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Continuous intracranial pressure monitoring in severe traumatic brain injury in children

**St.M. Iencean^{1,2}, A. Tascu^{3,4}, C.A. Apetrei², C. Gheorghita⁵,
Tsz-Yan Milly Lo⁶, Ian Piper⁷, A.St. Iencean²**

¹ Neurosurgery, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, ROMANIA

² Neurosurgery, "Prof. Dr. N. Oblu" Clinical Emergency Hospital, Iasi, ROMANIA

³ Neurosurgery, "Bagdasar-Arseni" Clinical Emergency Hospital, Bucharest, ROMANIA

⁴ Neurosurgery, "Carol Davila" University of Medicine and Pharmacy, Bucharest, ROMANIA

⁵ Neurosurgery, "Sf. Maria" Children Clinical Emergency Hospital, Iasi, ROMANIA

⁶ University of Edinburgh (Child Life & Health) / Royal Hospital for Sick Children (Paediatric Critical Care Medicine), UK

⁷ BrainIT Group Coordinator, Principal Health Care Scientist, Neuro-Intensive Care Monitoring Research, UK

ABSTRACT

We present the results of the Romanian team for the multi-center grant "Paediatric Brain Monitoring with Information Technology (KidsBrainIT). Using IT Innovations to Improve Childhood Traumatic Brain Injury Intensive Care Management, Outcome, and Patient Safety", acronym KidsBrainIT. Children aged 2 to 16 years who require intensive care management after sustaining traumatic severe brain injury are included in this study in three neurosurgical hospital: "Prof. Dr. N. Oblu" Clinical Emergency Hospital Iasi, "Sf. Maria" Children Clinical Emergency Hospital Iasi and "Bagdasar-Arseni" Clinical Emergency Hospital Bucharest. Continuous real-time intracranial pressure monitoring became a "gold standard" in TBI intensive-care management and ICP-lowering therapy is recommended when ICP is elevated above 20 mmHg or more. Continuous ICP and mean arterial blood pressure (MAP) monitoring allow calculation of cerebral perfusion pressure (CPP) and to establish of an optimal CPP. This study aims to improve the treatments and the outcomes in severe traumatic brain injury in children.

INTRODUCTION

Annually, over 50,000 new cases of cranio-cerebral trauma (TBI) occur in Romania; road accidents are the main cause of cranial traumas, which often cause cognitive, affective and behavioural disorders, with a particular impact on families and society. World Health Organization

Keywords

cerebral perfusion pressure,
traumatic coma,
intracranial pressure,
paediatric brain monitoring,
severe children brain injury



Corresponding author:
A. Tascu

'Carol Davila' University of
Medicine and Pharmacy,
Bucharest, Romania

tascu_alexandru@yahoo.com

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estimated that up to 90% of head injuries that receive treatment are mild, of which moderate and severe injuries represent 10%. In the European Union the yearly aggregate incidence of TBI hospitalizations and fatalities is estimated at 235 per 100,000.

Fortunately, TBI in children is much lower, without being able to make a reliable estimate because of research differences, but partial studies have shown that TBI in children represents about 14% of the total TBI. Also, children have a higher incidence of increased intracranial pressure (ICP) following TBI than adults (80% vs. 50%) and it is a major cause of morbidity and mortality in the paediatric age group.

In this report of the multi-center grant "Paediatric Brain Monitoring with Information Technology (KidsBrainIT). Using IT Innovations to Improve Childhood Traumatic Brain Injury Intensive Care Management, Outcome, and Patient Safety", acronym KidsBrainIT we present the results of our study for almost the past two years.

MATERIAL AND METHODS

Three neurosurgical hospital: "Prof. Dr. N. Oblu" Clinical Emergency Hospital Iasi, "Sf. Maria" Children Clinical Emergency Hospital Iasi and "Bagdasar-Arseni" Clinical Emergency Hospital Bucharest participated in this study that included children aged 2 to 16 years who require intensive care management after sustaining traumatic severe brain injury. A total of 941 children with traumatic brain injury received medical care during 16 months in these three neurosurgical departments, including minor, medium and severe brain traumas. Thirty-one patients needed intensive care and 9 children have been ICP and blood pressure monitored, but only four patients were included in this scientific project. As presented in the previous report in two cases the values of ICP were high and very high and cerebral decompression was performed; unfortunately, the initial clinical condition was extremely severe and evolution was not favourable in these cases. The third and fourth patients monitored showed elevated ICP values up to 28-30 mm Hg and 30 - 40 mm Hg, which were medically treated.



FIGURE 1: Case of children with severe TBI and continuous intracranial pressure monitoring

RESULTS

During 16 months in our three neurosurgical departments there were a total of 941 children with

traumatic brain injury and 31 patients needed intensive care and 9 children have been ICP and blood pressure monitored, but only four patients were included in this scientific project. The scientific report that on the mid-term results of this multi-centre grant presented the three cases: two children

with high and very high values of ICP and cerebral decompression, but not favourable evolution and the case of the third patient monitored with elevated ICP values up to 28-30 mm Hg, medically treated with a favourable evolution. The fourth case had oscillating high ICP values up to 30 - 45 mm Hg, but the extremely severe initial clinical condition has made its evolution not favourable.

DISCUSSION

Our number of 941 cases in 16 months should be interpreted by reference only for two areas in the country: two hospitals in Iasi and one in Bucharest, so it does not cover the entire country. This number of cases of paediatric TBI vary across clinical and epidemiological studies and till now our number of cases with ICP and CPP monitoring are few and a statistical analysis could not be conclusive, but all the cases from the centres included in the grant from the other countries were hoping to have a statistical significance.

Intracranial pressure and cerebral perfusion pressure monitoring are invasive methods but they assured an early detection of increased ICP and disturbance of cerebral perfusion pressure in children with severe TBI. As we have mentioned in another material about this grant, the relationship between ICP elevation and CPP values is known in the adult, but in the paediatric TBI the studies are not conclusive; so "Chambers et al. proposed age stratified critical levels of CPP: in the age groups 2-6, 7-10, and 11-16 years, CPP values of 43 mmHg, 54 mmHg and 58 mmHg, respectively, were associated with normal values of ICP and good outcomes".

Within the partnership between the centres involved in the finalization of this scientific research it has been achieved a distribution of the research work packages/tasks by partner: (1) Kids BrainIT infrastructure development; (2) multi-centre multi-national patient recruitment into the project; (3) data extraction, central data-bank development and implementation; (4) outcome assessment (6 and 12 months); (5) data artefact detection and cleaning; (6) physiological data analyse; (7) novel technology sub-study and (8) MRI outcome sub-study.

Anonymised clinical and physiological data from different centres are uploaded successfully into the data-bank using a secure http data upload service which ensures secured and encrypted transfer of fully anonymised data only. There are 48 patients

recruited successfully into the study to-date in all contributing centres.

An important novel technology sub-study refers to the hybrid diffuse optical technology device, which is available for testing in Barcelona and patients are recruited into this sub-study since Barcelona open for recruitment in May 2018.

In our recruited patients with ICP and CPP monitoring the performed manoeuvres were drug therapy, CSF drainage and decompressive craniectomy in accordance with modern therapeutic guidelines. Treatment used sedatives, analgesics; hyperosmolar therapy as intravenous mannitol and hypertonic saline to control intracranial hypertension; mild hyperventilation; barbiturates, temperature control and prophylactic anti-convulsants. The routine steroid treatment in children with severe TBI is not conclusive; it has to be individualized and rather it is not indicated because the potential harm from infectious complications. Decompressive craniectomy was performed for controlling intracranial hypertension and it was effective at ICP reduction.

CONCLUSIONS

The severe traumatic brain injury in children requires a multidisciplinary approach in each phase of management. The prompt diagnosis during the initial evaluation and then the multimodal monitoring must be followed by the management of intracranial hypertension. Continuous ICP and mean arterial blood pressure (MAP) monitoring allow calculation of cerebral perfusion pressure (CPP) and to establish of an optimal CPP. All of this has its role to minimize the pathophysiological damage to the brain. The goal of this study is to establish the best care for severe TBI children and to ensure a transfer to a wider clinical audience.

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Tailored approach for the resection of planum sphenoidale meningiomas

Oana-Mihaela Punga¹, Cristiana-Elena Moisesescu¹,
D. Iftimie¹, D. Adam^{1,2}

¹ Department of Neurosurgery, "Saint Pantelimon" Clinical
Emergency Hospital, Bucharest, ROMANIA

² "Carol Davila" University of Medicine and Pharmacy, Bucharest,
ROMANIA

ABSTRACT

Background and importance. Planum sphenoidale meningiomas are relatively rare tumours that can grow to a considerable size before determining noticeable symptoms. Modern imaging techniques can detect these tumours of varying size. Surgical resection of planum sphenoidale meningiomas can be performed by adapting the approach to the size of the tumour.

Clinical presentation. A 56-year-old woman presented with a small (2 cm in diameter) planum sphenoidale meningioma that was resected through a frontal craniotomy performed with a 4,5 cm trephine at the level of the frontal sinus. The second case is that of a 55-year-old woman that presented with a large planum sphenoidale meningioma (5,6 cm in the antero-posterior plane and 5,5 cm cranio-caudally) extending to the tuberculum sellae and sellar diaphragm, reaching the anterior wall of the third ventricle. In this case, a bifrontal craniotomy was performed with frontal sinus cranialization and resection of falx cerebri, achieving a Simpson II resection. Both cases presented a favourable postoperative evolution, without any deficits and an excellent cosmetic result.

Conclusion. The approach for tumours of the anterior skull base must be tailored to the size of the tumour. A minimally invasive approach through the frontal sinus should not be avoided in cases with small tumours.

Keywords

minimally invasive approach,
planum sphenoidale
meningiomas



Corresponding author:
Dragos Iftimie

"Saint Pantelimon" Clinical
Emergency Hospital,
Bucharest, Romania

iftimie.dragos@gmail.com

INTRODUCTION

Meningiomas are the most common primary intracranial tumours, arising from arachnoidal cells. They are benign, slow-growing tumours and the cognitive impairment as well as behavioural changes they can induce can easily be mistaken for dementia or depression¹.

Planum sphenoidale meningiomas are relatively rare tumours that originate from the flat surface of the sphenoid bone, anterior to the optic chiasm. They are closely related to tuberculum sellae tumours but with a different clinical presentation. Tuberculum sellae tumours determine early visual deficits even when lesions are small, due to their proximity to the optic chiasm. Therefore, planum sphenoidale meningiomas can grow to a considerable size before determining

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noticeable symptoms².

Modern imaging techniques can detect these tumours of varying size and surgical treatment is still the most commonly used treatment option. Approaches that are used may vary depending upon tumour size and location, adjacent neurovascular structures and surgeon's experience as well as preference³.

CLINICAL PRESENTATIONS

Case 1

A 55-year-old female, known with chronic viral hepatitis C and hypermetropic astigmatism with retinal angiosclerosis, was admitted in our department for headaches that appeared 3 months prior to presentation. The neurological examination was otherwise normal. A contrast MRI examination revealed a 2 cm in diameter intracranial extra-axial tumour at the level of the planum sphenoidale, the radiological aspect suggesting a meningioma (FIGURE 1).

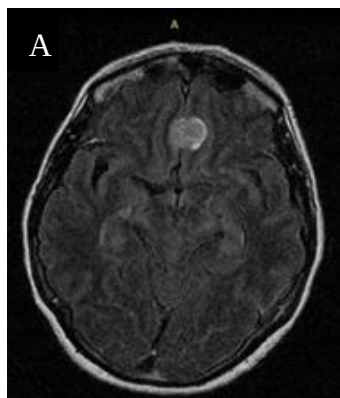
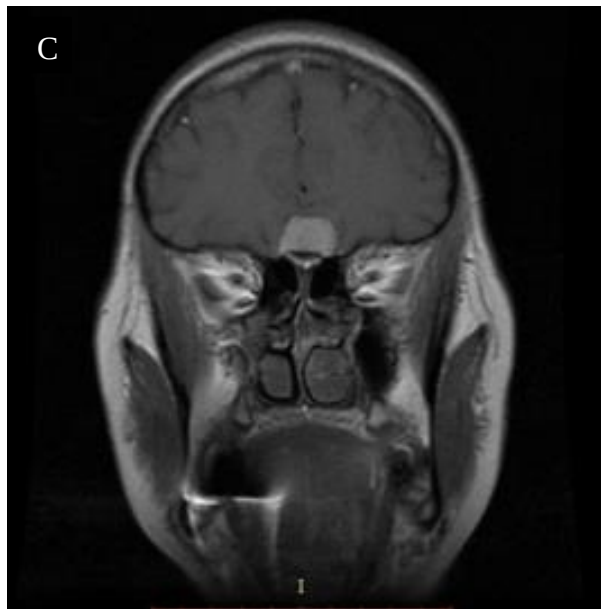
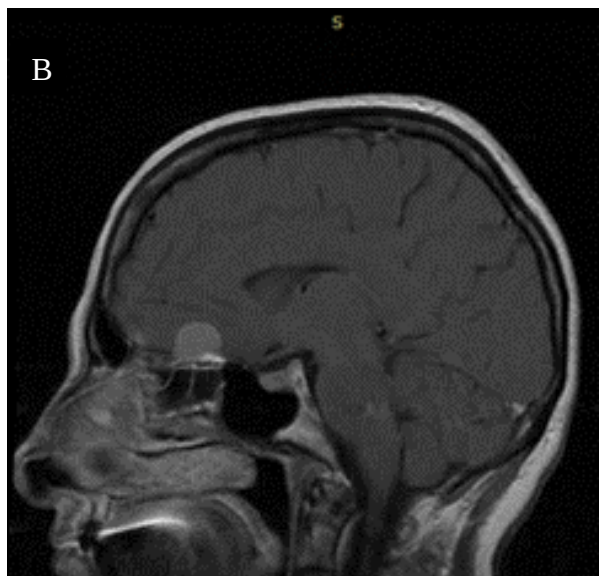


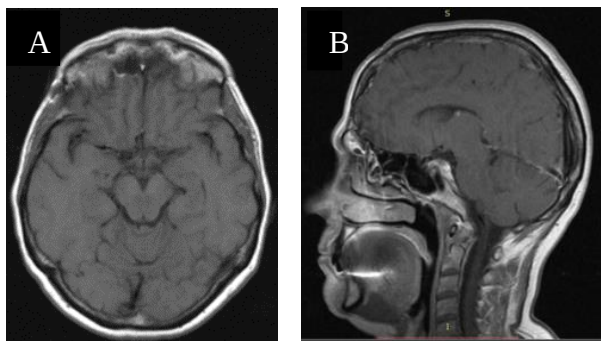
FIGURE 1. Axial (A), sagittal (B) and coronal (C) contrast MRI images revealing a planum sphenoidale meningioma



The approach was performed with a 4.5 cm trephine at the level of the frontal sinus (FIGURE 2) and the tumour was completely resected, while preserving the integrity of the olfactory tract. Postoperatively, the patient presented a favourable outcome with remission of headaches and no new neurological deficits. Postoperative control MRI confirmed total resection of the tumour (FIGURE 3).



FIGURE 2. Postoperative X-ray revealing the location of the craniotomy



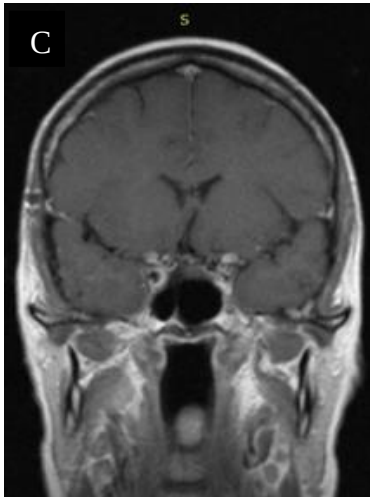


FIGURE 3. Postoperative axial (A), sagittal (B) and coronal (C) images of T1 with contrast MRI scan confirming the total resection of the tumour

Case 2

A 56-year-old woman was brought to the Emergency Department of our hospital for drowsiness and cognitive deterioration that began 3 months prior to presentation and progressively worsened. Neurological examination revealed right anisocoria, no motor deficits, positive Babinski on the left side and a GCS of 12 points.

The emergency native CT scan showed an isodense frontal tumor with bilateral extension and significant perilesional edema. The contrast MRI subsequently performed revealed a large extra-axial, isodense tumor with intense, homogenous enhancement, originating at the planum sphenoidale, imagistic features suggestive for a meningioma (FIGURE 4).

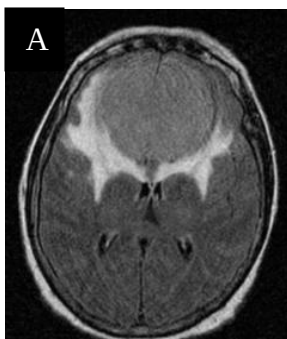
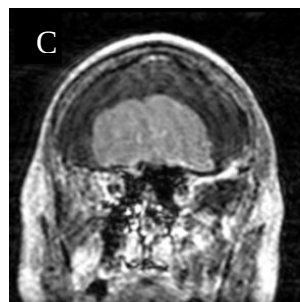
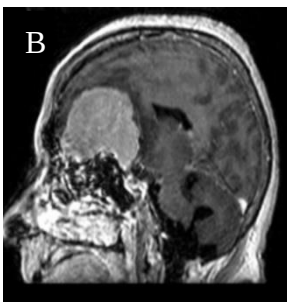


FIGURE 4. T1 weighted with contrast MRI in axial (A), sagittal (B) and coronal (C) planes that revealed a large planum sphenoidal meningiomas, 5.6 cm in the antero-posterior plane and 5.5 cm cranio-caudally



This tumour was resected through a large bifrontal craniotomy (FIGURE 5). After bone flap elevation and cranialization of frontal sinus, the dura mater was opened bilaterally and the anterior third portion of the superior sagittal sinus was ligated and resected. The tumour was completely removed with coagulation of dural insertion (Simpson II resection).

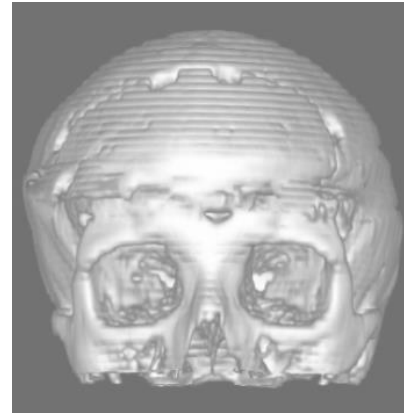


FIGURE 5. Bifrontal craniotomy performed for the resection of the large planum sphenoidale meningioma

Postoperatively, the patient presented a favorable evolution with no new neurological deficits. The control CT showed complete removal of the tumor (FIGURE 6) and the histopathological examination revealed a transitional meningioma (WHO grade I).

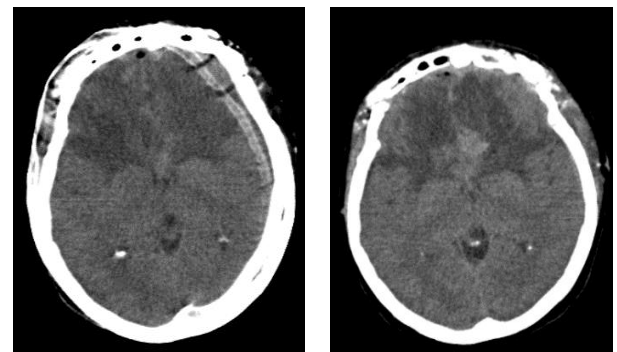


FIGURE 6: Postoperative CT scans that confirm a total resection of the tumor

DISCUSSIONS

We presented two cases of planum sphenoidale meningiomas of different sizes, both operated through a bifrontal approach, with the extent of craniotomy adapted to tumor size. In both cases, a total tumor resection was achieved with no surgical morbidity.

Planum sphenoidale meningiomas can be resected using different surgical routes, each with its advantages and disadvantages, allowing the

neurosurgeon to make decisions regarding the surgical strategy. The factors influencing it are: tumor size and its relationship to adjacent neurovascular structures, the patient's symptoms and the neurosurgeon's experience. There are various transcranial approaches to resect planum sphenoidale meningiomas: bicoronal subfrontal, unilateral subfrontal, pterional transsylvian, anterior interhemispheric, extended bifrontal, skull base techniques and fronto-temporal orbito-zygomatic^{4,5}.

The bifrontal craniotomy is generally used for most midline anterior cranial fossa lesions mainly because of the flexible operative working angles that it provides and for its generous exposure of the tumor⁶.

When compared with bifrontal craniotomy, the pterional approach avoids the frontal sinuses, averting the necessity to sacrifice the anterior superior sagittal sinus. It does not imply the necessity to manipulate both frontal lobes. This approach also allows early identification of the optic apparatus, therefore facilitating its protection during tumor resection^{7,8}.

Nakamura *et al.* compared in a series of patients, the bifrontal approach with frontolateral approaches, concluding that they prefer the frontolateral approaches that offer an adequate access to the tumor with less brain exposure while allowing a total tumor removal with a low morbidity rate⁹.

Also, a minimally invasive approach via a supraorbital incision and bone opening is also reportedly used quite frequently in removing these tumors¹⁰. Another option is the endoscopic endonasal approach. In one study, Ajlan *et al.* compared transcranial with endoscopic transnasal resection for anterior fossa tumors. While the transnasal endoscopic access associated fewer complications, the tumor resection rates were much lower compared to the transcranial approaches¹¹. Also, in a small single institution study, the endoscopic approach resulted in equal rates of resection with better outcomes and less trauma to the brain.¹²

However, in 2012 Komotar *et al.* published a meta-analysis of 60 studies including over 1,000 patients with tuberculum sellae, planum sphenoidale or olfactory groove meningiomas resected either via an endoscopic or transcranial approach. The results indicated that patients had

similar outcomes regardless of the approach with a higher rate of CSF leaks associated to the endoscopic approach¹³.

The transcranial approaches may be better suited for planum sphenoidale or tuberculum sellae meningiomas that are large, with significant lateral extension or vascular involvement. They offer better control and thus better tools to deal with vascular complications. Ultimately, the optimal approach is predicated by the experience of the surgeon and the patient's characteristics and should be determined on a case by case basis¹⁴.

CONCLUSIONS

The approach for meningiomas of the anterior skull base must be tailored to the size of the tumor. A minimally invasive approach through the frontal sinus should not be avoided in cases with small tumors.

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Biomarkers of the brain injuries - the future diagnosis standard in head trauma?

Brief literature review

**Andreea Elena Bîrlescu^{1,2}, Bianca Hanganu¹,
Andreea Alexandra Hleșcu^{1,2}, Irina Smaranda
Manoilescu^{1,2}, Beatrice Gabriela Ioan^{1,2}**

¹ "Grigore T. Popa" University of Medicine and Pharmacy, Dept. of Legal Medicine, Iași, ROMANIA

² Institute of Legal Medicine, Iași, ROMANIA

ABSTRACT

Acute head trauma is often a clinical challenge in diagnosing the brain damage, assessing its severity and prognosis, and establishing the optimal treatment. Different patients, with brain damage of apparent comparable severity according to the imaging examination, may have different neurological evolution or different response to therapy.

Minor traumatic brain injuries can induce a brief loss of consciousness or confusion, are usually benign, but sometimes they cause persistent and progressive brain symptoms in the long run. However, at present, there are no reliable methods that can diagnose properly minor traumatic brain injuries.

Biomarkers of the brain injuries allow the monitoring of both physiological and pathological processes. The identification of such biomarkers could allow a better understanding of the pathological processes involved in traumatic brain injuries, their diagnosis, prognosis and may facilitate the establishment of a better treatment regimen for these patients.

In this article, the authors make a brief review of the literature in which they analyse the biomarkers of the lesions of the various brain structures identified so far, which can be detected in biological fluids (blood, cerebrospinal fluid) and the advantages and limitations of their use in the current medical practice.

INTRODUCTION

Brain injury may be graded by Glasgow Coma Scale score (GCS) in: severe trauma, characterized by a GCS score of less than or equal to 8- the cerebral coma equivalent; moderate trauma, characterized by a GCS score of 9-12 [1], of which 10% of patients will experience neurological deterioration and cerebral coma and minor trauma, where the GCS score is between 13 and 15 [2].

Minor brain trauma can be characterized by the loss of consciousness of short duration- up to 30 minutes, or confusion, retrograde amnesia to the traumatic event of up to 24 hours, headache,

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Corresponding author:
Andreea Alexandra Hleșcu

"Grigore T. Popa" University of
Medicine and Pharmacy, Dept. of
Legal Medicine, Iași, Romania

andreea.velnic@yahoo.com

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vomiting (unrelated to intracranial hypertension) and/ or transient focal neurological signs or convulsions [1]. Most patients with minor brain trauma show favourable progression, but about 3% of cases have an unfavourable progression, with increased risk for intracranial haemorrhage and diffuse axonal injuries, the promoters of cognitive, motor and psychosocial deficits [2]. The morbidity associated with cerebral traumatic injuries (even minor) is considerable. Studies have shown that between 1 and 20% of patients with minor traumatic brain injuries develop persistent physical, cognitive and behavioural disorders [3], such as chronic dizziness, fatigue, headache, and amnesia. It is also important that in the clinic, minor brain injuries are more common than stroke, dementia and epilepsy, indicating their high prevalence and justifying the efforts to diagnose and treat them as accurately as possible.

Despite substantial efforts to clarify and improve the diagnostic criteria for minor traumatic brain injuries, compared to moderate and severe brain injuries, the former often remain a diagnostic challenge. This is largely due to the rapid resolution of acute signs and symptoms after a simple rest and the absence, in many cases, of objective neuroimaging evidence.

Current diagnosis regimens for minor traumatic brain injuries often face the difficulty of differentiating them from non-traumatic pathologies that may exhibit a similar symptomatology.

Currently, the gold standard for diagnosing and establishing the therapeutic management of traumatic brain injuries is the computer tomography (CT) exam. It allows the detection of various traumatic head injuries, such as cranial fractures, extra- and subdural hematomas, subarachnoid haemorrhage, cerebral contusion and laceration, cerebral edema, etc. With increased sensitivity and specificity and by using it in the clinic as a routine exam, the head CT scan surpassed the simple head radiography [1]. However, the head radiography retains its importance in the initial classification of traumatic brain injuries as complicated injuries (radiographically proven) or uncomplicated injuries (negative radiography), and thus contributes to establishing the necessary further investigations, such as CT scan or MRI, and the therapeutic management (hospital admission with or without surgery). Despite the superior results from classical

X-rays, modern imaging modalities such as CT scan and MRI are costly and entail a number of risks, including the risk of irradiation and the risk associated with the administration of the contrast substance [3]. Also, in many cases, minor traumatic brain injuries cannot be detected by CT scan. Under these circumstances, an additional diagnostic tool is necessary to detect patients at risk of developing further complications.

BIOMARKERS OF CEREBRAL LESIONS - PATHOPHYSIOLOGICAL BACKGROUND

Research on biomarkers of neuronal lesions began after the 1950s, and their interest has increased significantly over the past 25 years.

Biomarkers, also called biological markers, are natural characteristics that can be measured and interpreted objectively as indicators of biological processes or responses to therapeutic interventions [4]. Biomarkers are indicators of physiological, pathological or pharmacological processes. Each organ system has more or less specific biomarkers, and their analysis, either isolated or joined to other clinical investigations, allows monitoring of an individual's health status [2].

From the pathophysiological point of view, due to the brain injuries, the neuronal and astroglial network loses its structural integrity, cellular membranes are affected and secondary to these events, biomarkers are released in the cerebrospinal fluid and in blood, allowing for the diagnosis and prognosis of brain injuries [5].

Traumatic mechanical forces can determine cell damage due to shear, rupture and stretching of neurons, axons, glial cells and blood vessels, and the lesion will induce biochemical changes such as excitotoxicity, necrosis and apoptosis, oxidative stress and inflammation. Similar pathophysiological changes can also be seen in disorders induced by acute pathological brain injury such as stroke.

Sensitive and specific biomarkers that reflect the brain damage can provide important information about the pathophysiology of traumatic brain injuries and can predict abnormal CT results and/ or the development of residual deficits in patients suffering from minor traumatic brain injuries. Biomarkers could be diagnostic criteria for traumatic brain injuries and could be a valuable adjuvant to clinical and routine imaging. In particular, the possibility of using biomarkers in patients with minor

traumatic brain injuries could provide a rapid, differential, non-invasive and cost-effective diagnostic test to guide appropriate patients' triage and their early management [6].

BIOMARKERS OF BRAIN INJURIES –

PROMISING RESULTS

A wide range of proteins, of different origins and resulting from various pathways, have been studied as biomarkers for diagnosis and prognosis of brain injuries. However, the performance of many of these biomarkers has not been studied in the case of minor traumatic brain injuries [7].

At the level of the central nervous system, the lesion biomarkers studied to date are S100beta, Glial Fibrillary Acidic Protein (GFAP), Neuron-Specific Enolase (NSE), Alpha II Spectrin, Tau protein, Ubiquitin C-Terminal Hydrolase L1 (UCH-L1), Fatty-Acid-Binding Proteins (B-FABP, H-FABP) and IL-10.

Among the listed biomarkers, the most studied are S100 beta and Neuron-Specific Enolase (NSE), the values of which increase in hypoxic conditions, starting on the 2nd post-traumatic day and normalize at about 4 days after the trauma [2].

S100 beta is a dimer that binds cell calcium, is involved in cellular differentiation and neuronal proliferation and has a life span of about 2 hours. There are 19 types of such dimers, of which S100A1 (in skeletal muscles, heart, and kidneys), S100A1B (in astrocytes), S100B (in astrocytes and Schwann cells) and S100BB (in astrocytes). The low molecular weight of 21kDa allows the S100beta dimers to easily cross the blood-brain barrier, so that in brain injuries high levels of S100beta are found in the blood. Unlike the NSE, the plasma level of S100beta is not affected by hemolysis, 21.2 micrograms/ liter suggesting the installation of anoxic coma, and 15.2 micrograms/ liter indicates neuronal recovery.

Neuron-Specific Enolase (NSE) is an isoform dimer involved in glucose metabolism, which is normally not found in the peripheral blood. In patients with stroke, the NSE value increases, with higher values for patients with irrecoverable traumatic brain injuries compared to patients with favourable progression. Decreasing NSE values at 24-48 hours after the trauma usually indicates a good prognosis, while a value greater than or equal to 30 micrograms/ liter, 48 hours post-trauma, predicted death in 100% of the cases. As mentioned above, NSE values are influenced by hemolysis, which does not

allow its determination in peripheral blood. Apart from brain lesions, other sources of NSE may also be small cell carcinomas, neuroblastoma, haemorrhagic shock, femoral fracture, ischemia and local reperfusion.

Glial Fibrillary Acidic Protein (GFAP) is a monomer, being an intermediate protein derived from astroglial cells. GFAP has increased specificity for neuronal tissue, with high values in degenerative brain diseases, cerebral infarction, severe brain injury, and axonal injuries. GFAP is a predictive indicator for the recovery of anoxic cerebral coma, but studies conducted so far on this monomer are contradictory, and further research is needed on post-mortem biological products.

Ubiquitin C-Terminal Hydrolase L1 (UCH-L1) is a compound that plays a role in the elimination of oxidized neuronal proteins under both normal and pathological conditions. Initially, it was used as a histological marker for neurons. Recently, UCH-L1 has been found to have elevated values in the cerebrospinal fluid after a traumatic brain injury, which can be immediately detected post-traumatically, with elevated values lasting for about one week [2].

Both S100B and the combination of GFAP and UCH-L1 were promising in screening for CT positivity/negativity among patients with acute traumatic brain injury [8].

Alpha II Spectrin is a major component of the cortical membrane of the cytoskeleton, being present in axons and presynaptic terminations. It is a marker for apoptosis and necrosis in the post-traumatic initial stages and has high values in moderate and severe brain injuries [2].

Tau is a microtubule associated protein, which is necessary to maintain the structural integrity of the axons. Tau proteins have also other functions, such as nerve impulse transmission, synaptic activity, cellular proliferation, neurobiological development and neuroplasticity. Phosphorylation of Tau proteins is a normal metabolic process, while in both aging and neurodegenerative diseases, Tau proteins undergo hyper-phosphorylation, which determines their aggregation as fibrillar deposits. Post mortem studies on human corpses described different patterns of tauing, depending on the pathological phenotype. Recent studies also highlight the uniqueness of pathological models, including a model attributed to repetitive cerebral trauma,

although clinical correlations were relative [9].

Fatty-Acid-Binding Proteins (FABPs) are non-enzymatic cytoplasmic proteins involved in intracellular buffering and transport of fatty acids. These are 9 distinct protein types, each named after the tissue in which it was first detected. FABPs are rapidly released into circulation from the injured cells and are eliminated by the kidney, with a half-life of about 20 minutes. B-FABP was first identified in the rodent brain where it has a variable concentration depending on the animal's age (stage of development). Thus, in adult mice, B-FABP is usually produced at low concentrations and is detected only in glial cells of the white matter. Unlike B-FABP, H-FABP is also detected in neurons of the gray matter. B-FABP and H-FABP proteins have different brain tissue distribution, with the highest concentrations in the frontal lobe. However, in all brain structures it was observed that the level of H-FABP concentration is about 10 times higher than the B-FABP concentration. Studies show that these two proteins have greater susceptibility to minor cerebral lesions than the currently used markers, S100B and NSE respectively [10].

DIAGNOSTIC RELEVANCE OF BIOMARKERS OF CEREBRAL INJURIES

To date, biomarkers of cerebral injuries have been detected in cerebrospinal fluid and in peripheral blood. It has been found that in cases where the blood-brain barrier is intact, cerebral proteins are only present in small amounts in blood. The condition of the blood-brain barrier has, therefore, an important influence on the concentration of those proteins in the blood, which should be considered for the interpretation of the cerebral lesion-specific biomarkers [7].

The cerebrospinal fluid is in direct contact with the extracellular matrix of the brain, and its composition reflects the biochemical changes occurring in this organ. For these reasons, the cerebrospinal fluid could be an optimal source of brain damage biomarkers. Several cerebral lesion-specific biomarkers have already been described, including proteins that indicate the integrity of the blood-brain barrier and neuro-inflammation, as well as axonal, neuronal and astroglial lesions. Some proteins that are expressed in the central nervous system are also detectable in peripheral blood, albeit

at very low concentrations due to their dilution in the much larger volume of the extracellular plasma and matrix of peripheral tissues. Because peripheral blood sampling is much easier in practice than the collection of the cerebrospinal fluid, a series of cerebrospinal fluid biomarkers specific for minor traumatic brain injuries have also been evaluated in the peripheral blood. The low concentration of potential biomarkers in the peripheral blood is, however, a technical limitation on the use of most standard immunological tests. However, the number of potential biomarkers of cerebral lesions in the peripheral blood studied is steadily increasing as the analytical tools for detecting them become more and more sensitive [11].

Studies have shown that unique biomarkers do not have the specificity and sensitivity required for their use as diagnostic tools. For a biomarker to be useful its sensitivity and specificity should be very high to ensure diagnosis and prognosis assessment without the need for a CT brain exam.

So far, most research on biomarkers of minor traumatic brain injuries has been performed with unique biomarkers. The combination of different biomarkers has been suggested to enhance the diagnostic performance. Several studies have shown that combinations of biomarkers significantly increase diagnostic performance in various pathologies, such as sleep disorders, post-stroke subarachnoid haemorrhage, lung cancer or differentiation of post-traumatic brain injuries from other types of lesions. Furthermore, it has been suggested that some combinations of different clinical parameters, such as the age and types of biomarkers, e.g. inflammatory proteins, can improve the classification of lesions [7].

In a multicentre study, 13 cerebral biomarkers, all previously investigated in patients with stroke, were evaluated for their ability to correctly classify patients with minor traumatic brain injury, CT positive and CT negative, with a GCS score of 15 and showing at least one clinical symptom. Of the 13 biomarkers, the H-FABP and IL 10 proteins were the best single markers. These were further compared and combined with the better-studied S100B and GFAP markers. H-FABP was the best single marker, but when combined with GFAP, the overall performance increased from 32% to 46%, with a sensitivity of 100%. Proteins have been shown to be released from various types of injured cells. S100B and GFAP

were derived from astrocytic lesions, H-FABP from endothelial cells and neuronal cellular bodies, while IL10 is expressed by monocytes and macrophages [7].

Detection of cerebral lesions by the serum biomarkers is not a standard procedure in current clinical practice, although several proteins, such as S100B, NSE, myelin basic protein and GFAP show promising results [10]. Some biomarkers, such as S100B and GFAP, have been extensively studied in the blood of patients with minor traumatic brain injuries, but so far none seem to provide sufficient information [7].

DIFFICULTIES AND LIMITATIONS IN THE STUDY OF BIOMARKERS OF BRAIN INJURIES

The main difficulty facing biomarkers for brain damage is to know whether the measured proteins really come from the brain injuries. As shown above, regardless of their origin, single biomarkers do not have sufficient performance to be transformed into diagnostic tools. Biomarker combinations, however, have been shown to enhance diagnostic performance when proteins of different origins and pathways are combined, due to the complexity of the nervous system and the heterogeneity of the traumatic brain injuries [7, 8].

There are also other obstacles to the development of a series of blood biomarkers for minor traumatic brain injuries. The blood-brain barrier prevents the evaluation of the biochemical changes in the brain by using biomarkers in the blood, but this is possible, however, in the case of loss of blood-brain barrier integrity, which occurs in severe brain lesions. In addition, some potential biomarkers suffer a proteolytic degradation in the blood, and their levels may be affected by clearance in the blood through the liver or kidneys. The accuracy of immunoassays may also be affected by the binding of biomarkers to carrier proteins and extra-cerebral sources of biomarkers [12].

Biomarkers of the cerebral injuries have different delivery patterns, and this has limitations on their practical use. As a result, clinical applicability may be limited by the type of brain injury (traumatic, stroke, hypoxia-ischemia). Another important limitation in the analysis of cerebral biomarkers is their ambiguity in multiple lesions.

Despite the current limitations in the study and application of biomarkers of cerebral lesions in the current medical practice, biomarkers could be used in the future as an adjuvant, supplementing the traditional and neuro-imaging examination in the diagnosis and prognosis of patients with traumatic brain injuries [4].

CONCLUSIONS

Traumatic brain injuries may raise clinical challenges due to the diagnostic difficulties and the lack of specific prognostic tools. A special place in the traumatic pathology of the brain is occupied by minor traumatic brain injuries that, although characterized by immediate mild signs and symptoms, can induce long-term brain pathology with increased disability potential.

Biomarkers of cerebral injuries may be a new diagnostic standard for traumatic brain injuries, and in particular, minor ones that often cannot be detected by cerebral CT.

However, further studies are needed to identify the biomarkers or combinations of biomarkers with the highest sensitivity and specificity for cerebral injuries.

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Dual microcatheter technique for the treatment of a ruptured wide neck basilar tip aneurysm

Rares Filep, Dorin Nicolae Gherasim, Septimiu Popescu, Botond Tokes, Lucian Marginean

* Department of Interventional Radiology & Department of Neurosurgery, Emergency County Hospital, Targu Mures, ROMANIA

ABSTRACT

Endovascular treatment is a safe and efficient therapy for intracranial aneurysms with lower complication and mortality rates compared to surgical clipping. Wide-neck aneurysms still represent a challenge to complete and safe aneurysm occlusion in spite of techniques such as stent-assisted or balloon-assisted coiling, developed in order to achieve better occlusion rates. These techniques themselves may lead to further complications, so alternative methods such as the dual microcatheter technique were developed. This technique assumes that, via two microcatheters inserted into an aneurysm, simultaneous deployment of two coils achieves a stable coil frame without the use of adjunctive devices. The aim of this paper is to present a successfully treated basilar tip wide-neck aneurysm treated with the dual microcatheter technique.

Case report. A 46-year-old male patient with acute onset of severe headache presented in the emergency room with altered state of consciousness. Non-enhanced CT scan showed subarachnoid and intraventricular haemorrhage. CT angiography revealed a wide-neck basilar tip aneurysm. Digital subtraction angiography confirmed the presence of an aneurysm with a wide, 4.9 mm neck.

Dual microcatheter technique was chosen as the first treatment option, while a hypercompliant balloon was kept as backup. Two microcatheters were placed inside the aneurysm and two coils were introduced in order to form a stable framing coil mass that served as a support for further coils deployed in an alternately manner through each microcatheter. No procedural complication occurred, and the patient's evolution was uneventful with no neurological deficits at discharge.

Conclusion. The dual microcatheter technique is a safe and effective therapeutic option for wide-neck ruptured or unruptured intracranial aneurysms. Periprocedural complication rates are similar to simple coiling or balloon-assisted coiling, but lower than for stent-assisted coiling.

INTRODUCTION

Endovascular treatment has become the therapy of choice for intracranial aneurysms owing to its lower complication and mortality rates, as compared to surgical clipping (5). However wide-neck aneurysms with a neck diameter greater than 4 mm or a dome-to-neck

Keywords

subarachnoid haemorrhage,
cerebral aneurysm,
basilar artery,
endovascular treatment



Corresponding author:
Dorin Nicolae Gherasim

Department of Neurosurgery,
Emergency County Hospital,
Targu Mures, Romania

dorin.gherasim@gmail.com

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ratio less than 2, still represent a procedural challenge attributable to the risk of intraprocedural coil herniation, a higher number of thromboembolic complications and higher rate of long-term recanalization (6).

Different techniques have been developed to assist wide-neck aneurysm coiling by covering the neck during coil deployment, thus allowing denser packing and better long-term occlusion rates. Stents and balloons have been used for this purpose, but both techniques have their limitations. Stent placement might be difficult in tortuous vessel anatomy and is associated with delayed thromboembolic events and in-stent stenosis. Balloon-assisted coiling (BAC) requires temporary flow arrest and may be associated with increased risk of vessel rupture and thromboembolic complications (7).

One alternative to the above-mentioned procedures is a less used and under-reported method, the dual microcatheter technique (DMT),

which requires simultaneous placement of two microcatheters in the aneurysm sac and deployment of coils through both of them with the aim of achieving a stable coil frame without the use of adjunctive devices (1).

The aim of this paper is to present the case of a patient with a wide-neck basilar tip ruptured aneurysm, successfully treated using the DMT and to discuss its advantages and disadvantages compared to other techniques used for wide-neck aneurysm coiling.

CASE REPORT

A 46-year-old male patient presented in the emergency department with abrupt-onset severe headache. Clinical examination revealed a drowsy and confused patient (Hunt-Hess 3). Non-enhanced CT and CT angiography of the head performed on 64-channel machine (Siemens, Erlangen, Germany) showed a subarachnoid and intraventricular hemorrhage (mFisher 4) and a wide-neck basilar tip aneurysm. (FIGURE 1: a, b, c)

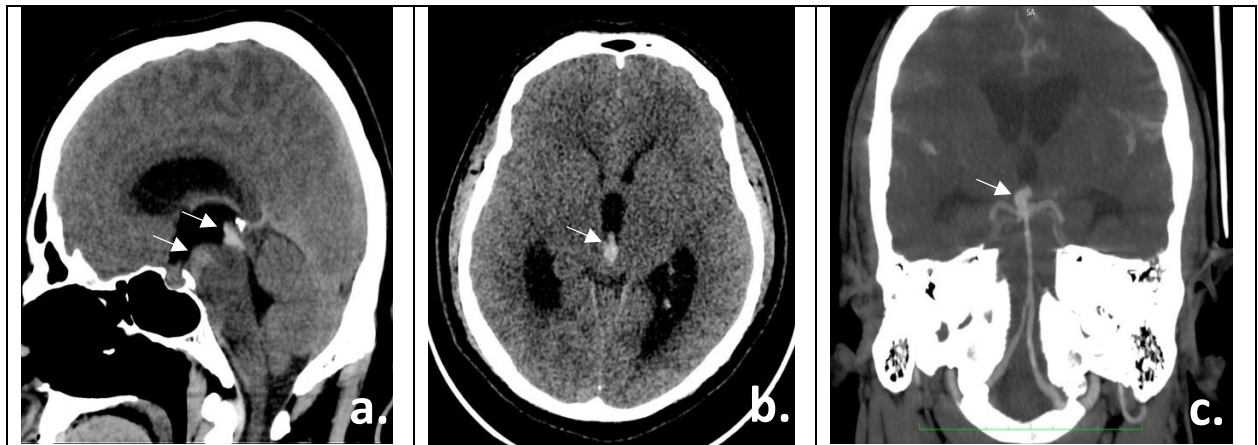


FIGURE 1. a. Sagittal NCCT image reveals a small amount of subarachnoid blood in the interpeduncular cistern and the 3rd ventricle (white arrows); **b.** Axial NCCT slice shows the blood clot in the 3rd ventricle (white arrow); **c.** Coronal CTA image reveals the basilar bifurcation aneurysm (white arrow)

NCCT = non-contrast computed tomography; CTA = computed tomography angiography

Digital subtraction angiography (DSA) and 3D rotational angiogram obtained on a Siemens biplane system (Siemens, Erlangen, Germany) showed the basilar tip aneurysm measuring 7.1/5.1/5.4 mm (CC/LL/AP diameters) with a neck of 4.9 mm (dome-to-neck ratio of 1.4), and a small secondary lobule along the left superior border of the aneurysm, thought to be the site of bleeding (FIGURE 2: a, b).

Under general anesthesia the right common femoral artery was accessed with a 6F Cordis sheath (Cordis, Fremont, California) and a 6F Chaperon guiding catheter (Terumo, Tokyo, Japan) was placed in the right vertebral artery (VA). A Headway 17 microcatheter (Terumo, Tokyo, Japan) was then advanced into the aneurysm and a Target 360 standard 5 mm x 15 cm coil (Stryker, Michigan, USA)

was deployed. At this point an intravenous bolus of 2500 units of heparin was administered. The coil was quite stable in the aneurysm sac without impingement on the basilar artery. (FIGURE 2: c.) We kept it attached to its introducer wire nevertheless, with the idea to keep it as support for further coils that will be inserted through a second microcatheter.

A 5F Cordis femoral sheath was inserted on the opposite side and a second Headway 17 microcatheter was introduced into the aneurysm via a 5F Navien support catheter (Medtronic, Minneapolis, USA) placed in the left VA. A 3D Axiom Prime 5 mm x 10 cm coil (Medtronic, Minneapolis, USA) was introduced through the second microcatheter, and by intertwining with the first coil,

formed a secure, stable coil mass throughout the entire volume of the aneurysm. (FIGURE 2: d, e) The second coil was detached, and an additional bolus of 2500 IU of heparin was administered. A third HydroCoil 3 mm x 8 cm coil (Microvention, California, USA) was introduced through the second microcatheter, followed by the careful detachment of the very first coil. Three further hydrogel-coated coils were introduced through both microcatheters, alternately, resulting in satisfactory occlusion of the aneurysm judged by the Raymond-Roy occlusion classification as 1 (FIGURE 2: f). The patient had an uneventful postoperative course and was discharged 2 weeks later without neurological deficits, with a modified Rankin scale 0.

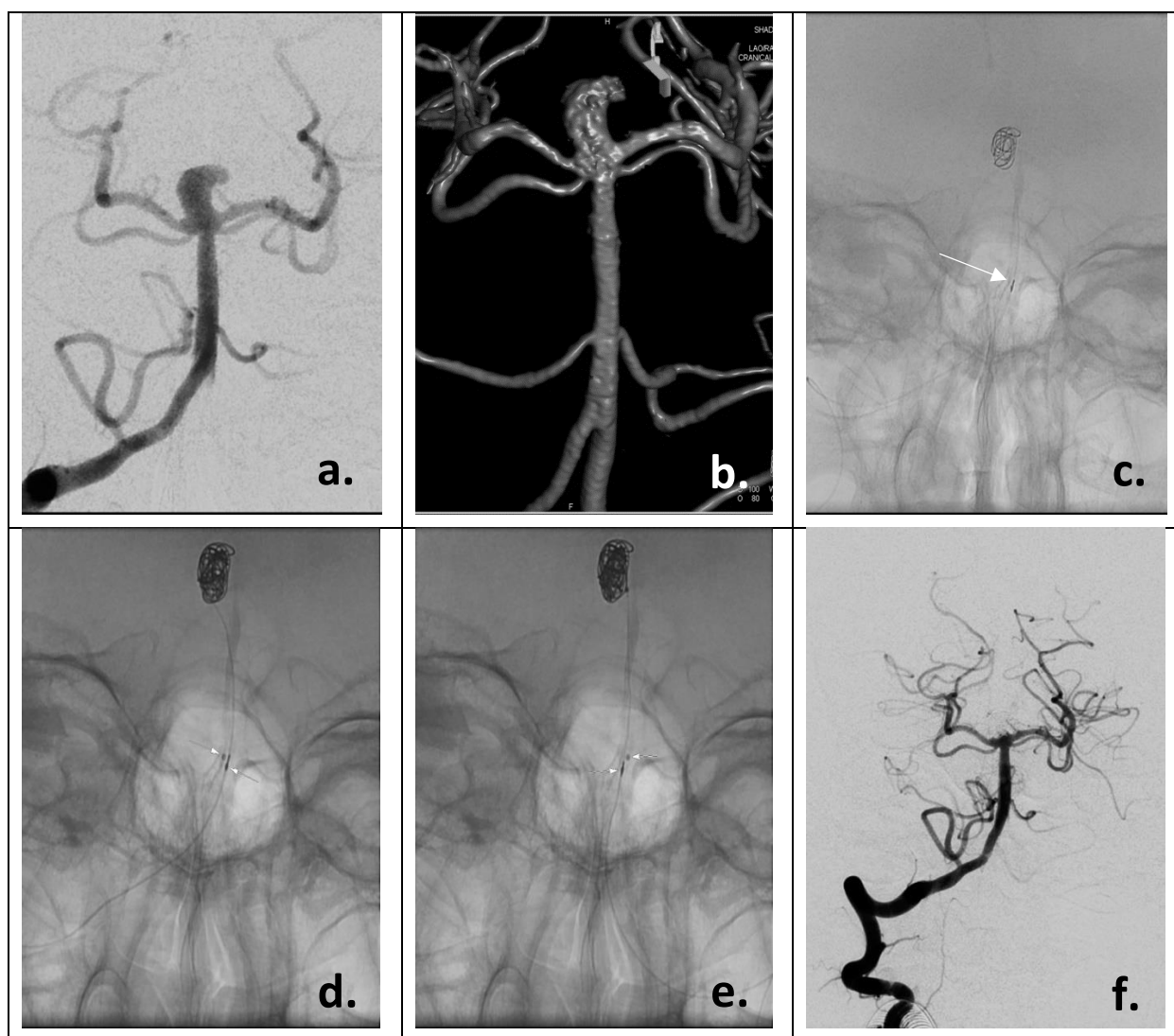


FIGURE 2. **a.** AP DSA image from a right VA injection shows a basilar tip aneurysm; **b.** 3D rotational angiographic reconstruction; **c.** AP unsubtracted image shows the first microcatheter and the first coil inside the aneurysm (white arrow); **d.** AP unsubtracted image

reveals the second microcatheter (white arrows) and a further coil inserted into the aneurysm; **e.** Further coils are deployed simultaneous through both of the microcatheters; **f.** Final control DSA angiogram shows the complete obliteration of the aneurysm. AP = anteroposterior, DSA = digital subtraction angiography

DISCUSSIONS

Since its introduction in 1998 by Baxter's group (4), DMT has been used as an alternative to balloon or stent-assisted coiling (SAC) for wide-neck intracranial aneurysms. It involves the use of two microcatheters inserted in the aneurysm sac followed by simultaneous or sequential deployment of coils. The general principle behind this technique is the stability obtained by the "entanglement" of the first two framing coils inserted simultaneously, thus creating a larger coil frame that prevents impingement on or herniation of the coil loops into the parent artery. One of the coils is usually detached at the end of the procedure thus conferring additional stability for further coils.

The technique is aimed at wide-neck saccular aneurysms with a dome-to-neck ratio less than 2, irregular aneurysms with multiple daughter sacs and complex configurations and aneurysms with a vessel emerging from the neck (5). We considered DMT as the first therapeutic option for our case while a balloon was kept as back-up in case the coils were not stable inside the aneurysm. SAC was excluded because the aneurysm was ruptured, and dual antiplatelet therapy was necessary. For a more detailed description of the technique we propose a step-by-step guide on how to approach aneurysms that are amenable to treatment with this procedure.

1. General procedural considerations

Endovascular treatment of intracranial aneurysms should be performed with the patient under general anesthesia. In our institution all catheters are continuously flushed with saline containing heparin (2500 IU heparin in 500 ml of saline). Our protocol is to administer a bolus of 5000 IU heparin intravenously after the deployment of the first coil, although during this procedure, 2500 IU were administered after insertion of both guiding catheters in order to prevent thromboembolic events, and 2500 IU following the deployment of the first coil.

2. Femoral artery access and guiding-catheter (GC) choice.

Uni- or bilateral access depends on how many GC's are needed. Generally, the dual microcatheter

technique can be safely performed through one GC. In the majority of cases the internal carotid arteries (ICA) or at least one of the vertebral arteries (VA) can easily accommodate one larger device, although cases with small VA's may require the use of two GC's in cases with posterior circulation aneurysms (4). Advantages of using a unilateral approach are the smaller complication rates related to femoral artery puncture and large vessel access, like arterial spasm, dissection and embolic events. Theoretically, using two GC's can lead to a two-fold increase in such complications. The use of two GC's can be avoided because the majority of 6 or 7 French (F) devices have a large enough lumen to contain both microcatheters. Disadvantages of using only one device are the difficulty of obtaining quality roadmaps or control angiograms with two microcatheters that occupy a large luminal area of a 6F GC, although this can be overcome with the use of a 7F device. Another disadvantage of two microcatheters inserted through the same GC is related to the risk of inadvertent forward/backward movement while manipulating them, which can lead to aneurysm perforation or dislodgement of the coil mass (4,3). Due to the limited experience with this technique we felt safer with a bilateral approach in order to avoid inadvertent microcatheter movement and to have access with a hypercompliant balloon if the coils were not stable or if rupture of the aneurysm occurred.

3. Aneurysm access

The first option is to try coiling the aneurysm with one microcatheter. If this fails due to coil herniation or impingement on the parent artery, the second microcatheter is positioned as follows. To anticipate the deployment behavior of the coils it is useful to divide the aneurysm in two imaginary compartments, each one occupied by one of the first two coils, a simple example is to have a proximal and a distal compartment, and to position the tip of the two microcatheters in the corresponding compartment (3).

4. Coil selection, deployment and detachment

Coil choice depends on the configuration of the aneurysm. For irregular aneurysms with multiple

daughter sacs soft coils are recommended to avoid perforation. If this is not the case, standard, complex coils are preferred due to their larger radial force providing a better “anchoring” inside the aneurysm. The first coils should be longer, thus minimizing the number of subsequent coils necessary for a dense final packing. After achieving a stable frame with the first two coils, one of them is detached and further coils are inserted until complete obliteration is obtained, while the other is left attached to its pusher-wire. The decision which coil to detach first is usually based on its stability: the more stable looking coil is to be detached first, because it provides a better scaffold for further coils. Another consideration to which coil should be detached first is the position of the microcatheter tip. It is safer to insert coils through the catheter sitting closer to the neck of the aneurysm than through the one positioned deeper inside due to the risk posed by the deep deposition of coils that might “push” the whole coil construct outside and into the parent vessel, consequently the one sitting deeper should be detached earlier (1,3,4).

5. Microcatheter removal

A potential risk of retrieving the microcatheters at the end of the procedure is the extraction of the coil mass outside the aneurysm. The best way to avoid this if the microcatheter's tip is deep inside the aneurysm, is to push gently on the pusher-wire of the last coil until the tip protrudes outside, and only afterwards to detach the coil (6).

DMT is a relatively under-used method for intracranial aneurysms compared to balloon or stent-assisted coiling, with only few case reports, series and retrospective studies published in the literature so far. The safety and efficiency of this approach has been assessed by Durst et al in their retrospective analysis of 100 wide-necked aneurysms (2). They reported a morbidity and mortality of 1% and 2% respectively. Intraprocedural rupture occurred in 3 patients (3%), 2 were successfully stopped immediately and 1 patient died due to massive hemorrhage and hydrocephalus. One other patient died as a consequence of the coils herniating in the parent vessel, obliterating the lumen and subsequent ischemic stroke. DMT was successfully carried out in 91 cases (91%). The remaining 9 failed due to the impossibility of stabilizing the coils inside the aneurysm.

Retreatment was necessary in 18% of cases after recanalization (2).

The relatively low major complication rate of DMT (3%) is similar to that reported for simple coiling (0.6-5.1%) or BAC (0.9-3.8%), but much lower than for stent-assisted coiling (SAC) (9.4-12.2%) (7). Two common downsides of BAC and SAC are the greater experience needed for device manipulation and the specific risks imparted by these devices on the procedure. Balloons add the risk of intraprocedural vessel rupture while stents are permanent intraluminal devices prone to in-stent stenosis and thrombosis, requiring long-term antiplatelet therapy with an additional hemorrhagic risk. Conversely, no special training is needed for DMT since the only devices used are those required for simple coiling, although special care is mandatory during aneurysm access, because two catheterization procedures mean an increased risk of wall perforation with either the guidewire or the microcatheters.

One major issue of DMT is the retreatment rate of 18% (7), that compared to BAC, between 5.7% and 15.6%, and SAC, between 4.3% and 13.3% (8) is relatively high. This is especially important for young patients due to their longer life expectancy, therefore a judicious use of DMT is necessary in this patient population.

CONCLUSIONS

The dual microcatheter technique is a safe and effective therapeutic option for wide-neck ruptured or unruptured intracranial aneurysms. Periprocedural complication rates are similar to simple coiling or balloon-assisted coiling, but lower than for stent-assisted coiling.

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New technologies for low-grade glioma surgery

Nicolae-Ştefan Bogaciu^{1,3}, Daniel Teleanu^{1,2,3}, A.V. Ciurea^{2,3}

¹ University Emergency Hospital, Bucharest, ROMANIA

² Sanador Clinical Centre Hospital, Bucharest, ROMANIA

³ "Carol Davila" University of Medicine and Pharmacy, Bucharest, ROMANIA

ABSTRACT

Brain surgery has come far from the primitive methods used thousands of years ago. In the last hundred years alone, we have come across countless breakthroughs like the invention of bipolar coagulation, the surgical microscope, microsurgical techniques and a large variety of surgical instruments. The latest years have brought us neuro-navigation, intra-operative imaging techniques and brain activity monitoring. Low-grade glioma surgery, in particular, has taken advantage a lot from all these new methods, bringing great benefits for the patients: the safe extent of resection has grown progressively and tumours located in eloquent areas that were thought until recently to be inoperable, have started to be removed in safe conditions. The purpose of this paper is to present these new technologies as a recap for neurosurgical professionals.

INTRODUCTION

Endovascular Brain surgery is one of the oldest procedures to ever be performed on a human being. Beginning as trephining, it has known a long period of slow development, only to become one of the top-edge sciences of modern time. It developed from somewhat barbaric procedures with little if any supporting scientific knowledge, to life-saving procedures performed on a macroscopic scale, to microscopic interventions with progressively smaller „collateral damage” and in the future it might turn into something we would call „molecular surgery”. The purpose of this paper is to highlight the technologies we nowadays use in low-grade glioma surgery, presenting their pearls and pitfalls, benefits and uses.

MATERIALS

Computer assisted neuro-navigation. The purpose of this tool in brain surgery is to integrate imaging studies obtained preoperatively with intra-op anatomy in order to localize more accurately the lesions subdue to surgery (PICTURE 1). A neuro-navigation system has the following main parts: a computer-station with built-in software, a receiver and trackers/pointers (PICTURE 2).

Keywords

intraoperative, imaging,
neuro-navigation,
low-grade glioma,
brain monitoring



Corresponding author:
Nicolae-Ştefan Bogaciu

University Emergency Hospital,
Bucharest, Romania

bnicolaestefan@yahoo.com

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PICTURE 1

PICTURE 2



The initial step is to upload the preoperative images in the computer. Patient is positioned and a patient-tracker is placed in the proximity of the patient's head. Landmark registration is performed and checked for accuracy and surgery can commence. Intra-operatively, the surgeon may navigate with different tools: pointers, microscope, standard neuro-navigated instruments (aspirator, ultrasonic aspirator, retractors etc.). Some systems allow injection of images directly into the microscope for compatible devices (PICTURE 3).



PICTURE 3

Neuro-navigation is not only useful for accurately localizing a lesion, but also for localizing vasculature and other normal anatomical structures that need to be avoided in glioma surgery. Image series used for neuro-navigation can be fused for better describing the anatomy and functionality of different brain areas: tractography, PET, MRI, CT, contrast-enhanced imagery etc. The advantages of using neuro-navigation in LGG (low-grade glioma) surgery consist of, but are not limited to: smaller scalp incisions, cranial flaps, dural incisions and corticotomies, safer dissection and tumour excision, reduced surgery time.

All these imply fewer post-operative complications from surgery, faster discharge, lower costs for patient care. The main disadvantage of neuro-navigation systems is that the position of the patient

when obtaining images and the position of the patient during surgery are almost never the same so the brain will have a shift during surgery compared to imaging. Another thing is that after beginning the excision of tumoral tissue, the landscape changes, but the images stay the same. Some solutions were developed for these problems. Other imaging studies may be performed intraoperatively to complete the preoperative study and to increase the accuracy of the neuro-navigation system. Intraoperative MRI is a known tool which performs the task well, but it is highly inconvenient. Its more readily available counterpart is intraoperative ultrasound. Tips for successfully removing tumours using neuro-navigation include: removing tumour tissue closer to eloquent areas first, when accuracy is better, performing en-bloc excisions as much as possible, avoiding cysts especially when they are large, until good accuracy is no longer an issue, „rebuilding” volume by placing cottonoids in resulting cavities. In spite of all issues, a surgeon will always find this tool useful and he will always have in mind the fact that he can never rely on solely this in performing his tasks.^{1,2,3,4} (PICTURE 4).



Intra-operative ultrasound. Ultrasonography (US) is a great mean of obtaining fast, cheap real-time images during brain surgery. Images are usually

obtained by using a probe of 4-8 MHz which is sufficient for acquiring images in a 2-6 cm distance from it. There are a few ways to use this tool: regular gray-scale brightness mode (B-mode), Contrast Enhanced Ultrasound (CEUS), elastosonography. US is of aid in all stages of brain tumour surgery, from the opening of the dura up to the resection of peripheral extensions of the tumour. As opposed to cortical lesions, subcortical lesions are more difficult to identify, and the site of the corticotomy may be tricky to choose. By using US, the surgeon can identify the subcortical tumour and choose an entry site as found suitable. During resection, the surgeon may use US to identify the depth and extent of the tumour and adapt the aggressivity of his resection accordingly. In the final stages of the surgery, one may use US for identifying residual tumoral tissue in the periphery of the mass. Not only US may be used for identifying the tumour, but also to characterize it. It can deliver information about the consistency of the tumour. For example, the surgeon may use this information to adapt the power of an ultrasonic aspirator, or to differentiate between low-grade glioma (LGG) and high-grade glioma (HGG): LGG are firmer than HGG (as assessed by elastosonography). CEUS brings even more information about the vascularization of the tumour, by real-time angio-sonography so that the surgeon may adapt his resection strategy and have even more information about the possible histological diagnosis (LGG are poorly vascularized as opposed to HGG). A common use for intraoperative US in brain surgery is enhancing accuracy of neuro-navigation systems by updating the pre-operative acquired images used for registration and navigation, with real-time images provided by intra-operative US. By doing so, the effects of brain shift and swelling may be partly counteracted.^{1,4-8}

Intraoperative CT. Although it is less preferred by neurosurgeons compared to other imagistic tools, intraoperative CT-scans may be found useful in glioma surgery. As the other intraoperative imaging studies (US, MRI), it allows a greater extent of surgical resection by providing real-time intra-operative information regarding tumour mass, as well as updating pre-operative neuro-navigation planning. We may consider some advantages regarding the cost (relatively low compared to intraoperative MRI), speed of the procedure and general benefits such as improving accuracy and extent of the resection.^{9,10}

Intraoperative MRI (ioMRI). Intraoperative magnetic resonance imaging is the preferred intraoperative imaging method for low-grade glioma surgery. It is also the most laborious, the most expensive, but more importantly the most accurate. IoMRI comes in two shapes: low field ($\leq 0,5$ Tesla) and high field ($\geq 1,5$ Tesla). Regardless of the power of the magnet, ioMRI aids the surgeon in extending tumour resection in both enhancing and non-enhancing lesions, with greater benefit in the latter. The use of intraoperative MRI associates with higher extent of resection which implies longer overall survival and free of symptoms survival in patients with gliomas. Setting up an operating room with an MRI device can get pretty challenging. Although there are tools that can be used within the area closest to the device (an area limited by the 5-gauss border, which is a line beyond which ferromagnetic instruments can be used), most instruments used for microsurgical resection, including microscope and ultrasonic aspirator, have to be used further away from the magnet. Residual tumour is observed with high fidelity on images acquired from intraoperative MRI and can be readily excised if feasible. The whole range of sequences can be studied: functional, connective or pathological areas can be identified. Newly acquired images are integrated into navigation systems making surgeon orientation precise.^{3,11–13}

Intraoperative brain mapping and awake craniotomy. Although neuroimaging techniques have a great contribution to identifying functional cerebral structures and their relationship to tumor masses, intraoperative brain mapping is the gold standard for establishing tumour surgical strategy for each individual case, especially in the case of low grade glioma (LGG) where it is commonly accepted that the extent of resection (EOR) is linked to increase in survival. Intraoperative electric stimulation is performed by using a bipolar probe with an electric intensity starting from 2mA, with increments of 1mA up to 6 mA in patients operated with local anaesthesia and up to 16 mA in patients operated with general anaesthesia. During the procedure, when a certain area of the brain is stimulated, it will produce a neurological disturbance which returns to normal after stimulation is stopped. Thereby the interested function is noted and the neurosurgeon can make a surgical decision of stopping the resection. Areas which when stimulated do not

generate a disturbance are considered safe for continuing resection. LGG are slow-growing and rarely present with major neurological deficits, so the benefit of intraoperative brain mapping is large in LGG surgery because you need to preserve functionality for the patient. Even more, tumour mass resection is considered to be linked to postoperative seizure control so the possibility of safely increasing the EOR with this procedure increases the chance of good seizure control. Intraoperative brain mapping even offers the opportunity for safe tumour resection in eloquent areas otherwise considered inoperable. An important factor that contributes to this fact is brain plasticity. Brain plasticity also offers the opportunity for re-intervention in LGG of eloquent areas where initial total resection could not be performed, but timing of such a re-intervention must be carefully planned in order not to be too late and face anaplastic transformation.^{10,14–16}

CONCLUSIONS

Low-grade glioma is a challenging pathology in the field of neurosurgery due to its infiltrative nature, especially when concerning eloquent areas of the brain. Safe resection of such lesions can be performed using a variety of instruments and procedures, but better results can be obtained by combining them. The goal is obtaining an increased extent of resection which is beneficial for the patient, improving survival and quality of life.

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Initial single centre experience with Barrel VRD stent in large neck aneurysms

Cristian Mihalea^{1,2}, Felicia Otilia Humulescu^{3,4}, Hazem Abdelkhalek^{1,5}, Sorin Pescariu⁶, Bogdan Valeriu Popa⁷, Horia Ples¹

¹ Department of Neurosurgery, "Victor Babes" University of Medicine and Pharmacy, Timisoara, ROMANIA

² Department of Interventional Neuroradiology, NEURI Brain Vascular Center, Bicêtre Hospital, Le Kremlin-Bicêtre, FRANCE

³ Bucharest University of Economic Studies, Faculty of Cybernetics, Statistics and Economic Informatics, ROMANIA

⁴ Bucharest University of Medicine and Pharmacy Faculty, Faculty of Dental Medicine, ROMANIA

⁵ Department of Neuropsychiatry, Tanta University Hospital, Tanta, EGYPT

⁶ Cardiology Department, "Victor-Babes" University of Medicine and Pharmacy, Timisoara, ROMANIA

⁷ Department of Radiology and Medical Imaging, "Floreasca" Clinical Emergency Hospital, "Carol Davila" University of Medicine and Pharmacy, Bucharest, ROMANIA

ABSTRACT

Introduction. Despite the use of new techniques, such as Y-stenting, the waffle-cone technique and intrasaccular flow disrupters the treatment of wide-neck bifurcation aneurysms is still challenging, especially for those where adjacent branches are arising at the neck level. Moreover, the use of flow diverter stents in bifurcation aneurysms has been proposed by several teams, although the results remain controversial.

This study is reflecting initial experience in our department with a relatively new device available on the market: Barrel VRD stent. The unique design feature of the device is the "belly-like" central part of the stent which protects the adjacent branches.

Methods. We retrospectively reviewed all patients in whom stenting with braided or laser-cut stents had been performed in our center. Three patients were identified and analyzed. Technical success, complications, immediate angiographic outcomes, procedural data, are reported here.

Results. One MCA bifurcation and two basilar tip large neck aneurysms with one branch arising from the neck level have been identified. Technical success was achieved in all procedures. Overall procedure-related morbidity and mortality was 0%. In the immediate post-treatment angiography, adequate occlusion (neck remnant or total occlusion) was observed in all patients. Short- and mid-term follow-up angiography showed adequate occlusion of the aneurysms.

Conclusions. In this small case series, retrospective single-center analysis we showed that Barrel VRD - stent assisted coiling is a safe and feasible technique.

Keywords

cerebral aneurysms,
Barrel stent,
endovascular treatment



Corresponding author:
Cristian Mihalea

Department of Neurosurgery, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

cristianmihalea@yahoo.com

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Moreover, it offers an elegant and effective endovascular solution for large neck basilar tip aneurysms on which the neurosurgical clipping remains challenging.

INTRODUCTION

Endovascular treatment is the standard first-line therapy for both ruptured and unruptured intracranial aneurysms [1-3]. Unfavorable anatomy as wide-neck aneurysms also require adjuvant therapy to be treated safely and efficiently [4, 5] knowing the fact that simple coiling or balloon-assisted coiling has a high risk of coil protrusion into the parent vessel. The use of stent-assisted coil embolization for wide-necked intracranial aneurysms has significantly expanded the range of aneurysms that are candidates for endovascular treatment [6-8]. However, single stent-assisted coiling in particular situations does not provide sufficient support when the neck of the aneurysm is centered on the bifurcation branches. In these cases, the use of two stents or Y-stenting has been proposed [9-12]. From technical point of view this technique remains challenging but it has high immediate and long-term occlusion rates [11]. The waffle-cone technique is a feasible alternative to Y-stenting and consists of deploying the distal end of a dedicated stent, such as pCONus (Phenox GmbH, Bochum, Germany) and PulseRider (Pulsar Vascular, San Jose, California, USA), inside the aneurysm sac and the proximal end in the parent artery. Coiling is performed through the expanded distal end of the stent. The main advantage of this technique is that both branches of the bifurcation are not involved in endovascular treatment. Small retrospective studies have evaluated and reported its safety and efficacy [13-15]. In asymmetric bifurcations where two or even three branches are arising from the neck level those techniques described above offer limited solutions and unpredictable branch protection during coiling. The use of flow diverters in wide-neck bifurcation aneurysms (WNBA) remains controversial owing to inconsistent patency of bifurcation branches covered by the stent and poor occlusion of the aneurysm at follow-up angiograms [16]. Targeted, large prospective multicenter studies are needed to evaluate the safety and efficacy of this treatment specifically for WNBA. Intracranial flow disruption devices, such as WEB (Woven EndoBridge; Microvention, Tustin, California, USA) are presently a feasible and efficient tool of WNBA treatment; moreover, retrospective and prospective studies

confirmed the high safety level and low morbidity and mortality rates [17,18]. Despite the advantages of flow diversion in the case of complex irregular shapes and bi-lobed aneurysms or asymmetrical bifurcations, placing the WEB device proved to be unfeasible or at least very challenging even in experienced hands. In this context a single stent with “belly-like” central part which protects the adjacent branches in WNBA seems to be a promising solution for this type of aneurysms. Here, we report our single-center experience with Barrel VRD - stent assisted coiling, with clinical and angiographic periprocedural results, in order to evaluate the safety and efficiency of this technique.

MATERIALS AND METHODS

Population

We retrospectively reviewed interventional neuroradiology database records to identify patients in whom stenting with laser-cut or braided stents had been performed. We identified three patients treated with this technique in our institution between April 2015 and August 2018. Demographic data, aneurysm location and size are summarized in Table 1. All aneurysms were unruptured; all of them were primary endovascular treatments. In all cases, the aneurysm neck was wide, with an average dome to neck ratio of 1.49.

The Barrel vascular reconstruction device

The Barrel device (Medtronic/Covidien, Irvine, California, USA) is a nitinol self-expandable, closed-cell laser cut micro-stent with electrolytic detachment system. Two main characteristics offer two this type of stent the feasibility for WNBA's treatments. Main advantage is that due to “barrel” design that is represented by the “belly-like” central part of the stent protects the adjacent branches. Secondly due to the property to be re-sheathable up to three times.

Endovascular technique

Dual antiplatelet therapy was prescribed 2 days before the procedure as in all stent-assisted coiling treatment. In all patients, endovascular treatment was performed using a monoplane angiography unit with three-dimensional rotational capability (Allura Monoplan; Philips, Best, The Netherlands) under general anesthesia and systemic heparinization. After the procedure, dual antiplatelet therapy

(Ticagrelor 2 × 90 mg/day and Aspirin 150 mg/day) was administered for the first 3 months, and aspirin 160 mg/day alone was administered for the following 9 months. In our department clopidogrel (Plavix 75 mg) was replaced by ticagrelor (Brilique 90 mg) due to multiples advantages of the last one and also knowing that 20-25% of the subjects are naturally resistant to clopidogrel. A baseline activated clotting time (ACT) was obtained prior to the bolus infusion of heparin (30 to 50 IU/kg body weight), and hourly thereafter. The bolus infusion of heparin was followed by a continuous drip (1000 to 1500 IU/h), with the purpose of doubling the baseline ACT. From the femoral arterial access, a 6 Fr 100 cm distal-access catheter (Envoy/Codman, USA) was placed into the internal carotid artery or in the dominant vertebral artery. In all procedures, the most challenging branch of the bifurcation was first catheterized in order to place the distal tip of the stent. Then the simple deploying by retrieving the 0.021-inch microcatheter (Rebar 18, Medtronic, Irvine, CA, USA) was performed similar to Solitaire AB stent. The convenient placement of the “belly-like” central part of the stent was analyzed during the deployment in subtracted and non-subtracted angiograms. In all procedures the Barrel stent used was BV 4065 (“belly” diameter was 6,5mm and 4 mm proximal end diameter and 3.5 mm distal diameter) and in case 1 and 3 the satisfactory positioning of the stent was achieved after a first deployment. The precise placement of the “belly-like” central part of the stent is relatively simple to archive by the first attempt (2 out of our 3 cases). In one case the good positioning was achieved after third attempt due to acute angle between left PCA basilar trunk and consecutive drop of the microcatheter while deploying the device. Each time the Barrel stent was safely re-sheeted inside Rebar 18 microcatheter and a new catheterization of the left PCA was done. In all three cases the aneurismal sac was microcatheterized easily through Barrel interstices after stent placement and detachment (no jailing technique was used). In all procedures, passing through both stents studs with 0.014-inch microguidewire was achieved without any technical incident. Finally, the aneurysm was coiled using detachable coils. After coiling in all three cases no collapse of the stent has been noticed neither thromboembolic event was noticed in the protected neck-sided branch.

Complications

No intra-procedural or delayed thromboembolic or hemorrhagic complication were noticed for all three cases treated in our department.

Follow-up protocol

At the end of the procedure, immediate control angiograms were obtained from all patients. Modified Raymond–Roy occlusion classification (RROC) was used for grading the occlusion status of coiled aneurysms. Patients underwent Angio-MRI at 3 months to reassess filling status of the coiled aneurysm, in-stent stenosis, and thrombosis. The modified Rankin scale was used for scoring neurologic status at discharge and follow-up.

RESULTS

All three treated aneurysms were un-ruptured. Procedural details and follow-up angiographic results are shown in Table 1. Treatment was successfully performed in all three cases. Angiographic results were categorized according to the revised RROC into one of the following groups: complete occlusion (RR1), remnant neck (RR2), or residual aneurysm (RR3) by two senior neuroradiologists in consensus. There was no evidence of in-stent stenosis or thrombosis during follow-up Angio-MRI.

DISCUSSION

Stent-assisted coiling represents a wide world accepted solution for the treatment of wide-neck cerebral aneurysms over treatment with conventional coiling targeting higher rates of complete occlusion and lower rates of recurrence at long-term follow-up. However, treatment of WNBA and fusiform aneurysms is requiring a higher level of interventional neuro-endovascular skills and frequently requires a second stent (that is, a Y-, X- or waffle-cone-stenting configuration [19–20]) or dedicated endovascular stents such as pCONus, PulseRider, and Barrel stent [21]. There are currently little clinical data on these last three devices available.

Despite the potential benefit of single stent-assisted coiling, complex aneurysms can pose a significant challenge for achieving immediate and durable

embolization. Specifically, for wide-necked aneurysms located at shallow angle arterial bifurcations, single stent-mediated coiling may provide insufficient support of the coil mass to prevent coil herniation through the aneurysm neck.

A special situation is represented by the aneurysms with branches incorporated in the aneurysm base; Kim *et al.* [22] published a study with 68 patients with 78 intracranial aneurysms treated with multiple endovascular techniques: single-catheter coiling, multi-catheter coiling, balloon-assisted coiling, stent-assisted coiling, and combined techniques. 5.8% morbidity have been reported in this study and no mortality. 10 out of 55 (18%) intracranial aneurysms had a recanalization from which six were retreated. It represents a significant proportion and, moreover, retreatments are even more challenging in this situation. In 2004, Chow *et al.* detailed the Y-stent technique [12], whereby double open-cell Neuroform stents (Boston Scientific, Fremont, CA, USA) were deployed sequentially — first, proximal to the arterial bifurcation, and then into each arterial branch followed by coiling of the aneurysm sac. This represented an efficient endovascular solution for bifurcation lesions that are too complex for coiling alone, remodeling technique, or single-stent assisted coiling. Several authors have evaluated this technique in retrospective single-center studies, mostly including unruptured aneurysms [9-11]. The safety was relatively limited: Bartolini *et al.* reported 10.0% procedure-related permanent neurologic deficits and 1.0% death [10]. However, in other studies, the rate of intra-procedural complications was lower, with 4.2% in the study by Limbucci *et al.* and 2.7% in the study by Yavuz *et al.* with mortality rates of 2.1% and 0.5%, respectively [9,11]. At long-term follow-up, the rate of complete aneurysm occlusion was high with 85.8% in the Bartolini study, 95.7% in the Yavuz study, and 93.6% in the Limbucci study. Several types of stents can be used for Y-stenting; mainly open-cell stents (Neuroform, Stryker Neurovascular, Fremont, California, USA) or closed-cell stents (Enterprise, Codman, Miami Lakes, Florida, USA) have been reported. Intrasaccular flow disruption devices, such as the WEB device, are specially designed for the treatment of WNBA and have shown a high level of safety, with morbidity and mortality at 1-month post-procedure of 2.7% and 0.0%, respectively [23]. The efficacy of this technique

also proved to be higher than single-stent assisted coiling, and adequate occlusion was reported in 82.0% of cases at 12 months follow-up (complete occlusion: 56.0% and neck remnant: 26.0%). Despite progressive technological improvements, such as the replacement of dual layer by single layer versions, and progressive decreases in the diameter of the micro-catheter used to deliver the device, there are still bifurcation aneurysms with challenging anatomy which are not suitable for this technique. More recently new WEB-balloon remodeling techniques have been described by Mihalea *et al.* [24] where the WEB device can be deployed and tilted in the aneurysm sac using so called “balloon remodeling technique” and it may represent a feasible solution for this type of wide neck bifurcation aneurysms. In this category of wide neck aneurysms with branches incorporated at the neck level are technically particular and we strongly believe that Barrel stents represents a feasible and efficient solution. Moreover, it offers a solution for those anatomies where Y-stenting is not a suitable solution as in recurrent branch anatomies like in the cases presented in this report (FIGURE 1, 2 and 3). Being a nitinol self-expandable, closed-cell laser cut microstent Barrel device is definitely less thrombogenic than braided stents that can be used for Y-stenting configuration. In our experience Y-stenting demands higher technical skills and prolonged duration of treatment and from this point of view the solution to protect the both side branches of an WBNA with only one stent is more elegant and particularly less susceptible to per-operative thromboembolic complications. Several particular anatomical conditions are feasible for this technique: a dome to neck ratio below 1,5; branches incorporated at the neck level usually with a smaller diameter (not suitable for stent deployment); poly-lobed bifurcation aneurysms; and asymmetry between the aneurysm plan and the bifurcation plan.

From a technical point of view, one of the main advantages over Y-stenting is represented by the fact that the stent micro-catheter (0.021-inch internal diameter) Rebar 18 in our cases, has to be placed only once at the level of desired branch and no recatheterization of the stent and second stent placement is needed.

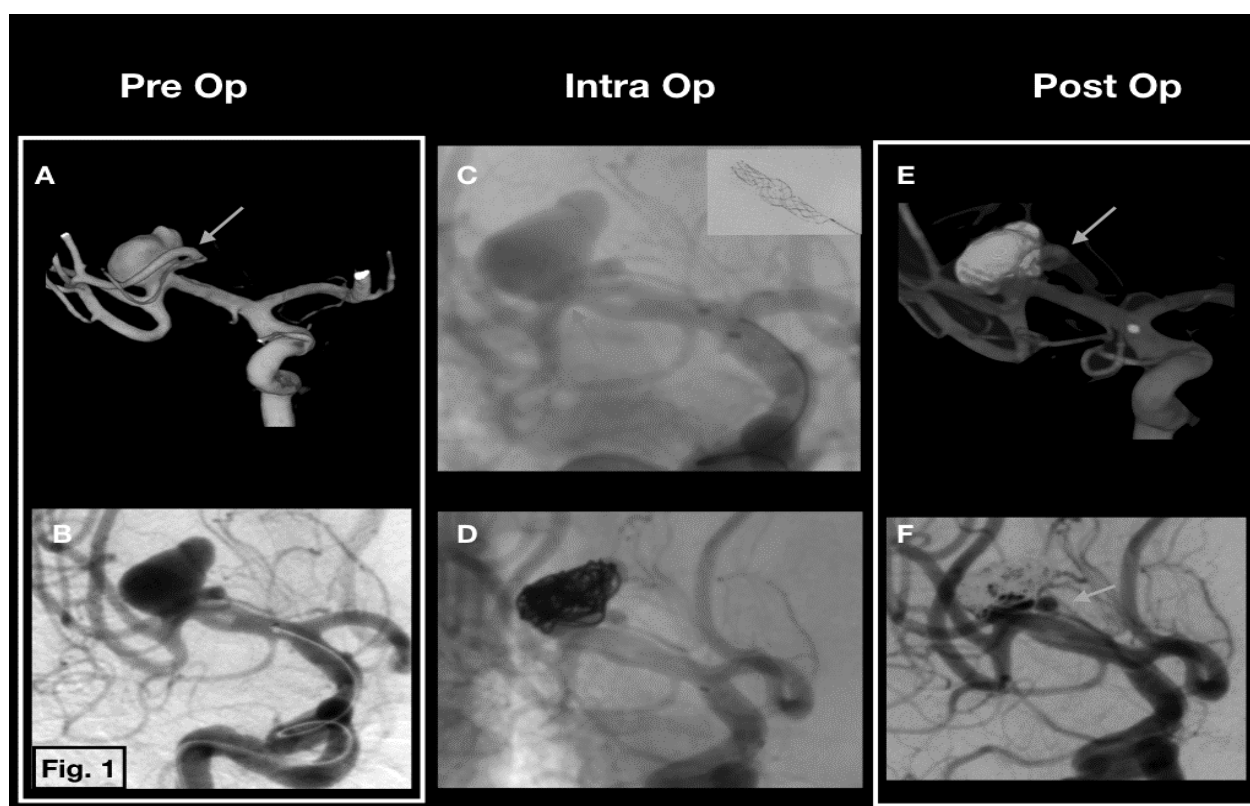


FIGURE 1. Right MCA bifurcation non-ruptured aneurysm with superior division of MCA arising from the neck level (yellow arrow). Barrel VRD was deployed in the inferior branch of the inferior division, the red arrow on Intra OP middle row (upper) indicates the radio-opaque markers protruding below the aneurysm neck. Post-Op pictures are demonstrating total occlusion of the aneurism sac and patency of the superior division of MCA.

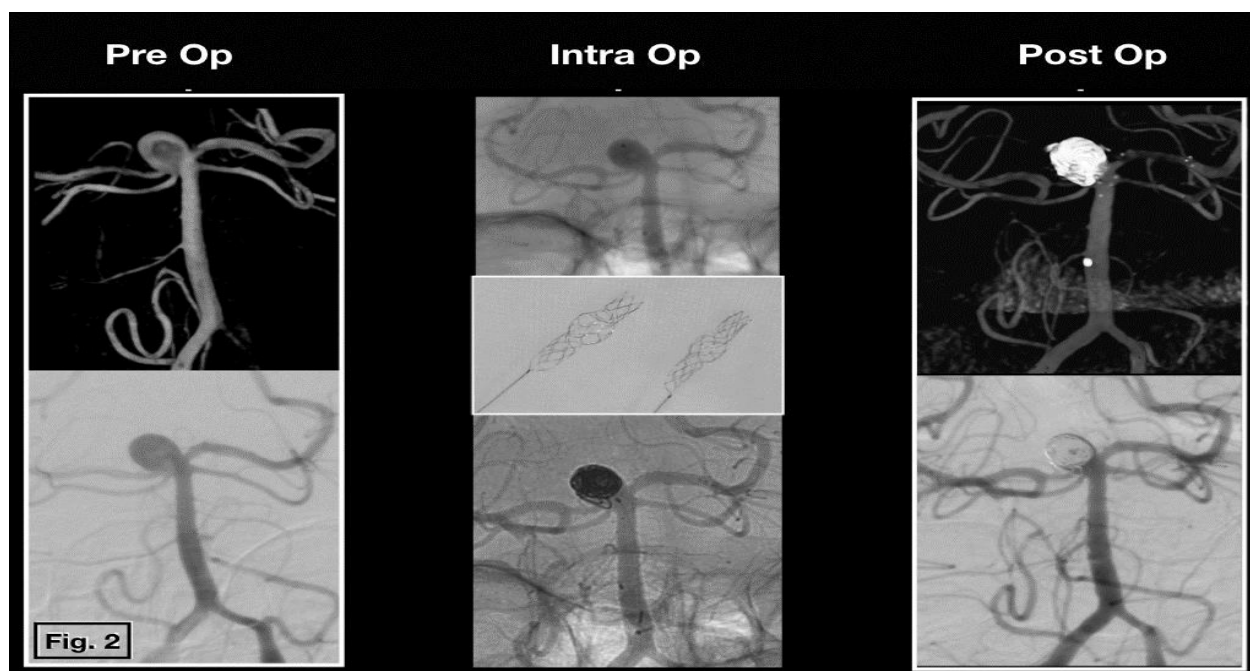


FIGURE 2. Basilar tip non-ruptured aneurysm with both PCA's arising from the neck level; Barrel VRD was deployed between the P1-P2 segment of left PCA and the middle third of basilar artery. Post-Op pictures (3DRA and subtracted 2D images) are demonstrating total occlusion of the aneurism sac and patency of the both PCA's and SCA's arteries.

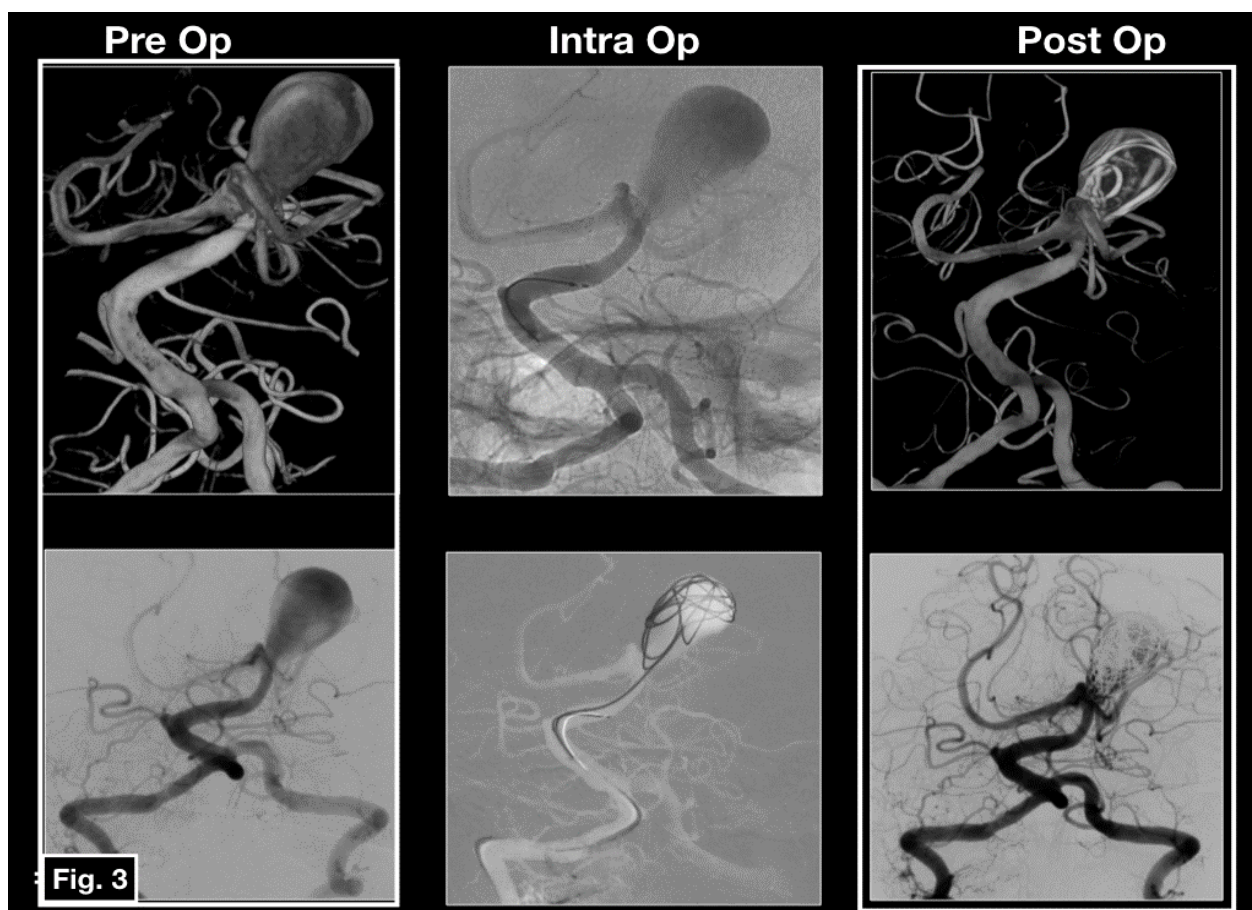


Fig 3. Giant basilar tip non-ruptured aneurysm with both PCA's arising from the neck level; Barrel VRD was deployed between the P1 segment of right PCA and the middle third of basilar artery. Red arrow indicating adequate apposition of the "belly" of the stent at the neck level with protection of both origins of PCA's. Post-Op pictures (3DRA and subtracted 2D images) are demonstrating adequate occlusion of the aneurism sac and patency of the both PCA's and SCA's arteries.

There is high visibility of the markers and positioning of the "barrel" at the neck level is clearly controlled under Road Map in conjunction with non-subtracted fluoroscopy (FIGURE 1 and 3; Intra-Op – middle row, upper image). In the same time the operator has to be aware that in angulated anatomies the stent positioning can be challenging and it requires re-shifting of the stent. Is always preferable the more distal start of deploying than more proximal one. In this way we adjusted permanently the "barrel" part till the best matching with the neck is achieved. In all cases the stent has been detached once the deployment was proper and in the second time micro-catheterism through the stent struts was done without any technical difficulties with an 0,017 coiling microcatheter (Echelon 10/Medtronic,USA) . Coiling of the aneurysm sac was achieved using coils that were 1 mm smaller than aneurysm maximal diameter. This strategy allowed safe coiling of the sac

and also avoided the micro-catheter expulsion from the aneurysm. In the current study, the initial immediate angiographic result was complete occlusion in all cases, and no recanalization occurred during follow-up. We found that this type of technique is useful in cases of asymmetrical WNBA, in which a WEB device is not a feasible solution and is less challenging than Y-stenting technique. In the same time, we are aware of the strong limitation of our small number of aneurysms treated by this technique and certainly further prospective studies comparing this technique with Y-stenting or WEB technique is needed in order to quantify the potential complication rates, long term angiographic outcomes.

CONCLUSION

WNBA remains challenging to endovascular treatment, although new devices that are dedicated

to this type of anatomy are available. Barrel stent seems to be a promising device and difficult anatomies where Y-stenting or WEB device were only technical solution are now suitable for this technique. Main advantage of the device is the possibility to protect complex bifurcations or even trifurcations and branches incorporated at the neck level. However, further study using this technique in a prospective study with a large population and a long follow-up period is warranted.

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COMPETING INTERESTS STATEMENT

No Competing Interests to declare.

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Correlations between clinical, imaging and histological findings in a patient with neurofibromatosis type 1 (von Recklinghausen's disease)

**Gabriela Florența Dumitrescu¹, Anca Sava^{1,2},
Ion Poeată^{1,2}, Danisia Haba^{1,2}, Bogdan
Dobrovăț^{1,2}, Nicoleta Dumitrescu¹, Camelia
Margareta Bogdănici^{2,3}, Claudia Florida Costea^{1,2}**

¹ "Prof. Dr. N. Oblu" Emergency Clinical Hospital, Iași, ROMANIA

² "Grigore T. Popa" University of Medicine and Pharmacy, Iași, ROMANIA

³ "Saint Spiridon" Emergency County Hospital, Iași, ROMANIA

ABSTRACT

Neurofibromatosis type 1 (NF1) or von Recklinghausen disease is one of the most common genetic diseases, affecting 1/4,000 individuals. It is transmitted by autosomal dominant inheritance and the gene NF1, which is responsible for the disease, is located on the long arm of chromosome 17. NF1 is characterized by varied expressions of the disease, even within the same family.

We present the case of a 22-year-old patient with NF1 admitted in the Department of Neurosurgery for a two months history of diffuse intercostal neuralgias that did not respond to treatment and discuss the histopathological and immunohistochemical features of her cutaneous and spinal neurofibromas.

Our case adds new data to the knowledge of the diverse biological behaviour of NF1, highlighting the fact that this condition is a complex disease even in the same individual. We report here a highly variability among neurofibromas in the same patient from a histopathological point of view. Our data are also important as they demonstrate the fact that the management of a patient with NF1, due to the various and complex manifestations of the disease, requires a multidisciplinary approach, including neurologist, neurosurgeon, ophthalmologist, plastic surgeon, dermatologist, radiologist and pathologist.

INTRODUCTION

Neurofibromatosis type I (NF1) is a complex neuro-cutaneous disease with dominant autosomal transmission, whose NF1 gene is located on Chromosome 17. The definitive diagnosis needs the existence in the same individual of two or more criteria from the following seven main elements: a). six or more café-au-lait spots, larger than 5 mm in puberty and larger than 15 mm after puberty, disseminated on the whole body;

Keywords

neurofibromatosis type 1,
cutaneous neurofibroma,
spinal neurofibroma,
pseudomeissnerian
corpuscle, ganglia cell,
immunohistochemistry



Corresponding author
Anca Sava

"Grigore T. Popa" University of
Medicine and Pharmacy, Iași,
Romania

dr.anca.sava68@gmail.com

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b). axillary and inguinal freckling (Crowe sign); c). two or more cutaneous or spinal nerve neurofibromas of any type or at least 1 plexiform neurofibroma; d). optic nerve glioma; e). two or more Lisch nodules (iris hamartomas); f). characteristic skeletal dysplasia; g). at least one first-degree relative affected by NF1 (parent, sibling, child) (1).

However, NF1 is characterized by varied expressions of the disease, even within the same family.

We present the case of a 22-year-old patient with NF1 fulfilling five main criteria of the disease and discuss the histopathological features of her cutaneous and spinal neurofibromas highlighting the fact that NF1 is a complex disease even in the same individual.

CASE PRESENTATION

A 22-year-old female patient was referred to Neurosurgery Department, „Prof. Dr. N. Oblu” Emergency Clinical Hospital Iași, with a two months history of diffuse intercostal neuralgias that did not respond to treatment.

The patient had a positive family history for von Recklinghausen's disease. She had an uncle (44 years-old), her father's brother, with NF1, who was diagnosed five months ago with plexiform neurofibromas of the spinal nerves (from D12 nerve roots to the sacral roots), the terminal segments showing the appearance of pelvic "masses".

Our patient's past medical history revealed a diagnosis of NF1 that was established when she was 8 years old as she has had already *café-au-lait* spots, disseminated on her limbs and trunk, and cutaneous soft, painless tumours, one of them located in her left retroauricular area.

The tumour was incompletely excised when the patient was 12 years old and the diagnosis of a cutaneous diffuse neurofibroma was histopathologically established, thus confirming the diagnosis of von Recklinghausen's (NF1) disease.

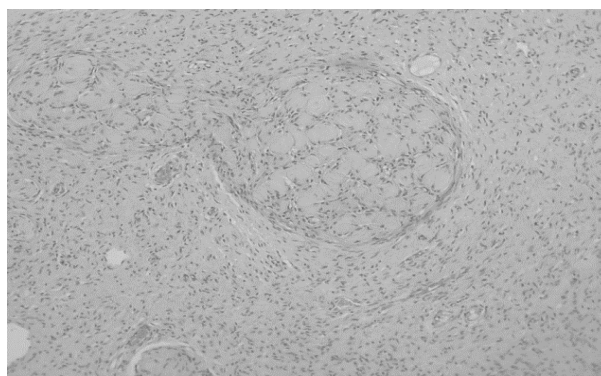
As the tumour slowly increased in size, after 9 years a head Magnetic Resonance Imaging (MRI) was performed, identifying the presence of a lesion that developed in the dermis and distorted the left temporo-occipital region (FIGURE 1).

The tumour was completely excised and the specimen was sent to the Pathology Department where it was processed using the standard histological technique. The immunohistochemical

stainings were performed using anti-S-100 protein antibody, anti-Vimentin antibody, and a two-step staining technique (EnVision+ Dual Link System-HRP, Dako). On histological examination, an intact epidermis covered a relatively ill-defined dermal tumoural proliferation of Schwann cells with hyperchromatic wavy nuclei, few aggregates of pseudomeissnerian corpuscles, associated with fibroblasts and normal appearing nerve bundles. Tumour mass infiltrated the hypoderm, entrapping adipocytes and distorting serous gland acini. Immunopositivity for Vimentin in randomly arranged fibroblasts and intense immunopositivity for S-100 protein in randomly arranged Schwann cells, but also in the cells of pseudomeissnerian corpuscles, established the final diagnosis: cutaneous neurofibroma with pseudomeissnerian corpuscles (FIGURES 2, 3, and 4).



FIGURE 1. MRI T2 SE scan revealed a cutaneous tumour in the left temporo-occipital region.



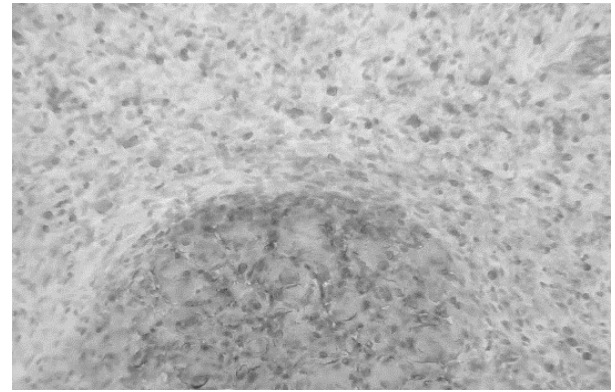
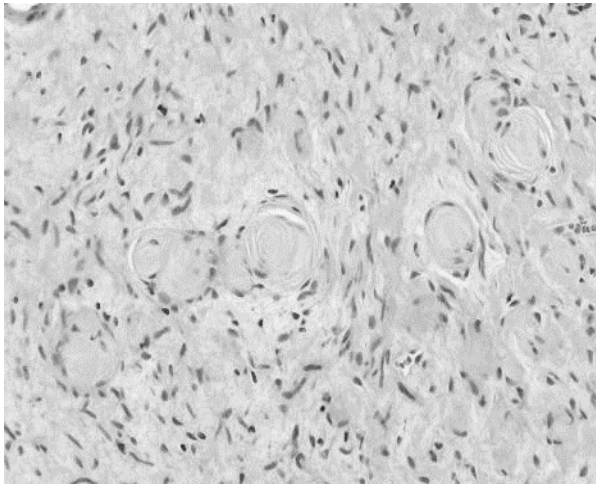


Figure 3. Intense immunopositivity for S100 protein in randomly arranged Schwann cells, but also in all cells located in the pseudomeissnerian corpuscles (anti - S100 protein, x 200).

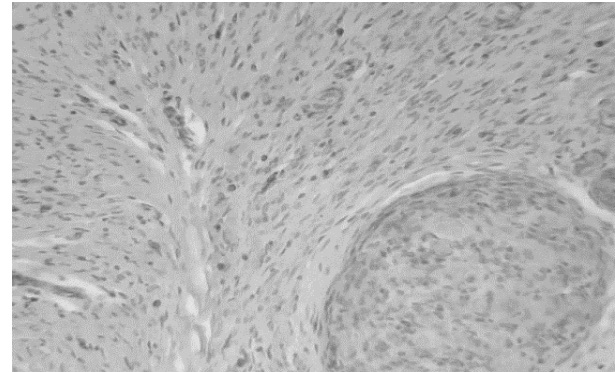
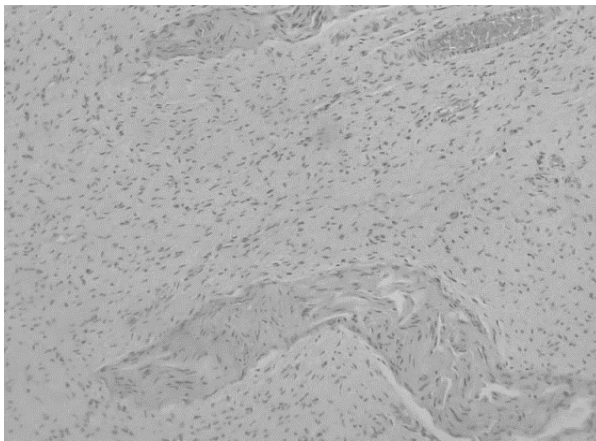


FIGURE 4. Immunopositivity for vimentin in randomly arranged fibroblasts (anti - Vimentin, x 100).

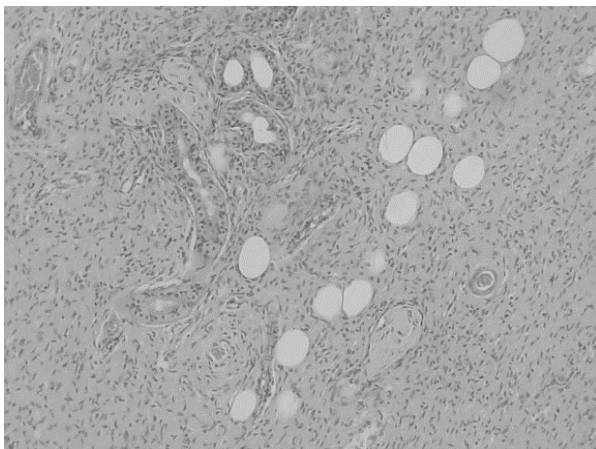


FIGURE 2. Cutaneous neurofibroma: a). Tumoral proliferation of Schwann cells with hyperchromatic wavy nuclei, which were intimately associated with fibroblasts and fine collagen strands. In some areas, there were aggregates of pseudomeissnerian corpuscles (HE, x100); b). tactile-like/pseudomeissnerian corpuscles (HE, x200). c). Small scattered fascicles of nerve bundles entrapped into the tumour mass (HE, x100); d). tumour mass infiltrated the hypoderm, entrapping adipocytes and distorting serous gland (HE, 1200).

One year later, on admission in our hospital due to diffuse intercostals neuralgias, the patient's physical examination revealed: axillary and inguinal freckling, six *café-au-lait* spots with diameters ranging from 1,5cm to 6 cm, located on the trunk, six cutaneous tumours that were soft, pink, painless, ranging from a few millimeters to 2 centimeters, which were located on the dorsal trunk and right shoulder (FIGURE 5).



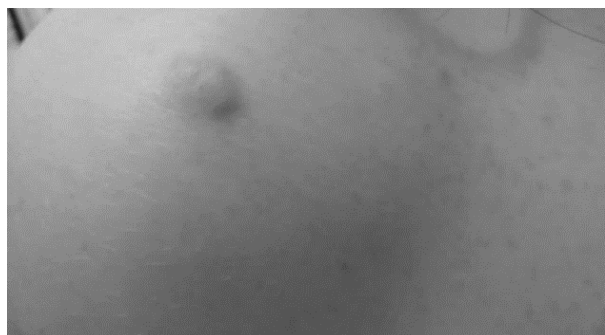


FIGURE 5. a). On the dorsal inferior trunk there were several "café-au-lait" spots, along with red, soft, depressible tumours. b). On the dorsal superior trunk there were three large (ranging from 2 cm to 6 cm in long diameter) "café-au-lait" spots; c). On her right shoulder area there was a cutaneous soft, pink-colored tumour, with a diameter of 1.5cm.

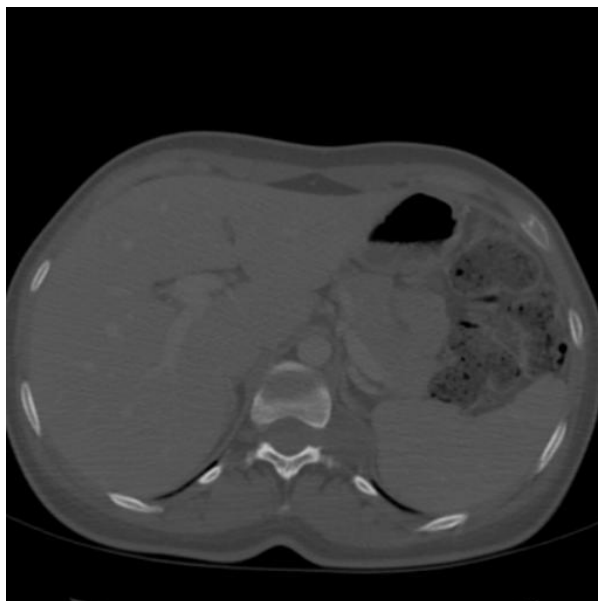


FIGURE 6. The contrast enhanced CT exam showed an intraforaminal and para-vertebral tumour formation with widening of the vertebral left foramen at D10-D11, with left paravertebral extension, being in contact with the superior pole of the left kidney. The nodular aspect of the lesion, visible in the sagittal plane, is associated with the inclusion of the left D10 and D11 spinal roots into the tumoural mass, as seen in the axial image. a). Axial section in a parenchymal window; b). Axial section in a bone window; c). sagittal section.

An abdominal CT scan was performed and revealed the existence of a left paravertebral solid tumour, which was developed intraforaminal and para-vertebral around the dorsal level D11. The tumour extended upward at the D10 level and downward at the D12 level, encompassing left D10 and D11 spinal

roots. The tumoural formation was solid, oval, well defined, with dimensions of 35/16 / 65mm (FIGURE 6).

The standard laboratory tests values were in the normal range.

Surgical intervention was performed by external approach at D11-D12 lateral level, with microsurgical total ablation of the tumour. The surgical specimen was sent to the Pathology Department of the same hospital for histopathological analysis.

The specimen was fixed in formalin, embedded in paraffin, cut at 5 µm and stained with hematoxylin-eosin (HE). On representative sections, immunohistochemical stainings were performed using anti-S-100 protein antibody, anti-Vimentin antibody, and a two-step staining technique (EnVision+ Dual Link System-HRP, Dako). Histological sections stained with HE showed a non-encapsulated tumour, consisting of neoplastic wavy Schwann cells, entrapped ganglion cells as the tumour extended to associated ganglia, a myxoid stroma, and delicate collagen fibers (FIGURE 7). S100 protein immunostaining highlighted neoplastic Schwann cell component and ganglia cells of the spinal root that were entrapped into the tumour (Figure 8). Vimentin immunostaining revealed numerous fibroblasts (FIGURE 9). The final pathological diagnosis was spinal neurofibroma with tumoural infiltration of the associated ganglia.

The ophthalmologic examination revealed myopia in both eyes (best corrected visual acuity in right eye was 1 with -1 D and in the left eye was 1 with - 0,5 D). The ophthalmoscopic examination showed normal appearance of the ocular fundus in both eyes. Direct photomotor reflex was bilaterally present. Intraocular pressure was within normal range: right eye = 12 mmHg and left eye = 13 mmHg. Both eyes presented many small, bright brown, oval, and dome-shaped irian nodules (Lisch nodules) (FIGURE 10).

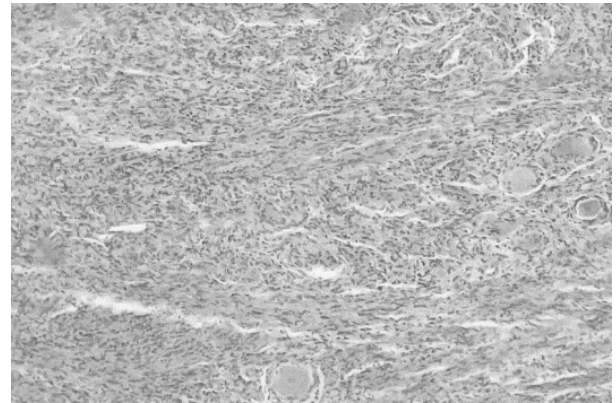
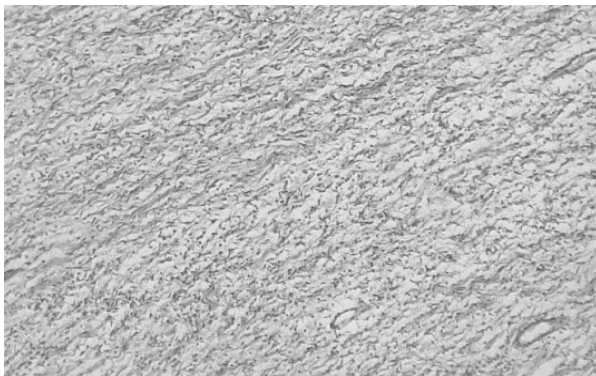


FIGURE 7. Spinal neurofibroma: a). non-encapsulated tumour made up of neoplastic wavy Schwann cells, a myxoid stroma, and delicate collagen (H-E, x100); Numerous ganglia cells entrapped into the tumour mass (HE, x100).

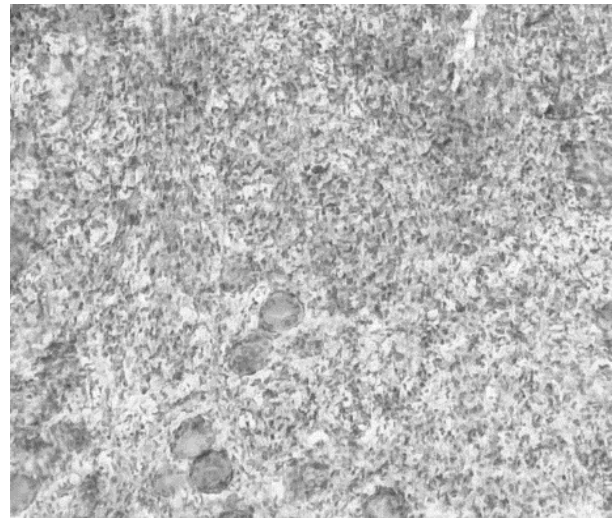


FIGURE 8. Immunopositivity for S100 protein in neoplastic Schwann cells and ganglia cells (anti-S100 protein, x 100).

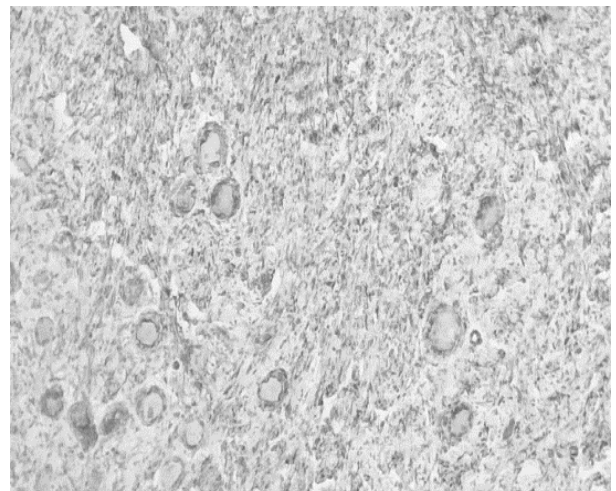


FIGURE 9. Immunopositivity for vimentin in randomly arranged fibroblasts (anti-Vimentin, x 100).

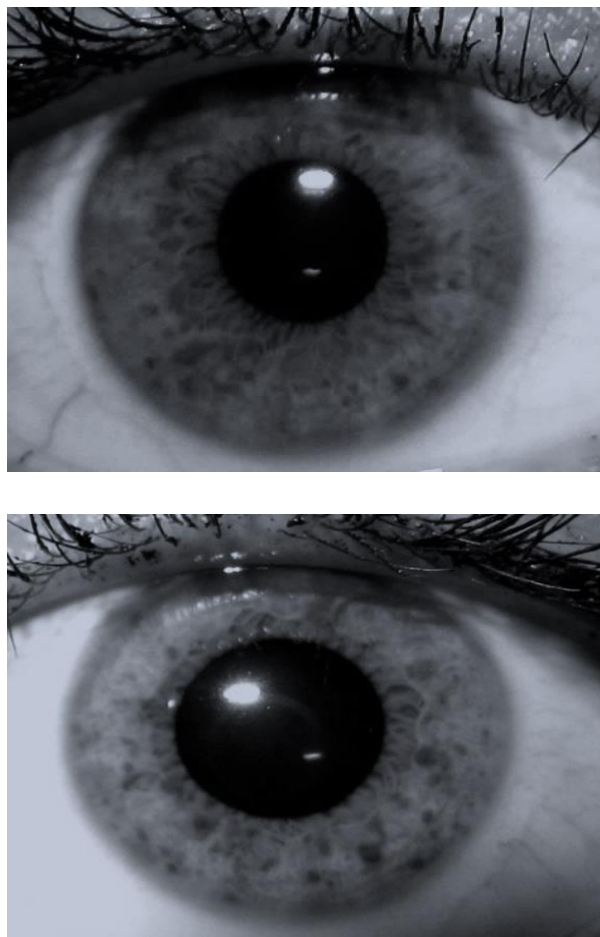


FIGURE 10. Numerous small Lisch nodules at both eyes [a]. right eye; b). left eye].

DISCUSSION

There are suppositions that Ebers Papyrus case #873 can represent the first mention of a case of neurofibromatosis type 1 (NF1) (2). The important landmarks in the history of the disease are the Irish neurosurgeon Robert William Smith, who, in 1849, realized a systematic review of clinical cases (3), and the German pathologist Friedrich Daniel von Recklinghausen (1833-1910), who fully described this condition in 1882. Von Recklinghausen introduced the term “neurofibroma” into clinical practice to define the benign tumours that accompany this disease. He was the first who found that these tumours develop from the peripheral nerve sheath, consisting of a mixture of Schwann cells and fibroblasts (4). In recognition of his discovery, the disease received his name.

However, there are different forms of neurofibromatosis that VM Riccardi, the director of the Baylor NF Program (1978-1990), attempted to

classify the disease in 1982 (5). He considered that there were eight types, but later, in 1986, Carey et al. proposed a new classification into only five types, as follows: NF1 - classical, NF2 - acoustic, NF3 - segmental, NF4 - CALM - familial and NF5 - NF-Noonan phenotype (6).

NF1 represents 90% of all cases with NF, being characterized mainly by multiple café-au-lait spots and neurofibromas along peripheral nerves.

Even though NF1 has been recognized as a clinical entity for more than a century, its etiopathogenesis was better understood only in 1990 when the NF1 gene was identified on chromosome 17. NF1 gene is a tumour suppressor gene that encodes a protein named neurofibromin (7), which is a negative regulator of the “rat sarcoma viral oncogene homologue” (RAS) (8).

Approximately 50% of the cases with NF1 disease represent new mutations and the expression of the disease is highly variable, both between and within families (9).

The most important hypothesis regarding the neurofibromas was that these tumours can develop only after both NF1 alleles have been lost in the Schwann cell lineage. When Schwann cells begin to proliferate, they recruit some other cells from their environment (10). As such, neurofibromas are complex tumours, consisting in a mixture of cell types: Schwann cells, fibroblasts, perineurial cells, and mast cells (7, 10).

It was also hypothesized that these different cellular phenotypes can represent divergent cellular differentiation pathways of multipotent precursor cells (11).

It was considered that the development of neurofibromas include the presence of a clonal population of NF1-/- Schwann cells in a microenvironment harbouring other cell types with an NF1+/- genotype. It was also hypothesised that the multipotent NF1+/- cells are the major source of different cell types found in the neurofibromas (11).

Neurofibromas developing in a NF1-affected individual can be classified according to their anatomical location into: cutaneous, subcutaneous, intraneural, and spinal nerve roots tumours (12).

Cutaneous neurofibromas generally appear during preadolescence. They are soft, pink coloured tumours, sessile or dome-shaped, being most numerous on the trunk and limbs. The tumour diameter usually varies between a few millimetres

and approximately 2 centimetres (11). It is considered that these benign tumours developed from small nerve tributaries of the skin (13). Histologically, cutaneous neurofibromas are nonencapsulated, loosely textured dermal mixed tumours, consisting of Schwann cells, neurons, perineurial cells, fibroblasts, and mast cells, but also adipocytes, epithelial cells, and axonal processes (11). All of these cellular elements are embedded in an abundant collagenous extracellular matrix.

Megahed (14) described ten histopathological variants of neurofibroma: classic, cellular, myxoid, hyalinized, epithelioid, plexiform, diffuse, pigmented, granular cell, pacinian. Subsequently, some other variants such as dendritic cell neurofibroma with pseudorosettes (15), lipomatous neurofibroma (16), and angioneurofibroma (17) have been reported. Pseudomeissnerian corpuscles can be seen in cutaneous neurofibromas, but not so frequently.

Using traditional histological staining as well as immunohistochemical staining (anti-S100 protein antibody and anti-Vimentin antibody) can be the proofs that the neoplastic component is made of Schwann cell. Neurofilament protein immunoreactivity (NFP) revealed the occurrence of residual axons within tumour nodules. Some authors highlighted the fact that, using factor XIIIa as an immunohistochemical marker, the pathologist can differentiate cutaneous neurofibromas from neurotized nevi and cutaneous schwannomas (18). Aggregates of pseudo-meissnerian corpuscles are frequent in diffuse cutaneous neurofibromas (19). As these structures consist entirely of Schwann cells, they can be highlighted with anti-S100 protein antibody immunostaining (20).

Our patient presented at least one cutaneous neurofibroma since he was 8 years-old, but the definitive diagnosis of NF1 was realized only after the surgical excision of the tumour (when patient was 12 years-old). Histological and immunohistochemical examinations identified diffuse cutaneous neurofibroma with clusters of organoid structures resembling Meissner corpuscles (pseudo-meissnerian structures), thus being in line with other researchers' findings.

The incidence of spinal involvement in NF1 patients varies among authors. Mautner et al. reported that spinal neurofibromas are found in up to 38% of NF1 patients but very few of them are symptomatic (21).

In a study of patients with NF1 made by Thakkar et al., 6% of patients had intramedullary tumours, 57% had intraforaminal tumours (dumbbell), and 33% had extradural tumours (22).

At the spinal level, patients with NF1 may have either one or more tumours that can develop in one or more spinal nerve roots. Usually, spinal tumours are diffuse or plexiform neurofibromas. Some authors found out that more frequently these spinal tumours are solitary neurofibromas (23), but others reported plexiform neurofibromas, which grow involving multiple nerve fascicles, branches and plexuses (24). Our patient had a solitary spinal neurofibroma, but her uncle had multiple plexiform spinal neurofibromas. Our article prove the fact that neurofibromas developing in a patient with NF1 can have different histological features, each of them displaying microscopical appearances more closely related to the histology of the region in which the tumour occurs, i.e., cutaneous neurofibroma exhibited pseudomeissnerian corpuscle, and spinal neurofibroma revealed Schwann cells arranged in bundles, reminding of spinal nerve histology.

The age at onset of symptoms caused by spinal neurofibromas can vary from 11 to 49 years (mean 32.8 years), but most cases present symptoms at adult ages (22 to 43 years) (25).

Spinal neurofibromas cause neurological symptoms in only 2% of NF1 patients, provoking both sensory and motor deficits due to compression of the spinal cord or nerve root (22). In a recent article, Mauda-Havakuk et al. analyzed the radiological findings of a series of thirty-four patients with NF1 with spinal neurofibromas. They classified spinal involvement into four types according to the anatomic location of the tumours along the spine and to their type of involvement of the spinal canal and foramina: 1. foraminal tumour; 2. "kissing" tumours; 3. paraspinal tumour; 4. intradural tumour (26). These authors reported that most spinal neurofibromas developed in the lumbo-sacral area and fell into group 1 (foraminal).

Our patient was diagnosed as having a spinal foraminal neurofibroma at the age of 22. As her left D10 and D11 spinal roots were entrapped into the tumour mass, the patient presented a two months history of diffuse intercostal neuralgias that did not respond to the treatment, thus imposing the surgical intervention.

Lisch nodules are hamartomas of the iris that are

also characteristic for NF1. They have variable dimensions and dome-shaped configuration. Some researchers reported that patients affected by NF1 and older than twenty could have an incidence of Lisch nodules of 100% (27). Lewis et al. found out that 92% of subjects aged 6 years and older had Lisch nodules, but their presence was not correlated to number of café-au-lait spots, number of neurofibromas, or severity of disease (28). Our patient, being in her third decade of life, also presented Lisch nodules in both her eyes.

Due to varied and complex manifestations of the disease, the management of a patient with NF1 requires a multidisciplinary approach. Once the diagnosis is established, clinical monitoring is needed to identify possible complications. As a result, annual assessment is required to reduce morbidity and improve the quality of life. This assessment should include: a) dermatological examination to analyze the progression of the existing neurofibromas and to identify possible new lesions; b). head and spine MRI, chest and abdomen imaging to detect the majority of complications that could be associated with this disease; c). full ophthalmological examination for early detection of optic nerve lesions; d). neurological examination for early detection of paresthesia, radiculopathy, muscle fatigue or muscle atrophy; e). removal of skin tumours for cosmetic or therapeutic purposes; f). education and psychological support for NF1 patient.

CONCLUSION

The patient described in this article is a very typical case of NF1, having six "café-au-lait" spots, six neurofibromas, axillary or inguinal freckling, Lisch nodules, and a first degree relative (her father's brother) with NF1. Our case presents a considerable interest because of a complete description of the natural evolution of NF1, highlighting the histological pictures of her cutaneous and spinal neurofibromas. Because the expression of the disease is highly variable, both between and within families, our study data are especially valuable as they also showed a highly variability among neurofibromas in the same patient from a histopathological point of view. These data are also important as they demonstrate the fact that the management of a patient with NF1, due to the various and complex manifestations of the disease, requires a multidisciplinary approach, including neurologist, neurosurgeon, ophthalmol-

ogist, plastic surgeon, dermatologist, radiologist and pathologist.

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Experience of choroid plexus papilloma in children at Mansoura University Hospital

Hatem Badr, Ahmad Zaher, Mohamed State, Amr Farid Khalil

* Mansoura University, EGYPT

ABSTRACT

Choroid plexus papilloma (CPP) are rare, benign tumours of neuroectodermal origin; they represent 1-3% of central nervous system (CNS) tumours in paediatric patients. Authors present their experience in the management of such lesion in Mansoura University Hospitals.

Methods. For children with Choroid plexus papilloma who were treated via microsurgical excision over 4 years from January 2012 to January 2016 in Mansoura University Hospitals, a retrospective analysis was done for age, sex, clinical manifestations, surgical treatment and follow up.

Results. Twenty-three paediatrics were treated over 4 years. Age ranged from (7 months - 8 years). There were 13 female and 10 males. Tumours were located in the lateral ventricle in all cases. Features of raised intracranial pressure were the predominant presentation. Total microsurgical excision was achieved in all cases. All cases had intraoperative blood loss < 100 ml with mean Haematocrit 28%. Follow up period (7-53 months). Complete relief of all symptoms was reported in all cases with no mortality. One of our patients needs postoperative ventriculoperitoneal shunt for persistent CSF leakage and another one required subdural peritoneal shunt for persistent subdural CSF collection.

Conclusion. Total excision of Choroid plexus papilloma is usually the rule with an excellent outcome. Routine external ventricular drainage for at least 3 days is effective in lowering shunt-dependent cases as it allows the release of bloody CSF and small tumour residue. With proper microsurgical technique through superior parietal lobule to access lateral ventricle then tumour coagulation at the same time of irrigation that helps the tumour to shrink and thus, decrease the incidence of bleeding. The tumour vascular pedicle should be resected with the last part of the tumour to avoid pedicle retraction that may lead to ventricular haemorrhage.

INTRODUCTION

Choroid plexus papilloma (CPPs) are benign neoplasms of the choroid plexus, a structure made from tufts of villi within the ventricular system that produces cerebrospinal fluid (CSF) [13, 24]. Lateral ventricle of the brain is the commonest site of CPPs in paediatrics, but they can occur in adults too. Although the major percent of these tumours are considered benign in nature, a small percent is classified to be malignant [1, 3].

CPPs represent about 1% of intracranial neoplasms but this percentage tends to be higher in children (2-4%). The most common

Keywords

choroid plexus papilloma,
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Corresponding author:
Hatem Badr

Mansoura University, Egypt

hatembadr1@gmail.com

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location is the atrium of the lateral ventricle in paediatric population while 4th ventricle represents the commonest location in adults. Cerebellopontine angle (CPA), 3rd ventricle, and parenchyma of the cerebrum are considered rare locations of these tumours [20].

Clinically infants and children with CPP presented with; headache, vomiting, progressive head enlargement and excessive crying, as reported by the patients mothers, usually caused by hydrocephalus that results from; CSF pathway obstruction, CSF overproduction, or arachnoidal fibrosis due to recurrent occult bleeding from tumour [8].

Computed tomography (CT) and magnetic resonance imaging (MRI) show iso- or hyperdense, T1 isointense, and T2 hyperintense masses inside the ventricles that enhance with contrast, generally associated with hydrocephalus [17].

Grossly, these tumours arise as well-circumscribed cauliflower-like exophytic growths from the ventricular wall. Histologically, choroid plexus papilloma appears as papillary proliferation with a fibrovascular core lined by a single layer of monotonous cuboidal to columnar epithelium with a basement membrane [5].

Gross total excision is considered the main line of treatment of these tumours as it is associated with excellent outcomes after surgery. Moreover, adjuvant radiotherapy can be used for progressing tumours that were treated by subtotal resection. A meta-analysis of 566 choroid plexus tumours found no difference in survival when comparing patients with recurrent CPPs and those with stable disease [10].

Choroid plexus tumours can be distinguished from each other via mouth intestinal bacteria (MIB-1) labelling, status of p53, and histology into CPP, atypical papilloma, and carcinoma, and this differentiation can direct follow-up and adjuvant treatment plans later on [22].

In management of choroid plexus papilloma, there are two main problems: treatment of associated hydrocephalus, rich tumour vascular supply that is medially located in these young patients, can lead to a hazardous intraoperative blood loss. Preoperative embolization, to minimize risk of intraoperative loss, is associated with exposure to radiation and also to vessel injury and stroke [21].

We present our experience in management of such lesions in the neurosurgical department located at Mansoura University Hospitals.

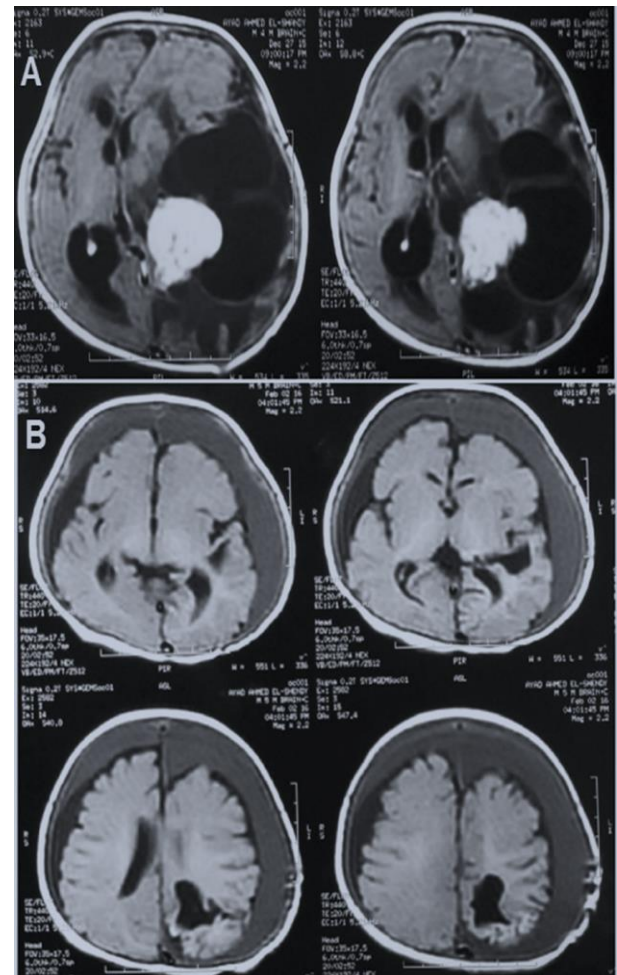


FIGURE 1. A 2-year-old female child with left lateral ventricle choroid plexus papilloma. A: preoperative MRI brain with contrast; B: 3-month follow up MRI brain with subdural CSF effusion and total tumour excision.

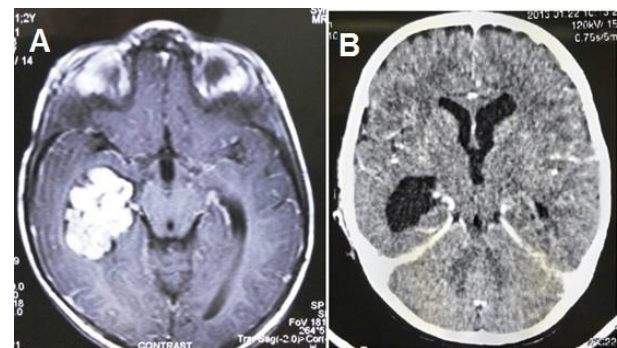


FIGURE 2. A 6-year-old female child with right lateral ventricle choroid papilloma. A: preoperative MRI brain with contrast, B: 1-month follow up CT brain with contrast showing total tumour excision.

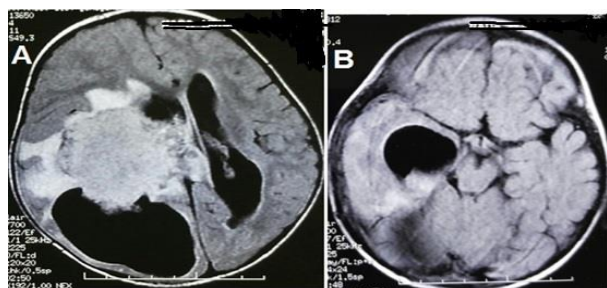


FIGURE 3. Right lateral ventricle choroid papilloma which was managed by microsurgical resection. A: preoperative MRI brain, B: 3-month follow up MRI brain showing no residual or tumour recurrence.

METHODS

Retrospective analysis of children with choroid plexus papilloma who were treated by microsurgical resection over 4 years from January 2012 to January 2016 in Mansoura University Hospitals.

Each patient was subjected to complete medical history taking, through physical examination, routine pre-operative laboratory tests, and radiological studies (CT and MRI brain). The tumour size was calculated as the maximum diameter of the lesion measured by CT and MRI.

All research activities were approved by Mansoura University local ethical committee.

Post-operative complications were classified into two categories; major or minor. Denovo permanent neurological deficits and functional status worsening were classified as major complications. Minor complications included temporary post-operative problems that faded with time like transient cranial neuropathy, temporary postoperative seizures, deep venous thrombosis (DVT), or wound healing problems such as infection, cerebrospinal fluid (CSF) leak, and pseudo meningocele.

The collected data were coded, processed and analysed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (SPSS Inc, Chicago, IL, USA). Qualitative data was presented as number (frequency) and Percent. Quantitative data was expressed as median (range).

RESULTS

TABLE 1: Demographic, clinical, operative, and follow up data.

Variable	Range or number
Age (month)	39 (7 – 96)
Sex	
Male	10 (43.47%)
Female	13 (56.52%)

Variable	Range or number
Symptoms	
-Headache	13 (56.52%)
-Vomiting	8 (34.78%)
-Progressive head enlargement	9 (39.13%)
-Excessive crying	6 (26.08%)
Tumour size (cm)	3.1 (2.4 – 4.2)
Calcification	3 (13.04%)
Major complications	0 (0%)
Mortality	0 (0%)
Minor complications	2 (8.69%)
-CSF leakage	1 (4.34%)
-Persistent subdural effusion	1 (4.34%)
Follow up (month)	20 (7-53)
Need for shunt	2 (8.69%)
Residual in follow up CT	0 (0%)

Twenty-three paediatrics were treated via microsurgical resection over 7 years. Age ranged from (7 months - 8 years). There were 13 females (56.52%) and 10 males (43.47%). Features of increased intracranial pressure were present in all our cases with varying combination like headache, vomiting, excessive crying, and progressive head enlargement.

All cases were evaluated preoperatively via CT and MRI brain. Lateral ventricle of the brain was the site of the CCP in all our paediatric cases. The CT scans showed a mass that was lobulated, globular, and brightly enhancing in the lateral ventricle. Median tumour diameter measured by CT or MRI was 3.1 cm. Calcification was diagnosed radiologically in 3 cases (13.04%), whereas all the cases had varying degrees of hydrocephalus. In all patients, MRI showed an enhancing mass in the lateral ventricle that was isointense on T1- and hyperintense on T2-weighted images.

Total microsurgical excision was performed via the transcortical approach through the superior parietal lobule in the all patients who had the tumour located the lateral ventricle trigone. The tumour was identified and then, its surface was coagulated. Moreover, it was excised after shrinking its size via combined coagulation and irrigation. Coagulation, then division of the vascular tumour pedicle was achieved on removal of the last tumour part.

Routine closed ventricular drainage was applied in all patients to allow CSF drainage for three days post-operatively. That ventricular drain was removed after exclusion of ventricular hematoma by CT scan and absence of red colour in the draining CSF fluid. In one case (4.34%), CSF leakage from the operative

incision occurred and that child needed ventriculo-peritoneal shunt for persisting hydrocephalus. Another patient (4.34%) needed subduro-peritoneal shunt because of persistent, subdural effusion.

The follow-up ranged from 7–53 months (median: 20 months). All patients experienced no symptoms at follow-up as well as the post-operative CT and MRI showed no residual lesions.

DISCUSSION

Choroid plexus papilloma are considered as WHO grade I tumours and are among the most common tumours in the paediatric group less than 2 years. They are of neuroectodermal origin representing 1–3% of central nervous system (CNS) tumours in paediatric patients [23].

Choroid plexus papilloma has been reported to be associated with Aicardi syndrome [4, 25, 28] and Li-Fraumeni syndrome [6]. Leptomeningeal dissemination may occur [7].

Usually, CPPs occur in the lateral ventricles in paediatric population, while the 4th ventricle is the commonest location in adults; other rare sites included 3rd ventricle and the cerebellopontine angle (CPA). CPPs have also been reported in other regions like the suprasellar area, frontal lobe, and cerebellum [17]. In our study, all tumours were located in the lateral ventricle (23 cases).

In children, before closure of the sutures and fontanelles, the sequel of raised intracranial pressure such as blindness will be difficult to manifest. Seizures or mental changes may be the only presentations of these lesions while tumours involving the 4th ventricle may manifest itself with cerebellar signs. Cerebellopontine angle CPPs have been reported to cause cranial nerve deficits [8]. The predominant clinical features in our study can all be traced back to raised intracranial pressure that is consistent in all of our patients.

Clinical picture of CPP in paediatrics includes; headache, vomiting, progressive head enlargement and excessive crying. These are usually caused by hydrocephalus that results from CSF pathway obstruction, excessive CSF production, and recurrent occult bleeding from the tumour that results in arachnoidal fibrosis and adhesions [8].

In our study, headache was present in 56.52 % of cases while vomiting was experienced in 34.78 % of cases. Moreover, progressive head enlargement and excessive crying were reported by the mothers of in

39.13 and 26.08% of our cases respectively.

The mean value of maximum tumour diameter in our study was 3.1 cm, while the study conducted by Safaee and his colleagues included cases with median diameter of 3 cm in the total resection group [21].

Calcification was detected in CT in 13.04% (3 cases) in our study cases. This is consistent with the findings reported in the literature stating that choroid plexus tumours calcification can be detected radiologically in around 4–20% of cases [9, 19].

Surgical gross total excision of the tumour should be attempted in all cases of choroid plexus papilloma [2]. As these tumours are highly vascular, great care should be taken during surgery to avoid excessive blood loss that may lead to mortality, as reported in some series, especially in young children. Securing the main arterial supply of the tumour, which is usually a branch of choroidal artery, is of crucial importance to avoid hazardous intraoperative bleeding followed by coagulation of the tumour and en bloc or piecemeal removal [15].

Regarding surgical excision for paediatric CPPs, there is a surgical opinion stating that there is some sort of benefit from delaying surgery till hydrocephalus develops. That is because this delay lessens the length of the corridor to the ventricles and widens the space surrounding the lesion making it more surgically accessible. The drawback to this delay is that hydrocephalus may not be the presenting symptom, leading to more tumour growing that may lead to neurological deficit that may not resolve after surgical resection [11, 16].

In addition, the drawbacks to a watchful waiting on dealing with such tumours are many. Initially, repeated general anaesthesia will be needed for MRI for follow up which will be burdensome and not devoid of risks. Moreover, although CT scan may alleviate the need for MRI but excess radiation exposure will carry risk to the child as well [11].

We reported that blood loss in this study was less than 100 ml in every patient. No major complications or mortality were reported in our study. Major complications reported in another series were rare, that may be attributed to the fact that these modern studies were conducted at a tertiary care centres [21].

Compared to published series from the modern microsurgical era, our observed morbidity was very minimal, once again confirming that these tumours can

be safely resected in both children and adults [14, 27, 29].

Whereas complete surgical excision is the ideal treatment, it could be impossible to accomplish in some cases, due to excessive blood loss or due to tumour infiltration into the surrounding vital structures. If significant residual tumour is left or recurrence is diagnosed, redo-surgery may be an option after sometime. Moreover, adjuvant therapy has been reported to be another option [18].

Pneumocephalus, pneumoventricle, subdural effusions, persistence of hydrocephalus (in those not previously shunted), and new onset hydrocephalus are the most common reported complications after surgical intervention [21, 26]. Total surgical removal of these tumours is associated with excellent survival that reaches 100% at 10-year follow up as reported in the literature [14].

In our series, only two cases required post-operative shunts; one needed ventriculoperitoneal shunt due to persistent CSF leakage, and the other needed subduroperitoneal shunt for persistent subdural CSF collection.

Although some studies have described neurocognitive sequelae related to surgery for CPP [12, 16], our study is not large enough to make any significant conclusions with respect to differential outcomes in children compared to adults.

Safaee and his associates also reported a 22 % incidence of temporary swallowing dysfunction that required percutaneous endoscopic gastrostomy tubes, tracheostomy, or both, with no difference in the incidence when comparing patients who received gross total resection with the subtotal resection group [21].

The prognosis for CPP patients treated with gross total resection (GTR) is excellent, with a report of 100% survival at 5 years after surgical resection in many series including ours, and adjuvant therapy is not indicated in these patients. Radiotherapy is not necessary after GTR, and its usefulness should be reserved for recurrent disease. Unfortunately, the prognosis for patients with choroid plexus carcinoma CPC is guarded, with an overall 5-year survival rate of 26-50%. GTR is generally considered the most important prognostic factor for CPC as was confirmed in our analysis [14].

Several limitations can be noted in this current study. Small sample size limits the statistical power of our analysis, but is an unfortunate and inevitable

consequence of studying such a rare tumour. Moreover, this study is a single centre study that could affect the validity of our results as it serves a localized population.

CONCLUSION

Total excision of Choroid plexus papilloma is usually the rule with excellent outcome. Routine external ventricular drainage for at least 3 days is effective in lowering shunt dependent cases as it allows release of bloody CSF and small tumour residue. With proper microsurgical technique through superior parietal lobule to access lateral ventricle then tumour coagulation at the same time of irrigation that helps the tumour to shrink and thus, decrease the incidence of bleeding. The tumour vascular pedicle should be resected with last part of the tumour to avoid pedicle retraction that may lead to ventricular haemorrhage.

AUTHORS CONTRIBUTIONS

This work was carried out in collaboration between all authors. Author Amr Farid, designed the study, Author Mohamed State wrote the protocol, Author Ahmed Zaher managed the literature research, Author Hatem Badr performed the statistical analysis and revised the final manuscript. All surgical procedures were carried out by the same surgical team including the four authors. All authors read and approved the final manuscript.

ABBREVIATIONS

CPC	Choroid plexus carcinoma.
CPP	Choroid plexus papilloma.
CPA	Cerebellopontine angle.
GTR	Gross total resection.
MIB-1	Mouse intestinal bacteria.
MRI	Magnetic resonance imaging.

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Hydatid cyst of the quadrigeminal cistern. A case report for unusual location with literature review

**Saif Saood Abdelrazaq¹, Abdullah H. Al Ramadan²,
Ali Adnan Dolachee³, Mohammed Maan
AbdulAzeez⁴, Ali Saud Abdulrazzaq⁵, Amar Saeed
Rashid⁶, Samer S. Hoz⁵**

¹ Neurosurgery Department, Al Sadar Teaching Hospital, Najaf, IRAQ

² Department of Neurosurgery, King Faisal Specialist Hospital and
Research Centre, Riyadh, SAUDI ARABIA

³ Department of Neurosurgery, College of Medicine, Al Qadisiyah
University, IRAQ

⁴ College of Medicine, University of Baghdad, Baghdad, IRAQ

⁵ Neurosurgery Department, Neurosurgery Teaching Hospital,
Baghdad, IRAQ

⁶ Department of Neurosurgery, College of Medicine, Kufa University,
Baghdad, IRAQ

ABSTRACT

Intracranial hydatid cyst involves supratentorial area and mainly affecting the middle cerebral artery territory with the predilection of the partial lobe. It can be single - which is the most common - or multiple up to 35 cysts. They tend to be huge at the time of symptomatic presentation especially when they are presented as a solitary lesion with a slow growth rate around 1.5 cm/year, however, it is variable and it can be up to 10 cm/year. Surgical treatment is mandatory for all patients once the correct diagnosis is made, except for patients with multiple organ involvement in poor general conditions and deep-located cysts. The existence of hydatidosis in the cisternal spaces must not be neglected given the capacity of *E. granulosus* larvae to disseminate via the CSF. In this case report; two and half years' male child presented with a history of 2 attacks of generalized seizure for the last 72 hours with the head circumference at the upper normal limit for his age. This paper presents the first case report demonstrating a primary single hydatid cyst located in the quadrigeminal cistern in a child. We concluded that in spite of the feasibility of the imaging and the high suspension of cerebral hydatid cyst, still, the reports show more locations which can be described as unusual although for a head to toe suspected distribution of hydatid disease is already understood. An eminent medical and surgical (if indicated) treatment of the primary cerebral hydatid cyst are always effective and recommended.

INTRODUCTION

Choroid Echinococcosis could be characterized as a zoonotic infestation caused by cestode species of the genus *Echinococcus* (1).

Keywords

neurosurgery,
hydatid,
quadrigeminal cistern,
case report



Corresponding author:
Mohammed Maan AbdulAzeez

College of Medicine, University of
Baghdad,
Baghdad University, Iraq

mohammed.wwt@gmail.com

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It is most commonly involving the liver then lungs. (2) Intracranial involvement occurs in 1-2% of Echinococcosis and 50-70% of these cases affect the paediatric age group. (3) It showed slightly male preference in most of the case series. (4,5,6,7,8) Geographically endemic area of hydatid disease includes some of South America countries like Argentina, Brazil, Chile, Peru and Uruguay, France, Italy and Greece in Europe, Turkey, Israel, Lebanon, Syria and Jordan in the Middle East, China, Iran, and India in Southeast Asia and Tunisia in Africa. (9)

Intracranial hydatid cyst involves supratentorial area and mainly affecting the middle cerebral artery territory with the predilection of the partial lobe. It can be single - which is the most common - or multiple up to 35 cysts. (10,11,12) They tend to be huge at the time of symptomatic presentation especially when they are presented as a solitary lesion with a slow growth rate around 1.5 cm/year, however, it is variable and it can be up to 10 cm/year. (13) Surgical treatment is mandatory for all patients once the correct diagnosis is made, except for

patients with multiple organ involvement in poor general conditions and deep-located cysts. (14) The existence of hydatidosis in the cisternal spaces must not be neglected given the capacity of *E. granulosus* larvae to disseminate via the CSF. (15)

This paper presents the first case report demonstrating a primary single hydatid cyst located in the quadrigeminal cistern in a child.

CASE SCENARIO

Two and half years' male child presented with history of 2 attacks of generalized seizure for the last 72 hours with head circumference at the upper normal limit for his age.

Initial lab workup was done to exclude metabolic derangements the patient was sent for neuroimaging. The general lab tests were within normal ranges and the brain MRI showed a midline rounded cystic lesion, 5x3 cm in size, located in extra-axially in the quadrigeminal cistern and extend infratentorially to compress the cerebellum downward along with bilateral dilated lateral ventricles (FIGURE 1).

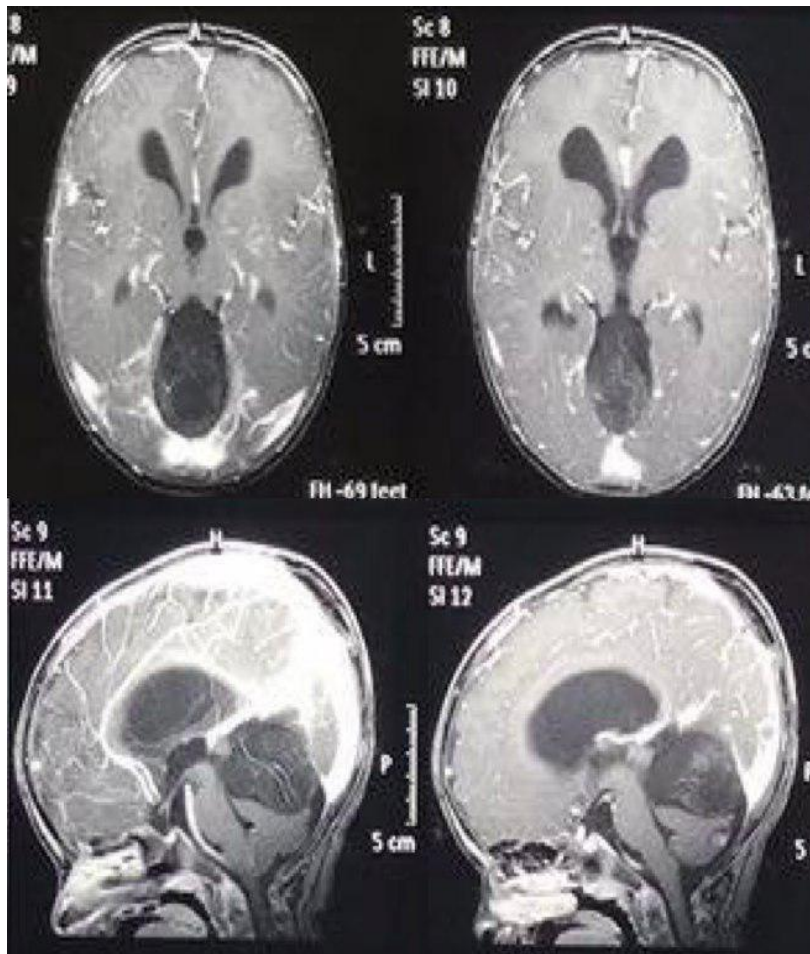
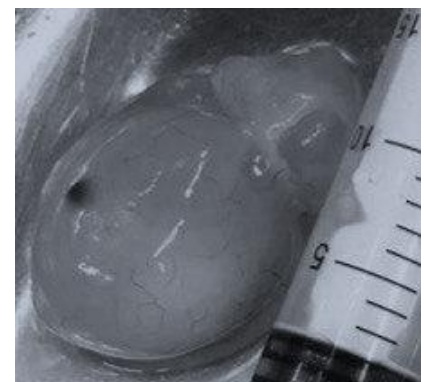


FIGURE 1. Pre-operative brain MRI showing a midline rounded cystic lesion, 5x3 cm in size, located in extra-axially in the quadrigeminal cistern and extend infratentorially to compress the cerebellum downward along with bilateral dilated lateral ventricles. The lesion was hypointense and homogenous in T1 with intensity higher than CSF, hyper-intense in T2 and showed no enhancement in contrasted image, also there was some vivid inclusions within the upper part of the cyst.

FIGURE 2. the delivered intact hydatid cyst.



The lesion was hypo-intense and homogenous in the T1 sequence of the MRI with intensity higher than the CSF, hyperintense in the T2, and showed no enhancement in the contrasted image, also there were some vivid inclusions within the upper part of the cyst.

At that point, the top differential diagnosis included were epidermoid, dermoid and arachnoid cysts only, because that location was an unusual location for a hydatid cyst and the age of the patient was too young for a hydatid cyst.

The decision was to do a surgical resection or fenestration according to the intra-operative

findings. we planned to delay the CSF shunting option as the sulci were not effaced, the young age of the patient and the surgery would remove the cause of the obstruction of the CSF pathways.

The surgery conducted at the next day, an intra-tentorial supra-cerebellar approach was done via midline occipital craniotomy. The cyst was a typical hydatid cyst. The cyst resected as one piece via initial dissection and then delivered using Dowling's hydro-dissection technique (FIGURE 2,3).

The postoperative course went uneventfully. The histopathology confirms the diagnosis, further workup excluded other organs involvement.

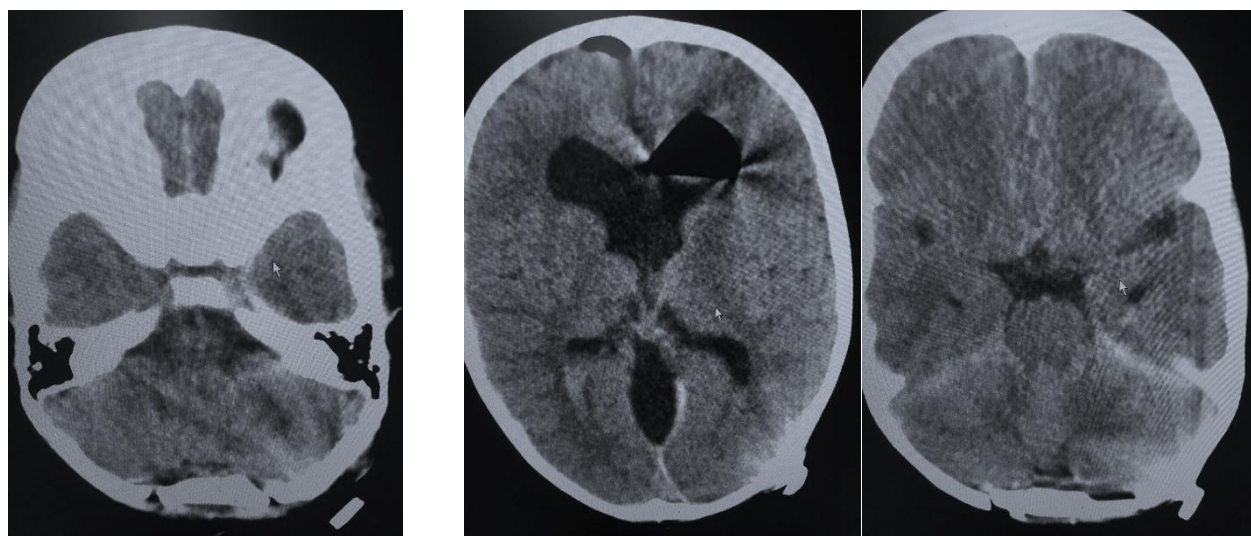


FIGURE 3. Early postoperative axial brain CT scan showing resection cavity

TABLE 1. Intracranial Cisternal Hydatid cysts: Case Report in English Literature

No.	Authors	Age/Gender	Complain	Diameter	Location	Treatment
1	Rumboldt et al (27)	50 Year/ Male	Headache	30 mm	Premedullary Cisten	Surgery
2	Beskonakli et al (28)	33 Year/ Male	Headache and impair vision	N/A	Interpeduncular Cistern	Surgery
3	Sanli et al (29)	7 Year/ Male	Symptoms of high Intracranial pressure	25 x 25 mm	Ambient Cistern	Surgery
4	Kizilca et al (37)	45 Year/ Female	Symptoms of high Intracranial pressure	N/A	Premedullary Cisten	Surgery
5	The authors of this case report	2.5 Year/ Male	Seizure	50 x 30 mm	Quadrigeminal Cistern	Surgery

DISCUSSION

Variant locations of hydatid cyst were reported in the literature including aqueduct of Sylvius (16), Frontal lobe associated with massive edema and raise in the intracranial pressure (17), temporal lobe with midbrain herniation. (18)

Thalamic hydatid cyst was managed surgically through the transcallosal approach in a child who presented with left-sided weakness. (19)

An interosseous lesion involving the skull estimated to represent 3-4% of the lesion involving the skeleton which evident in 2% of all hydatid cyst. (20)

Spinal hydatid cysts are estimated at less than 1%, they are usually extradural and tend to rupture intraoperative more than other location. (21)

Meckel's cave can be involved with extension to the Cerebellopontine angle and the middle fossa. (22)

Brainstem hydatid cyst was reported in middle age woman presented with a headache and progressive hemiparesis. (23) both cases of Meckel's cave and Brainstem hydatid cysts were treated with decompression first prior to the removal to decrease the chances of intraoperative rupture. (22,23)

Cerebellar lesion with mass effect causing obstructive hydrocephalus was encountered in a child with a progressive headache followed by signs and symptoms of high intracranial pressure. (24)

Intraventricular involvement was estimated between 1.3 - 16.6% of multiple case series for intracranial hydatid disease with overall good outcome after surgical excision. (25) Other unusual locations include the seller and the para-sellar regions were reported. (26)

Cisternal hydatid cysts were reported to involve the pre-medullary, the interpeduncular and the ambient cisterns. (27,28,29) (Table 1)

An intermittent headache can be the only presenting symptoms even with a huge cyst. (30) In a Large series from China, headache and vomiting were the most common symptoms, this finding was supported in the literature as well.

Seizure attacks, focal neurological deficits, and skull deformities were reported. Papilledema was frequent in the ophthalmological examination especially in patients with high intracranial pressure, optic atrophy was seen as well. (4,31,32)

The Magnetic Resonance Imaging (MRI) thought to be more sensitive than the computed tomography (CT) to identify the pericystic layer and to

differentiated the hydatid cyst from the other similar cystic lesions like the epidermoid cyst, however, CT scan is more sensitive to identify the calcified lesions. (33)

Serious complications related to the rupture of the hydatid cyst include recurrence, cerebral vasospasm and infarction, hydrocephalus, anaphylactic shock, chemical meningitis, and even death. (34)

In two series of long-term follow up for cerebral hydatidosis in children, it can be concluded that the improvements of the imaging facilities lead to early recognition and improve the outcome. Poor prognostic factors can be identified including delay in the treatment, the rupture of the cyst at the presentation or intraoperatively, and poor control of the systemic disease. Single versus multiple cyst and age at the presentation was not identified as prognostic factors, however, some authors consider the multiplicity as a malignant form of the disease. (35,36)

Review of all the available literature reveals that our case is the first reported case of hydatid cyst located in the quadrigeminal cistern which was removed successfully.

CONCLUSION

In spite of the feasibility of the imaging and the high suspension of cerebral hydatid cyst, still, the reports show more locations which can be described as unusual although for a head to toe suspected distribution of hydatid disease is already understood. An eminent medical and surgical (if indicated) treatment of the primary cerebral hydatid cyst are always effective and recommended.

ABBREVIATIONS

CT: computed tomography
MRI: magnetic resonance imaging
CSF: cerebrospinal fluid

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Cerebral pilocytic astrocytoma with spontaneous intratumoral haemorrhage in the elderly - a rare entity. A case report and review of the literature

Amit Narang, Varun Aggarwal, Divya Kavita, Chandni Maheshwari, Prajjwal Bansal

* Baba Farid University of Health Sciences. Faridkot. Punjab, INDIA

ABSTRACT

Pilocytic astrocytomas (PA) are histologically are low-grade tumours, commonly found in the paediatric and young adult population. Although cases of adult and elderly pilocytic astrocytomas are described in the literature, they are quite uncommon. The rate of PAs with spontaneous bleeding is very less, with a high occurrence in children than in adults, moreover, that is in cerebellar PAs. Cerebral PAs with intratumoral haemorrhage in the older age group is extremely rare. We present a case of a 60-year female presenting with acute neurological compromise resulting from an acutely haemorrhagic Left temporal pilocytic astrocytoma. She was managed surgically with evacuation of tumoral haemorrhages, as well as resection of the tumour. Postoperatively the patient made a remarkable recovery.

INTRODUCTION

Pilocytic astrocytoma (PA) is commonly a paediatric central nervous system glial tumour. Adult occurrence is rare, especially in elderly population. [6,2] The most common sites of PAs origin are cerebellum, optic chiasma, hypothalamus, and to a lesser extent, cerebral hemispheres, brain stem and spinal cord.[6] Reports of tumours with intratumoral haemorrhage in elderly population are extremely rare. Here we present a 60 years old female who presented with left temporal intratumoral bleed mimicing Intracerebral haemorrhage.

CASE SUMMARY

Ours is a 60-year-old female who was a known case of hypertension and was poorly compliant to anti-hypertensive medications. She had complaint of sudden onset of altered sensorium and slurring of speech. There was no history suggestive of Trauma. Patient was taken to a nearest clinic and was managed conservatively on the line of Intra Cerebral Hemorrhage (ICH), and was discharged after seven days. Three days after the discharge patients attendants brought the patient

Keywords

astrocytoma,
cerebral pilocytic
astrocytoma,
elderly population,
intratumoral hemorrhage,
tumor excision



Corresponding author:
Varun Aggarwal

Guru Gobind Singh Medical College
and Hospital Faridkot, Punjab,
India

drvarunaggarwal86@gmail.com

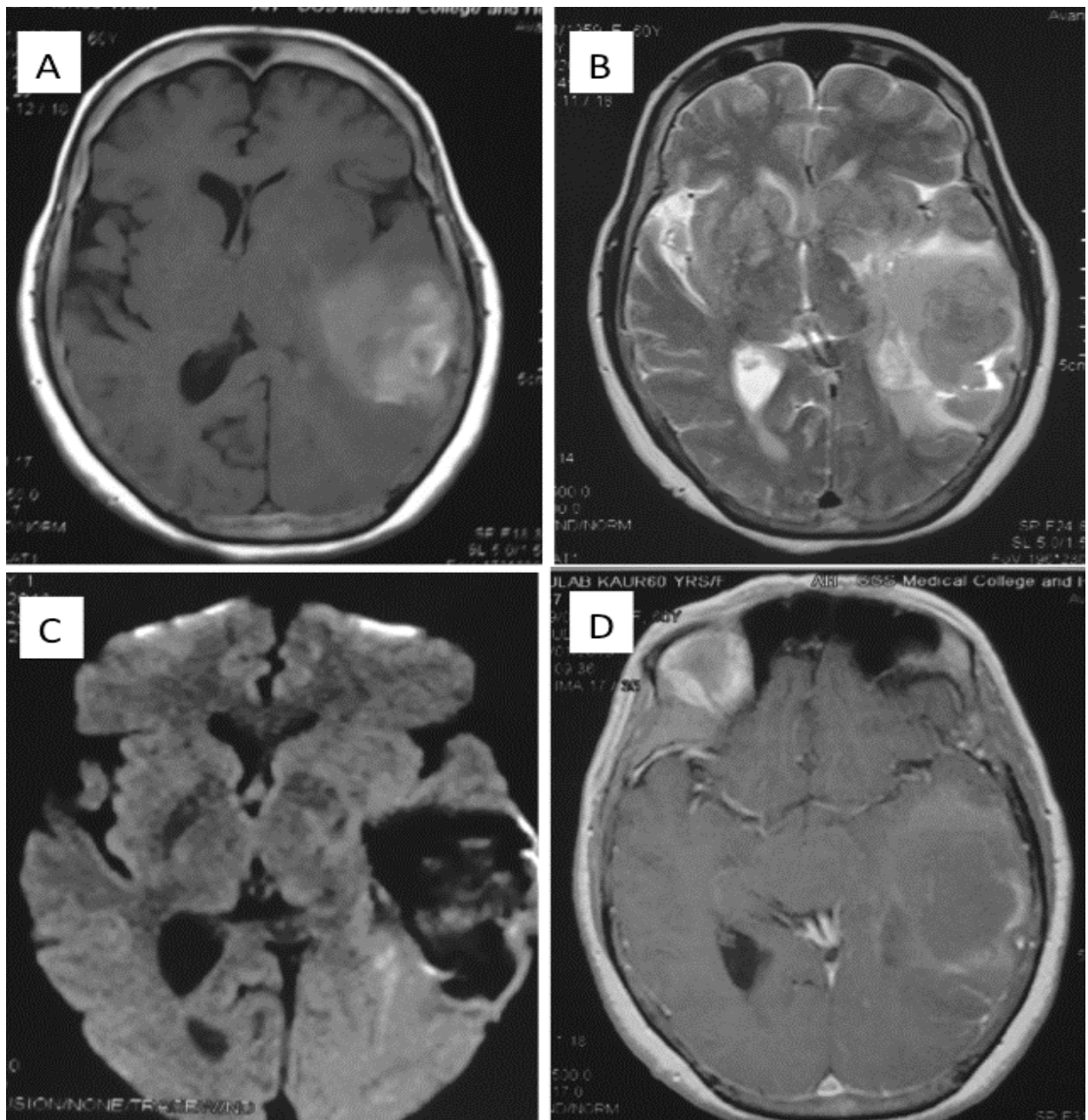
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to our hospital for second opinion. On presentation her GCS was E3V3M5. Contrast MRI Brain was done which was suggestive 48 x 34 mm altered signal intensity lesion in left temporoparietal cortex with vasogenic edema and with mass effect in the form of midline shift of 6.4 mm towards right. The lesion was hypointens on T2, T1 with marginal T1 hyperintensities, hyperintens on flair and intens blooming in gradient images. In post contrast studies subtle marginal enhancement noted. By enlarge, radiological features were suggestive of left Temporal ICH with mass effect. [Fig-1]. Patient was taken up for surgery. Left frontotemporal craniotomy and eva-

uation of intracerebral hematoma was done. Intraoperatively brain was bulging and there was large hematoma in Rt temporal lobe, brain tissue all around the hematoma was greyish, soft and suckable this tissue was excised all around and was sent for biopsy. Post operatively NCCT was done suggestive of complete evacuation of ICH with reduced mass effect [Fig-2]. Histopathology was suggestive of pilocytic astrocytoma (WHO grade I). Patient improved significantly and discharged on 5th Post op day with GCS E4V4M6.

FIGURE 1. A -T1, B -T2, C- DW, D- post contrast MRI showing lesion in left temporal lobe



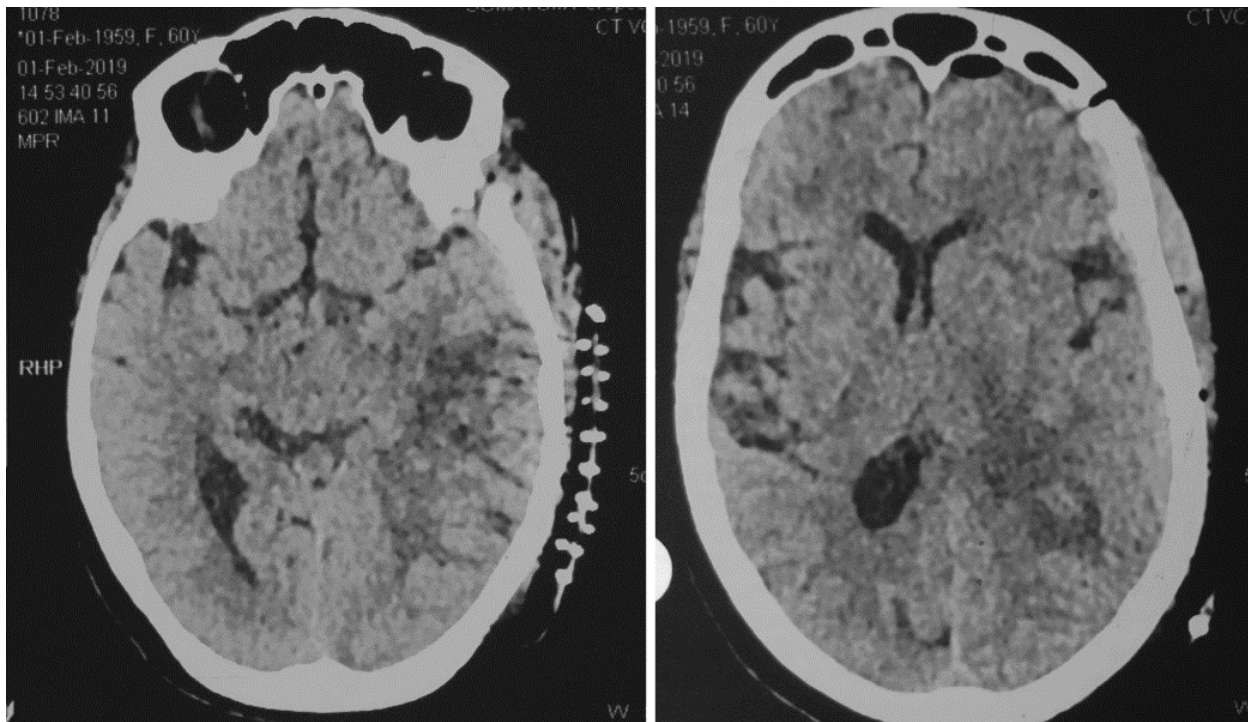


FIGURE 2. First post op day NCCT head showing Complete evacuation of hematoma and reduced mass effect

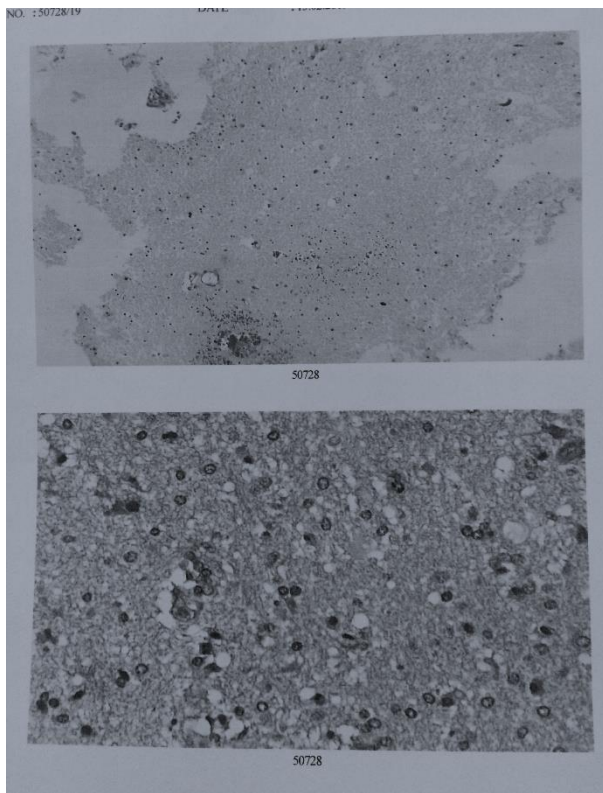


FIGURE 3. Histopathology was suggestive of low grade astrocytic tumor with abundant eosinophilic granular bodies- pilocytic astrocytoma (WHO grade I)

DISCUSSION

PA is a histological subtype of astrocytomas, which accounted for approximately 15% of central nervous system (CNS) tumours. PAs are considered World Health Organization (WHO) grade I tumours, which have relatively distinct histological appearance and well demarcated boundaries. [1,5]. This tumour has much higher occurrence among children and adolescents than elderly. Common age group for PAs is 5 to 14 years, followed by 0 to 4 years and 15 to 19 years, however, pilocytic astrocytoma rarely occur over the age of 60. [2]

Patients having a pilocytic astrocytoma may present with sensory motor deficit, gait disturbance, headaches, cranial nerve deficits and hydrocephalus, depending on the exact location. The most common sites of these tumour origin are cerebellum, optic chiasma, hypothalamus, and to a lesser extent cerebral hemispheres, brain stem and spinal cord. [1] Most of glial tumours, such as high-grade astrocytomas, oligodendrocytes, and mixed astrocytomas, have propensity for intratumoral bleeding. However, intratumoral hemorrhage is very rare among patients with PA. [6]

The rate of PAs with spontaneous bleeding is approximately 8%, with a high occurrence in children than in adults, which is mostly in cerebellar PA [6].

Relatively limited amount of literature is available on PAs with intratumoral haemorrhage in older age group. Although vascular necrosis and tumour invasion are the primary causes of bleeding in high-grade gliomas, the mechanisms underlying low-grade gliomas remains unclear. [3] Previous literature have demonstrated that spontaneous bleeding in PAs is due to interaction of various factors, which includes specific pathological changes in vascular structures of tumour, such as proliferation of vascular endothelial cells, hyaline degeneration and interstitial degeneration. Sun S. et al [6] suggested in their study, the vascular histology of bleeding tumour reveals a poorly developed capillary bed and thin vessel walls. Bleeding tumour blood vessels, although rich in collagen have fewer elastic fibres and poor compliance, which can escalates the chances of tumour rupture. As reported previously the reticular vessels are more prone to rupture, which suggests an association between tumour capillary type and bleeding tendency.[4] In addition, intratumoral bleeding is associated with tumour growth, intratumoral vascular invasion, rupture of an encased aneurysm and coagulopathies. Notably, higher arterial pressure and acute intracranial hypertension are also the predisposing factors. Previous studies also suggest that calcification may contribute to intratumoral bleeding. [6,4]. It has been found that the spontaneous bleeding of PAs is also associated with tumour VEGF expression.[7]

The patient in our case report developed spontaneous intratumoral hemorrhage, but the cause of bleeding is still not clear. Therefore, we speculate that intratumoral bleeding may be attributed to tumour vascular abnormalities and hypertension.

PAs patients with intratumoral bleed leading to raised intracranial tension requires emergency neurosurgical care. Surgery is the preferred the treatment for PAs with hemorrhage, which permits simultaneous removal of tumor and hematoma. Tumors that occurred in the brain stem or visual pathway usually cannot be completely removed by surgery, though the residual tumors may cease to grow, or grow slowly, or even regress. Therefore, a long-term follow-up is required for patients with complete and partial resection. The patients treated with subtotal resection may require post op chemotherapy and radiotherapy, but it is still a

matter of debate. The prognosis of patients with PAs is generally good. The location of the tumour and the extent of the resection can play an important role in the prognosis of PAs patients. Reoperation may be considered for most patients with recurrent PAs. Patients with partial resection of tumour can have a higher risk of recurrence. [8] literature suggests that a longer follow-up period is required for PAs patients with intratumoral haemorrhage.

CONCLUSION

Based on the collective results from the present clinical experience and other related studies, we suggest that cerebral PAs with spontaneous intratumoral haemorrhage is extremely rare, especially in elderly patients over the age of 60 years. We agree with the literature that to completely remove the tumour and hematoma; surgery is probably the most effective treatment option. Long-term follow-up after surgical treatment of PAs with intratumoral haemorrhage is crucial to identify and treat the recurrence if any.

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Traumatic posterior fossa extradural hematoma. A comprehensive analysis of cases from a tertiary care centre in Southwestern Rajasthan

Vibhu Shankar Parashar, Vivek Kumar Kankane,
Gaurav Jaiswal, Tarun Kumar Gupta

* Department of Neurosurgery, Rabindra Nath Tagore Medical College & M.B. Groups of Hospital, Udaipur, Rajasthan, INDIA

ABSTRACT

Background. Extradural hematoma of posterior fossa (PFEDH) is less common and there are not many articles about PFEDH. These patients can deteriorate very rapidly due to compression over brainstem. Thus, early identification and immediate intervention can save the lives of these patients.

Objective. This study aims to conduct a comprehensive analysis of patients with PFEDH and evaluate the postoperative outcome which may be of help to make further preventive strategies.

Methods and Materials. The study included 16 patients admitted with traumatic PFEDH from July 2016 to July 2018 at R.N.T. Medical College & M.B. Groups of Hospital Udaipur, southwestern Rajasthan, India. We have retrospectively reviewed the data. Analysed factors were gender, age, Glasgow Coma Scale (GCS), Noncontrast CT scan findings, associated brain injury, type of intervention, Glasgow Outcome Scale (GOS). GOS was assessed at discharge, at 3 months and 6 months follow-up.

Results. Out of a total of 16 patients, 11 were male and 5 were female with age ranging from 05-46 years. 12 patients had GCS 13-15 at admission and only one of them had GCS < 8. 15 patients underwent surgical intervention. At 6 months follow-up, 12 patients had good recovery GOS is 5.

Conclusion. Early detection and immediate evacuation of PFEDHs should be done if causing fourth ventricle, basal cistern or brain stem compression. It may be rapidly fatal due to the expansion of hematoma leading to brainstem compression, tonsillar herniation, and/or obstructive hydrocephalus. Early detection and immediate evacuation lead to a better outcome in these patients.

INTRODUCTION

PFEDH is an uncommon trauma sequel accounting for only 4% to 12.9% of all EDHs^[1,2]. In PFEDH clinical progress may be silent and slow, but sudden deterioration may occur without significant warning signs. Because of limited space in posterior fossa, comparatively small volume can cause clinical deterioration. The patient may deteriorate very rapidly due to compression over the brainstem usually without

Keywords

posterior fossa,
extradural hematoma,
traumatic,
Glasgow outcome Scale



Corresponding author:
Vivek Kumar Kankane

Rabindra Nath Tagore Medical
College & M.B. Groups of Hospital,
Udaipur, Rajasthan,
India

drvarunaggarwal86@gmail.com

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any prior warning sign. Thus, early intervention before progression to herniation is lifesaving. Early diagnosis by cranial computed tomography and emergent evacuation is vital for a good outcome [3].

MATERIAL AND METHODS

In our study, we have retrospectively reviewed the data from July 2016 to July 2018 at tertiary care hospital in R.N.T. Medical College & M.B. Groups of Hospital Udaipur, southwestern Rajasthan. We found 16 cases of traumatic Extradural Hematoma (EDH) which were located in the posterior fossa.

The Data was analysed for clinical presentation, Glasgow Coma Scale (GCS) at admission, mode of injury, radiological findings, any other associated

intracranial traumatic lesion, type of intervention and postoperative outcome. Postoperative scans, within 6-12 hour of surgery were acquired in all cases. Outcomes were assessed on the basis of Glasgow Outcome Score (GOS) divided into good (normal, moderate disability) and poor (severe, vegetative, dead) outcome at 3 months, 6 months of follow-up. We also assessed the prognosis of posterior fossa EDH depending on the compression over the fourth ventricle, basal cistern and brain stem. All patients were divided in two groups. Group A were those who showed isolated PFEDH and in group B were those patients who showed PFEDH associated with brain injury.

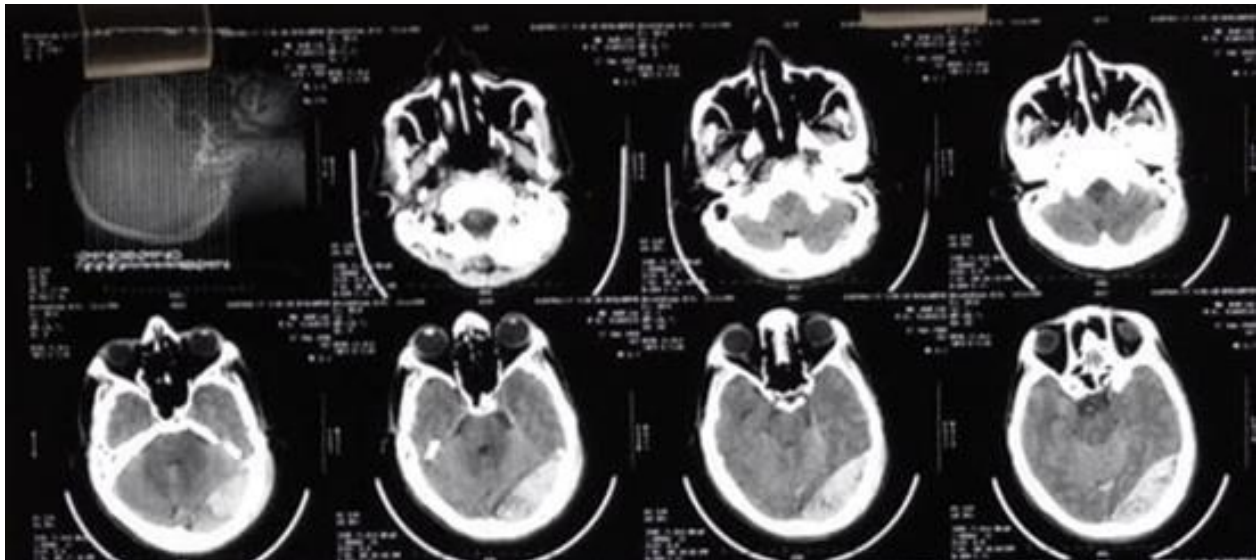
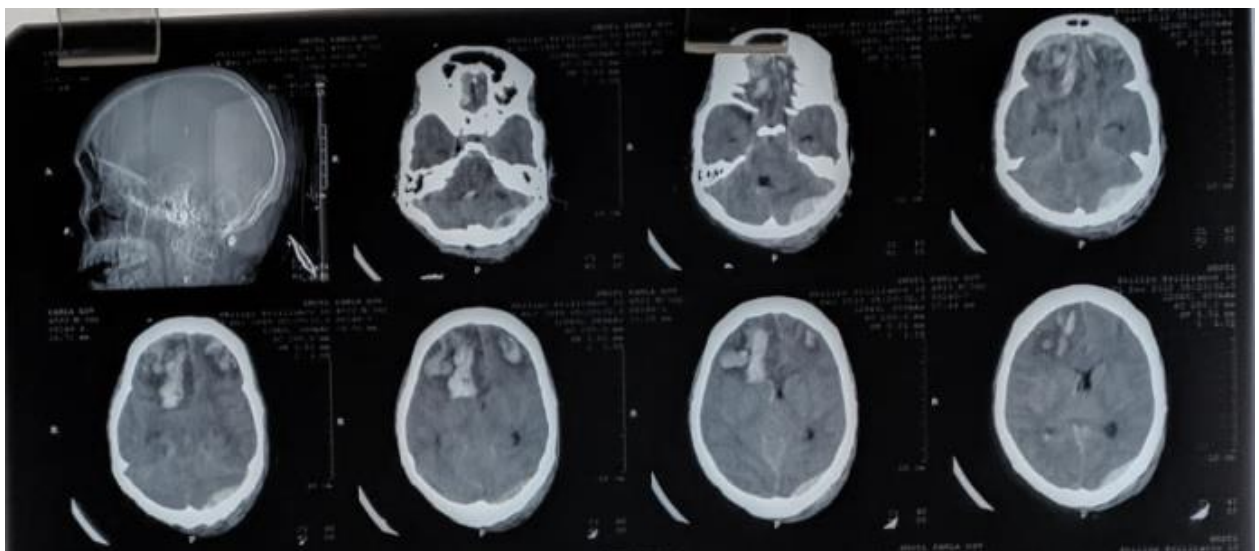


FIGURE 1. NCCT head revealed Left posterior fossa Extradural Hematoma with supratentorial extension

FIGURE 2. NCCT head revealed left posterior fossa Extradural Hematoma with bilateral frontal intracerebral hematoma



RESULTS

A total of 16 cases of PFEDHs were admitted to our tertiary care centre during 24 months from July 2016-July 2018. The mean age of patients was 28.6 years (range 5-46 years). 3 (18.75%) of them were below 18 years. 5 (31.25%) of them were Females (TABLE 1). Outcome was better in paediatric patients.

Most common mode of injury was road traffic accident (n= 11, 68.75%), rest were either fall from height (n = 04, 25%) or assault (n =1, 6.25%) (TABLE - 2). Most common associated radiological finding is occipital bone fracture followed by supratentorial

extension of EDH and frontal contusions (TABLE 3).

15 patients underwent surgical evacuation. At 6 months follow-up, 12 (75%) patients had good recovery and one patient died (6.25%) (TABLE 4). Patients with PFEDH with associated brain injury had lesser GCS Score on admission with increased volume of EDH, increased hospital stay. Outcome was poor in PFEDH patients with associated intracranial injury as compared to those with isolated PFEDH. (TABLE 5)

TABLE 1. Correlation of Gender and Age and outcome analysis

Total cases	Number. of patients (N=16)	AGE<18 Yrs	AGE>18 yrs	Percentage (%)	Good outcome (GOS 3-5)	Poor outcome (GOS1-2)
Gender						
Male	11	03	08	68.75%	10	01
Female	05	00	05	31.25%	03	02
Age						
Pediatric patients (<18)	03			18.75 %	03	00
Adults	13			81.25%	10	03
Total	16			100%	13	03

TABLE 2. Correlation of mode of injury, GCS at admission and outcome analysis

	No. of patients	Percentage	Good outcome (GOS 3-5)	Poor outcome (GOS 1-2)
Mode of injury				
Road traffic accident	11	68.75%	09	02
Fall from height	04	25%	03	01
Assault	01	6.25%	01	00
GCS at admission				
13-15	12	75%	12	00
9-12	03	18.75%	01	02
3-8	01	6.25%	00	01
Total	16	100%	13	03

TABLE 3. Analysis of clinical presentation and radiological findings

	Number of patients	Percentage
Clinical presentation		
Headache	10	62.5%
Altered sensorium	06	37.5%
Vomiting	08	50%
Radiological findings		
Occipital bone fracture	12	75%
Frontal contusions	01	6.25%
Supratentorial extension of EDH	02	12.5%
Hydrocephalus	01	6.25%
Intraventricular hemorrhage	01	6.25%

TABLE 4. Outcome based on GOS (Glasgow outcome score)

Outcome based on GOS	Discharge	At 3 months	At 6 months
GOS 5	11	12 (75%)	12 (81.25%)
GOS 4	03	01 (6.25%)	No follow up
GOS 3	00	01 (6.25%)	01 (6.25%)
GOS 2	01	01 (6.25%)	01 (6.25%)
GOS 1	01	-	-

TABLE 5. Analysis of patients with isolated PFEDH and those with associated brain injuries

Parameters	Isolated PFEDH (Group A)	PFEDH and associated brain injury (Group B)
Total patients	13(81.25%)	03(18.75%)
Radiological findings		
Occipital bone fracture	10(76.9%)	02(66.7%)
Frontal contusions	-	01(33.3%)
Supratentorial extension of EDH	-	02(66.7%)
Hydrocephalus	-	01(33.3%)
Intraventricular hemorrhage	-	01(33.3%)
GCS (admission)		
15-13	11	01
12-9	02	01
8-3	00	01
Management		
Surgical evacuation	11	03
Conservative	02	00
Failed conservative and operated	01	00
GCS (discharge)		

15-13	13	01
12-9	00	01
8-3	00	01
Good outcome (GOS 3,4,5)	12	01
Poor outcome (GOS1,2)	01	02

DISCUSSION

Traumatic brain injury is emerging as the most common cause of morbidity and mortality in both developed and developing countries. PFEDHs are reported to constitute 0.1–0.3% of all cranial traumatic conditions. Loss of consciousness and vomiting are the most frequent presenting features of PFEDH which comprises around 10% of EDH. A history of occipital bone fracture combined with these symptoms should raise suspicion of PFEDH. Lucid interval is classically seen in EDH; however, it is uncommon in PFEDH and in children. A rapid deterioration is a feature of these lesions. Thus, all patients need to undergo imaging promptly in order to diagnose the lesions.

Unlike supratentorial EDHs where the source of bleeding is usually the middle meningeal artery in temporo-parietal EDHs and the anterior ethmoidal artery in frontal EDHs.^[4] PFEDHs have a venous origin in 85% of the cases and develop as a result of injury to the transverse or sigmoid sinuses secondary to occipital bone fracture.^[5] However, an extradural hematoma can develop without fracture. Since most of the PFEDHs are of venous origin and expand slowly, it takes longer for the clinical picture to develop in PFEDH and it is of vital importance to use imaging methods for early diagnosis. Currently, NCCT scan is the imaging of choice in brain trauma.

In the literature it has been reported that PFEDHs are most commonly encountered in the first decade.^[6,7] In our study, 03 (18.75%) cases were paediatric patients. Male gender dominated in our group, which is in line with data in the literature. This fact is explained by greater liability to trauma at work, road accidents and alcoholism in men. A leading cause of PFEDHs in our series were road traffic accidents, although in paediatric patients the most common mode of injury was falls. In all the female patients, the reason for traumatic PFEDH was attributed to sitting on vehicles as pillion riders and indicating the lack of support in the vehicles.

The majority of PFEDHs were unilateral with prevalence on the left side (93.75%). In one patient

(6.25 %) the PFEDH was bilateral and similar observation was reported by Karasu *et al.* Fracture of occipital bone is a common feature (in 58-95% of PFEDH) even though not all of them are visible on plain X-rays of the skull. 75% of our patients had fracture of occipital bone, or parietal bones in occipital region on the side of extradural hematoma.

Whereas some authors reported the occurrence of coexisting lesions in 23 - 50% of cases. We also observed them in three of our patients. The most common associated intradural lesion was supratentorial extension of EDH, brain contusion followed by a subdural collection and acute hydrocephalus.

Bozbuga *et al.* reported 73 cases in 1999, the largest series on PFEDH till now. Out of 73, they operated 53 cases^[6]. 89% of operated patients had a good recovery, and 5.4% died. Malik *et al.* published another series of 61 patients in 2007^[8]. Of these 48 were managed surgically, 36 (59%) had a good recovery and 15% died. Roka *et al.*^[9] reported 43 patients in 2008, of these 33 were operated and were followed up for 79 months with 81.8% good recovery in the operated patients and 3% overall mortality^[9].

In our study 15 patients underwent surgical evacuation. During 6 months follow-up, 12(75%) patients had good recovery and one patient died (6.25%). This was similar to study by Jang *et al.*^[10] and Balik *et al.*^[11]. Jang *et al.*, in 2011, published the review of 34 patients with 96 months follow-up^[10]. Nineteen patients underwent surgical evacuation with 73.7% having a good recovery and 5.3% mortality.

Three series comprised paediatric cases only., Gupta *et al.* in 2002^[12], Sencer *et al.*, in 2012^[13] Prasad *et al.* in 2015^[14], and published paediatric series with 18, 40 and 18 cases, respectively. Sencer reported good recovery in all cases. Prasad's series had 94.4% patients with good recovery. Both these series showed better outcomes in paediatric age group. Outcome was better in paediatric patients in our study.

Admission GCS is the single most important

factor that determined the immediate and long-term outcomes. Patients with additional intracranial findings had relatively poor GCS at admission and categorically much poor outcomes. Patients with mass effect over brainstem had lesser GCS Score on admission with increased volume of EDH, increased hospital stay and increased mortality^[15]. Nonsurgical management is a viable option in select patients with low EDH volumes, but option should be kept for surgical evacuation in such patients for better outcome.

CONCLUSION

PFEDH is a rare entity and posterior fossa is an unfavorable location. They are usually associated with occipital bone fractures. Early diagnosis and emergent evacuation lead to good outcome.

PFEDH may be rapidly fatal due to the expansion of hematoma and compromise of the posterior cranial fossa space leading to brainstem compression, tonsillar herniation, and/or obstructive hydrocephalus which are associated with worse outcome.

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Secondary (Duret) brainstem haemorrhage may not always represent a fatal event. Review of literature and report of four cases

Martin Hanko¹, Branislav Kolarovszki¹,
Kristián Varga¹, René Opšienák¹, Pavol Snopko¹,
Radoslav Hanzel¹, Kamil Zeleňák²

¹ Clinic of Neurosurgery, University Hospital in Martin, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, SLOVAKIA

² Clinic of Radiology, University Hospital in Martin, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, SLOVAKIA

ABSTRACT

Background. Secondary brainstem haemorrhage (eponymously called Duret haemorrhage) is a well-known complication of transtentorial brain herniation or of rapid decompression of intracranial space. It is considered to be a consequence of arterial rupture, venous infarction or ischemia-reperfusion injury and it is regarded as a harbinger of an unfavourable outcome for the patient. Despite this, several case reports describing good outcome after Duret haemorrhage preceded by evacuation of an expansive traumatic intracranial mass lesion, an episode of intracranial hypotension or lumbar drainage have been published.

Case description. We present four cases of patients with secondary brainstem haemorrhage linked to an episode of intracranial hypertension due to various reasons who were treated at our clinic. The first patient suffered a small brainstem haemorrhage that was described on his initial CT scan presumably as a result of massive intracranial expansion caused by an acute subdural haematoma and this Duret haemorrhage markedly expanded after the subdural haematoma was evacuated by means of a decompressive craniectomy. The next two patients developed Duret haemorrhage after the evacuation of intracranial haematomas. The fourth patient presented with posttraumatic cerebral oedema complicated by a subtle Duret haemorrhage displayed on his initial CT scan and this bleeding remained stable even after a bilateral decompressive craniectomy. One patient passed away, one remained in a persistent coma and two survived with a light neurological deficit.

Conclusions. However ominous a newly discovered Duret haemorrhage may be, it alone should not discourage us from the further intensive treatment of our patients as their outcome may considerably vary. The extent of this bleeding, type and severity of underlying brain injury and complete clinical status and history of our patients should all be taken into account when deciding about patients' prognosis.

INTRODUCTION

Originally described by a French surgeon Henri Duret^[6], secondary

Keywords

Duret haemorrhage,
intracranial hypertension,
prognosis, secondary
brainstem haemorrhage



Corresponding author:
Branislav Kolarovszki

Jessenius Faculty of Medicine in
Martin, Comenius University in
Bratislava, Clinic of Neurosurgery,
University Hospital in Martin
Kollárova 2, 036 59 Martin,
Slovakia

kolarovszki@jfmmed.uniba.sk

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brainstem haemorrhages or eponymously Duret haemorrhages are a feared consequence of a transtentorial brain herniation or of a decompression of the intracranial space by means of craniectomy or by removal of an intracranial mass lesions^[16,21,22].

They can occur with a delay of only 30 minutes after the initial insult and primarily affect the ventral midline parts of the pons and the mesencephalon, but never the medulla oblongata^[7,15,26]. Because such haemorrhages often irreversibly destroy the brainstem reticular formation, functional centres and descending pathways, their prognosis is usually very poor with patient either dying or surviving for a limited amount of time with a severe deficit, often unconscious and ventilator-dependent^[15,18,26]. However, case reports of patients suffering Duret haemorrhage and achieving a highly favourable outcome with a gentle or no persistent neurological deficit are known^[1,2,3,8,11,16,20]. Currently, the question of whether a diagnosis of Duret haemorrhage should discourage us from an aggressive treatment is debated. In this work we review the available knowledge concerning secondary brainstem haemorrhage with attention paid on its pathogenesis and outcome of patients who suffer it. We also present four cases of our patients with Duret haemorrhages which resulted in various outcome.

CASE PRESENTATIONS

Case A

A 50 years old man was found unconscious with a right-sided mydriasis. He had a history of chronic alcoholism and ethylic liver disease. The emergency ambulance was called, he was intubated and

sedated, then transported to our hospital. After arrival, his GCS score was 4 (1-1-2), he was anisocoric with bilateral absence of pupillary and corneal reflexes and with a decerebrate response to painful stimuli. CT scan verified an acute left-sided subdural haematoma 24 mm thick, descending transtentorial herniation, enlargement of the right lateral ventricle, midline shift of 21 mm and a small interhemispheric haemorrhage. There was also a subtle Duret haemorrhage located in the pons (FIGURE 1A). The patient was immediately brought to the operating room and a decompressive craniectomy with an evacuation of the subdural haematoma was performed. He was then kept sedated and ventilated with circulatory support by norepinephrine until a control CT scan was performed 6 hours after the surgery. It revealed a reduction of the midline shift to 3 mm, however remains of the subdural haematoma were present and new bilateral intracerebral haemorrhages occurred together with a bleeding into the third and fourth ventricle. Massive enlargement of the pontine haematoma that was now extending into mesencephalon was described. Perimesencephalic cisterns were bilaterally compressed (FIGURE 1B). Based on these findings the patient's prognosis was considered highly unfavourable and no other surgical intervention was indicated, we continued in a palliative care. The sedation and mechanical ventilation were discontinued (the patient remained unconscious with GCS 3), oxygen and norepinephrine support was further provided. 14 hours after the surgery our patient died due to failure of cardiorespiratory functions.

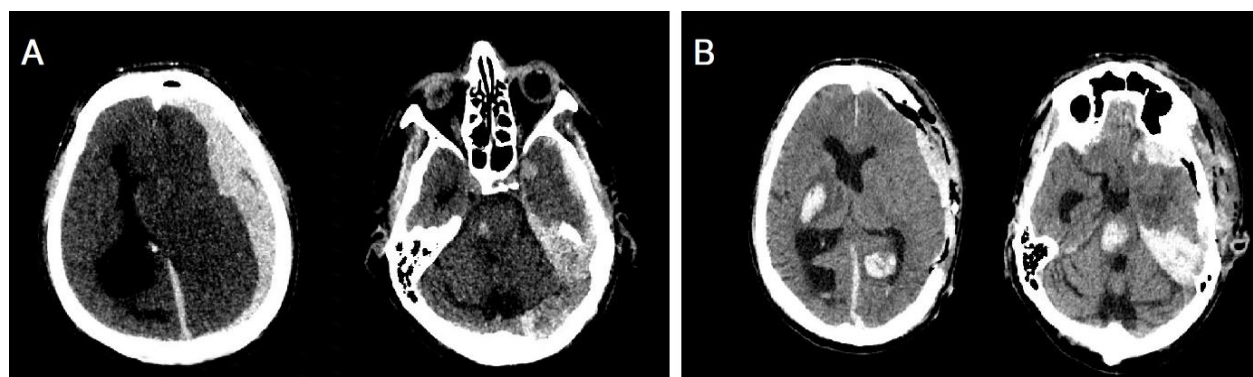


FIGURE 1. Preoperative CT scan (A) revealing a massive acute subdural haematoma 24 mm thick, smaller interhemispheric acute subdural haematoma, enlargement of the right lateral ventricle, midline shift of 21mm, and a subtle Duret haemorrhage located in the pons. After a decompressive craniectomy (B) the midline shift had resolved however remains of subdural haematomas are apparent. New intracerebral haemorrhages together with progression of pontine bleeding are visible.

Case B

This 64 years old man with a history of arterial hypertension, liver steatosis, lung resection due to tuberculosis and chronic obstructive pulmonary disease underwent a right-sided decompressive craniectomy with an evacuation of an acute posttraumatic haemorrhage into a chronic subdural haematoma. Two months later he was admitted again for a planned cranioplastic surgery using an autologous bone flap. At that time, he was fully conscious, well-oriented and communicating with a moderate left-sided hemiparesis persistent since the event of his traumatic brain injury. He underwent the cranioplasty without any serious complications and without any changes in his neurological status immediately after surgery. Approximately 8 hours later the patient had an epileptic seizure that terminated after a 5 mg intravenous dose of diazepam, he however remained non-responsive, his right-sided pupil was enlarged. The attending neurosurgeon indicated an immediate CT scan which revealed an epidural haematoma 47 mm thick at the site of reimplanted bone flap, midline shift of 19 mm, compression of lateral ventricles and perimesencephalic cisterns and a transtentorial herniation of the right-sided temporal lobe. The patient was transported to the operating room with pupils already bilaterally mydriatic and non-reactive. Emergent evacuation of the epidural haematoma was performed and the bone flap was returned with drainage tubes placed into the epidural space. The patient remained sedated and ventilated until the next CT scan 8 hours later which revealed a recent haemorrhage into right-sided basal ganglia, all four ventricles and a Duret haemorrhage into the upper pons and mesencephalon. 24 hours later the sedation and mechanical ventilation were discontinued and a tracheostomy was performed. At that time the patient was unconscious with GCS 3, he had irregular pupils with a slight right-sided mydriasis, absent pupillary reflex and present corneal reflex, spontaneously ventilating. He was later transferred to a nursing home and remained in persistent coma with his neurological status unimproved (as reported from his last known clinical check 2 months after the surgery).

Case C

A 63 years old woman pedestrian was struck by a car and subsequently transported to a peripheral

hospital, unconscious with GCS 7 (1-1-5), present pupillary reflex, sedated and intubated. CT scan was performed revealing a skull base fracture, pneumocephalus, traumatic subarachnoid haemorrhage, small subdural haematoma over the right hemisphere and a small haemorrhagic contusion in right temporal lobe. She also suffered numerous smaller lung contusions. 24 hours later she was transferred to our institution due to a progressive oedema of the right hemisphere with an enlargement of the haemorrhagic contusion in the right temporal lobe. Decompressive craniectomy and evacuation of the haemorrhagic contusion was subsequently performed and the patient remained sedated for following 24 hours. A control CT scan revealed two subtle Duret haemorrhages (one located in the pons and one in the mesencephalon) both with a diameter of approximately 1 cm (FIGURE 2). No further surgical intervention was indicated. Two months later she underwent autologous bone flap replantation and a ventriculo-peritoneal shunt insertion due to development of a posttraumatic hydrocephalus. After the surgery she remained conscious with GCS 14 (4-4-6), disoriented with signs of organic psychosyndrome - slightly bradypsychic, occasionally agitated and verbally aggressive. Her only persistent motoric deficit was a right sided ptosis.



FIGURE 2. Postoperative CT scan verifying basally located remains of haemorrhagic contents and a subtle Duret haemorrhage in the pons.

Case D

A 27 years old patient who suffered a motorcycle accident was immediately sedated and transferred to our clinic due to a CT verified posttraumatic cerebral oedema, subarachnoid haemorrhage, non-expansive right-sided acute subdural haematoma, intracerebral haematomas in both frontal lobes and a small Duret haemorrhage located in his ventral mesencephalon. Prior to sedation he had GCS 8 (1-2-5), he was isocoric with pupillary reflex bilaterally preserved. Due to a presence of non-expansive haemorrhagic intracranial lesions only an intraparenchymal intracranial pressure sensor was initially inserted but 12 hours later the patient developed a refractory intracranial hypertension with pressure values exceeding 40 mmHg and a bilateral decompressive craniectomy was performed. However, because of a CT verified Duret haemorrhage the patient's prognosis was considered unfavourable. The postoperative CT revealed stabilized intracranial findings with an adequate decompressive effect of the bilateral craniectomy with the brainstem haemorrhage being stable and non-expanding. The sedation was discontinued and the patient was later discharged to a peripheral hospital surprisingly achieving a highly favourable outcome: GCS 15 and a slight right sided hemiparesis and facial nerve palsy.

DISCUSSION

Henri Duret (1849-1921), a French surgeon and a pioneer of neuroscience focused his aim in neurological research on localising of functional areas in the brain, describing the vascular supply of the central nervous system and investigating pathomechanisms of traumatic brain injuries [27]. In experimental conditions he had described mechanisms of intracranial hypertension by simulating intracranial mass lesions and correctly assumed brainstem (especially medulla oblongata) as a centre of cardiorespiratory functions. He had also noted a disturbance in the cerebral tissue perfusion during periods of increased intracranial pressure and had observed microscopic haemorrhages located in the floor of the fourth ventricle which were associated with episodes of increased intracranial pressure [6,27]. Despite of having inaccurately linked these bleedings to an increased cerebrospinal fluid pressure at the moment of primary brain injury and despite a fact

that these haemorrhages might not even be true secondary brainstem bleedings, Duret haemorrhages have remained an eponymous term for secondary brainstem haemorrhagic lesions caused mostly by intracranial hypertension and following the transtentorial herniation [21,27].

Causes of Duret haemorrhage

Duret haemorrhage is typically a result of a descending transtentorial brain herniation. Cases of a brainstem haemorrhage preceded by an occurrence of an intracerebral haematoma [19,21], acute subdural haematoma [1,10,17,20,21], cerebral infarction [19] or diffuse cerebral oedema caused by hyponatremia [11] are known. On the other hand, several cases of the Duret haemorrhage following an episode of intracranial hypotension which can also provoke a descending transtentorial herniation have been reported. Cardinale et al. have published a case of the Duret haemorrhage in a patient after a decompressive craniectomy complicated by an episode of intracranial hypotension and a paradoxical brain herniation presenting as the sinking skin flap syndrome [4]. Similarly, Yuan et al. have described a case of the Duret haemorrhage in a patient with lumbar drainage following an operation of a thalamic tumour [28]. There is also a report of a patient who suffered a brainstem haemorrhage caused by a postoperative lumbar pseudomeningocele and associated intracranial hypotension [3]. Interestingly, even a rapid decompression of the intracranial space by means of evacuation of an expansive intracranial haemorrhage [2,8,13,22] or by means of a decompressive craniectomy [16,17,25] can result in the Duret bleeding.

Incidence

In their autopsic research of haemorrhagic stroke Nedergaard et al. have observed an incidence of the Duret haemorrhage in 45% of intracerebral haemorrhages, 15% of cerebral infarctions and 36% of aneurysm haemorrhages [19]. In a clinico-pathological report of Klintworth, Duret haemorrhage was typically associated with intracranial lesions complicated by a rapidly expanding intracranial haemorrhage or brain oedema or with a surgical decompression of intracranial space even in slowly growing lesions with overall incidence of 16.5%, specifically 31.5% for

intracerebral haemorrhages, 21.5% for subdural haematomas and 11.6% for cerebral infarctions ^[13]. In a non-missile brain injury, Graham *et al.* have reported an incidence of the Duret haemorrhage in 51% of autopsies ^[9]. However, almost 20% of these haemorrhages could only be discovered during microscopic examination ^[9] and this fact leads us to expect that radiological examination will underestimate the incidence of secondary brainstem haemorrhages in surviving patients.

Pathogenesis

Unlike primary brainstem haemorrhage which could be a result of a spontaneous arterial rupture, direct traumatic injury to the brainstem or of a rupture of vascular malformation, secondary brainstem haemorrhage typically presents with a delay and is mostly a consequence of the descending transtentorial herniation or follows a rapid decompression of the intracranial space ^[16,21]. There are several main explanations for pathogenesis of the Duret haemorrhage. The theory of an arterial origin of the Duret haemorrhage assumes that a descending transtentorial herniation causes a displacement and angulation of the brainstem with an elongation and straining of the perforating arteries extending from the basilar artery which is fixed in its upper end by the posterior communicating arteries and the posterior cerebral arteries. This tension results in either vasospasm or rupture of the perforating arteries and causes the Duret haemorrhage ^[12,15,21,26]. The very appearance of the Duret haemorrhage is highly dependent on the volume and rate of expansion of the underlying intracranial mass lesions and also on variations of systemic blood pressure and blood inflow into the perforating arteries during the episodes of transtentorial herniation. Slowly expanding intracranial mass lesions do not usually cause the Duret haemorrhage ^[7,12]. An extremely rapid descending transtentorial herniation causing acute brainstem ischaemia results in early death of the patient without an episode of the secondary brainstem bleeding (which is prevented by the disturbed blood flow in perforating arteries) ^[12]. Based on experimental research on animal model, Klintworth has postulated that the Duret haemorrhage arises during two possible scenarios: The transtentorial herniation can extensively displace the perforating branches of the basilar

artery. If sufficient blood flow in these vessels is retained, they are prone to rupture and cause secondary brainstem haemorrhage ^[12]. Evacuation of the intracranial mass lesion causing transtentorial herniation and perforating vessel damage (mechanic or ischaemic) can also provoke Duret haemorrhage in a situation when the blood flow into these damaged arteries is restored causing them to bleed even more extensively than during transtentorial herniation only, especially in situation of elevated systemic blood pressure ^[12,14,15,24]. It is possible that all types of blood vessels in the ventral brainstem are damaged in a manner of an ischaemia-reperfusion injury and are later prone to cause a massive secondary brainstem haemorrhage ^[14]. The theory of reperfusion injury is supported by a report of Sim *et al.* who have observed an enhancement of ventral pontomesencephalic area on CT angiography in a patient with a transtentorial herniation due to bilateral chronic subdural haematoma and acute tentorial subdural haematoma. After a burr-hole drainage of chronic haematomas was performed, a massive Duret haemorrhage in the area of previous parenchymal enhancement occurred. The contrast extravasation probably demonstrated damaged perforating arteries ^[24]. Arterial origin of Duret haemorrhage is also supposed when based on a report by Chew *et al.* who have performed a post-mortem CT angiography on a patient who died due to a middle cerebral artery aneurysm rupture associated with a transtentorial herniation and a secondary brainstem haemorrhage. Multiple linear enhancing foci corresponding to ruptured paramedian perforating arteries found in autopsy were detected in the central pons ^[5]. Theory of a venous infarction arises from an observation of venous congestion in the brainstem in patients with a supratentorial mass lesions, perivenous localisation of several Duret haemorrhages and a fact that the veins are thin-walled vessels easily compressed by an external pressure, specifically at the site of the tentorial notch. Compression can cause the veins to thrombose and result in venous brainstem haemorrhages ^[12,15,21,23]. This explanation has been however questioned because secondary brainstem haemorrhages often extend anatomical regions of the venous drainage and the evacuation of intracranial mass lesions can rather provoke Duret haemorrhage than prevent it ^[12]. Observations of a brainstem ischaemia with no secondary

haemorrhage in patients with the transtentorial herniation also challenges this theory of pathogenesis^[26].

Favourable outcome of patients suffering a Duret haemorrhage

Despite being considered a predictor of infaust prognosis, several reports describing a favourable outcome of patients with the Duret haemorrhage caused by various types of intracranial pathologies have been published. Dramatic recovery has been reported by Ishizaka et al.: A patient with an idiopathic subdural haematoma and preoperatively described Duret haemorrhage underwent evacuation of the subdural haematoma and despite of a severe preoperative neurological deficit his status resolved to a persistent oculomotor palsy only^[10]. Similarly, Nguyen et al. have described a patient with an acute subdural haematoma and a Duret haemorrhage achieving a favourable outcome (dysarthria and no motor deficit) after an evacuation of a subdural bleeding^[20]. Stiver et al. have also reported a favourable outcome of a young woman who developed a Duret haemorrhage after an evacuation of an epidural haematoma by means of decompressive craniectomy^[25] and another case of favourable outcome after an evacuation an epidural haematoma in a patient with a Duret haemorrhage has been published by Fujimoto et al.^[8]. A report by Park et al. describes a patient who suffered a Duret haemorrhage after a burr-hole drainage of bilateral chronic subdural haematomas and survived with his only persistent deficit being a gentle gait disturbance^[22]. Lonjaret et al. have published a case report of patient with a Duret haemorrhage triggered by a decompressive craniectomy for an acute subdural haematoma resulting in a favourable outcome with no neurological deficit^[16]. Kamijo et al. have reported a favourable outcome (gentle hemiparesis) in a patient with a severe hyponatremia causing a transtentorial herniation and a Duret haemorrhage^[11]. A favourable outcome with persistent internuclear opthalmoplegia only in a patient with a Duret haemorrhage due to an intracranial hypotension has been published by Bonow et al.^[3]. In paediatric patients, Beier and Dirks have reported a favourable outcome in two patients with Duret haemorrhage preceded by a traumatic brain injury^[1]. When summarized, most of patients surviving with favourable outcome have suffered a brainstem

haemorrhage of a limited extent only^[1,2,3,8,20], however exceptions exist^[11,16,22]. Younger age of these patients could be a factor predicting a favourable outcome^[1,11,16,20]. A typically reported persisting neurological deficit in patients with the favourable outcome is often a cranial nerve weakness^[1,3,8,10,11,16], or various subtle forms of the organic psychosyndrome and a cognitive deficit^[1,25].

Analysis of our case series

The first three patients (A,B,C) described in our work represent cases of Duret haemorrhage provoked or worsened by a rapid decompression of intracranial space combined with a decompressive craniectomy in 2 of 3 patients. The explanation of this phenomenon could be based on the theory of reperfusion into the damaged pontine perforating vessels as initially postulated by Klintworth^[12,13,14,24]. Alleviation of a significant pressure on the brainstem had most likely increased the blood inflow into mechanically and metabolically injured vessels in the pontomesencephalic region and resulted in the secondary brainstem haemorrhage (or its significant expansion in one case). The patient D probably suffered a Duret haemorrhage due to a massive cerebral oedema with a mass effect that displaced the brainstem and distorted the mesencephalic perforating arteries thus causing them to rupture because of a combination of metabolic and mechanic damage^[12,15,21,26]. It is possible that due to patient's younger age and absence of complicating diagnoses the perforators remained relatively stable even after the alleviation of the intracranial hypertension by means of decompressive craniectomy and the secondary brainstem haemorrhage did not expand. Two of our four patients had achieved a good outcome and this was probably caused by a smaller extent of the pontine haemorrhage and a younger age of patient D. Chronic liver disease present in two patients with unfavourable outcome could play a role as a potential negative prognostic factor as it can negatively affect the function of the blood coagulating system, however a definite conclusion can only be made when relating to a larger group of patients.

CONCLUSIONS

Massive elevation of intracranial pressure, decompression of the intracranial space by means of

craniectomy or intracranial bleeding evacuation can make the patient susceptible to the secondary brainstem (Duret) haemorrhage. Such bleeding, typically localised in the midbrain and pons has been considered a significant predictor of poor prognosis. Despite of this, outcome of patients suffering the Duret haemorrhage can considerably vary as presented in our report. When deciding about the prognosis of a patient with the Duret haemorrhage, attention should be paid to the type and severity of the underlying brain injury, patient's clinical status and history and at last but not least to the extent of the very brainstem bleeding.

ABBREVIATIONS

CT: computed tomography
GCS: Glasgow Coma Scale

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Spinal extradural meningioma en plaque with nerve root attachment and extracanal (intrathoracic) extension. Review of literature on management and case report

Morgan E.¹, Hakkou M.², Mellaoui A.², Poluyi E¹,
El Ouahabi A.²

¹ Lagos University Teaching Hospital, Idi-Araba, Lagos, NIGERIA

² Faculte de Medicine et de Pharmacie, Mohamed V. University,
Souissi Rabat, MOROCCO

ABSTRACT

Meningiomas are relatively common primary spinal tumours, being the second most common intraspinal tumours probably after vertebral haemangioma.

It constitutes about 25% of all intraspinal tumours; however, in the presence of extradural spinal lesions, the diagnosis of meningioma is uncommon and often not among the first two considerations. Purely extradural spinal meningioma, especially of the "En plaque" variety, usually simulate malignant disease (metastatic diseases and lymphoma) and may result in inadequate therapy, however, the presence of nerve root attachment is even rarer.

Our case report is that of an entirely cervicothoracic extradural en-plaque meningioma (WHO grade 1) with a nerve root attachment (right C7) and intrathoracic extension. We highlighted the issues in diagnosis, operative intervention and long-term follow-up.

INTRODUCTION

Meningiomas account for about a quarter of all intraspinal tumours and literature has shown that it is the second commonest primary intraspinal tumour [1]. The majority of spinal meningiomas are entirely intradural and this is seen in about 10% of cases.

There is an extradural spinal extension, but attachment to spinal nerve root and/or intrathoracic extension are not a frequent finding [2]. Meningiomas located purely in the extradural space are very rare and, therefore, are not often listed in the differential diagnosis of spinal extradural lesions [2].

We present a case report of purely extradural meningioma "en plaque" of the spine that was noticed to be attached to right C7 nerve root which create a bias for preoperative diagnosis of spinal schwannoma (intradural extramedullary) with extradural extension.

Keywords

spinal extradural
meningioma,
intrathoracic extension,
case report



Corresponding author
Morgan Eghosa

Lagos University Teaching Hospital,
Idi-Araba Lagos,
Nigeria

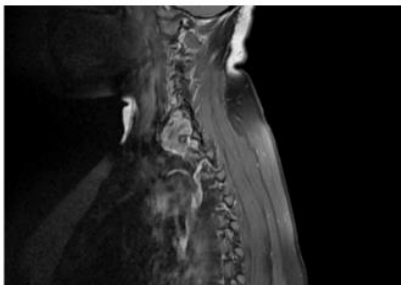
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CASE REPORT

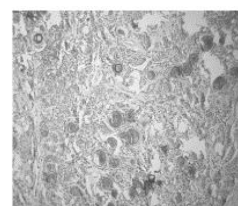
We report a case of a 28-year old woman with no previous significant medical history presented with 2-month history of progressive spastic tetraparesis (with muscle power in most muscle groups being 4) associates with right brachio-cervical hyperesthesia involving C6/C7 distribution. Cervico-thoracic magnetic resonance imaging (MRI) done was reported as intradural extramedullary tumour (schwannoma) extending from C4-T1 vertebral level by the radiologist with attachment to right C7 nerve root. Lesion was iso-hypointense on T1WI and enhances on T2WI as shown in IMAGE 1 and IMAGE 2

IMAGES 1**IMAGES 2**

perioperatively, the tumour was accessed via C4 -T1 laminectomy, and it was entirely extradural extending from C4-T1 with right C7 nerve root attachment and extending to the intrathoracic region anteriorly as shown in intra-operative images 1 and 2. The tumour was firm, fibrous, highly vascular and dissectible, tumour resected with coagulation of the attachment to right C7 nerve root but the intrathoracic component left in-situ.

INTRAOPERATIVE IMAGES 1**INTRAOPERATIVE IMAGES 2**

Both frozen section and definitive histopathological/immunohistochemical analyses confirmed meningioma "en plaque" (WHO grade 1) as shown in histology slides below.

HISTOLOGY 1**HISTOLOGY 2**

Post operatively, there was an initial loss of sensory modality of right C7 nerve root distribution which improved subsequently in conjunction with motor functions (preoperative tetraplegia) after six (6) weeks of function education and rehabilitation. Follow up is been done regularly using both clinical and radiological tools and there has not been change in improvement achieved postoperatively and also the size of the intrathoracic component.

DISCUSSION

Meningioma is one of the commonest central nervous system (CNS) tumours which is essentially a benign tumour. Majority are intracranial, with about 90% supratentorial, but spinal meningioma account for between 1.2%-12.5% of all meningiomas [3,4,5]. Meningioma arises from arachnoid cap cell (meningiothelial cell in the arachnoid villi just like any meningioma elsewhere).

The prevalence of extradural meningioma in literature ranges from 3.3% and 21.4% of all cases of spinal meningioma [6].

Tumours occur more in female to male of ratio 4:1 with a peak incidence between 5th and 6th decades of life. Almost about 80% occur in the thoracic spinal region [6]. Majority of these lesions are intradural extramedullary and are placed ventral or ventrolaterally to the dura. However, about 10% do extend to the extradural space [2]. The presence of a "sole" extradural spine meningioma is entirely rare [2]. Common tumours located in the spinal extradural space are metastatic spinal tumour and lymphoma, hence the dilemma in preoperative diagnosis which was also emphasis by Saryedekar et al in the two cases reported by them [7].

Our patient reported above had purely extradural spinal "en plaque" meningioma with right C7 nerve root attachment and intrathoracic extension. The occurrence of "en plaque" variety of meningioma is rarer. Moreso, the presence of nerve root attachment with or without intrathoracic extension is even much more a rarity. Only 16 cases in literature have shown extradural spinal meningioma adhering/proximity to spinal nerve root.

Tuli et al in their case report of a 42-year old lady with T4-T6 extradural spinal meningioma revealed attachment to left T5 spinal nerve root. The presence of extradural meningioma with or without nerve root attachment remain a puzzle and been described as a

paradox in view of absence of arachnoid cap cell in the extradural space.

Several theories have been ascribed to the occurrence of an entirely extradural spinal meningioma and possibility of nerve root adherence. Reasons adduced for these in literatures include migration of arachnoid tissue into the extradural space, or extradural spinal meningioma could arise from ectopic or separated arachnoid tissue around the periradicular nerve root sleeve, which is the point of contact of the spinal leptomeninges directly into the dura. This probably explains the attachment to nerve root [2].

Another reason alluded to the occurrence of spinal extradural meningioma is that the periradicular dura which is said to be less thick, may have vestigial remnants of the superficial layer of the embryonal arachnoid mater and villi [6].

Also, it has been suggested that islands of arachnoid tissue that may have migrated into the extradural space can be the source of the meningioma [2,6].

An entirely spinal extradural meningioma especially of the 'en plaque' variety poses a dilemma in pre-operative diagnosis [2, 7]. In this index case, a pre-operative diagnosis of C4-T1 schwannoma of the spine in view of its location and C7 nerve root attachment.

Intraoperative frozen section histopathological analysis is a necessity in view of other possibility such as metastatic spine tumour and lymphoma [8]. In this index case, the frozen section was done which showed a meningioma en plaque. This was done for decision making as regards extent of tumour resection.

The extradural tumour with its attachment to the right C7 nerve root was resected and point of C7 nerve root adhesion was coagulated. However, the thoracic extension was left in-situ. Saryedekar et al in their work shows the importance of intraoperative frozen section with near total resection of spinal extradural meningioma en plaque [7].

This strategy will give the best postoperative outcome, as prognosis depends on the extent of tumour resection [8].

Another consideration in the operation is to decide whether to open the dura or not. However, in consideration of the pathogenesis of the lesion from the dura nerve root sleeve and not from the external part of the spinal dura. It may be necessary to only

peeled off the tumour from the dura. Saryadekar et al in the two cases reported shows that the tumour was stripped off the dura with no durotomy done [7]. Though there is essentially no consensus on whether the dura should be excised or not, However, it is necessary that the dura be opened to rule out intradural extension of the meningioma which is seen in literature to account for about 10% of cases [2].

Tuli et al. reported 12 cases out of 47 supposedly pure extradural spinal meningioma who had durotomy, three (3) of these 12 patients was noticed to have intradural extension. This buttresses the importance of durotomy in hitherto purely extradural spinal meningioma. We had to open the dura to be very sure that there was not intradural component of the tumour as done in standard procedure [6].

Issues relating to long term outcome still remain an item of debate. Issues been debated such as gross total resection versus incomplete resection, benign versus malignant meningioma remain an important factor in considering long-term outcome following operation for extradural spinal meningioma.

Literature has revealed that this tumour may have a local malignant potential despite been a relatively benign tumour. Also, worse prognosis is seen with incompletely tumour resection due to bony involvement or paraspinal extension [2, 3, 8]. In the index case been reviewed, all except the thoracic extension was excised. Tumour has remained static after a regular follow-up period of over 2 years.

CONCLUSION

Spinal extradural meningioma is a rare tumour, even more with the 'en plaque' variety with spinal nerve

root attachment. In view of the prevalence of between 3.3% to 21.4%, it is essential that cases of extradural spinal meningioma should be entertained in conjunction with common tumours such as metastatic spine disease and lymphoma and in doubtful cases Intraoperative frozen section and durotomy are essential in operative decision making either to do gross total resection or partial. For the incompletely resected tumours, long-term follow-up period using both clinical and radiological monitoring tools is essential.

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The evaluation of long-term screw pull-out rates following posterior thoracolumbar fusion surgery with short and thin pedicle screws

Umit Kocaman¹, Hakan Yilmaz²

¹ Izmir Cigli Region Education and Research Hospital, Department of Neurosurgery, Izmir, TURKEY

² University of Health Sciences Izmir Bozyaka Education and Research Hospital, Department of Neurosurgery, Izmir, TURKEY

ABSTRACT

Background. The aim of this study was to evaluate screw pull-out rates after fusion operations with short and thin pedicle screws.

Methods. A total of 200 posterior lumbar and thoracolumbar fusion operations performed at our clinic with short and thin pedicle screws (5.5x35 mm) were retrospectively evaluated. The patients were assessed with computed tomography postoperatively on the day of surgery and at the 6th month. Single groove retraction of the transpedicular screw was evaluated as pull-out. The results were evaluated by the 'number of pull-out cases / total number of cases' and also the 'total number of pull-out screws / total number of screws used' ratios.

Results. There were 112 (56%) female and 88 (44%) male patients with a mean age of 58 years. The total number of screws used in the 200 cases was 1188. There were 88 (7.4%) thoracic pedicle screws, 1056 (88.9%) lumbar pedicle screws and 44 (3.7%) sacral pedicle screws used. No pull-out was found in the control CTs taken postoperatively. Left side T11 and T12 pull-out was observed in one case and left L4 pull-out was observed in another case in the control CTs taken at the postoperative 6th month. Pull-out was observed in 2 (1%) of the 200 cases and 3 (0.25%) of the 1188 screws.

Conclusions. All the short and thin pedicle screws used had passed the pedicle length and neurocentral junction. The use of a 5.5x35 mm screws in fusion operations is less invasive than using longer and thicker screws while the pull-out rates may be similar.

INTRODUCTION

Posterior lumbar and thoracolumbar fusion operations constitute an important part of neurosurgery practice. The major problems after these operations are screw pull-out, adjacent segment degeneration, deterioration of instrumentation integrity, and fusion insufficiency. Various preventive measures such as post-cement screw application and porous coated screw application are rarely used to prevent screw pull-out, while the tendency is to use long and thick screws. The general

Keywords
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pedicle,
screw



Corresponding author
Hakan Yilmaz

University of Health Sciences Izmir
Bozyaka Education and Research
Hospital, Department of
Neurosurgery, Izmir, Turkey

dr_hakanyilmaz@hotmail.com

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preference is to use 6.5x45 mm, 6.5x50 mm, 6.0x45 mm, 6.0x50 mm screws for the lumbar and thoracolumbar junction. Screws 7.0 mm thick or 55 mm long are also in use for the lumbar region. Although long and thick screw applications increase spine stability, they also create surgical risk [2,4,12].

We investigated the pull-out rates in the cases where we used screws that were shorter and thinner than those generally used in thoracolumbar fusion operations. We would like to share our experiences on surgical safety in posterior lumbar and thoracolumbar fusion surgeries in this regard.

METHODS

A total of 200 posterior lumbar and thoracolumbar fusion operations performed with short and thin pedicle screws between 2016 and 2018 at the Izmir Cigli Regional Training Hospital's Neurosurgery Department were evaluated retrospectively. This evaluation was performed only in patients who underwent posterior segmental instrumentation and fusion with 5.5x35 mm transpedicular screws. Cases where screws of a different size were used as necessary and those that required revision for postoperative screw malposition were not included in the study. An evaluation was made with preoperative CT in all cases and a screw length of 35 mm was used after it was deemed to be adequate to reach the neurocentral junction. The patients were evaluated with computed tomography postoperatively on the day of surgery and at the 6th month. Single groove retraction of the transpedicular screw was evaluated as pull-out. The results were evaluated by the 'number of pull-out cases / number of cases' and the 'total number of pull-out screws / total number of screws' ratios.

STATISTICAL ANALYSIS

Descriptive statistical methods were used in the evaluation of the data. The results were expressed as mean $\pm$ standard deviation and frequency (%).

RESULTS

The 200 patients included in the study consisted of 112 (56%) females and 88 (44%) males. The mean age was 58 years and the age range was 22-78 years. The primary pathology was narrow lumbar canal in 100 cases, lumbar spondylolisthesis (grade 1) in 26 cases, degenerative type lumbar spondylolisthesis (grade 1) in 24 cases, post-traumatic burst fracture requiring

posterior thoracolumbar fusion in 22 cases, post-traumatic burst fracture requiring posterior lumbar fusion in 6 cases and primary or recurrent lumbar disc hernia with segmental instability in 22 cases (TABLE 1). The number of screws used in the 200 cases was 1188. These consisted of 88 (7.4%) thoracic pedicle screws, 1056 (88.9%) lumbar pedicle screws and 44 (3.7%) sacral pedicle screws (TABLE 2). No pull-out was found in any patient on the control CTs taken the same day postoperatively (FIGURE 1,2). Left T11 and T12 pull-out was observed in control CTs performed at the postoperative 6th month in 1 case who had undergone thoracolumbar fusion (FIGURE 3). Left L4 pull-out was observed in 1 patient who had undergone surgery due to narrow lumbar canal. Both patients underwent revision surgery. Pull-out was therefore observed in 2 (1%) of the 200 cases and 3 (%0.25) of the 1188 screws.

Pathology	Female	Male	Total
narrow lumbar canal	59	41	100
isthmus type lumbar spondylolisthesis (grade 1)	13	13	26
degenerative type lumbar spondylolisthesis (grade 1)	13	11	24
burst fracture requiring thoracolumbar fusion	12	10	22
lumbar disc herniation with segmental instability	12	10	22
burst fracture requiring posterior lumbar fusion	3	3	6
Total	112	88	200

TABLE 1. The distribution of the cases where short and thin pedicle screws were applied according to the primary pathology and gender.

Pathology	Lumbar pedicle screw	Thoracic pedicle screw	Sacral pedicle screw
narrow lumbar canal	558	0	12
isthmus type lumbar spondylolisthesis (grade 1)	66	4	14

degenerative type lumbar spondylolisthesis (grade 1)	206	6	8
burst fracture requiring thoracolumbar fusion	130	78	0
lumbar disc herniation with segmental instability	54	0	6
burst fracture requiring posterior lumbar fusion	42	0	4
Total	1056	88	44

TABLE 2. The distribution of the screws used.

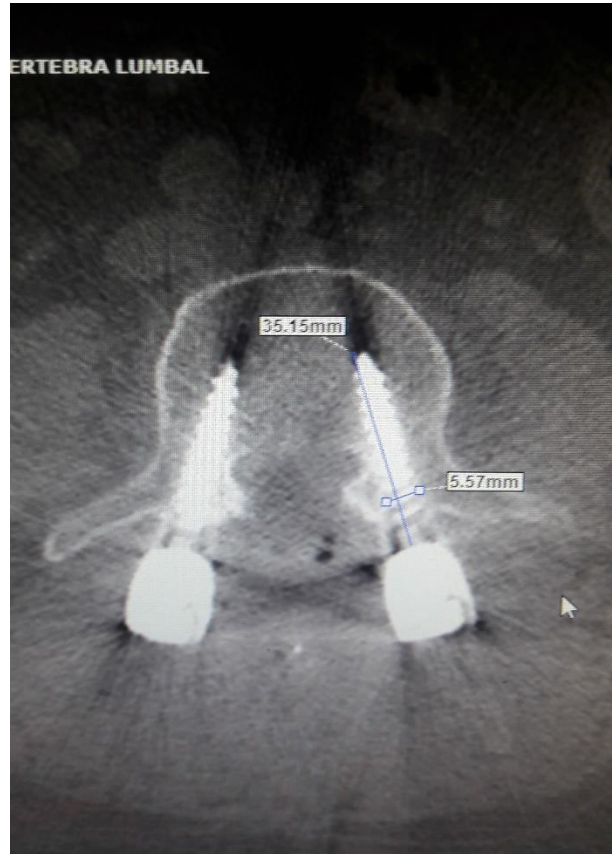


FIGURE 1,2. Spinal CT sagittal and axial images of the posterior lumbar fusion operation where short and thin pedicle screws (5.5 mm-35 mm) was used.



FIGURE 3. Left side T12 screw pull-out of a patient on the spinal CT axial image who was inserted a short and thin pedicle screw.

DISCUSSION

The mechanisms preventing pull-out are thought to be large screw outer diameter, low screw inner diameter, short intergroove distance, and a strong bone structure. The most important of these has been shown to be a large screw outer diameter. It is believed that a length that goes past the neurocentral junction is sufficient in terms of stability. However, pericortical and even bicortical screw lengths that markedly go past the neurocentral junction are used in practice [2,4].

No significant correlation was found between the screw length and the force needed to create pull-out in the cadaver study of Diaremes et al. Bone density seemed to be a more important factor in their study [5].

Karami et al. compared the force needed to create pull-out in mid-body, pericortical and bicortical screws in their cadaver study. The force needed to create pull-out increased as the screw depth increased. However, a statistically significant difference was only found between mid-body and bicortical screws [7].

There are also studies reporting opposite results in the literature [5]. Our study provides the results of the pull-out evaluation of screws with a thickness of 5.5 mm and invasion depth of 35 mm that were used to go past the neurocentral junction.

There was no significant difference between our pull-out rates during 6-month follow-up after 5.5x35 mm short and thin pedicle screws were inserted and the results of long and thick pedicle screw use in the literature [4,5,6]. It is possible that long and thick screws will be more effective in terms of spine stability according to Denis' three-column theory [3,8]. However, all screws went past the pedicle length and neurocentral junction with short and thin pedicle screw use. The importance of short pedicle screws in terms of surgical safety increases when it is considered that spinal surgery makes up a significant part of neurosurgical practice and a large number of surgeries are performed by surgeons with various levels of experience. The anterior, antero-lateral and lateral areas of the pedicle screw application area are surrounded by arterial and venous structures with very high flow. Although rare, damage to these structures during the screw implantation stage carries a high mortality rate [1,9,10,11]. Most of these surgeries are elective and concern the spine and any mortality creates a difficult situation.

Vascular damage can occur at 3 different stages: pedicle probe implantation, tapping, and screw implantation [10,11]. We believe that using a 35 mm screw at the pedicle probe placement stage will improve surgical safety and may decrease the probability of invading the main vascular structures in case of lateral malposition.

According to the results of this study, we recommend short pedicle screw use in appropriate cases after considering the risk-benefit balance. Every patient needs to be evaluated separately. Biomechanical studies can evaluate the stability of short pedicle screws more clearly. Our results indicate that the pull-out rates of short pedicle screws that reach the neurocentral junction are similar to those of long screws.

The critical point here is that each patient should be evaluated according to his/her spine characteristics and the length of the screw to be used should be chosen so as to reach the neurocentral junction during preoperative planning.

Using a 5.5 mm screw instead of a 6.0 / 6.5 mm screw makes it easier to stay within the pedicle boundaries. It decreases the risk of pedicle burst during screw implantation and allows the use of a thicker screw when revision is required. Our results indicate that the pull-out rate for 5.5 mm screws is similar to thicker screws. Specific planning may be required for each patient in the presence of comorbid situations such as advanced osteoporosis, scoliotic deformity and rheumatic diseases.

CONCLUSION

The use of a 5.5x35 mm screw during posterior lumbar and thoracolumbar instrumentation and fusion operations is less invasive than using longer and thicker screws and the pull-out rates may be similar.

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Traumatic complete transection of dorsal spinal cord un-associated with spinal fracture or subluxation. Management review

Guru Dutta Satyarthee, Satyajit Panda

* Department of Neurosurgery, Neurosciences Centre, AIIMS New Delhi, INDIA

ABSTRACT

Complete transection of spinal cord is an extremely rare occurrence, and usually associated with spinal instability, fracture or spondylolisthesis and also have associated systemic polytrauma involving multiple organs injury. However, a complete transection of spinal cord unassociated with fracture or dislocation or without abnormality on X-ray and CT scan imaging is extremely uncommon. Kalfas et al. observed 11.2 % of cases had cord transection in the study of sixty-two cases spinal cord-injured patients, who underwent spinal MRI, were additionally had evidence vertebral injury. In 2010, Cha et al reported the first case of transection of cord in the cervical region in a 34- year- adult male, as the first case in literature, which was not associated with any vertebral body fracture or dislocation. Authors report an interesting case, 15-year boy, who had complete transection of the spinal cord associated with polytrauma following a motor vehicle accident, spinal X-ray and CT scan imaging was unremarkable, however spinal MRI scan established the diagnosis. Briefly, imaging, management and pertinent literature are reviewed.

INTRODUCTION

Acute spinal injury can present with a spectrum of pathology including vertebral body fracture, dislocation, cord contusion, but spinal cord transection represents very uncommon occurrence^[1-8] However mostly such cord transection is reported with spinal column injury in form of fracture, dislocation or spondyloptosis. However, unassociated with fracture dislocation is uncommon. In 2010, Cha et al was first to report a case of cervical cord transection of cord in a 34- year- male, which was not associated with fracture or dislocation.^[1,2] However, in a detailed radiological review, Kalfas et al. reported his observation of sixty-two spinal cord-injured patients, who underwent spinal MRI evaluation within the first thirty six hours of sustaining spinal injury, seven cases had evidence of anatomical cord transection with various types of fracture and dislocations.^[3] Spinal cord injury is usually associated with severe traumatic injury involving spine and other body

Keywords

complete spinal cord transection, magnetic resonance imaging study, associated injury, management



Corresponding author
Guru Dutta Satyarthee

Department of Neurosurgery,
Neurosciences Centre, AIIMS New
Delhi, India

duttaguru2002@yahoo.com

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organs. However, paediatric population can sustain various grades of Spinal cord injury without evidence of a radiographic abnormality, and acronym SCIWORA (spinal cord Injury without radiographic abnormality) was coined in the year 1982 by Pang and Wilberger for describing cases sustaining spinal cord injury and presenting with clinical symptoms of traumatic myelopathy, however, no radiographic or computed tomographic scan shows evidence of spinal fracture or instability.^[1] SCIWORA is considered rare in adults, but relatively commoner in children. In the paediatric cases, SCIWORA represents about 8 to 19% of all paediatric spinal cord injuries^[4]. However, MRI can show presence of in cases of SCIWORA. SCIWORA lesions have predilection for cervical spine commonly but can affect the thoracic or lumbar spine although much less frequently. SCIWORA in adults is rare, but is of considerable importance because of the potential problems of management inherent in the diagnosis. Authors report a case, who sustained complete transection of spinal cord but without association of vertebral column fracture or dislocation. Kalfas et al. reported observation of sixty-two spinal cord-injured patients, who underwent spinal MRI evaluation within the first thirty-six hours of sustaining injury, showed presence of anatomical cord transection in 7 cases.^[3]

CASE ILLUSTRATION

A 15-year-old male pillion rider presented to emergency services with the complaints of inability to move associated with numbness involving both lower limbs following a high-speed road traffic accident. He wore helmet and received initial first aid was given at primary health centre, evaluation on arrival to our emergency services, he had history of loss of consciousness for ten minutes, when regained consciousness, complained of severe pain in the abdomen. On arrival at hospital his pulse rate was 160 per minute and blood pressure was 70/40/mm Hg. Immediately resuscitation started with colloid and blood transfusion started, with momentary recovery of blood pressure followed by fall. GCS was E3VTM5 and pupils were normal size briskly reacting to light with motor evaluation showed flaccid paraplegia with absent deep tendon jerks.

The X-ray chest and cervical spine was normal. Non-contrast computed tomography of cervical

spine showed was essentially normal with no evidence of fracture, subluxation or compromise of spinal canal. (FIGURE 1) cranial computed tomography scan head showed presence of multiple contusions with diffuse cerebral edema with absence of midline shift. Ultrasound abdomen revealed presence of hemoperitoneum, CT scan abdomen revealed presence of hepatic tear with hemoperitoneum.



FIGURE 1. Computed tomography scan spine of 15-year male, sagittal section image of spine showing no evidence of fracture or dislocation.

He was planned for emergency surgical exploration by trauma surgery team. He suffered cardiac arrest in casualty while shifting to operation theatre, but revived and immediately shifted to operation theatre and underwent emergency laparotomy under general anaesthesia. A midline laparotomy done; two liters of blood mixed collection were drained. Intraoperative, solid organs were examined, showed presence of grade -3 liver laceration on anterolateral

surface in the second segment with bile staining with serosal tear found on greater curvature of stomach and associate retroperitoneal hematoma in ascending and descending mesocolon and gastric tear was also repaired, sub hepatic drain was placed and mesh laparostomy was carried out.

In the post- operative phase, MRI of whole spine was carried out to causes of paraparesis, showed non visualization of the spinal cord from upper

border of D3 to lower border of D5 vertebra with retraction of upper and lower cord segment suggestive of complete cord transaction. (FIGURE 2) Foci of blooming seen in the retracted upper cord at D3 level suggestive of hemorrhage. In the proximal part of the transacted cord there was a linear T2 hyperintensity at D1-D3 level might be wallerian degeneration. T2/STIR hyperintensity seen in the supraspinous and interspinous ligaments from C7 to D10 levels suggestive of sprain in ligaments.



FIGURE 2. MRI, spine, T2 weighted image, sagittal section image of spine showing discontinuity of dorsal spinal cord at level of D3 to lower border of D5 vertebra with retraction of upper and lower cord segment suggestive of complete cord transaction. Foci of blooming seen in the retracted upper cord at D3 level suggestive of haemorrhage.

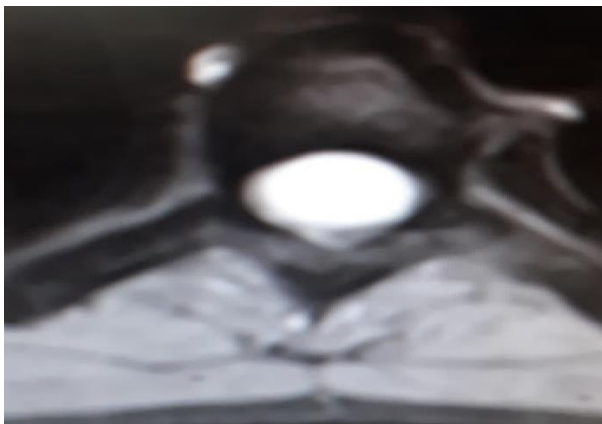


FIGURE 3. Magnetic resonance imaging study of dorsal spine, axial section, T2 weighted image of showing absence of spinal cord signal.

DISCUSSION

The incidence of SCIWORA is considered highest among children below eight years also being predisposed by presence of weaker neck muscles, and relatively heavy head and more horizontal orientation of facet joints and associated greater elasticity of vertebral ligaments. The cervical spinal cord is most commonly involved ^[5]. SCIWORA involvement in the thoracic is rare and contributes for about 10 to 13% of all paediatric SCIWORA cases. ^[4,5] The commonest cause of thoracic SCIWORA is high velocity trauma, including motor vehicular high-speed vehicular collisions, severe distraction injuries related to lap belts and crush injuries in slow-moving motor vehicles ^[5] other includes sports injuries, assault or gunshot injury and falls.

In most cases, SCIWORA occurs as a result of hyperextension forces or from a direct frontal impact to the face and May to occur during sports such as diving, wrestling, and baseball. However, Cha et al put forward combined hyperflexion-hyperextension mechanism for cervical cord transection. ^[2] In children, such movement of the vertebral column allows the musculoskeletal system to move beyond the normal physiological range of motion without the risk of fracture, however injury to the spinal cord is caused contusion or ischemia due to temporary occlusion of vertebral arteries followed by a spontaneous return of vertebrae to their original Venous congestion within the compressed spinal cord is also a pathogenic factor. The onset of clinical symptoms is delayed from a few minutes to 48 hours after injury in about 50% of patients. This latency is associated with repeated micro-insults to the spinal cord from striking against the unstable vertebrae. Various spinal cord pathology includes, signal cord swelling, contusion or oedema, however cord transaction is uncommon. ^[5]

Patients may present with variety of clinical

presentation depending on severity of injury and location of involvement of spinal cord includes transient weakness, paraesthesia, numbness, paraparesis, quadriplegia, complete cord transection syndrome and Brown-Sequard syndrome.^[17]

CT scan spine is best for assessing the associated bony injuries which may need concomitant treatment consideration but does not assess the cord itself. MRI is considered as investigation of choice and is often performed acute phase in the context of recent traumatic spinal injury and picks up spinal cord pathology, associated extramural hematoma, or hematomyelia, or ligament injury, which that may or may not be confirmed by trauma CT. The role of acute MRI is usually to assess for the presence of acute pathologies treatable such as an epidural haematoma or cord compression, which can be targeted by surgical decompression. The identification of significant cord trans section can potentially contraindicate surgery. Kalfas et al analyzed cases had spectrum of lesions including anatomical spinal cord transection in seven cases, other finding were 28 cases had spinal cord deformity secondary to extrinsic compression, 21 had focal cord enlargement/swelling, hyperintensity intramedullary lesions noted in 17 cases, and rest two cases had disc herniations.^[3]

Boese et al. analyzed 114 patients, on admission, neurologic deficit assessed by the American Spinal Injury Association impairment scale was an in 28%, B in 17%, C in 31%, and D in 25%. On basis of MRI, they categorize finding. Type I noted in 43% cases with no MRI abnormalities and 57% exhibited abnormal scan results (Type II): 6% revealed extra neural (Type Ima), 38% intramural (Type Ibis) and 13% combined abnormalities (Type Sic).^[15]

Pang classified MRI finding into five common patterns, first type is complete cord disruption represents most severe injury predominantly involving upper cervical and thoracic spine in younger children as a result of flexion injury. second being major cord haemorrhage with axial MRI showing haemorrhagic involvement of greater than 50% of cord, next is a minor cord haemorrhage, fourth is isolated cord edema and fifth pattern is groups of patients presenting with acute clinical neurologic deficit consistent with SCIWORA and with no evidence of injury in the cord on MRI study.^[17]

Prognosis depends on spinal cord pathology and associated spinal injury. For isolated spinal cord

injury case with only cord oedema have most favorable prognosis but intermediate for cord oedema and contusion and remains worse for cord contusion and associated intramedullary hemorrhage. The prognosis for spinal cord transaction still remains very poor. However, in cases with SCIWORA, associated extrinsic compression caused by vertebral body fragment and disc must be surgically corrected. In cases with fracture may need spinal fixation and fusion. Management of spinal cord transection is still a mystery, and no clear solution seems in the pipeline in near future.^[6-9]

Satyarthee advocated ideally care management acute traumatic spinal cord injury should commence immediately at the moment of traumatic impact, continue during safe evacuation, immediate resuscitation by trained paramedics, adequate immobilization, and proper prehospital care, and emergence transportation to a specialized hospital after prompt resuscitation, a detailed neurologic evaluation, pertinent neuroimaging studies, medical intervention including maintenance of airway and circulation, augmentation and maintenance of target level mean arterial pressure, avoidance of any hypotensive episodes, assessment and appropriate care of associated systemic injury, early surgical spinal decompression as judiciously needed.^[8] However, these are effective in minor cord injury, but for complete transection of spinal cord, situation remains gloomy.^[8-10]

Tabakow et al observed management of cases suffering complete spinal cord injury remains an unsolved clinical problem because of the lack of spontaneous regeneration of injured central axons.^[13] Exact management is still not available.^[10-16] Various suggested method are suggested mostly on experimental basis. Olfactory ensheathing cells support axon outgrowth in the olfactory system, and transplantation after spinal cord injury lead to axon regeneration and improvement in recovery. Thornton et al. observed rats with mid-thoracic transection and olfactory ensheathing cells transplantation, and for assessing connectivity across the transection, pseudorabies virus injected into muscles of hind-limb and finally noted presence of large number of serotonergic axons crossed the rostral scar border and the area of neurofilament-positive axons in the injury site.^[11] Authors concluded olfactory ensheathing cells transplantation can increase axonal growth across

the injury site and may promote recovery of proprioception circuit.

Tabakow et al reported 38-year-old with ASIA A injury at 21 months. The olfactory bulbs were removed to obtain a culture containing olfactory ensheathing cells and olfactory nerve fibroblasts. The cultured cells were transplanted following resection of the glial scar. He improved to ASIA C with improved trunk stability, partial recovery of the voluntary movements of the lower extremities, and an increase of the muscle mass in the left thigh. Neuroimaging confirmed grafts producing bridge over left side of the spinal cord with majority of the nerve grafts implant, and further neurophysiological examinations confirmed the restitution of the integrity of the corticospinal tracts.^[13]

CONCLUSION

Every cases with suspected head injury sustaining can presenting with shock and paraplegia, a high index of suspicion for cord transaction should also be considered, although rarer. It is highly imperative that paediatrician, neurosurgeons, orthopaedician and emergency physician should be aware for entity total spinal cord transection.

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Post traumatic isolated ipsilateral oculomotor nerve palsy. An uncommon presentation

**Praveen Kumar¹, Sharad Pandey², Kulwant Singh¹,
Mukesh Sharma¹, Prarthana Saxena²**

¹ Department of Neurosurgery, Sir Sunder Lal Hospital, IMS, BHU, Varanasi, Uttar Pradesh, INDIA

² Department of Neurosurgery, P.G.I.M.E.R. Dr Ram Manohar Lohia Hospital, New Delhi, INDIA

ABSTRACT

The common causes of isolated third nerve palsy are microvascular infarction, intracranial aneurysm, diabetes, hypertension and atherosclerosis. Here we are presenting a case of 26-year female presenting with a history of head injury two months back. She presented with ptosis on the left side. On computed tomography, a large left-sided chronic subdural hematoma with significant midline shift was found. Isolated ipsilateral third nerve palsy is a rare presentation with unilateral chronic subdural hematoma. Improvement in ptosis after surgery indicate a good neurological outcome.

INTRODUCTION

Chronic subdural Hematoma is a collection of liquefied old blood between the duramater and arachnoid membrane of brain. It is first described by Virchow as "Pachymeningitis hemorrhagica interna" in 1857. Later Trotter put forward the theory of traumatic rupture of bridging veins as a cause of what he named "subdural hemorrhagic cyst". Chronic SDH is commonly present in elderly patients After a trivial Trauma [1,2]. Unilateral chronic SDH is more common in comparison to bilateral SDH [3]. Chronic SDH is a common presentation in people taking anticoagulant or antiplatelet drugs. Commonly Chronic SDH Patients present with Headache, Vomiting, Hemiparesis, Ataxia, Altered Consciousness, Seizures, Urinary incontinence [4]. Patients with Chronic SDH rarely present with vertigo and nystagmus upward gaze palsy, and isolated third nerve palsy [5,6,7]. Isolated third nerve palsy presented with ptosis is rare presentation in post-traumatic chronic SDH patients.

CASE REPORT

We are presenting a 26-year-old female patient, non-hypertensive,

Keywords

ptosis,
third nerve palsy,
chronic subdural hematoma
(chronic SDH)



Corresponding author
Sharad Pandey

Department of Neurosurgery,
P.G.I.M.E.R. Dr Ram Manohar Lohia
Hospital, New Delhi, India

drsharad23@yahoo.com

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non diabetics, not on antiplatelet drugs. She presented with history of Head Injury two months back. No initial CT Head was done at the time of injury. Patient was conscious, cooperative and well orientated at the time of admission. Patient's vitals were within normal limit. All hematological investigations were normal. She presented with complaining of headache after one month of head injury, headache was not severe in nature and relieving on taking analgesic. There was no vomiting, hemiparesis, gait disturbance and urinary incontinence. After one and half month of head injury she complaining of dropping of left upper eyelid and patient vision was 6/9 in left eye. Left eyeball was placed outward and downward due to loss of adduction and elevation [FIGURE 1]. Left side pupil was mid dilated but fundus examination was normal. A CT Head was done showing large left side fronto-temporo-parietal chronic subdural hematoma with significant midline shift [FIGURE 2]. Patient was taken up for left sided two burr hole drainage of subdural hematoma under general anesthesia. Post operatively patient has no significant complaints and patient was put on antiepileptic medications. Her Neurological and clinical condition improved after surgery. Patient left eye ptosis and eyeball position improved same day after the surgery. Patient discharge from the hospital after 3 days in a stable condition. Improvement in ptosis after surgery indicates good neurological outcome and this was due to brainstem compression and transtentorial (Uncal) herniation which cause compression of oculomotor nerve.

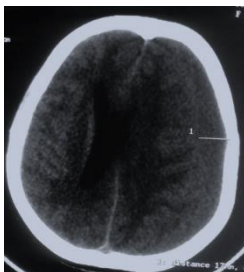


FIGURE 1. (A) severe ptosis of left eye with outward & downward displacement of eyeball (B) pre-operative CT head showing left fronto-temporo-parietal chronic subdural hematoma with significant midline shift and mass effect.

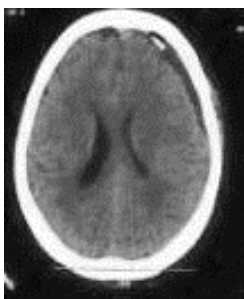


FIGURE 2. (A) Postoperative improvement in ptosis & position of eyeball (B) postoperative CT showing no residual hematoma.

DISCUSSION

Oculomotor nerve supplies all the extraocular muscle of eye except superior oblique and lateral rectus muscle. It also supplies the striated muscle of the levator palpebrae superioris and the smooth muscle concerned with accommodation namely the sphincter pupillae and ciliary muscle. In a complete lesion of the nerve the eye movement restricted in upward, downward and inward direction. Patient complaining of diplopia. There is drooping of upper eyelid due to paralysis of levator palpebrae superioris. Chronic subdural hematoma represents one of the most frequent intracranial hemorrhages encountered in the neurosurgical department, with elderly people being more frequently affected [8]. In an elderly patient brain undergo atrophied leads to 11% increase in extra cerebral space [9]. The other predisposing factors are head injury, alcohol abuse, coagulopathic disorder, antiplatelet drugs [10]. A history of head injury due to trivial trauma is presented in 60- 80% of the elderly patients [11, 12]. Most of the patient presented with complaining of headache, vomiting & hemiparesis. Isolated Third nerve palsy presented with ptosis is a rare presentation. The most common causes of isolated Third Nerve Palsy are microvascular infarction, intracranial aneurysm, Diabetes, Hypertension, Atherosclerosis. (13, 14)

CONCLUSION

Ipsilateral third nerve palsy in post-traumatic unilateral chronic subdural hematoma is a rare condition. Improvement in ptosis after surgery indicates good neurological outcome as in large chronic subdural hematoma brain shift to opposite site leads to brainstem compression and transtentorial (Uncal) herniation which cause compression of oculomotor nerve [15]

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Nil

CONFLICT OF INTEREST

There are no conflicts of interest.

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Endoscopic management of intraventricular shunt-related cystic compartment in paediatric patients

Ahmed Zaher, Amr Farid Khalil, Mohamed State, Hatem Badr

* Department of Neurosurgery, Faculty of Medicine, Mansoura University, EGYPT

ABSTRACT

Background. Intraventricular uniloculated compartments are relatively seen frequently in children previously treated with ventriculoperitoneal shunts for hydrocephalus. These compartments may present before shunt insertion and even as an end result to the shunt gliosis. Although the availability of different surgical modalities for the management of such loculations but till now there is no consensus about a single therapeutic approach for its management. Objective: The aim of this study is to assess the role of neuroendoscopy in management of uniloculated compartments, in pediatric cases who underwent shunting for hydrocephalus, to avoid multiple shunt insertion and even to eliminate the need for the preexisting shunt system.

Patients and Methods. We retrospectively studied 44 consecutive previously shunted patients with isolated intraventricular compartment who underwent 58 endoscopic procedures by a single surgeon during the period between February 2015 and February 2018. These procedures included endoscopic cyst fenestration, intraventricular septum pellucidotomy, foraminoplasty and additionally third ventriculostomy in some cases was added to the previous procedures. Multiloculated hydrocephalus and cysts related to the tumours were excluded. Clinical, radiological and surgical data were assessed.

Results. The most common cause of a single loculation in those patients was neuroepithelial cyst (20 cases) followed by post shunt isolated compartment (12 cases), meningitis (8 cases) and four cases of intraventricular haemorrhage. The patient's age varied from two months up to seven years (mean = 3.2 years). The follow-up period was ranged from (2-49 months) with the mean of 12.3 months. The overall success of restoration of communication between the uniloculated compartment and the ventricular system was achieved in 36 patients (81.8%), with 28 (63.6%) patient needed only one shunt and eight (18.2%) patients became independent of their previous shunts. Fourteen repeated endoscopic procedures were considered necessary in ten patients for either reopening of a closed stoma and/or shunt revision and finally, eight patient (18%) required additional shunt insertion during follow up period. The complications encountered were minor and reversible (CSF leak in two cases, infection in two cases, subdural fluid collection in four cases) with no mortality.

Conclusion. Minimal invasive endoscopic technique is a useful operative alternative to control uniloculated compartments in patients with previous ventriculoperitoneal shunts. It does not only simplify the existing shunt system by restoration of the communication between the loculated compartment and the draining shunt but it may eliminate the need for external shunt in some cases as well.

Keywords

loculated hydrocephalus, endoscopy, fenestration



Corresponding author
Ahmad Zaher

Department of Neurosurgery,
Faculty of Medicine, Mansoura
University, Egypt

azaher2005@hotmail.com

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INTRODUCTION

Intraventricular septation may lead to formation of an isolated CSF cystic component which may become enlarged even if the shunt system is functioning. Such enlarging intraventricular loculation may be attributed to altered CSF dynamics as result of separation between the ventricular catheter tip and the site of CSF production [14].

Variable anatomical and radiological forms of loculations were described according to the site of obstruction and consequent CSF accumulation including either uniloculated or multiloculated. Identification and distinction between the two forms is crucial because everyone has a particular different pathogenesis, treatment and prognosis [7].

Loculated hydrocephalus usually develops after episodes of neonatal meningitis or germinal matrix hemorrhage. Occlusion of the foramen of Monro, the aqueduct, and the outlet foramina of the fourth ventricle may result from shunt infection and its consequences like ventriculitis and ventricular septations. However, isolated intraventricular compartment may evolve after insertion of ventriculoperitoneal shunt via other mechanisms rather than shunt infection [11, 14].

Direct ependymal trauma during shunt insertion, collapse of shunted ventricular compartment with subsequent obstruction of the catheter tip perforations by proliferating fibrillary astrocytes and over drainage of existing shunt may play important roles that may stimulate the enlargement of an isolated shunt related compartment [14].

The management of such complex condition is challenging to most neurosurgeons. The main goal of treatment is to elevate the manifestation of increased intracranial pressure by creating a free connection between the isolated compartment and the ventricular system cavity via converting them into a solitary component that will be drained by a single ventricular catheter with little morbidity and mortality [8, 19].

Multiple treatment strategies for intraventricular loculation are available but the best choice of the proper procedure remains controversial. This group of patients presented with intraventricular compartments related to ventriculoperitoneal shunts often require multiple and repeated operations. These patients usually necessitate either traditional shunt revisions alone or in combination with other procedures like insertion of multiple

perforated catheter, craniotomy with transcallosal fenestration, stereotactic aspiration, endoscopic cyst fenestration, septostomy, foraminoplasty or third ventriculostomy [18, 20].

Recent advancement of neuroendoscopy and the higher incidence of complication associated with traditional shunt revision or open craniotomy have shifted many neurosurgeons to the different endoscopic techniques as simple and minimal invasive alternatives to solve this complex condition [9].

PATIENTS AND METHODS

From February 2015 to February 2018, forty-four consecutive paediatric cases presented with shunt related cystic compartments and a preexisting ventriculoperitoneal shunts were operated at "Neurosurgical Department of Mansoura University Hospitals" by a single surgeon using neuroendoscopic techniques. Our study included 28 boys and 16 girls; their ages ranged from two months to seven years (mean 3.2 years). The follow up period ranged from (2-49 months) with the mean of 12.3 months. Cases of multiloculated hydrocephalus or uniloculated hydrocephalus without previous shunt insertion were excluded from our study. Tumour related cysts were also excluded.

We retrospectively reviewed the patient's data retrieved from the patient charts which included: patient history, clinical examination, radiological investigations, operative data, patient outcome, shunt independency, the need for additional shunts and the prerequisites to repeat endoscopic procedures.

Plain x-ray to the shunt system, CT scan and MRI brain with or without gadolinium were done to all patients preoperatively. CSF sample was obtained and examined to exclude CSF or shunt infection prior to endoscopic procedures.

Endoscopic surgery was indicated when the patients had clinical deterioration in the form of progressive enlargement of head size, development of manifestations of intracranial hypertension, worsening of the focal neurological deficits, gait disturbance or refractory epilepsy. The previous clinical manifestations had been correlated with radiological signs of the cyst enlargement and/or shunt malfunctioning. Cognitive dysfunction was not

considered as an indication for surgical management.

Our aim of endoscopic surgery was to connect the isolated compartment to the ventricular cavity in order to drain both of them by the same shunt in order to simply the pre-existing shunt device and to avoid implanting another device whenever possible.

In all patients, surgery was done under general anaesthesia. The entry point was tailored individually in every case according to the cyst location and the location of the previous shunt entry point. A proper burr-hole location and the direct surgical corridor were the most critical points for proper cyst fenestration and shunt revision simultaneously.

Different angles rigid lens endoscopes (0°, 30°, 70° Karl-Storz rigid Gaab System) were used. The endoscopic sheath has an outer diameter of 6 mm and working channel of 2 mm. After endoscopic introduction, continuous irrigation was essential for clear identification of key anatomical landmarks and proper visualization of cyst wall as well as the proximal end of the pre-existing ventricular catheter. Initial cyst fenestration was performed in a thin, translucent and relatively a vascular segment of the cyst wall by the use of bipolar electrocoagulation. Dilation and enlargement of the initial stoma was continued by with the aid of Fogarty balloon catheter, punches, and sharp scissor to fashion a wide stoma that secure a free CSF passage and minimize the incidence of reclosure of the stoma. Coagulation and devascularization of the cyst wall were done in order shrink the cyst wall and hold the cyst growth.

Other endoscopic procedures like endoscopic revision of the shunt, septum pellucidotomy, foramioplasty and third ventriculostomy were done in combination with endoscopic cyst fenestration to advance the communication of CSF isolated compartments.

Any bleeding point was secured with continuous irrigation, bipolar electrocoagulation and tamponading with embolectomy balloon catheter to achieve a non-vascular surgical field as well as the site of fenestration. At the end of the surgery, the endoscopic sheath was retrieved under continuous irrigation to clear out the surgical field from any blood clots or any surgical debris.

Clinical outcome was defined as improved, unchanged or worsened. Developmental delay was not considered in post-operative clinical outcome

assessment. Epilepsy was defined to be improved if the attacks were controlled after withdrawal or even reduction of the dose of antiepileptic drugs. If the head circumference remained stable or slightly reduced in size, this was considered as a postoperative sign of improvement.

Routine postoperative CT brain was done to all patients twenty-four hours after surgery. Follow up CT and MRI brain were done routinely 3 months after surgery. The procedure was considered to be successful when endoscopic procedure was able to restore the continuity between the cyst and the ventricular system cavity without the need to insert additional shunt devices. Repeated endoscopic procedures were considered when the patient experienced recurrence or progression of his clinical manifestations that were concomitant with progressive cyst and/or ventricular enlargement on follow up CT and/or MRI images.

RESULTS

Progressive enlargement of the head size was the most common presenting symptom in our patients (28 cases, 63.6%) followed by seizures (14 cases, 31.8%), headache (10 cases, 22.72%), focal neurological deficits (10 cases, 22.72%) and gait disturbance in 6 patients (13.6%) (TABLE 1).

The non-colloidal neuroepithelial cysts were the most prominent underlying cause of intraventricular unilateral compartments with preexisting shunts in our study (Twenty cases, 45.5%) while uniloculated cysts related to either previous shunt insertion or shunt infection represented the second most common cause (Twelve cases, 27.3%) followed by meningitis (eight cases, 18.2%) and neonatal intraventricular haemorrhage (four cases, 9%) (TABLE 2).

Endoscopic fenestration of cyst wall was done in all patients. Other additional endoscopic procedures that were required to be done simultaneously with the endoscopic cyst fenestration included either endoscopic third ventriculostomy (six patients), septum pellucidotomy (ten patients) or foraminoplasty (six patients).

During the previous endoscopic procedures, shunt revisions were indicated in only six patients (33%) who had non-colloidal neuroepithelial cysts whenever 20 out of 24 patients (83%) of shunt related cysts, postmeningitic cysts and post-

haemorrhagic cysts required endoscopic shunt revisions.

Throughout the follow up periods, the previous endoscopic procedures were successful to restore the connection between the isolated compartments and the ventricular system cavities in 36 patients (81.8%).

Simplification of the previous shunt systems were achieved in 28 patients (63.6%) who required only a single device, while eight patients needed additional shunt system, the remaining eight cases (18.2%) became shunt independent after previous endoscopic procedures and shunt removal (TABLE 2).

Fourteen repeated endoscopic procedure were done in 10 patients for either reopening of the stoma in ten procedures or shunt revisions in the remaining other procedures. (2 cases due to gliosis and 2 due to debris). Finally, eight (18.2%) patients required additional shunt insertion after failure of restoration of a proper connection between the isolated compartments and the ventricular system cavities with failure of a single shunt to drain the dilated cavities.

As regard clinical outcome, most patients n=28 (63.6%) presented with progressive head enlargement showed either stabilization or slight reduction in their head size. Headache was improved in eight patients from 10 patients (80%) with only two patients sustained to complain of headache after successful fenestration. Ten from 14 patients (72%) presented with epilepsy achieved clinical improvement by either absence of their epileptogenic attacks after withdrawal of antiepileptic treatment or reduction of the doses of their treatment regimens, whenever two patients (14.2%) remain dependent on the same drug regimen and another two patients required addition of another antiepileptic drug to control his seizures.

We had no mortalities among our patients whenever the procedure related morbidities were minimal including two of CSF leakage, two cases of superficial wound infection and four cases of subdural fluid collection.

TABLE 1. Clinical presentation and postoperative clinical outcome.

<i>Clinical presentation</i>	<i>No. (%)</i>	<i>Clinical outcome</i>		
		<i>Improved</i>	<i>Stable</i>	<i>Worsening</i>
Head enlargement	28 (63.6%)	14 (50%)	12 (43%)	2 (7%)
Seizures	14 (31.8%)	10 (72%)	2 (14%)	2 (14%)
Headache	10 (22.7%)	8 (80%)	2 (2%)	0
Focal neurological deficit	10 (22.7%)	6 (60%)	4 (40%)	0
Gait disturbance	6 (13.6%)	4 (66.7%)	2 (33.3%)	0

TABLE 2. Number of required shunts and repeated endoscopic procedures in relation to different etiologies.

<i>Etiology</i>	<i>No. of patients</i>	<i>No. of required shunt</i>			<i>Repeated endoscopic</i>
		<i>No shunt</i>	<i>One shunt</i>	<i>Additional shunt</i>	
Neuroepithelial cyst	20	6	14	0	0
Shunt related cysts	12	2	10	0	2
Meningitis	8	0	2	6	8

Intraventricular age	4	0	2	2	4
Total no. and %	44 (100%)	8 (18%)	28 (64%)	8 (18%)	14 (24%)

TABLE 3. Repeated endoscopic procedure in ten patients.

<i>Type of the procedure</i>	<i>No.</i>	<i>%</i>
Closed fenestration	10	71.4
Shunt revision	4	28.6
<i>Gliosia</i>	2	14.3
<i>Obstruction form debris</i>	2	14.3

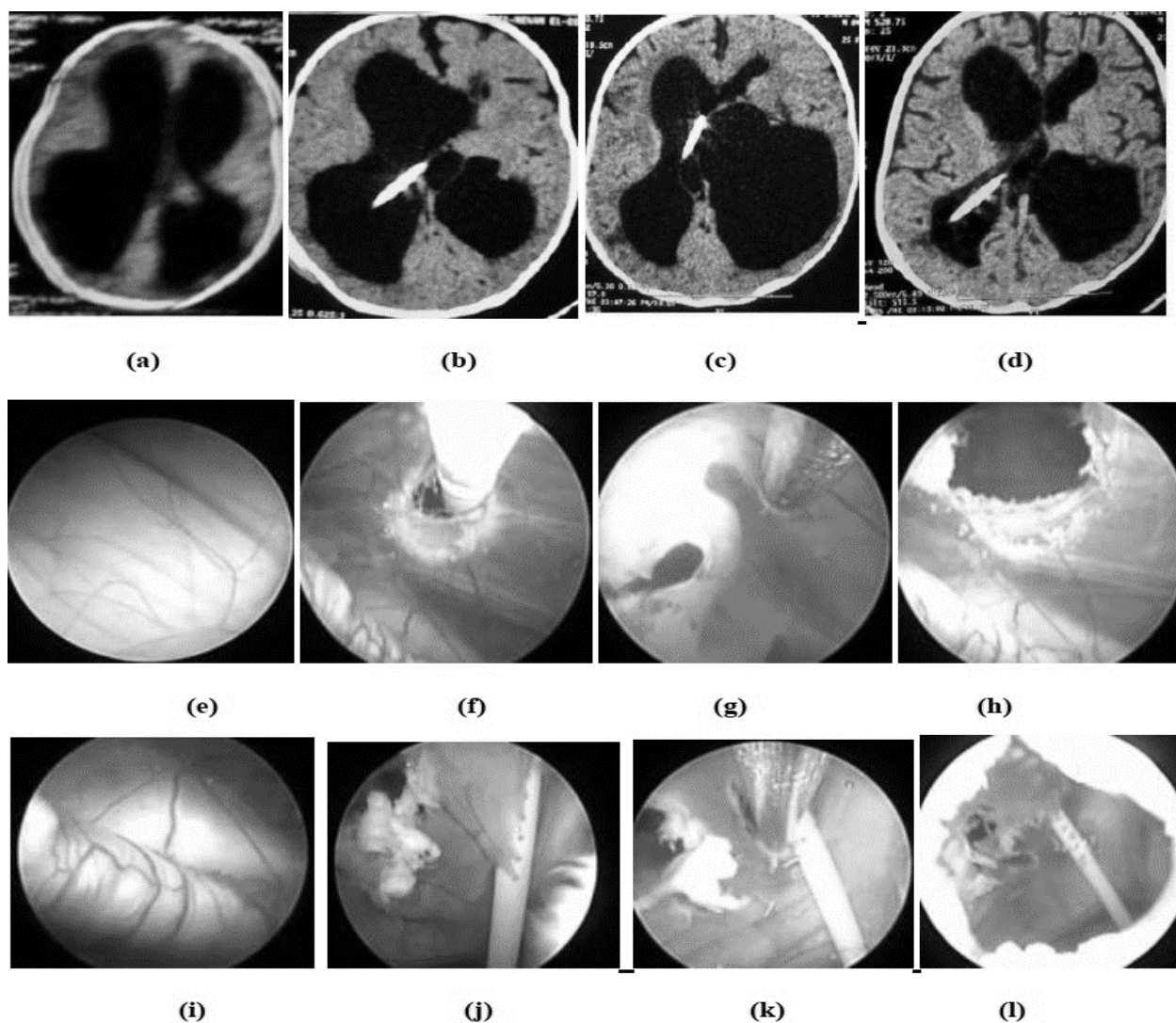


FIGURE 1. a-l: Radiological and intraoperative endoscopic photographs of a case of shunt related cyst. a) Preoperative CT. b) CT after insertion of a shunt. c) Three months follow up CT after shunt insertion with development of shunt related cyst. d) CT after

endoscopic fenestration and shunt revision with improvement of hydrocephalus e) Endoscopic view of the cyst wall. f) Opening of the cyst. g) Coagulation and shrinkage of the wall of the cyst. h) Fenestrated cyst with adherent shunt. i) Shunt adherent to the inner cyst wall. j) Occlusion of the shunt perforations by proliferation of the cyst wall. k) Sharp dissection of the shunt from the adherent cyst. l) Endoscopic view after shunt revision and cyst perforation.

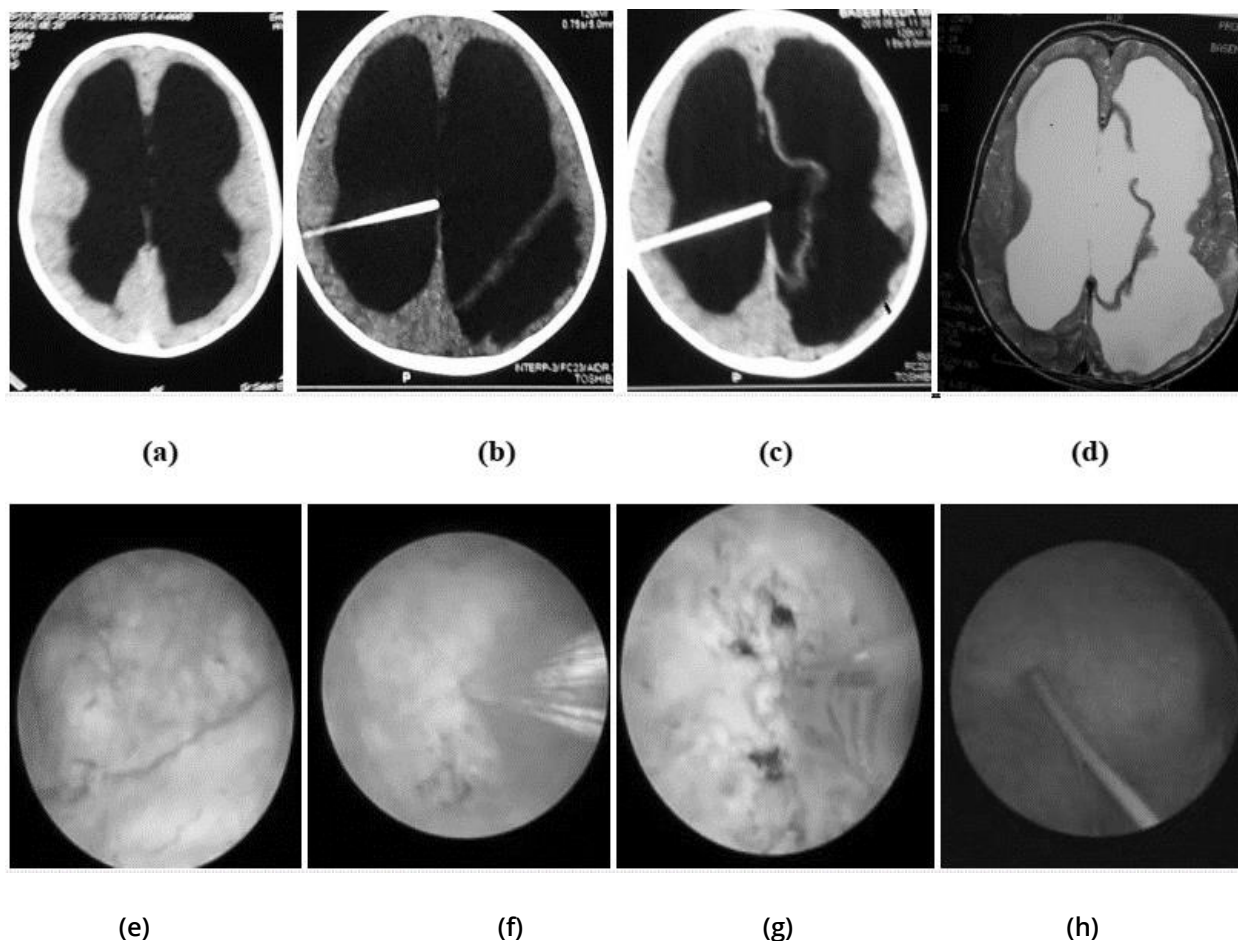


FIGURE 2. a-f: Radiological and endoscopic photographs of a case of post-haemorrhagic hydrocephalus. a) Preoperative CT. b) CT after insertion of the shunt with early formation of a cyst. c) CT after three months with progressive cyst enlargement. d) T2-MRI after cyst fenestration with good communication. e) Endoscopic view of thick cyst wall. f) Bipolar perforation of the cyst wall. g) Sharp dilatation of the stoma. h) Endoscopic view of the shunt within the ventricle through the performed stoma.

DISCUSSION

Uniloculated intraventricular discrete CSF filled compartment has been defined as a particular diagnostic entity by Cushing since he reported his first case of intraventricular unilocular compartment [1]. Subsequently Salmon in 1970 reported five cases of uniloculated hydrocephalus [17].

Non-colloidal neuroepithelial cysts are the most common underlying etiological causes for uniloculated hydrocephalus which may lead to obstruction of normal ventricular pathways with subsequent cystic dilation of one segment of the ventricular system, e.g. foramen of Monro or aqueduct and formation of uniloculated

compartment. Excess CSF drainage via previously inserted ventricular catheters within a previously communicating ventricular system can cause ventricular morphological changes and possibly leads to isolation of ventricular compartments. Moreover, CSF over drainage might result in unilateral ventricular collapses or obstruction of foramen of Monro or aqueduct [4, 7].

Failure of the previous shunt may result from collapse of the isolated compartment around the tip of the catheter with subsequent obliteration of ventricular catheter fenestrations by reactive proliferation of fibrillary astrocytes [12].

Although the pathogenesis of univentricular

loculation is not well known but the most accepted theory is that the inflammatory reaction related to previous shunt insertion, infection and intraventricular hemorrhage are the triggering factors for subependymal gliosis that may enhance the formation of glial tufts which occlude the holes of the ventricular system and act as a nidus for ventricular septations [11, 18]. Regardless of the accurate mechanism, the problem progress steadily toward greater complexity with time and traditional treatment ultimately require repeated surgeries with increasingly complex shunt devices [1].

The synonyms and classification of complex hydrocephalus are still interchangeable and unclear in the literatures. Spennato et al. published a classification for variable types of ventricular loculation defined by the location and number of compartments [19]. According to the previous proposed scheme "uniloculated" and "multiloculated" are broadly defined based on anatomical factors only [1]. These categories should be further subdivided into physiologically simple or physiologically complex based on whether CSF absorption is normal or impaired [2]. Differentiation between the previous entities is of great importance as their pathogenesis, surgical outcome and prognosis are quite different [6].

The clinical features of loculated hydrocephalus are not specific and are difficult to recognize because they often arise in a neurologically compromised infant or child with a previous history of hydrocephalus, neonatal meningitis or intraventricular haemorrhage. In our study the progressive head enlargement was the most common presenting symptom in 28 cases (63.6%) followed by seizures in 14 cases (31.8%) headache in 10 cases (22.7%), focal neurological deficit in 10 cases (22.7%) and gait disturbance in 6 cases (13.6%).

Intraventricular loculation with previous ventriculoperitoneal shunt is a complex disorder that is difficult to treat. Those patients usually require repeated shunt revisions. Furthermore, those patients may need division and lysis of intraventricular septations either surgically through transcallosal craniotomy or through endoscopic techniques [13, 16].

The best advantages of the endoscopic procedures over transcallosal craniotomy are limited invasiveness and short postoperative recovery time. Nowadays the recent technical improvement in

endoscopic techniques and high morbidity associated with multiple shunt revision or transcallosal craniotomy has shifted neurosurgeon toward the minimally invasive endoscopic techniques for lysis of intraventricular septae simultaneously with endoscopic shunt revisions [5].

Our objective in management of a single intraventricular loculation in a previously shunted patient was to restore the continuity between the isolated compartment and the ventricular system cavity to create a single cavity with the intent of simplifying or removal of the previous shunt system and reducing the need for repeated procedure. The proposed goal has been achieved in thirty-six patients (81.8%) with simplification of the previous shunts in 28 patients (63.6%); out of them eight patients (18.2%) became shunt independent after endoscopic cyst fenestration and additional endoscopic foraminoplasty, septum pellucidotomy or third ventriculostomy.

Shunt malfunctioning was found in most cases of our series (34 cases, 77%) due to either collapse and adhesive scarring of the cyst around the catheter tip or occlusion of the catheter perforations by debris or proliferating epithelial tufts. We used bipolar coagulation for safe dissection of the catheter tip from the adherent collapsed cyst wall to avoid catastrophic intraventricular bleeding which may happen in absence of endoscopic control.

In his series of 31 pediatric patients with uniloculated hydrocephalus, El-Ghandour treated 9 cases of uniloculated hydrocephalus with preexisting shunt system demonstrating reduction of shunt revision rate from 2.7 per year before fenestration to 0.25 per year after fenestration with simplification of four previous complex shunt systems and all patients required single repeated endoscopic procedures [6]. Lewis et al. reported 34 cases of both multiloculated and uniloculated hydrocephalus and shunt revision rate dropped from 3.04% prior to endoscopy to 0.25 after the procedure and 50% of the patients shunted prior to endoscopy required repeat endoscopic procedures [12].

In our series 90 revisions were required in 32 patients prior to endoscopy with shunt revision rate was 2.98/year which have been reduced to 0.27 after endoscopic fenestration as only four patients required endoscopic shunt revision. Ten patients (22.7%) of our series required fourteen repeated endoscopic procedure for opening of a closed

fenestrae or endoscopic shunt revision. The explanation of small percentage of repeated endoscopic procedure, in our cases compared by previously mentioned series is that we have 20 cases of neuroepithelial cysts presented to us with malfunctioning shunts and none of them required to repeat surgery. Moreover, we have only 12 cases of post meningitis and post haemorrhagic uniloculated hydrocephalus in which 8 cases required 12 repeated endoscopic surgery and only two patients with shunt related cysts had a single repeated endoscopic surgery

During repeated endoscopic procedures, ten cysts required reopening of closed stoma and four ventricular catheters required reopening of the closed stoma either due to gliosis in two cases or obstruction of the catheter openings by a debris in the other cases. Ultimately, eight patients (18.2%) "Six with post-meningitis loculations and two with post-haemorrhagic loculations" required insertion of additional ventricular catheters after failure of repeated endoscopic procedures to achieve proper communication with persistent undrained intraventricular loculated compartments.

In the context with the experience of other endoscopic surgeons, we found that sharp dissection, employment of wide fenestrations of at least one cm and coagulation of the cysts wall ensured the success of the procedure and reduced the chance of recurrence [10, 15].

Previous series of endoscopic fenestration of loculated hydrocephalus highlighted the combination of endoscopic procedures to achieve better success and moreover may help shunt independence [6, 20]. The obvious advantages of leaving one shunt in complex hydrocephalus are fewer opportunities for obstruction, rupture, infection and gliosis [3].

Septum pellucidotomy, foraminoplasty and third ventriculostomy were employed in our cases in combination with endoscopic cyst fenestration and shunt revision that have been succeed to achieve simplification of the previous shunt systems in (63.6%) and elimination of shunt dependency in eight patients (18%). The immaturity and deficient absorptive capabilities of scared subarachnoid space by a previous inflammatory process may be responsible for the lower shunt independent incidence in our study in line with others series [2, 12].

Nida and Haines who advocate transcallosal craniotomy for division and lysis of intraventricular septation criticized the endoscopic approaches by their limited ability to control intraoperative bleeding which may obscure the operative field [13]. However, intraoperative haemorrhage presented no great problem and did not result in termination of any procedure in this series. Haemorrhage was controlled by continuous irrigation with warm lactated ringer solution and occasionally monopolar and bipolar coagulation were helpful to control any bleeding point. Moreover, proper coagulation of site of fenestration may help to minimize the incidence of intraoperative bleeding.

As regard clinical outcome 28 patients (63.6%) who presented with head enlargement had stabilization or decline in their head circumference. Epilepsy was controlled in ten patients (72%) out of fourteen patients presented with seizures. Focal neurological deficient was improved in six patients (60%) and gait disturbance was improved in four patients (67%). Development delay was excluded from postoperative assessment as developmental improvement is not correlated with the change of the cyst size. Our results are going with the previous series which assessed the postoperative clinical outcome, in addition to radiological improvement of hydrocephalus [6].

Our morbid complications were minimal and reversible including CSF leakage in two cases which stopped within few days after medical therapy, four cases of subdural hygroma that resolved spontaneously during follow up and only two cases of superficial wound infection which improved with antibiotic and repeated dressing.

CONCLUSION

Intraventricular loculations in previously shunted patients is among the most challenging scenarios encountered by a neurosurgeon. This complex disorder has a relatively evolving course in the form of ongoing worsening with time that requires increasingly difficult surgical procedures. The main objective in management of such cases is to reduce the number of surgical procedures more than improving the quality of life of the patient. Endoscopic surgical techniques are attractive minimal invasive alternatives that may help to achieve treatment objectives with minimal postoperative morbidity.

AUTHORS CONTRIBUTIONS

This work was carried out in collaboration between all authors. Author Amr Farid, designed the study, Author Mohamed State wrote the protocol, Author Ahmed Zaher managed the literature research, Author Hatem Badr revised the final manuscript. All surgical procedures were carried out by single surgeon and assisted by the same surgical team including the four authors. All authors read and approved the final manuscript.

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The use of folic acid in the prevention of spinal bifida. Knowledge, attitude, and practice of women of childbearing age in low income rural communities

Eghosa Morgan¹, Nosa Akpede², Emmanuel Friday Osagiede², Vivian Ajekweneh², Francis Erah², Victoria Aishetu Momoh³, Mohammed Irumhekhai Momoh³, Ezemwenghian Aikomien Morgan¹, Ese Tracy Osagiede⁴

¹ Department of Surgery, Ambrose Alli University, Ekpoma, NIGERIA

² Department of Community Medicine, Irrua Specialist Teaching Hospital, Irrua, NIGERIA

³ Department of Community Medicine, Ambrose Alli University, Ekpoma, NIGERIA

⁴ Accident and Emergency Unit, Irrua Specialist Teaching Hospital, Irrua, NIGERIA

ABSTRACT

Background. Spinal Bifida is a congenital malformation of the spine that typified defect of the neural tube with devastating neurological, psychosocial and developmental burden to the growing child with associated huge financial burden to the parents, community and the country. Past and present studies have shown strong evidence to indicate that folic acid supplementation during the periconceptional period reduces the occurrence of spinal bifida in children.

Aim. To assess the knowledge, attitude, and practice of use of folic acid during the periconceptional period among women of childbearing age in two rural communities in Edo State, Nigeria.

Materials and methods. A prospective cross-sectional study of 170 women between the ages of 15 and 49 years recruited through a multi-stage sampling technique. The survey instrument was a structured interviewer-administered questionnaire. The data was analysed using Statistical Package for Social Sciences (SPSS) version 21 and presented as charts, tables, and associations tested with Chi-square at a statistical level of significance set at $p < 0.05$.

Results. One hundred and twenty-two (71.8%) of the respondents showed good knowledge, 147(86.5%) had a positive attitude, and 106 (62.4%) had a good practice of use of folic acid. There was a statistically significant association between respondents' age, marital status, level of education, occupation, and their knowledge of the use of folic acid as well as with their attitude towards the use of folic acid. However, the practice was mainly associated with the socio-demographic variable of each household.

Conclusion. The use of folic acid during the perinatal period for the prevention of

Keywords
folic acid,
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Corresponding author
Eghosa Morgan

Department of Surgery, Ambrose Alli
University Ekpoma and Irrua
Specialist Teaching Hospital, Irrua,
Nigeria

morganeghosa@gmail.com

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spinal bifida is found to be absent in about two-fifths of the study population, a number found to be alarming despite the high level of good knowledge and attitude towards the use of folic acid. There is, therefore, an urgent need to step up more advocacy and health education to women of childbearing age to increase the uptake of folic acid for effective reduction of the incidence of spinal bifida.

INTRODUCTION

Spinal bifida is part of a group of birth defects called neural tube defects (NTDs) which are caused by the abnormal closure of the embryonic neural tube between 22 and 28 days after conception.¹ The neural tube is the embryonic structure that eventually develops into the baby's brain and spinal cord as well as adjacent tissues. There are two major types of spinal bifida: spinal bifida occulta as seen when the vertebral defect or malformation is covered by skin and hence hidden, and spinal bifida cystic characterized by a cystic protrusion. Spinal bifida cystic is further subdivided into meningocele in which the protrusion contains meninges and cerebrospinal fluid, and may or may not be covered by skin or myelomeningocele is the most severe form where the protrusion which contains spinal cord and nerves is exposed to the exterior.² The worldwide incidence of spinal bifida varies between 0.17 and 6.39 per 1000 live-births.³ In Nigeria, however, the general incidence of neural tube defects has been reported at rates of 2.75 to 7 per 1000 livebirths.^{4,5}

Past and ongoing studies have shown that the use of folic acid has significantly reduced the occurrence of spinal bifida and other neural tube defects. The relationship between apparent folate deficiency and spinal bifida was hypothesized as early as 1965. This prompted the conduction of randomized control trials by the medical research council where they found that women with the previous history of NTD-related pregnancies reduced the risk of occurrence by 70% by taking 4000 micrograms of folic acid daily. In 1984, Hungarian randomized control trial found 100% reduction in risk of having the first occurrence of NTD-affected pregnancy among women who took 800 micrograms of folic acid daily^{6,7} although the exact mechanism by which folic acid prevents spina bifida, and other NTDs is still not known, its role in the synthesis, repair, and methylation of DNA especially in rapidly growing cells is instructive. The world health organization recommends that all women of

childbearing age consume 400 micrograms of folic daily and that women with pregnancies previously affected by NTDs consume 5000 micrograms of folic acid daily.⁸ Women should consume these amounts in the periconceptional period as it takes eight weeks to reach the optimal serum level of folic acid.⁹

METHODOLOGY

This is an eight-month (June 2017 to January 2018) prospective cross-sectional study involving 170 women of child bearing age attending the Primary Health Care Facility at Usugbenu and Opoji, Edo Central Senatorial District, Edo State, Nigeria. This study was carried out by the use of an interviewer-administered questionnaire with emphasis on the following areas: Knowledge of use of folic acid in the prevention of spinal bifida among women of child bearing age, compliance to use of folic acid among women of childbearing age, and factors that influence use of folic acid among women of child bearing age.

Data were analyzed using SPSS version 21. Descriptive and inferential statistics were used to describe and interpret the data with the level of statistical significance set at $p < 0.05$.

RESULTS

Majority of the respondents 90 (52.9%) were between age 30-39, while only 5 (2.9%) were less than 20 years. All the respondents 170 (100%) were females. Those married were 131 (77.1%) while 4 (2.4%) were cohabiting. A total of 84 (49.4%) respondents had secondary education, while 34 (20%) has primary education. Most of the respondents 79(46.5%) were self-employed while 6(3.5%) were students. Most of the respondents had been pregnant 70(41.2%) while a total of 19(11.2%) had not been pregnant before. (TABLE 1).

Majority 127 (74.7%) have not had Spinal bifida child, while 43 (25.3%) have had a Spinal bifida child in the past (FIGURE 1). Seventy-nine (46.5%) said they had had a Miscarriage while 91(53.5%) said they had not had any Miscarriage (FIGURE 2).

In scoring for "KNOWLEDGE," 11 points were considered from the questionnaire, and a score of > 7 points was graded as "GOOD," a score of 5 -7 was graded as "FAIR," while a score of < 5 was graded as "POOR." In scoring for "ATTITUDE," 8 points were considered from the questionnaire, and a score of > 4 was graded as "POSITIVE," while a score of ≤ 4 was

graded as "NEGATIVE." In scoring for "PRACTICE," 6 points were considered from the questionnaire, and a score of >3 was graded as "GOOD," a score 2 -3 was graded as "FAIR" while a score of < 2 was graded as "POOR." In scoring for "DETERMINANTS," 5 points were considered from the questionnaire, and if > 2 "NO" were ticked, it was graded as "STRONG" while if ≤ 2 "NO" were ticked it was graded as "WEAK" (TABLE 2).

There was a statistically significant relationship between age group, marital status, level of education, occupation, number of pregnancies had and spinal bifida. However, there was no statistically significant relationship with the number of miscarriage (TABLE 3A). There was a statistically

significant relationship between, level of education and occupation. However, there was no statistically significant relationship with age group, spinal bifida child, pregnancies had, marital status and miscarriage (TABLE 3B). There was a statistically significant relationship between age-group, marital status, level of education and number of pregnancies had. However, there was no statistically significant relationship with having spinal bifida child (TABLE 5). There was a statistically significant relationship between age group and occupation, but there is no statistically marital status, level of education, number of pregnancies had, spinal bifida child and miscarriages (TABLE 7).

TABLE 1. Socio-demographic characteristics of respondents.

VARIABLE	FREQUENCY (n=170)	PERCENT (%)
Age group(year)		
< 20	5	2.9
20-29	46	27.1
30-39	90	52.9
40-49	29	17.1
Mean ± SD = 28.41±0.73		
Marital status		
Single	21	12.4
Married	131	77.1
Widowed	14	8.2
Co-habiting	4	2.4
Level of education		
Primary	34	20.0
Secondary	84	49.4
Tertiary	52	30.6
Occupation		

Employed	58	34.1
Unemployed	27	15.9
Self-employed	79	46.5
Student	6	3.5
Pregnancies had		
None	19	11.2
1-3	39	22.9
4-6	70	41.2
7-9	35	20.6
>9	7	4.1

FIGURE 1. Prevalence of spinal bifida.

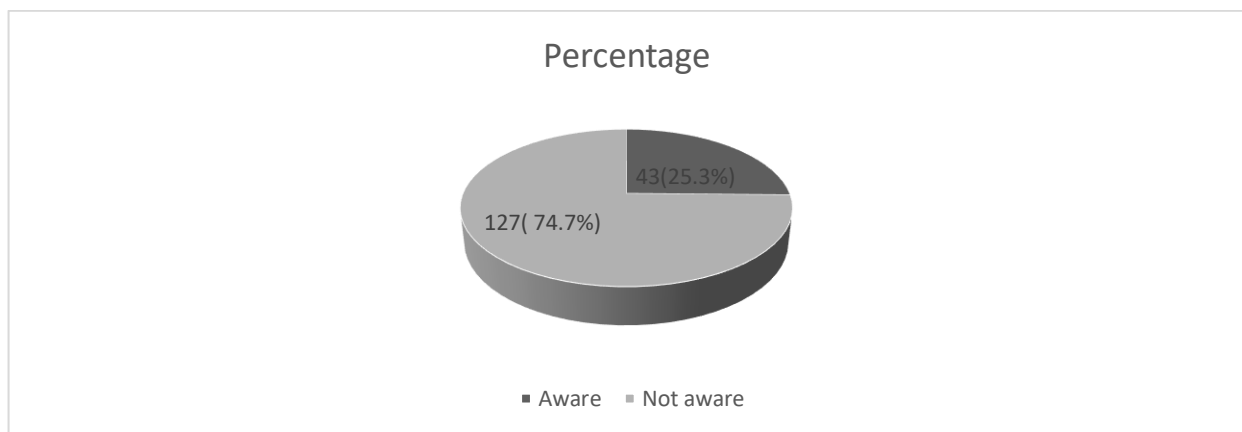


FIGURE 2. Prevalence of Miscarriages.

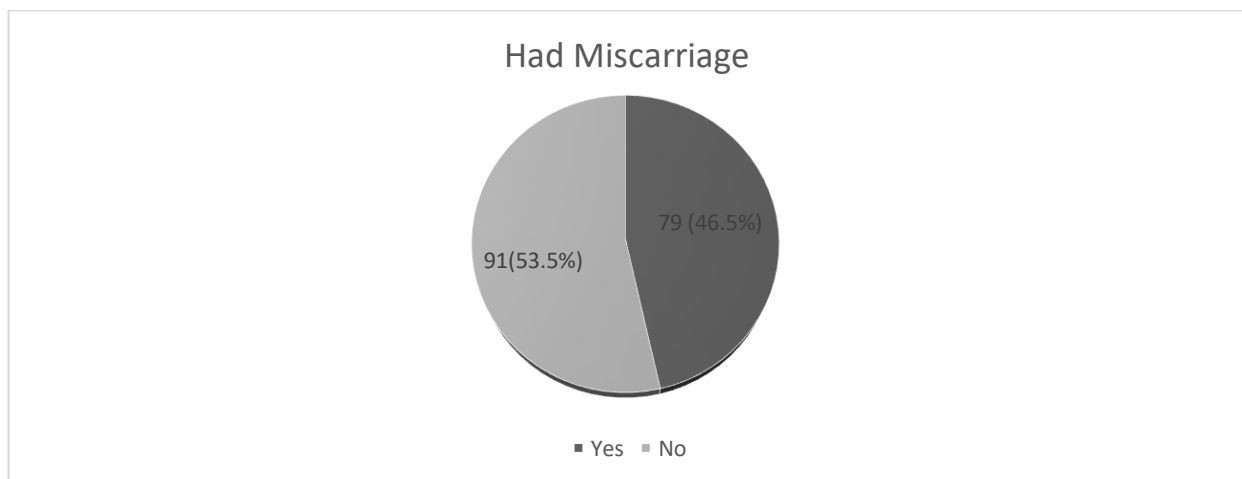


TABLE 2. Respondents knowledge, attitude, practices, and determinants in the use of folic acid in the prevention of spinal bifida.

Variable	Frequency (n=170)	Percent (%)
Knowledge		
Good	122	71.8
Fair	36	21.2
Poor	12	7.1
Attitude		
Positive	147	86.5
Negative	23	13.5
Practice		
Good	106	62.4
Fair	49	28.8
Poor	15	8.8
Determinants		
Strong	9	5.3
Weak	161	94.7

TABLE 3A. Association between socio-demographic characteristics of respondents and their knowledge on the use of folic acid in the prevention of spina bifida.

DEMOGRAPHIC	KNOWLEDGE OF RESPONDENT			
VARIABLE	GOOD (%)	FAIR (%)	POOR (%)	TOTAL (%)
Age group (years)				
< 20	1(20)	2(40)	2(40)	5(100)
20-29	27(58.7)	14(30.4)	5(10.9)	46(100)
30-39	74(82.2)	12(13.3)	4(4.5)	90(100)
40-49	20(70)	8(27.6)	1(2.4)	29(100)
Total	122(71.7)	36(21.2)	12(7.1)	170(100)
X² = 20.280 p=0.002				

Marital status				
Single	8(38.1)	6(28.6)	7(33.3)	21(100)
Married	98(74.8)	28(21.4)	5(3.8)	131(100)
Widowed	12(85.7)	2(14.3)	0(0)	14(100)
Cohabiting	4(100)	0(0)	0(0)	4(100)
Total	122(71.7)	36(21.2)	12(7.1)	170(100)
$X^2 = 29.775 \quad p < 0.001$				
Level of education				
Primary	22(64.6)	4(11.8)	8(23.6)	34(100)
Secondary	56(66.6)	26(31)	2(2.4)	84(100)
Tertiary	44(84.7)	6(11.5)	2(3.8)	52(100)
Total	122(71.7)	36(21.2)	12(7.1)	170(100)
$X^2 = 25.662 \quad p < 0.0001$				
Occupation				
Employed	48(82.8)	8(13.8)	2(3.4)	58(100)
Unemployed	13(48.2)	8(29.6)	6(22.2)	27(100)
Self-employed	58(73.4)	18(22.8)	3(3.8)	79(100)
Student	3(50.1)	2(33.3)	1(16.6)	6(100)
Total	122(71.7)	36(21.2)	12(7.1)	170(100)
$X^2 = 18.262 \quad p = 0.006$				

TABLE 3B. Socio-demographic characteristics of respondents and knowledge on the use of folic acid in the prevention of spinal bifida.

DEMOGRAPHIC VARIABLES	KNOWLEDGE OF RESPONDENT			
Pregnancies had	GOOD (%)	FAIR (%)	POOR (%)	TOTAL (%)
None	11(57.9)	3(15.8)	5(26.3)	19(100)
1-3	24(61.5)	11(28.2)	4(10.3)	39(100)

4-6	53(75.7)	15(21.4)	2(2.9)	70(100)
7-9	28(80)	7(20)	0(0)	35(100)
>9	6(85.7)	0(0)	1(14.3)	7(100)
Total	122(71.7)	36(21.2)	12(7.1)	170(100)

$\chi^2=19.714$ $p=0.011$

Had Spinal bifida child

Yes	39(90.7)	3(7)	1(2.3)	43(100)
No	83(65.3)	33(26)	11(8.7)	127(100)
Total	122(71.7)	36(21.2)	12(7.1)	170(100)

$\chi^2=10.182$ $p=0.006$

Had a Miscarriage

Yes	61(77.2)	15(19)	3(3.8)	79(100)
No	61(67.1)	21(23.1)	9(9.8)	91(100)
Total	122(71.7)	36(21.2)	12(7.1)	170(100)

$\chi^2=3.169$, $p=0.205$

TABLE 4A. Sociodemographic characteristics of respondents and attitude on the use of folic acid in the prevention of spina bifida.

DEMOGRAPHIC VARIABLE	ATTITUDE OF RESPONDENT		
	POSITIVE (%)	NEGATIVE (%)	TOTAL (%)
Age group (years)			
< 20	3(60)	2(40)	5(100)
20-29	38(82.6)	8(17.4)	46(100)
30-39	82(91.1)	8(8.9)	90(100)
40-49	24(82.8)	5(17.2)	29(100)
Total	147(86.5)	23(13.5)	170(100)

$\chi^2 = 5.579$ $p=0.134$

Marital status

Single	15(71.4)	6(28.6)	21(100)
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Married	114(87)	17(13)	131(100)
Widowed	14(100)	0(0)	14(100)
Cohabiting	4(100)	0(0)	4(100)
Total	147(86.5)	23(13.5)	170(100)

$X^2 = 6.912$ $p=0.075$

Level of education

Primary	24(70.6)	10(29.4)	34(100)
Secondary	73(86.9)	11(13.1)	84(100)
Tertiary	50(96.2)	2(3.8)	52(100)
Total	147(86.5)	23(13.5)	170(100)

$X^2 = 11.512$ $p=0.003$

Occupation

Employed	52(89.7)	6(10.3)	58(100)
Unemployed	17(63)	10(37)	27(100)
Self-employed	72(91.1)	7(8.9)	79(100)
Student	6(100)	0(0)	6(100)
Total	147(86.5)	23(13.5)	170(100)

$X^2 = 15.667$ $p=0.001$

Pregnancies had

None	15(78.9)	4(21.1)	19(100)
1-3	29(74.4)	10(25.6)	39(100)
4-6	64(91.4)	6(8.6)	70(100)
7-9	33(94.3)	2(5.7)	35(100)
>9	6(85.7)	1(14.3)	7(100)
Total	147(86.5)	23(13.5)	170(100)

$X^2 = 9.111$ $p=0.058$

TABLE 4B. Sociodemographic characteristics of respondents and attitude on the use of folic acid in the prevention of spinal bifida.

DEMOGRAPHIC VARIABLE	ATTITUDE OF RESPONDENT		
Had Spinal bifida child	POSITIVE (%)	NEGATIVE (%)	TOTAL (%)
Yes	38(88.4)	5(11.6)	43(100)
No	109(85.8)	18(14.2)	127(100)
Total	147(86.5)	23(13.5)	170(100)

 $X^2=0.178$, $p=0.673$ **Had a Miscarriage**

Yes	70(88.6)	9(11.4)	79(100)
No	77(85.6)	14(15.4)	91(100)
Total	147(86.5)	23(13.5)	170(100)

 $X^2=0.576$, $p=0.448$

TABLE 5A. Socio-demographic characteristics of respondents and practice on the use of folic acid in the prevention of spinal bifida.

DEMOGRAPHIC VARIABLE	PRACTICE OF RESPONDENT			
	GOOD (%)	FAIR (%)	POOR (%)	TOTAL (%)
Age group (years)				
< 20	1(20)	2(40)	2(40)	5(100)
20-29	22(47.8)	16(34.8)	8(17.4)	46(100)
30-39	64(71.1)	22(24.4)	4(4.4)	90(100)
40-49	19(65.6)	9(31)	1(3.4)	29(100)
Total	106(62.4)	49(28.8)	15(8.8)	170(100)

 $X^2 = 17.821$ $p=0.007$ **Marital status**

Single	8(38.1)	5(23.8)	8(38.1)	21(100)
Married	82(62.6)	44(33.6)	5(3.8)	131(100)

Widowed	12(85.7)	0(0)	2(14.3)	14(100)
Cohabiting	4(100)	0(0)	0(0)	4(100)
Total	106(62.4)	49(28.8)	15(8.8)	170(100)

$\chi^2 = 35.461$ $p < 0.001$

Level of education				
Primary	13(38.2)	17(50)	4(11.8)	34(100)
Secondary	53(63)	26(31)	5(6)	84(100)
Tertiary	40(77)	6(11.5)	6(11.5)	52(100)
Total	106(62.4)	49(28.8)	15(8.8)	170(100)

$\chi^2 = 17.314$, $p = 0.002$

Occupation

Employed	43(74.2)	9(15.5)	6(10.3)	58(100)
Unemployed	10(37)	15(55.6)	2(7.4)	27(100)
Self-employed	49(62)	23(29.1)	7(8.9)	79(100)
Student	4(66.7)	2(33.3)	0(0)	6(100)
Total	106(62.4)	49(28.8)	15(8.8)	170(100)

$\chi^2 = 15.131$, $p = 0.019$

Pregnancies had

None	8(42.1)	3(15.8)	8(42.1)	19(100)
1-3	25(64.1)	10(25.6)	4(10.3)	39(100)
4-6	41(58.5)	27(38.6)	2(2.9)	70(100)
7-9	28(80)	7(20)	0(0)	35(100)
>9	4(57.1)	2(28.6)	1(14.3)	7(100)
Total	106(62.4)	49(28.8)	15(8.8)	170(100)

$\chi^2 = 37.809$ $p = 0.000$

TABLE 5B. Socio-demographic characteristics of respondents and practice on the use of folic acid in the prevention of spinal bifida.

DEMOGRAPHIC VARIABLE	PRACTICE OF RESPONDENT			TOTAL (%)
	GOOD (%)	FAIR (%)	POOR (%)	

Had Spinal bifida

Yes	32(74.4)	10(23.3)	1(2.3)	43(100)
No	74(58.3)	39(30.7)	14(11)	127(100)
Total	106(62.4)	49(28.8)	15(8.8)	170(100)

 $\chi^2=4.717$, $p=0.095$ **Had a Miscarriage**

Yes	56(70.9)	22(27.8)	1(1.3)	79(100)
No	50(54.9)	27(29.7)	14(15.4)	91(100)
Total	106(62.4)	49(28.8)	15(8.8)	170(100)

 $\chi^2=11.326$, $p=0.003$

TABLE 6A. Socio-demographic characteristics of respondents and the determinants on the use of folic acid in the prevention of spinal bifida.

DEMOGRAPHIC VARIABLE	DETERMINANTS OF RESPONDENT		TOTAL (%)
	STRONG (%)	WEAK (%)	

Age group (years)

< 20	1(20)	4(80)	5(100)
20-29	6(13)	40(87)	46(100)
30-39	2(2.2)	88(97.8)	90(100)
40-49	0(0)	29(100)	29(100)
Total	9(5.3)	161(94.7)	170(100)

 $\chi^2=10.981$ $p=0.012$ **Marital status**

Single	3(14.3)	18(85.7)	21(100)
Married	6(4.6)	125(95.4)	131(100)
Widowed	0(0)	14(100)	14(100)

Cohabiting	0(0)	4(100)	4(100)
Total	9(5.3)	161(94.7)	170(100)

$X^2 = 4.526, p=0.210$

Level of education

Primary	2(5.9)	32(94.1)	34(100)
Secondary	3(3.6)	81(96.4)	84(100)
Tertiary	4(7.7)	48(92.3)	52(100)
Total	9(5.3)	161(94.7)	170(100)

$X^2 = 1.117 p= 0.572$

Occupation

Employed	2(3.4)	56(96.6)	58(100)
Unemployed	4(14.8)	23(85.2)	27(100)
Self-employed	2(2.5)	77(97.5)	79(100)
Student	1(16.7)	5(83.3)	6(100)
Total	9(5.3)	161(94.7)	170(100)

$X^2 = 80.26 p=0.045$

TABLE 6B. Socio-demographic characteristics of respondents and the determinants on the use of folic acid in the prevention of spinal bifida.

DEMOGRAPHIC VARIABLE	DETERMINANTS OF RESPONDENT		
	STRONG (%)	WEAK (%)	TOTAL (%)
Pregnancies had			
None	3(15.8)	16(84.2)	19(100)
1-3	2(5.1)	37(94.9)	39(100)
4-6	4(5.7)	66(94.3)	70(100)
7-9	0(0)	35(100)	35(100)
>9	0(0)	7(100)	7(100)

Total	9(5.3)	161(94.7)	170(100)
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$\chi^2=6.549$, $p=0.162$

Had Spinal bifida child

Yes	0(0)	43(100)	43(100)
No	9(7.1)	118(92.9)	127(100)
Total	9(5.3)	161(94.7)	170(100)

$\chi^2=3.218$, $p=0.073$

Had Miscarriage

Yes	4(5.1)	75(94.9)	79(100)
No	5(5.9)	86(94.1)	91(100)
Total	9(5.3)	161(94.7)	170(100)

$\chi^2=0.016$, $p=0.900$

DISCUSSION

This research was carried out to assess the knowledge, attitude, and practice of use of folic acid in the prevention of spinal bifida among women of childbearing age in ECLGA of Edo State. The research also assessed the relationship between socio-demographic factors and knowledge and use of folic acid in the prevention of spinal bifida. A total of 170 women, all of childbearing age, were interviewed. The mean age is 32 years with the highest proportion of participants 90(52.9%) consisting of those within the age group 30-39 years.

Majority of the participants were married 131(77.1%) as compared to singles 21(12.4%), widows 14(8.2%), cohabiting (2.4%). Up to 84(49.4%) had secondary education, 52(30.6%) had tertiary education, and 34(20.0%) had primary education. We observed that the majority of the respondents 71.8% had good knowledge about the use of folic acid in the prevention of spinal bifida. This is in sharp contrast to a study done on awareness of mothers about birth defects in Ibadan, in which only 15.8% knew that birth defects could be prevented.¹⁰ In another study in Ibadan, only 11.8% knew that folic acid could prevent birth defects although as much as 98.3% were using folic acid in the current pregnancy.¹¹

64.6% awareness of folic acid was reported in Jos.¹² In Port Harcourt, 94.4% knew about folic acid, but only 24.1% knew folic acid could prevent birth defects.¹³ The high awareness in this study is quite encouraging. It could be explained by the proximity of the respondents to a tertiary health facility (Irrua Specialist Teaching Hospital) which gives them access to health education through campaigns or interactions with resident health personnel. Also, there is routine education of women during antenatal visits, as most respondents stated.

We also observed that certain socio-demographic factors had a demonstrable influence on knowledge of folic acid use in the prevention of spinal bifida. Age, marital status, level of education, occupation, previous pregnancy and having babies with spinal bifida in the past were significantly associated with knowledge of the use of folic acid whereas factors like religion and number of miscarriages were not. These observations are by earlier observations.^{11, 14-18} On the aspect of attitude towards the use of folic acid, most of the respondents 86.5%. Showed a positive attitude. Sociodemographic factors significantly associated with this positive attitude were level of education ($p=0.003$), occupation ($p=0.001$).

More than half of the respondents 62.4 had a good practice which compares favorably with the result of the study done in Jakarta, Indonesia where 64% of respondents claimed to have been compliant with the use of folic acid.³³ In another study done in Canada, 71% were compliant with the use of folic acid,³⁵ while only 22.3% of the women in a study in Denmark showed compliance¹⁹. The differences between our observation and between the results in previous reports could be due to the difficulty in measuring the actual practice of use of folic acid by women of childbearing age, for example in the Jakarta study²⁰; two parallel results were obtained from the same respondents using qualitative and quantitative tools.

There was a statistically significant relationship between age ($p=0.007$), number of miscarriages ($p=0.003$), marital status ($p=0.000$), level of education ($p=0.002$), number of pregnancies had (0.000). A number of pregnancies had the highest statistical significance.

Determinants of use of folic acid showed statistically significant relationship with certain sociodemographic factors such as with age group such as women between 30-39 years had strong score while women less than 20 years had weak score reason for which may be due to teenage unplanned pregnancy, ignorance and late antenatal booking which is in keeping with the study done in South-western Nigeria.¹⁷ In our study, the occupation had the highest statistical significant relationship ($p=0.045$). This shows that employment empowers these women making them better placed to use folic acid. Also, employment is also related to an older age.

CONCLUSION

We concluded that

1. The knowledge of the use of folic acid among women of childbearing age in ECLGA is good. Furthermore, attitude and practice of use of folic acid match the knowledge and compares unfavourably with the levels reported from other places.
2. The level of knowledge, attitude, and practice on the use of folic acid among women of childbearing age in ECLGA are dependent on age, marital status, level of education, occupation, number of pregnancies, previous child with spinal bifida.

RECOMMENDATION

We recommend that:

1. The government and health institution should work closely with stakeholders in the health sector to create more public enlightenment campaigns to increase awareness about spinal bifida and use of folic acid either in their diet or as medication in its prevention especially among women of childbearing age
2. Communities should organize forums where a health worker enlightened member about the benefits of the use of folic acid by women of childbearing age while also answering any questions they may have.

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