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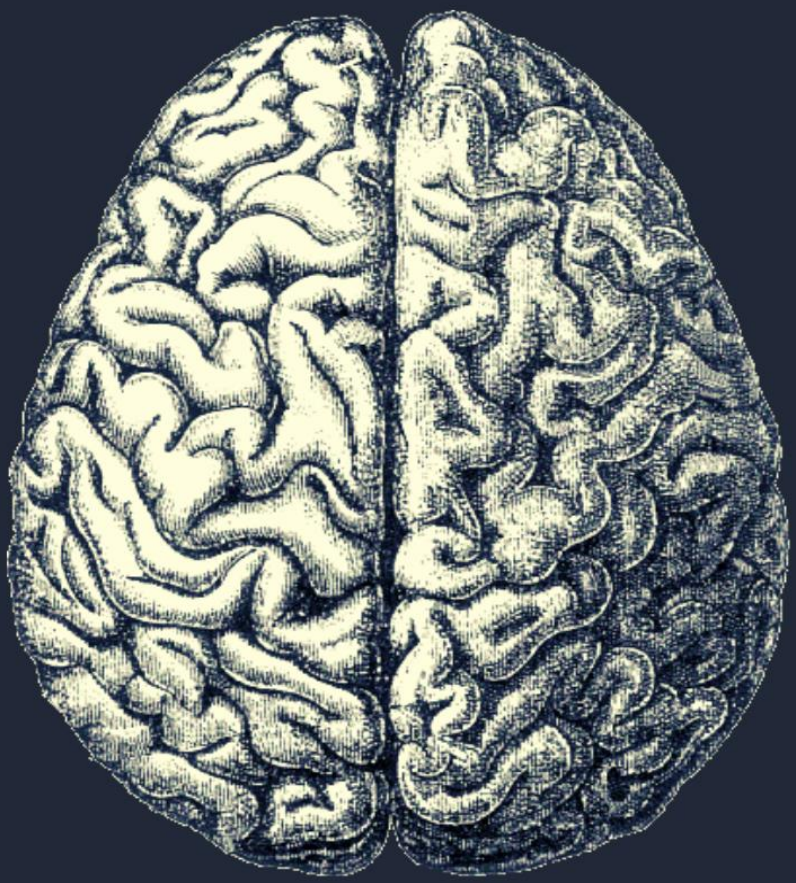

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Active hydrocephalus with aqueduct stenosis to an old woman. Case report

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ABSTRACT

Introduction: Aqueduct stenosis (AS) in old people is a rare pathological entity. I report a case of a 66 years old woman with severe ataxia, cognitive deterioration, loss of sphincters control (gatism). Clinical, neuro-radiologic and therapeutic considerations are discussed.

Case presentation: A 66 years old woman with a 6 months history of mild cerebral trauma by car accident without losing consciousness, present 2 months before hospitalization severe ataxia, cognitive disorders, gatism. At the time of trauma, brain scanner performed in another institution showed minimal fronto-basal cerebral contusions and blood collection around the brain stem. One month after a new unenhanced brain scan all previous lesions are gone. At admission, an abnormal enlargement of lateral and third ventricles are remarked both on unenhanced CT and MRI scan of the brain explained by cerebral aqueductal stenosis. Ventricular open pressure was 350 mm H_2O. A ventriculoperitoneal shunt with a variable pressure valve was installed. The surgery went uneventful and the patient recovered as expected. 6-month follow-up visit the patient was symptom-free, with a fine intellectual recovery.

Keywords
aqueductal stenosis (AS), different pressure hydrocephalus, old people, surgical techniques, ventriculoperitoneal shunt with variable pressure valve

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INTRODUCTION

Abnormal enlargement of lateral and third ventricles due to aberrant accumulation of CSF induced by a AS, generally implies a congenital etiology; to those people that survive, an alternate CSF drainage pathway via the extracellular space (ECS) of the brain, with increasing resistance to CSF outflow with deep white matter ischemia, leads to symptoms onset in 3%-10% of adult hydrocephalus. To old persons, AS is much rarer (1)(2).

PHYSIOPATHOLOGY AND AETIOLOGY

A 66-year-old woman, teacher, has a previous 6 months history of a mild cerebral trauma by car accident without losing consciousness. At the time of trauma, brain scanner performed in another institution showed minimal fronto-basal cerebral contusions and blood collection around the brain stem. One month after a new unenhanced brain scan

all previous lesions are gone. 2 months before hospitalization the payient present: headaches, dizziness, loss of coordination, severe ataxia, cognitive disorders, loss of sphincters control. Upon physical examination, the patient has an oral temperature of 37°C (98.6°F), blood pressure was 154/90 mm Hg, pulse was regular with a rate of 76 beats/min, her heart sounds are normal. She is unable to stand, due to a severe feeling of imbalance. She has a severe ataxia, the power was normal in all 4 limbs, with mild spasticity, no Babinski sign. Sensation to pinprick and temperature, the joint position and vibration sense are intact bilaterally. She has a sustained horizontal gaze-evoked nystagmus looking to the left and right, with a down beating nystagmus on downward gaze. The gag reflex is diminished. The tongue movements are normal. Routine laboratory analysis findings, including a complete blood cell count, a basic metabolic panel with renal function tests, blood sugar level, lipid profile, prothrombin time and concentration were normal. A fine opthalmologic, psihyatric and psyhologic clinical evaluation was performed: fundus oculi was normal, but severe cognitive disorders, especially affecting memory, attention were reported. Noncontrast CT scan of the head and cerebral & spine MRI to exclude a possible obstructive cause of hydrocephalus an AS was performed (Fig. 1).

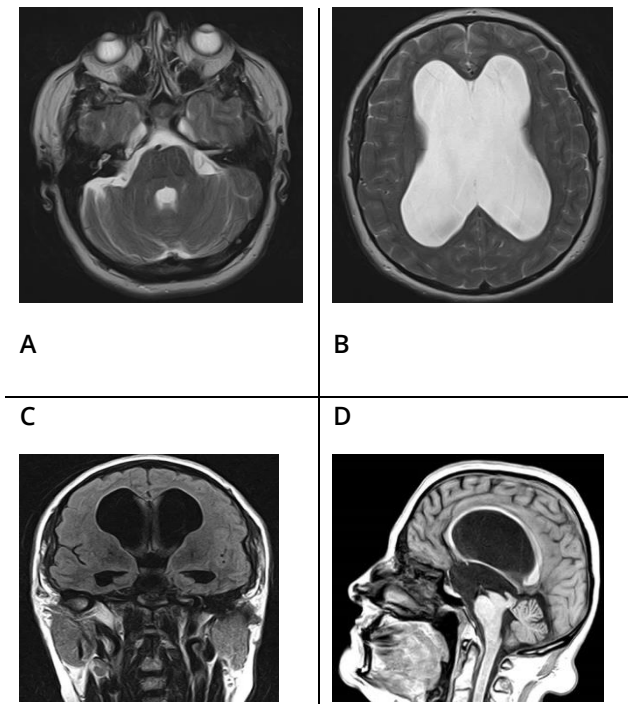

Figure 1. Pre-operative MRI A & B T2 axial, highlighting the 4th ventricle and the lateral ventricles, C &D T1 coronal and sagittal demonstrates the extent of hydrocephalus by AS.

A fine treatment tunnig using surgical shunt diversion with variable valve was installed (a Strata II variable valve – Metdronic was used); ventricular open pressure was 350 mm H2O. The surgery went uneventful and the patient recovered as expected. 6 month follow-up visit the patient was symptom free, with a fine intellectual recovery. Unenhanced brain scanner demonstrate significant remission of the ventricular size (Fig. 2).

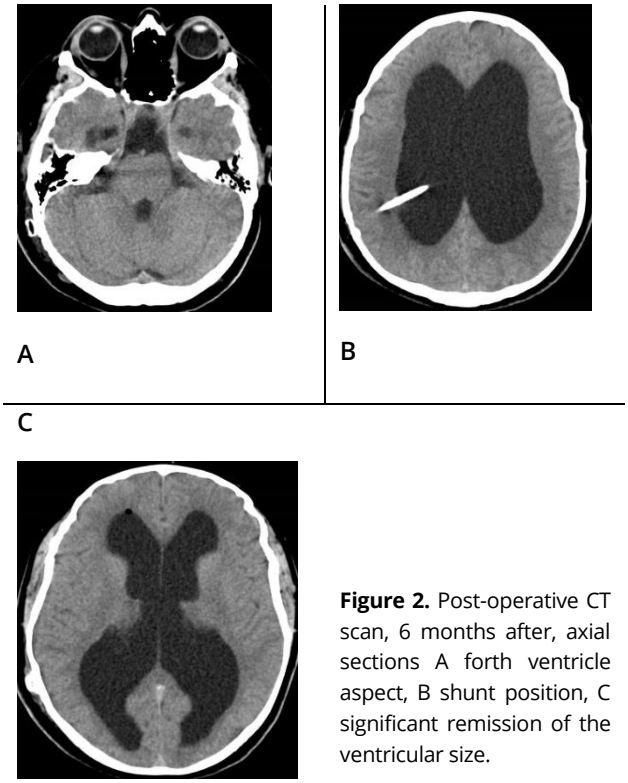

Figure 2. Post-operative CT scan, 6 months after, axial sections A forth ventricle aspect, B shunt position, C significant remission of the ventricular size.

Discussions

Aqueductal stenosis (AS), is a pathological entity, generating abnormal enlargement of lateral and third ventricles due to aberrant accumulation of CSF, with normal 4th ventricle responsible for 20% of cases of hydrocephalus (3). More frequent in children 16-60% - its incidence ranges from 0.5 to 1.0 in 1,000 births, with a recurrence risk in siblings of 1.0% to 4.5%, it may be inherited in an X-linked recessive manner, see Bickers-Adams-Edwards syndrome (4). AS appears less in adult 3-10% - as an acquired abnormality and is rare in elderly people.

Historical data: LIAS - late-onset idiopathic aqueductal stenosis (5) was first described by Spiller in 1902, Schlapp and Gere in 1917 suggested the pathological relationship between AS and congenital hydrocephalus. Dandy resume this idea in 1920, 1945 (6)(7). From 1930 to 1977 there are more than 20 bibliographic references with this subject (8), subsequently, many works were performed elucidating the diagnosis and treatment.

Concerning etiology, there are several extrinsic and intrinsic causes for AS. However there is no correlation between aqueduct caliber and hydrocephalus: a partial stenosis may coexist with normal-sized ventricles; also complete stenosis it is difficult to admit at least on a microscopic scale, in a patient who has reached adulthood, in the absence of a macrocephaly - weighty argument for congenital origin, because there are possible alternate CSF drainage pathway via the extracellular space (ECS) of the brain, also late onset of congenital origin of AS (1)(5)(8)(9). The main causes of AS (1)(3-5)(8-12) are:

-congenital with large range incidence between 3.7:1,000,000 to 1:2000, rarely it may be inherited in an X-linked recessive transmission Bickers Adams Edwards syndrome: with congenital AS, corpus callosum and corticospinal spinal tracts agenesis, absence of medullary pyramids. Congenital AS can present later in adult age due to compensation of CSF flow dynamics during childhood and normalization of clinical symptoms (10);

-acquired with different causes: extrinsic and intrinsic. Extrinsec causes can generate AS by mechanic compression;

-tumors: posterior third ventricle mass, tectal plate glioma, pineal and posterior fossa tumor: metastasis, hemangioblastoma, glioma – even a subependymal astrocytoma, vestibular schwannoma, meningioma in contact with tentorial incisura;

-posterior fossa arachnoid cyst;

-cerebral vascular malformations: Galen malformation, basilar megadolico basilar trunk lifting the floor of the third ventricle;

-malformative causes: Chiari and Dandy Walker malformations;

-aquired causes: Paget's disease – by venous compression of bone origin, Guillain Barré syndrome, syphilis, sarcoidosis.

Intrinsec causes can be multiple:

-idiopathic or “simple”, late-onset idiopathic AS especially in the elderly, apparently without a precise cause, not uncommon; aqueduct caliber could be obliterated by subarachnoid-villous system age alteration, or even narrowed with normal ependymal cells in the lumen, without gliosis of the surrounding tissues;

-reactive gliosis with glial cell and fibers proliferation, without ependyma (the residual lumen is not outlined by ependyma) as a reaction to:

1. subarachnoid hemorrhage (SAH) after an aneurysm rupture, posttraumatic – as in our case, neurosurgical interventions in elderly subjects after surgical sacrifice of CSF. resorption pathways, heavy bleeding, posterior cerebral fossa with opening of the fluid system;
2. toxic agents: a widespread ependymitis and ventriculitis generating AS at the time of scarring viral (urlian), bacterial, tuberculous, lymphomatous, carcinomatous, toxoplasmosis;
3. increased resistance to CSF flow, see deep white matter ischemia in late adulthood, venous hypertension, developmental venous anomaly draining bilateral medial thalami (12).

-intraventricular high pressures may generate vascular problem, decreased secretion, gradual increase in resorption capacities: trans-ependymal, choroid plexuses, optic nerve sheaths, large vessel adventitia, lymphatic pathways, residual gradient.

-biochemistry changes and physical properties of enclosures with visco-elastic walls, under persistent residual gradient generating structural changes of cerebral mantle.

According to the histopathological classification of Russell in non-tumoral AS there are four types (13-15):

1. “congenital atresia” – generating global caliber stenosis, with normal histology, due to a malformation of abnormal development.
2. "forking"aqueduct”- 2 distinct channels, in a sagittal plane, one behind the other, may communicate, may enter the ventricle independently, or end blindly are separated by normal nervous tissue expression of an incomplete fusion of the median fissure, reducing the lumen and/or perturbing the laminar flow of CSF.
3. "septum formation"- a webs or diaphragms, more frequent at the lower end of the aqueduct, gradually becomes a tiny sheet from prolonged pressure and dilatation of the canal above.

4. “gliosis” - characterized by proliferation of glial cells and overproduction of glial fibers, the residual lumen is not outlined by ependymal, usually a reaction to irritant agents, such as hemorrhage – see our case, infection, or toxic agents, and is often part of a widespread ependymitis of the ventricles. In such cases transition to chronicity involves different pathophysiological mechanisms acting simultaneously (10).

Clinical features in AS reflects the acute or chronic picture of the evolution of the disease (4)(5)(8)(10)(16)(17), due to alterations of CSF dynamics, with acute or compensated stages, explaining in congenital origin, undiagnosed aspects during several years: enlarging infant head size, bulging fontanelles, gaping cranial sutures, setting sun phenomenon, in X-linked form (Bickers-Adams-Edwards syndrome) profound intellectual disability, bilateral adducted thumbs. Subjective aspects in acute or subacute stages: headaches in attacks or continuous, variable seat, vomiting especially in posterior fossa tumor, decreased conscious state; in compensated stages episodes of headaches and nausea more severe in the morning and diplopia by abducens nerve palsy in intra-cranian hypertension syndrome, dizziness, somnolence, in adults with late-onset idiopathic AS more commonly have chronic onset of neurological symptoms, also pure akinesia with gait freezing (18). Objective aspects are variable in acute decompensated stage – see the present case, with: comitial crises, episodes of graying out of vision, papillary stasis on fundus oculi, Parinaud syndrome - upward gaze and accommodation failure, pupillary contraction abnormality, nystagmus, paralysis of extrinsic musculature, intracranial hypertension syndrome with Cushing triad - hypertension, reflex bradycardia, respiratory irregularities, rhinorheea, "bobble head doll" syndrome with repetitive antero-posterior head movements; sphincter disorders are generally limited to urination disorders of varying severity: from pollakiuria to urinary incontinence in the final stage, rarely accompanied by anal incontinence, impaired consciousness, disturbance of the conscious level up to coma by brain engagement. In chronic stages: walking apraxia, standing disorder, with widening of the support polygon, retropulsion, falls; head wearing in a slight lateral inclination, ataxia, gait disturbance, bipyramidal and cerebellar syndrome by white matter tracts pressure surrounding the ventricles, increased reflexes, paroxysmal attacks with hypertonicity of the axial muscles and limbs in opisthotonus, spastic weakness of lower limbs with gait disturbance, akinetic mutism is the most serious ultimate form of motor disturbance, neuro-psychological tests detect degradation, with visual-spatial or constructive difficulties associated with motor performance disorders; so called "the nonverbal learning disabilities syndrome" Fletxher 1995. There are also: behavioral changes of cognitive function, mental fatigue, attention disorders, depression, disinterest, temporal disorientation, sluggishness up to 40%, also abulia; vegetative disorders: tachypnea, bradycardia /tachycardia, hyperthermia, hypopituitarism disorder; diabetes; obesity.

In adults, with A.S. there are 3 possible situations (19)(20)

1. active hydrocephalus with PIC average > 12 mm Hg - unclear decompensation mechanism with possibly congenital aqueduct stenosis, after head trauma, infection, hemorrhage, even stenosis secondary to hydrocephalus, itself secondary to a more distal obstacle, thus forming a vicious circle hydrocephalus-stenosis-hydrocephalus.

The disjunction of ependymal cells under the effect of ventricular distension explains the classic transependymal resorption see LOVA concept: long standing open ventriculomegaly in adults; important congenital hydrocephalus found in adults, even with transependymal resorbtion, justified by an AS, with macrocephaly, cognitive troubles with subnormal QI, intracranial hypertension syndrome, spastic weakness of lower limbs with gait disturbance, loss of sphincters control (gatism).

2. compensated chronic hydrocephalus (symptomatic condition, with non-progressive hydrocephalus): average PIC </ = 12 mm Hg, with A or B waves. The pressure is normal only in appearance, because above a low mean value there are pathological waves (A and / or B). The transependymal pressure gradient persists, maintaining or worsening ventricular distension.

The triad of HAKIM & ADAMS (1965) bringing together movement disorders, psycho-intellectual disorders and sphincter disorders, classic "normal presssure hydrocephalus". Bi or unisymptomatic forms (isolated motor or mental disorders, exceptionally sphincter disorders) are not rare. Bret-Chazal (18) appreciate that the terminology "normal

pressure" is ill suited, because the intracranial pressure in this condition is not always normal, see our case.

3. arrested chronic hydrocephalus (asymptomatic, inactive with non-progressive ventriculomegaly when the intracranial pressure (ICP) returns to normal, despite the remaining dilated ventricle): average PIC </ = 12 mm Hg, without wave A or B, is a chronological stage in the natural history of a hydrocephalus not a constant situation, has applicability in all progressive, active hydrocephalus in adults, the evolution is in bursts, appear after shunt or endoscopic third ventriculostomy (ETV)

In AS the main studies (20-22) are:

-unenhanced brain scanner identifies a possible cause of hydrocephalus, the ventricular dilation, permit reproducible measurements such as the bifrontal index, highlight parenchymal abnormalities, peri-ventricular hypodensities, the degree of visibility of the subarachnoid spaces: dilated, normal, erased, see basal cisterns, Sylvian valleys. Brain scanner in dynamic may quantify hydrocephalus, evaluate hydrocephalus after treatment.

-cerebral MRI may precise topography of a possible obstruction; may show funnelling superiorly of Sylvius aqueduct, distinguish the extent of obstructive hydrocephalus of the lateral and third ventricles with the 4th ventricle not dilated, transependymal resorption and signal abnormalities in the subependymal zone, images of leukoencephalopathy reflecting vascular processes more distant from the ventricles, monitorise the hydrocephalus during treatment. Useful MRI protocols in AS are: sagittal T2 with the absence of flow-void signal intensity at the aqueductal level, obstructing web; on sagittal CISS and three-dimensional constructive interference in steady-state (3D-CISS): decreased aqueductal stroke volume; phase-contrast MR imaging: peak systolic velocity; cine cardiac-gated phase-contrast MRI: aqueductal CSF flow after aqueductoplasty with stenting (21)(22). In patients with AS and in controls, the apparent diffusion coefficient (ADC) in four regions in the centrum semiovale on midsagittal FIESTA or CISS image proof deep white matter ischemia (DWMI), increasing resistance to CSF outflow through the ECS of the brain and in late adulthood may contribute to the development of symptoms in adult onset AS (9). Another useful studies are PET to prove cerebral functional activity and angiography: to demonstrate megadolico basilar trunk, aneurysm of the ampulla of Galen, or for the study of venous return circulation, intimately linked to the dynamics of CSF.

In AS surgical treatment (5)(23-25) is based on:

1.treatment of the cause: excision of the responsible tumor

2.ventriculo-peritoneal shunt with valve, as in my case, with possible shunt complications - infection, obstruction and overdrainage.

3.endoscopic third ventriculostomy (ETV) can be considered the best surgical procedure for obstructive hydrocephalus caused by AS, restoring physiological circulation of CSF; to patients with obstructive triventricular hydrocephalus, with increased intracranial pressure, translucent membranous stenosis or aqueduct obstruction, prestenotic dilatation of the aqueduct.

4.aqueductal plasty (AP) could be performed alone or as an adjunct to third ventriculostomy, with or without a silastic stent, with few indication today. This procedure it's a logic, but also a high risky procedure with important complications rate after the tectal plate dorsal and midbrain tegmentum ventral trauma: diplopia, dysconjugate eye movement, trochlear palsy.

5. the endoscopic trans-fourth ventricle - retrograde aqueductoplasty with stent placement especially in cases of supratentorial slit ventricles.

Conclusions

This case could be a plea to demonstrate that AS may generate not only a chronic noncommunicating hydrocephalus with a potential normal pressure, as seen later in adults and very rare in elderly people, but also active hydrocephalus installed after a posttraumatic subarachnoid hemorrhage.

The lack of anatomo-pathological confirmation of Sylvius aqueduct to explain AS, may generate speculations to explain active as like chronic noncommunicating hydrocephalus by gliosis or even by the presence of a small and slow growing periaqueductal microglioma.

An active patient survey should be mandatory.

Abbreviations

CSF - cerebro-spinal fluid

AS - aqueductal stenosis
LIAS - late-onset idiopathic aqueductal stenosis
ECS - extracellular space of the brain
PIC - intracranian pressure
AP - aqueductal plasty
ETV - endoscopic third ventriculostomy
RA - retrograde aqueductoplasty by the endoscopic trans-fourth ventricle, with stent placement
VP - ventriculo-peritoneal shunt

Founding and Conflicts of Interest
This study received no funding.
The author declare no conflict of interest.

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Particular management strategy for intraprocedural coil migration during endovascular treatment of intracranial aneurysm

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ABSTRACT
Migration of coils represents one of the most challenging complications of endovascular management of cerebral aneurysms with a potentially catastrophic result. In this article, we present the successful management of a coil migration during the endovascular occlusion of an anterior communicating artery aneurysm. A stent fixation technique was used with good vascular repermeabilisation. The reported frequency, risk factors and management strategies are also discussed.

Keywords
coil migration,
stent fixation technique

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INTRODUCTION

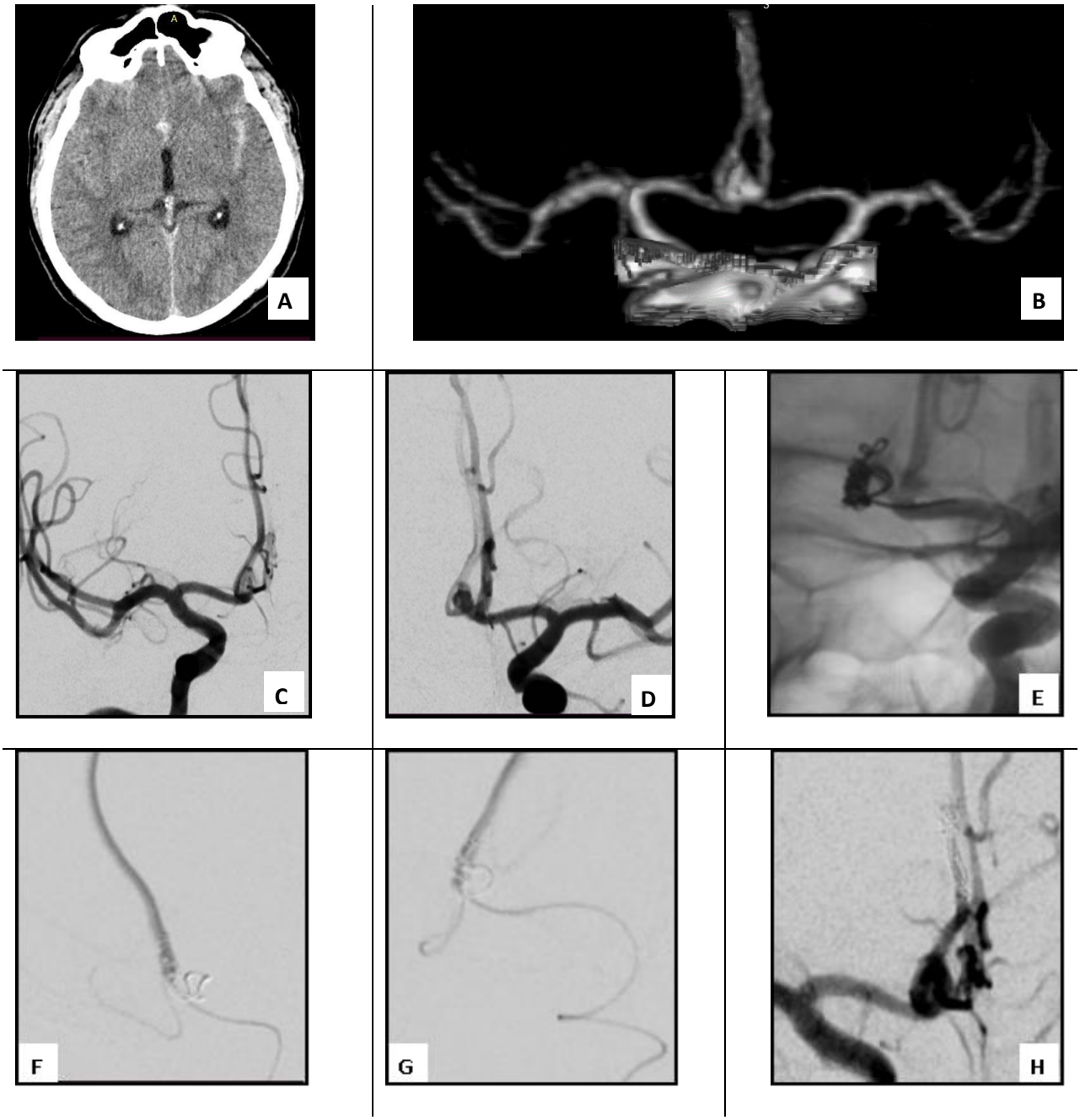
Cerebral aneurysms occlusion by endovascular coiling is considered the main treatment in most neurosurgical centres in the world. With this evolution of treatment, numerous studies have reported coil migration as significant intraprocedural complication which can lead to catastrophic neurological consequences without proper management. The reported rates of coil migration that range from 2% to 6% have not significantly changed over time. However, the outcome of patients with this complication has been greatly improved as a result of development of different techniques and devices for retrieval or repositioning of the migrated coils. In this paper we present a particular management strategy for correction of a distal coil migration in a patient undergoing endovascular coil embolization of an anterior communicating artery aneurysm. We also summarize the current literature describing the management of intraprocedural coil migration [2,4].

CASE PRESENTATION

A 44-year-old man addressed to emergency department from a local hospital for severe headache started in the same day. A head CT-scan investigation was performed immediately and showed a mild subarachnoid haemorrhage in the interhemispheric fissure and both

Sylvian fissures. The CT angiography demonstrated an anterior communicating artery aneurysm as source of hemorrhage. The patient was immediately transferred to our hospital for further treatment. At admission he was confused and presented mild nuchal rigidity. His past medical history included hypertension with no regular treatment. The patient was scheduled for an endovascular aneurysm occlusion for the next day. A written informed consent was obtained prior to the treatment from the family.

The intervention was performed on a biplane angiography system (INFINIX, Toshiba, Canon Medical System) under general anesthesia by our neurosurgical team with many years of experience in neuroendovascular interventions. Femoral artery access was established with a 6 F/11 cm sheath from Merit Medical. Different angled cerebral angiography was performed to clarify the relationship of aneurysm / neck / arterial branches. The aneurism was injected from both carotid artery but with a better visualisation from the left side injection.



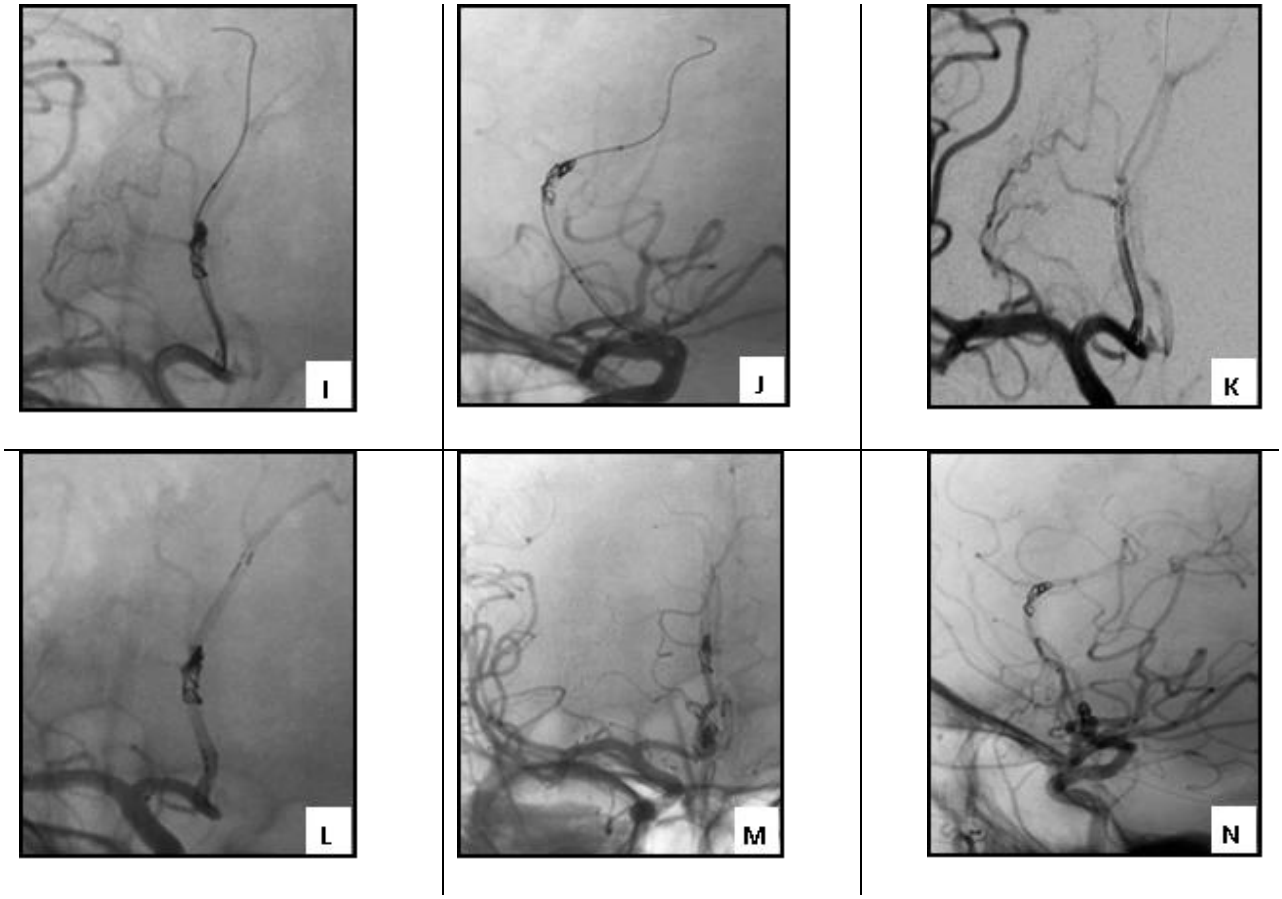


Fig. A. Diagnostic head CT; - **B** – Brain Angio-CT showing a CoA aneurysm; **C, D** – DSA right and left ICA demonstrating a CoA aneurysm: **E** – Partially coil migration to right A2; - **F, G** – Frontal and lateral view with attempt of coil retrieval; - **H** – DSA image with distal coil migration and arterial occlusion; -**I, J** – Microguide and microcatheter passing the coil; **K** – DSA image showing slightly right A2 repermeabilisation; -**L** DSA showing total right A2 repermebilization by coil fixation with a detachable intracranial stent; **M, N** Frontal and lateral view demonstrating adequate coils occlusion of the aneurysm.

A 6F Chaperon guiding catheters (Microvention) was carefully advanced over 0.035 glidewire up to the proximal segment of the left internal carotid artery. A Prowler 10 microcatheter (Codman J&J) was then very carefully advanced over a 0.014 Transed microwire (Boston Scientific) and positioned into the aneurysm sac. One 4/8 mm GALAXY G3™ XSFT coils (Cerenovus Johnson&Johnson) was then inserted and detached into aneurysm. At the beginning of the introduction of the second coil 3/4, the tip of the microcatheter descended to the aneurysm neck. As soon as it was detached, the flow carried a part of the coil from the aneurysm to A2 segment of the right anterior cerebral artery. The next contrast injection demonstrates thrombosis of the right A2 without flow distal to the migrated coil. The right A2 was then catheterized through the left A1 with an Excelsior 10 microcatheter. The microcatheter was advanced proximal to the migrated coil, and 5 ml Heparin solution was infused. The microcatheter was passed carefully distal to the coil, and a 3/30 mm Atlas 2 stent (Stryker) was deployed and successfully fixed and stabilized the migrated coil. The following injection demonstrates a good repermeabilisation of the right A2 segment. A new aneurysm microcatheterization with a Prowler 10 microcatheter was obtained. A complete angiographic occlusion of the aneurysm was obtained after the safe insertion and detachment of other two coils (2/ 8 mm GALAXY G3™ XSFT and 1.5/ 4 mm GALAXY G3 Mini). The microcatheter is then carefully retracted and a DSA acquisition is performed to check the permeability of all vessels. Finally, the entire guiding system is retracted with a compressive dressing of the femoral puncture site. The patient was placed into intensive care and received 75mg clopidogrel and 100mg aspirin daily. Postoperatively the patient remains neurologically

intact. A cerebral CT scan was performed 7 days postoperatively and showed the total SAH resorption. The patient was discharged home after 17 days of hospitalisation in good neurological condition.

Discussion

With the increasing use of spiral embolization techniques, the migration of these removable implants during endovascular embolization of intracranial aneurysms has become a potentially serious intraprocedural complication. The phenomenon of prominence and / or migration of a coil can most often manifest itself on the circulatory hemodynamics at the level of arterial vascularization by creating a thrombogenic nidus that can have an occlusive or embolic effect. Occlusions of the major parent artery or distal vessels branches may result in a large territory infarct with sever neurological consequences.

Even if coil migration is not a common occurrence the incidence reported in the literature varied between 0.5–6% [1,2,3].One of the largest retrospective studies on 1811 patients demonstrated an incidence of coil migration phenomenon of 2,5% [2,3,4]. Higher incidences of this phenomenon have been reported in early studies (Casasco et al, 5.6%) compared to more recent studies (Abdalkader et al, 0.3%). This discrepancy in reported rates it could be in part related to use of the term 'coil migration' in literature for different related situation like coil malpositioning, partial coil stretching, partial prolapse, and total displacement of coils from the aneurysmal cavity. On the other hand, the continuous development of coils and embolization techniques has led to a decrease in the complication rate due to the migration phenomenon[3,5].

Coil migration could be classified depending on the time of detection in acute intraprocedural or delayed postprocedural migration (after completing the coiling procedure).

A number of factors such as anatomical, flow and techniques have so far been described as being responsible for coil migration in the treatment of cerebral aneurysms. There have been reports that have shown a direct relationship between the increased risk of coil migration and the increased width of the aneurysm neck, the presence of vascular conditions and high flow conditions [2,3]. From a technical point of view the unstable configuration, the early detachment and the oversized/undersized use of the coils are the main factors for the migration of the coils.

Coil migration management can vary depending on the migration time (acute or delayed), the location of the migrated coil (proximal or distal) and the permeability of the target vessel and the eloquence of the vascular territory. Thus, endovascular retrieval or fixation techniques, surgical extraction and conservative treatment have been described as management methods in coil migration. Migrated coil retrieval methods should be considered when the migration occurs intraprocedurally and may include stent retrievers, Snaring, Alligator, and Merci devices, aspiration and wire recanalization techniques. The fixation technique by deploying a stent across the migrated coil to restore the arterial flow may be applied in cases in which coil displacement occurs in tortuous and distal intracranial vessels or unsuccessful coil retrieval. The open surgical option must be carefully considered due to its complexity, extremely high risk of morbidity which usually outweighs the potential benefits.

Conservative medical management with antiplatelets and/or anticoagulation should be the first option when the migrated coil is too distal to safely pursue, or there is no associated vessel occlusion and as a possible option following unsuccessful attempts at recovery.

Conclusions

Coil migration during cerebral aneurism endovascular treatment it can have a devastating course in the absence of proper management. Even if no “gold standard” method has been identified for retrieval or repositioning migrated coils, several techniques and devices have proven effective in managing this type of complication. The management of our case demonstrates that stent fixation of a distal migrated coil can be used successfully to rescue patients with this potentially devastating complication.

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Talk and Die Syndrome. A comprehensive review

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ABSTRACT

The "Talk and Die" Syndrome is described as the clinical deterioration following a mild to moderate traumatic brain injury. In the face of this event, individuals are able to articulate recognizable words and then deteriorate within 48 hours of the injury. This syndrome represents a major public health challenge due to its high morbidity and mortality rate; it develops from an intracranial haemorrhage causing an increase in intracranial pressure and leading the person to a neurological crisis with focal signs, coma and later death.

INTRODUCTION

The talk and die syndrome represents a major public health challenge because of its high mortality and disability rate, it can occur at any age, but the risk is significantly higher as the age increases [1]. People who

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"talk and die" after a head injury may suffer late complications that may be highly preventable if detected early [1,2]. Intracranial hematoma is the main reason why a patient whose injury does not appear serious at first, subsequently dies [1,2]. [3].

The high risk of death following this event is that the victim initially appears stable after receiving an apparently minor head trauma, while intracranial hemorrhage either inside or outside the brain is ongoing. Major warning signs include loss of consciousness on impact and severe headaches. If the hemorrhage progresses without being treated in time, the affected person may fall into a coma and even die [4].

The epidemiological study by Dylan Dean et al. found that patients who talk and died were older (median age, 81 years; interquartile range, 67-87 years), normotensive (median systolic blood pressure, 138 mm Hg; interquartile range, 116-160 mm Hg), commonly fall-injured (71.3%), and often (52.4%) died in non-trauma hospitals [5].

The prognosis is related to the amount of hemorrhage found at the time of diagnosis, so it is essential to take early action regarding the management and follow-up of these individuals, especially if they are high-risk groups such as elderly adults [6]. Based on the above, the objective of this review is to provide information that favors the detection and timely treatment of this syndrome, thus having an impact on the reduction of deaths due to this cause.

Definition

"Talk and die" represents a small number of patients with mild head trauma who, due to intracranial causes, deteriorate and die [7]. Really et al in 1987 first introduced the term "talk and die," used to describe a group of patients with potentially recoverable head injuries in whom the primary injury was not severe enough to destroy higher cognitive function. Their ultimate demise was thought to represent a combination of secondary brain injury as well as other potentially preventable factors. For this reason, patients who talk and die have been the focus of multiple studies, most of which were relatively small with limited ability to identify associated factors [1].

The main cause leading to this syndrome is penetrating trauma [8]. In lower frequency are also found falls (28%), traffic accidents (20%), road traffic accidents (19%), assaults (11%), unknown cause (9%), bicycle (3%) and suicide (1%) [9].

Injury severity is associated with risk factors such as older age, lower Glasgow scale score on admission, higher injury severity score (ISS), hypotension on arrival and comorbidities such as congestive heart failure, chronic kidney disease, liver cirrhosis and hematological disorders, subdural hemorrhage, contusion and vault fracture) [10]. Therefore, it is essential to perform a multifocal approach in these individuals in terms of the etiology of the injury, pre-hospital care, initial treatment including the neurocritical care unit and surgical treatment in order to avoid progressive deterioration and multi-organ failure leading to death during the postoperative period [11,12].

Mechanism of injury

The magnitude of the brain injury and the time of duration depends on the severity of the resulting concussion, which is defined as a transient interruption of brain functions caused by a mechanical force. Memory, consciousness, motor control or brainstem functions may be temporarily disrupted or impaired during this phenomenon. The mechanical deformation of brain tissue in a concussion injury is sufficient to interfere with both the functions of polarized neuronal membranes and synapses and render numerous brain neurons temporarily dysfunctional. A concussion is usually not sufficient to cause structural damage, but may result in abnormal brain metabolism for weeks after the initial injury [13].

The basic physiological sequelae that constitute the state of vulnerability induced by traumatic brain injury appear to be due to cellular ionic and metabolic alterations [14]. These pathological changes in the aging brain may trigger secondary brain injury contributing to more severe and irreversible damage in middle-aged and elderly patients, which explains why age plays an important role in the prognosis of those affected [15].

In the growing attempt to understand the pathophysiology of fatal non-projectile head injuries, three grades of diffuse axonal injury have been identified. In grade 1, histologically, axonal injury is seen in the white matter of the cerebral hemispheres, corpus callosum, brainstem and, less frequently, the cerebellum; in grade 2, there is also a focal lesion in the corpus callosum; and in grade 3,

there is also a focal lesion in the dorsolateral quadrant(s) of the rostral brainstem. It is worth mentioning that focal lesions can only be identified microscopically in most cases [16].

Intracranial hematomas are the most frequent cause of deterioration in head trauma patients, so rapid diagnosis and decompression are the most important factors in saving these patients. [17]. The above is due to the increasing volume of accumulated blood which causes a progressive increase in intracranial pressure that can even force the brain down through the foramen magnum causing a brain herniation. This compresses the brain stem with such force that the centers controlling consciousness, respiration, heart rate and blood pressure cease to function, resulting in coma and death [4].

The area in which the intracranial hemorrhage occurs will be a determining factor in its pathophysiology. Intra-axial hemorrhages occur directly in the substance of the brain due to the rupture of blood vessels caused by impact [4]. As for traumatic intraventricular hemorrhages, regardless of the presence or absence of neurological deficits should have close follow-up by emergency physicians because of the possibility of acute obstructive hydrocephalus requiring prompt surgical evacuation before unexpected but avoidable deterioration occurs [12].

On the other hand, among extra-axial hemorrhages, there are epidural, subdural and subarachnoid types of hemorrhage; the latter, for example, its mechanism is that blood leaks into the subarachnoid space, filled with cerebrospinal fluid and reaches the ventricles, causing severe headache, nausea and vomiting. Meanwhile, in subdural hematoma, the bridging veins that drain the surface of the brain into the venous sinuses are torn generating a low-pressure venous hemorrhage. Among the adverse consequences of hemorrhage is hydrocephalus, which, if uncontrolled, can lead to coma and death. Another complication is an intense vasospasm, which can be so marked that it restricts blood flow to that region of the brain, leading to ischemic stroke [4]. Vasospasm is proposed as the cause of secondary ischemic hypoxia associated with a high incidence of acute subdural hematomas and brain swelling. Suggestions for further testing this hypothesis and implications for preventive management are discussed [13].

It is recognized that an apparently minor head injury can cause diffuse cerebral edema with serious consequences. Among the two possible mechanisms described by McCrory are, first, cerebral hyperemia and increased blood volume as a result of disordered cerebrovascular autoregulation, commonly known as "malignant cerebral edema". The second is due to true cerebral edema [18].

The distinction between cerebral swelling and cerebral edema was made by Klazko, who observed that cerebral edema could be cytotoxic or vasogenic and that both could occur after craniocerebral trauma. Therefore, the mechanism of death would be a transtentorial herniation of the brain stem as a consequence of elevated intracranial pressure, which would affect the cardiorespiratory centers of the brain stem [18]. Findings from diffusion MRI and apparent diffusion coefficient (ADC) mapping suggest that cellular swelling is predominant in the peripheral area for a period of 24 to 72 hours while cells in the central area of the contusion undergo shrinkage, disintegration and homogenization [19].

Clinical manifestations

The fact that the patient is talking implies a less severe primary brain injury, but does not necessarily place the patient in the mild head injury category (GCS 13-15) as there are cases with an eye-opening score of 2 or 3, a verbal score of 3 and a motor score of 5 or 6 (GCS of 10-12), which gives a GCS between 9 - 12, placing the patient in the moderate injury group, which of course is associated with a worse prognosis [20]. In addition, in children admitted with head trauma caused primarily by motor vehicle accidents or falls, they had initial Glasgow Coma Scale scores equal to or greater than 9 and demonstrated irritability and restlessness just prior to deterioration [21].

The main primary clinical manifestation is a severe headache followed by problems with speech, vision and even coma. It should be noted that at the beginning people usually do not present any symptoms, but in the course of time may manifest severe headaches, weakness and confusion resulting from lesions of intracranial masses and increased intracranial pressure (ICP) that were progressively established [22]. The mean age, the degree of midline shift observed on computed tomography (CT) and the presence of subdural hematoma are the main factors influencing the

evolution (recovery or death) of patients who talk [23].

The difference between those with and without a lucid period is related to the degree of primary lesion by diffuse white matter impingement and the presence of ventriculomegaly with large sulci rarely found in lucid patients [24]. In the study by Kim et al. it was observed that the median age of patients who died due to hematomas was 82.5 years, compared to 54.0 years for patients who died from refractory ICP elevations ($p = 0.003$). Hyponatremia occurred during the first 7 days in 38.9% of patients who died due to hematomas and in only 14.3% of patients in the ICP group ($p = 0.236$). No seizures were observed in any of the patients in either group. Skull fractures were present in four of the 18 (22.2%) patients who died of hematomas, in contrast to four of the seven (57.1%) patients who died of refractory ICP [25].

The presence of a fracture line proved to be significant, as it was accompanied by approximately 38% intracranial abnormalities versus 6% in non-fractured cases. In addition, high-volume hematomas are associated with more brain injury after a worse clinical course of the patient prior to evacuation, but evacuation does not improve executive functioning in these individuals. Early detection of any asymptomatic intracranial pathology allowed immediate transfer of patients to the neurosurgical center, where surgical treatment was performed, when indicated, without mortality or morbidity [26,27].

In 2 cases of severe traumatic brain injury (TBI) with acute subdural hematoma in which cerebral blood flow (CBF) and cerebral blood volume (CBV) measurements were obtained before evacuation of the subdural hematoma and immediately after removal. The younger patient had the highest preoperative CBF. Thus, it is possible that the cerebral circulation is more easily compromised in older patients; however, it is also possible that the brains of younger patients are more tolerant to similar low levels of CBV [22]. Likewise, patients whose CBF returns to normal 2-3 weeks after severe traumatic brain injury after being abnormally low in the acute phase of the injury can be expected to achieve a good neurological outcome [28].

Diagnosis

To diagnose an intracranial hemorrhage we can detect as warning signs: loss of consciousness at the moment of impact, nausea, vomiting, severe headache, focal neurological deficits, confusion, lethargy, any change in neurological status, seizures, use of antiplatelet drugs, anticoagulants and individuals with coagulopathies that result in poor clotting ability [4]. Despite the above, diagnosis is often slowed down by the lack of knowledge of these signs on the part of medical personnel and by the existence of underestimation predictors such as the characteristics of the lesions (severe cranial and pelvic lesions), the characteristics of the patients (middle-aged and conscious) and the time of day (nocturnal) [29].

Generally, the level and duration of consciousness is related to the prognosis of those affected, for this reason, it is common to assume that the individual is stable after he/she speaks after having suffered a brain injury, however, this is the trigger for these patients to have a high mortality rate despite the fact that they may be potentially survivable [30]. Although talking indicates a non-lethal impact brain injury, deterioration is a marker of poor prognosis. Thus, outcome depends on early recognition of deterioration and rapid removal of mass lesions. The challenge for emergency physicians is to distinguish patients at risk for deterioration from the many patients evaluated after traumatic brain injury [31].

The following are independent predictors of outcome (in order of importance): Glasgow Coma Scale score after deterioration into coma, highest intracranial pressure during the patient's evolution, degree of midline shift, type of intracranial injury, and patient age. In contrast, the mechanism of injury, the Glasgow Coma Scale verbal score during the lucid interval, and the time to deterioration or to surgical intervention did not influence the final outcome [32]. The diagnostic value of GCS ≤ 8 for severe TBI in patients with multiple injuries has low sensitivity (56.1%) but higher specificity (82.2%). Because of the low sensitivity of GCS, we suggest the use of the anatomic scoring system with AIS head ≥ 3 to define severe TBI in patients with multiple lesions [33].

Computed tomography (CT) constitutes a gold standard in the evaluation of patients after TBI. None of the available guidelines address the role of repeat CT as a follow-up procedure after head injury in pediatric patients. Experience suggests that a repeat CT scan should be a routine component of

postoperative management, especially in pediatric patients after neurosurgery or in a barbiturate coma [34]. Age, type of injury, loss of consciousness, posttraumatic seizures, otorhinolaryngologic bleeding, vomiting, scalp injury, and polytrauma were not found to be predictors of a positive CT scan. GCS score on admission, focal neurologic deficits, and fractures detected by skull radiography were found to be statistically significant predictors of positive CT findings [35].

Studies have found considerable variation among institutions and individual physicians in ordering CT scans for patients with minor head injuries. Although emergency physicians were selective in ordering CT, the yield of radiography was very low across hospitals. These findings suggest great potential for a more standardized and efficient use of CT of the head, possibly through the use of a clinical decision rule [36]. Increased pulsatility index after mild to moderate TBI is cause for concern about the possibility of further neurological deterioration so CT and Doppler measurements could be combined to detect on admission patients at risk of secondary neurological deterioration in order to improve their initial disposition [37].

Forensic autopsy is important in patients with "Talk and Die" to clarify the causal relationship with the head injury in relation to any other forensic disputes. The deaths of these patients raise medicolegal questions, about the precise causes of death and the possible correlation of death with the head injury, especially when such deaths occur after a prolonged period of time following the event [30]. In an investigation of 13 autopsies with examination of the brain, it was found that 5 patients died with severe brain injuries not complicated by iatrogenic factors and 4 patients died with associated severe injuries. Iatrogenic factors significantly complicated the death of 40% of the patients, a considerable alarming figure [12].

Using a decision tree analysis, studies have found hypotension and low cerebral perfusion pressure (CPP) to be the best predictors of death [38]. Other parameters are also found to be predictors of mortality such as (in order of importance): Glasgow coma scale score after deterioration into coma, the highest intracranial pressure score during the patient's evolution, the degree of midline shift, the type of intracranial injury, and the patient's age. In contrast, the mechanism of injury, the Glasgow Coma Scale verbal score during the time interval between lucidity and clinical deterioration or until the patient underwent surgery, did not prove to influence the final outcome [32].

Evidence suggests that 92% of patients with ICP plasma levels greater than 15 µg/ml or D-dimer levels greater than 5 µg/ml died regardless of their level of consciousness on admission, whereas all patients recovered well when their ICP levels were less than 2 µg/ml or D-dimer levels were less than 1 µg/ml. Thus, it was revealed that plasma ICP and D-dimer levels on admission are reliable prognostic markers of head injury. Using these markers, patients with unfavorable outcomes (progressive brain injury), such as the talk anddeteriorate type, could be easily identified on admission [39]. The D-dimer value was significantly higher in the talk and die group at any time and was considered the best coagulation/fibrinolytic parameter to monitor from the early stage of injury predicting outcome [40,41].

Treatment

The most important factors in saving these patients are prompt diagnosis and immediate surgical decompression before irreversible brain damage occurs [42]. In 1983, a uniform protocol for the initial treatment of patients with head injuries was introduced, based on knowledge of the epidemiology of head injuries, the importance and frequency of preventable factors in the region, and also adjusted to the specific geographic conditions. This protocol is guided by the level of consciousness prior to arrival at the hospital, the initial assessment of the level of consciousness and neurological status on arrival at the hospital and, finally, subsequent changes in the level of consciousness and neurological status [43].

Most people admitted to the emergency department for traumatic brain injury are discharged after one or two days [3]. The study by Eric Cecala Peterson et al. found that all patients were managed with observation in the intensive care unit and hyperosmolar therapy to maintain serum osmolarity at 300. Overall, 7 of 13 (54%) suffered clinical deterioration with a mean of 4.5 days after the injury. Of those injured with immediate surgical decompression, all had good results and returned to work. There was no difference in contusion or edema volumes between patients with and without clinical deterioration. Based on this series and experience in

other TBI patients, prophylactic hypertonic saline (HTS) infusions are no longer used in the setting of head trauma. Management of these patients with intensive care unit, admission and early intracranial pressure monitoring is recommended. If they deteriorate despite these measures, rapid bifrontal decompression may lead to good functional outcomes [44]. Potential adverse events that have been associated with HTS include renal failure, central pontine myelinolysis rebound ICP elevation [45].

For individual therapeutic management there is currently the use of transcranial Doppler (measuring mean cerebral artery systolic, diastolic and mean cerebral artery (MCA) flow velocities and a derived value, pulsatility index, jugular venous oxygen measurement, intracranial pressure waveform analysis and near infrared spectroscopy. In addition, it has been suggested that the complexity of the lesion may necessitate the administration of combinations of neuroprotective agents acting at various steps in secondary self-destructive injury cascades. Each cascade may have its own critical window for treatment, so sequential or concurrent combinations of therapeutic agents may be necessary. For example, administration of a single intravenous bolus of Mg salts for up to 12 h after injury has demonstrated improvement in neurological recovery after injury in rats [46].

Studies by the Adelaide Head Injury Group suggest that the beneficial effects of Mg may be related to the positive mRNA regulation of beta-amyloid precursor protein (APP), which is a normal component of neurons and there is evidence of its role in the repair and regeneration of these cells. On the other hand, the APOE genotype, specifically the apolipoprotein 4 allele, has been associated with increased odds of having a poor outcome at 6 months, increased odds of having plaques of amyloid protein deposits, and have a 10-fold increased risk of Alzheimer's disease [46].

Controversy exists regarding prehospital intubations in patients with severe and moderate head injuries. It is unclear whether field intubations actually improve neurologic outcome or survival. Failed attempts at field intubations may increase out-of-hospital time and increase the risk of aspiration or hypoxia. Hypoxia and hypotension have been found to worsen outcome in head trauma [47].

With respect to surgical procedures, all strategies of craniotomy, decompressive craniectomy, and initial trepanation appear to be effective, but the superiority of each procedure has not yet been established. Since Glasgow Coma Scale (GCS) scores, age, papillary reaction, and computed tomography findings are strongly correlated with outcome, each factor has been investigated as an indicator of resiliency [48]. Individuals with CT-proven anisocoria, trephination of the skull prior to transfer resulted in uniformly good results without complications. Time to relief of intracranial pressure was significantly shorter with trephination and neurological outcomes were not different [49]. As for craniotomy for evacuation of hematomas and/or intracranial contusions, it was the most common treatment recorded (performed in 30% of all cases), followed by treatment of barbiturate coma (8%) and decompressive craniectomy (6%) [50].

Repeated use of CT should be a routine component of postoperative management, especially in pediatric patients after neurosurgery or in a barbiturate coma, because it prevents such revelations as a case of a previously undetected acute epidural hematoma in the right frontoparietal region with mass effect that displaced contiguous brain tissue to the contralateral side and, following this finding, the hematoma can be evacuated and bleeding from the ruptured middle meningeal artery can be stopped without any problems [34].

Preventing secondary insults will remain the primary goal of treatment, but the next major advances in the treatment of head injury are likely to be through cell biology, with therapy. Targeting specific intracellular targets and perhaps promoting genes that lead to repair and regeneration [46].

Conclusions

In order to reduce the morbimortality rate of the talk and die syndrome, it is essential to educate the population about the risks of suffering apparently mild or moderate cranioencephalic traumas that are not monitored by a health professional. In turn, in the medical field, specifically in the area of emergency and traumatology, health personnel should be educated about this syndrome in order to increase clinical suspicion and with it, the strict and constant monitoring of the vital functions of these patients, in order to be able to detect in time possible warning signs that can prevent serious sequelae and

even death of those affected. It should be noted that this syndrome can affect any age group; however, greater emphasis should be placed on high-risk populations such as older adults and individuals who use anticoagulants or antiplatelet drugs.

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Essentials of nimodipine in neurocritical care patients

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ABSTRACT

Nimodipine is a drug belonging to the group of calcium channel blockers, very well tolerated, widely recognized for its central action as a vasodilator preventing vasospasm secondary to aneurysmal subarachnoid haemorrhage. It is currently approved as a drug used in the treatment of this type of haemorrhage, mainly because it is effective in reducing neurological deficits due to delayed cerebral ischemia. In addition, due to its relaxing action on the cerebral vascular musculature and its facility to cross the blood-brain barrier, it has multiple functions in other types of cerebral vascular lesions such as ischemic stroke and other neurological conditions involving stress or cell death. Its role as a prophylactic agent in the treatment of migraine and its effect as a neuroprotective agent have also been evaluated.

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Introduction

Calcium channel blockers act by blocking the entry of calcium ions into vascular and cardiac smooth muscle cells during membrane depolarization. Its inhibition causes essentially relaxation of arterial vessels, because muscle contraction is highly dependent on calcium influx. This is why the main effects of calcium channel blockers are relaxation of arterial and vascular smooth muscle cells, resulting in arterial vasodilatation [1]. In general, they are indicated in the treatment of hypertension and other major cardiovascular disorders; however, their use has also been suggested in the management of cognitive disorders and other neurological disorders [2].

Based on the above, the pharmacological effect of vasodilators on cerebral blood flow, such as calcium channel blockers, has been extensively studied and evaluated in different pathological conditions that compromise cerebral vascular integrity. Nimodipine, being lipophilic, can cross the blood-brain barrier; in fact, studies have shown that nimodipine is more lipophilic than nifedipine and its volume of distribution in the brain of rats was three times greater than that of nifedipine [3].

Early pharmacological studies characterized nimodipine as a potent cerebral vasodilator drug [3]. Subsequently, several studies confirmed the cerebral vasodilator activity of nimodipine and mentioned that, in addition to its calcium antagonist action on the smooth muscle of cerebral blood vessels, nimodipine may have direct neuronal effects [3]. Thus, different studies were developed to identify its efficacy in different brain alterations that generate some degree of compromise in the cerebral vascular endothelium, such as traumatic brain injury, stroke and migrainea.

One of the main complications following a subarachnoid hemorrhagic stroke is arterial spasm, which is caused by the presence of blood in the subarachnoid space [4]. Nimodipine plays an important role in inhibiting reflex vasospasm, thus acting as a neuroprotector. It has also been shown that the prophylactic use of nimodipine in patients with aneurysmal subarachnoid hemorrhage reduces the risk of ischemic brain damage, a frequent complication of this event [5,6]. In this review, the essential aspects of nimodipine for the management of patients in the neurocritical state are presented.

Pharmacological aspects of nimodipine

Nimodipine (C21-H26-N2-O7) is a drug belonging to the group of second-generation 1,4-dihydropyridine calcium channel blockers [7]. It has been used for various situations since the 1980s, where it was initially implemented in the management of systemic arterial hypertension but later approved by the Food and Drug Administration (FDA) for the treatment of vasospasm after aneurysmal subarachnoid haemorrhage [7-9]. It is not widely used, since its use is mainly aimed at the management of patients with this type of stroke [10].

Mechanism of action

Voltage-dependent calcium channels (VDCCs) are widely distributed throughout the body and their function is to regulate the excitability and secretion of different cell types. Nimodipine binds to the alpha-1 subunits containing the voltage sensor and transmembrane pores of L-type VDCCs, acting as a negative allosteric modulator of the function of this channel [7,8]. Four alpha-1 isoforms have been identified within the L-type class of which Cav1.2 or Cav1.3 are those that are widely expressed in the cardiovascular system and in neurons, therefore, they are of great importance in the pathophysiology of the central nervous system (CNS), because they have a high relationship with cells involved in the regulation of the neurovascular unit [8].

During depolarization of the smooth muscle cells of blood vessels, there is an influx of calcium ions; nimodipine acts by blocking these channels, preventing this influx and causing vasodilatation [7]. In addition, it has a high lipid solubility, so it has a preference for acting on cerebral blood vessels and can cross the blood-brain barrier [7,10]. In this way, it has an effect on cerebral blood flow by having the ability to reverse the persistent pathological activation of L-type channels in cerebral arteries, which are responsible for reflex vasoconstriction in case of injury [8,11].

Clinical utility of nimodipine in neurocritical care

Haemorrhagic stroke

Nimodipine is an FDA-approved drug included in the general treatment of aneurysmal subarachnoid haemorrhage (aSAH) [12,13]. It has the ability to reduce the risk of cerebral ischemia and improves clinical prognosis. The dose recommended by clinical practice guidelines is 60 mg orally every 4 hours

during the first 48 hours after the onset of symptoms or when the patient's hemodynamic status permits, and is maintained for the following 21 days [12,14]. If the enteral route cannot be used, it is recommended to use intravenous nimodipine, gradually increasing up to 2mg/h, avoiding arterial hypotension; it should be switched to the oral route as soon as possible [12].

The most frequent complication of aSAH is delayed cerebral ischemia, which is believed to be the product of multiple processes such as angiopathic micro- and macrovasospasm, loss of autoregulation, cortical depolarization, microthromboembolism, and heterogeneity of capillary transit time [8,15,16]. It has been postulated that cortical depolarization propagates from the nucleus and vulnerable regions, causing additional ischemia both adjacent to the core lesion and in distant regions with compromised perfusion due to large vessel vasospasm; when nimodipine is used, cortical depolarization is initiated less frequently and less severely, decreasing the risk of delayed cerebral ischemia [8].

Several studies have demonstrated the efficacy of nimodipine in improving neurological status following this type of hemorrhagic event [17,18]. Philippon et al [19] conducted a prospective randomized double blind study in patients with aSAH to determine whether the use of nimodipine reduces the severity of ischemic deficits secondary to vasospasm and found that, although not observed in all cases, nimodipine effectively decreases the occurrence of neurological deficits due to vasospasm. Pickard et al [20] conducted a prospective trial with the aim of establishing the effect of nimodipine on the incidence of ischemic events and proven cerebral infarction, and on the reduction of death and severe disability after subarachnoid hemorrhage; it was shown that the use of oral nimodipine 60 mg every four hours is well tolerated, reduces cerebral infarction and improves outcome after subarachnoid hemorrhage. Finally, in a similar study, Petruk et al [21] concluded that treatment with nimodipine in poor-grade patients with subarachnoid hemorrhage results in an increase in the number of good outcomes and a reduction in the incidence of delayed neurologic deterioration due to vasospasm.

The efficacy of nimodipine in the context of subarachnoid hemorrhage has also been evaluated in children. Song et al [22] conducted a prospective randomized controlled clinical trial in children with subarachnoid hemorrhage, with the aim of evaluating the effect of prophylactic nimodipine in preventing vasospasm and improving outcomes in this type of patient. As a result, they concluded that prophylactic nimodipine cannot reduce the incidence of vasospasm in children with subarachnoid hemorrhage, but may improve short-term brain function

On the other hand, Sriganesh et al [23] evaluated the effect of intra-arterial nimodipine on regional cerebral oxygen saturation (rSO2) and systemic hemodynamic indices during therapy for cerebral vasospasm following aSAH. Analysis of the results showed that there was no change from baseline in ipsilateral and contralateral rSO2 after administration of intra-arterial nimodipine, but there was a significant decrease in mean arterial pressure and total peripheral resistance index. These latter hemodynamic changes could offset any potential effect of intra-arterial nimodipine to improve rSO2. Further studies are needed to corroborate this theory

Several studies have also been conducted comparing the effectiveness of nimodipine with other calcium channel blockers in the treatment of patients with aSAH. One of these is the study by Schmid-Elsaesser et al [24] where they evaluated the efficacy of magnesium (nature's physiological calcium antagonist) versus nimodipine to prevent delayed ischemic deficits after aSAH. They showed that, in the magnesium group, 15% experienced clinical vasospasm and 38% experienced angiographic/transcranial Doppler vasospasm, compared to 27% and 33% of patients in the nimodipine group, respectively [24]. The authors conclude that the efficacy of magnesium in the prevention of delayed ischemic neurological deficits in patients with aSAH is comparable to that of nimodipine and further studies are needed to better define its role in these neurological circumstances and on its combined administration with nimodipine.

Ischemic stroke

Most strokes are ischemic, i.e., caused by reduced blood flow with obstruction of small and large vessels. This sudden loss of blood supply is associated with a massive influx of calcium ions into neurons, which is the common pathway leading to

cell death [25]. It is proposed that inhibition of calcium entry by the use of calcium channel blockers could protect neurons and reduce neurological deterioration after stroke

Several studies have investigated the efficacy of nimodipine in improving clinical outcomes after ischemic stroke. Steen et al [26] conducted a study in pigtailed monkeys, which were subjected to 17 minutes of complete cerebral ischemia followed by 96 hours of intensive care treatment. They evidenced that the neurological outcome at 96 hours after ischemia was significantly better in nimodipine-treated monkeys than in controls, and a histopathological scoring system yielded a significantly better mean score for the treated group than for the untreated group [26].

In the randomized, double-blind, multicenter clinical trial conducted by The American Nimodipine Study Group, a positive finding was that patients treated with nimodipine had a 30% reduction in the frequency of clinical worsening compared to placebo within 18 hours after stroke [27].

However, the results compared with those of other clinical trials are contradictory. In the study by Kaste et al [28], where the hypothesis that nimodipine would improve functional outcome in acute hemispheric ischemic ischemic stroke was tested, no differences in functional outcome were observed between treatment groups. Similarly, in a Cochrane meta-analysis where randomized controlled trials comparing a calcium antagonist versus a control in people with acute ischemic stroke were included, it was found that calcium antagonists showed no effect on the primary outcome (RR 1.05; 95% CI: 0.98 to 1.13) or on death at the end of follow-up (RR 1.07, 95% CI 0.98 to 1.17); therefore, the authors concluded that no evidence was found to support the use of calcium antagonists in patients with acute ischemic stroke [29]. Further studies are needed to clarify whether the use of nimodipine in ischemic stroke is beneficial or not.

Uses of nimodipine in other neurological conditions

Calcium channel antagonists, such as flunarizine, are used as a drug for migraine prophylaxis, so the role of nimodipine in the treatment of this condition has been studied [30]. Nimodipine could intervene in the pathophysiology of migraine by blocking the entry of calcium into the smooth muscle cells of cerebral vessels, preventing the vasomotor manifestations of migraine. The possibility of a neurogenic mechanism of action has also been studied [31].

Recent case reports have elucidated the efficacy of nimodipine in the treatment of prolonged hemiplegic migraine (HM) linked to the ATP1A2 gene mutation [32]. The case was reported by Dannenberg et al [32] where a girl diagnosed with MH developed drowsiness, confusion, nausea, vomiting, photophobia, left hemiparesis and unilateral central facial palsy, after two days of headache. Initially, levetiracetam and dexamethasone were administered, but due to the persistence of symptoms, nimodipine was added on the sixth day to prevent new spasms [32]. Nimodipine infusion rapidly improved the patient's symptoms and was well tolerated, and within 12 hours improved left arm motor function. The authors concluded that nimodipine treatment should be considered for prolonged migraine attacks in patients with ATP1A2 mutations.

On the other hand, clinical and experimental data have attributed a neuroprotective effect to calcium channel blockers, specifically nimodipine. This is why Leisz et al [33] conducted a study with the aim of evaluating the relationship of nimodipine treatment on the in vitro neurotoxicity of various cell types subjected to stress. Schwann cell lines, neuronal cells and astrocytes were treated for 24 hours with nimodipine and incubated under osmotic, oxidative and heat stress conditions. The results demonstrated a cell type-independent protective effect of prophylactic treatment with nimodipine, through decreased activation of caspase 3 and 7, and increased activation of CREB (cyclic adenosine monophosphate response element-binding protein) and AKT (proteinkinase B) signaling. The authors suggest that these investigations should be continued in vivo to determine whether these mechanisms can be transferred to patient tissues.

Similarly, Herzfeld et al [34] analyzed the neuroprotective effects of nimodipine on Neuro2a neuroblastoma cells after the application of cell death inducers (surgery-associated stress, such as heat or mechanical stress). The results indicated that nimodipine significantly decreased ethanol-induced cell death by up to 9% at all concentrations tested; in addition, heat-induced cell death was reduced by 2.5% and mechanical treatment-induced cell death was reduced by up to 15%. These findings

demonstrated that nimodipine rescues Neuro2a cells from stress in a mild but significant manner,

Adverse effects and limitations of use of nimodipine

Nimodipine is generally well tolerated, but its use is correlated with some side effects related to its vasodilator property. Hypotension is the most frequently reported adverse effect compared to placebo treatment [35]. Hajizadeh et al [36] conducted a study with the aim of determining adherence to oral nimodipine administration in patients admitted with aSAH. They found that 39% of patients who started nimodipine in the neurosciences intensive care unit reduced the dose due to excessive falls in blood pressure, and transient discontinuation occurred in 2% patients [36]. They concluded that most patients with aSAH did not complete 21 days of nimodipine and hypotension was the main reason for the change or suspension of the dose. However, the hypotensive effect can be minimized by generating control of the blood pressure by reducing the dose given to the patient.

Other adverse effects of the drug include headache, dizziness, flushing, nausea, diarrhea, edema of the feet, rash and palpitations. An increase in serum liver enzyme concentrations has also been reported in patients on intravenous treatment with nimodipine, but it is reversible and is thought to be due to the ethanol in the intravenous formulation and not to nimodipine [35]. Isolated cases of confusion with psychosis and myocardial ischemia during treatment with nimodipine have been reported [35].

Intrathecal administration of dihydropyridines has been suggested with the aim of decreasing Cerebrospinal Fluid (CSF) concentrations of these drugs, with lower systemic concentrations and fewer systemic side effects, mainly hypotension [37]. Etminan et al [37] reviewed data from intrathecal application of a slow-release nimodipine EG-1962 microparticle system to improve outcome and prevent delayed cerebral ischemia following subarachnoid hemorrhage. Given the strong rationale for investigating the effects of EG-1962 in patients suffering from subarachnoid hemorrhage, they initiated two clinical trials on intracisternal and intraventricular application of EG-1962.

Hänggi et al [38] also described the development of sustained-release nimodipine microparticles that can be administered directly into the subarachnoid space or brain ventricles to improve the outcome of patients with aSAH. Eight injectable formulations of nimodipine microparticles in poly (DL-lactide-co-glycolide) (PLGA) polymers were tested in vitro. Their efficacy has been tested and it has been concluded that Nimodipine-PLGA microparticles significantly attenuate angiographic vasospasm.

Among the contraindications, a history of hypersensitivity reaction to nimodipine is an absolute contraindication, while hepatic insufficiency and hypotension are relative contraindications for its administration. Finally, it is relevant to mention that nimodipine is not safe during pregnancy (category C) and should only be used in these circumstances if there is a strong risk-benefit ratio; breastfeeding is also contraindicated while taking the drug due to possible harmful effects on the baby [1].

Final recommendations

The efficacy of nimodipine in improving outcomes in the treatment of aneurysmal subarachnoid hemorrhage is well established in the literature. Its pharmacological approach is aimed at reducing the harmful effects of subarachnoid blood, prevent aneurysm rebleeding, and treatment to reduce the risk of delayed cerebral ischemia or vasospasm [39]. It would be interesting to further investigate the mechanisms by which nimodipine decreases aSAH-associated complications and whether it has any impact on neurological conditions following the occurrence of the event

It is also important to investigate the effects of nimodipine on ischemic strokes, which constitute a large percentage of the events encompassed within the context of acute neurological pathology. As noted above, there is much controversy regarding the possible effects of nimodipine in the management of patients with ischemic stroke and it is essential to clarify these concepts. Likewise, future scientific research should be directed to investigate the action of nimodipine not only at the level of the cerebral vasculature, but also in the central nervous system as a whole, since it has been mentioned about the possible neuroprotective effects in other neurological pathologies.

Finally, further research is needed on microparticulate systems that have a sustained release formulation of nimodipine administered directly into the central nervous system by various

routes, such as intraventricular, which have been tested in patients with subarachnoid hemorrhage [40]. It is necessary to establish whether this method of local administration could be more beneficial than the oral presentation of nimodipine, since with the latter the concentrations administered to the vulnerable brain may be very low due to side effects such as systemic hypotension.

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Multiple intracranial aneurysms in subarachnoid haemorrhage. Which one has bled? A diagnostic dilemma

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ABSTRACT

This paper is intended as an illustrative teaching case. It gives a porotype case of a patient with subarachnoid haemorrhage and multiple intracranial aneurysms, where the CT data is non-conclusive as to the source of haemorrhage. The paper then discusses the diagnostic challenges and management pearls, pertaining to such scenarios. The paper concludes with a few "take-home points" that summarise the criteria to be applied in such cases.

Keywords
subarachnoid haemorrhage, multiple intracranial aneurysms

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CASE DESCRIPTION

A 39-year-old male patient with autosomal dominant polycystic kidney disease (ADPKD) presented to the emergency department with a sudden-onset, severe headache and vomiting followed by an altered level of consciousness (GCS:10-E2M5V3). A computed tomography (CT) scan of the head revealed diffuse subarachnoid hemorrhage (SAH) (the typical star-shape sign), but did not give a clue for the source of bleeding (figure 1.A). Cerebral CT angiography (CTA) revealed two intracranial saccular aneurysms in the anterior communicating artery (Acom) and the right middle cerebral artery (MCA); of 7 mm each with no vasospasm observed (figure 1.B,C). However, it could not be determined from the CTA data which aneurysm has ruptured. Cerebral catheter angiography is not available in our country. Thus, the team assumed that the ruptured aneurysm was located at the Acom, and planned the surgery accordingly. The patient underwent surgery on the day of admission. Intraoperatively, it was evident that the anterior communicating artery (Acom) was indeed the source of bleeding. The aneurysm was clipped and secured, without complications. Early postoperative cranial CT scan showed 2 clips in position with no other significant findings (figure1.D). The patient had an uneventful recovery and he remained well.

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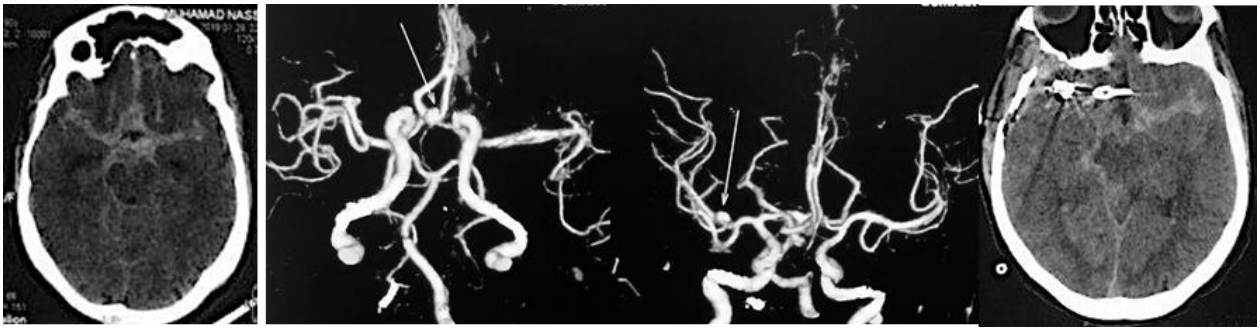

A B C D

Figure. A 39-year-old male patient with autosomal dominant polycystic kidney disease (ADPKD) presented to the emergency department with a sudden-onset, severe headache and vomiting followed by an altered level of consciousness (GCS:10-E2M5V3). A: An initial cranial CT scan showing SAH in the basal cisterns (the typical star-shape sign) with no clue to the source of bleeding. **B and C**: A cerebral CT angiography- 3D reconstruction- revealing multiple intracranial saccular aneurysms in the Acom (B inferior view with an arrow pointing to the Acom aneurysm) and the right MCA (B anterior view with an arrow on the superiorly directed, right MCA aneurysm); both aneurysms are regular, rounded-shaped, have no murphy's teat and, have a size of 7 mm each with no vasospasm noticed. **D**: An early, post-operative cranial CT scan showing 2 clips in position with no other significant findings

Discussion

The incidence of Multiple intracranial aneurysms (MIAs) amongst all patients with aneurysms is around 15-33.5% [7] [4] [10]. Hypertension has been identified as the risk factor most commonly associated with MIAs [2]. MIAs are more common in women, with a female to male ratio of 5:1. The ratio is even higher (11:1) in patients with three or more aneurysms [10]. Overall, the anterior communicating artery (Acom) is the most common location for intracranial aneurysms (35%) [8]. Common sites for multiple intracranial aneurysms include the posterior communicating artery (PCA) the middle cerebral artery (MCA), the anterior communicating artery, and the ophthalmic artery [10].

In patients with SAH and MIAs, verifying the source of bleeding is not always a straightforward task. Furthermore, misidentification of the true ruptured aneurysm is a major cause of post-operative re-bleeding and mortality. In one series that examined a cohort of 76 patients with SAH and MIAs, the rate of false localization of the ruptured aneurysm was 9%, resulting in rebreeding and mortality at the rates of 5.3% (n=4/76) and 2.6 (n=2/76), respectively [6]. The rate of rupture site misidentification is even higher in patients with a non-definitive bleeding pattern on initial CT scan, quoted at 16.2% [11]

The only absolute evidence for aneurysm rupture is angiographic dye extravasation or the "smoking gun" sign [10]. This is, however, an uncommon sign that indicates a grim prognosis [10]. Other highly accurate angiographic findings include focal spasm, aneurysm shape irregularities (Murphy's Teat), larger size, focal mass effect and aneurysm shape shifts on repeat imaging [3, 10]. While these signs have a high predictive value of the rupture site, they are fairly rare [10].

Clinical signs are less reliable when it comes to identifying the site of hemorrhage. Reports on their usefulness vary, with a sensitivity range of 7-33%[10] [1]. Sometimes, the CT scan shows a clear hemorrhage pattern that suggests the source of the bleeding [5]. Nevertheless, where there is a diffuse, symmetrical pattern of hemorrhage or localized bleeding along with numerous aneurysms in the vicinity, the CT is unable to delineate the site of rupture [5]. One reliable sign is that might give a clue to the site of rupture is the location of the epicenter of hemorrhage (area with most contraction) on CT or MRI [3].

In our case, none of the above-mentioned radiological signs were present, and hence prediction of the site of the ruptured aneurysm was responsibility of the treating neurovascular team. In this case, the Acom was presumed to be the ruptured site given the frequency of these aneurysms and the fact that they are more prone to rupture than MCA aneurysms. In this case, the surgery was directed only at the ruptured Acom aneurysm. Some surgeons opt for the treatment of all significant aneurysms at the time of surgery to

reduce the risk of late re-bleeding, while others recommend treating the ruptured aneurysm only [12]. In either case, prompt identification and treatment of the ruptured aneurysm remains a priority, as it has significant implications on patient outcomes. In fact, it has been shown that the most common cause of late re-bleeding is the originally ruptured aneurysm which was not identified at the time of initial surgery [9].

It is not yet determined whether MIAs are associated with worse surgical outcomes. However, several risk factors have been investigated for their prognostic significance in patients with SAH and MIAs. One population-based study has shown that for patients > 70 years of age, the prognosis is less favorable for those with SAH and multiple aneurysms as compared to those with SAH and a single aneurysm [7]

In summary, the present case has illustrated the potential challenging nature of SAH in patients with MIAs and emphasized on the importance of adopting a systematic, step-wise progression through preoperative planning, and the critical impact this has on surgical outcomes.

Take-home points:
- Patients with MIAs and SAH present a challenge to the neurovascular surgeon.
- When the bleeding pattern on the initial CT scan is non-definite, meticulous examination of the CTA and/or DSA data becomes very important and should take into consideration the following criteria [3]
-CT/MRI: Where is the area exhibiting the greatest concentration (Aka. The epicenter of SAH)?
-CTA/DSA: Where is the area with local vasospasm?
-Morphology: Is there a “Murphy’s teat” – a daughter cyst- or an area of irregularity- in any of the aneurysms?
-Size: Which aneurysm is larger?
- If none of the above criteria applies, as in this case, then the judgment of the treating team is critical. The caveat is that, when such a time-sensitive decision is required, it is safer to assume that the Acom is culprit site, as it is the predilect site of intracranial aneurysms, and is , hence, overall the most common site of rupture.

Abbreviations

ADPKD: Autosomal dominant polycystic kidney disease
GCS: Glasgow coma scale
EMV: Eye movement and verbal response
CT: Computed tomography
SAH: Subarachnoid haemorrhage
3D: Three dimensional
Acom: Anterior communicating artery
MCA: Middle cerebral artery
CTA: Computed tomographic angiography
MIAs: Multiple intracranial aneurysms
MCA: Middle cerebral artery
PCA: Posterior communicating artery
N: number
MRI: Magnetic resonance imaging
DSA: Digital substraction angiography
Aka: Also known as

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Intracranial myopericitoma. A case report of a rare tumour in a rare location in an AIDS patient

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ABSTRACT
Myopericytoma is a benign, soft tissue tumor probably derived from perivascular myoid cells. They are usually found in subcutaneous tissues in the extremities. Intracranial localization of myopericitoma is exceedingly uncommon. We report a 43 years old male patient with incidentally found myopericitoma of the posterior fossa. Patient was operated and tumor was completely removed. Patient was subsequently diagnosed with acquired immunodeficiency syndrome due to human immunodeficiency virus infection. One year after operation tumor showed no signs of recurrence, but patient developed progressive symptoms of AIDS and started highly active antiretroviral therapy (HAART). Connection of intracranial myopericitoma appearance and HIV/AIDS has been reported before, but clear connection is yet to be elucidated.

Keywords
AIDS/HIV,
myopericitoma,
intracranial tumour

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INTRODUCTION

Myopericytoma represents a rare benign lesion most frequently found in soft tissue. However, it may arise in any other location. Clinical, neurological and radiological features are unspecific with symptoms arising due to compression of surrounding structures. Surgical resection is the treatment of choice with excellent prognosis. Pathology examination provides the definite diagnosis, but the differential diagnosis is wide. Intracranial location is exceedingly uncommon, and we found only several case reports described in the literature2,7. Connection of intracranial myopericitoma appearance and human immunodeficiency virus infection has been reported before, but causal connection is yet to be elucidated1.

We present a case of a 43 years old male with incidentally found myopericitoma of the posterior fossa. One year after the operation patient was diagnosed with acquired immunodeficiency syndrome due to human immunodeficiency virus infection.

CASE REPORT

We present a case of a 43 years old male gynecologist who was first examined 6 years ago because of typical migraine headaches, when brain computed tomography (CT) showed small dural based extra axial hyperdense lesion in the posterior region of foramen magnum without significant compressive effect, which was confirmed with brain magnetic resonance imaging (MRI). The patient was motivated for further intermittent follow-up and consecutive MRI showed no signs of lesion expansion and patient remain neurologically intact without symptoms and any complains for almost 6 years. However, patient skipped the last two fallow-ups since he was clinically suspected for COVID-19 infectious disease, although three consecutive PCR tests were negative. Shortly after resolution of respiratory symptoms patient abruptly developed ataxia and gait disturbance with severe neck pain after which he was admitted in our emergency department and brain CT scan showed significant enlargement of extra axial lesion in the posterior cranial fossa with signs of cerebellar and fourth ventricle compression, but without signs of hemorrhage nor hydrocephalus (Figure 1).

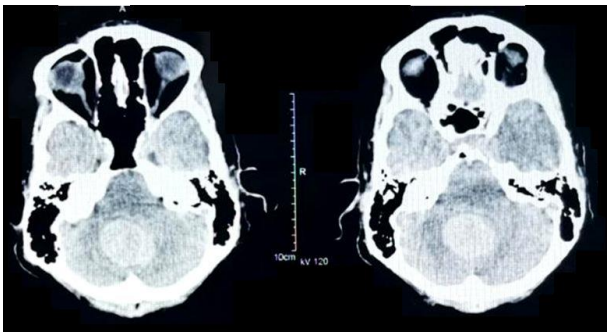

Figure 1. First brain CT after development of signs and symptoms of cerebellar dysfunction, showing tumor in the cerebellum.

Patient was transferred to Neurosurgical clinic of Clinical center of Serbia. At department admission he presented with cerebellar symptomatology including ataxia, asthenia and astasia-abasia complex without muscle weakness accept of mild bilateral thigh flexors weakness. Also, global hyperreflexia with atypical plantar reflex bilaterally was noted. His past medical history was insignificant. Brain MRI showed large intradural extra-axial ovoid shaped tumor measuring 36 x 31 x 33 mm in diameter (LL x AP x CC) located at the posterior midline aspect of foramen magnum and with signs of cerebellar and fourth ventricle compression (Figure 2). Patient was prepared for neurosurgical intervention, and MRI angiography was performed to visualize V3 and V4 segments of vertebral arteries, and fortunately they were distant from the tumor.

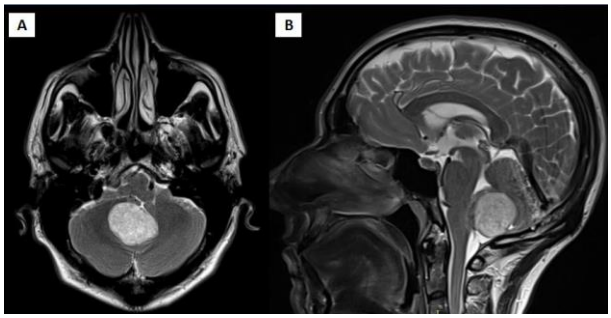

Figure 2. Brain MRI showing tumor in the posterior aspect of foramen magnum: (A) axial plane, (B) sagittal plane.

On the day of surgery, extremely rare situation occurred. Namely, four consecutive transfusion cross-matching blood tests using activated Papain showed positive inter-reaction. However, after our Blood Transfusion Institute provided enough units of blood, we proceeded with intervention, and the patient was operated in the sitting position. The skin was incised on the midline from the occipital protuberance down to the upper cervical region. The midline plane was opened between the posterior muscles, up to the occipital protuberance and down to the spinous process of C2. Bone opening was performed using a drill and Kerrison rongeurs. We decided to perform small right unilateral approach instead of large medial bone opening, since we wanted to avoid occipital sinus injury. Posterior margin of foramen magnum has been also removed. The dura was incised in a Y-shaped fashion and retracted with stitches. After dura opening and retraction of right cerebellar hemisphere, a tumor with insertion on the midline portion of dura was brought into view. The plan was to be perform tumor debulking with the ultrasound aspirator, however since tumor was highly vascularized, we decided to coagulate and liberate dural insertion, after which the tumor was removed in one piece (Figure 3).

Operation and early postoperative period were uneventful. Blood loss during operation was minimal, and there was no need for a blood transfusion. Patient recovered well, and preoperative cerebellar symptomatology was less

pronounced. Control brain CT showed complete tumor removal. Patient was discharged on the 4th postoperative day. The conjugation of morphological, histopathological and immunohistochemical studies allowed the final diagnosis of intracranial myopericytoma. After 6 months patient was without symptoms, and control brain CT showed no signs of tumor recurrence. However, one year from operation patient suffered rapid weight loss, several episodes of recurring fever and profuse night sweats with extreme and unexplained profound fatigue. After investigations patient was diagnosed with acquired immunodeficiency syndrome due to human immunodeficiency virus (HIV) infection. Patient recently started highly active antiretroviral therapy (HAART).

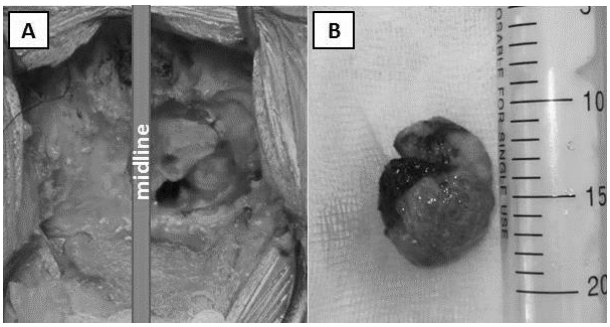

Figure 3. (A) Intraoperative image showing right unilateral approach during dura opening phase, (B) tumor after removal.

Discussion

Myopericytoma is a benign tumor originating from the myoid perivascular cells6. It is often diagnosed in middle-aged patients, and most commonly arises in subcutaneous tissue of distal extremities or sometimes in retroperitoneal space. Granter et al. described the first case of myopericitoma and called it perivascular myoma3. According to current nomenclature, these tumors correspond to a continuum morphological spectrum, including myofibroma, myopericitoma and glomangiopericytoma5. First case of intracranial localization of myopericytoma was described by Rousseau et al. Since then only several cases of intracranial localization have been described8. We present a case of an intracranial myopericitoma with even more rare localization in the posterior cranial fossa. To our knowledge this is the second case of myopericitoma with posterior fossa localization.

In the described cases patients had a wide range of age, with slight female predominance7. Our patient is a 43 years old male patient. The histological findings were similar in all cases from the literature with tumor composed of large thick walls vessels with myxoid changes, lined by elliptical and oval/spindle endothelial cells7. Differential diagnoses included meningioma, solitary fibrous tumor/haemangiopericytoma and angioleiomyoma. However, in all cases, as well as in our patient, immunohistochemical studies confirmed diagnosis of myopericytoma.

Regarding tumor origin, some studies showed unusual molecular changes such as t(7;12)(p22;q13) and del(6)(q12q15)6. Also, some authors postulate a probable relation between Epstein-Barr infection in AIDS patients and myopericytoma development1,4. Our patient was probably HIV positive many years before operation, and AIDS symptoms appeared soon after intracranial surgery. Although reports on this peculiar association have been described in the literature, more data are needed to clearly show a connection between these entities.

Intracranial myopericytoma is a low-grade slow growing tumor, with excellent overall survival. In all cases described in the literature only one patient died and it was due to other cause7. One year after the operation, our patient is without neurological symptoms and without signs of tumor recurrence. However, his general condition is worsening due to AIDS.

In conclusion, intracranial myopericytoma is a rare benign neoplasm, successfully treated by surgery and with excellent follow-up. Connection of intracranial myopericitoma appearance and HIV/AIDS is yet to be elucidated.

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Analysis of functional outcome of single and double level lumbar discectomy

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Keywords
lumbar PIVD,
functional outcome,
RODI,
RDQ,
BQ

ABSTRACT

Introduction: Functional improvement in lumbar PIVD patients can be assessed either objectively like improvement in SLRT, relief in pain, etc or subjectively using different types of scales. In our study, we have used Revised Oswestry Disability Index (RODI) score, Ronald–Morris disability questionnaire (RDQ), The Back Bournemouth Questionnaire (BQ) to analyse functional outcome in single and double level lumbar PIVD patients pre-operatively and post-operatively.

Method: It is a prospective study including 80 patients of lumbar PIVD who failed to respond to conservative treatment. Patients were clinically evaluated and disability scales viz- RODI, RDQ & BQ were recorded. After lumber discectomy, patients were again assessed and scored as per disability scales at 1 month, 6 months and 1 year postoperatively.

Result: RODI, RDQ and BQ scores were calculated at pre-operatively and post-operatively 1, 6 and 12 months and statistically analysed. The mean RODI scores at pre-operative and postoperative 1, 6, and 12 months were 72, 18, 10, and 6 respectively. The mean RDQ scores at pre-operative and postoperative 1, 6, and 12 months were 15, 5, 3, and 2 respectively. Similarly, the mean BQ scores at pre-operative and postoperative 1, 6, and 12 months were 51, 12, 8, and 4 respectively. Statistically, significant improvement was seen in mean scores of all 3 functional scales and maximum changes were observed after 1 month. Statistically, significant improvements were observed in 54 out of 62 patients (87%). Three questions of BQ related to the patient social and family activities, anxiety and depression were separately compared pre and post-operatively and they showed a statistically significant improvement.

Conclusion: Overall 87% of patients had a significant improvement in functional assessment using RODI, RDQ and BQ scales. On comparing single and double level discectomy patients, the functional improvement was similar in follow up of one year. Social and family activities (SFA), depression and anxiety of the patients improved significantly over 1 year.

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Introduction

Lumbar disc prolapse has been thoroughly evaluated in terms of its epidemiology [14], physiology [33] and outcome after discectomy [22, 26, 34]. Proper patient selection and surgical technique can provide an excellent outcome. Different discectomy procedures are carried out for the treatment of lumbar disc prolapse. Postoperatively 75-90% of patients get relief from radicular pain [4,5,9,17,20,21].

According to Asch et al, in a prospective study of 200 patients, the outcome was significant, which was determined by six parameters including pre-operative ODI (Oswestry disability index) and the ODI at 1 and 10 days, 6 weeks, and 6 months and 12 months postoperatively. One of the most common causes of the poor outcome is the poor definition of selection criteria for surgery, which varies fourfold to fivefold between different communities and countries [3].

Risk factors associated with poor outcome include work off over 3 months, psychosocial problems including poor educational level, smoking, and obesity (30). According to Weber's study, the first symptom to improve following successful surgery is the radicular pain, typically followed by improvement in motor function, and finally the resolution of sensory loss. Sensory loss may be permanent persisting at 10-years follow-up in 35% of patients [31, 32].

The restoration of normal function after discectomy in lumbar PIVD patients is considered a key outcome. Assessment of functional improvement can be done either objectively, like improvement in SLRT, relief in pain, improvement in movement, or subjectively with the help of different types of scales. Functional assessment scales are comprised of a self-reported questionnaire and having a standardised format that yields a measure with known reliability and validity. Thus, we performed our study to analyse the functional outcome after lumbar discectomy using the Revised Oswestry Disability Index (RODI) score, Ronald–Morris disability questionnaire (RDQ) and The Back Bournemouth questionnaire (BQ). We are also comparing the degree of improvement after single and double level lumbar discectomy along with the effect of surgery on SFA, depression and anxiety.

Methodology

This prospective study was conducted in the Department of Neurosurgery at our institute between February 2017 to September 2018. Eighty patients with symptoms and signs of lumber PIVD, diagnosed as a case of single and double level Lumbar PIVD by Magnetic resonance imaging (MRI) were enrolled in the study after informed consent. The study was approved by the institutional ethical committee.

Inclusion criteria:

- Signs and symptoms of lumbar PIVD correlating with MRI findings.
- Not responding to conservative management of 6 weeks or more.
- Needs Primary Lumbar Discectomy without fusion.

Exclusion criteria:

- Previous spinal surgery.
- More than 2 level discs prolapsed.
- Lumbar disc prolapsed associated with spondylolisthesis or severe degenerative disease.
- The patient having red flag signs.

- spinal fractures
- primary malignancy, metastasis or infection
- cauda equine syndrome or severe neurological compromise

- Intra-op complications – Dural tear, root injury.

Patients were clinically evaluated and disability scales viz- RODI, RDQ & BQ were recorded. After lumber discectomy, patients were again assessed and scored as per disability scales at 1 month, 6 month and 1 year postoperatively.

Data were summarised as MEAN ± SE (standard error of means). Groups were compared by repeated measures One-way analysis of variants (ANOVA) and the significance of the mean difference between the groups were compared by Tuckey's HSD (honestly significant difference) post hoc test. A two-tailed p-value < 0.05 was considered as statistically significant. The analysis was performed on STATA software.

Functional Status Questionnaires: The following functional status questionnaires, completed by the patients, were taken into account for this study. The

researcher was present during the measurements (at pre-op, post-op 1 month, 6 months, and 1 year) to help patients complete the questionnaires.

Functional status questionnaires:
1. Revised Oswestry disability index (RODI): The Oswestry Disability Index is an index derived from the Oswestry Low Back Pain Questionnaire used by clinicians and researchers to quantify disability for low back pain.

This validated questionnaire was first published by Jeremy Fairbank et al. in Physiotherapy in 1980. The self-completed questionnaire contains ten topics. Each topic category is followed by 6 statements describing different potential scenarios in the patient's life relating to the topic. The patient then checks the statement which most closely resembles their situation. Each question is scored on a scale of 0–5 with the first statement being zero and indicating the least amount of disability and the last statement is scored 5 indicating the most severe disability. The scores for all questions answered are summed and then multiplied by two to obtain the index (range 0 to 100). Zero is equated with no disability and 100 is the maximum disability possible.

Scoring:
- 0% –20%: Minimal disability
- 21%–40%: Moderate Disability
- 41%–60%: Severe Disability
- 61%–80%: Crippling back pain
- 81%–100%: These patients are either bed-bound or have an exaggeration of their symptoms

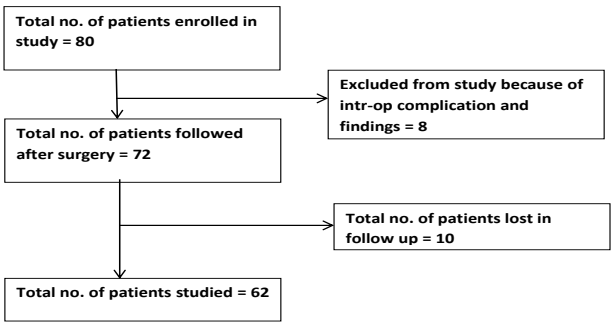
2. The Roland-Morris Disability questionnaire (RDQ) contains 24 yes/no items. Patients are asked whether the statements apply to them that day (the last 24 hours). The RDQ-24 score is calculated by adding up the number of "yes" items, ranging from 0 (no disability) to 24 (maximum disability). The clinical improvement over time can be graded based on the analysis of serial questionnaire scores. Total improvement can be reflected as a percentage of initial score.

3. The Back Bournemouth questionnaire (BQ) is a comprehensive multi-dimensional core outcome tool assessing patients' outcomes of care in a routine clinical setting. It is a short, self-report questionnaire, developed by J. Bolton. The questionnaire consists of seven core items, which are: pain intensity, function in activities of daily living, function in social activities, anxiety, depression levels, fear-avoidance behaviour and locus of control behaviour. Each item is rated on a numeric rating scale (NRS) from 0 to 10:
0= Much better
5= no change
10= much worse.

The score for each measure is added. This can produce a value between a minimum score of 0, and a maximum score of 70. A higher score reflects a higher degree of impact on a patient's life.

RESULTS

Out of 80 patients, 10 patients were lost in the follow-up, 5 patients showed intra-operative mobility which needed stabilization, two patients had post-op foot drop and one patient had intra-operatively CSF leakage due to Dural tear. After exclusion of these patients, 62 patients were studied.



Post-operative CT scan, 6

Out of 62 patients, 47 (76%) patients were male and 15 (24%) were female. Age ranged between 22 years to 63 years. The mean age was 38.8± 9.88 years (mean±SD). Thirty-four (55%) patients had history of insidious onset of pain and twenty-eight (45%) patients had history of sudden onset pain. Patients were categorised into 4 categories based on the duration of pain i.e. <3 months, 3 months – 1 year, 1year- 3 years and > 3 years. Twenty (32%) patients had complaints of radicular pain for less than 3 months, fourteen (26%) had pain since one year, thirteen (21%) patients had history of pain since 3 years and fifteen (21%) patients had pain for more than 3 years. Knee reflex was decreased in 4 (6%) and normal in 58 (96%) patients but ankle reflex was

decreased in 59 (95%) and normal in 3 (5%) patients. plantar reflex was absent in 45 (73%), equivocal in 13 (21%), absent in 2 (3%) and normal in 2 (3%) patients. 31 (50%) patients had paraspinal muscle spasm on examination. 7 (11%) had lumbosacral scoliosis because of unilateral pain and muscular spasm. Out of 80 patients, 60 (97%) had positive straight leg raising test (SLRT) while 2 (3%) had negative SLRT. 25(40%) patients had bilateral positive SLRT whereas 17 (27%) patients had left-sided positive SLRT and 18 (29%) patients had right-sided positive SLRT (Table 1).

Table 1. Clinical parameters of patients

Parameter		No. of patients
Age profile of the study population		
Number of cases		62
Sex	**Male**	47
	Female	15
Minimum age (years)		22
Maximum age (year)		63
Mean age ± SD		38.80 ± 9.88
Clinical parameters		
Occupation	Light work	20
	Moderate work	19
	Heavy work	23
Pain onset	Insidious	34
	Sudden	28
Duration	< 3 month	20
	3month- 1year	14
	1year - 3 year	13
	>3 year	15
Knee reflex	Normal	58
	Decrease	4
Ankle reflex	Normal	3
	Decrease	59
Planter reflex	Normal	2
	Decrease	2
	Equivocal	13
	Absent	45
Paraspinal muscle spasm	Present	31
	Absent	31
Spinal deformity (scoliosis)	Present	7
	Absent	55
SLRT	Positive	25+17+18 (B/L+LT+RT)
	Negative	2

Out of 62 patients, 27 (44%) patients were diagnosed as a case of L4-L5 PIVD, 27 (44%) patients had L5-S1 PIVD and 8 (12%) patients had both L4-L5, L5-S1 PIVD. At L4-L5 disease level, 15 patients had Central disc herniation, 5 had right paracentral and 7 had left paracentral disc herniation on MRI lumbosacral spine. Out of 27 L5-S1 PIVD patients, 19 had Central disc herniation, 10 had right paracentral disc herniation and 8 had left paracentral disc herniation (Table 2).

Table 2. Level of disease and methods of surgery

Parameter		No. of patients
L4—L5 PIVD	Central	15
	RT Paracentral	5
	LT Paracentral	7
	Total	27
L5-S1 PIVD	Central	19
	RT Paracentral	10
	LT Paracentral	8
	Total	27
L4-L5, L5-S1		8
Method of Discectomy	Open	41
	Microscopic	18
	Endoscopic	2
	Percutaneous	1

Patients underwent different types of discectomies that are by open method, microscopic endoscopic, and percutaneous. Open laminectomy and discectomy were performed in 41 (66%) patients. Microscopic, endoscopic and percutaneous discectomies were performed in 18 (29%), 2 (3%) and one (2%) patient respectively (Table 2).

The mean RODI scores at pre-operative and postoperative 1, 6, and 12 months were 72, 18, 10, and 6 respectively. The mean RDQ scores at pre-operative and postoperative 1, 6, and 12 months were 15, 5, 3, and 2 respectively. Similarly, the mean BQ scores at pre-operative and postoperative 1, 6, and 12 months were 51, 12, 8, and 4 respectively. A one - way repeated measures ANOVA was run on the 62 patients to determine, if there were any changes in the mean RODI, RDQ, BQ scores over time (pre-op; post-op at 1 month, 6 month, and 1 year) (figure 1 and 2). Results showed that there was a statistically significant difference in the mean RODI, RDQ, BQ scores over time that is pre-op vs post-op 1 month, 6 month, and 1 year period ($p=0.000$). Tukey's post-hoc test revealed no statistically significant differences between the RODI, RDQ, BI scores observed 1-month post-op vs 6-month post-op, and 6-month post-op vs 1-year post-op ($p>0.05$). However, a statistically

significant difference was observed between mean RDQ scores 1-month post-op vs 1-year post-op (p=0.013), whereas, mean RODI and BQ scores 1-month post-op vs 1-year post-op were statistically non-significant (Table 3).

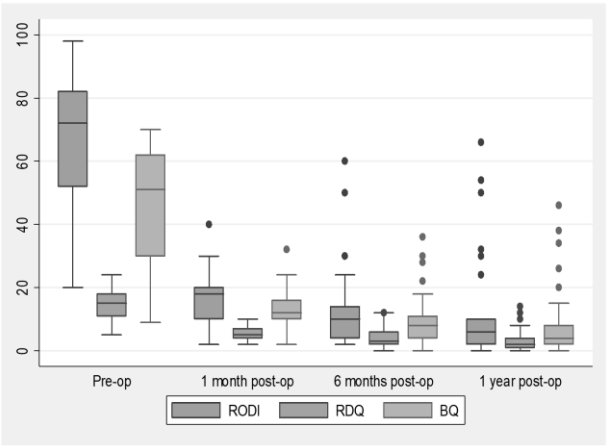


Figure 1. Changes in RODI, RDQ, BQ scores and their mean

Table 3. Pre-op versus post-op changes in different functional score system

Changes in Mean RODI Scores in Single/ Double Level Discectomy patients			
Time	**Contrast**	**S.D**	**Tukey p-value**
1 month post-op vs pre-op	-54.516	2.73	0.000
6 month post –op vs pre-op	-54.064	2.73	0.000
1 year post-op vs pre-op	-55.000	2.73	0.000
Changes in Mean RDQ scores in single/ double level discectomy patients			
1 month post -op vs pre-op	-9.032	0.654	0.000
6 month post –op vs pre-op	-10.322	0.654	0.000
1 year post-op vs pre-op	-11.032	0.654	0.000
Changes in Mean BQ scores in single/ double level discectomy patients			
1 month post-opvs pre-op	-34.516	2.142	0.000
6 month post –op vs pre-op	-37.484	2.142	0.000
1 year post-op vs pre-op	-38.612	2.142	0.000

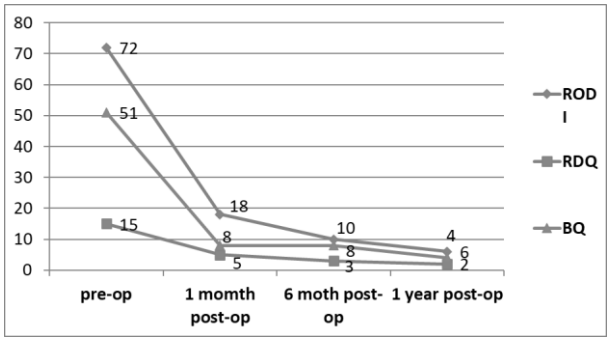


Figure 2. Mean of ODI, RDQ and BQ

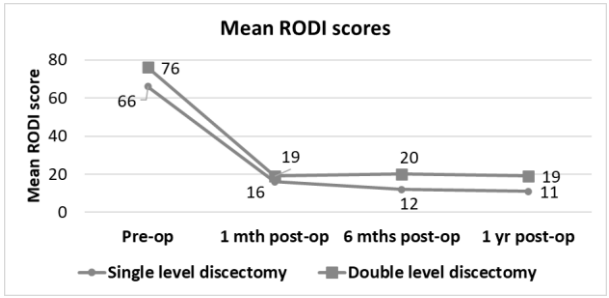


Figure 3. Changes in mean of RODI scores in single level vs double level discectomy patients

Patients were categorised in 2 categories based on the level of discectomy performed, i.e single level discectomy (SLDG) and double level discectomy (DLDG). In SLDG patients (n=54), the mean RODI scores were 65.67±2.76, 16.18±1.06, 11.92±1.58, and 10.95±2.05, at pre-operative, and postoperative 1month, 6 month, 1 year respectively. Similarly, the mean RDQ scores were 14.42±4.79, 5.38±2.38, 4.11±3.16, 3.44±3.64, and mean BQ score 46±18.10, 12.35±6.11, 9.16±8.01, 7.85±10.63 at pre-operative and respective post-operative follow up. In DLDG patients (n=8), the mean RODI scores were 75.75±5.57, 18.75±3.42, 19.50±7.87, and 18.87±9.10, at pre-operative, and postoperative 1month, 6 month, 1 year respectively. Similarly, the mean RDQ scores were 15.63±4.0, 6.62±3.11, 5.20±3.73, 4.25±5.03 and mean BQ score 50.38±16.12, 14.63±8.19, 13.12±12.73, 13.25±17.99 at pre-

operative and respective post-operative follow up (figure 3, 4 and 5). Changes in RODI, RDQ, and BQ scores at the respective intervals were compared between these two groups using a mixed ANOVA test. The difference of change in RODI, RDQ, and BQ scores over time in both groups was found to be statistically non-significant (P=0. 701, P=0.992, P=0.962 respectively). This finding showed that a similar degree of improvement occurred in both SLDG and DLDG.

Sub questions of BQ related to patient's anxiety, depression, social, and family activities (SFA) were compared pre-operatively and post-operatively. The mean ± S.D SFA scores at pre-operative and post-operative at 1 year were 7.65 ± 2.26 and 3.32±1.40 and this difference was statistically significant (P=0.000) (Table 4 and Figure 6).

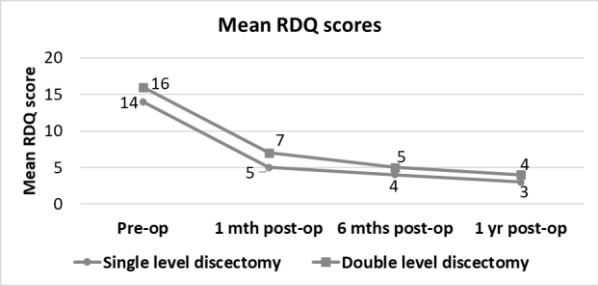


Figure 4. Changes in mean of RDQ scores in single level vs double level discectomy patients

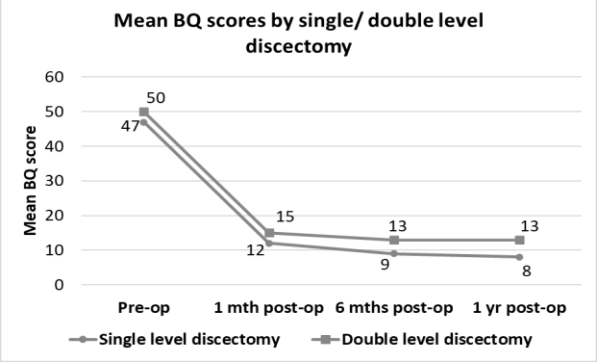


Figure 5. Changes in mean of BQ scores in single level vs double level discectomy patients

Table 4. Changes in psychosocial status (sub-questions of BQ)

Sub-question of BQ	Pre-op		Post-op		p-value
	Mean of diff.	S.D	Mean of diff.	S.D	
Social and family activities	7.650	2.26	3.32	1.40	0.000
Anxiety	5.50	2.53	1.42	1.37	0.000
Depression	5.50	2.53	0.71	1.08	0.000

Similarly, the pre and 1 year post-op anxiety scores were 5.73 ± 2.53 and 1.42± 1.37 respectively and the difference was statistically significant (P=0.000). The pre-op and 1 year post-op depression scores were 5.50 ± 2.53 and 0.71± 1.08 respectively and the difference was statistically significant (P=0.000) (Table 4 and Figure 6).

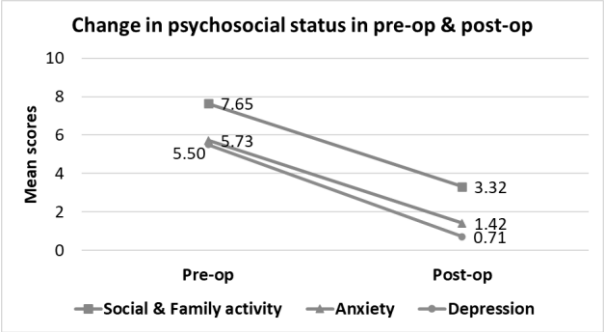


Figure 6. Changes in psychosocial status (sub question of BQ)

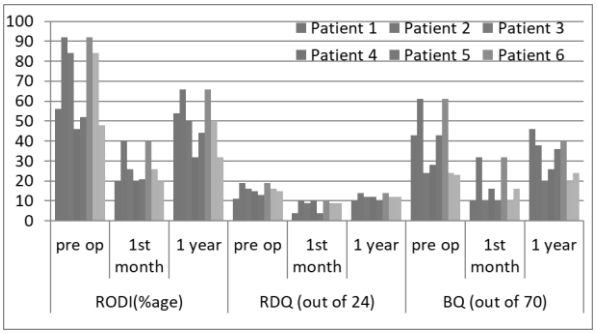


Figure 7. Functional assessment of not significantly improved patients

Discussion

Patients were assessed functionally with RODI, RDQ, and BQ at admission and after surgery at 1 month, 6 months, and 12 months. The RODI scores at pre-operative, post-operative 1, 6, and 12 months were 72, 18, 10, and 6 respectively. The RDQ scores at pre-operative, post-operative 1, 6, and 12 months were 15, 5, 3, and 2 respectively. Similarly, the BQ scores at pre-operative, post-operative 1, 6, and 12 months were 51, 12, 8, and 4 respectively. A gradual statistically significant improvement was seen in mean scores of all 3 functional scores. Maximum changes were observed after 1 month follow up in most of the patients as mentioned in the statistical table and diagram (Table 2 and Figure 1). Pre-

operative functional scores of each patient were compared with post-operative scores separately and the result showed that gradual, statistically significant improvement seen in 54 (87%) patients and 8 (13%) patients did not show statistically significant improvement, after the initial decrease in scores (figure 7). Among the patients who did not show improvement, four patients were in the RODI category 5 and 4 patients were in RODI category 3 pre-operatively. These patients were evaluated with MRI lumbosacral spine and among these two patients had developed Spondylolisthesis at operated level, four patients had foraminal stenosis due to facet joint hypertrophy and two patient's MRI showed increase degenerative changes at the operated level. Among two patients those who had developed post-op listhesis, one patient had undergone L4-L5 discectomy through open method and another patient had undergone L4-L5, L5-S1 double level discectomy (Table 5).

Table 5. MRI findings in patients not showing significant improvement

Spondylolisthesis	**2**
Foraminal stenosis	4
Canal stenosis	2

Many previous studies measured functional assessment with the help of different tools like SF-36, SF-24, PROLO scores, ODI scores or self-made objective criterias of improvement and many other [1,2,8,10,11,12,15,18,23,25,27,28,29]. Joel N Abramowitz categorized patient's outcome into 3 groups Good, Fair & Poor. A good outcome was defined as a situation where the patient had returned to the premorbid level of activity and was not limited by residual symptoms and was not taking narcotic medications. A fair outcome was defined as a situation where the patient did not return to work or was taking narcotic medications but improved after surgery. A poor outcome was defined as a situation where the patient had no improvement. In his study of 108 patients, 72 patients showed Good outcome, whereas 34 patients showed fair and 2 showed poor outcome [19]. Lewis et al (1987) divided the outcome as completely relieved, same or worse. 100 patients were followed for 5 - 10 years [16]. The results of lumbosacral Discectomy appeared favourable as compared to Weber's study [31, 32]. In the study of Junge et al - out of 381 patients 89% and 86% were followed up for 6 months and 12 months respectively. Low back pain of 6 or more on Visual Analog Scale, reduced working ability of more than half a year, no return to the previous job, regular visits to treating physicians, or hospital stay have been chosen as a criteria for the bad outcome. The outcome was categorized into good, moderate, and bad. Good- None of the above-mentioned criteria, Moderate -one or two of the criteria if back pain is between 0 and 3. Bad - Two criteria and back pain more than 3 or all of these criteria. 51.5% had a good outcome, 28.4% moderate, and 20.11 % bad outcome at 12 months follow up. There was no difference in 6 months outcome and 12 months outcome [13]. It is evident from above that for analyzing the outcome of lumbar disc disease various authors have chosen criteria that differ from study to study and the duration of follow up also differs significantly. These assessments were done by clinicians, so functional assessment of patients can be overestimated. That's why in our study, the functional assessments of the patients were done with the help of RODI, RDQ, AND BQ scores. These questionnaires were filled by patients themselves; hence there were chances to plot their functional assessment in a better way. Our results were comparable to other studies.

Most of the long term studies with follow up of more than 5 years are retrospective and most of the short term studies with short follow up of 2 years and less are prospective. Studies with short term follow up showed better outcomes than long term results. Further studies that included patients with severe degenerative spine or with neurological deficit showed unsatisfactory results. Salenius and Laurent reported satisfactory early results in 70% of patients that was decreased to 56% after 6 to 11 years of observation[24]. Frymoyer et al, in a retrospective study with a minimum 10-year follow-up, reported a 38% failure rate because of persistent symptoms or the need for reoperation [7]. Dvorak et al found that 23% of patients still complained of severe low-back pain and 45% had residual sciatica after 4 to 17 years follow-up [34]. In Spangfort's analysis of 2504 patients, more than 30% of patients complained of persistent low back pain, while sciatic pain was found in 23% of the patients [26].

Single and double level discectomy patients were compared along with changes in the mean of RODI, RDQ, and BQ scores over the defined follow-up time. Both groups of patients showed significant improvement over time. Further, both these groups were compared to see the degree of improvement over 1 year with the help of difference in the mean RODI, RDQ, and BQ scores measured at pre-operatively and one-year postoperatively and both these groups showed a similar degree of improvement (figure 3, 4, and 5).

Some patients of lumbar disc disease had anxiety and depression and some patients had affected their social and family activities. Hence 3 questions of BQ related to the patient social and family activities, anxiety and depression were separately compared pre and post-operatively. Mean of differences of means at pre-op and post-op 1 year of these sub-questions showed the statistically significant improvement over time. (Table 4 and Figure 6)

Complication:

Four patients experienced complications in our study. The intra-operative cerebrospinal fluid leak was present in one patient due to a dural tear, two patients had unilateral post-operative foot drop, and 1 patient developed postoperative superficial wound infection (Table 6).

Table 6. Complications

Complication	No of patients
CSF leak due to dural tear	1
Post-op foot drop	2
Superficial wound infection	1

Limitations:

This is a single centred study so the study population is less. Follow up period is one year as this is a prospective study and having time limitation. Further, prospective study is needed, which include large sample size and long follow up period so the results can be better plotted on population.

Conclusion

87% (n= 54) of patients had statistically significant improvement on functional assessment scales i.e RODI, RDQ, and BQ. Most of the patients who did not show statistically significant improvement were in ODI category 4 or 5. No statistically significant differences were seen on comparing single and double level discectomy on follow up of one year i.e similar trends of improvement were seen in single level versus double level discectomy patients. SFA, depression, and anxiety of the patients improved significantly over 1 year.

Acknowledgements

I am thanking Dr Arvind Kumar Singh, Associate Professor, Deptt. Of Community Medicine, Dr RMLIMS, Lucknow for statistics and valuable advice during my study.

Abbreviations

ODI: disability index
PIVD: prolapsed intervertebral disc
RODI: revised Oswestry Disability Index score,
RDQ: Ronald–Morris disability questionnaire
BQ: The Back Bournemouth questionnaire
MRI: Magnetic resonance imaging
ANOVA: One-way analysis of variants.
HSD: honestly significant difference
SE: standard error of means.
SLRT: straight leg raising test
SLDG: single level discectomy
DLDG: double level discectomy
SFA: social and family activities

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Possible predictive markers in surgical decision making in patients with degenerative or isthmic lumbar spondylolisthesis

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ABSTRACT

Background: Although age, comorbidity, duration and severity of symptoms, slippage degree, and flexion-extension slipping stability during X-ray imaging are effective in making a surgical decision in patients with spondylolisthesis, these factors are rarely based on definitive evidence. The aim of this study was to determine the efficacy of clinical, radiological and biochemical findings in surgical decision making in these patients.

Materials and methods: Patients' data including age, gender, degree and type (i.e. degenerative or isthmic) of the spondylolisthesis, urinary incontinence, neurogenic claudication were recorded. Radiological imaging studies (lumbar dynamic X-ray, computed tomography, magnetic resonance imaging), serum glucose, C-reactive protein and erythrocyte sedimentation rate values of the patients obtained during hospital admissions were evaluated.

Results: Forty patients were followed conservatively and 12 patients were treated surgically. Degenerative spondylolisthesis was seen in 22 patients. Nine patients had neurogenic urinary incontinence and 19 patients had neurogenic claudication. When the patients were divided into two groups with and without surgical treatment, the presence of the pars defect, slipping distance in a neutral position and slipping distance in flexion position was significantly different between groups. A positive correlation was found between pars defect and surgical treatment. Likelihood ratio test results revealed that the presence of pars defect, neurogenic claudication and neurogenic urinary incontinence could be the best parameters in decision making the surgical treatment.

Conclusion: The presence of pars defect, neurogenic claudication and urinary incontinence could be the best parameters that may help the surgeon to make the surgical treatment decision.

INTRODUCTION

Lumbar spondylolisthesis which described as slipping of a vertebral body over the adjacent vertebral body may be caused by a combination

of osteoarthritis and degenerative changes in the disc and facet joints. This slipping may lead to varying degrees of spinal stenosis, resulting in mechanical low back pain associated with hip and leg pain clinically (1).

In literature, it is advocated that these patients should be treated with conservative treatment as the first choice, but surgical treatment should be applied when this treatment fails (2-5). Today, surgical treatment options include decompression and fusion to slipping vertebrae with instrumentation (6-11). However, other clinical studies have demonstrated that there will be no difference in spine fusion between instrument use and non-use (12), some of the systematic reviews have reported that the use of instrumentation can increase the likelihood of obtaining spinal fusion (1).

In clinical practice, it is generally reported that the patient's age, comorbidity, duration and severity of the symptoms, degree of slippage, and flexion-extension slipping stability during X-ray imaging are effective on making of the surgical decision, but these factors are rarely based on definitive evidence. It is generally believed that patients with symptoms of neural compression due to spondylolisthesis can be useful for simple decompression and less extensive fusion surgery, and extensive fusion surgery is generally recommended when serious "instability" is detected (12).

This study aimed to determine the efficacy of clinical, radiological and biochemical findings in surgical decision making in patients with degenerative or isthmic lumbar spondylolisthesis.

Materials and methods

Patient groups

This single-center retrospective study was conducted after approval by the Local Ethics Committee for Clinical Trial. In this study, the information of patients who were treated with conservatively and surgically was included between January 2015 and December 2018. ICD-10 (International Statistical Classification of Diseases and Related Health Problems) coding was used to scan hospital records.

Patients were divided into groups according to gender, whether there was a pars defect, according to the degree of spondylolisthesis, and whether surgical treatment was performed.

Patients with missing data, patients coded with the wrong ICD-10 code, patients with pathological spondylolisthesis due to a tumor, rheumatic disease, and infection, and patients in the pediatric age group (<16 years) were excluded from the study. Furthermore, patients with cauda equine syndrome which is considered as an emergency procedure, patients who underwent spinal surgery including unilateral or bilateral fenestration, hemilaminectomy, laminectomy, laminarthrectomy, laminotomy, foraminotomy, discectomy, flavectomy, sequestrectomy including anterior interbody fusion between adjacent vertebrae, instrumented fusion (with/without decompression) including intervertebral stabilization such as transforaminal interbody fusion (TLIF), anterior lumbar interbody fusion (ALIF) or posterior lumbar interbody fusion (PLIF), extreme lateral lumbar interbody fusion (XLIF) were ruled out from the study. Moreover, vascular claudication and other conditions/ joint problems limiting walking capacity have been ruled out

Materials

The patients' parameters including the age, gender, degree of spondylolisthesis according to Meyerding grade, type of the spondylolisthesis (degenerative or isthmic spondylolisthesis according to the evidence of the pars defect), presence of the radiculopathy pain, urinary incontinence and neurogenic claudication were recorded. Radiological images (lumbar dynamic X-ray, computed tomography (CT), magnetic resonance imaging (MRI), serum glucose, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) values of the patients obtained during hospital admissions were evaluated. The approach for measurements acquisition was adopted after review of available literature (13,14).

Surgical method

After general anesthesia applied to the patients who were considered surgery, paravertebral muscles were dissected by midline incision while the stabilization level was determined by scopy while in prone position and stabilization was applied to the vertebrae using transpedicular screws. A standard laminectomy was performed to remove spinal cord compression. Following hemostasis, surgical layers were closed according to anatomy and the operation was terminated. The patients walked on the first postoperative day after wearing a lumbosacral corset.

Biochemical analysis

Study results were obtained from the venous blood samples of the patients taken at their initial admission to the hospital. ESR (reference range <20 mm / h) was measured using an analyzer (ESR 40, Cystate Diagnostics). Serum glucose (reference range 74-109 mg/dL) and CRP (reference range 0.15-5 mg/dL) levels were obtained by the immunoturbidimetric method using an analyzer (Roche Diagnostic COBAS c501).

Table 1. Table shows the patients' data according to the gender. *Chi-Square test, Mann Whitney U test, p<0.05*

		GENDER			
Variable		**Male**	**Female**	**X^2 / Z**	**p**
Pars defect	Degenerative	4 (18.2%)	18 (81.8%)	0.229*	0.632
	Isthmic	4 (13.3%)	26 86.7%)		
Meyerding grade	1	3 (27.3%)	8 (72.7%)	3.453*	0.178
	2	5 (17.2%)	24 (82.8%)		
	3	0 (0.0%)	12 (100.0%		
Treatment modality	Conservative	7 (17.5%)	33 (82.5%)	0.596*	0.440
	Surgery	1 (8.3%)	11 (91.7%)		
Number of screws	0	7 (17.5%)	33 (82.5%)	0.916*	0.633
	4	0 (0.0%)	4 (100.0%)		
	6	1 (12.5%)	7 (87.5%)		
Incontinence	no	6 (14.0%)	37 (86.0%)	0.391*	0.532
	yes	2 (22.2%)	7 (77.8%)		
Radiculopathy pain	no	7 (26.9%)	19 (73.1%)	5.318*	**0.021**
	yes	1 (3.8%)	25 (96.2%)		
Claudication	no	5 (15.2%)	28 (84.8%)	0.004*	0.951
	yes	3 (15.8%)	16 (84.2%)		
Glucose		93.50 (81-206)	95.00 (79-140)	-0.038	0.970
C-reactive protein		2.61 (0-28)	4.36 (1-54)	-0.311	0.755
ESR		10 (9-46)	19 (5-71)	-0.210	0.834

(*) Chi-Square test

Number of patients (%) or median (minimum-maximum) value

X2: Chi-Square score, Z: Z score, ESR: erythrocyte sedimentation rate

Statistical analysis

The power analysis for the results of this study was performed using the "Gpower 3.1" package program and it was concluded that the patients included in the study were sufficient to form the study.

Chi-Square test, Kruskal Wallis test, and Mann-Whitney U test was used to compare the nonparametric data between the groups (p <0.05). Parametric data were analyzed using Independent Samples t-test (p<0.05).

Spearman's rho Correlation test was used to determine the relationship between the parameters (p <0.05).

ROC-Curve test and Logistic Regression test were used to determine the predictive markers in the decision of surgical treatment. The likelihood ratio test was used to estimate the "best" variable in decision-making in patients undergoing surgery (p <0.05).

RESULTS

Fifty-two patients (male = 8, female = 44) were included in the study. Nine patients (17.31%) had neurogenic urinary incontinence and 19 patients (36.54%) had neurogenic claudication. Twenty six patients (50%) suffered from radiculopathy pain. Serum glucose median values were 94.5 (79-205) mg / dL, CRP median values were 4.29 (0-54) mg / dL, and ESR median values were 19 (5-71) mm / hour.

When the patients were divided into two groups according to their gender, no statistically significant difference was found in terms of study parameters except radiculopathy pain (X2 = 5.318, p = 0.021) (Table 1).

Forty of the patients were followed conservatively and 12 patients were treated surgically. When the patients were divided into two groups with and without surgical treatment, there was found a statistically significant difference in terms of pars

defect (X2 = 4.202, p = 0.040) (Table 2). On the other hand, there was a statistically different between the two groups in terms of the slipping distance in the neutral position of the patient (t = 3.113, p = 0.006) and slipping distance in flexion position of the patient (t = 3.380, p = 0.003). However, changing the degree of the slippage angle was not different between the groups. In non-operated patients, the median slipping distance position was 0.22 ± 0.18 mm and the slippage angle was 7.03 ± 9.1 degrees in the neutral position while the mean slipping level was 0.24 ± 0.22 mm and the slippage angle was 7.26 ± 0.31 degrees in the flexion position (Figure 1 and Figure 2). In operated patients, the median slipping distance was 15.52 ± 13.78 mm and the slippage angle was 6.78 ± 5.49 degrees in the neutral position while the mean slipping distance was 17.26 ± 14.11 mm and the slippage angle was 4.93 ± 5.61 degrees in the flexion position (Figure 3 and Figure 4).

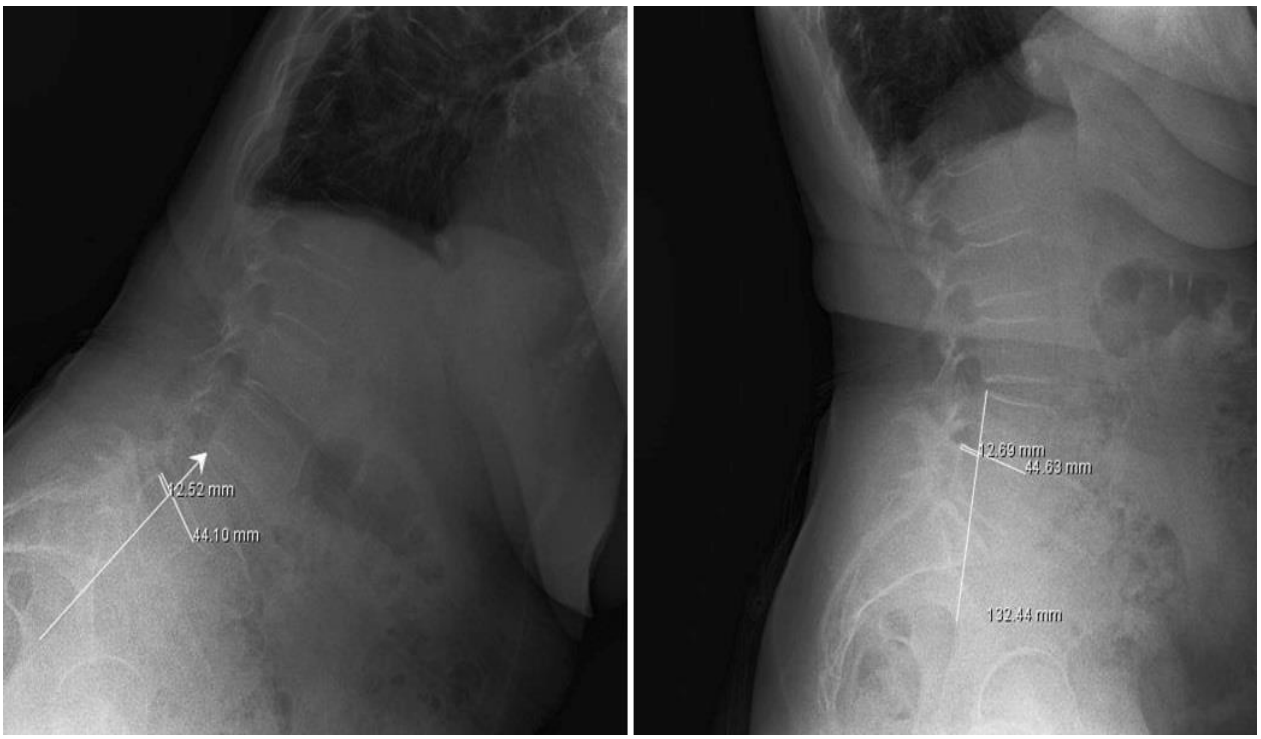

Figure 1. Lumbar dynamic X-ray images which were obtained in the neutral position and in flexion position showing the slipping distance of patient who was not operated.

Table 2. Table shows the data of patients who were treated surgically and conservatively. *Chi-Square test and Mann Whitney U test, p<0.05*

		TREATMENT MODALITY			
Variable		**Conservative**	**Surgery**	**X^2 / Z**	**p**
Gender	male	7 (87.5%)	1 (12.5%)	0.596*	0.440
	female	33 (75.0%)	11 (25.0%)		
Pars defect	Degenerative	20 (90.9%)	2 (9.1%)	4.202*	**0.040**
	Isthmic	20 (66.7%)	10 (33.3%)		
Meyerding grade	1	9 (81.8%)	2 (18.2%)	0.953*	0.621
	2	23 (79.3%)	6 (20.7%)		
	3	8 (66.7%)	4 (33.3%)		
Number of screw s	0	40 (100.0%)	0 (0.0%)	52.000*	**<0.001**
	4	0 (0.0%)	4 (100.0%)		
	6	0 (0.0%)	8 (100.0%)		
Incontinence	no	33 (76.7%)	10 (23.3%)	0.004*	0.947
	yes	7 (77.8%)	2 (22.2%)		

Radiculopathy pain	no	22 (84.6%)	4 (15.4%)	1.733*	0.188
	yes	18 (69.2%)	8 (30.8%)		
Claudication	no	27 (81.8%)	6 (18.2%)	1.219*	0.270
	yes	13 (68.4%)	6 (31.6%)		
Glucose		94 (79-206)	98 (83-139)	-1.055	0.292
C-reactive protein		4.33 (0-28)	4.03 (1-54)	-0.421	0.673
ESR		19 (5-71)	10 (6-51)	-0.941	0.347

(*) Chi-Square test
Number of patients (%) or median (minimum-maximum) value
X2: Chi-Square score, Z: Z score, ESR: erythrocyte sedimentation rate

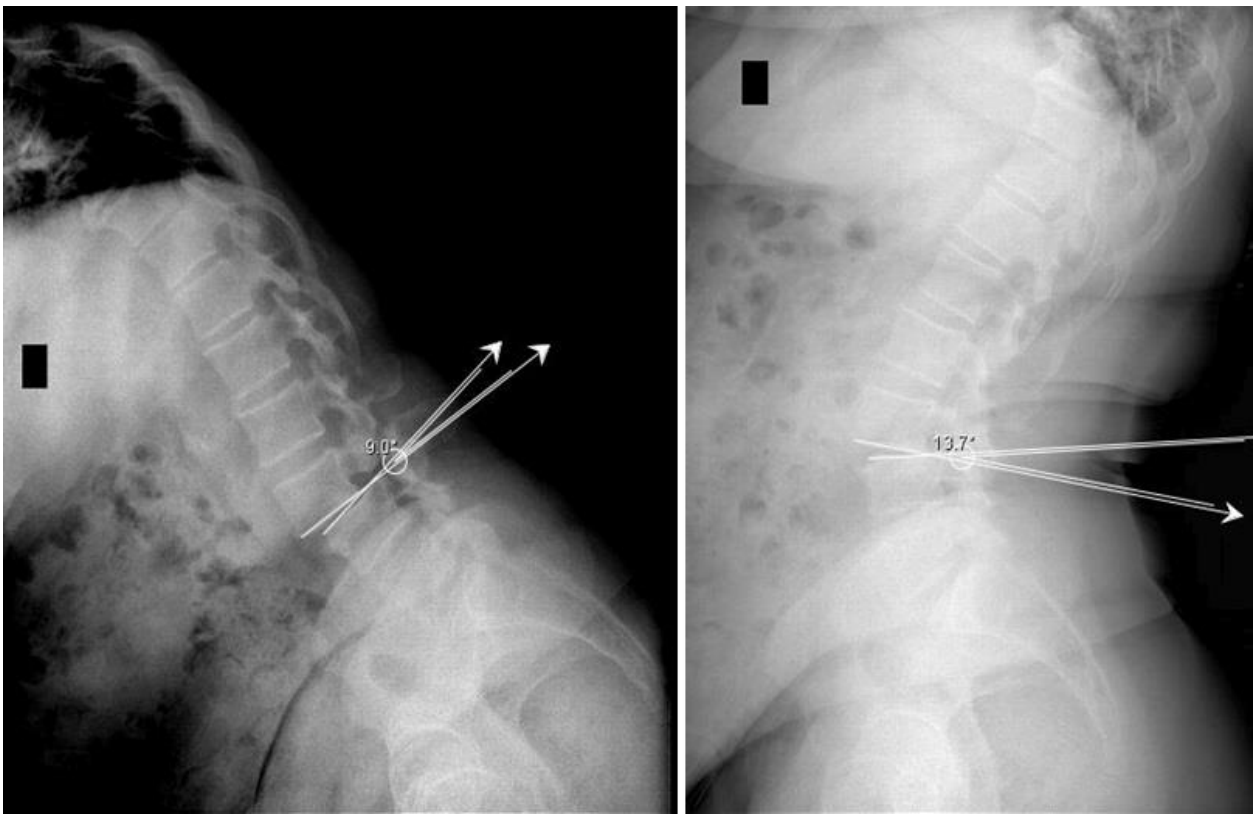

Figure 2. Lumbar dynamic X-ray images which were obtained in the neutral position and in flexion position showing the slippage degrees of patient who was not operated

Table 3. Table shows the patients' data according to the type (i.e. degenerative and isthmic type) of spondylolisthesis. *Chi-Square test and Mann Whitney U test, p<0.05*

		TYPE OF SPONDYLOLISTHESIS			
Variable		**Degenerative**	**Isthmic**	**X^2 / Z**	**p**
Gender	male	4 (50.0%)	4 (50.0%)	-0.229*	0.632
	female	18 (40.9%)	26 (59.1%)		
Meyerding grade	1	10 (90.9%)	1 (9.1%)	14.605*	**<0.001**
	2	10 (34.5%)	19 (65.5%)		
	3	2 (16.7%)	10 (83.3%)		
Treatment modality	Conservative	20 (50.0%)	20 (50.0%)	4.202*	**0.040**
	Surgery	2 (16.7%)	10 (83.3%)		
Number of screw s	0	20 (50.0%)	20 (50.0%)	4.885*	0.087
	4	0 (0.0%)	4 (100.0%)		
	6	2 (25.0%)	6 (75.0%)		

Incontinence	no	22 (51.2%)	21 (48.8%)	7.981*	**0.005**
	yes	0 (0.0%)	9 (100.0%)		
Radiculopathy pain	no	13 (50.0%)	13 (50.0%)	1.261*	0.262
	yes	9 (34.6%)	17 (65.4%)		
Claudication	no	12 (36.4%)	21 (63.6%)	1.307*	0.253
	yes	10 (52.6%)	9 (47.4%)		
Glucose		93.00 (79-139)*	96.5 (83-206)*	-1.076	0.282
C-reactive protein		3.96 (1-17)*	4.58 (0-54)*	-0.771	0.441
ESR		19 (5-71)*	14 (6-68)*	-0.600	0.548

(*) Chi-Square test
Number of patients (%) or median (minimum-maximum) value
X2: Chi-Square score, Z: Z score, ESR: erythrocyte sedimentation rate

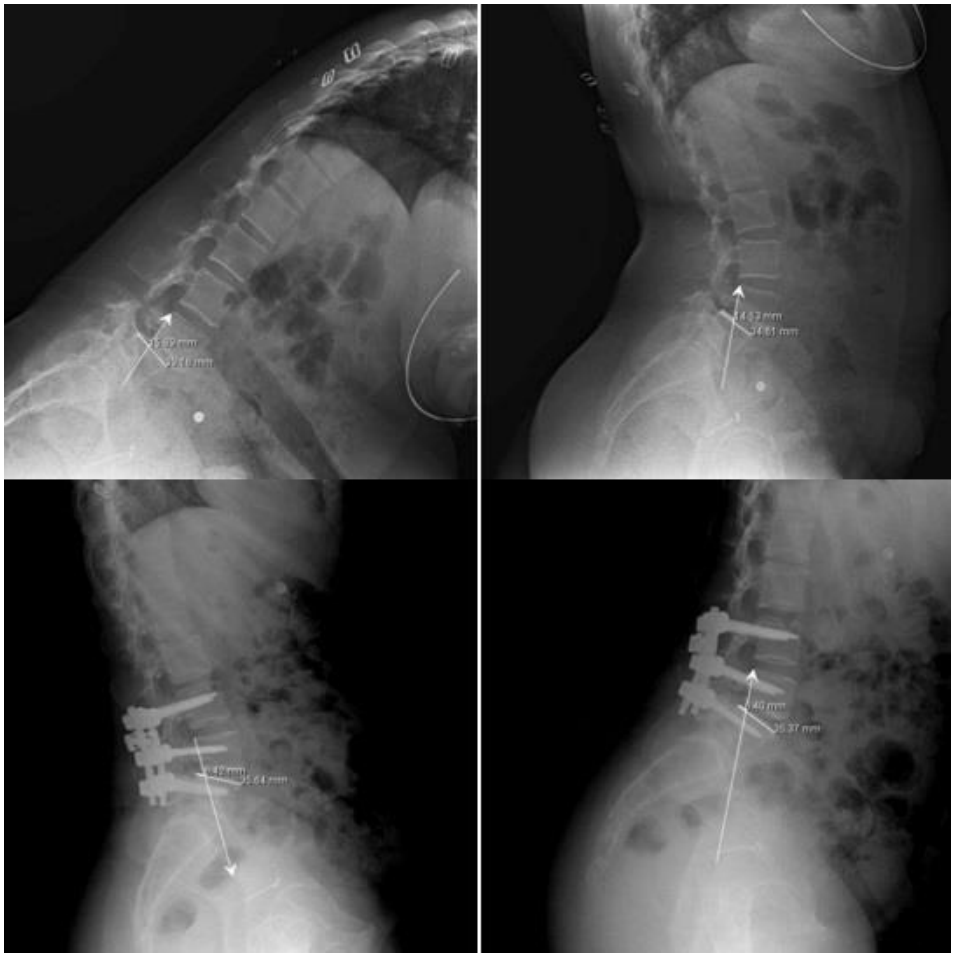

Figure 3. Lumbar dynamic X-ray images which were obtained in the neutral position and in flexion position showing the slipping distance of patient who was operated.

Table 4. Table shows the data of patients according to the grade (i.e. Meyerding grade) of spondylolisthesis. *Chi-Square test and Kruskal Wallis test, p<0.05*

		GRADE OF THE SPONDYLOLISTHESIS				
Variable		**1**	**2**	**3**	**X^2 / Z**	**p**
Gender	male	3 (37.5%)	5 (62.5%)	0 (0.0%)	3.453*	0.178
	female	8 (18.2%)	24 (54.5%)	12 (27.3%)		
Pars defect	Degenerative	10 (45.5%)	10 (45.5%)	2 (9.1%)	14.605*	**0.001**
	Isthmic	1 (3.3%)	19 (63.3%)	10 (33.3%)		
Treatment modality	Conservative	9 (22.5%)	23 (57.5%)	8 (20.0%)	0.953*	0.621

	Surgery	2 (16.7%)	6 (50.0%)	4 (33.3%)		
Screw s Number	0	9 (22.5%)	23 (57.5%)	8 (20.0%)	7.319*	0.120
	4	0 (0.0%)	4 (100.0%)	0 (0.0%)		
	6	2 (25.0%)	2 (25.0%)	4 (50.0%)		
Incontinence	no	11 (25.6%)	23 (53.5%)	9 (20.9%)	3.030*	0.220
	yes	0 (0.0%)	6 (66.7%)	3 (33.3%)		
Radiculopathy pain	no	8 (30.8%)	13 (50.0%)	5 (19.2%)	2.916*	0.233
	yes	3 (11.5%)	16 (61.5%)	7 (26.9%)		
Claudication	no	4 (12.1%)	21 (63.6%)	8 (24.2%)	4.539*	0.103
	yes	7 (36.8%)	8 (42.1%)	4(21.1%)		
Glucose		92 (81-139)	94 (79-206)	97 (80-125)	0.375	0.829
C-reactive protein		4 (1-17)	2.61 (0-54)	5 (1-28)	0.539	0.764
ESR		20.50 (9-59)	19 (5-71)	10 (5-68)	0.978	0.613

(*) Chi-Square test
Number of patients (%) or median (minimum-maximum) value
X^2: Chi-Square score, Z: Z score, ESR: erythrocyte sedimentation rate

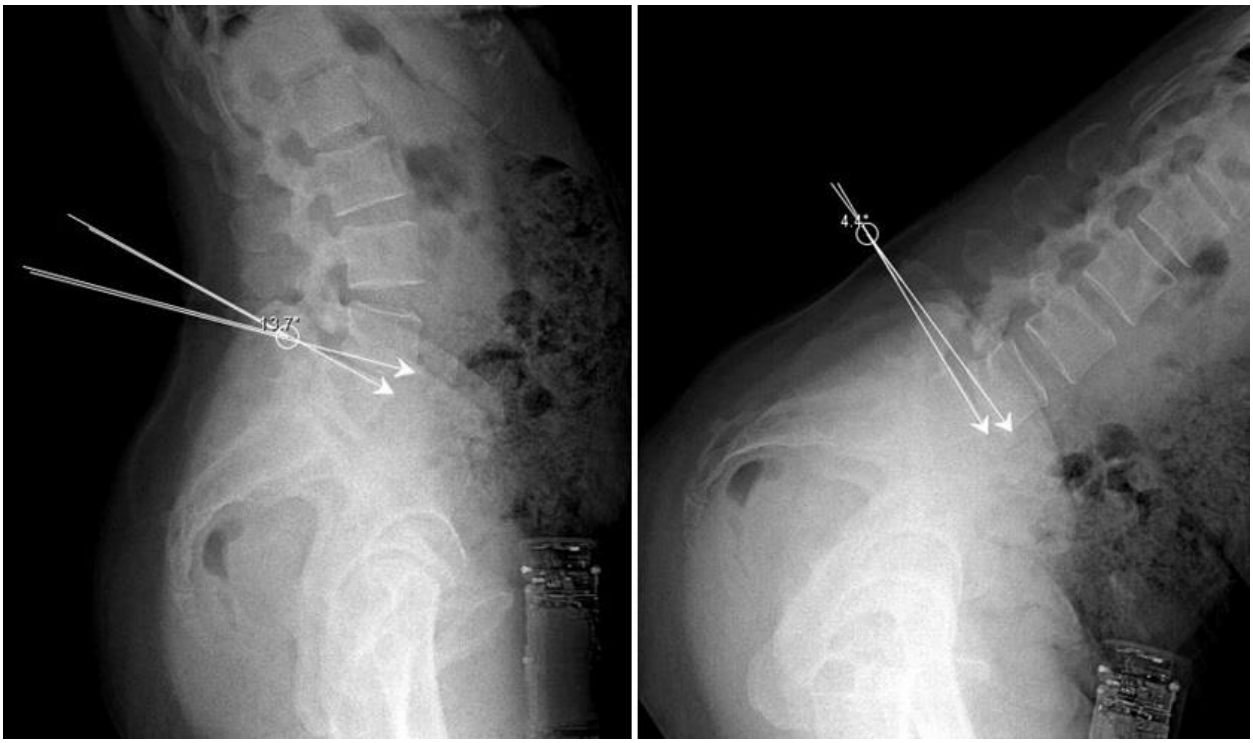

Figure 4. Lumbar dynamic X-ray images which were obtained in the neutral position and in flexion position showing the slippage degrees of patient who was operated

Degenerative spondylolisthesis was seen in 22 patients (male=4, female=18) and isthmic spondylolisthesis was found in 30 patients (male=4, female=26). When the patients were divided into two groups according to their pars defect (degenerative spondylosisthesisvs isthmic spondylolisthesis), the grade of spondylolisthesis (X2= 14.605, p <0.001), surgical treatment (X2= 4.202, p = 0.040) and urinary incontinence (X2= 7.981, p = 0.005) was found to be different between the groups (Table 3).

Eleven patients (21.15%) had grade 1, 29 patients (55.77%) had grade 2 and 12 patients (23.08%) had grade 3 spondylolisthesis. When the patients were divided into three groups according to the degree of spondylolisthesis, only the pars defect was found to be different between the groups (X2= 14.605, p = 0.001) (Table 4).

At the end of the correlation analysis applied to the data of all patients, a positive correlation was found between the gender and radiculopathy pain (r

= 0.320, p = 0.021), between pars defect and the grade of spondylolisthesis(r = 0.491, p <0.001), between the pars defect and receiving the surgical treatment (r = 0.284, p = 0.041), between the pars defect and urinary incontinence (r=0.392, p=0.004), between the urinary incontinence and radiculopathy pain (r=0.356, p=0.010) and between urinary incontinence and neurogenic claudication (r = 0.392, p = 0.004). However, a negative correlation was seen between the age and pars defect (r = -0.390, p = 0.004).

At the end of the ROC-Curve test and Logistic Regression tests, it was determined that no parameter could be a sensitive and specific predictive marker in the decision of surgical treatment. However, the likelihood ratio test results revealed that the presence of pars defect (X2 = 10.576, p = 0.001), the presence of neurogenic urinary incontinence (X2 = 8.203, p = 0.004) and the presence of neurogenic claudication (X2 = 8.003, p = 0.005) could be auxiliary parameters in decision making the surgical treatment (Table 5). Besides, it was considered that the angulation change or slipping distance in the slipping spine segment detected on dynamic X-Ray images was not sensitive or specific or an auxiliary parameter in decision making the surgical treatment.

Table 5. Table shows the best possible markers to make a decision of the surgery in patients with spondylolisthesis. *ROC-Curve test and Likelihood Ratio test, p<0.05*

	ROC-Curve test		*Likelihood Ratio* test	
Variable	**Area**	**p**	X^2	**p**
Pars defect	0.667	0.082	10.576	**0.001**
Meyerding grade	0.575	0.434	0.001	0.973
Incontinence	0.496	0.965	8.203	**0.004**
Radiculopathy pain	0.608	0.259	1.468	0.226
Claudication	0.588	0.362	8.003	**0.005**

Discussion

It has been shown in the literature that loss of height in the disc space, facet joint hypertrophy, hypertrophic ligamentumflavum, subchondral sclerosis, the presence of osteophyte, multifudis atrophy and presence of the “pars interarticularis” fracture may cause either severe canal stenosis and foraminal stenosis and anterior and / or lateral slipping in the vertebrae (3-5). Isthmic spondylolisthesis may result from a stress fracture, acute fracture or elongation defect. It is typically seen in children aged 5-7 years, but the defect can reach and be seen in adulthood. Lesions often occur in L5 - S1 but in trauma cases above the L5 level. It may be asymptomatic or may cause low back pain, hamstrings stiffness, knee contractures, and bladder and bowel incontinence (15).

In a study, degenerative changes in the lumbar spine were examined in 3 groups and group 1 patients had transient dysfunction; Group 2 patients had an unstable spine and group 3 patients had re-stabilization. It was reported that group 1 patients benefited more from conservative treatment, conservative approaches were applied to those in the early stage of group 2 patients, while conservative treatments were inadequate and fusion surgery was performed in late group 2 patients. Group 3 patients had severe stenosis and these patients underwent spinal decompression with or without instrumentation (16). In another study, it was suggested that the micro-instability period could be unnoticed. Therefore, a classification was formed by scoring the changes in X-ray, CT, and MRI for a decision on which the treatment would be done in these patients. According to the classification, it was aimed to provide early diagnosis and treatment to the patient in the period of micro-instability (17,18).

In our study, it was thought that the complaint of radiculopathy pain occurred mostly in women, but gender did not affect other study parameters. On the other hand, it was found that most of the patients (n = 30) had pars defect and 10 of them had surgical treatment. Most of the patients had grade 2 spondylolisthesis (n = 19) and most of them (n = 40) were treated conservatively, whereas surgical treatment was preferred in patients with pars defects (n = 10), and most patients (n = 43) did not have urinary incontinence.

Most of the patients (n = 30) had pars defect and 19 patients had grade 2 and 10 patients had grade 3 spondylolisthesis. Surgical treatment was applied to 2 patients without pars defect and 10 patients with pars defect; 6 of these patients had grade 2 and 4 had grade 3 spondylolisthesis. Although it was seen that most of the patients with grade 2-3 isthmic spondylolisthesis underwent surgery, it was thought that type or grade of spondylolisthesis could not be a criterion for deciding on the surgical treatment because of a small number of patients.

Correlation analysis showed that pars defect may be an important factor in the formation of spondylolisthesis and neurogenic urinary incontinence. It was also thought that urinary incontinence may also occur if the patient had symptoms and signs of radiculopathy pain or neurogenic claudication. However, it was argued that there was no statistical relationship between the degree of spondylolisthesis and the findings of radiculopathy pain, neurogenic claudication or urinary incontinence. ESR or CRP values, which are known as acute and / or chronic inflammation markers, could not be correlated with any parameters. With this result, it was argued that pars defect and / or spondylolisthesis detected in patients could not be the result of an inflammatory process.

On the other hand, at the end of the ROC-Curve analysis, it was concluded that none of the parameters evaluated in this study could be a predictive marker in deciding on surgical treatment. However, Likelihood Ratio test results demonstrated that the presence of pars defect in the patient, the presence of neurogenic claudication and urinary incontinence findings could be the parameters that may help the surgeon to decide on surgical treatment. However, it was thought that the degree of spondylolisthesis could be ineffective in deciding for surgical treatment.

Some limitations of this study are as follows: First, the retrospective character of this study limited the discussion of the mid-term or long-term follow up results of the patients. Second, the number of the study population was very small. Nevertheless, it can be easily said that the results of this study were very impressive and novel to discuss the predictive markers in deciding on surgical treatment. Third, in some cases, determining the correct level to identify spondylolisthesis was a challenge due to the difficulty in counting spinal levels with the possibility of lumbar-sacral segments or sacralized lumbar segments or a variable total number of spine levels. Fourth, because some MR and / or CT images were from external institutions, they could not be evaluated retrospectively. Therefore, the relationship between the X-Ray images and CT / MR images which could support more relevant data was not investigated. Finally, the present study included computerized abstracted information that required personal measurements that could be prone to random error.

Conclusion

At the end of this study, it was seen that the presence of pars defect (isthmic spondylolisthesis) in the patient, the presence of neurogenic claudication and urinary incontinence findings could be the parameters that may help the surgeon to make the surgical treatment decision. However, it was considered that the presence of the radiculopathy suffering of the patient or the grade of spondylolisthesis could be ineffective in the decision of surgical treatment.

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Surgical site infections in neurosurgery. Case series in a single centre

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Abstract

Background: Surgical site infections in neurosurgery are serious due to their proximity to the central nervous system and their management is a challenge. The aim of our work is to report surgical site infections (SSI) in patients who underwent brain or spinal surgery and to describe their characteristics.

Materials and method: We conducted a retrospective study involving patients who underwent surgery in our facility's neurosurgical emergency department over 5 years from January 2015 to December 2019. The data were collected from medical hospital and follow-up records.

Results: Fifty-eight cases of SSI were identified out of 2889 operations in total, for a frequency of 2%. The series consisted of 36 men (62.07%) and 22 women (37.93%). The average age was 43.9 years (19-72 years). 46 patients (79.31%) had undergone urgent surgery and 12 patients (20.69%) for delayed surgery. 40 patients (68.97%) had undergone cranial intervention and 18 patients (31.03%) underwent spinal surgery. The identified germ was Staphylococcus aureus in 13 cases (76.48%). Mortality was 13.8% (8 out of 58 cases).

Conclusion: The majority of microorganisms that cause the infections contaminate the surgical site intraoperatively. Preventive measures can reduce the rate of surgical site infections.

Keywords
infections,
neurosurgery,
surgical site

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Introduction

The incision of the skin barrier to perform the surgical procedure connects the inner environment with the external environment. Post-operative infections are the result of exogenous or endogenous contamination not controlled by the body's local and general defenses. This iatrogenic risk rises due to increased accessibility of surgical procedures and the development of surgical services activity. Surgical site infections (SSI) are a challenge for all surgical services. Neurosurgical site infections are severe because of their proximity to the central nervous system and their potential complications. SSI support also has a significant financial impact [1]. Understand the risk factors and identify the pathogens germs are essential to the management.

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The purpose of our work is to report surgical site infections in patients who have had cranial and spinal surgery in a neurosurgical emergency unit and to describe their characteristics.

Materials and method

This is a retrospective study that focused on patients operated in a neurosurgical emergency department of our institution over a period of 5 years from January 2015 to December 2019. Patients who underwent neurosurgical procedures and follow-up postoperatively were included. The data were collected from medical hospital and follow-up records.

The variables studied were: age, sex, patient origin, type of intervention, antibiotic prophylaxis, surgical indication and site of intervention, duration of surgery, type of germs identified, evolution. Quantitative variables were presented as an average. The qualitative variables in the form of a percentage. Urgent surgery was defined as a surgical procedure that was performed within the first 48 hours of admission, and delayed surgery was a procedure that took after 48 hours. The classification of Narotam [2] was used to classify the type of intervention into categories to determine the potential to develop sepsis: clean, clean with foreign body, clean-contaminated, contaminated, dirty.

Results

Fifty-eight cases of surgical site infections were identified out of 2889 operations in total, for a frequency of 2%. The average age was 43.9 years (19-72 years). The series consisted of 36 men (62.07%) and 22 women (37.93%). 34 patients (58.62%) lived in urban areas and 24 patients (41.37%) in rural areas. 46 patients (79.31%) had undergone urgent surgery and 12 patients (20.69%) for delayed surgery. 40 patients (68.97%) had undergone cranial intervention and 18 patients (31.03%) underwent spinal surgery.

According to Narotam's classification, surgical procedures were clean in 4 cases (6.3%), clean-contaminated in 6 cases (9.4%), contaminated in 16 cases (25%), and dirty in 32 cases (59.4%). The average duration of the intervention was 260 minutes with extremes ranging from 45 minutes to 540 minutes. The average length of hospitalization was 13 days with extremes of 6 days to 45 days. All patients had benefited from prophylactic antibiotics.

Table 1 summarizes the characteristics of patients who developed a surgical site infection.

Table 1. General characteristics of patients with SSI

Variables	Number of patients	Percentage (%)
Sex		
Female	22	37.93
Male	36	62.07
Origin		
Rural	24	41.37
Urban	34	58.62
Type of surgery		
Urgent	46	76.31
Delayed	12	20.69
Wound classification		
Clean	04	06.30
Clean-contamined	06	09.40
Contamined	16	25.00
Dirty	32	59.40

Table 2. Initial procedure performed to patients and diagnosis of the SSI

Variables	Number of patients	Percentage (%)
Craniotomy procedures		
Traumatic	36	90.00
Tumoral	02	05.00
Infectious	02	05.00
Spine surgery procedures		
Traumatic	08	44.44
Degenerative	07	38.89
Tumoral	03	16.67
Diagnosis of SSI in cranial location		
Superficial wound infection	07	17.50
Osteitis	02	5.00
Meningitis	24	60.00
Abcess or empyema	07	17.50
Diagnosis of SSI in spinal location		
Superficial wound infection	06	33.33
Meningitis	02	11.11
Deep infection	10	55.56

Initial surgical indications in cases of surgical site infection at the cranial level were traumatic in 36 cases (90.00%), tumor, and infectious each in 2 cases (5.00%). The supratentorial location was reached in

34 cases (85%), and infratentorial in 6 cases (15%). The distribution of the type of cranial infection was: superficial wound infections in 7 cases (17.50%), osteitis in 2 cases (5.00%), meningitis in 24 cases (60.00%), abscess or empyema in 7 cases (17.50%).

In the cases of surgical site infection at the spinal level, the surgical indications were traumatic pathologies in 8 cases (44.44%), degenerative in 7 cases (38.89%) and tumors in 3 cases (16.67%). The location of the infection was cervical in 1 case (5.55%), dorsal in 10 cases (55.56%), dorsolumbar in 4 cases (22.22%), and lumbar in 3 cases (16.67%). The type of infection at the operative site after spinal surgery was: superficial wall infection in 6 cases (33.33%), meningitis in 2 cases (11.11%), and deep infection on osteosynthesis material in 10 cases (55.56 %). Table 2 summarizes the indications for the initial procedure and the type of infections presented by patients.

Hyperleukocytosis was found in 24 patients (41.37%) and an increase in the c-reactive protein in 26 patients (44.82%). The culture was positive in 29.31%of cases (17 patients). The most frequently identified germs were: Staphylococcus aureus in 13 cases (76.48%), Pseudomonas aeruginosa 1 case (5.88%), Escherichia coli 1 case (5.88%), Proteus mirabilis 1 case (5.88%), Enterobacter cloacae 1 case (5.88%). Full recovery without significant neurological sequelae was in 75.9% of cases. Six patients had epilepsy (10.3%). In all mortality was 13.8% (8 cases) in the series.

Discussion

Prevalence and risk factors

In our series, the prevalence of postoperative neurosurgery infections was 2%. The rate varies between 0.5% and 8% in studies [1,3–5]. The effect of prophylactic antibiotics helps to control the infection rate of less than 5% [6]. In our study, the low rate could be explained by routinely prophylactic antibiotics in all patients. Antibiotic prophylaxis alters the morbidity of surgical operations. The rate of postoperative meningitis is decreased by antibiotic prophylaxis [7].

Several risk factors for surgical site infections have been reported [5,8–11]. A long operation duration has been reported by several studies [8,9,11,12]. An intervention time of more than 4 hours increases the risk of developing a SSI [8,13]. In our series, the average duration was 4 hours and 20 minutes which was relatively high. Males were considered as a risk factor [13]. However, another study [14] showed that male sex, age, alcohol consumption, and steroid use were not associated with increased incidence of spinal SSI.

An urgent surgery remains an important risk factor for SSI [8]. In our work, 79.3% of postoperative infections were admitted through emergencies. Patients admitted as an emergency, especially in the traumatic setting, carry scalp injuries contaminated by foreign debris. In our study, the initial procedure of the SSI was considered clean in only 6.3% of cases. The presence of foreign bodies was significantly associated with a risk of developing postoperative infection [5,8]. Other risk factors for SSI were: a high American Society of Anesthesiologists score (ASA) [12,13], sinus opening [8], an intervention considered contaminated [10,12], a CSF leak [13,14].

Closure of surgical wounds by staples and use of dural substitute was also reported as risk factors in a study [11]. In the same study, craniotomy was identified as a risk factor and a complicated surgical procedure as a predictor in the development of SSI [11]. Tumor surgery was the most difficult type of intervention for deep infections [4]. In our study, traumatic surgery was the most performed intervention because our unit was dedicated to the management of neurosurgical emergencies.

The surgeon's experience plays a role in the risk of infection [12]. An experienced surgeon contributes to the reduction in the duration of the operative procedure and therefore to the reduction of postoperative infectious complications. Postoperative drainage would increase the risk of infection [12].

Several general factors have been reported as purveyors of post-operative infections. These factors associated with postoperative infection were: diabetes [5], intraoperative blood transfusion [12], use of immunosuppressors [15], urinary tract infection, and smoking in spinal surgery [14]. In our series, diabetes was found in 10 patients and no patients had immunosuppressors medication.

Pathological entities of SSI

The superficial wound infection and flap osteitis are not grouped into the same category of infections. Although the pathophysiology is similar, their consequences and their management are very different. In the case of superficial wound infection,

antibiotics alone or debridement can be achieved. In the case of osteitis, aggressive surgery associated with re-reconstruction can be required. In our series, superficial wound infections were 26% of all SSI.

Deep infections that affect the central nervous system are serious and can be accompanied by significant morbidity with a high risk of neurological damage. Meningitis was commonly found and can have lethal complications. In our series, meningitis is the most common infection after cranial procedures but its frequency was lower in the spinal procedures. Ventriculitis is an evolutionary complication of meningitis that affects the cranial ventricular cavities and often causes severe damages. In our series, no cases of ventriculitis were observed.

Intracranial suppurations most often develop by contiguousness with a local outbreak, but also by the hematogenic path of parenchyma. In our series, intracranial suppurations were diagnosed in 7 out of 40 patients or 17.50%.

The most common complication in our series at the spinal level is an infection on osteosynthesis material. The use of foreign materials is a predictor in the development of SSI.

Pathogen germs

Before starting antibiotic treatment, bacteriological documentation is imperative to guide antibiotic therapy for these postoperative bacterial infections depending on the germ in question and its sensitivity. The bacteriological examination of the CSF and the samples from the surgical site is essential and culture was performed to identify pathogens germs. The germs implicated in postoperative infections are different from those identified in community-acquired infections. In our series, the most frequently identified pathogenic germ was staphylococcus aureus in 76.48% of cases. The most common pathogens in the literature are Staphylococcus aureus [3–5] and gram-negative bacilli [4,5,16] namely Acinetobacter baumanii [5,17] and Pseudomonas aeruginosa [16,17], and Escherichia coli [16,17]. Other germs such as Propionibacterium acnes can also be found [3,10]. The majority of microorganisms that cause the infections contaminate the surgical site intraoperatively.

The ecosystem of the unit must be known to allow the prescription of a good probabilistic antibiotic therapy taking into account the bacterial resistance specific to each institution. The management of SSI requires a multidisciplinary approach. The urgency of starting antibiotic therapy varies from situation to situation, but delays in some cases, such as meningitis and intracranial suppurations, can be lethal. The choice of antibiotic is based on bacteriological data and the antibiotic. The front door must be treated urgently if it exists. Corticosteroids could decrease the penetration of antibiotics and the use of mannitol may be preferable during the first 48 hours.

Prevention

Efforts in operating theatres to improve the quality of care, the determination of clean and dirty circuits can significantly reduce the rate of post-operative infections. Recommendations for SSI prevention are surgical handwashing and the use of antibiotic prophylaxis [10]. Decolonization oriented towards Staphylococcus aureus reduces the frequency of SSI [18]. Postoperatively, other recommendations are the observance of rigorous asepsis when handling drains and dressings, as well as strictly enclosed maintenance of the drainage system. Surgical drainage of the surgical site should not exceed 48 hours.

Conclusion

This study presents the profile of surgical site infections, and the germs involved in our neurosurgical emergency unit. The most common germs are staphylococcus aureus and less commonly gram-negative bacilli. The majority of microorganisms that cause the infections contaminate the surgical site intraoperatively. Preventive measures can reduce the rate of surgical site infections.

Abbreviations

SSI: Surgical site infections
CSF: Cerebrospinal fluid

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Awake focussed craniotomy for oedematous/large brain lesions. A pilot study for safety and feasibility

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Keywords
anaesthesia, awake craniotomy, brain tumour, keyhole surgery

ABSTRACT

Aim: Awake craniotomy has been proven to be safe and effective. It has generally been used for non-edematous conditions. If done in edematous states, large craniotomies are advised. Here, we report the combined use of techniques of awake anaesthesia and focussed craniotomy for dealing with large/edematous brain lesions.

Materials and methods: This was a prospective single-centre study from May to October 2019. Included were adult cooperative patients presenting with edematous brain lesions. A completely awake cycle was used using ring scalp block, Dexmedetomidine loading, and maintenance infusion, and use of Midazolam and Fentanyl. The dural flap was lifted limited to the lesion, and sometimes in stages to tackle the bulging brain. Data was collected for resection volume, pain scores using visual analogue scale (VAS) during the surgery, seizures, complications, new deficits, blood loss, duration of surgery, ICU, and postoperative hospital stay.

Results: Fifteen patients underwent the procedure. Pathologies were high-grade gliomas (7), low-grade gliomas (3), tuberculoma (2), metastasis (1), ependymoma (1), and meningioma (1). Fourteen patients underwent total, and one underwent subtotal excision. Brain bulge could be handled with the staged opening of the dura and intratumoral decompression. No patient required postoperative ventilatory support. Intraoperative pain scores ranged from 2-3. The duration of surgery ranged from 60-280min. Blood loss ranged from 75-300ml. Postoperative stay varied from 3-20 days. There were two intraoperative seizures (managed), two CSF leaks, and two infections. Two patients developed transitory motor deficits.

Conclusion: Awake focussed craniotomy was found safe and effective for large/edematous brain lesions in appropriately selected patients.

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Introduction

Awake craniotomy (AC) has been proven to be safe and effective in several conditions, including low-grade gliomas, epilepsy surgeries, and vascular diseases.2,12,13 It provides several advantages over craniotomy done under general anesthesia (GA). Firstly, it gives the ability to use intraoperative monitoring of eloquent regions, including speech, motor, and visual areas. Secondly, pulmonary complications due to intubation, ventilation, etc., that can occur with GA can be avoided. Thirdly, positional complications like ulcers, spinal torsions, etc. can also be prevented. Since the level of sedation is lesser than GA, the AC is essentially more physiological. The use of newer drugs like Dexmedetomidine has proved to be safe and effective in awake craniotomies, perioperative, and ICU situations.1,3.

AC has been generally used in non-edematous conditions, possibly due to the apprehension of intraoperative brain bulge. If done in edematous states, large craniotomies have been advised.4 Also, for the lesions with midline shift, the asleep-awake-asleep cycle has been used, and the data regarding the size of craniotomy is missing.5 Small craniotomies are associated with lesser operative time, blood loss, wound complications, etc. than large craniotomies. We have reported minicraniotomy and endoscopic-assisted excision of deep-seated brain tumors and hematomas in the past.8,9 In this article, we report the combined use of techniques of awake and focussed craniotomies for dealing with large or edematous brain lesions.

Materials and methods

This was a prospective study done at a single center from May 2019 to October 2019. Institutional ethics committee permission was taken. The trial was registered under the clinical trials registry of India with reference number CTRI/2019/05/019338.

Patient inclusion criteria were adult cooperative patients presenting with large or edematous brain lesions defined as either the tumor volume 30 cc3, or edema volume 60 cc3, or the total volume of tumor + edema 60 cc3. Patient denying taking part in the study, or with cardiac or respiratory illnesses were excluded from the study. Karnofsky status and Minimental status examination (MMSE) were calculated both before and after the surgery.

Anesthesia protocol

Patients were explained about the procedure and habituated with the types of questions to be raised before the surgery. Once in the operation theatre, glycopyrrolate 0.2mg, fentanyl 100mcg, and Ondansetron 4mg were administered intravenously, and an oxygen mask (O2) was applied. Monitoring included an electrocardiogram, pulse oximetry, blood pressure (BP), End-tidal CO2, and urine output. Ring scalp block was performed with 20 ml of 0.5 percent bupivacaine. The infiltration was given in the territories of Supraorbital, Supratrochlear, Zygomaticotemporal, Auriculotemporal, Lesser occipital and Greater Occipital nerves. The incision site was again infiltrated with 2% Lignocaine and 1:100,000 Adrenaline. Infusion of Dexmedetomidine (1ug/kg/hr) was then started and stopped 10 minutes before the neurocognitive testing. The level of sedation was assessed by the Ramsay sedation score and was maintained between a score of 3 to 5 until neurocognitive testing was started. Bispectral index monitoring was not available at our center and was not used in any of the cases.

Figure 1. Shows the patient positioning. An 'L' shaped rod allows the surgeon to work in a sterile field and anesthetist to have face accessible for interacting with the patient and emergency airway management if the need arises.

Surgical protocol: We defined focussed craniotomies as bone opening not more than 1 cm and dural opening not more than 0.5 cm of tumor edges. All surgeries were done by the same surgeon. A preoperative dose of antibiotic (Ceftriaxone) and 4mg of Dexamethasone was given in every case. Patients were placed supine with neck tilt in order to make the surgical trajectory as perpendicular to the ground as possible. A three-pin Mayfield head clamp was applied for immobilization. Patients were

allowed to move their limbs within the limits of safety. An L-shaped stand was placed right across the patient's face, and draping was done in a way to have the face always accessible to the anesthetist (figure 1).

The scalp flap was elevated according to the need, and a small craniotomy was lifted depending upon the lesion. The deeper the lesion, the smaller the craniotomy was made, according to the inverse funnel-shaped principle of keyhole surgeries. The brain bulge, if anticipated, was tackled with the initial small opening of dura, tumor decompression and later rest of the dural opening if needed. The bipolar cautery settings were used at the minimum. Cold saline was always kept ready to abort the seizure if it happens. The lesions were resected with the standard bimanual dissection technique. Cortical mapping with direct cortical stimulation was done in the last five cases. It was initially assessed over the exposed surface, and the absence of the eloquent region allowed the resection. Mapping was repeatedly done during the procedure, along with the clinical testing. There was no difficulty in achieving the hemostasis in any of the cases. Stopping the Dexmedetomidine raised blood pressure to be normal, and asking the patient to cough confirmed the hemostasis. Dura was closed, the bone was reposited, and standard closure techniques were followed in all the cases.

Table 1. Demographic details of the patients.

S. No.	Age in Years / Gender	Loc.	Side	Diagnosis	Tumor vol. (cc^3)	Edema vol. (cc^3)	Hydro-cephalous	Resection	Intraope --rative brain bulge	Blood loss (ml)	Duration of surgery (min)	Procedure related complication
1.	55/M	PF	Right	Metastasis	5.4	60	Absent	Total	Present	100	60	Intraoperative seizure
2.	25/F	AF	Left	Recurrent HGG	36.6	66.32	Absent	Total	Present	200	120	CSF leak, infection
3.	30/M	AP	Left	Tuberculoma	14.4	75	Absent	Total	Present	75	60	None
4.	32/M	PF	Right	Recurrent HGG	40	100	Absent	Subtotal	Present	150	200	CSF leak, infection
5.	45/M	MF	Left	Tuberculoma	37.63	67.32	Absent	Total	Present	100	150	None
6.	53/M	PF	Right	Convexity meningioma	22.8	110.7	Absent	Simpson Grade 1	Present	200	120	None
7.	40/M	AF	Right	HGG	38.5	22	Absent	Total	Present	200	150	None
8.	34/M	AF	Left	Ependymoma	42.75	20.4	Absent	Total	Present	200	280	None
9.	45/M	PF	Right	HGG	40.1	21	Absent	Total	Present	180	200	None
10.	24/M	PF	Left	HGG	44.5	23.2	Absent	Total	Present	300	180	Transient speech slurring
11.	30/F	AP	Right	HGG	40.2	21.1	Absent	Total	Present	250	210	None
12.	40/M	PF	Right	LGG	38.5	24.5	Absent	Total	Present	250	180	Intraoperative seizure
13.	22/M	AP	Right	LGG	40.2	23.1	Absent	Total	Present	250	150	Transient shoulder weakness
14.	29/M	AP	Left	HGG	30.5	40.2	Absent	Subtotal	Present	250	200	None
15.	42/F	MF	Left	LGG	41.2	21.2	Absent	Total	Present	200	220	None

Postoperative care

Postoperatively, they were given IV antibiotics for three days, and oral antibiotics for five more days. Dexamethasone, anticonvulsants, and analgesics were given for a minimum of one week and tapered thereafter.

Surgical resection

The resection was termed as gross total resection (GTR) (100% removal), near-total (91-99% removal), subtotal (STR) (51-90% removal), and tumor biopsy (<10% removal). These were determined based on a comparison of preoperative and postoperative imaging volumetrically.

The duration of surgery was calculated from the time of incision to the last stitch. Subtracting the amount of irrigation fluid from the drain fluid and weighing the gauges after surgery calculated blood loss.

Pain score

Patients were asked to rate the degree of maximum pain during the surgery on the visual analog scale (from 0-10, where 0 means no pain, and 10 means life-threatening pain).

Results

Fifteen adult patients (12 males, 3 females) ranging from 22-55 years were operated in the study period. The diagnosis included high-grade gliomas (7), low-grade gliomas (3), tuberculoma (2), metastasis (1), Ependymoma (1) and meningioma (1). Three gliomas were previously operated and were recurrences. All tumors were located either cortically or subcortically. Seven patients had a history of seizures before the surgery. The demographic details, including the location of tumors, are given in table 1.

Neurological status and deficits

The preoperative MMSE of the patients ranged from 22-30 (mean = 27.26 ± 2.49). Postoperatively at six weeks MMSE ranged from 28-30 (mean = 29.38 ± 0.76). The preoperative Karnofsky status of the patients ranged from 50-100 (mean = 77.33 ± 15.79), and it improved to range from 80-100 (mean = 91.53 ± 8.98) at six weeks. There were four patients with prior hemiparesis. One of them had an increase in shoulder weakness that resolved in six weeks. Another patient had new speech slurring, which resolved in four weeks. For these two patients, the surgery had to be stopped after the new deficit. None of the patients had a permanent new neurological deficit.

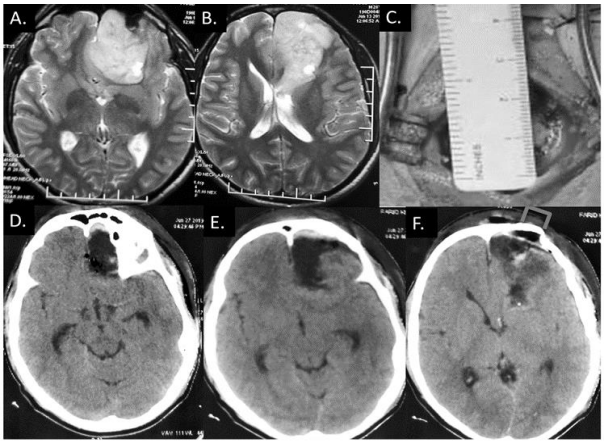

Figure 2. A & B shows the T2 weighted MRI with a large left parafalcine mass arising from the ventricle approached with awake minicraniotomy. C shows the 3cm sized bone opening. D-E shows the postoperative scan of the patient showing complete tumor excision. The red bracket shows the minicraniotomy on the scan.

Tumor volume and perilesional edema

Lesion volume ranged from 5.4cc3 to 44.5 cc3. The mean tumor volume was 34.21 ± 11.30 cc3. Perilesional edema volume ranged from 20.40 cc3 to 110.7cc3 with a mean of 46.4 ± 31.2 cc3.

Surgical resection

The dura was opened in a limited manner over the tumor or just more than the tumor. Fourteen patients underwent total, and one underwent subtotal excision of the masses (due to tumor invasiveness). Focussed craniotomies were lifted based on the methodology described. Figure 2 shows a Parafalcine mass arising from the ventricular wall (Ependymoma) approached through an awake frontal minicraniotomy. One of our patient (Case 4) had a significant bulging brain and for it staged dural opening and tumor resection was carried out. In the end, the brain was lax (figure 3). One patient (recurrent grade III glioma) had a previous large craniotomy. Going through it needed resection of a wedge of normal brain tissue to tackle the bulging brain. Therefore a new minicraniotomy with a direct trajectory was planned that allowed us to hit the tumor only and prevent the venous compression of the normal brain (figure 4). There was no difficulty in achieving hemostasis in any of the cases.

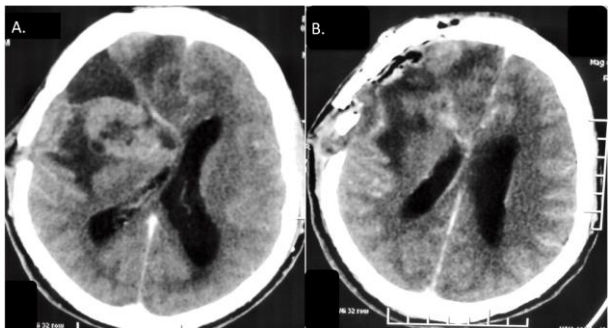

Figure 3. 'A' is the preoperative MRI of a large recurrent glioma grade III. 'B' shows the postoperative scan of the patient. The dura was opened in a staged manner with the tumor resection to tackle the bulging. The mass could be excised subtotal due to its invasion into the surrounding eloquent region.

Blood loss and duration of surgery

Average blood loss was 146.66 ± 57.37 ml. Although

no direct objective comparison was made with the cases done under GA, the blood loss was found subjectively equal to them. The mean duration of surgery was 131.33 ± 61.86 min, and similar was observation for it.

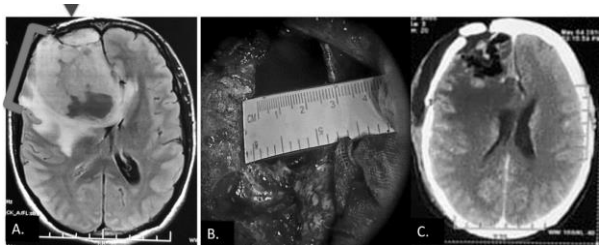

Figure 4. A Shows the preoperative scan of the patient with a large mass. It shows the prior site of craniotomy (I) and a newer approach (II). B shows a 3 cm size width dural opening. C shows the postoperative scan of the patient with a newer mini-craniotomy site visible and total resection of the mass.

Intraoperative vitals

Mean blood pressure fell by 12.66 ± 4.16 mm Hg, and the mean pulse fell by 13.06 ± 5.79/min after the bolus dose of Dexmedetomidine.

Pain score

Postoperatively, patients were asked to rate their maximum level of pain on a score of 1-10 (1-minimum, 10-maximum as possible). The pain score for all the patients ranged from 2-3, with the mean score being 2.6 ± 0.63.

Postoperative hospital stay

All patients could be discharged without any new neurological deficit with a mean hospital stay of 7 ± 4.08 days ranging from 3-20 days.

Complications

There was one event of intraoperative focal facio-brachial seizure, which possibly occurred due to the high value of bipolar coagulation. It was managed with pouring cold saline over the brain and giving 1.5mg Midazolam intravenously. On reducing the value of bipolar coagulation, there was no other seizure. One case (recurrent GBM) developed a cerebrospinal fluid leak, which was controlled with the resuturing of the wound. Another patient (recurrent glioma - grade III) developed a wound site infection, which required prolonged antibiotics. We believe both the latter complications should not be attributed to the AC since they were recurrent cases and can happen with craniotomies under GA also. There was one case of speech slurring (recovered in 6 weeks) and one case of shoulder weakness (recovered in 2 weeks). Neuromonitoring in the speech slurring case was not done, while in the shoulder weakness case didn't show the localization of the shoulder area. There was no procedure-related permanent morbidity or mortality. No case of any pressure-related injury or cautery burns etc. happened.

Follow-up

One patient of metastasis (Case 1- metastasis from melanoma) succumbed to his illness one month later. Another patient - Tuberculoma with TBM (case 3), also died one month later due to basal infarcts. Rest patients were neurologically intact, having a follow-up of 3-6 months.

Discussion

AC has been done for a long time.6,7 However, the safety and efficacy of small craniotomies in edematous brain lesions have not been described before. Traditionally, for AC, a large bone flap has been recommended to avoid brain compression at the edges.4 The present set of technology with the newer concept of keyhole surgery allows us to explore in this direction.10,11 This study is probably the first one in the literature to report the safety and feasibility of focussed AC for large or edematous brain lesions.

We found that small craniotomies were beneficial in large or edematous lesions, contrary to the previous observation.4 The reasons may be the usage of principles of keyhole surgery. We found three things to be required for awake focussed craniotomies.

1. Patient selection: All patients were adults and cooperative, as is required for all awake surgeries.
2. Proper positioning: Patients were positioned to make the operative site highest and trajectory perpendicular to the ground. This made the surrounding brain to fall apart and pushed the tumor out towards us. We used a Mayfield head clamp to make these positions. It also inhibited any untoward movement of the patient.
3. Small craniotomy: This avoided the compression of the surrounding brain and veins between

tumor and dural edges. Points 2 & 3 are explained in Figure 5.

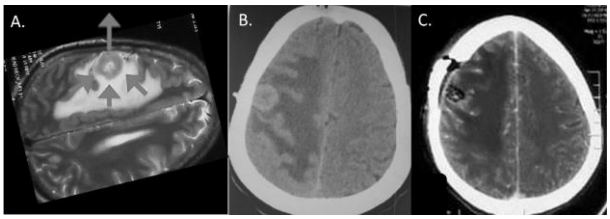

Figure 5. Shows the technique through which small craniotomy works. 'A' is the preoperative MRI of the patient showing a small metastasis with significant perilesional edema. If proper positioning is made with the tumor at the highest position, the edematous forces (red arrows) will aid in forcing it out. Since the site of the craniotomy is near to the tumor, no brain tissue/veins get compressed between the edges of the tumor and dura. 'B' shows the marker CT depicting a radio-opaque marker at the site of the mass. 'C' shows the postoperative scan with a small craniotomy. Note the surrounding cortex expands and takes space of the tumor.

The face was always accessible to the anesthetist that provided the ability to use non-invasive ventilation or laryngeal mask airway ventilation if the need arise, although we didn't need them in any of the cases. The duration of the action of Bupivacaine is 4-8 hours and this allowed us to perform the surgery with minimal pain. Dexmedetomidine decreased the blood pressure and pulse rates mildly but these were always under control. This drug also has an analgesic effect which allowed the procedure to be performed for the convexity meningioma and parafalcine mass (cases 6 and 8).

The cases in our series were heterogeneous with tumor size ranging from 5.4 cc3 to 44.5 cc3, and edema volume ranging from 20.40 cc3 to 110 cc3. This showed that the procedure was safe in cases with high intracranial pressure, in lesions of various etiologies, and with a variable amount of tumor size and edema.

The GA helps in decreasing the intracranial pressure (ICP) by deep sedation. However, during its reversal, it also makes the patient susceptible to a sudden rise in ICP, BP, pulse rate, etc. which can create postoperative complications like hematomas. We believe that awake surgeries are more physiological than the surgeries done under GA. The level of sedation, heart rate, BP, ICP, etc. are close to the baseline in the awake state, while all of these vary a lot in the GA state. Although there were cases of operative site hematoma in Taylor et al. series,13 we found none in our series. We believe that after tumor removal, the stoppage of Dexmedetomidine leading to the restoration of BP and asking the patient to cough helped in confirmation of hemostasis, which carried to the postoperative state.

The average blood loss and operative duration were similar to the personal experience of the surgeon. A direct objective comparison was not possible with surgeries done under GA due to the variability of the diagnosis and vascularity of the tumors operated. There was no procedure-related complication apart from one intraoperative seizure, which was easily controlled with cold saline and Midazolam.

The costs of the procedures done under awake conditions are less due to the lack of need of anesthesia gases, endotracheal tube, and postoperative ICU stay. The cost of Dexmedetomidine with Midazolam is very less compared to the anesthesia gases and ventilatory support. These factors play a very important role in resource-limited settings.

Limitations of our study include small sample size and a single team's experience, which may create bias. A multicenter randomized controlled trial between craniotomies under awake and GA conditions will be better to show its superiority/inferiority for the rates of the degree of surgical resection, duration, blood loss, and brain bulge. The intraoperative seizure is a critical limitation of AC, but these can be managed as mentioned. All tumors were located near the surface in our series, and safety and efficacy in deeper lesions need to be established. However, despite these limitations, this study shows the safety and feasibility of awake focussed craniotomies in large or edematous brain lesions.

Conclusion

Awake focussed craniotomy was found safe and effective for large or edematous brain lesions in appropriately selected patients.

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Essentials of cerebral fat embolism syndrome. A hidden enemy in trauma

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ABSTRACT

Fat embolism syndrome typically appears after an asymptomatic period of 24 to 72 hours and is typically manifested by the clinical triad of respiratory failure, neurological manifestations and petechiae, together with analytical alterations such as anaemia and thrombopenia. Respiratory distress is the most common symptom. Cerebral fat embolism is an incomplete form of fat embolism, which does not meet all the diagnostic criteria; in fact, it may appear without the presence of respiratory failure; Therefore, its early diagnosis is a challenge in the trauma patient.

Introduction

Fat embolism syndrome occurs when fat enters the circulation and may embolize and may or may not present clinical manifestations [1,2]. It is a potentially serious complication of fractures, with a reported incidence of 0.5 to 3.5% in isolated fractures of the long bones and 5 to 10% in patients with polytrauma. [3,4] The mortality rate is 5 to 15% [5]. Due to its association with polytrauma, it is much more frequent in the third and fourth decade of life [5,6]. It has also been associated, but to a lesser extent, with non-traumatic conditions such as orthopedic procedures, bone marrow transplants, extensive burns, closed-chest cardiac massage, acute pancreatitis, liposuction, parenteral lipid infusion, fatty liver, diabetes mellitus, osteomyelitis, rupture of a Tarlov's cyst, and other non-traumatic conditions [5,7,8], or even more rarely, a case was reported after chest surgery in a patient with empyema [9]. This complication can target the vascularization of the brain and generate severe ischemic accidents. Considering the potential of this pathological condition to negatively impact the integrity of the central nervous system, and that it is little known by medical students and primary care physicians, the aim of this review is to present basic concepts about its pathophysiological mechanism, important aspects for its early detection and approach.

Pathophysiological mechanisms of cerebral fat embolism

Cerebral fat embolism is caused by lipid droplets that travel through the bloodstream, subsequently blocking small vessels, especially at bifurcations [1,3,10]. This occurs in patients with long bone fractures, so it implies that there is bone trauma with exposure of the medullary fat, and that fat emboli subsequently enter the venous system [3,6,11,12,13]. They all travel into the pulmonary circulation and in the presence of right-to-left shunts pass into the systemic circulation [14]. There are several hypotheses that attempt to explain the pathophysiological mechanism of this disease.

Mechanical theory

Approximately 100 years ago, specifically in 1924, an author by the name of Gauss posited that bone marrow adipose cells could access venous sinusoids due to increased intramedullary pressure following trauma [1]. These adipose cells have proinflammatory and prothrombotic attributes [15]. As the venous system travels back toward the heart, they precipitate platelet adhesion and increased fibrin production, forming an embolus and increasing the risk of embolizing the pulmonary arterial circulation when the vessels form capillaries [16]. Capillary obstruction triggers interstitial bleeding, edema, alveolar collapse and reactive vasoconstriction. Massive fat emboli can also cause macrovascular obstruction and shock. Even in special cases such as in the permanence of a patent foramen ovale, fat cells can enter the arterial circulation [17].

Biochemical theory

Another hypothesis put forward is biochemical. This supports the fact that the clinical manifestations of fat embolism are caused by a proinflammatory state [1]. Bone marrow adipose cells are broken down by tissue lipases to form glycerol and toxic free fatty acids, which cause injury to pneumocytes and pulmonary endothelium, triggering a cascade of proinflammatory cytokines that lead to respiratory failure [18-20]. This theory helps to explain the cases of non-traumatic fat embolism. Experiments in animal models support this hypothesis [1].

However, these results are derived from general concepts. The toxic properties of free fatty acids were demonstrated around 1950 [1]. Since then, fatty acid infusions have been used in animal models to induce embolism-like changes in the circulation and lung. An example of this is the use of triolein to induce fat embolism syndrome and investigate a "second hit" phenomenon in rat models. Lung damage after injection of another toxin has been found to be worse in rats that had a history of this clinically resolved triolein-induced syndrome than in rats that were exposed to the toxin alone [1].

However, it would be interesting to continue with this type of research to determine the precise degree of severity of pulmonary involvement and, specifically, of brain damage.

Clinical presentation

As previously mentioned, clinical manifestations are usually delayed from 24 to 72 h, and some authors speak of an onset from 12 to 72 hours [21,22]. However, only one case of hyperacute CGD has been reported, whose clinical signs appeared 2 hours after an automobile accident, where the patient reported

fractures of the right femur, tibia and fibula, in addition to non-specific symptoms during the first hours, the subsequent development of the symptoms was of bad prognosis for the patient, with almost no improvement after a few days [23,24].

Typical symptoms of fat embolism syndrome include respiratory failure, cerebral dysfunction and petechial rash. Respiratory manifestations appear in almost 100% of patients, neurological symptoms are usually transient appearing in 80% and petechial exanthema in 20 to 50% of cases and is the most specific, but the most delayed sign [25,26].

Clinically, the syndrome can be variable from headache to diffuse encephalopathy, lethargy, convulsion, coma, pyramidal symptoms, aphasia, visual and auditory hallucinations, sexual hallucinations, aggressive behavior and pupillary paresis [2,27]. Other manifestations described are renal failure, myocardial depression, jaundice and fever. Patients with pure cerebral fat embolism have no respiratory symptoms and a history of cranioencephalic trauma [2,28].

Diagnostic approach

The clinical evolution of the patient must be considered, i.e., that he/she presents respiratory and neurological alterations and, in some cases, cutaneous petechiae after a fracture of long bones, orthopedic surgeries, or due to non-traumatic causes such as sickle cell anemia, which produces infarcts in the bone tissue. On the other hand, the use of imaging is one of the best methods to confirm the diagnosis, and thus exclude other clinical impressions such as diffuse axonal injury [1,2,29,30].

Magnetic resonance imaging (MRI) is considered the method of choice for diagnosis, because it is able to capture the lesions that occur in the brain. MRI can commonly show a characteristic pattern of microemboli in the gray and white matter or cytotoxic edema, evidencing "lesions" by dots in the gray matter that form an image similar to a star field in T2 and DWI [1,2]. This pattern is true in most cases, varying in time the number of lesions that may appear, i.e., an MRI performed during the first hours of neurological dysfunction may or may not show lesions in white matter, but a star field pattern may be present. Another pattern found in DWI and T2 sequences, and whose significance is associated with a worse prognosis, corresponds to confluent bilateral periventricular and subcortical cytotoxic edema. Finally, T2/FLAIR sequences may show areas of hyperintensity probably associated with vasogenic edema [1,2,31].

Therapeutic approach

Treatment is essentially coadjuvant; when one of these cases occurs, it is common to use heparin, dextran, aspirin, albumin and steroids, which are ineffective in treating the disease. Currently, case reports have opted to include statins in their list, due to their anti-inflammatory mechanism rather than their cholesterol-lowering action; where the use of high doses of the drug had a result considered satisfactory, improving neurological functions. However, there is a lack of studies to support it [1,2].

In the case of patients with cerebral embolism, care of neurological manifestations and complications focuses on frequent neurological observation. These patients may develop cerebral edema which, although manageable, increases the risk of morbidity, mortality and disability [29-31]. Continuous monitoring of intracranial pressure should be performed in these cases. Although clinical diagnosis is still considered the preferred diagnostic method for this syndrome, studies have shown that MRI is useful, in cases where there is no head trauma, to assess the severity of cerebral fat embolism and to predict the functional prognosis. In general, sedation and neuromuscular blockade for trauma patients should be titrated so as to keep the patient comfortable, without affecting their serial neurological examinations and, in addition, allowing them to tolerate mechanical ventilation [1,2,29,31].

Prognosis

Usually, almost 80% of patients experience spontaneous resolution of symptoms, however, 3% to 8% die. It has been described that the prognosis could be associated to the promptness with which the symptoms appear, suggesting that when presenting in less than 12 hours, the morbimortality is higher [1-6].

Conclusions

Cerebral fat embolism or fat embolism syndrome is a disorder characterized by the appearance of respiratory, neurological and cutaneous dysfunction symptoms (petechiae) frequently found in people who have suffered long bone and pelvic fractures. This pathology requires an adequate diagnosis and

treatment, in order to reduce the morbimortality associated with it, even though there is no treatment oriented to the cause of it. For the time being, few changes have been described in the literature for this disorder, however, small trials are beginning to make inroads in terms of therapies that may be considered effective in the future.

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Spinal conditions in geriatric patients in developing countries. A four years institutional experience

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ABSTRACT

Background: The spinal injury in an elderly patient is associated with higher mortality and an increased frequency of life-threatening complications and specifically spinal cord injuries. The aim of this study is to study the prevalence of geriatric spinal neurosurgical conditions in the Neurosurgical Department at Khoula Hospital, Muscat, Sultanate of Oman.

Results: 171 patients were admitted due to spinal pathologies, which will be the main focus of the present study with an average age of 70.7 years. The male-to-female ratio was (1.5:1). Degenerative conditions were the most common spinal diagnosis (90.6%) followed by traumatic accidents (2.9%). Most of the patients underwent surgical intervention (78.9%). The majority of the patients (91.2%) of the patients stayed in the hospital for less than 15 days. There was a significant difference between the age of patients above and below 75 years the gender (p=0.003) and between the length of stay and type of intervention (P<0.005).

Conclusion: Spinal cord-related pathologies are a growing cause of mortality and morbidity worldwide, because of the increasing number of elderly people due to an increasingly rising life span worldwide. In the present study, degenerative conditions were the most common spinal diagnosis followed by traumatic accidents.

Keywords
spinal causes,
geriatric,
elderly,
neurological deficits

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INTRODUCTION

Over the past years, the evolution of new medical equipment and enhancing of technology and neuroanesthesia and ICU, have expanded the daily neurosurgical practise. (1). The aging population in western civilization places an increase demand on health system in terms of number and special needs. (1). The elderly population is defined as adults aging 65 years or older. (2). Within Europe, people aged 80 years and older is projected to double from 5% to 9% in 2040. (3). With the increase age, the presence of comorbid conditions probability increase makes the need for specific measures necessarily. (4). Elderly population are not exempt from neurosurgical practise. (5). On the other hand, with this population increase, neurosurgeon workload will

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involve these patients in greater portions. (5). Moreover, an injury in an elderly patient is associated with a higher mortality and an increased frequency of life-threatening complications and specifically spinal cord injuries. (6). As the incidence of traumatic spinal cord injury in elderly rises, neurosurgeons are increasingly faced with difficult discussions regarding management. (7. The most common mechanism of traumatic spinal cord injuries are falls and they occur frequently due to age-related deteriorations.

Traumatic spinal cord is associated with greater morbidity in elderly (7). A previous study done by Al-Saadi et al investigating the prevalence of low back pain (LBP) among Sultan Qaboos university staff in Sultanate of Oman showed that the prevalence of LBP among them was 44.7% among the included cohort, in which majority (68%) of them were suffering from the pain for more than one year. Among those who had LBP for more than one year, 73.5% were less than 50 years old (8). Carpal tunnel syndrome one the most comments neuropathies with a peak age of 50-54 and second peak 75-84. (2)

The aim of this study is to retrospectively analyse the prevalence of peripheral nerve and spinal cord injuries in Sultanate of Oman. The traumatic spinal injuries service is shared between the neurosurgery department and the ortho-spine department. The current article dealt only with cases admitted under neurosurgery department. The health care services in Oman is considered as having one of the best health care systems in the world according to World Health Organization reports (9,10). The Department of Neurosurgery in KH is the main neurosurgical center in the country with average admissions of 1600 patients annually (11,12). In the present study, we chose a cut of age of 65 years and older according to the local definition, taking into account the increase in life span throughout the last few decades and the improvement in the quality of life that results from many changes in all social and health care sectors in the country.

Methods

Study group

This is a retrospective study conducted at Khoula Hospital located in Muscat, Sultanate of Oman. The study was approved by the Research Ethical Committee at Khoula Hospital/ Ministry of health (PRO122020072). Medical records of 171 patients who are above the age of 65 and admitted to the neurosurgical ward and diagnosed with spinal and peripheral nerve conditions, from the period of January 2016 to 31st December 2019 were included. The study includes both Omani and non-Omani patients. Patients with the following features are excluded:

- Non elderly patient (below 65 years).
- Non neurosurgical conditions and neurosurgical conditions other than spinal and peripheral nerve diseases.
- Elderly with spinal conditions admitted under orthospine department.
- Outside the study period (from 1st January 2016 to 31th December 2019).
- Patients with missing or incomplete data.
- Data collection:

Data was obtained from the health information system included: patient demographics (age, gender), presenting symptom, previous surgical history, preoperative and postoperative Glasgow coma scale (GCS), radiological findings, indication for surgery, diagnosis, length of hospital stay (LOS), length of ICU admission and treatment proposed. Then the information classified into continues and categorized variables and analyzed accordingly.

Data analysis

Research database was analyzed and processed using the statistical package for the social sciences (SPSS) software (version23). The categorized variables were cross-tabulated using frequency tables and pie charts or bar charts. Chi-square test was used to obtain the significance of the association between categorized variables, using a P value of ≤ 0.05 as the cut-off for significance. The numerical variables were summarized by their medians, means, and ranges, and the categorical variables were described by their counts and relative frequencies. All the p values were 2-sided, and a p value < 0.05 was considered to be significant in all the analyses.

Results

Table 1 showing demographic characteristics of the included cases in the present study. We have total of 669 patients admitted in neurosurgical department at Khoula hospital in Muscat the capital city of Sultanate of Oman in four years' period (from 2016 to 2019). Out of those 669 patients, 171 patients

were admitted due to spinal and peripheral nerve pathologies, which will be the main focus of the present study. Fifty-four and four tenths % of the study cohort were more than 75-year-old. Male to female ratio was (1.5:1). Degenerative conditions were the most common spinal diagnosis (90.6%) followed by traumatic accidents (2.9%). Most of the patients underwent surgical intervention (78.9%). Majority of the patients (91.2%) stayed in the hospital less than 15 days.

Table 1. Demographic characteristics of the patients

Category	Number of patients (%)
Number of patients admitted each year	
2019	202 (30.0%)
2018	172 (25.7%)
2017	154 (23%)
2016	141 (21.3%)
Total number of admitted neurosurgical cases (2016-2019)	669
Total number of spine cases	171
Age	
≥75	93 (54.4%)
< 75	78 (45.6%)
Gender	
Female	69(40.4%)
Male	102(59.6%)
Spinal diagnosis	
Degenerative conditions	155 (90.6%)
Traumatic	5(2.9%)
Infection	4 (2.3%)
Peripheral nerve disease	7(4.1%)
Type of interventions	
Surgical	135 (78.9%)
Conservative	36(21.1%)
Length of stay (LOS)	
≤ 15 days	156 (91.2%)
>15 days	15 (8.8%)

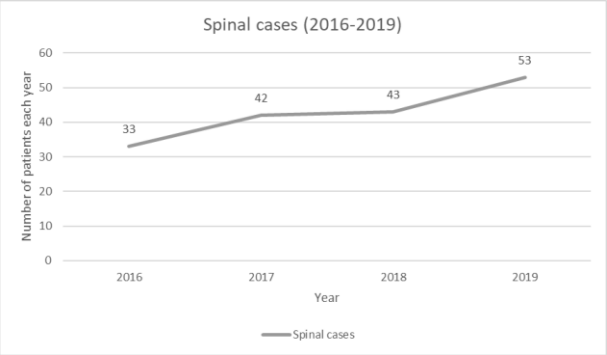

Figure 1. Total number of admitted patients with spinal cases in each year

Figure 1 represents the total number of admitted patients with spinal diagnosis in each year. As seen in the graph, spinal cases were continuously raising among the study years with the highest number of cases in 2019 (n=53, 31.0%).

Table 2 showing the association between the age of the patients with spinal pathologies and the gender. It demonstrates that there was significant difference between age of patients above and below 75 years the gender, in which male patients were more commonly found to belong into the older age group (p=0.003).

Table 2. The association between the age of the patients and other variables (gender and GCS)

		Gender	
		Male	**Female**
AGE	less than 75	46	47
	more than 75	56	22
P-value		0.003	

Table 3. The association between the LOS (length of stay) of the patients and other variables (age and type of intervention)

Length of stay (LOS)	**Age**		**Type of intervention**	
	< 75years	≥ 75 years	Surgical	Conserv -ative
less than or equal to 15 days	86	70	129	27
more than 15 days	7	8	6	9
P-value	0.530		0.005	

The association between the LOS of the patients and other variables (age and type of intervention) is shown in table-3. There was no significant relationship between the age of the patients (more and less than 75 years) and LOS (15 days as a cut off value), (p=0.530). Also it represents that there was a significant difference between LOS and type of intervention (surgical vs conservative), (P<0.005).

Discussion

Increasing life expectancy, along with rising health care related expectations is producing an important workload across all medical fields, considering that most medical diseases increase in frequency with age, more elderly will require neurosurgical care including the spinal cord related diseases. Additionally, with the advances in diagnostic and surgical techniques spinal neurosurgical diseases have led more patients to be treated in a better quality and quantity which explains the continuously raising neurosurgical cases generally and spinal cases specifically among the present study years (1,2). One hundred seventy-one patients were admitted due to spinal pathologies, which will be the main focus of the present study. 54.4% of the study cohort were more than 75-year-old (range 65-68). Another study done by A Gulati et al showed a mean age of 73 years (range 65-88). Male to female ratio was (1.5:1). Inglis et al. conducted a study that showed was in the same line of our study in which 61% of the cases were males. This can be explained by the fact that males are more predisposed to injuries in their daily life activities, as well as the fact that Omani count population states that the male to female ratio in Oman is 180.8 males per 100 females (6,13).

Degenerative conditions were the most common spinal diagnosis followed by traumatic accidents in our study. Correspondingly, Chibbaro et al conducted a study that demonstrate that degenerative spinal diseases were one of the most common procedures performed in along with cranial procedures for tumour resection, and burr hole for chronic subdural hematoma among elderly patients over the two separate time periods (1983-1985 and 2003-2005) which shows the high incidence of those group of diseases. For traumatic spine injuries, it was reported that most of the injuries were due to falls from less than standing height, which may emphasize the age-related reduced capability of the spine to withstand the mechanical stress as only 13% of traumatic injuries occurs due to violent acts and automobile accidents as reported by DeVivo et al (14,15). Carpal tunnel syndrome (CTS) was also reported as it is the most common entrapment neuropathy worldwide and in the present study (2). The few previous studies in the prevalence of peripheral nerve diseases among elderly suggested a bimodal age distribution with a peak between ages 50–54 years, and a second peak between 75–84 years, which is the reason why it's important to take such group of diseases in consideration among geriatric age group (2).

In the current study, most of the patients underwent surgical intervention (78.9%). In contrast, another study shows that 77% of patients were treated conservatively, specifically in traumatic spine injuries (6). Treatment decision making in elderly patients in more arguable than younger age, as they are less likely to withstand the physiological and pathological insult of surgery and more likely to develop post-operative complications, additionally, they often have spine instability requiring extensive surgery with a poor neurological prognosis, and consequences of healthcare issues associated with living with more significant neurological deficit (7)

We found that, 91.2% of the patients stayed in the hospital less than 15 days. In accordance to our study, Chibbaro et al reported a period of stay between 6-8 days, In the other hand, the median hospital stay for patients was 136 days in a study done by A Gulati et al. Those variations are due to the differences in the type of injury, type of intervention, the pre-existing medical conditions and other related factors (1,6). The lack of a long-term rehabilitation center in the country might be another contributing factor to this. As patients should be cleared for discharge home when the safety of the mobility is guaranteed.

The present study also demonstrates that there is significant difference between age of patients above and below 75 years the gender, in which male patients were more commonly found to belong into the older age group. This can due to the fact that increased life expectancy in developing countries in the last few decades, due to better medical scrutiny of the elderly, better knowledge and practice by neurosurgeons and all other associated physicians and surgeons in the elderly patient's management, which improves the patient's ability to practice their

daily life and predispose them to more spinal related injuries and their consequences. (2)

The current study found that there was no significant relationship between the age of the patients and LOS. Also it represents that there is a significant difference between LOS and type of intervention (surgical vs. conservative), (P<0.005). Osteoporosis and other typical spinal problems of advanced age, multiple comorbidities, and the lessened physical performance that goes along with age are accompanied by markedly heightened expectations on the part of our older patients. Thus, the value of different treatment strategies needs to be rationally assessed due the risk of prolonged stay in the hospital (increased LOS) (3). Surgical decision making for this age group is a multifactorial process so its advocated that chronologic age must be evaluated in the light of patient's clinical status to define eligibility for surgery (16,17).

Limitations

There were several limiting factors in the present study. It was a retrospective, single-centered study over a period of four-years. Thus, a number of confounding factors found, for example, the degree of advancement in modern medical technology and the availability of modern diagnostic facilities. Cases admitted under the orthopedic department were not included which might present a large number of patients. The follow-up was not included in the data of the present study. Additionally, the oncological causes of spinal related disorders were not mentioned and discussed in the present paper, as they will be discussed in a separate paper along with all other neurosurgical tumors.

Conclusion

Spinal cord related pathologies are growing cause of mortality and morbidity worldwide, because of the increasing number of elderly people due to an increasingly rising life span worldwide. In the present study, degenerative conditions were the most common spinal diagnosis followed by traumatic accidents. Special care must be taken when dealing spinal cases due its potentially high morbid outcomes, especially among geriatric age group due to the age-related reduced capability of the spine to withstand the mechanical stress.

Abbreviations

Length of hospital stay (LOS)
Carpal tunnel syndrome (CTS)

Availability of data

From medical records of patients from the "Al-Shifa Health Information System" of Ministry of Health in Sultanate of Oman used in Khoula hospital.

Authors contributions

AM and OT: Report writing, data collection and analysis
TS: Research design, analysis and review.
All authors have read and approved the manuscript.

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Fibrous dysplasia of sphenoid bone presenting as a case of loss of vision

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ABSTRACT

Background: Fibrous dysplasia is a fibro-osseous lesion of unclear aetiology wherein normal bone is replaced by abnormal fibrous tissue and immature bone. Fibrous dysplasia is associated with a defect in osteoblastic differentiation and maturation that originates in the mesenchymal precursor of the bone & is well documented to affect craniofacial structures.

Case description: A case of the lesser sphenoid wing fibrous dysplasia is described which presented with symptoms of pressure effects on the optic nerve, managed subsequently with microsurgical decompression of the nerve.

Conclusion: Craniofacial fibrous dysplasia is an uncommon entity which can present with loss of vision, wherein the visual prognosis depends upon timed & adequate surgical intervention.

Keywords
fibrous dysplasia, sphenoid wing, orbit

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INTRODUCTION

Fibrous dysplasia is associated with a defect in osteoblastic differentiation and maturation where normal medullary bone is replaced with a variable amount of abnormal and structurally weak fibrous and osseous tissue. It is of particular interest to neuro-ophthalmologist as it can affect craniofacial bones wherein encroachment on the paranasal sinuses, orbit, and foramina of the skull can produce variety of ophthalmological symptoms. Here in a case is described of fibrous dysplasia of lesser sphenoid wing presenting with optic nerve compression & visual loss.

CASE REPORT

A 45-year-old female housewife presented with holocranial headache for 1 year which was dull aching, moderate intensity, and gradually progressive, non-pulsatile, no specific aggravating factors, relieved on medication. There was no history of vomiting, seizures, trauma, aura and photophobia, facial pain & anosmia. She also complained of

blurring of vision followed by gradual progressive painless, visual deterioration in right eye for 2 months. There was no history of painful movements of eyeball, reddening/ congestion, diplopia, proptosis, epiphora/ glare. She didn't complain of tunnelling of vision & had no history suggestive of hormonal changes.

Examination revealed the visual acuity in right eye as 6/60 & left eye 6/12 unchanged with pinhole, pupillary response was normal in left eye whereas relative afferent pupillary defect was present in right eye. On perimetry, paracentral scotoma was observed on right side while left side was normal. Fundus examination, extraocular movements & conjunctiva were normal on both sides. On CT scan of brain, orbit & skull base, diffuse expansion of medullary cavity with ground glass bone matrix with no contrast enhancement & intact cortices was noted involving bilateral greater & lesser wing of sphenoid, bilateral anterior clinoid processes & pterygoid plates with orbital wall & roof thickening on both sides causing narrowing of bilateral optic canals (right more than left) (Fig.1). Blood investigations were normal.

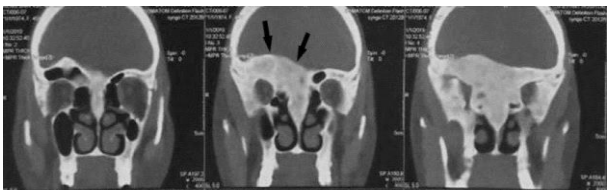


Figure 1.

Based on imaging findings, a provisional diagnosis of fibrous dysplasia was made. Right frontal craniotomy was performed and optic nerve decompression was achieved by drilling of right anterior clinoid process and orbital roof. Intra-operatively right sphenoid wing , frontal bone, anterior clinoid process and orbital roof was found to be thickened and bone was spongy and vascular while the optic nerve seemed to be compressed in optic canal, with thinning of intracanalicular portion. Optic nerve decompression was done till orbital apex (Fig 2a &2b).

Histopathological examination revealed irregular trabeculae of woven bone within fibrous tissue which lacked osteoblastic rimming suggestive of fibrous dysplasia. Post operative CT scan showed significant drilled out bony portion at right orbital roof thus demonstrating decompression of the optic nerve as compared to preoperative scans (Fig 3 & 4). Visual acuity in right eye as assessed at the end of 1 month & 2 months of follow up period was 6/36 & 6/24 respectively, hence showing betterment; along with improvement in headache.

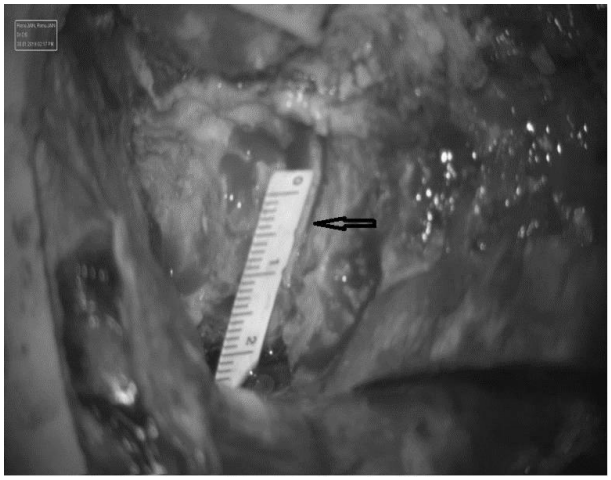
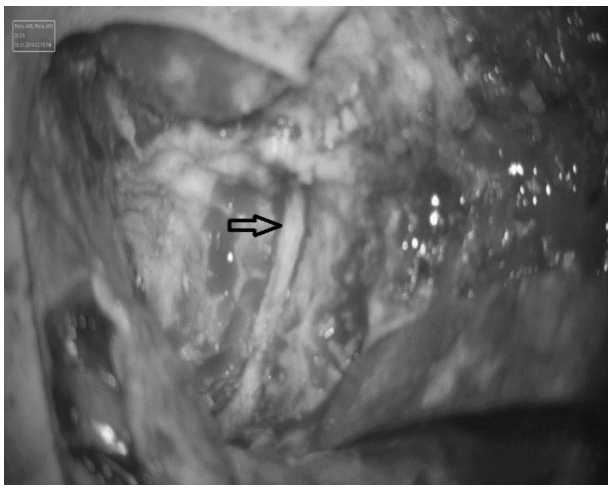


Figure 2a.



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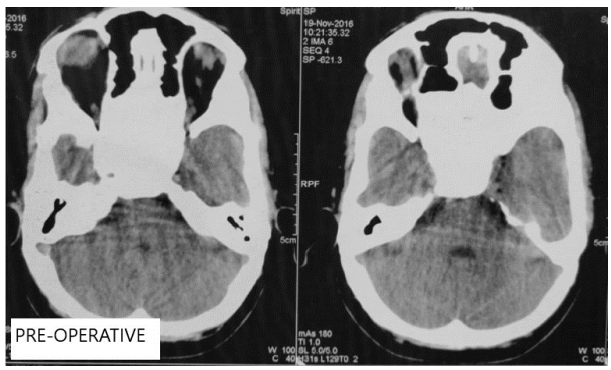

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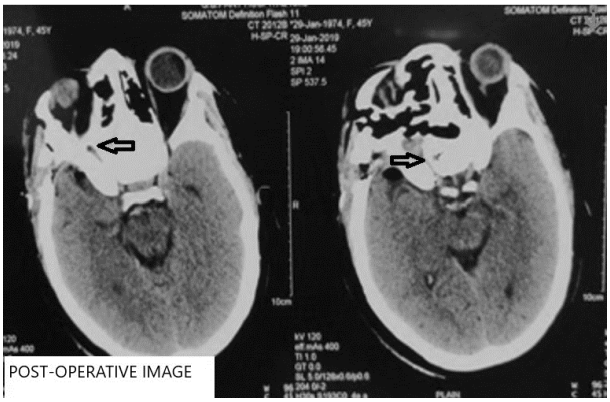

Figure 4.

Discussion

Fibrous dysplasia was first recognized by von Recklinghausen in 1891 and further characterized and named by Lichtenstein in 1938. It is one of the most common benign skeletal disorders and can affect any bone in the body [2]. It is most common in adolescents and young adults, and progression decreases after puberty [2]. There are three types of fibrous dysplasia: monostotic (the most common, accounting for 70% of cases), polyostotic, and McCune-Albright syndrome. McCune-Albright syndrome is characterized by polyostotic fibrous dysplasia, endocrine hyperfunction (which can lead to precocious puberty in female patients), café au lait pigmentation of the skin, and other extraskeletal abnormalities [1].

Fibrous dysplasia has a predilection for the skull base; particularly the ethmoid (most common) followed by sphenoid, frontal, maxilla bones & orbits [5]. Consequently, patients with fibrous dysplasia may exhibit local cosmetic deformity (the most common manifestation), headaches, proptosis, impaired ocular movement, and loss of visual acuity [2].

Based on radiographic features, fibrous dysplasia is classified into 3 types, the pagetoid, or "ground-glass," pattern is the most common (56% of all cases); it appears as a mixture of dense and radiolucent areas of fibrosis. The sclerotic pattern (23% of cases) is uniformly dense. The cystic pattern (21%) is characterized by an spherical or ovoid lucidity surrounded by a dense bony shell.[3]

Involvement of the orbit leading to visual loss is the most feared complication, and surgical decompression may be warranted in acutely or progressively symptomatic patients (or in both) [1,2]. Radiotherapy and chemotherapy have no role in the treatment of fibrous dysplasia, and the former may increase the risk for malignant degeneration (most commonly osteosarcoma) [3,4].

Fibrous dysplasia may be complicated by aneurysmal bone cyst formation [1]. Malignant degeneration occurs in 4% of cases of fibrous dysplasia and is more common with the monostotic type. The interval between the diagnosis of fibrous dysplasia and evidence of sarcomatous degeneration is long, with a mean of 15 years. Close imaging follow-up with serial CT and MRI is essential in patients with known fibrous dysplasia. Worsening pain, development of a soft tissue mass, or elevation of alkaline phosphatase levels should raise concern for malignant degeneration [2].

Conclusion

Fibrous dysplasia of the sphenoid bone, although not a common entity, can present with symptoms of visual loss. Timely intervention & adequate microsurgical decompression of the optic nerve results in good postoperative visual outcome and is of prognostic significance.

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The impact of lockdown on incidence of neurosurgery trauma patients in India

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Abstract

Objective: Covid19 pandemic challenged the global healthcare system and both developed and developing countries responded with their might to fight this global pandemic. Road traffic accidents are a major cause of morbidity and mortality in India and we studied the impact of lockdown on neurosurgery trauma patients in a tertiary care centre in India.

Methods: Indian government announced complete lockdown on 25th march 2020 and India remained in complete lockdown till 31st May 2020. We included the patients admitted from 1st January 2020 to 24th March 2020 in pre lockdown period and25th march to In this cross-sectional study we divided the patients into two groups of pre lockdown and lockdown period and incidence of neurosurgery trauma patients was assessed for Road Traffic Accident, assault, hit by animal and fall from height.

Result: In our study 491 patients were admitted in pre lockdown and 369 patients were admitted in lockdown period. Road traffic accident patients were more in pre lockdown 39.5% (n=194) as compared to lockdown period 31.2% (n=115). However, cases of assaults were more in the lockdown period (14.6%, n=54) as compared to pre lockdown (3.9%, n=19). The death rate in neurosurgery trauma patients reduced significantly in lockdown (7.3%, n=27) as compared to pre lockdown (21.8%, n=107).

Conclusion: The COVID19 pandemic induced lockdown resulted in a decrease in motor vehicle movements which further decreased the incidence of RTA and related trauma however incidence of assault-related trauma and cases increased significantly in this period. The overall outcome of such patients improved probably due to better utilization of available health care facilities.

Keywords
assault,
India,
lockdown,
road traffic accidents,
trauma

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Introduction

The first reports of Covid19 disease started to appear from various parts of China and it gradually spread in European nations first and then USA while in India initial cases were reported in January 2020.1 Indian government on first announced a public participation lockdown and on 24th March, 2020 ordered an unprecedented nationwide lockdown for 21 days and subsequently extended till 31st May 2020.2 This absolutely indispensable and globally appreciated rigorous lockdown froze the world's largest democracy. This lockdown made everything to stand still in a country of second largest population and

caused significant decrease in motor vehicular activities.3 This resulted in subsequent decrease in the cases of neurosurgery trauma patients. Although India has only 1% of the motor vehicles of the world yet nearly 37000 persons died in 2019.4 Impact of lockdown on cases of road side accidents and assault cases, their prevalence and the effective healthcare provided to the victims is not assessed properly in world medical literature. We tried to study the impact of lockdown on number of cases and efficacy of treatment provided to the patients admitted in India in our study.

Aims and objectives

To study the impact of lockdown on trauma cases in a hospital in India.

To study the quality of health care in terms of operations and survival of the trauma patients during Covid19 pandemic and difference in level of care during and without lockdown.

Materials and methods

This was a retrospective cross-sectional study done in our hospital which is the biggest tertiary referral centre of India. All patients who presented with history of trauma during the lockdown between 26th march 2020 to 31st may 2020 were compared with a comparative period of 67 days between 19th January 2020 to 25th march 2020. We included all the patients who presented to our trauma centre. Our study was aimed to study the patients with a history of road traffic accidents (RTA), fall from height, domestic accidental injuries, injuries, sports-related injuries, assault injures, or injuries caused by animals. We collected data on trauma patients from our hospital's electronic database. The following data were collected on a standard data abstraction sheet: baseline characteristics, mode of injury, type of RTA, treatment given and hospital outcome.

Statistical analysis

We analyzed the data by using a statistical package for social sciences for Windows (SPSS Inc. released 2007, version 23.0. Armonk, NY, USA). Dichotomous variables were compared by using the chi-square test. The factors associated with the profile of trauma patients during these two study periods were determined by bivariate logistic regression analysis and their 95% confidence intervals (CI) calculated. A two-sided p-value of less than 0.05 was considered statistically significant.

Observations and results

In this study total 860 patients were enrolled based on inclusion and exclusion criteria. We found in this study that total 491 patients were admitted in pre lockdown and 369 in lockdown. These patients were classified into patients of RTA, assault, fall from height and others. The total number of patient admitted in lockdown was less as compared to pre lockdown period in our trauma centre. (Table 1)

Table 1. Total patients admitted in pre lockdown and lockdown period (April 2021)

Percent	Total number of patients admitted	Percent
Pre-lockdown	491	57.1
Lockdown	369	42.9
Total	860	100.0

This study suggested that more young patients were reported in our causality trauma centre indicating a more burden of accidental injuries during pre lockdown period as compared to lockdown period. In this study admission of male patients was more during pre lockdown period (n= 373, 76% in pre lockdown v/s n=276, 74.3% in lockdown) as compared to lockdown which suggested that road traffic accidental trauma in males during pre lockdown period. However admission of female patients was slightly more during lockdown period (n=93, 25.2%) as compared to pre lockdown (n=118, 24%). This suggested a rising trend of injuries amongst females during lockdown which we further investigated in our study. We found that more females were subjected to assault (n=54, 14.6% during lockdown v/s n=19, 3.9% in pre lockdown) during pre lockdown period and most cases were of domestic violence. Also in this study there was a slight increase in admission of children during lockdown period (n=26, 7%) as compared to pre lockdown period (n=26, 5.3%). (Table2)

Table 2. Mode of injury in patients admitted in lockdown and pre lockdown period

			Time period		Total
			Pre lockdown	Lockdown	
Mode of injury	Fall	Count	66	50	116
		% within Lockdown	13.4%	13.6%	13.5%
	Hit	Count	3	2	5

		% within Lockdown	0.6%	0.5%	0.6%
	RTA	Count	194	115	309
		% within Lockdown	39.5%	31.2%	35.9%
	Assault	Count	19	54	73
		% within Lockdown	3.9%	14.6%	8.5%
	Others	Count	209	148	357
		% within Lockdown	42.6%	40.1%	41.5%
Total		Count	491	369	860
		% within Lockdown	100.0%	100.0%	100.0%

In this study more patients were admitted with history of road traffic accidents (n=194, 39.5%) during pre lockdown period as compared to lockdown (n=115, 31.2%) suggesting a statistically significant fall in incidence of road traffic accidents in lockdown (p value <.05). However the admissions of patients with history of assault was more in lockdown period (n=54, 14.6%) as compared pre lockdown (n=19, 3.9%). There was a statistically significant increase in number of cases of assault in lockdown period reflected in our study. (Table3)

Table 3. Outcome of patients in lockdown versus pre lockdown period

			Lockdown		Total
			Pre	Post	
Outcome	Left against medical advise	Count	72	40	112
		% within Lockdown	14.7%	10.8%	13.0%
	Deaths	Count	107	27	134
		% within Lockdown	21.8%	7.3%	15.6%
	Abscond	Count	7	3	10
		% within Lockdown	1.4%	0.8%	1.2%
	Transferred to other departments	Count	40	33	73
		% within Lockdown	8.1%	8.9%	8.5%
	Discharges	Count	265	266	531
		% within Lockdown	54.0%	72.1%	61.7%
Total		Count	491	369	860
		% within Lockdown	100.0%	100.0%	100.0%

In this study the outcome of patients was improved in lockdown period with deaths due to trauma was more in pre lockdown period (n=107, 21.8%) as compared to lockdown period (n=27, 7.3%). Similarly discharges were more in lockdown period (n= 266, 72.1%) as compared to pre lockdown period (n=265, 54%).

Discussion

We worked on a hypothesis that lockdown will halt all the motor vehicular activities in the country and will cause significant decrease in cases of road traffic accidents and associated injuries.5 This was also projected in IJCMR by Nandkishore M Harne et al in 2020.6 As according to our hypothesis, this study also showed that patients admitted due to road traffic accidents were decreased by 8% during lockdown as compared to pre lockdown. This fall in number of road traffic cases was due to reduced vehicle activities and also due to reduced demand and supply ratio of essential commodities during lockdown period. This reduced economic activities and fall in motor vehicle accidents was also observed in other countries like UK.7

During the testing times of Covid19 disease this fall in cases of accidents was a breather in terms of burden on already stretched healthcare system. We found a slight increase in pediatric populations admitted with history of trauma in our hospital between the two periods during lockdown period (n=26, 7%) as compared to pre lockdown period (n=26, 5.3%) but not significant statistically. More likely the cause of this finding was children being more at home and hence more prone to injuries and domestic violence in lockdown period.8,9 In this study we found increased incidence of assault and accidental injuries amongst females during lock down period in our study which was suggesting of increased cases of domestic violence and related assault in this section of society.10Similar data was found in the studies published in Lancet journal suggesting increased incidence of rage and anger during the period of lockdown mainly due to economical constraints and psychological breakdowns. Increased incidence of assault has been reported in other parts of world too during lockdown.11 The pan-global lockdown has aptly been described as “the world's largest psychological experiment”.12 A review of multiple studies done on the effect of quarantine published by The Lancet shows that quarantine in the past has been associated with increased fear and anger among other emotions that may have perpetrated

assaults.13 In this study we found a statistically significant difference in outcome of patients admitted with history of trauma. This study suggested that lesser number of admissions during lockdown successfully helped to provide better healthcare to these patients.

Conclusion

This study concluded that during lockdown the number of trauma cases was decreased as compared to pre lockdown period. The cases of road traffic accidents were decreased in our hospital but the incidence of assault was increased during lockdown period. Incidence of assault in case of females increased and also there was increase in injuries in pediatrics age group during lockdown period.

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Indirect revascularization in an Iraqi child with Moyamoya Disease

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ABSTRACT

Background: Moyamoya disease (MMD) is a rare cerebrovascular disease characterized by bilateral stenosis starting at the supraclinoid internal carotid artery (ICA), with the development of a collateral network of vessels. It is an established cause of stroke in the pediatric age group. Despite its increasing prevalence in various parts of the world, it remains largely underrecognized in the Middle East, particularly in Iraq. This is the first case of MMD in an Iraqi patient undergoing surgery.

Case description: A 12-year-old boy presents with a 3-months history of progressive behavioural changes. MRI revealed diffuse infarcts of different ages. MRA and CT angiography revealed extensive asymmetrical steno-occlusive changes of the supraclinoid ICAs extending into the anterior and middle cerebral arteries, with the development of a collateral network in the basal ganglia. Indirect revascularization of the right side by encephaloduroarteriomyosynangiosis (EDAMS) was performed. The clinical status of the patient improved during the follow-up and the MRA showed a re-establishment of the blood flow to the MCA.

Conclusion: MMD should be recognized as a cause of stroke or recurrent TIAs in the Iraqi population, particularly in pediatric patients. EDAMS is an effective revascularization procedure with good results in pediatric patients.

Keywords
internal carotid artery, stenosis, Moyamoya, revascularization, EDAMS

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INTRODUCTION

Moyamoya Disease (MMD) is a rare chronic idiopathic neurovascular disorder characterized by progressive bilateral steno-occlusive changes starting at the supraclinoid internal carotid artery (ICA) and extending distally to involve proximal parts of the anterior & middle cerebral arteries (ACA & MCA) [1]. The resulting hypoxia leads to the development of a compensatory network of dilated vasculature at the basal ganglia, giving the characteristic Moyamoya (Japanese for "puff of smoke") appearance on cerebral angiography [2].

First described in 1957 as “Hypoplasia of the bilateral internal carotid arteries” [29], the term “Moyamoya” was coined in 1969 by Suzuki and Takaku [2]. Originally, this disease entity was thought to be unique to East Asian populations, particularly Japan. However, it has

increasingly been identified in western populations [3, 4], and has become a recognized cause of stroke in pediatric patients [5]. Nevertheless, it remains a rare entity with varying prevalence across ethnic groups, ranging from 6 per 100,000 in Japan to a tenth of that in Europe [3, 4, 16-18]. It has a female predominance, with the female-to-male ratio ranging between 2:1 and 4:1 [16,19].

Some individual case reports and small series of MMDs have been reported in Middle Eastern individuals [6-14], but there are no large series or long-term studies available in the literature. Only one case of moyamoya syndrome in an Iraqi patient has been reported in the literature, in which surgical revascularization has not been performed [15]. To the best of our knowledge, this is the second case report of MMD in an Iraqi patient and the first to be successfully treated by cerebral revascularization.

CASE PRESENTATION

A 12-year-old boy was brought by his parents, who described a 3-month history of progressive behavioral changes and decreased school performance. His physical and neurological examination was unremarkable. Routine blood and urine investigations were normal. Magnetic Resonance Imaging (MRI) showed signs of diffuse cortical and deep matter infarcts, as well as an old frontal infarct (Figure 1).

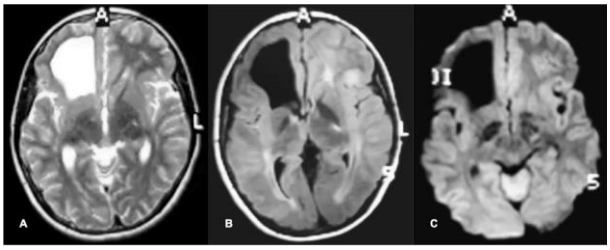

Figure 1. Axial MRI of the brain. **A-B:** T2-weighted & FLAIR images showing diffuse high signal intensities in the cortical and deep frontoparietal peri-ventricular regions. A large frontal porencephalic cyst, probably caused by an old infarct, can be seen as well. **C:** DWI image of the brain showing restricted flow in the abovementioned areas.

Magnetic resonance angiography (MRA) & computer tomographic angiography (CTA) (Figure 2) revealed asymmetrical steno-occlusive changes of the anterior circulation with an extensive deep collateral network at the basal ganglia. These modalities showed generalized stenosis of the intracranial right ICA with severe near-occlusive narrowing of its supraclinoid segment extending to the first few millimeters of the right ACA & MCA. The left supraclinoid ICA is completely occluded with obliteration of its proximal intracranial segments, and the proximal parts of the left ACA and MCA are completely occluded. The vertebrobasilar system and the posterior cerebral arteries (PCAs) were normal with no signs of stenosis, and the posterior communicating artery (Pcom) was intact on both sides, providing flow to the MCAs. As an endovascular facility was inaccessible at our center, no catheter angiography was performed.

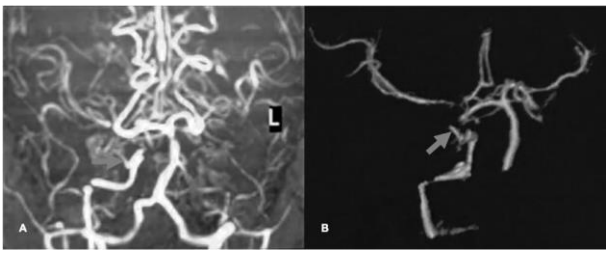

Figure 2. Brain MRA **(A)** and CTA **(B)** showing asymmetric stenosis of the anterior circulation with an extensive vascular network at the basal ganglia. The right ICA shows stenosis with near-occlusive narrowing of its supraclinoid segment extending to a few millimeters of the right ACA & MCA.

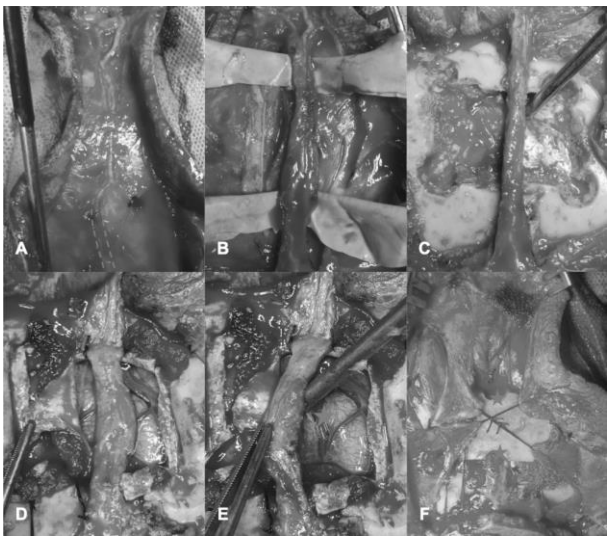

Figure 3. Revascularization by EDAMS. **A-B:** a linear incision is made along the course of the STA (dashes) with the aid of Doppler U/S and the artery is dissected and mobilized. **C-D:** a 5x5 cm craniotomy is created underlying the STA, and the dura opened and reflected in a cruciate fashion, with special care to preserve the middle meningeal artery. **E:** the STA and strips of temporalis muscle are sutured to the cortical surface adjacent to cortical MCA branches (star). **F:** reimplantation of the bone

flap after creating opposing notches (stars) to accommodate passage of the STA with its perivascular tissues.

A definitive diagnosis of asymmetrical MMD was made based on MRI and MRA criteria, and the patient underwent a right-sided extracranial-intracranial (EC-IC) bypass.

Indirect revascularization was performed by Encephalo-duro-arterio-myo-synangiosis (EDAMS), demonstrated in Figure 3. A linear incision was made along the course of the STA with the aid of Doppler U/S, after which the STA was dissected along with its perivascular tissue, and mobilized to allow safe drilling of 4 burr holes to make a 5 by 5 cm craniotomy. The dura was then opened and reflected in a cruciate fashion, with special care to preserve the middle meningeal artery (MMA). Afterwards, the STA was laid on & sutured to the cortical surface adjacent to cortical MCA branches. Strips of temporalis muscle were also reflected and attached to the cortex around the STA. The bone flap was re-implanted after preparation by creating opposing burr hole notches to accommodate the passage of the STA with its perivascular tissues.

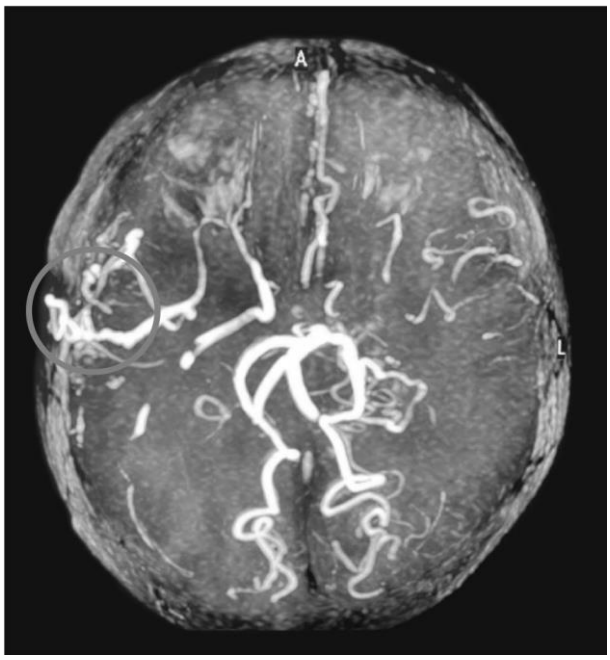

Figure 4. MRA performed 6 months following indirect revascularization (EDAMS) of the right side shows establishment of collateral blood flow from the STA to the frontal and parietal cortical territory of the MCA (circle).

There were no surgical complications, and the postoperative recovery was uneventful. The patient was discharged home with protective headgear at day eight postoperatively, and the parents were informed of the need to perform left-sided revascularization. At his six-month follow-up appointment, the parents reported a noticeable improvement in the patient's behavior and school performance. The follow-up MRA confirmed the re-establishment of collateral blood flow to the right MCA (Figure 4).

Discussion

Moyamoya disease versus syndrome

An important distinction when discussing moyamoya phenomena is differentiating moyamoya disease from moyamoya syndrome. MMD is characterized by bilateral, albeit sometimes asymmetrical, changes in the ICAs and eventually ACAs and MCAs. When these changes are coupled with certain well-documented associated conditions, or when the changes occur unilaterally, it is referred to as moyamoya syndrome [5]. Bilateral disease eventually develops in 40% of those with unilateral vasculopathy.

Our patient presented with bilaterally diseased cerebral circulation, with no associated risk factors and physical exam and laboratory investigations revealed no findings. Therefore, his condition is classified as moyamoya disease.

Presentation

MMD has a bimodal age distribution of disease onset (with peaks at ages 5-9 and 45-49) [19]. Pediatric patients are more likely to present with ischemic symptoms such as stroke, transient ischemic attacks (TIAs), or seizures. Hemorrhagic presentations are seen in both age groups, albeit at a much higher rate in adults [16, 20]. Our pediatric patient presented with ischemic symptoms that are consistent with established patterns in patient presentation.

Diagnosis

Diagnosis of MMD is generally based on clinical and radiological characteristics. MMD should be in the differential diagnosis of any patient presenting with neurological deficits or unexplained symptoms attributable to cerebral ischemia, particularly in the pediatric age group. Diagnosis can be confirmed by radiological evaluation, primarily with MRI, MRA and catheter angiography. Specific MRI sequences can detect cerebral infarction in its early and late stages, as was the case with our patient. FLAIR imaging also

enables the detection of chronic hypoxia, which manifests as linear high signals along the cortical sulci; the so called "ivy sign" [21]. A highly suggestive finding on T1 & T2-weighted images is the absence of ICA, ACA and MCA signal voids on the affected side, and the appearance of tortuous signal voids at the level of the thalamus and the basal ganglia, brought about by the development of collateral vessels in that region [22].

Catheter angiography is the most valuable tool for definitive diagnosis of MMD by detecting the steno-occlusive changes in the supraclinoid ICA extending to the ACA and MCA, and can visualize the leptomeningeal and/or basal collateral networks; the moyamoya or "puff of smoke" vessels. It also allows staging of the disease using the Suzuki grading system [2].

Due to concerns about cost, invasiveness and availability of catheter angiography, criteria have been established for diagnosing MMD based on MRI and MRA alone [23]. This criteria establishes a definitive diagnosis of MMD based on three conditions; namely the documentation of stenosis or occlusion at the terminal portion of the ICA and the proximal portions of the ACA and MCA on MRA, an abnormal vascular network in the basal ganglia seen on MRA or MRI, and the observation of the abovementioned two points bilaterally. In pediatric patients, the latter condition is not necessary for a definitive diagnosis. A staging system based on MRA findings alone has also been proposed [24], and is summarized in table 1. Using that system, our case would be categorized as grade II. This corresponds to grade III in the catheter angiography-dependent Suzuki grading system (stenosis of the ACA and MCA with patent Pcom and extensive collateral network at the basal ganglia).

Table 1. MRA-based grading system for MMD [24]

Vessel Changes	Score
ICA	
• Normal	0
• Stenosis of C1	1
• Discontinuity of C1 signal	2
• Invisible	3
MCA	
• Normal	0
• Stenosis of M1	1
• Discontinuity of M1 signal	2
• Invisible	3
ACA	
• Normal A2 and its distal signal	0
• A2 and its distal signal decrease	1
• Invisible	2
PCA	
• Normal P2 and its distal signal	0
• P2 and its distal signal decrease	1
• Invisible	2
Total	**0-10**

0-1: Grade 1; 2-4: Grade 2; 5-7: Grade 3; 8-10: Grade 4

Treatment

The mainstay of treatment for MMD is surgical revascularization using intact STA as an alternative source of blood flow. This has been shown to be a safe and effective treatment option that has reduced the incidence of strokes and TIAs in patients with MMD, with 96% of them having a 5-year stroke-free period and enhanced day-to-day activities [20, 23, 25].

There are no established surgical indications for patients with MMD, and some authors encourage surgical intervention in asymptomatic cases as neurological status at the time of surgery is stated to be the most significant predictor of long-term outcomes [20].

Surgery consists of direct STA-MCA bypass, indirect bypass techniques or a combination of both, with each modality having its own benefits and pitfalls. Direct revascularization provides an immediate augmentation of cerebral blood flow to the stenotic arteries, but due to the technical difficulties in anastomosing small-caliber vessels, its use is limited in pediatric patients. On the other hand, indirect revascularization is a less technically demanding technique, in which highly vascular tissues are approximated to the cortical surface to promote angiogenesis and enable the passive development of collateral EC-IC vessels. This offers excellent long-term outcomes comparable to those of direct revascularization, but improvement in cerebral blood flow is delayed and collateral vessels might take up to 3-4 months to develop [23].

Many techniques of indirect revascularization have been developed since the description of the disease in 1969, including encephalodurosynangiosis (EDS), encephalomyosynangiosis (EMS), encephaloduroarteriosynangiosis (EDAS), EDAMS, omental flaps transplantation, and placement of multiple burr holes [1].

We have reported the first case of MMD in an Iraqi patient to be successfully treated, using the EDAMS procedure of indirect revascularization. The aim of this procedure is to nourish the frontal and parietal cortical territories of the MCA. It combines the EDAS and EMS techniques thus maximizing the amount of vascular tissue involved in the synangiosis [26]. The very small size of the STA in our patient rendered direct bypass non-feasible. However, due to the long course of the vessel, its re-routing into the cortical surface was possible. Long-term follow-up data has shown EDAMS to be a safe and effective treatment modality for adults and older children with MMD [27, 28].

The reporting of such rare cases in the Iraqi population should warrant higher vigilance and the consideration of MMD as differential diagnosis in patients presenting with ischemic stroke, particularly children.

Conclusion

We present the second case of moyamoya disease in an Iraqi patient and the first to be successfully treated by indirect surgical revascularization, using the EDAMS technique. The article emphasizes the importance of recognizing this disease as a cause of stroke or recurrent TIAs in the Iraqi population, particularly in the pediatric age group.

Abbreviations

ACA: anterior cerebral artery
Acom: anterior communicating artery
CTA: computer tomographic angiography
DWI: diffusion-weighted imaging
EC-IC: extracranial-intracranial
EDAMS: encephaloduroarteriomyosynangiosis
EDAS: encephaloduroarteriosynangiosis
EDS: encephalodurosynangiosis
EMS: encephalomyosynangiosis
FLAIR: fluid attenuation inversion recovery
ICA: internal carotid artery
MCA: middle cerebral artery
MMA: middle meningeal artery
MMD: moyamoya disease
MRA: magnetic resonance angiography
MRI: magnetic resonance imaging
PCA: posterior cerebral artery
Pcom: posterior communicating artery
STA: superficial temporal artery
TIA: transient ischemic attack
U/S: ultrasonography.

Authors' contributions

S.S.H: Data collection
A.O.A: Manuscript drafting
Z.F.A: Manuscript revision
M.A.A: Manuscript revision

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Gastroparesis as a complication in the patient with traumatic brain injury

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ABSTRACT

Patients with acute neurological diseases (traumatic brain injury, hemorrhagic or ischemic stroke, spinal cord injury or tumour) may present with various systemic alterations such as changes in cardiovascular and respiratory response, gastrointestinal function disorders, metabolic and endocrinological abnormalities, coagulopathies, among others. Head injury increases the risk of malnutrition due to multiple factors related to nutrient intake, abnormalities in energy expenditure, eating behaviour disorders, gastrointestinal changes, and medication side effects.

Gastrointestinal conditions include gastroparesis, which is defined as a delay in gastric emptying in the absence of mechanical obstruction. These patients often report nausea, vomiting, pain, postprandial fullness and abdominal swelling. Although the exact mechanism by which it occurs in traumatic brain injury is not known, it is related to complications such as intracranial hypertension, so it is most often seen in cases of severe trauma. Therefore, the objective of this review is to expose basic and practical concepts about gastroparesis and its approach.

Introduction

Traumatic brain injury (TBI) is one of the most frequent acute brain pathologies that constitute a serious public health problem worldwide due to its high mortality and number of cases of permanent disability after its occurrence [1]. The most recent data provided by the Centers for Disease Control and Prevention (CDC) estimates that for the year 2019 there were about 61,000 TBI-related deaths in the United States, which is approximately166 deaths every day [2]. This condition can be caused by a blow, jolt or penetrating head injury that disrupts the normal functioning of the brain [2]. TBI, especially severe TBI (Glasgow Coma Scale < or equal to 8), is associated with many consequences, the most common being altered consciousness, coma, movement and gait disorders, memory impairment - learning, among others; however, the occurrence of gastrointestinal dysfunction in patients, such as gastroparesis, has been reported days after traumatic brain injury [3].

The incidence of gastroparesis (GP) in TBI ranges around 45-50%, and is closely related to the severity of trauma and intracranial hypertension [4]. GP is a well-documented finding among patients with severe TBI [5]. GP is defined as delayed gastric emptying in the absence of mechanical obstruction [6-8]. In these patients, a temporal profile of delayed emptying has been described during the first 2 weeks post-trauma with subsequent improvement [4]. Although the exact cause of GP in TBI is unknown, altered nerve signaling to the stomach appears to be a factor [9]. Other factors that promote its onset are inflammation, sepsis, hydroelectrolytic alterations (hypokalemia, hypomagnesemia), hyperglycemia, frequently used drugs (opioids, furosemide, hydantoin, antacids, corticosteroids, among others), renal and hepatic dysfunction, and liver dysfunction [4,6].

Considering the relevance of this topic in the care of the neurocritical patient and the lack of current evidence to know the impact of this condition, the objective of this review is to present basic concepts related to the pathophysiological process, general approach and future perspectives of gastroparesis in patients with traumatic brain injury.

General information on gastroparesis in patients with TBI

It has been shown that more than 50% of patients with severe traumatic brain injury do not tolerate enteral feeding, which presents itself in the form of vomiting, abdominal distension, delayed gastric emptying, esophageal reflux and decreased intestinal peristalsis [10]. The above suggests that gastrointestinal dysfunction is a frequent entity following TBI and that the association between the severity of brain injury and enteral feeding intolerance appears to be related to the existence of a link between the central nervous system and the non-functioning gut [10].

As mentioned above, one of the factors involved in such intolerance consists of delayed gastric emptying or gastroparesis [11]. Gastroparesis and altered gastric accommodation are the result of a neuromuscular dysfunction of the stomach. Kao et al [11] conducted a study where they evaluated the half-time of gastric emptying of liquid meals in patients with moderate to severe TBI, finding that head trauma can cause significantly prolonged gastric emptying [11]. Other studies have shown that TBI can also induce a decrease in both intestinal contractility and transit and an increase in inflammation in intestinal smooth muscle, which may indicate that motility is inhibited in the small intestine due to inflammatory damage secondary to brain injury [10].

On the other hand, delayed gastric emptying has been frequently observed in patients with intracranial hypertension (IH). Increased intracranial pressure (ICP) causes a large increase in sympathetic activity, which is responsible for several of the systemic and peripheral gastrointestinal symptoms [12]; this increase in turn can lead to changes in GI motility and in water and electrolyte absorption. Similarly, Madroszkiewicz et al [13] conducted a study to evaluate the effects of acute and chronic ICP on gastric myoelectric activity and found that the most significant changes in gastric activity were

observed in patients after severe traumatic brain injury with acute IH.

Pathophysiological aspects

Under normal conditions, food is liquefied in the stomach by the digestive action of gastric acid and antral contractions [14]. These antral contractions, essential for the crushing of solid food and gastric emptying, are mediated by extrinsic vagal innervation (gastric branches from the anterior and posterior vagal trunks) and intrinsic cholinergic neurons [14,15]. Nitrergic neurons mediate intrinsic inhibitory mechanisms, which facilitate pyloric relaxation and intragastric peristalsis. These neurons are essential for gastrointestinal (GI) muscle relaxation prior to contraction, and are responsible for downstream inhibition prior to upstream contraction, which is induced by excitatory neurons (cholinergic neurons) [14].

These inhibitory and excitatory neuronal effects are transmitted through interstitial cells of Cajal (ICC), fibroblast-like cells (positive for platelet-derived growth factor receptor α - PDGFRα), and smooth muscle cells of GI muscles. This causes the muscular layer of the stomach to behave like a multicellular electrical syncytium so that coordinated contractions, which are initiated in the proximal stomach and involve the entire circumference of the stomach, can propagate into the antropyloric region [14,16,17].

PDGFRα-positive ICCs and fibroblast-like cells are considered to be the pacemaker cells of the gastrointestinal tract and possess the ability to transmit electrical signals (Figure 1) [17]. In gastroparesis, delayed gastric emptying is associated with decreased antral motility and, in some patients, pyloric sphincter dysfunction due to neuromuscular dysfunction [14].

On the other hand, after traumatic brain injury, primary tissue damage (somatic and axonal) induced by mechanical damage to the brain causes the release of intracellular and intraaxonal contents, as well as the extravasation of blood products [18]. In response to this tissue damage, local activation of microglia occurs. At the same time that the local microglial inflammatory response occurs, brain infiltration and accumulation of peripheral immune cells is generated, which enter due to alterations in the blood-brain barrier after TBI [19]. These cells mediate inflammatory processes through the production of a variety of inflammatory cytokines, chemokines, adhesion molecules, reactive oxygen and nitrogen species, among others [18].

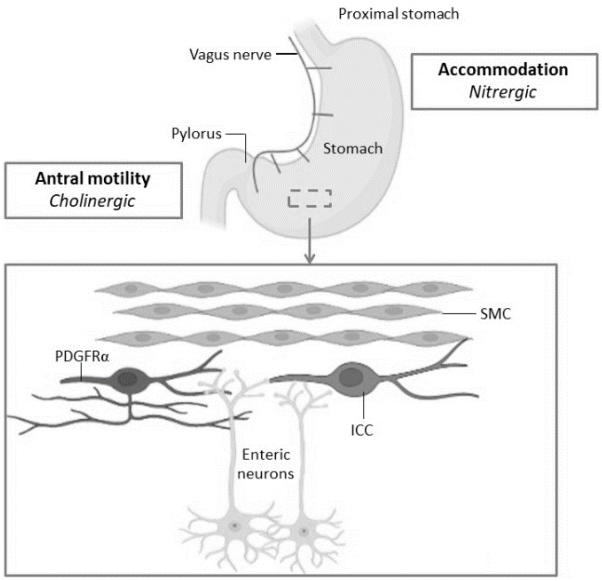

Figure 1. Mechanisms of antral motility, accommodation and gastric emptying. Created by authors with BioRender.

Some studies have shown reductions in the number of ICC in the stomach body of patients with gastroparesis [20,21]. This reduction in ICC could impair conduction of electrical activity through the electrical syncytium and thus interfere with coordinated gastric electrical rhythms, peristalsis and gastric emptying [14]. Both the decrease in the number and damage of ICCs in the stomach of some patients with gastroparesis have been associated with a decrease in the number of M2 anti-inflammatory macrophages, which express the mannose receptor (CD206) and heme oxygenase 1 (HO1) and are responsible for mediating cellular repair. In this way, M2 macrophages protect neural tissue against the effects of oxidative stress and inflammation [14,20].

Thus, a possible explanation for the occurrence of gastroparesis as a complication of an episode of TBI is that a decrease in the number or damage of ICC in patients with a reduced number of M2 anti-inflammatory macrophages would generate a deficiency in the protection of neural tissue against the effects of oxidative stress and inflammation. Ultimately, these events could result in gastric intrinsic neural dysfunction, which would be the cause of gastroparesis

Clinical and diagnostic considerations

GP manifests itself through a wide array of signs and symptoms, including nausea (predominant symptom), vomiting, pain (burning or burning), early satiety, postprandial fullness, abdominal distension, bloating, and upper abdominal discomfort. GP-associated pain is mainly located in the epigastrium, is described as persistent or nocturnal, and is often reported after a meal (food-induced pain) [8,9]. The severity of gastroparesis is assessed by the degree of nutritional impairment or weight loss or by the degree of delayed gastric emptying (e.g., the proportion of food retained in the stomach for a given number of hours), which will be influenced by the method and foods used to test overall stomach function. Similarly, there are several symptom severity scales to assess clinical signs and symptoms [14].

In the neurocritical patient with enteral feeding by nasogastric tube (NGT), increased gastric residuals and intolerance to enteral feeding are typically reported [9]. This delays adequate nutrition, favors aspiration of gastric contents and pneumonias, thus prolonging hospital stay, increasing medical costs and contributing to a higher risk of mortality [4, 6, 9].

Diagnosis

The diagnosis of GP is based on the presence of signs and symptoms and the demonstration of delayed gastric emptying. It should be emphasized that, before assessing gastric motor activity or emptying rate, it is necessary to exclude other possible causes of symptoms. Generally, people in whom GP is suspected require upper endoscopy to exclude mechanical obstruction or ulcer disease. While endoscopy is often normal in patients with delayed gastric emptying, in severe cases, endoscopy may reveal food debris in the stomach, the so-called bezoarsLaboratory tests should rule out water and electrolyte disorders, and glycemia and thyroid function should also be requested. Subsequently, gastric motor function tests can be considered [8,9].

As previously mentioned, documentation of delayed gastric emptying is essential for a definitive diagnosis. The evaluation of gastric emptying includes a variety of methods [22-24]. Currently, scintigraphy is the most widely used diagnostic technique and is considered the gold standard for documenting delayed gastric emptying; using this technique, a radioactive substance is administered and two-dimensional images show the emitted radiation [7, 24, 25]. Carbon 13 (13C)-octanoic acid or 13C-acetic acid breath analysis is used in some institutions, but requires more time than the 1- or 2-hour scintigraphy tests [6, 8]. Other diagnostic methods include ultrasound but depend on a specialized operator [6]. When gastric emptying tests are inconclusive, particularly in those patients with pronounced postprandial fullness or early satiety, measurements of gastric accommodation can also be estimated by validated methods such as positron emission tomography (PET/CT) and magnetic resonance imaging (MRI), or by screening tests such as proximal stomach size on gastric scintiscan (taken immediately after ingestion of a radiolabeled meal) or by a water or nutritive drink loading test [26].

In the intensive care setting, the most commonly used method for assessing gastric emptying is the measurement of gastric residual volume (GRV) [24,25], which can be accomplished by connecting a 50 ml syringe to an NGT and aspirating the residual contents. Another way to measure VGR is to connect a drainage bag to the end of an NGT and lower the bag below chest level for 10 minutes [27]. Delayed gastric emptying is often designated when the GRV is 250 ml or more. However, factors such as patient position (low or high elevation from the head of the bed), feeding port tube location (deeper in the body of the stomach or near the gastroesophageal junction), and the internal diameter of the feeding tube (narrow or wide) may affect the GRV [23,24].

Therapeutic approach to gastroparesis in the setting of TBI

The treatment of GP focuses on 2 pillars:

1) Restoration of water and electrolyte balance, glycemic control, suspension of drugs that alter gastric motility (pro-gastroparasitics) and modifications in the diet provided, which should be low in volume and lower in calories, but with shorter intervals between servings [28]. Higher kcal and weight meals are associated with longer emptying times. The diet should preferably be liquid and fat-free; fat intake releases cholecystokinin which can further delay gastric emptying. High fiber foods are recommended to prevent the formation of bezoars [6]. In patients with TBI, actual energy needs can be up to 60% higher than expected values [29]. Therefore, it has been emphasized that, in terms of

complications and survival, nutritional support is beneficial for neurocritical patients [30]. Enteral nutrition instead of parenteral nutrition is generally the preferred means of nutritional support. It is indicated for maintaining and restoring electrolyte balance, in addition to providing nutritional [31]. Enteral nutrition can be instituted through many routes, such as NGT and nasoenteric tubes, or by gastrostomy or jejunostomy that simultaneously decompresses the stomach and allows enteral nutrition [32]. Particularly in patients with TBI, GP makes oral nutritional support difficult. To overcome the difficulties associated with GP, transpyloric placement of the feeding tube has been recommended [9, 33]. However, tube displacement and difficulties in passing the tube through the pylorus are common problems. In addition, the need for transpyloric feeding has been questioned, as it does not result in a significant decrease in complications [34]. Therefore, strategies have been developed to improve gastric motility with intragastric enteral feeding.

2) The administration of drugs to stimulate and improve gastric emptying and reduce nausea and vomiting. Several prokinetic agents have been shown to achieve this goal. These drugs increase antral contractility, correct gastric arrhythmias, and improve coordination of antroduodenal movements [6,28]. With recent advances in research on prokinetic agents, the following three categories of drugs are frequently used in GP patients.

Dopamine antagonists: Metoclopramide is a dopamine antagonist with both central and peripheral activity [6]. It acts on dopaminergic (D2) and serotonergic (5-HT3) receptors, and stimulates the release of acetylcholine in myenteric plexus neurons [28]. In addition to its antiemetic effect, it has prokinetic activity [6]. It is more effective in short-term treatments, no longer than 15 days [8]. The usual dose is 10 mg IV 3 or 4 times a day and the dose may be doubled in severe cases. Although frequently used, it may cause neurological symptoms with long-term use [28]. Side effects are related to central dopaminergic blockade causing sporadic acute dystonic reactions, facial spasms, parkinsonian symptoms and asthenia [6, 8, 28]. Domperidone is another dopamine antagonist, but with peripheral activity only [6]. It has a prokinetic and antiemetic action and has a particularity, it does not cross the blood-brain barrier, therefore, it does not produce extrapyramidal side effects [28]. Superior efficacy and tolerability have been suggested for domperidone over metoclopramide [35, 36]; therefore, it has been considered as the drug of choice. The dose is 10 mg distributed in 4-6 daily intakes [28]. Like metoclopramide, it can produce hyperprolactinemia [6].

Substituted benzamides: Cisapride facilitates acetylcholine release from myenteric plexus neurons through a 5-HT4 receptor-mediated effect [6]. Superior efficacy and tolerability have been suggested for cisapride over metoclopramide [37]. However, due to the increased risk of QT interval prolongation with cardiac arrhythmias, its use in routine clinical practice has been restricted [1]. Cinatapride is another non-antiemetic prokinetic. It is a 5-HT4 receptor agonist. It facilitates the release of acetylcholine. Unlike its predecessor cisapride it does not produce QT interval prolongation or severe cardiac arrhythmias. The usual dose is 1 to 2 mg distributed in two daily doses [28].

Antibiotics: Erythromycin is a macrolide that stimulates gastroduodenal motilin receptors. It is the most potent prokinetic, with a significant improvement in gastric emptying. However, it has no antiemetic action [6]. The dose is 300-750 mg/day distributed in 3-4 intakes, preferably IV [28]. Due to its antibiotic properties, long-term use may lead to the induction of resistant strains. There are other possible side effects such as ototoxicity and pseudomembranous colitis, which limits long-term use in patients with gastroparesis. In addition, the problem of tachyphylaxis makes long-term use less attractive. Concomitant hyperglycemia may interfere with or block its prokinetic property [28].

Future perspectives

Traumatic brain injury remains a major cause of mortality, morbidity and economic burden worldwide, and will always be a frequent entity in neurocritical care settings, since its main causes are falls and motor vehicle accidents, which are events that occur on a daily basis in our environment [38,39]. In first world countries, there has been a trend towards reducing TBI incidences driven by

public health interventions such as seat belt legislation, helmet use, and workplace health and safety standards [38]. In underdeveloped countries, as is the case in Latin America, these established prevention standards are not complied with by the majority of their inhabitants, which leads to a higher number of TBI cases in emergency departments. Therefore, the appropriation and acquisition of knowledge on this subject is fundamental.

Knowing the pathophysiological aspects and degrees of severity would help to understand the mechanisms by which different complications occur after TBI, as well as to evaluate the good or bad prognosis of functional recovery and to anticipate the rehabilitation needs of patients.

Gastrointestinal alterations, in this case gastroparesis, as a complication associated with severe TBI is no exception, since there are large gaps in knowledge, its pathophysiology and inconsistencies among published studies on this subject. For this reason, neurogastroenterological research, which aims to improve the understanding of the physiology and pathophysiology of the digestive neurological subsystems from which functional symptoms arise, has aroused great interest within the scientific community. Similarly, research on the relationship between gastroparesis and intracranial hypertension should be expanded, as it has been suggested that correction of these gastric abnormalities may facilitate the recovery of patients with brain lesions.

On the other hand, neuronutrition is also a line of research that has gained strength in recent years, due to the importance of nutrition in patients with neurological disorders; it is necessary for the proper functioning of respiratory muscles, cardiac function, the balance of the coagulation cascade, electrolyte and hormone balance, and renal function, as well as influencing functional recovery and the overall cost of medical care. The need to identify and treat the patient with malnutrition or impaired gastrointestinal function is a critical aspect of patient management [40]. The above explains why research on gastroparesis in the context of TBI is essential to improve specific and overall patient outcomes with general involvement, and thus reduce the rate of secondary complications such as pulmonary aspiration or malnutrition, overall morbidity, mortality, and disability.

Conclusion

Traumatic brain injury remains a pathological condition with a considerable burden of disease worldwide. Gastroparesis is a complication that substantially influences morbidity, mortality and disability in the traumatic brain injury patient by intervening in the nutrition process, among many others. Although its pathophysiology is not clearly known, early treatment of its symptoms can substantially improve the prognosis.

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A reverse brain herniation (RBH) after ventriculoperitoneal shunt (VP) in posterior fossa tumour with obstructive hydrocephalus. A rare and fatal complication

Lamkordor Tyngkan, Avatar Singh, Abdul Rashid Bhat

Keywords
posterior fossa tumour,
hydrocephalus,
reverse brain herniation,
ventriculoperitoneal shunt

Abstract

The risk of hydrocephalus in posterior fossa tumour is quite high (71- 90%), cerebrospinal fluid (CSF) diversion procedures like ventriculoperitoneal (VP) shunt, Endoscopic third ventriculostomy (ETV) and external ventricular drainage (EVD) are emergency procedures and may improve symptoms like headache and vomiting. However, post-operative deterioration after CSF diversion should alert the clinician to the possibility of RBH which is rare (3%) and has a high mortality. We report a case of a 12-year female child with a left cerebellar lesion with hydrocephalus. VP shunt was done and her pupils revert back to normal size, two hours post-surgery her pupils become dilated and not reacting to light, an urgent CT was done which showed reverse brain herniation. Reverse brain herniation is a very rare complication after the CSF diversion procedure with a poor prognosis.

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Introduction

Obstructive hydrocephalus secondary to posterior fossa tumour is quite common, occurring in 71–90% of children with posterior fossa tumors.1The optimal management of hydrocephalus in a child with a posterior fossa tumor is a topic of debate.2 The question of whether to place an external ventricular drain (EVD), insert a ventriculoperitoneal shunt (VPS), perform an endoscopic third ventriculostomy (ETV), or defer CSF diversion procedures before resective surgery depends on the clinical presentation and individual surgeon practice; there exists no class I evidence to guide management.3Cerebrospinal fluid (CSF) diversion procedure carry the risk of reverse brain herniation (RBH) which is rare and associated with significant mortality. RBH may aggravate hydrocephalus and cause hemorrhagic infarction of the brainstem and cardiorespiratory disturbance. 4, 5 we report case of left cerebellar lesion with obstructive hydrocephalus that developed fatal reverse brain herniation after ventriculoperitoneal (VP) shunt.

CASE REPORT

A 12-year female child presented to surgical emergency department with complaints of headache since 2 months and altered sensorium since 2 hours. On examination Glasgow Coma Scale (GCS) was E1V1M2 (4/15), pupils bilaterally dilated not reacting to light, Magnetic resonance imaging (MRI) showed left cerebellar heterogenous enhancing lesion with hydrocephalus. Urgent intubation and right ventriculoperitoneal shunting was done, CSF came out under high pressure. Post surgery patient pupils revert back to normal size and reacting to light and patient was shifted to Neuro ICU as she was not extubated. However after 2 hour of surgery her pupils become dilated and not reacting to light again, urgent NCCT (non contrast computed tomography) was done which showed decompressed ventricles with shunt tip in situ and revesre brain herniation. Surgical decompression of posterior fossa tumours was planned but patient relatives didn't give consent for surgery and unfortunately patient died after 3 days.

DISCUSSION

To the best of our knowledge only three cases of revesre brain herniation (RBH) after CSF diversion procedure in posterior fossa tumour with hydrocephalus has been reported in the literature.

Obstructive hydrocephalus secondary to posterior fossa tumors is quite common, occurring in 71–90% of children with posterior fossa tumors.1 CSF diversion procedures are emergency procedure in these cases; however, post-operative deterioration in the condition of the patient after CSF diversion should alert the clinician to the possibility of RBH of the brain. RBH is the least understood of the brain herniation syndromes and is a rare complication of VP shunt with an incidence of 3%.6 Cuneo et al. reported that cerebellar mass (65%) is the commonest lesion associated with RBH, followed by lesions of CP angle (13%), the pons (11%), and the fourth ventricle. It usually occurs when the mass originates near the incisura, when drainage of the lateral ventricles relieves obstructive hydrocephalus, or when the opening in the tentorium is large.4 Galen's vein lies immediately above the posterior tentorial incisura. Herniation of the vermis through the notch displaces Galen's vein upward against the splenium and the unyield¬ing free edge of the falx. Acute compression of Galen's vein may produce hemorrhagic infarction in the diencephalon and the adjacent white matter if venous collateral channels fail.4

Direct compression of the brainstem and downward tonsillar herniation may be present. The clinical picture includes signs of pontine compression (obtundation, hyperventilation, decerebrate rigidity, and small fixed pupils), midbrain compression (loss of upward gaze and pupils which may be fixed and dilated). Compression of the brainstem nuclei causes severe bradycardia and asystole.4, 5 In our case as tumour was large possible cause of reverse brain herniation (RBH) into the supratentorial compartment, was a sudden decrease in the supratentorial pressure due to the shunt.

Gurajala I et al. showed that Interruption of VP shunt and prompt institution of mechanical ventilation immediately after clinical diagnosis of RBH may have reduced the extent of herniation. Even though RBH has significant mortality, surgical decompression should be undertaken as soon as possible even in cases of severe RBH.8 Our patient was only mechanically ventilated because patient relatives denied for any surgical intervention.

The mortality associated with RBH is significant. In the series by Cuneo et al, only seven cases out of a total of 52 reviewed were diagnosed antemortem and the mortality was 100%. Cases reported later in the literature had a better outcome. In about 25% of the patients, ventricular drainage is directly responsible for precipitation of the herniation.5, 6, 8, 9 Hence, patients who undergo CSF diversion should be observed closely for reverse brain herniation (RBH) postoperatively.

Table 1. Reported cases of reverse brain herniation (RBH) after CSF diversion in obstructive hydrocephalus secondary to posterior fossa tumour

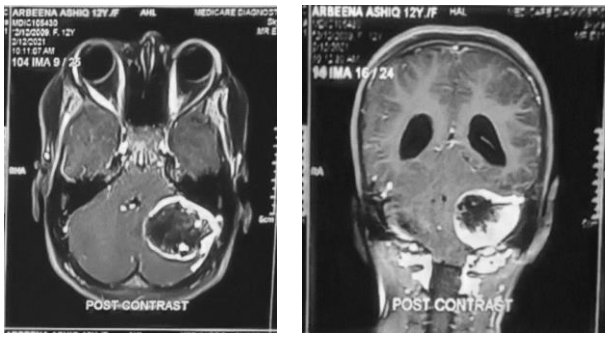
Case	Author	Year	Age / Sex	Location of tumour	Treatment	Out-come
1	Singha SK et al[9]	2009	57/M	Midline posterior fossa (Involving vermis and both cerebellum) hemangioblatoma with hydrocephalus	ETV + suboccipital craniectomy and tumor decompression.	Uneventful

2	Gurajal l et al[8]	2012	45/M	Right cerebellopontine (CP) angle tumours with hydrocephalus	VP shunt + Tumour decompression	Discharged with nasogastric tube
3	Marappan K et al[10]	2018	3.5/F	4th intraventricular tumour	VP shunt	Not avail-able
4	Present case	2021	12/F	Left cerebellar lesion	VP shunt	Expired

ETV- Endoscopic third ventriculostomy; VP- Ventriculoperitoneal

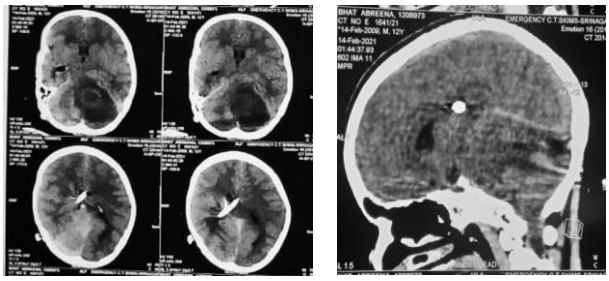
Conclusions

Ventriculoperitoneal shunt for obstructive hydrocephalus with posterior fossa tumour can be complicated by reverse brain herniation which is a rare complication and can be fatal if prompt diagnosis and intervention is not done. Surgical decompression should always be done even in a case of severe RBH.



A. **B.**

Figure 1. (**A**) axial CEMRI image showing left cerebellar lesion with heterogeneously enhancing lesion; (**B**) Coronal MRI image showing left cerebellar lesion with hydrocephalus.



A. **B.**

Figure 2. NCCT (**A**) axial image showing decompressed ventricles with reverse brain herniation; (**B**) saggittal image showing raised tentorium with revesrse brain herniation.

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A rare occurrence of primary basal ganglia germinoma in an adult patient. A case report and literature review

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ABSTRACT

Background: Basal ganglia germinomas (BGGs) represent a diagnostic and management neurosurgical dilemma. Because of the rarity of these tumors in adults, the management strategies are not well defined.

Case description: A 24-year-old man was presented with progressive left-sided hemiparesis. Cranial computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated a heterogeneous lesion with few microcystic nodules, seen involving the right basal ganglia with calcification. A stereotactic brain biopsy (SBB) was obtained. Histopathology revealed BGG. The patient received whole-brain radiation therapy (WBRT) and reported marked improvement in symptoms with no recurrence during a follow-up period of four years.

Conclusion: BGG should be considered a part of the differential diagnosis in young adults presented with hemiparesis and a heterogeneous lesion in the basal ganglia. Standard recommendations for the management of such rare lesions in adults are needed.

Keywords
basal ganglia,
germinoma,
radiation therapy

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INTRODUCTION

Intracranial germinomas represent 0.5 to 3% of all intracranial tumors. [2-4,5,7] They are mostly found in the pineal and suprasellar regions. [1-7] Rarely, they arise from the basal ganglia and are sparsely reported in the literature. [1-7] Adults with an established diagnosis of basal ganglia germinoma (BGG) are exceedingly rare. [5] Only thirteen cases of primary BGG have been reported to date. BGGs are difficult to treat due to their deep anatomical position inside the brain, making them rarely susceptible to total eradication. Management practices range from stereotactic brain biopsy (SBB) to partial or more aggressive resections and even empirical radiation without a prior histological diagnosis, plus radiation therapy (XRT) and chemotherapeutic agent administration. [1-5,7]

Adult BGGs have rarely been investigated in isolation. Thus, the natural history remains mostly undefined, and the therapeutic paradigms have not been standardized yet. This article is intended to discuss a good outcome for a young adult diagnosed with BGG, using a minimal intervention strategy. We also provide a review of the relevant literature.

CASE DESCRIPTION

A previously asymptomatic 24-year-old male was presented to our facility after experiencing five months of isolated progressive left-sided weakness. The vital signs and all other systemic clinical parameters were normal. The neurological evaluation was grossly intact aside from left-sided hemiparesis (Grade 4/5 Medical Research Council) and left-sided deep tendon hyperreflexia. His gait pattern was characterized by dragging his left foot while walking.

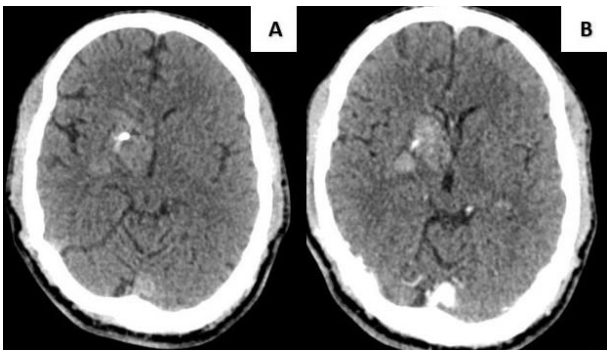

Figure 1. Preoperative cranial CT scan demonstrates a mildly hyperdense irregular lesion in the right basal ganglia with dense calcification (**A**) and a heterogenous, moderate enhancement in the postcontrast study (**B**).

Initially, a plain and intravenous contrast cranial computed tomography (CT) scan (Figure. 1) was performed, showing a mildly hyperdense lesion with moderate post-contrast enhancement and containing an area of calcification in the right basal ganglia. Cranial magnetic resonance imaging (MRI) demonstrated a heterogeneous signal intensity lesion with few microcystic nodules in the right basal ganglia with calcification on pre-contrast images (Figure. 2). The lesion showed mild hypointensity on T1-weighted images (Figure. 2A), hyperintensity on T2-weighted images (Figure. 2B) and fluid-attenuated inversion recovery images, and moderate heterogeneous patchy enhancement in postcontrast T1-weighted images (Figure. 2E). There was evidence of patchy restricted diffusion in diffusion-weighted imaging (Figure. 2C). After a negative comprehensive check-up, including spinal MRI, whole-body CT scan, HIV serology, ophthalmic examination, and positron emission tomography scan without abnormalities, amongst the differential diagnoses entertained was primary basal ganglia germinoma, followed by other less likely differentials of pilocytic astrocytoma, primitive neuroectodermal tumor, and cryptococcus meningitis.

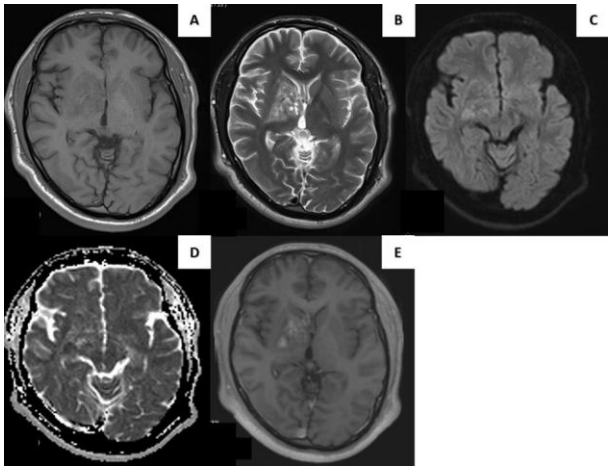

Figure 2. Preoperative cranial MRI demonstrates a right basal ganglia lesion with mild hypointensity on the T1-weighted sequence (**A**) and heterogeneous hyperintensity with microcystic nodules on the T2-weighted sequence (**B**). The lesion shows patchy restricted diffusion in the form of a patchy high signal with a high B value of DWI (**C**) and a low signal apparent diffusion coefficient (**D**). The lesion shows patchy enhancement in the postcontrast T1-weighted sequence (**E**).

SBB was performed on the patient. Histopathological evaluation (Figure. 3) revealed nests of neoplastic cells separated by thin fibrous septa. The neoplastic cells were large and polygonal with distinct eosinophilic cytoplasm and a vesicular nucleus with a conspicuous nucleolus. No fibrillary background, trophoblastic cells, rosette formation, or neutrophils were noted. Mitosis (2-4/HPF) and large areas of necrosis and hemorrhage were present in the tumor. There were a few scattered lymphocytes. The tumor cells were strongly and diffusely positive for placental alkaline phosphatase (PLAP), Beta-human chorionic gonadotropin (B-HCG), and CD117. However, they were negative for glial fibrillary acidic protein, synaptophysin, chromogranin, isocitrate dehydrogenase 1, oligodendrocyte transcription factor 2, S100, epithelial membrane antigen,

myogenin, CD 20, and CD 30. The Ki-67 index was 40-50%, and INI-1 was preserved. A diagnosis of basal ganglia germinoma was made based on histological findings.

The blood serum sample showed an elevated B-HCG of 563 mlU/mL and a normal alpha-fetoprotein (AFP) of 3.5 µg/L. The cerebrospinal fluid (CSF) sample showed an elevated B-HCG of 350 mlU/mL and a normal AFP of 1.1 µg/L. No atypical cells were detected in the CSF sample.

The patient received whole-brain radiation therapy (WBRT) using a volumetric modulated arch therapy technique with a total dose of 24 Gy in 15 fractions over four weeks, followed by a tumor boost of 16 Gy in 10 fractions over two weeks. Repeated blood serum, three months post-XRT, showed a normal B-HCG of 0.4 mlU/L. Over a four-year follow-up, the patient significantly improved after XRT and had no tumor recurrence on the MRI (Figure. 4).

Discussion

Adults with primary BGGs are uncommon, and their natural history and treatment are rarely the topic of published work.[5] We performed a literature search of the following databases on May 17, 2021: PubMed and Google Scholar. We included adult patients (age ≥ 19) with germinoma located in the basal ganglia (Striatum, Pallidum, Subthalamic nucleus, and substantia nigra) (Table. 1). Patients with a tumor mainly located in the thalamus were excluded from the review. Adding our case, thirteen patients were diagnosed with pure germinoma, and one patient was diagnosed with germinoma mixed with syncytiotrophoblastic giant cells. Six tumors were right-sided, six tumors were left-sided, and two tumors were bilateral. All of the patients were men. The median age at diagnosis was 24.5 years old (the range was 19-31 years)

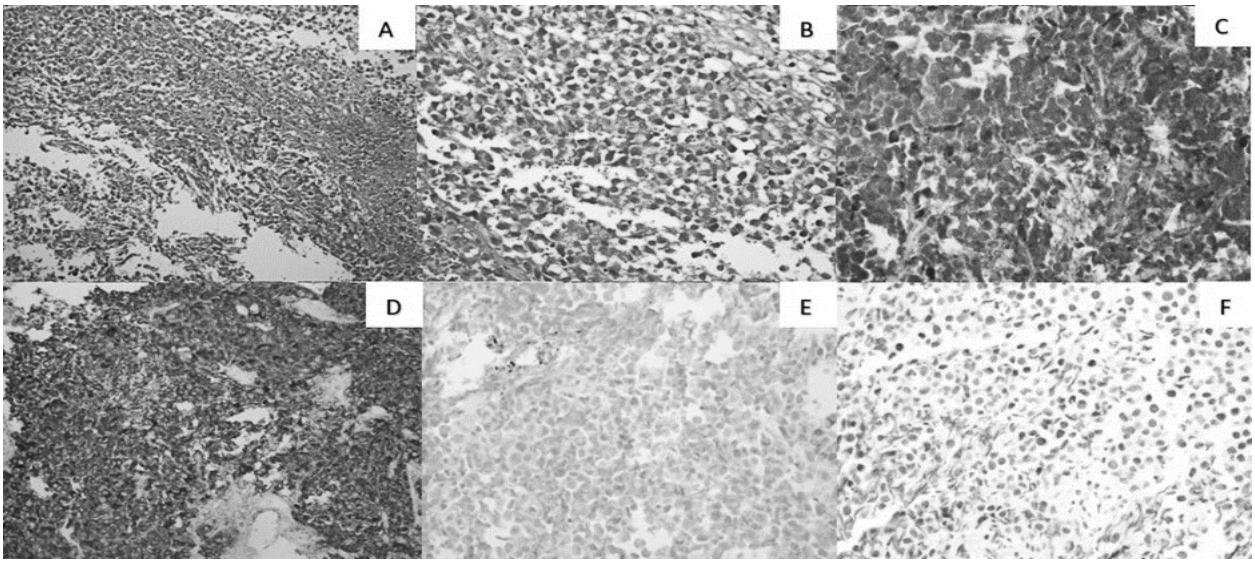

Figure 3. Histopathology of right basal ganglia germinoma. The lesion shows sheets of cells having abundant eosinophilic cytoplasm, pleomorphic nuclei with prominent nucleoli, 20x, 40x HE (A **& B**). The tumor cells are strongly and diffusely positive for B-HCG (**C**) and PLAP (**D**) immunostain and negative for synaptophysin (**E**). INI-1 is preserved (**F**).

Table 1. Clinical characteristics of reported adult cases of primary basal ganglia germinoma

Source	Age/Sex	Presentation	ICH signs ǂ	Duration (Months)	AFP (S/C)	HCG (S/C)
Elizabeth J et al. 2002	21/M	Hemiparesis, Speech difficulty	Yes	12	NA/NA	NA/NA
Sonoda Y et al. 2008	24/M	Hypokinesia	No	6.9	+/NA	-/NA
	31/M	Hemiparesis, Hypokinesia	No	6.9	-/-	-/-
	29/M	DI, Personality change	No	11.4	-/-	-/-

Phi JH et al. 2010	19/M	Hemiparesis	No	8	-/NA	-/NA
Lin JC et al. 2012	24/M	Bizarre behavior	No	0.5	-/NA	-/NA
Vialatte de Pemille C et al. 2016	21/M	Hemiparesis	No	NR	-/-	-/-
Wei X-H et al. 2016	31/M	Headache	Yes	NR	-/NA	NA/NA
	19/M	Hemiparesis	No	NR	-/NA	+/NA
	21/M	Hemiparesis, Polydipsia	No	NR	-/NA	-/NA
	30/M	Hemiparesis	No	NR	-/NA	-/NA
	29/M	Hemiparesis	No	NR	-/NA	-/NA
Woo PYM et al. 2017	21/M	Hemiparesis	No	24	-/NA	-/NA
Our case, 2021	24/M	Hemiparesis	No	5	-/-	+*/+*
ǂ *ICH signs reported: Headache, Vomiting, dysphagia, Papilloedema 6th cranial nerve palsy.* **beta subunit of HCG*						
Keywords: M: male; ICH: Intracranial hypertension; NR: Not reported; S: serum; C: Cerebrospinal fluid; NA: Not applicable; -: normal level; +: High level, DI: Diabetes insipidus.						

Table 2. Magnetic resonance imaging findings before stereotactic brain biopsy of reported adult cases with primary basal ganglia germinoma

Source	MRI Findings						
	Enhancement	Mass effect	Hemorrhage	Cyst formation	Calcification	DR	Other
Elizabeth J et al. 2002	+	+	+	+	NR	NR	Multiple lesions
Sonoda Y et al. 2008	+	+	-	-	-	NR	-
	+	-	-	-	-	NR	-
	+	+	-	-	-	NR	Multiple lesions
Phi JH et al. 2010	-	-	-	-	-	NR	Bilateral
Lin JC et al. 2012	+	-	NR	+	NR	NR	Bilateral
Vialatte de Pemille C et al. 2016	+	-	NR	NR	NR	NR	Multiple lesions
Wei X-H et al. 2016	+	+	-	+	NR	NR	CA, multiple lesions
	NR	+	-	+	NR	Yes	CA, multiple lesions
	+	-	-	+	NR	Yes	CA, multiple lesions
	+	-	-	+	NR	NR	CA, multiple lesions
	+	+	-	+	NR	NR	Multiple lesions
Woo PYM et al. 2017	NR	+	+	+	NR	Yes	Early CA
Our case, 2021	+	+ *minimal*	-	+	+	Patchy	None
Keywords: NR: Not reported; DR: Diffusion restriction; CA: cerebral atrophy.							

Table 3. Treatment protocols and outcome of adult patients with primary basal ganglia germinoma

Source	SBB	Surgery	XRT					CTX	Outcome	Recur-rence
			Type	Total (Gy)	Fractions	Duration (weeks)	Boost (Gy/Fractio-ns/weeks)			
Elizabeth J et al. 2002	No	TR	Yes (Type NR)	NR	NR	NR	NR	Yes	Minimal improvement	No

Sonoda Y et al. 2008	Yes	No	LB	60	NR	NR	NR	Yes	Partial response	No
	Yes	No	No	-	-	-	-	Yes	Complete response	Yes
	Yes	No	No	-	-	-	-	Yes	Complete response	Yes
Phi JH et al. 2010	Yes	No	BG + WV	50.4 + 36	NR	NR	NR	Yes	Complete remission	No
Lin JC et al. 2012	Yes	No	CSRT	NR	NR	NR	NR	Yes	Complete resolution	No
Vialatte de Pemille C et al. 2016	Yes	No	CSRT	24	NR	NR	16/NR/NR	No	NR	NR
Woo PYM et al. 2017	No	NTR	CSRT	NR	NR	NR	NR	Yes	Complete resolution	No
Our case, 2021	Yes	No	WBRT	24	15	4	16/10/2	No	Mark improvement	No

Keywords: SBB: Stereotactic brain biopsy; TR: Total resection; LB: Local brain; BG: Basal ganglia; WV: Whole ventricle; NTR: Near-total resection; NR: Not reported; XRT: Radiation therapy; CSRT: Cerebrospinal radiation therapy; WBRT: Whole-brain radiation therapy; CTX: Chemotherapy.

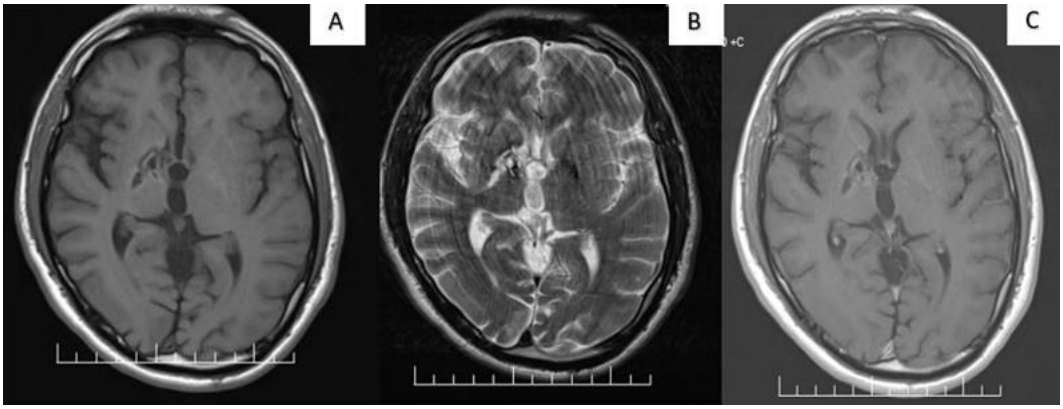

Figure 4. Cranial MRI of the previously treated basal ganglia germinoma at the last follow-up demonstrates stable disease with surrounding gliosis and post-radiation changes with secondary ex-vacuo dilation of the ipsilateral frontal horn of the lateral ventricle in T1 and T2-weighted images (A **& B**). No new lesion was detected in the post-contrast T1-weighted image (**C**).

Presenting symptoms included hemiparesis (71.4%), hypokinesia (14.2%), psychiatric symptoms (14.2%), diabetes insipidus (14.2%), headache (7.14), and speech difficulty (7.41%). Signs and symptoms of increased intracranial pressure such as headache, vomiting, papilledema, dysphagia, and sixth cranial nerve palsy were found in two patients at the initial presentation. Diabetes insipidus due to the coexisting suprasellar lesion was evident in two patients. At the onset of symptoms, patients seek medical attention after a median of 9.3 months (range: two weeks to two years). Serum AFP and HCG were measured in (13/14) cases. Elevation of serum AFP and HCG was detected in one patient and two patients, respectively. CSF testing for AFP and HCG was not routinely performed.

In all patients, cranial MRI was required for radiological diagnosis (Table. 2). Eight patients had multiple lesions - in the internal capsule (4 cases), thalamus (3 cases), frontal lobe (2 cases), septum pellucidum (1 case), pineal (1 case), suprasellar (2 cases), corpus callosum (1 case), frontotemporal gyri (1 case) regions, as well as the basal ganglia. In five individuals, the initial study revealed ipsilateral cerebral hemiatrophy, indicating wallerian degeneration. The patterns seen in the MRI were varied and were related to the duration of the disease before admission. The MRI patterns ranged

from a subtle patchy lesion seen in the T2-weighted sequence with no contrast enhancement to a large lesion with a mass effect and vivid contrast enhancement. Some BGGs displayed hemorrhagic and cystic components or calcification. Hydrocephalus was evident in four cases.

Reported therapeutic strategies are outlined in (Table. 3). SBB was performed in seven cases and craniotomy in two (reported 1 Transylvanian approach) patients. Postoperative imaging in craniotomy patients revealed one complete resection and one near-total resection. Seven patients received XRT (3 craniospinal, 1 whole-brain, 1 basal ganglia with whole-ventricle, and 1 local brain technique). Seven cases received platinum-based antineoplastic regimens to mitigate XRT toxicity. However, chemotherapy alone did not seem to improve survival.

Follow-up imaging (> 3 months) was available for eight patients. While most reported marked improvement in symptoms, some reported poor neurological outcomes. In general, all treated tumors by XRT tend to show no recurrence on subsequent imaging or progression to the contralateral side.

Our patient, for example, is notable for being: 1. diagnosed in an adult patient, 2. diagnosed in a middle Eastern patient, 3. located in the basal ganglia, 4. not associated with ipsilateral cerebral atrophy, and 5. successfully managed with a minimal treatment strategy, 6. showed no recurrence during the follow-up period. As far as we know, such a case has never been described before.

Conclusion

BGGs are rare entities, and a high degree of suspicion is needed for their diagnosis, especially in young adults with hemiparesis and a heterogeneous basal ganglia lesion on cranial MRI. Early detection of such lesions is critical, as a delay in intervention may result in poor neurological recovery. SBB followed by WBRT seems to be a minimal and safer treatment strategy for managing such lesions.

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A case of sellar epidermoid tumour with haemorrhage

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ABSTRACT

Introduction: Intracranial epidermoid cysts are congenital inclusion tumours. Cerebellopontine angle and parasellar locations are the common locations. This is a report of an intrasellar epidermoid cyst with haemorrhage, which is rare.

Case report: A 70-year-old female presented with bifrontal headache, vertigo, and nasal discharge. Contrast-enhanced Magnetic resonance imaging [MRI] showed heterogeneously enhancing lesion in sella turcica. Internal hemorrhagic foci were seen. Computed tomography [CT] scan showed a slightly hyperdense tumour of sella. Transnasal transsphenoidal excision was done. Hemorrhagic and colloid material came out. Histopathological examination showed cyst lined by stratified squamous epithelium with keratohyalin granules and keratin flakes, suggestive of an epidermoid cyst.

Discussion: Usually epidermoid cyst is hypodense in CT scan. But hyperdensity can occur due to calcification of keratinized debris, increased protein content, and recurrent haemorrhage. Enhancement with gadolinium in MRI is mild and in cyst wall. Haemorrhage and enhancement are probably due to foreign body granulation tissue developing from leakage.

Keywords
sella turcica, epidermoid cyst, haemorrhage, microsurgery, endoscopy

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INTRODUCTION

Intracranial epidermoid cysts are congenital inclusion tumors arising from the remnants of epithelial tissue during the closure of neural tube [1,2]. They constitute 0.8-1.2% of intracranial tumors. Cerebellopontine angle is the most common location. But they can be seen in parasellar, suprasellar, middle fossa, and diploic locations. Intrasellar location is rare. MacCarty et al. reported four cases of sellar epidermoid with suprasellar or parasellar extension [3].

CASE REPORT

A 70-year-old female presented with bifrontal headache, vertigo, and nasal discharge. She had systemic hypertension, diabetes mellitus, and dyslipidemia. Neurological examination was noncontributory. Visual fields were normal. Pupillary reaction was normal. There was mild ataxia on walking.

Contrast enhanced Magnetic resonance imaging [MRI] showed heterogenously enhancing lesion in sella turcica [Fig.1]. Coronal image showed capsular enhancement and thin sellar floor. Internal

hemorrhagic foci were seen. There was no compression on optic chiasm. Computed tomography [CT] scan showed slightly hyperdense tumor of sella [Fig. 2]. Septation was seen in right half of sphenoid sinus.

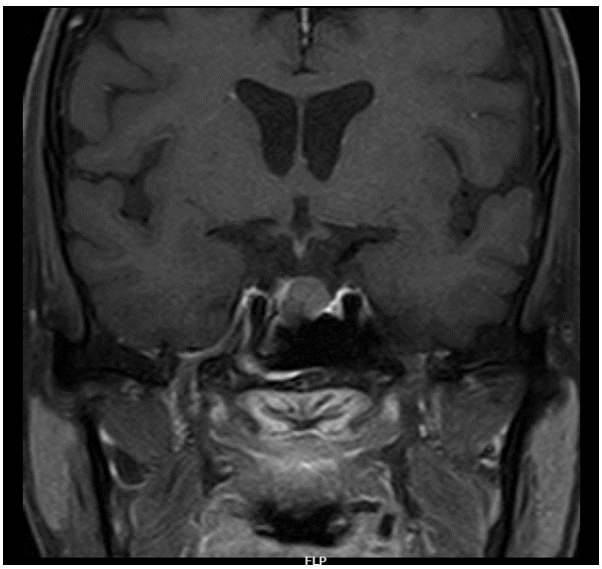

Figure 1. MRI coronalimage showing heterogeneous tumor with capsular enhancement and thin sellarfloor

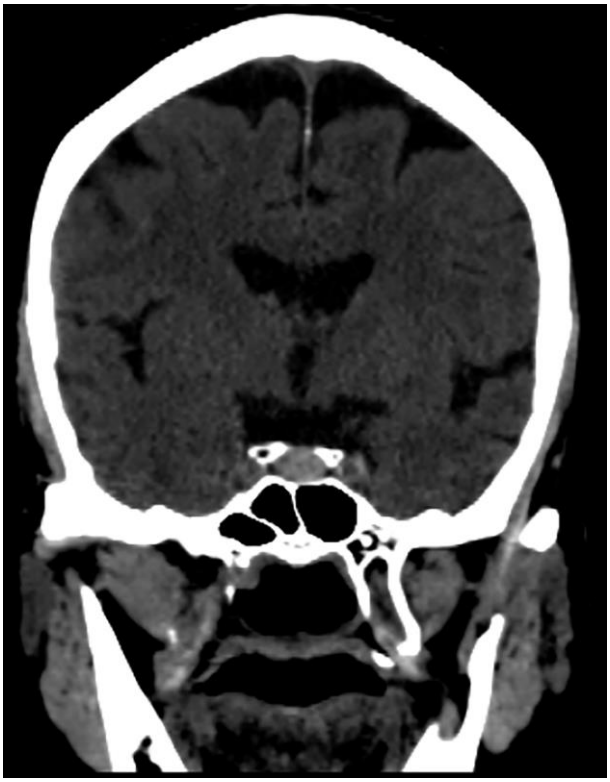

Figure 2. CT scan showing hyperdense tumor of sella

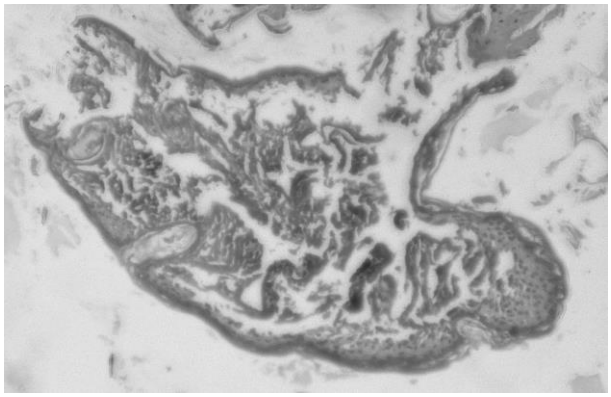

Figure 3. Cyst linedby stratified squamous epithelium and hemorrhage with inflammatory cells

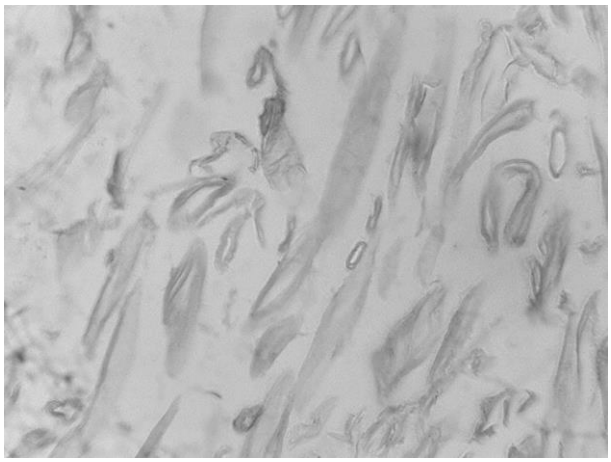

Figure 4. High powerview of keratin flakes

Transnasal transsphenoidal excision was done. Left side was chosen because of sphenoid septation on right side. Left sphenoidal ostium was found following middle turbinate. Ostium was enlarged. Dura was opened and piecemeal decompression was done. Hemorrhagic and colloid material came out. Decompression was done till increased urine output was noticed. Fat pad was used for closing the sphenoid.

She recovered clinically. Hourly urine output was in normal range. Hormonal levels such as thyroid function tests, cortisol, and prolactin were within normal limits. Postoperative CT scan showed gross total removal. Initial squash cytology showed fibrocollagenous fragments, cells with round nuclei and eosinophilic cytoplasm, and red blood cells. This was suggestive of inflammatory tissue with hemorrhage. Histopathological examination showed cyst lined by stratified squamous epithelium with

keratohyaline granules and keratin flakes [Fig. 3, and 4]. Immunohistochemistry was positive for p63, suggestive of squamous differentiation. The features are of an epidermoid cyst.

Discussion

The clinical presentations of sellar epidermoid tumors are frontal headache, bitemporal hemianopia, visual loss, diplopia, amenorrhea, galactorrhea, diabetes insipidus, failure of sexual development, and endocrine disturbances [2,3,4,5]. Presentation with features of pituitary apoplexy also is reported6.

The usual finding in CT scan is a hypodense lesion, due to lipid and cholesterol content [1,2]. But hyperdensity can occur due to calcification of keratinized debris, increased protein content, and recurrent hemorrhage. Epidermoid tumor appears hypo-, iso- or hyper-intense on T1-weighted MRI7. On T2-weighted imaging, it appears hyper-intense. Heterogeneous appearance also is described. Diffusion weighted imaging of MRI shows a restricted pattern as hyperintensity. The cyst appears insinuating into nearby structures. Enhancement with gadolinium is mild and in cyst wall. Differential diagnoses are pituitary adenoma, craniopharyngioma, arachnoid cyst, Rathke's cleft cyst, and dermoid cyst. Pituitary adenomas are usually solid and has homogeneous enhancement8. Craniopharyngioma has calcifications in CT and mixed solid and cystic appearances in MRI7. Arachnoid cyst is isointense to cerebrospinal fluid(CSF) in all sequences. Dermoid cyst resembles fat and appear hyperintense in T1-weighted image. Because of avascular nature, hemorrhage is rare in epidermoid cyst9. Hemorrhage and enhancement are probably due to foreign body granulation tissue developing from leakage.

Surgery is by endonasal transsphenoidal microsurgery or by endoscopic endonasal transsphenoidal approach [2,3,5,6]. Often, the adherence of capsule with neurovascular structures prevented complete removal of the cyst wall. Modification of endoscopic endonasal approach according to the extent of the tumor, can help in gross total removal2. Total removal prevents recurrence with malignant change in future.

On histopathological examination, epidermoid cyst is lined by keratinizing stratified squamous epithelium10. Keratohyaline granules are basophilic granules in the cytoplasm of granular cells. Keratin flakes also can be seen. The cyst is filled with keratin debris, lipid, and water. Immunohistochemical positivity for p63 is useful in confirming squamous differentiation [11]. Dermoid cyst is lined by simple stratified squamous epithelium1. Rathke's cleft cyst is lined by simple cuboidal or columnar epithelium with goblet cells. Carcinoma in situ can occur in residual epidermoid cyst as a sequelae of inflammatory response to recurrent rupture and foreign body reaction [1,2].

The sellar tumors which were reported to present with hemorrhage are pituitary adenomas, craniopharyngiomas, epidermoid cyst, undifferentiated sarcoma, tuberculoma, atypical teratoid/rhabdoid tumor, and primary melanocytic tumor [12,13,14,15,16]. So these differential diagnoses also should be considered in case of a hemorrhagic sellar tumor.

Conclusion

This is a report of an intrasellar epidermoid cyst with hemorrhage, which is rare. CT scan showed hyperdensity due to hemorrhage. There was enhancement with contrast in MRI. Hemorrhage and enhancement occur due to inflammatory tissue. Transsphenoidal microsurgery and endoscopic endonasal approach are the preferred surgical methods. Total resection is necessary to prevent malignant transformation.

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Hyperbaric oxygen therapy. Application in traumatic brain injury

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Keywords
hyperbaric oxygenation, traumatic brain injuries, brain hypoxia-ischemia, inflammation, neuroprotection

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ABSTRACT

The extent and progression of neurological impairment in traumatic brain injury depend significantly on the area of perilesional gloom, where neuronal apoptosis occurs. Inhibition of apoptosis becomes a therapeutic strategy to preserve brain tissue and promote functional recovery. Hyperbaric oxygen therapy is a treatment by which 100% oxygen is administered, with the aim of achieving a higher pressure than atmospheric pressure at sea level, to decrease ischemia and intensity of inflammatory processes triggered, compromising the viability of the tissues. For mild traumatic brain injury, studies indicate that hyperbaric oxygen therapy is no better than sham treatment. For acute treatment of moderate to severe traumatic brain injury, although the methodology is questionable in certain studies due to the complexity of the brain injury, hyperbaric oxygen therapy has been shown to be beneficial as a relatively safe adjunctive therapy. The objective of this review is to discuss aspects related to the pathophysiology of traumatic brain injury, the mechanism of action of hyperbaric oxygen therapy, and correlate these results with the use of this therapy in the prevention of neuronal injury, supported by original studies reported in the scientific literature

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Introduction

Traumatic Brain Injury (TBI) is generated when there is a sudden acceleration-deceleration process inside the skull caused by all kinds of external forces, among which traffic accident is one of the most common causes [1]. It is considered a major global health problem, being one of the main causes of death and disability, entailing functional, social and economic consequences [2,3] Brain injury in cranial trauma is triggered in two stages, the first occurs immediately after the initial mechanical impact, and in most patients is terminated before admission to the medical institution, representing a permanent neuronal loss [1,4]. Subsequently, within hours, days, and sometimes even weeks, given the insufficient oxygen supply of the surrounding regions, biochemical and metabolic processes are generated that culminate in the apoptosis of neuronal cells [4].

Considering the fact that energy metabolism in the brain is based on aerobic processes, Hyperbaric Oxygen Therapy (HBOT) has been proposed in recent years as a neuroprotective strategy directed towards the containment of secondary processes, in addition to the preservation and reactivation of the penumbra area [5,6]. The objective of this review is to discuss aspects related to the pathophysiology of traumatic brain injury, the mechanism of action of hyperbaric oxygen therapy, and correlate these results with the use of this therapy in the prevention of neuronal injury, supported by original studies reported in the scientific literature.

How hyperbaric oxygen therapy works?

HBOT targets TBI-induced ischemia by exposing patients to an environment that exponentially increases the amount of O2 inspiration, producing hyperoxia in the plasma, and consequently, an accentuation of O2 supply for diffusion to brain tissue, where hypoxia can be decreased, and thus, prevent neuronal death [7,8]. For mild TBI, studies indicate that HBOT is no better than sham treatment [9]. For acute treatment of moderate to severe TBI, although the methodology is questionable in certain studies due to the complexity of the brain injury, HBOT has been shown to be beneficial as a relatively safe adjunctive therapy [7,9].

The therapeutic effects in moderate TBI, are attributed to several pathophysiological mechanisms, including: increased arterial oxygen pressure and oxygen levels in brain tissue, increased diffusion velocity and effective oxygen diffusion distance, reduction of brain tissue edema and intracranial pressure, neuronal protection from ischemic death by acceleration of collateral circulation, stimulation of angiogenesis and neurogenesis accompanied by repair of injured microcirculation, and prevention of microthrombus formation [7,8,10]. Other studies have shown that repetitive application of HBOT after moderate TBI attenuates reactive astrogliosis and glial scarring, in addition to decreasing the expression of inflammatory mediators [11]. Additionally, research in murine models with moderate TBI induced and treated with HBOT showed improvement in spatial learning and memory [7,12].

During the acute phase of severe TBI, the metabolic demands of the brain increase, but O2 delivery to the brain is limited due to a reduction in cerebral blood flow, as well as diffusion barriers caused by capillary endothelial edema [7,8,13]. This O2 deficiency causes failures in cellular respiration and other aerobic biochemical events, activating the anaerobic machinery, with consequent depletion of cellular energy (ATP), and finally, cell death [8]. The crisis resulting from inadequate O2 supply produces electrolyte imbalance, secondary to the lack of energy for the normal function of the Na+/K+ ATPase pump within the cells of the nervous system [8,14,15]. This imbalance leads to increased calcium influx, resulting in considerable release of excitatory neurotransmitters, and further disruption of mitochondrial metabolism, resulting in excessive accumulation of free radicals and as the neuroinflammatory response continues, apoptosis-mediated proteins initiate the process of cell death [8,16].

Mechanism of neuroprotection

Most of the damage following TBI occurs due to a secondary process. This includes cell death, oxidative stress, neuroinflammation and glutamate excitotoxicity [14,15,17]. Baratz-Goldstein et al [7]. showed how immediate and delayed HBOT, can ameliorate the elevation of reactive astrocytes seen after moderate TBI, successfully preventing the demyelination process [7]. In addition, it has been reported that following TBI, there is a decrease in previously elevated inflammatory processes, such as inhibition of caspase 3, TNF-α expression, NF-κB,

upregulated microglia, and elevation of IL-10 [13,18,19]. Based on the above, it can be said that HBOT exhibits multiple mechanisms of neuroprotection (Table 1). Considering the above, when additional O2 is available for diffusion through the capillary endothelium, anaerobic metabolism is converted back to aerobic metabolism, allowing mitochondria to restore depleted cellular energy [8,16].

The upregulation of Nrf2 was suggested as one of the mechanisms that help protect neuronal loss [18]. Yang et al [19]. evaluated HBOT treatment following intracerebral hemorrhage in murine models, finding that this intervention upregulated microglia characteristics, potentially decreasing diminished neuronal loss [19].

Another explanation for the neuroprotective qualities of HBOT in moderate TBI is related to changes in cerebral blood flow [7,8]. HBOT stimulates vasoconstriction, leading to a decrease in cerebral blood flow. This mechanism promotes neuroprotection as it reduces trauma-induced intracranial pressure and cerebral edema, thus improving cognitive functions [8,16]. This effect on cerebral blood flow after the use of HBOT is mainly attributed to a decrease in the concentration of nitric oxide in the brain, as well as to an inclination in the production of reactive oxygen species [20]. Following this treatment, dependent improvements in general motor function, cognitive and behavioral tests, neurological function and locomotor coordination have been observed [8].

Proteomic studies, have observed that in acute TBI there is a decrease in the levels of pAkt/Akt, pGSK3β/GSK3β, and β-catenin, which facilitates neuronal apoptosis. He et al [13]. demonstrated increase in these proteins after instituting HBOT [13].

Table 1. Neuroprotective effects of hyperbaric oxygen therapy

Reduces inflammation	Induces Bcl-2 and Bcl-xl, reduces Cas-3
Inhibits neutrophil adhesion to endothelial cells	Inhibits permeability of mPTP
Decreases IL-8, TNF-α and MMP-9; increases IL-10	Decreases endothelin levels and regulates blood flow
Inhibits TLR4 and NF-κB expression	Reduces intracranial pressure
Inhibits apoptosis	Promotes neurogenesis and angiogenesis.
Increases PaO2 of brain tissue.	Enhances Nrf2 and HO-1
Preserves tissue metabolism	

Importance

Neuroinflammation is well established as a key secondary injury mechanism after TBI, and has long been considered to contribute to sustained damage after brain injury [5,21]. With HBOT, the effect of high pressure, increased solubility and O2 diffusion characters are expected to improve oxygenation, modulation of inflammation and immune function, as well as promote angiogenesis [1].

Comprehensive management of traumatic brain injury generally aims at maintaining oxygenation and perfusion, so hyperbaric oxygen has been proposed as a complementary therapy for TBI, both for the preservation of the functional capacity of the affected person, as well as for the increase in survival rate [2,6,9].

Efficacy

The prognosis of traumatic brain injury clearly depends on the cell death and survival processes occurring within the injured tissues, so neuroprotective therapies aim to improve function within the remaining viable perilesional brain tissue [16].

Increased oxygen supply under hyperbaric conditions facilitates oxygen diffusion into the injured tissue, improving cellular energy metabolism, which attenuates cell signaling and cytosolic ischemic cascades, thereby reducing programmed cell death and subsequent necrosis [22]. Many studies have consistently corroborated that HBOT compared with standard care significantly improves markers of oxidative metabolism in the relatively uninjured brain [22].

HBOT may also counteract vasodilation of capillaries within hypoxic tissues, thus minimizing extravascular fluid accumulation, reducing cerebral vasogenic edema and intracranial pressure [16]. This is why it has been postulated that HBOT stimulates the restoration of antioxidant, angiogenic, neurogenic and anti-inflammatory gene expression. This translates into greater neurological recovery, as evidenced by the improvement of the Glasgow score [5,13,23]. To obtain the benefits described above, this therapy should be started within the first hours, and several sessions should be established [5].

Generalities

HBOT is a therapeutic option that consists in the inhalation of 100% oxygen, in a sealed hermetic chamber that increases the pressure to more than one absolute atmosphere (ATA); (ATA=101.3kPa) [1,3,4,5,16,24]. Generally, a pressurization of 1.5-3.0 ATA is used for one or more times a day, for one or two hours [25]. This ensures the administration of a higher partial pressure of oxygen in the blood, improving mitochondrial metabolism and tissue oxygenation [5,6,16]. The benefits found in this therapy have allowed recommending its use in a large number of pathological conditions (Table 2), which is increasing over the years.

HBOT allows hemoglobin to be saturated to 100% and the volume of oxygen fraction bound to plasma to be elevated [4,16]. The latter can be used more easily than that bound to hemoglobin, so that oxygen is supplied even in conditions with erythrocyte deficit; therefore, HBOT causes an increase in oxygen transport in the blood, increasing the force of oxygen diffusion in the tissues [16].

Table 2. Indications for hyperbaric oxygen therapy

Traumatic brain injury [6]	**Cerebral palsy**
Stroke [6]	Decompression sickness [6,16]
Anoxic brain injury [6]	Carbon monoxide poisoning
Cerebral edema*[7]	Minimization of tissue damage induced by radiotherapy [4,16]
Ictus [7]	Enhancing skin grafts [4,16]
Spinal cord injury*[7]	Autism* [16]
Acute central retinal artery insufficiency*[7]	Multiple sclerosis* [16]
Traumatic ischemia [7]	Air or gas embolism [4]
Gas gangrene [4]	Compartment syndrome [4]
Intracranial abscess [4]	Osteomyelitis [4]
Burns [4]	Wounds [4]

Non-approved use

HBOT has been in use for more than 50 years, but its application in the treatment of traumatic brain injury has been performed since the early 1960s [7]. In 1966, the first study reporting the neuroprotective effect of this therapy in rats was published by Coe & Hayes [26]. Almost immediately, Dunn & Lawson [27]. demonstrated reduced mortality in a canine model with cerebral contusion, and since then, studies on the effect of HBOT on blood flow, cerebral edema and intracranial pressure have been carried out.

Conclusion

Traumatic brain injury is a common health problem that causes permanent sequelae and considerably decreases the functional capacity of the sufferer. Unfortunately, to date there is no treatment or intervention that fully ensures neurological functionality. Hyperbaric oxygen therapy is a therapeutic option with the potential to decrease neuronal death by improving oxygen supply to the injured brain, thus controlling inflammation and apoptotic processes. The effectiveness of the intervention, however, depends on prompt medical attention and constant monitoring of hemodynamic and neurological variables.

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Epidemiological, demographic and clinical profile of traumatic brain injury patients. A prospective analysis at a level one trauma centre in northern part of India

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ABSTRACT

Context: Traumatic brain injury is a major public health problem worldwide with increasing incidence and severity in developing countries**.** In India, it becomes a huge burden on society with a lack of proper preventive measures, public awareness, traffic sense and pre-hospital care. Therefore, we studied the epidemiological profile and factors predicting outcome.

Aims: To study the epidemiological, demographic profile of TBI patients to help to improve the healthcare facilities.

Setting and design: It is an observational prospective study.

Methods and materials: Overall 2134 patients with TBI were enrolled. The data was collected according to the predesigned proforma. The demographic, epidemiological, clinical variables were analysed to determine the current trends and outcomes.

Result: The male: female ratio was 2.21:1 with most cases from the age group of 21-30 years (29.42%). RTA was the mode of injury in 64.48% of cases. Overall mortality was 10.91%. Overall descriptive data was suggestive of poor outcome in old patients, referred cases, acute SDH and brainstem lesions, hypoxic and hypotensive patients, associated injuries, pre-existing disease and with higher Rotterdam and ISS scores.

Conclusion: The outcome is dependent on factors like geographical, demographic, pre-hospital, and patient-related. With knowledge about the causes, patterns, and distribution the prognosis of TBI patients can be improved.

INTRODUCTION

Traumatic head injury is one of the common causes of mortality and morbidity in the world. It has been estimated that, annually around 60-70 million people are affected globally. In India around 1.4-2 million

persons are affected and 1 million loose their life every year . A study at a tertiary care institute has reported that the occurrence of TBI is approximately 42.5% in rural and 57.5% in urban area .1 The incidence of head injury is increasing mostly due to excessive use of motor vehicles in low and middle income countries (LMIC) .2-3 It affects patients of all age groups with young aged persons between 20-40 yr being the majority . Males are more commonly affected than females . The most common cause is RTA (around 60%) followed by falls (20-30%), assault (10%) and sports injury(10%) .4 India is leading the world in deaths due to road accidents . Neurological status at the time of presentation is the most important prognostic factor with others being the age , CT finding , associated injury , vital parameters , mode of injury , and others . The outcome is dependent on severity of primary injury and is a reflection of secondary insult like hypoxia , hypotension , raised ICP , cerebral ischemia. So early recognition and prevention of secondary insult results improvement in neurological status . With detailed knowledge of the clinical and demographic profile of TBI , we can provide the appropriate management and thus get the desired favourable outcome.

The aim of this study is to determine epidemiology and demography of TBI , clinical status, severity of head injury , associated comorbid conditions and the final outcome . To our knowledge, this is one of the largest data registry in the world and certainly the largest in India.

Materials and methods

This study was done at SMS medical college and hospital , Jaipur which is a tertiary care level 1 trauma center in northwestern part of India . It was conducted between april 2017 to march 2019 . A total no of 2134 patients were inducted into the study based on the inclusion criteria :1) Clinical diagnosis of TBI , 2) Clinical indication for CT scan and 3) informed consent obtained according to local and national requirements . The ethical clearance was obtained from the institutes ethical committee.

This was a prospective observational study . The data was collected and patients were followed upto final outcome . Data obtained was entered into a proforma . Data that was collected included demographic parameters , mode of injury ,GCS on admission and discharge ,associated findings , CT findings ,treatment given , duration of hospital and ICU stay and outcome including Glasgow outcome scale .Injury severity and Rotterdam score were calculated for every patient. Based on GCS ,TBI cases were graded as mild (13-15) , moderate (9-12) and severe (<8) and Glasgow Outcome Scale (GOS) was used to know the final outcome.

The data collected was analyzed and compiled with multiple variables showing current trends and demographic profile.

Results

A total no of 2134 patients were inducted into the study . Majority of the cases were from rural parts of jaipur . The no of cases from urban and rural areas were 45.82% and 54.17% respectively.

Age and Sex

The total no of male and female were 68.89% and 31.11% respectively . Most patients affected were in the age group of 21–30 years (29.42% cases) followed by 31–40 years (22.68% cases) (Table 1) . The mean age of patients who survived and died was 33.24 + 14.5 and 41.36 + 17.8 years respectively . The outcome was best in patients < 20 years of age and worst in patients >60 years age with 13.61 % of overall deaths.

Mode of injury

Figure 1. Distribution on basis of mode of injury

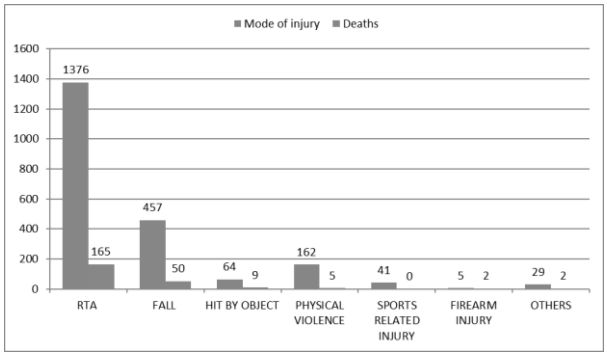

Table 1. Distribution of age adjusted mode of Injury and outcome

Age In yrs n (%)	Total cases n=2134	Mode of Injury RTA	Fall	Assault	Sports	others	Deaths n (%) Injury
0-10	191 (8.95)	41(21.47)	130(68.06)	nil	12(6.28)	8(4.19)	8(4.18)

11-20	233(10.91)	128(54.93)	54(23.17)	15(6.43)	24(10.30)	12(5.15) 12(5.15)
21-30	628(29.42)	511(81.36)	43(6.85)	29(4.61)	5(0.79)	40(6.36) 74(11.78)
31-40	484(22.68)	357(73.76)	69(14.26)	34(7.02)	nil	24(4.96) 56(11.57)
41-50	232(10.87)	144(62.06)	54(23.27)	26(11.20)	nil	8(3.44) 40(17.24)
51-60	153(7.16)	71(46.41)	35(22.87)	45(29.41)	nil	2(1.31) 14 (9.15)
>60	213(9.98)	124(58.21)	72(33.80)	13(6.10)	nil	4(1.88) 29(13.61)
Total	2134	1376(64.48)	457(21.41)	162(7.59)	41(1.92)	98(4.59) 233(10.91)

Severity of Injury

49.10% had mild, 31.02% had moderate and 19.86 % severe injury . Severe injury was more common with acute SDH, contusions , and brainstem lesions . 39.38% patients having severe injury died.

Clinical and radiological findings

CT finding;

The most common CT finding was multiple lesion with 60.82% cases followed by normal CT finding in 36.18% cases and acute SDH in 32.7% cases . Other findings were Skull bone fracture (34.3%), contusion (30.13%), acute EDH (24.5%), SAH (17.29%), ICH (11.57%), diffuse axonal injury (9.93) ,brainstem injury (8.76%), and chronic SDH (3.56%) cases (Table 2). Mortality with acute SDH was maximum in 20.99% cases.

Table 2. Description of Various CT findings with severity of injury and fatal outcome.

CT finding	Total no of cases no(%)n=2134	Severity of injury (GCS on admission) no(%)			Deaths no(%)
		mild	moderate	severe	
Normal CT	772 (36.18)	678(87.82)	86(11.13)	8(1.03)	13(1.68)
Acute EDH	523 (24.50)	381(72.84)	78(14.91)	64(12.23)	41(7.84)
Acute SDH	698 (32.70)	154(22.06)	299(42.83)	245(35.10)	176(25.21)
Contusion	643 (30.13)	218(33.90)	223(34.68)	202(31.41)	135(20.99)
ICH	247 (11.57)	116(46.96)	76(30.76)	55(22.26)	29(11.74)
SAH	369 (17.29)	265(71.81)	54(14.63)	50(13.55)	43(11.65)
Brainstem Lesion	187 (8.76)	32 (17.11)	94(50.26)	61(32.62)	19(10.16)
Skull bone fracture	732 (36.18)	465(63.52)	211(28.82)	56(7.65)	29(3.96)
Multiple lesion	1298(60.82)	708(54.54)	356(27.42)	234(18.03)	167(12.86)

Loss of consciousness was maximally associated with acute SDH , ICH , and brainstem lesions whereas normal CT and contusion mostly presented with history of headache. Hypotension and hypoxia was mostly associated with brainstem lesions with 34.75% and 40.55% incidence respectively. Pupillary reactivity was absent in patients with mass effect , uncal herniation and brainstem lesions. Seizure was seen in association with contusion in most (36.39%) cases. (Table 3)

Table 3. Association of CT finding with clinical spectrum

CT finding	LOC	SBP(mmHg)		SPO_2%	Pupil		Seizure	
	No	Yes	<90	>90	<90	>90	R	NR	No	Yes
										<5min	>5min
Acute EDH	220(42.06)	134(23.70)	169(32.31)	29(5.54)	494(94.45)	34(6.50)	489(93.49)	364(69.59)	159(30.40)	458(87.57)	65(12.42)
Acute SDH	145(20.77)	114(16.33)	439(62.89)	72(10.31)	626(89.68)	143(20.48)	555(79.51)	510(73.06)	188(26.93)	541(77.50)	157(22.49)
ICH	78(31.57)	69(27.94)	100(40.48)	34(13.76)	213(86.23)	57(23.07)	190(76.92)	169(68.42)	78(31.57)	202(81.78)	45(18.22)
Contusion	389(60.49)	90(13.99)	164(25.50)	62(9.64)	581(90.35)	65(10.10)	578(89.89)	501(77.91)	142(22.08)	409(63.60)	234(36.39)
SAH	102(27.64)	143(38.75)	124(33.60)	32(8.67)	337(91.32)	54(14.63)	315(85.36)	278(75.33)	91(24.66)	338(91.59)	31(8.40)
Brainstem Lesion	21(11.22)	34(18.18)	132(70.58)	65(34.75)	122(65.24)	76(40.55)	111(59.35)	62(33.15)	125(66.84)	175(93.58)	12(6.41)
Skull fracture	323(44.12)	132(18.03)	277(37.84)	12(1.63)	720(98.36)	76(10.38)	656(89.62)	701(95.76)	31(4.23)	709(96.85)	23(3.14)
Multiple lesion	780(60.09)	326(25.11)	192(14.79)	102(7.85)	1196(92.14)	231(17.79)	1067(82.20)	976(75.19)	322(24.80)	1154(88.90)	144(11.09)

R-Reactive,NR-Non Reactive

Clinical features

Loss of consciousness was most the most common presentation in 81.77% cases with vomiting and ENT bleed being the next two in 73.94% and 52.62% cases respectively. Spinal injury was present in 0.98%

cases. The overall seizure incidence was 32.28%. (Table 4)

Associated injuries

Associated injuries were found in 21.23% cases with facial injury being the most common in 61.58% followed by orthopedic injury 56.07 %. Among these 453 cases , 77(16.99%) expired . Out of the total 77 patients expired with associated injury most common were with orthopedic injury 41.55% followed by chest injury 25.97 %.

Complications

Chest infection was seen in 21.39 % patients especially in patients in ICU and on ventilator support . Post operative wound infection was seen in 3.56 % patients . About 7.87 % patients had CSF leak and of which 48.80 % developed meningitis and 8.33% patients died . Hydrocephalus was seen in 4.59% cases and CSF diversion was performed in 85.71% of these cases . Post traumatic epilepsy was diagnosed in 2.10% cases.

Table 4. Distribution of symptoms, frequency of Associated injuries and various complications

Clinical presentation Total no of cases no (%) n=2134	Associated injury Total cases (%) n=453	Complications Total no of cases no (%)n=2134
LOC 1745(81.77)	Orthopedic injury 254(56.07)	Chest Infection 456(21.39)
Vomiting 1578(73.94)	Chest injury 123(27.15)	Hemiparesis 297(13.91)
ENT bleed 1123(52.62)	Facial inury 279 (61.58)	Cognitive deficit 245(11.48)
Headache 726(34.30)	Abdominal injury 65(14.34)	Meningitis 82(3.84)
Seizure 689(32.28)	Spinal injury 21(4.63)	CSF leak 168(7.87)
Hypoxia 339(15.88)		Pressure ulcer 230(10.78)
Hypotension 249(11.66)		Hydrocephalus 98(4.59)
Spinal injury 21(.98)		Epilepsy 45(2.10)
Associated injury 453(21.23)		Wound infection* 23(3.56)
		Facial palsy 356(16.68)

LOC-loss of consciousness, *Percentage of Wound infection was calculated from no of operated patients (n=645).

Management and Outcome
Management

645 cases were operated out of which 16.74% patients died (Table 7) . Burr hole was done for 11.16% cases, craniotomy in 64.34% , Decompressive craniectomy for 20.47% and skull base repair in 4.03% cases .The outcome was poor in patients with decompressive craniectomy and craniotomy With evacuation of SDH (Table 5). Patients managed in ICU were 612(28.67%) with 54.72% operated patients and 42.32% conservatively managed patients . Deaths in ICU was seen in 209(89.70% of all deaths) of which 136(38.52%) were of operated patients.

Table 5. Description of operative intervention pone

Total no of cases% Associated Injury Management Conservative Deaths Operated Deaths
Normal CT 772(36.18) 213(27.59) 772(100) 13(1.68) nil nil
Depressed Fracture 279(13.07) 127(45.51) 96(34.40) 6(6.25) 210(75.26) 12(5.71)
Acute EDH 523(24.5) 148(28.29) 296(56.59) 13(4.39) 227(43.40) 28(12.33)
Acute SDH 698(32.7) 176(25.21) 274(39.25) 45(16.42) 424(60.74) 131(30.89)
ICH 247(11.57) 54(21.86) 165(66.80) 16(9.69) 82(49.69) 13(15.85)
Contusion 643(30.13) 45(6.99) 322(50.07) 57(17.70) 321(49.92) 78(24.29)
Multiple Lesion 1298(60.82) 348(26.81) 762(58.70) 124(16.27) 536(41.29) 43(8.02)

The numbers here are more than 645 because of multiplicity of the lesions in same patient.

Table 6. Overall outcome of all patients

Total no of cases % n=2134
Discharged Total= 1901 (89.08) GOS 5 1406 (65.89) 4 215 (10.07) 3 184 (8.62) 2 96 (4.49)
Deaths (GOS 1) Total= 233 (10.91) In ICU 209 (89.70)* In Ward 24 (10.30)*

*Percentage of deaths in ICU and ward are calculated with respect to total no of deaths n=233

The overall mortality was 10.91%. The mean ISS and Rotterdam were 11.3 and 2.1 respectively which were much higher for deceased patients. Patients with non reacting pupil, hypotension, hypoxia, history of alcohol/drug intoxication, pre-existing systemic disease and severe head injury performed poorer than others. (Table 7)

Table 7. Various parameters showing total survivals and deaths

Total Survived % Died % n=2134
Age year (mean) 31.65± 15.1 33.24 ± 14.5 41.36 ± 17.8
Sex Male 1470(68.89) 1311(89.18) 159(10.81) Female 664(31.11) 590 (88.85) 74(11.14)
ISS mean 11.3(10.2-12.4) 10.6 (10.0-11.2) 26.5(23.2-29.7)
Rotterdam score mean 2.1(1.6-2.8) 1.8(1.5-2.1) 3.9(3.5-4.3)
GCS on admission mean 13.4(12.1-14.7) 12.0(11.0-13.0) 5.2(4.5-5.9)
Pupil Reactive 1591(74.83) 1534(96.41) 57(3.58) Non reactive 543(25.44) 367(67.59) 176(32.41)
Blood pressure (SBP) <90 mmHg 249(11.69) 156(62.65) 93(37.35) >90 mmHg 1885(88.33) 1745(92.57) 140(7.42)
SPO_2 <90 % 339(15.89) 216(63.71) 123(36.28) >90% 1795(84.11) 1685(93.87) 110(6.12)
Alcohol/drug intoxication 310(14.52) 243(78.38) 67(21.61)
Pre-existing systemic disease 163(7.63) 131(80.36) 32(19.63)
Management Conservative 1489(69.78) 1364 (91.60) 125(8.39) Operated 645(30.22) 537 (83.26) 108(16.74)
Severity of injury* Mild (13-15) 1048 (49.10) 1036(98.85) 12 (1.1) Moderate(9-12) 662 (31.02) 608(91.84) 54 (8.15) Severe (<8) 424 (19.86) 257(60.61) 167 (39.38)

ISS-injury severity score,SBP-systolic blood pressure

*grading done on the basis of GCS on admission and percentage calculated for each subgroup.

Discussion

Traumatic brain injury is a major global public health issue. There is continous rise in incidence in developing countries accounting to increased industrialization and surge in vehicles without improving the infrastructure. It is also associated with huge socioeconomic losses. Therefore complete understanding of its epidemiology and characteristics is necessary. There has always been some limitation in catering proper healthcare services to these patients due to lack of detailed good quality data , inadequate policies , proper guidelines, funding and public awareness .

In our study , the patients from urban and rural areas were comparable . This was probably due to lack of high quality trauma care in rural India. The mortality among these cases was 25.89%. More than 85% cases were of low or middle income groups . The males outnumbered the females with male:female ratio of 2.21:1. The mean age was 31.65± 5.1 years reflecting the increase in TBI incidence among young adults in similar view as in other studies .[4-5]

RTA was the most common mode of injury followed by falls. It was the commonest mode in young adults and males and was responsible for more severe injuries. This was because of less traffic sense, overspeeding , not using helmet or seatbelt and drunk driving . While in pediatric and geriatric population fall was more common. Gururaj et al[6] also studied about the increasing trend of falls among children. Whereas fall remains the most common cause in developed world and with aging Indian population it has now emerged as most frequent cause in older individuals.[7] Mechanism of injury is an significant predictor of outcome in TBI.[8-9]

Acute SDH was the most common single intracranial lesion detected in 32.70% cases and was also associated with poor outcome with mortality of 25.21%. Narwade N et al[10] reported SDH in 16.83% cases. The severity of TBI was more in patients with cortical lesions and these patients also had more incidence of seizures, LOC, pupillary non reactivity. CT findings such as mass effect, midline shift, presence of cerebral edema and SAH also effect outcome.[11-12] Around 30.22% patients were operated, mostly with severe or moderate TBI. According to McHugh et al, hypotension, hypoxia and hypothermia were also an independent risk factors for poor outcome.[13]Prehospital care also determines the favourable outcome with early diagnosis and effective intervention.[14] We see a lack of prehospital care in this part of India. In India due to lack of emergency services majority of the patients do not get appropriate management in early periods and major deaths that occur, do so within first 2 hours after injury.[15] Severe injury is directly related to poor outcome. In our study 39.38% patients with severe injury died. The severity can be graded on the basis of GCS on admission, ISS, and Rotterdam score. Previous studies have also shown them as the major

determinant.[16,18-19] The overall mortality was 10.91% while other studies by Row Bothom[17] and khursheed et al[18] had mortality of 17.55 and 27.8% respectively. Mortality was more with severe injuries, operated and patients shifted to ICU. The prognosis of these patients is mostly dependent upon the prehospital factors, neurological status (GCS) at the time of admission[19] , age , mechanism of injury , ISS [18], Rotterdam score[18] , associated injuries , presence of hypoxia and hypotension[13,9] .

All patients with severe injury do not have poor outcome. In our study also, 60.61% patients with severe injury survived and thus aggressive and timely management of all patients is necessary. Also early and appropriate care is a major factor in avoiding secondary injuries and death .[20] With detailed understanding of these factors , we can develop new plans, formulate better policies, increase public awareness. This all will lead to improvement in early diagnosis and management. The data of this study may be used for prognostication, formulation of hypothesis, developing prognostic models[21].

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Letter to the editor. Face-off between glioma and meningioma

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ABSTRACT

Gliomas are malignant, and intrinsic cerebral tumours may cause tumour-infiltrative oedema. Meningiomas are mostly benign, extrinsic cerebral tumours that do not infiltrate the surrounding parenchyma. Meningiomas may give rise to vasogenic oedema in the peritumoral tissue.[1] The radiological diagnosis of cerebral tumours may be non-conclusive on conventional MRI in few cases, and diagnosis must rely on histopathological analysis. [2] We report a case that has an atypical clinical presentation with nonconclusive MRI brain, and finally, histopathology confirmed the diagnosis.

Keywords
angiomatous meningioma, meningioma mimicking glioma, meningioma versus glioma, glioblastoma MRI, meningioma MRI

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CASE

A 56-year-old male patient presented with a nine months history of progressively increasing urinary frequency and urgency. The patient was seen by a urologist, and he operated for benign prostate hypertrophy, but his symptoms were not relieved. Then, he referred to a neurologist for further evaluation. After being admitted to the hospital, a detailed history and clinical examination were made. Higher mental function examination showed decreased attentiveness, vigilance, problem-solving and defect in motor programming with usual insight, judgment, language functions, and memory. Neurological examination showed bilateral grade III Papilledema, right spastic hemiparesis (MRC grade 4/5), and the right plantar response was extensor. MRI brain was suggestive of a large SOL with the solid cystic component is noted in the left frontal lobe, size 6.6x4.8x5.6 cm with flow voids of vessels within the lesion. There is significant surrounding oedema with a midline shift of 1.8 cm towards the right side with uncal herniation. Post-contrast sequences show moderate enhancement of solid component and wall enhancement in the cystic part. Thin enhancement is noted along the overlying dura in the left frontal lobe. Spectroscopic sequences show increased choline-creatine ratios in solid component of the lesion ranging from 2 to 4, suggestive of the neoplastic lesion. Radiological features that raise the possibility of glioma are significant perilesional oedema, hypervascularity of the tumour, difficulty to localise (intra versus extra-axial), multilobulated

looks aggressive in nature, heterogeneous enhancement and spectroscopy findings. The patient was operated on, doing well and histopathology report suggestive of Angiomatous Meningioma.

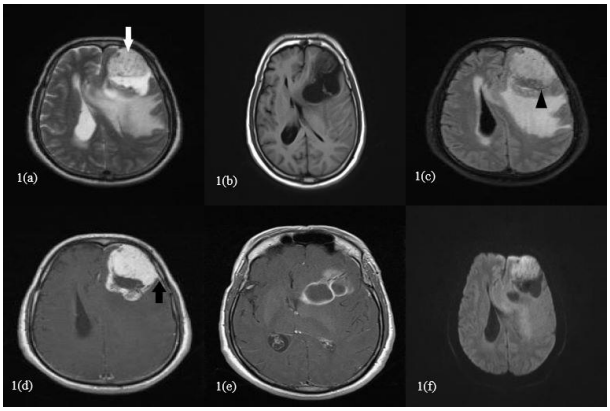

Figure 1. 1(a) T2 shows a hyperintense lesion with flow void signals of vessels inside the solid component (white arrow); 1(b) T1shows iso to hypointense lesion; 1(c) FLAIR shows CSF cleft sign (black arrowhead) and significant perilesional oedema; 1(d) T1 Contrast shows homogenous solid component enhancement with Dural Tail sign (black arrow); 1(e) T1 contrast shows cystic peripheral enhancement; 1(f) Diffusion shows mild restriction.

Discussion

Meningiomas are the commonest and around 20-30% of the primary tumour of the brain. However, Angiomatous Meningioma (AM) are very rare tumours.[3] The MRI characteristics features of AM are T1 iso to hypointense and T2 hyperintense with solid cystic components with significant perilesional oedema and flow void signals of vessels with homogenous enhancement commonly and dural tail sign. The higher brain oedema thought to be due to increased capillary permeability due to hypervascularity and vascular endothelial growth factor (VEGF) secretion.[4] The most typical site is cerebral convexity, and it is relatively more common in males and has a good prognosis.[4,5] There are few cases reported where glioblastoma can mimic meningioma on MRI with the dural tail sign (thickening and enhancement of the adjacent dura), CSF cleft sign (a perimeter of CSF between the tumour and brain parenchyma), and broad dural contact. Moreover, cerebral angiography can reveal tumour feeders commonly associated with meningioma.[6] AM is a highly vascular more than 50% vascular component, rare benign tumour with distinct radiological features.[7] To conclude, good clinical history and examination is the gold standard to localise the lesion and to avoid unnecessary iatrogenic burden to a patient and focused radiological examination will give a near accurate diagnosis.

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