporal lobe with a striking shadow of the thrombosed aneurysm and absence of the left ICA proximal to the clinoidal segment on MRA (Figure 1 A-D). The patient couldn't afford the catheter angiography at that time.

We opted to treat him conservatively with regular clinico-radiological follow-up. A 3-month follow-up MRI showed a reduction in the size of the aneurysm, loss of flow void signal intensity, and his symptoms improved. At the 9-month follow-up, the patient was neurologically intact and did not experience headaches over the last three months. His brain MRI and MRA cerebral revealed a complete resolution of the cavernous aneurysm, no mass effect on the temporal lobe with the disappearance of the aneurysmal shadow, and the absence of the left ICA on MRA (**Figure 1 E-H)**. A 9-month follow-up digital subtraction angiography (DSA) showed complete occlusion of the left ICA just distal to its origin with sufficient collateral circulation from the right ICA. No aneurysmal filling was detected (**Figure 2**). The patient remained asymptomatic at the last follow-up. No further investigations were planned, and annual clinical assessment follow-up visits were scheduled.

Discussion

CCAs are rare and constitute approximately 2-9% of all intracranial aneurysms [5]. They are predominantly asymptomatic, are discovered incidentally, and have a benign natural history with a low risk of rupture and complications. However, they may become symptomatic due to mass effects from an enlarged aneurysmal mass [6,14]. It is known that CCAs rarely cause rupture and subarachnoid hemorrhage (SAH) since the cavernous sinus is composed of thick double-dural membranes, which lay over the sphenoid body [16]. The optimal management strategy for CCA aneurysms remains controversial. Since CCAs are known to have a low propensity for a life-threatening sequela, conservative management with serial follow-up imaging seems to be a reasonable strategy. However, there are several compelling reasons to treat this entity, including a rupture with the formation of carotid-cavernous fistula, an increase in the size of the aneurysm on follow-up imaging, progressively worsening headache, and erosions of the sphenoid sinus. These signs and symptoms should be analyzed by a multidisciplinary team (neuro-endovascular and microsurgical) to choose the optimal treatment plan [1,6,14].

Aneurysms arising from the circle of Willis are likely to cause spontaneous SAH leading to a devastating neurological condition. On rare occasions, these aneurysms may undergo spontaneous thrombosis causing symptoms related to a local mass effect and or distal thromboembolism of the parent artery. Complete thrombosis of aneurysms occurs at a lower incidence in comparison to partial thrombosis (13-20% vs. 60%); generally, it tends to occur in large (>15mm) and giant (>25mm) aneurysms [2].

The association of ipsilateral ICA occlusion with giant CCA is rare, with only 18 reported cases in the literature [1]. Theories addressing the coexistence of these two pathologies and their progression is a matter of contentious debate due to a limited number of reported cases and the variability in the characteristics, progression, and management strategies. One explanation is that the large thrombosed CCA tends to compress on the ICA against the anterior clinoid process and causes stenosis of the parent artery [8,15]. Other proposed theories include direct stretch and compression of the parent artery by the giant aneurysm and proximal propagation of an intramural thrombus [12]. On the other hand, thrombosis of the parent artery can be initially formed in association with giant

CCA due to the presence of tough dural folds, bony structures along with the natural bend of the artery at this location, which facilitate parent artery deformity, blood flow stasis and eventually thrombosis. The resultant decreased flow into the aneurysm leads to intra-aneurysmal clot formation [2].

In our case, the treatment decision was challenging because the patient was young and had an acute presentation with abducent palsy of 3 weeks duration. However, the absence of ICA ipsilateral to the giant CCA led us to choose conservative management with regular follow-up imaging in the absence of a defined management strategy for these lesions. Then the patient did well with complete resolution of symptoms at nine months follow-up.

Table 1. Characteristics and follow-up of patients with CCA aneurysm and ipsilateral ICA occlusion that were treated conservatively

Authors	**Age-Year/ Sex**	**Side**	**Clinical presentation**	**Imaging at presentation (MRI and DSA)**	**Imaging at F/U (MRI and DSA)**	**Clinical outcome**	**Treatment**
Gautier, 1986. (14)	65/F	left	CN III, IV, VI palsies	**CCA:** (23mm) Thrombosed **ICA:** occluded	-	Opthalmo paresis persisted	The patient refused treatment
Sato et al. 1990 (15)	49/M	left	Headache, CN III, VI, V1 palsies	**CCA:** (3cm) partial thrombosed (MRI flow void) **ICA:** occluded	-	improved	
Kurokawa et al. 2001. (10)	50/F	Right	Headache, CN III, VI, and V1 palsies.	**CCA:** (25 mm) not thrombosed. **ICA:** Intact.	**CCA:** has heterogenous thrombus on MRI but has no flow in DSA. **ICA:** Occlusion of petrous segment. (Time from diagnosis: 2 years).	Only CN III palsy resolved.	The patient refused treatment.
Tsutsumi al., et 2002 (11)	74/M	right	Cavernous sinus syndrome	**CCA:** complete thrombosis (no flow on DSA) **ICA:** occluded	-	NA	
Dehdashti et al. 2003 (4)	31/F	Right	Headache, CN III, and VI palsies.	**CCA:** (30 mm) has heterogenous thrombus on MRI but has no flow in DSA. **ICA:** Intact.	**CCA:** partial resolution (aneurysm decrease in size). **ICA:** Occlusion at the origin. (Time from diagnosis: 18 months).	Neurologically intact.	The patient refused treatment.
Perrini al., et 2005(16)	47/M	Right	Headache, CN V1, V2 palsies.	**CCA:** (28mm), complete thrombosis **ICA**: mild stenosis	**ICA:** Occlusion at the origin. (Time from diagnosis: 6 weeks	CN V palsy persist headache and diplopia resolved	Treated conservatively with anti-platelet
Vasconcellos al., et 2009 (7)	47/F	Right	Headache, CN III, IV, V1, V2, VI palsies.	**- CCA:** giant	**ICA:** Occlusion (Time from diagnosis: 6 months)	CN V palsy persist headache and diplopia resolved	

	44/F	Left	Headache, CN III, IV, VI, V 1, V2 palsies.	**CCA**: giant	**ICA:** Occlusion (Time from diagnosis: 6 months)	CN VI palsy persist headache and diplopia resolved	
	65/F	Right	Headache, CN III, IV, VI, V1 palsies.	**CCA:** giant, partial thrombosis **ICA:** partial occlusion	**ICA**: Occlusion (Time from diagnosis: 5 years)	CN palsies persist , headache and diplopia resolved	
	84/F	Left	Headache, CN III, IV, VI, V 1, V2 palsies.	**CCA**: giant, partial thrombosis (heterogenous thrombus on MRI but has no flow in DSA). **ICA**: Occlusion at the origin.	-	CN III, VI palsies persist, CN IV, V partially improved, headache and diplopia resolved	
Sastri al. et 2013 (9)	65/F	Left	CN III, IV, VI, V 1, V2 palsies.	**CCA**: giant, partial thrombosis. **ICA**: Occlusion at the origin.	-	Ophalmo paresis improved, CN V persist	Treated conservativ ely on aspirin
	55/F	Left	Seizure, decrease vision, CN III, IV, VI, V1, V2 palsies.	**CCA:** (28mm) partial thrombosis **ICA**: Occlusion at the origin.	-	Ophalmo paresis improved, Decrease d Vision persist	Treated conservativ ely on aspirin
Das al.,et 2018(3)	45/M	Left	Headache, transient unconsciou sness	**CCA**: (23mm) partial thrombosis **ICA**: Occlusion at the origin.	-	Neurologi cally intact	Treated conservativ ely on aspirin
Present cases 2022	18/M	Left	Headache, CN VI palsy.	**CCA:** (28 mm) has heterogenous thrombus on MRI but has no flow in DSA. **ICA:** Occlusion.	**CCA:** complete resolution (no aneurysm detected). **ICA:** Occlusion at the origin. (Time from diagnosis: 9 months).	Neurologi cally intact.	Treated conservativ ely on aspirin

Shaded rows represent the patients with complete follow-up imaging.
ICA - Internal carotid artery, DSA - Digital subtraction angiogram, MRI - Magnetic resonance imaging, CCA - Cavernous carotid aneurysm.

In our case, a total of fourteen patients with concurrent ICA occlusion and CCAs have been treated conservatively, highlighting the natural history of this unusual association [2, 3, 4, 8, 16, 11 - 13, 15] (Table 1). Unfortunately, follow-up imaging was reported only in 7 patients, and, more specifically, concurrent follow-up MRI and DSA were available only in 3. Hence, only these 3 cases can be used to assess the actual progression of this disease with a high degree of certainty (Table 1-shaded rows) [3,8].

Lawton et al. proposed a new classification of thrombotic aneurysms based on anatomic relationships between the aneurysm, thrombus, and

lumen [9]. They defined the completely thrombosed aneurysm as one with the classic signals of thrombus on the brain, Computed tomography (CT) scan/MRI, and the DSA showing no filling of the lumen [9]. Of the abovementioned three cases, two cases had a complete thrombosis at presentation, and they end with varying degrees of aneurysmal regression on follow-up [3]. The other patient had a non-thrombosed aneurysm at the initial imaging, which progressed to complete thrombosis at the 2-year follow-up [8]. The association between the CCA-ICA occlusion, degree of thrombosis, and outcome cannot be inferred due to the limited number of cases and limited follow-up.

The timeline for the occurrence of the two pathologies (i.e., CCA and ICA occlusion) and which one is present at the presentation, and which one progress with the patient's symptoms is to be answered. For the fourteen cases that have been treated conservatively, eight patients had complete occlusion of the ICA at the presentation. The other six patients have either intact ICA at the initial investigation (2/14) or partially stenosed ICA at the presentation (2/14), with the initial occlusion status of the remaining two patients not mentioned. All the six cases of initially not occluded ICA end with complete occlusion but with variable duration and extension of occlusion. Those cases with delayed occlusion of ICA in the association of ipsilateral CCA (6/14) had a reported time for the occlusion to occur to be from 6 weeks to 5 years with a mean of 18.9 months. The location of the occlusion is at the origin of the ICA from the common carotid artery, with only one patient having a localized occlusion of the petrous and cavernous ICA [2, 3, 4, 8, 16, 11 -13, 15] (Table 1). Obviously, the limited number of cases produces this heterogenicity in the reported findings, and future studies are recommended to continue recruiting more patients and equally important that the patients should have a full radiological follow-up. This will have a profound impact on understanding this unique association, its related pathophysiology, and, most importantly, how to optimize treatment and prevention.

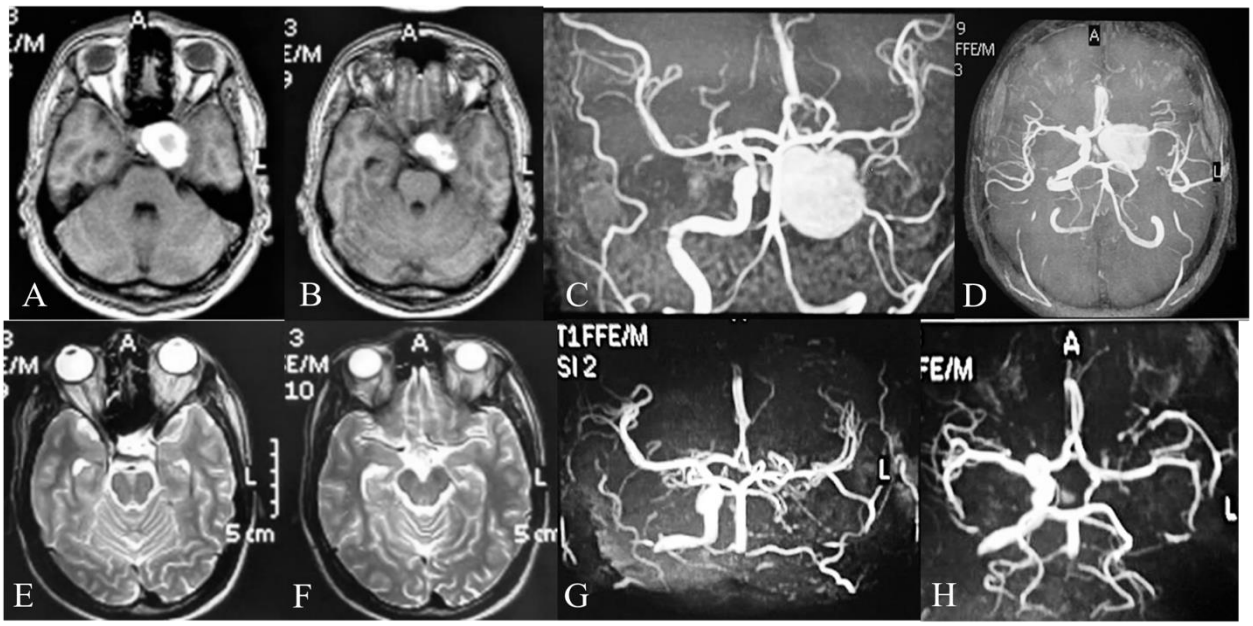

Figure 1. Brain MRI and MRA At presentation (A-D) showed a giant Left cavernous ICA aneurysm with mass effect on the left temporal lobe (A, B) with a striking shadow of the thrombosed aneurysm and absence of the left ICA proximal to the clinoidal segment in MRA (C, D). At 9-month follow-up (E-H) there is complete resolution of the aneurysm, no mass effect on the temporal lobe (E, F) with the disappearance of the aneurysmal shadow, and the same absence of the left ICA MRA (G, H).

CONCLUSION

The association of giant CCA and ICA occlusion on the same side is a rare phenomenon with no current consensus on the appropriate follow-up and management strategy. In this report, we described the first case of spontaneous complete disappearance of a giant CCA in the setting of ipsilateral ICA occlusion with complete resolution of symptoms at nine months of follow-up.

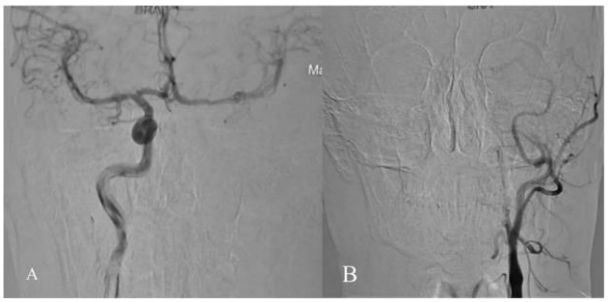

Figure 2. A 9-month follow-up DSA showed complete occlusion of the left ICA just distal to its origin with sufficient collateral circulation from the right ICA. No aneurysmal filling was detected in both (A) and (B).

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Mature cystic teratoma of spinal cord in an adult. A rare tumour

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ABSTRACT

Aim: Reporting a rare case of mature cystic teratoma of spinal cord in an adult

Background: Teratomas of the central nervous system are rare lesions accounting for less than 0.5-2% of all CNS tumors. Most of these are found in pediatric age group and favor sellar - suprasellar, pineal and sacro-coccygeal regions. Their occurrence in spinal cord in an adult is incredibly rare.

Case presentation: A 22-year-old male presented with low back ache and weakness of both lower limbs. Clinical examination and radiological workup revealed presence of a cystic lesion causing diffuse enlargement of the cord from L1 to L5-S1. Histo-pathological examination of the excised lesion revealed it to be teratoma.

Conclusion and clinical significance: Mature teratoma of the spinal cord in adults is extremely rare occurrence. However, this diagnosis should be kept in mind when evaluating a cystic lesion of cord even in adults. Maximal safe resection of the lesion results in prolonged deficit free survival.

Keywords
spinal teratoma.
adult teratoma,
cauda equina,
conus medullaris

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BACKGROUND

Teratomas of the central nervous system are rare lesions. Barring the sacro-coccygeal region, their occurrence in spinal cord is a rarity. They constitute only 0.5% of intraspinal tumors.

CASE PRESENTATION:

A 22-year-old male had presented with complaints of weakness of both lower limb in the last three months. He had difficulty in clearing the feet off the ground. This was associated with altered sensation in the left leg in a below knee distribution where he was not able to feel the temperature of water properly when bathing. He had a history of low back ache on and off for 4 years which was relieved by rest and analgesics. There were no 'red flags' till his presentation with weakness. He denied any history of trauma, lumbar puncture, bowel or bladder incontinence or fever. He was not forthcoming about his sexual history probably due to cultural reasons.

On examination, his vitals were normal, and the local examination of spine did not reveal any stigmata of spinal dysraphism. There was no

deformity. The power in both ankle dorsiflexors and great toe extensors was 3/5. It was largely unaffected in all other muscle groups. Sensory examination revealed almost complete loss to touch, pain, and temperature in left L4 to S1 distribution and by about 25-30% in S2 to S4 distribution. Bilateral knee and ankle jerks were absent, and planters were mute. MRI imaging revealed a large irregular intradural lesion of spine extending from L2 to L5-S1 junction which was hypointense on T1 and hyper intense on T2 with irregular enhancement on contrast (Fig. 1)

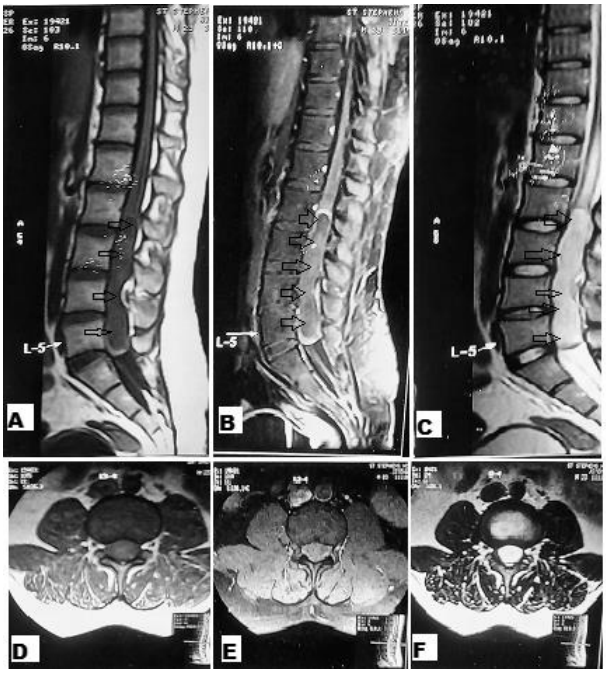

Figure 1. Preoperative MRI shows the lesion extending from upper border of L2 vertebra to lower border of L5.It has typical cystic appearance , hypo intense on T1 (A & D) with enhancement of walls on contrast (B & E). The contents are hyperintense on T2 (C & F) along with a syrinx in the cord. The lesion itself is pointed with hollow arrows.

The patient underwent L1-L5 laminectomy. On dural opening, a thick-walled lesion was found adherent to the conus and cauda roots. On opening the cavity, greenish pus-like fluid was drained. The wall was dissected piecemeal, and a small residual was left over one of the roots. The intraoperative picture was indicative of an epidermoid cyst. Histopathogical picture showed presence of all three germ cell layer derivatives indicative of a mature teratoma. Post operative period was complicated by presence of CSF leak which abated after removal of drain , pressure dressing and keeping the patient in prone position for 3 days. Before discharge on 10th day, the patient's motor status had improved to 4/5 in both ankle dorsiflexors and great toe extensors. He had a residual sensory loss of about 50% in left L5 and S1 distribution. He has been followed up for last seven years and he has recovered a power of 5/5 in all muscle groups with minimal sensory loss in left S1 distribution. Follow up MRI showed presence of a residual lesion at the tip of conus which was mildly hyperintense on T1 with no contrast enhancement and hypointense on STIR (Fig2). This is consistent with fatty tissue which may have been the small fragment that was left attached to one of the roots intraoperatively.

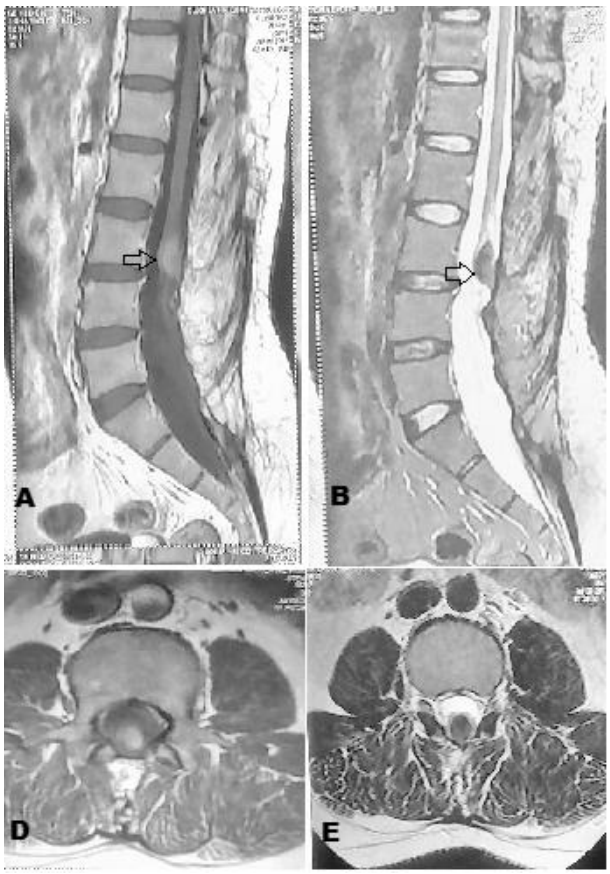

Figure 2. MRI image at eight years follow up shows residual lesion (marked with hollow arrows) opposite the lower half of L3 vertebra which is hyperintense on T1(A&D) and hypointense on STIR (B & E) indicating fatty tissue. There is no evidence of syrinx.

Discussion

The spinal tumors are classified according to their location. The IDEM lesions constitute about 55% of all spinal tumors. The most common IDEM tumors in

adults are nerve sheath tumors and meningioma [1]. Virchow reported the first spinal teratoma. This occurs more frequently in children with spinal dysraphism and is associated with various malformations like spina bifida, tethered cord, and split cord malformations of various types [2-7]. Sloof et al in their series of 1322 patients of spinal cord tumors, identified only 2 patients with teratoma [8]. Al-Sarraj et al had seven cases with a histological diagnosis of teratoma in a series of 25,000 cases over a period of 15 years [9]. Thus, spinal cord teratomas are in general very rare. Moreover, they occur far less frequently in adults.

Spinal teratoma in adults can have variable presentation and in general have a set of presenting symptoms like other IDEM lesions. However, there is a significant alteration in frequency of these symptoms compared to IDEMs in general. Usually, there is nothing in presentation that points specifically to the diagnosis. In our case, the patient presented with syndrome suggestive of a conus-cauda lesion. Poeze et reviewed 31 cases of intramedullary teratomas and found motor dysfunction to be the most common presentation (71%), followed by changes in reflexes, sensory changes, urinary changes, and pain [6]. Far less common were sexual disturbances and anal sphincter disturbances. On the other hand, a prospective study in 107 patients of IDEM tumors by Tarantino et al found pain to be the most common presentation followed by sensory deficits. The motor deficits at presentation were distant third (12%) [10].

Specific diagnosis of teratomas on imaging is difficult. They, in general have a picture like other IDEM tumors. On MRI, they appear lobulated or cystic, with variable signal intensity and enhancement consistent with the different solid and cystic components of the tumor [11, 12]. CT imaging is nonspecific and reveals differences in densities within the tumor consistent with different tissue types [13]. The role of imaging is more for preoperative planning and the decision regarding location of the tumor in relation to the cord rather than a definitive diagnosis.

Ultimately, the diagnosis of teratoma rests on histopathological demonstration of all the three germ layers in the specimen. Currently there are two proposed theories for the origin of spinal teratoma, the misplaced germ cell theory and the dysembryogenic theory [14, 15]. Regardless of the origin, the prognosis of teratoma is dictated by the classification into mature, immature, and malignant. The mature ones have an overall benign course once resected. However, the malignant teratoma as the name suggests, have an aggressive and stormy course with poor prognosis. The primary mode of treatment is surgical resection, and the goal is decompression of the neural tissue without causing further deficits. However, complete resection is a realizable goal in about 50% of cases and should always be attempted with patient safety in mind [16]. However, many authors suggest not attempting a complete resection citing the logic that these are slow growing tumors affording a large window period for picking up a recurrence and that the rate of recurrence with partial and complete resection is very similar (11% vs 9%) [17,18].

The overall prognosis for mature teratoma of spine is good following surgical resection with most patients reporting either improvement or stabilization of symptoms. However, most case reports [3, 6] have a short follow up. The patient in our case was followed up for approximately 8 years and showed improvement of all symptoms except mild sensory abnormality in left S1 dermatome. The rarity of these lesions in adults makes it difficult to design a long-term study of disease progression. Currently, there is no evidence supporting any role for chemotherapy or radiotherapy for mature teratoma following resection [19].

CONCLUSION AND CLINICAL SIGNIFICANCE

Spinal mature teratomas in adults are very rare. The clinical presentation is like any other IDEM tumor or conus-cauda lesion. Imaging modalities also do not offer any specific distinguishing features from other similar lesions in the region. However, this differential diagnosis must always be considered when evaluating a radiological picture of cystic lesion of the spinal cord. The treatment rests on maximal safe surgical resection with an attempt for complete resection. These patients are likely to have a prolonged near deficit free course even in the long term.

List of Abbreviations

MRI: Magnetic resonance Imaging
T1WI: T2 Weighted image
T2WI:T1 Weighted image
IDEM: Intradural extramedullary

CT: Computer tomography
CSF: Cerebrospinal Fluid
STIR: Short tau inversion recovery

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Incomplete Currarino triad in an adult woman. A case report

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ABSTRACT

Introduction: Currarino Syndrome (CS) is a rare entity characterized by a triad of sacral agenesis, anorectal malformations, and pre-sacral masses. CS is typically diagnosed during the first decade of life.

Case Description: We present a rare case of incomplete Currarino syndrome manifesting in a 36-year-old lady who presented with back pain, urinary retention, anal paresthesia, and lower limb weakness. The patient underwent multiple laminectomies and partial resection of an epidermoid cyst and regained function.

Conclusion: Although rare, the possibility of Currarino syndrome should be entertained in adult patients with lower lumbosacral symptoms and a pre-sacral mass. A thorough physical examination and strategic pre-operative planning are mandatory to maximize patient outcomes.

Keywords
Currarino syndrome, sacral agenesis, epidermoid cyst

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INTRODUCTION

Currarino syndrome is a rare entity with a set of complex congenital anomalies. It manifests clinically as a triad of sacral bony defects, anorectal malformations, and pre-sacral masses, such as anterior meningocele (1,2). This condition is usually diagnosed during the first decade of life and diagnosis in adults is rare (3,4). Both sporadic and inherited cases have been reported, with an estimated incidence of 1 in 100,000 of the population (5,6). Here, we report a rare case of an incomplete Currarino syndrome (sacral agenesis, epidermoid cyst with no anorectal malformations) manifesting in adulthood.

CASE DESCRIPTION

A 36-year-old female presented with a two-week history of lower back pain, urinary retention, and anal numbness. She had no history of trauma. Her examination was significant for sacral anesthesia and weakness in ankle plantar and dorsiflexion -Medical Research Council (MRC) scale 4/5 -. Magnetic resonance imaging (MRI) of the lumbosacral

spine and pelvis revealed sacral agenesis and an intradural cystic lesion extending from the level of the second lumbar vertebrae (L2) to the sacrum with an anterior meningocele (Figure 1).

Multiple laminectomies (from L2 to sacrum) were performed through the posterior approach. . The cystic lesion was identified and durotomy revealed a soft white pearly lesion suggestive of epidermoid tumor which was partially resected as it wrapped most nerve roots with an adherent surrounding capsule. The histopathological analysis revealed flakes of keratinous materials with strips of unremarkable squamous epithelium consistent with epidermoid cyst (Figure 2).

The patient had an uneventful recovery and was discharged on a course of steroids and referred to a bladder training program. On her one-month follow-up, her bladder function was back to normal as were her lower limb power and peri-anal sensation. The MRI showed a decrease in the size of the epidermoid cysts and anterior meningocele (Figure 3).

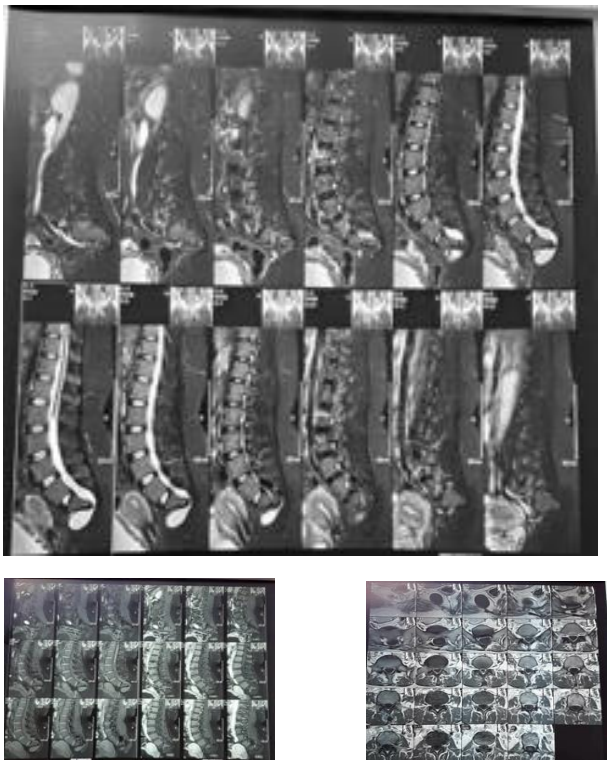

Figure 1. A, B MRI sagittal view of the lumbosacral spine T1 and T2 showing an intradural mass hypointense in T1 and hyperintense in T2 extending from L2 to the sacrum and turning anteriorly to the. Partial agenesis of the sacrum is also evident. C: MRI axial view showing cystic cavity in the sacral spine extending anteriorly in the pelvis through a widened sacral foramen.

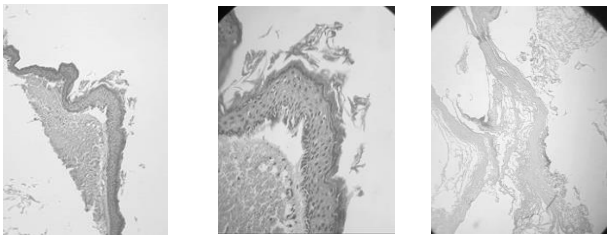

Figure 2. Pictures of histopathology showing flakes of keratinous materials with strips of unremarkable squamous epithelium consistent with epidermoid cyst.

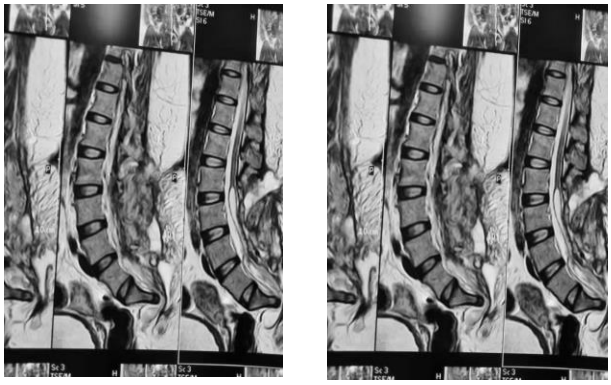

Figure 3. Post-operative MRI T1 and T2 sagittal view showing operative site from L2 to the sacrum and decrease in the size of the intradural lesion and the anterior meningocele.

Discussion

Sacral agenesis is a congenital deformity that ranges from partial agenesis of the unilateral sacrum to complete bilateral sacral agenesis (7-9). In a normal pregnancy, the incidence of sacral agenesis is between 0.005 and 0.1%. However, 16-20% of sacral agenesis patients have diabetic mothers. Sacral agenesis is associated with an increased incidence of spinal dysraphism, and currarino triad. (10)

Spinal meningocele is a posterior protrusion of meningeal elements out of the spinal canal, usually seen in the lumbosacral region. An anterior sacral meningocele is a meningeal protrusion into the presacral, retroperitoneal, and intraperitoneal space as a consequence of partial anterior sacral agenesis (11). Anterior sacral meningoceles may occur anteriorly through a defect in the body of sacrum or anterolaterally through an enlarged intervertebral foramen or coalesced foramina as in our case (12) Such improper development can result from other coexisting abnormalities in the skin, subcutaneous tissues, spine, and internal organs. Anterior sacral meningocele occurs sporadically, but familial cases have been reported in literature as part of the Currarino triad. (13)

The most common presacral masses are teratomas and anterior sacral meningocele, while dermoid tumors, lipomas, pelvic hamartomas, leiomyosarcoma, and carcinoid tumors have all been documented in literature but are very uncommon. Our case had an epidermoid cyst which is exceptionally uncommon, with a frequency of 4% among patients with Curarrino triad in adulthood. (14)

Currarino traid is rare in adults and should be diagnosed early to prevent life-threatening complications, such as meningitis, rectal fistulas, and malignant transformation. Approximately, 80% of the patients with the classic triad are recognized during the first decade of life. (15) Urinary symptoms and chronic constipation are amongst the most common manifestations of Currarino triad (16) Other clinical presentations include gynecological anomalies, spinal cord tethering, perianal sepsis, and meningitis (17).

Sacral bony defects are pathognomonic for this triad. Pelvic X-ray is the initial imaging modality of choice (18). On MRI, epidermoid cysts appear as a well-defined cystic mass generally with no perilesional edema (19). MRI can also define the extension of presacral mass and may detect other malformations. Prenatal ultrasound and fetal MRI could be used to identify the presence of a presacral mass during in-utero and is indicated when a history of maternal Currarino triad is present. (20)

The variable set of complex anomalies associated with Curranio mandates a multi-disciplinary management approach. Surgical management involves correction of the anorectal malformations before attending to any existing pre-sacral masses (18,21) . The anterior sacral meningocele is surgically managed through the posterior sagittal approach to provide full perineum exposure by incision from the sacrum to the anus. In our case, the trans-dural pathway was accessed by sacral laminectomy, which permits the excision of the intradural epidermoid cyst (18,21). Given the high level of morbidity and mortality associated with this condition, timely diagnosis and precise pre-operative planning are paramount to maximize patient outcomes (22).

Conclusion

Although rare, the possibility of Currarino syndrome should be entertained in adult patients with lower lumbosacral symptoms and a pre-sacral mass. A thorough physical examination and strategic pre-operative planning are mandatory to maximize patient outcomes.

Abbreviations:
CS: Currarino Syndrome;
MRC: Medical Research Council;
MRI: Magnetic resonance imaging;
L2: second lumbar vertebrae.

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The curious case of commitment to religion and prayer in extreme long term survival anaplastic astrocytoma patient

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ABSTRACT

Anaplastic astrocytoma WHO (World Health Organization) grade 3 represents about 7% of all primary brain tumours in the adult population. The standard treatment protocol involves safe surgical resection, chemotherapy and radiotherapy. Advances in therapeutic protocols have been noted over the past few decades, but the prognoses are still poor with a median survival of 31 months.

We present a case of a male patient who is alive 25 years after the initial diagnosis and treatment of anaplastic astrocytoma WHO grade 3. The patient was operated and reoperated two times due to local tumour recurrence in the first two years after the initial diagnosis. After the last operation, the patient abandoned medical therapy and started praying. The patient is still alive without any clinical or radiological signs of tumour recurrence.

Keywords
anaplastic astrocytoma,
long-term survival,
prayer,
religion

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INTRODUCTION

Anaplastic astrocytoma WHO (World Health Organization) grade 3 represents about 7% of all primary brain tumors in adults. The standard protocol for its treatment involves safe surgical resection, chemotherapy and radiotherapy. Advances in therapeutic protocols have been noted over the past few decades, but the prognoses are still poor [1]. Median survival is 31 months, and relative 5-year survival is about 23.6% and 10-year survival is only about 15.1% [2, 3]. However, it has been observed in clinical practice that some patients live longer than expected.

We present a case report of a patient who is alive even 25 years after the initial diagnosis and treatment of anaplastic astrocytoma WHO grade 3, without any symptoms. and neurological deficits.

CASE REPORT

We present a case of a mail patient who was examined for the first time in our institution when he was 23 years old. Patient present with

epileptic seizure and headache, in early spring 1998. After a few seizures, brain computer tomography (CT) was performed and it showed infiltrative expansive lesion in the right temporal lobe and basal ganglia (Figure 1). Patients had left homonymous hemianopsia. After standard preoperative preparation, the patient was operated on in 1998, and maximal tumor reduction was achieved. The histopathological finding showed anaplastic astrocytoma WHO grade III (Figure 2). A few weeks after the operation he was on chemotherapy with Lomustine (CCNU), 200 mg/m2, and radiotherapy with 60 Gy in 30 fractions, which was well tolerated. Patient had excellent recovery.

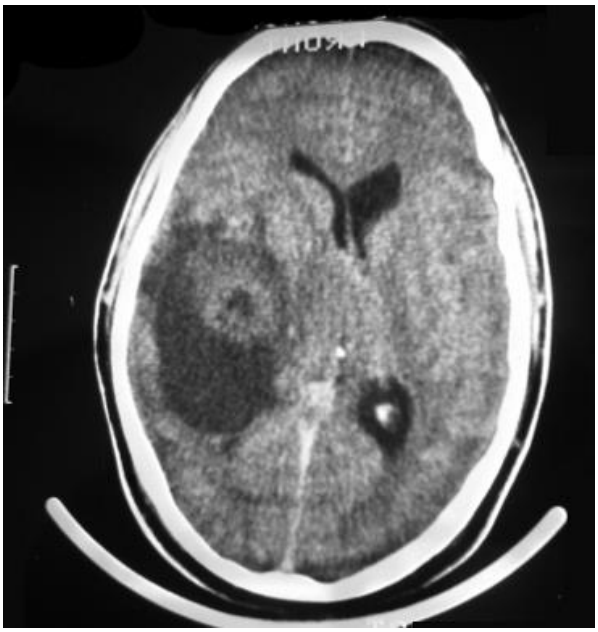

Figure 1. Initial brain computed tomography (CT) performed right before first operation in 1998 showing expansive lesion of the right temporal lobe with perifocal edema.

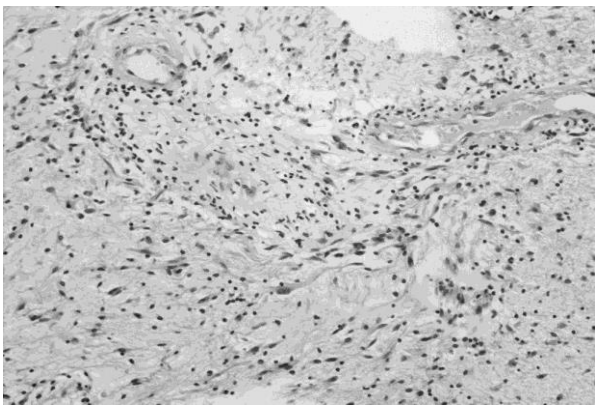

Figure 2. Histopathological finding of anaplastic astrocytoma WHO grade 3 (after first operation).

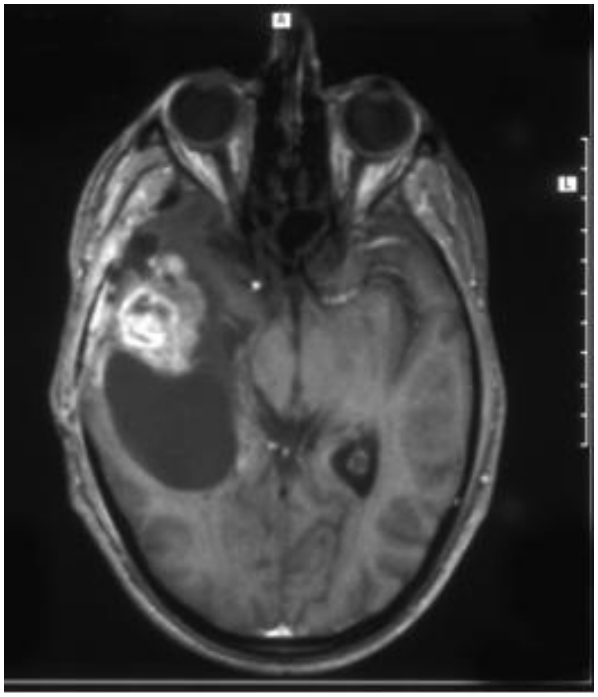

Figure 3. Magnetic resonance imaging (MRI) before third and last operation in 1999 showing tumor recurrence.

However, five months after the first operation, patient was reoperated due tumor recurrence with a significant compressive effect and clinical and radiological signs of the brain herniation. After this operation, the patient was in good condition for another 5 months, after which he was again hospitalized because of the exacerbation of epileptic seizures with poor seizure control. The magnetic resonance imaging (MRI) was immediately performed, and showed a tumor recurrence in the frontal part of the right temporal lobe with significant perifocal edema (figure 3). Patient was reoperated once again with maximal tumor reduction. The histopathological finding again showed anaplastic astrocytoma WHO grade 3 without signs of further malignant progression. The oncologist prescribed Carmustine (BCNU), 100 mg/m2, but patient rejected any further therapy. His neurological status improved significantly, with only residual left sided homonymous upper quadrant-anopsia at hospital discharge. Instead of any other therapy, the patient turned to prayer, and agreed only to further clinical controls. During the next few months, the patient only had occasional headaches, and control MRI in 1999 indicated small residual tumor with 1 cm in diameter. Next year, the control MRI showed a stationary finding without tumor progression.

Patient was symptom free, without epileptic seizures. Patient also abandoned antiepileptic therapy, and continued only praying. He went to a monastery and soon became an Orthodox Christian monk within the Serbian Orthodox Church.

In 2014, i.e. 14 years after the last control, patient visited our hospital due to symptoms of sciatica, and brain and spine MRI was performed, and there were no signs of tumor presence (figure 4). Spine MRI showed degenerative changes without significant duroradicular compression, so the patient received conservative treatment, which led to a complete resolution of symptoms, and after a year, the patient was without any complaints, with completely normal neurological finding.

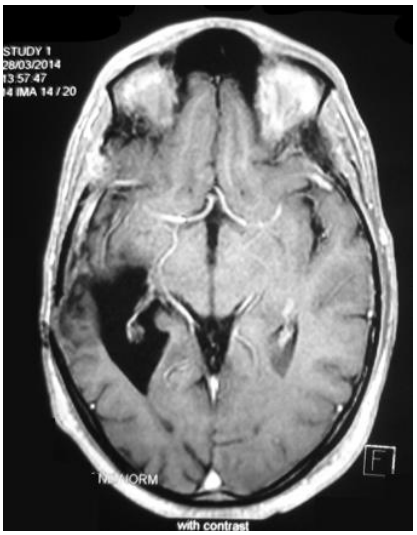

Figure 4. Control magnetic resonance imaging (MRI) from 2014 without signs of tumor presence.

Today, almost 25 years after the initial treatment, the patient lives at the Chilandar Monastery on the Mount Athos in Greece (figure 5A). He spends about 8 hours per day in a prayer, and every day he drinks two drops of oil from a cresset placed in front of the Icon of Virgin Mary (Greek: Panagia Tricherousa, meaning "Three-handed Theotokos"), one of the most revered icons of the Serbian Orthodox Church (figure 5B).

Figure 4. Picture A is showing the Chilandar Monastery on the Mount Athos in Greece. **Picture B** is showing the icon of Virgin Mary. Pictures are downloaded from the open-access internet.

Discussion

Our patient's survival period after the treatment of anaplastic astrocytoma WHO grade III is significantly longer than the median survival time. Furthermore, he has been living without any symptoms for more than a 2 decades. What makes this case particularly noteworthy is the role of religiousness in the patient's recovery. Patient started praying following the third operation. Subsequently he started practicing prayer for several hours per day. After the initial period of living as a novice in a monastery, he became a Serbian Orthodox Church monk.

Religion, medicine, and healthcare have been interrelated in all population groups since the beginning of history [4, 5]. Over the past 50 years, different studies have found aspects of religiousness to be positively associated with well-being, considered in a nonclinical sense as life satisfaction or happiness. Feelings of optimism and hope have been speculated to be potential mediators of the influence of religiousness on well-being. The positive aspect of religiousness is characterized by "a secure relationship with God, a belief that there is meaning to be found in life, and a sense of spiritual connectedness with others" [6]. Numerous studies discuss the influence of religion and spirituality not only on mental health, but also on health behavior. Besides, there is growing evidence that reducing stress and negative emotions paired with the involvement of religiousness and spirituality should have a favorable impact on a host of physical diseases and on the response of those diseases to treatment [7-9]. Until recently, religiousness and spirituality were set aside in clinical practice. But in the last two decades some of articles on the relationship of religiousness and health have been published in academic literature [10]. It has been shown that religiousness and spirituality are significantly related to positive physiological functions. A positive effect of prayer has been shown on cardiovascular functions in the population with a high risk for cardiovascular disease. It has also been found that those who are more religious have a lower blood pressure [5]. Also, despite the difficulty in defining and measuring spirituality, a growing literature describes its importance in cancer patients and is connectivity with survivorship. Religious beliefs influence patients' decision-making with respect to both aggressive care at the end of life as well as complementary therapies during treatment

[11]. In our case, the patient refused all therapy and turned exclusively to religion, and he grew stronger in his faith, so that today he spends more than 8 hours a day in prayer. Furthermore, given the fact that the intact immune function is critical for health maintenance and disease prevention, including the control of malignant disease, particularly significant are the findings of a positive relationship between religiousness/spirituality and immune functions [12, 13]. High religiousness and spirituality has been related to significantly higher white blood cell count, total lymphocyte count, total T cells, and cytotoxic T cell activity [5]. In light of such findings, we can presume that in the case of our patient his intense prayer, as an aspect of religiousness and spirituality, contributed significantly to maintaining a good condition of his immune functions. Also, to our knowledge, this is the first case of spontaneous regression of anaplastic astrocytoma WHO grade 3 tumor recurrence. Although extremely rare, similar scenarios are described in literature as isolated case reports, such as significant regression of grade IV astrocytoma or glioblastoma multiforme (GBM). In this case authors hypothesized a plausible antineoplastic role of levetiracetam and dexamethasone [14]. Although a similar explanation could be given in our case, since our patient was also treated with similar combination of drugs. However, our patient stopped all his drug therapy, including antiepileptic drugs while the tumor was still radiologically present. Therefore, the clear temporal association between this therapy and the absence of tumor in our patient cannot be fully explained in this way.

Kumar and Koshy described a case of a middle age women with a high-grade glioma of corpus callosum, e.g. a grade 3 anaplastic oligodendroglioma, who was operated and treated with chemotherapy and radiotherapy. The patient presented with tumor recurrence 5 years after the first operation. After another surgery the patient refused radiation therapy, and was given temozolomide and dexamethasone intermittently, with continuation of levetiracetam therapy. MRI performed at 10-month follow-up showed significant remission [15]. Although in this case a significantly longer survival than expected was achieved, a complete remission of the disease was not achieved, and the patient receives therapy all the time, which is assumed to have an antineoplastic effect as well, while in our patient any form of medical therapy is completely ruled out, and most importantly, there are no signs of tumor recurrence, neither clinical nor radiological.

Cancer is usually considered to be the worst of all illnesses and most people equate cancer with death [16]. Numerous studies have examined relationships between religiousness and spirituality and either the onset or the outcome of cancer, including cancer mortality. Most of these studies have found that those who are more engaged in religion, spirituality, and pray have a lower risk of developing cancer or have a better prognosis [5]. For example, one study exploring the influence of religiousness on breast cancer survival has shown an association between the lack of religiousness and poor breast cancer survival among African American women [17]. Another study revealed an association between low levels of religious involvement and the risk of colon cancer [18]. In our case patient's overall health, and especially length of survival is far beyond those expected for the given disease, since he is in good condition, without any signs or symptoms of tumor presence.

However, the most impressive research on the relationship between religiousness/ spirituality and physical health is in the area of mortality. Namely, it has been found that religiousness/spirituality is a predictive factor of greater longevity in 75% of all cases [5]. It has also been shown that prayer is one of the most frequently used forms of complementary and alternative medicine [11]. Prayer can be defined as "the raising up of one's mind to God". Also, prayer may be considered as the conscious act of opening oneself or activating a connection to a higher being. Several types of prayer have been described, including: a) petitioner prayer, which is considered to be some specific request either for oneself or for others; b) colloquial prayer, i.e. a conversational type of prayer in which someone may ask for personal guidance, forgiveness, or general blessings; c) ritual prayer, which includes prayers from books; and d) meditative prayer, which includes reflection upon and adoration of the divine. Specifically, it has been shown that one of the most frequent prayers is disease-centered prayer, which is directly related to patients' illness [11]. Based on the account of our patient, we can observe that his prayer comprises aspects of all the above-mentioned types.

Our patient's case shows that prayer, as an additional way of positive personal attitude to one's illness, could be considered as a possible supplementary suggested method, parallel to conventional medical treatment. Based on this particular case and on the previous studies on the relationship between religiousness/spirituality and health, we can presume that prayer may have positive influence on the overall physical and psychological health state in cases of brain malignancies as well as in other cases of malignant diseases.

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Global neurosurgery: the need of the hour for developing countries

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ABSTRACT
Global neurosurgery is relatively a new sub-discipline of global surgery. It is an area of study, research, practice, and advocacy that focuses on enhancing health outcomes and promoting health equity for all individuals around the world who are afflicted by neurosurgical disorders or require neurosurgical care. Low- and middle-income countries (LMICs) around the world have not benefited from advances in neurosurgery; most have little or no neurosurgical capacity in their entire country. The need of the hour is that a global problem necessitates a global response with a common vision and objectives.

Keywords
global neurosurgery, developing countries, low- and middle-income countries

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INTRODUCTION

Global neurosurgery is relatively a new sub-discipline of global surgery.1 "Global neurosurgery" can be defined as an area of study, research, practice, and advocacy that focuses on enhancing health outcomes and promoting health equity for all individuals around the world who are afflicted by neurosurgical disorders or require neurosurgical care.2 It should be made sure that neurosurgery is completely integrated into the growth of the global surgery movement. Every year, 5 million crucial neurosurgical cases go untreated, all of which are in low- and middle-income countries.3 A sufficient number of medical professionals, facilities, and training programs for neurosurgery are still lacking in the majority of underdeveloped countries. The World Health Organization (WHO) and World Federation of Neurosurgical Societies (WFNS) have had a very positive role in global neurosurgery. Research is an integral part of global neurosurgery and according to studies, despite having a high disease burden, low- and middle-income countries have a poor representation in research publications.2 The need of the hour is that a global problem necessitates a global response with a common vision and objectives.

DISCUSSION

Global neurosurgery is a subset of global surgery that lives in relative obscurity in the context of global health. Despite its recent popularity, global neurosurgery has been around for decades, with amazing work

being done all over the world. Because of the individual and collective efforts of neurosurgeons around the world, modern neurosurgery has become one of the most complex specialties in healthcare. Massive advances in patient care have transformed the field, transforming previously inoperable cases into standard practice. This progress has affected countless lives, but its impact has been disproportionate. Low- and middle-income countries (LMICs) around the world have not benefited from advances in neurosurgery; most have little or no neurosurgical capacity in their entire country.[4]

When it comes to surgical subspecialties such as neurological surgery, access to care ranges from uneven to non-existent in some cases. Many parts of the world, particularly in LMICs, have one neurosurgeon for every 10 million people, making access to neurosurgical care a luxury rather than a right.[2] Research is an essential component of global neurosurgery. It can help to shape policy, support training, and spread new ideas. Furthermore, and particularly in the developing world, research educates the public about disease trends, interventions, outcomes, and potential barriers to quality, safe, accessible, and affordable care. But according to studies, despite having a high disease burden, low- and middle-income countries have a poor representation in research publications.[2] The Global Neurosurgery Committee (GNC) Action Plan aims to advance relevant research, particularly in developing countries.[5,6]

The Lancet Commission on Global Surgery was formed in 2013 with the mission of "developing and assembling the best evidence on the state of surgery worldwide". The following is a summary of their report's findings:

- 5 billion people worldwide do not have access to “safe, affordable surgical, and anesthesia services when needed”.
- 9 out of 10 people in LMICs lack access to basic surgical treatment.
- 18.6 million people die each year due to lack of essential surgical care, more than 3 times the number of deaths due to HIV/AIDS, tuberculosis, and malaria.
- 143 million additional surgical procedures are needed in LMICs each year.
- 2.2 million more surgeons, anesthetists, and obstetricians are needed.
- The cost of addressing this need is estimated at US $350 billion by 2030.
- The cost of not responding to this need will result in losses estimated at US $12.3 trillion over next 15 years.[6]

The first step in addressing the global demand for safe, affordable, and equitable neurosurgical care is to identify current resources and needs. To provide the necessary data, research efforts at both the global and local levels are required. The WFNS GNC is actively involved in studies to determine the global neurosurgical workforce, broken down by country-specific numbers and markers, in order to determine where the greatest need exists and where additional efforts should be directed to address those needs. Knowing the density of neurosurgeons in a country, however, is only the first step; educational programmes are required to train more neurosurgeons. The distribution of training centres around the world is being studied, but the barriers to training access are still being investigated. Once a sufficient number of neurosurgeons have been trained, the issue of limited resources and the need for appropriate neurosurgical equipment that is both suitable and sustainable in various LMICs remains. Programs such as the WFNS Foundation Neurosurgical Equipment Support aim to provide donated equipment to LMIC neurosurgeons who would not otherwise be able to afford it. The GNC is currently analysing the WFNS programme to determine the suitability and sustainability of such equipment in LMIC settings, as well as the effectiveness of such equipment donation programmes.[5]

Role of WHO in Global Neurosurgery

WHO is the United Nations (UN) health technical branch, and its primary functions include:

1. Provide leadership and engaging partnerships
2. Shape the research agenda
3. Develop norms and standards
4. Articulate ethical, evidence-based policy options
5. Provide technical support
6. Monitor and assess health situations and trends.[7]

Most of the world's populations face ongoing challenges in gaining access to safe, timely, and affordable surgical care, as well as financial risk protection. Global neurosurgery, in particular, has a

significant need to increase the neurosurgical workforce, which includes all sub-specialty fields, particularly paediatric neurosurgery. Furthermore, good imaging and other equipment are required to provide an optimal means of providing comprehensive neurosurgical service delivery. Despite ongoing challenges at WHO, persistent underfunding, political wrangling, bureaucracy, and significant criticism, there have been significant successes and positive ongoing efforts to make the world a healthier, better place. There is no other international body or Member State capable of providing coordinated global leadership or commanding such global respect; no other body can bring all 194 Ministers of Health together in an international forum to set global health priorities. Most LMICs rely on WHO at all levels, particularly the Country Office, which is viewed as an essential ally of the local health ministry; WHO remains a vital asset to achieving a healthier world. By working directly with WHO at all levels and optimising WFNS interactions, including the WHO liaison committee, global neurosurgery would do well to consider WHO as an advantageous, strong, and willing partner.[7]

Role of WFNS in Global Neurosurgery

WFNS is the largest neurosurgical organisation, with over 49,000 neurosurgeons from almost every existing neurosurgical society worldwide. It was founded in 1955 to promote neurosurgery camaraderie among neurosurgeons. Several committees play critical roles under the auspices of the WFNS. The Foundation's activities are organised around three pillars:

1. Education
2. Development of network of training centers
3. Provision of neurological equipment to developing countries.[8]

Recommendations and future directions in global neurosurgery

- Expand the accumulation of human resources.
- By increasing capacity at existing training facilities and launching new programmes, more neurosurgeons, nurses, operating room staff, and anaesthetists need to be taught.
- To address the current deficit as soon as feasible, the idea of task-sharing training for non-neurosurgeons in basic and emergency neurosurgery should be investigated.
- Encourage LMICs to conduct research in neurosurgery. For contributions coming from LMICs, removing the financial obstacles to publication should be taken into consideration.
- Encourage innovative ideas that are useful and economical.
- By cultivating personal connections with significant organisations, neurosurgery can become a prominent player in the global surgery community.[2]

More articles on the outcomes of global neurosurgery measures implemented in low-resource countries will aid in the formulation of future strategies. It is a source of pride that neurosurgeons from developed regions have banded together to spread the benefits, love, and joy of neurosurgery to their underserved brothers and sisters. The collaboration and coordination of various societies such as the World Federation of Neurological Surgeons (WFNS), the Asian Congress of Neurological Surgeons (ACNS), the Neurosurgery Outreach Foundation (NOF), and the Foundation for International Education in Neurological Surgery (FIENS) would be a watershed moment in making neurosurgery truly global.[9]

A sufficient number of medical professionals, facilities, and training programmes for neurosurgery are still lacking in the majority of underdeveloped nations. Dedicated neurosurgical beds, beds in intensive care units, and hospitals with the capacity for neurosurgery are all in short supply. Computed tomography, magnetic resonance imaging, and specialist neurosurgery tools are further amenities. Additionally, there are the same issues with neurosurgeons being overrepresented in metropolitan areas as opposed to suburban ones. The main causes of the delayed progress in neurosurgery services in underdeveloped nations have been recognised as poor coordination amongst neurosurgical societies, limited funding, and poor development in neurosurgery education programmes by the governing bodies in those countries. The current measures taken by numerous institutions, organisations, societies, and people, particularly those from high income nations, have led to an increase in the number of qualified neurosurgeons in LMICs. To assure the sustainability of neurosurgery services, self-reliance with

committed education and training should be built in every nation. The ultimate goal of structuring neurosurgery education, human resources, and facilities in all nations around the world should be the equality of access to neurosurgical treatments by all people.[10]

A worldwide solution with a common vision and objectives is necessary for a global problem. The authors call on like-minded neurosurgeons to get together, begin the process of developing consensus within the international neurosurgery community, and work with other stakeholders in the provision of global surgical care.

Conclusion

The world's low- and middle-income countries have not profited from advancements in neurosurgery. The majority of developing countries still struggle with a lack of medical professionals. However, in recent years, the sector has started to coalesce and important initiatives have been taken to create a cohesive voice. Large-scale collaboration through multilateral, multinational participation is the only real answer to the problems we face in global neurosurgery. The future of global neurosurgery looks promising as the key actors have started working together toward this final resolution.

List of Abbreviations

LMIC: Low- and middle-income country
LMICs: Low- and middle-income countries
GNC: Global Neurosurgery Committee
UN: United Nations
WFNS: World Federation of Neurosurgical Societies
WHO: World Health Organization
ACNS: Asian Congress of Neurological Surgeons
NOF: Neurosurgery Outreach Foundation
FIENS: Foundation for International Education in Neurological Surgery

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An insight into artificial intelligence and its role in neurosurgery

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ABSTRACT

To acquire a wide range of technical skills, neurosurgeons undergo extensive and drawn-out training. Additionally, neurosurgery necessitates a significant amount of preoperative, intraoperative, and postoperative clinical data collection, decision-making, care, and recovery. The significance of artificial intelligence in neurosurgery has significantly increased during the past ten years. The potential of artificial intelligence to improve diagnostic and prognostic outcomes in neurosurgery is quite promising. It is important to clinical therapy because it helps neurosurgeons make crucial decisions during surgical interventions to improve patient outcomes and it enhances their abilities to give patients the finest interventional and non-interventional care possible. Furthermore, the acquisition, processing, and storage of clinical and experimental data are all greatly influenced by artificial intelligence. Its application in neurosurgery can lower surgical care expenses and offer top-notch medical treatment to a larger population. This article examines the use of artificial intelligence in preoperative, intraoperative, and postoperative care for both interventional and non-interventional aspects of neurosurgery, including diagnosis, clinical decision-making, surgical operation, prognosis, data collection, and research in the field.

Keywords
artificial intelligence,
machine learning,
deep learning,
neurosurgery

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INTRODUCTION

In the context of medicine, "artificial intelligence" (AI) literally refers to "a robotic doctor" and can be understood as "a machine capable of thinking." Neuroscience is still far from comprehending human intelligence, and AI technology is still far from constructing an "artificial brain." Currently, "artificial intelligence" methods use wholly new technologies to solve very conventional and logistical problems.[1]

The field of neurosurgery is grueling work. Neurosurgeons must have significant training, endurance, physical dexterity, outstanding hand-eye coordination, the ability to make wise decisions, leadership and organisational abilities, compassion, communication skills, and the ability to operate in a team.[2] In 1988, Kwoh and colleagues performed the first robotic brain surgery that was guided by computerised tomography.[3] The gap between people and machines has been closed by recent technological advancements, allowing computers to replicate and even surpass natural human ability to produce so-called "artificial intelligence."[4]

AI technologies may make it possible to quickly and thoroughly analyse the vast amounts of clinical data produced in contemporary healthcare settings at a level that is otherwise not attainable for humans. By pushing the boundaries of clinical diagnosis, clinical decision-making, and prognostication, AI may subsequently improve clinical practice. Moreover, AI may enter the operating theatre and provide more accurate procedures with fewer errors if integrated with surgical robotics and other surgical adjuncts like image guidance. There has been little published about potential drawbacks to increased clinical automation, despite the great hoopla surrounding the imminent medical AI revolution. Both direct and indirect effects could be among them. Directly, flawed, insufficiently taught, or poorly comprehended algorithms may yield false results, which may have a significant effect. A clinical workflow that is increasingly automated may unintentionally worsen the deskilling of human doctors due to over-reliance, inadequate understanding, overconfidence, and a lack of necessary monitoring.[5]

In comparison to people, machines, algorithms, and AI have a higher level of safety since they can work continuously without experiencing physical or mental exhaustion. Additionally, machines are better able to learn and recognise patterns that are not immediately apparent to humans[6], revealing difficult-to-discern linkages[7]. AI can help neurosurgeons by decreasing surgical mistake rates, cutting expenses for prognosis, diagnosis, and treatment, increasing access to high-quality healthcare, and giving patients more control over their own decision-making processes.

Discussion

Artificial intelligence and neurosurgery

The clinical speciality of neurosurgery generates a lot of data due to the routine usage of cutting-edge medical technologies and medical information systems. These elements make the application of AI technology in the field of neurosurgery more likely to succeed. To design an AI-based project in neurosurgery, it is necessary to first analyse the present demand for and implementation of these technologies, as well as to identify research areas that have the potential to benefit from AI.[8]

Neurosurgery could be transformed by AI, machine learning (ML), and deep learning (DL). While ML, a subfield of AI, integrates computer science and statistics to enable computers to discover patterns through direct studying of data via experience, independent of external programming, AI tries to imitate the behaviour of intelligent individuals in computers.[9,10] AI has the potential to increase the precision of neurosurgery diagnosis and treatment, as well as give neurosurgeons fast access to useful and efficient tools for preoperative, intraoperative, and postoperative care. AI is able to identify tiny abnormalities and deformities in clinical data and neuroradiological images that are invisible to human sight. A subtype of machine learning called DL is built on neural networks, which has numerous layers of learning algorithms.[11] By giving recommendations to foster consensus among neurosurgeons on surgical approaches, AI can lower variances in patient outcomes while also improving prognosis and cutting expenses.

Role of AI in preoperative, intraoperative and postoperative phases of neurosurgery

AI can support surgeons in the preoperative stage of neurosurgery by helping to diagnose the condition, choosing patients for the best course of treatment, and guiding patients in making the best choices.[10] AI can improve surgeon performance and lower neurosurgery-related errors during the intraoperative stage of the procedure. AI in postoperative care can forecast outcomes, spot potential issues after surgery, and monitor data for better recovery and aftercare.

Role of AI to push the boundaries of neurosurgical research

AI and artificial neural networks can be helpful tools for understanding how intricate the nervous system is. Over the past ten years, increased data processing capacity and data accumulation have improved AI's performance in surgical research. Combining brain-computer interface (BCI) and AI can enable the creation of future robots and help paralysed individuals regain some of their sensory and movement abilities.[12]

A major drawback of AI-assisted research in neurosurgery is a small sample size when compared to the huge data that machine learning has processed in other fields of science and industry. It is

crucial to follow the guidelines of evidence-based medicine when organising research that makes use of AI technology, since these guidelines ensure the accuracy of the results and, as a result, boost their value for patients.

Challenges associated with use of AI in neurosurgery

Neurosurgical use of AI is not entirely risk-free. When AI is used too heavily in neurosurgery, there may be both direct and indirect harmful effects. At the most basic level, hardware and software issues can result in blunders during surgical procedures as well as incorrect interpretations of clinical data, lab results, and image scans that result in incorrect diagnoses.[5] At the secondary level, a surgeon may become discouraged from gaining the skills necessary to master surgical techniques if they rely too heavily on AI for surgical interventions. It can be dangerous to rely too much on algorithms to diagnose and treat disorders of the neurological system.[4]

The idea that AI will replace professionals in the medical field has been one of the concerns surrounding its adoption. It is crucial to keep in mind that the patient is at the centre of medicine, and the benefit to the patient should be the main factor in determining whether AI can benefit medicine or not. AI shouldn't replace humans, but rather should collaborate with them to complement their abilities and enhance their performance in order to deliver the best care possible.[4]

The cost of using AI in neurosurgery is another issue. The long-term advantages of lessening surgeons' effort, enhancing data management, and decreasing mistake, however, can offset the initial expense of AI training and operation.[4] In order to uphold ethical standards, the introduction of AI in neurosurgery needs to be carefully regulated and monitored.[13] To prepare the next generation of surgeons with cutting-edge technology, AI should be used in medical and surgical training as early as possible even at undergraduate level.[4]

Conclusions

To provide patients with the best results possible, neurosurgery can use AI to its advantage. AI has the potential to improve surgeons' preoperative, intraoperative, and postoperative skill sets in neurosurgery. Humans and machines can collaborate to improve healthcare delivery quality by acquiring, processing, and interpreting images, selecting patients for the most appropriate surgeries, improving intraoperative work, postoperative follow-up, and facilitating access to high-quality healthcare. Future widespread adoption of AI in neurosurgery will necessitate further study, funding, and multidisciplinary cooperation.

List of Abbreviations

AI: Artificial intelligence
ML: Machine learning
DL: Deep learning
BCI: Brain-computer interface

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