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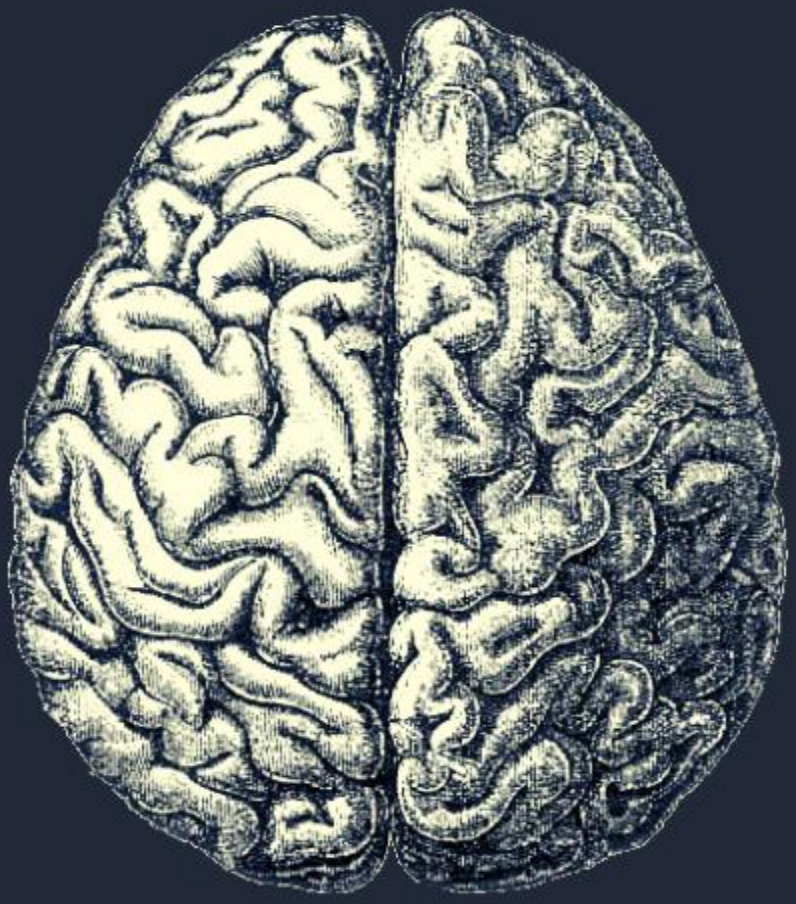

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150 years since the birth of Harvey Williams Cushing

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The first practitioner physicians of modern neurosurgery are Sir William Macewen, (1848-1939) with 21 surgical interventions, and Sir Victor Horsley (1857-1916) who performed 10 skull surgeries in 1886. (1)

During this time, the most important character in the development of neurosurgery was Harvey Cushing. The complex personality of Harvey Cushing becomes evident after reading the monumental biography written by John Fulton. Cushing was a genius with exemplary determination, working strength and an extraordinary perseverance. Like any genius, he was a difficult person, hard to collaborate with. These difficulties were minor in the light of his great achievements. (2)

It seems a sacrilege to criticize a human being who almost by himself abolished the terrible spectre of the "cerebral fungus" which was the common result of surgeries performed in that era.

Harvey Williams was born on April 8, 1869, in Cleveland, Ohio, and died on October 7, 1939 in New Haven, Connecticut. Between 1887 and 1891 he studied at Yale College, and continued his studies and graduated from the Harvard Medical School in 1895 *cum laude*. He studied for four years at Johns Hopkins Hospital in Baltimore under the famous surgeon W.S. Halsted. (1)

His collaboration with Halsted influenced Cushing's career. Halsted used local anaesthesia with cocaine in the vicinity of nerves. After he injected his own hand, he developed a cocaine addiction, which kept him away from his patients and the operating room. This allowed young Cushing to take on responsibilities closer to those of a senior surgeon, helping him advance in his career. (7)

Harvey Cushing also trained brain surgery techniques with Theodor Kocher in Bern and Charles Scott Sherrington in Liverpool. During his collaboration with Kocher, the "Cushing reflex" was described, which highlighted the relationship between blood pressure and intracranial pressure. He also studied intracranial pressure with Kocher. Together with Sherrington he had contributions to the cortical localization of brain centres (10).

Keywords
neurosurgery, Harvey Williams Cushing

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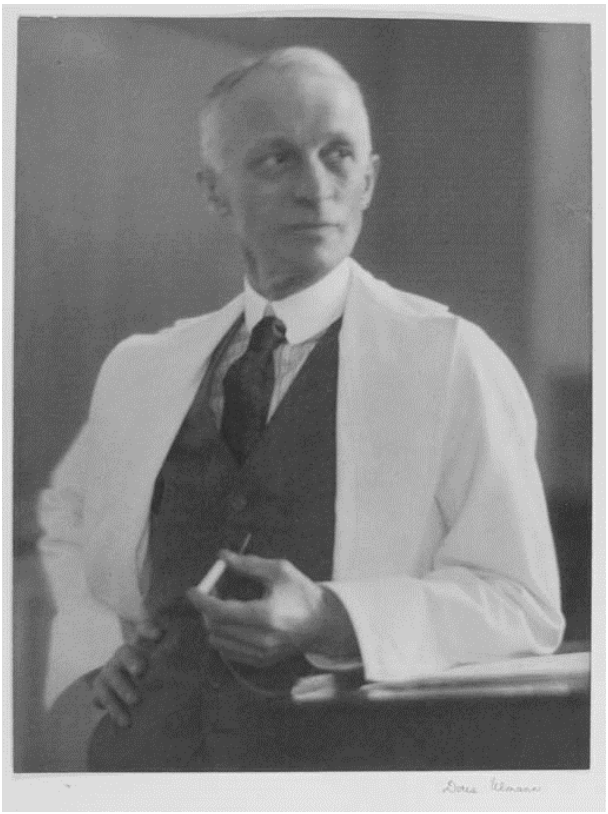
Cushing's best friend was Osler, the famous father of American internal medicine, and one of four professors who founded the Johns Hopkins Hospital. Cushing won the Pulitzer Prize in 1926 with his book "*Life of Sir William Osler*". He was a surgeon in the same hospital from 1902 to 1912. (3) In 1903 he obtained the title of Associate Professor in surgery. (6) Cushing managed neurological cases. In 1904 he presented "The Special Field of Neurological Surgery" with a great amount of enthusiasm in front of the Medical Academy in Cleveland. (1)

He became chief surgeon at Peter Bent Brigham Hospital in Boston and professor of surgery at Harvard Medical School. Cushing joined Yale in 1933. (3)

Cushing came from two generations of physicians. He married his childhood sweetheart, Katharine S. Crowell, on June 10, 1902 in Cleveland, Ohio. They had five children: two boys and three girls. One of his daughters married James Roosevelt, the son of the president of the United States in that time (Franklin D. Roosevelt). (4)

In his professional life Cushing was a "tough hombre". Nurses were sometimes reduced to tears and residents had nervous breakdowns due to Cushing's withering scorn and sarcasm. He demanded of his team work 98 hours per week. This took a toll on his wife and children. (5) One can see Cushing's character in how he behaved upon the death of his eldest son in a car accident at the age of



22. He received the news early in the morning. He notified his wife, and then he went to the hospital to perform scheduled surgeries. (1) He smoked a lot, drank very little, did not approve of alcohol in the family, disapproved of jazz, movies, fashion, telephones, friends, women in medicine, women

Harvey Cushing (Boston)

Thierry de Martel (Paris)
Paul Martin (Brussels)
Daniel Petit-Dutaillis (Paris)
Tracy Putnam (Boston)
Jean Morelle (Louvain)
John Fulton (New Haven)
William Welch (Baltimore)
Richard Meagher (Boston)
Francis Grant (Philadelphia)
Norman Dott (Edinburgh)
Frank Fremont-Smith (Boston)
Frédéric Bremer (Brussels)
Sir Charles Sherrington (Oxford)

Dimitri Bagdazar (Bucharest)
Percival Bailey (Chicago)
Georges Schaltenbrand (Hamburg)
Frederic Schreiber (Detroit)
Richard Light (Boston)
Herbert Olivecrona (Stockholm)
Arnold Klebs (Nyon)
Hugh Cairns (London)
Ignaz Oljenick (Amsterdam)
George Armitage (Leeds)
Gaston DeCoppet (Berne)
Franc Ingraham (Boston)
Geoffrey Jefferson (Manchester)
Otfrid Foerster (Breslau)

Wilder Penfield (Montreal)

smoking, and young men who did not attend classes. (5)

His patients knew another Cushing - wonderful and elegant manners, absolute dedication and empathy. (5)

He was of medium height, elegant, with a depressing smile and pleasant manners. He had charm and charisma, and he was proud of his own attire. He was a good speaker, but a terrible listener, with a tendency to interrogate his interlocutor. He used to follow his scientific ideas even if it meant sacrificing his friends (an example of this is Walter Dandy). His lack of diplomacy sometimes got him in serious trouble, such as the episode in 1917 in France when he was enrolled in the United States Army. Only the intervention of General Pershing saved him from court martial, following an incident that was rather a stupid verbal exchange. (2) After this episode, between 1917-1919, he was the director of the "US Army Base Hospital No 5". (6)

PROFESSIONAL ACTIVITY

When he entered neurosurgery, postoperative mortality was about 50%. His ability and surgical technique were able to decrease it to 10%. As mentioned above, he spearheaded the eradication of "cerebral fungus". (4)

Cushing's major interest was brain tumours. Between 1912 and 1938 he published 5 books, and he had a database of 2023 brain tumours. (7) In 1931, in Bern, at the first International Neurology Congress (August 31st - September 3rd), Harvey Cushing presented his memorable paper on 2000 brain tumour surgeries, a presentation which remained famous among neurologists and neurosurgeons. In the room there also were 25 of his pupils and at least 1,000 listeners. (7) During the presentation, no one remained outside the meeting room, says John Fulton. During this congress, Harvey Cushing organized a dinner to which he invited the great personalities who were there. The seating arrangement was personally guided by Harvey Cushing. From the image you can see that our countryman Dumitru Bagdasar was placed on the left of the great Cushing; this shows the appreciation and friendship felt by the American neurosurgeon for him.

Dr. Dumitru Bagdasar, subsequently university professor and minister of health in Romania (?)(1945-1946), specialised in neurosurgery at Peter Bent Brigham Hospital from 1927-1929 with his mentors Harvey Cushing and Percival Bailey. Prof. A. V. Ciurea (Bucharest) together with Dr. Pleș Horia (Timisoara) visited the Boston hospital. Two articles written by Dumitru Bagdasar during his work in the United States (Treatment of brain gummas and intracranial chordoblastomas) can be found up to this day.

There are several letters addressed by Harvey Cushing to the Romanian neurosurgeon mentioned in Dr. Dumitru Bagdasar's "Work and character" ("Muncă și caracter"). Cushing's affection for doctor Bagdasar is evident from these letters. Here is one of the letters:

Dear Bagdasar,

I wonder if I have answered you regarding the receiving of the delicious book that you have sent me on the art of Romanian peasants. If I did not, it was an omission. We liked it very much.

I hope that you and your wife are making satisfying progress. We are often talking about you here. I have seen your countryman researcher, Grigore Popa, in London, at the University College. He made an excellent paper on the circulation of the pituitary gland and hypothalamus.

With warm regards, I remain forever yours,

Harvey Cushing

Together with Louise Eisenhardt, he wrote a monography about brain meningiomas, another passion of Professor Cushing.

The most famous meningioma patient of Cushing was General Leonard Wood, from the US Army. General Wood was chief of military personnel in the USA, himself a military surgeon. In 1899 the General suffered a craniocerebral trauma, apparently without consequences until 1902, when he developed paresthesia in the left lower limb, and then epilepsy. In 1905 he underwent a surgery to remove a tumour mass located at the calvaria and an epidural tumour section. The Jacksonian seizures continued. In 1910, Professor Cushing performed surgery in two steps four days apart to remove an intracranial parasagittal meningioma. General Wood had a complete recovery. No doubt that the General's personal fame helped Cushing to obtain the position of chief surgeon in the new Peter Bent Brigham hospital. In 1927 General Wood came again to Doctor Cushing, this time in Boston, with spastic

left hemiparesis and ipsilateral hemianopsia. Cushing re-operated the tumour relapse without apparent complications, but the General died unexpectedly a few hours later as a result of a haemorrhage with intraventricular effraction. Cushing commented later: "*I was never so upset because of the death of a patient. He was so close to success. He was a great man.*" (8)

Between 1896-1912 he performed almost 200 surgeries intervention on children, attempting to establish paediatric neurosurgery as a sub-specialty (9).

Cushing studied the pituitary gland (1912), adding to his international reputation. He was the first person who described pituitary gland disorders, now called 'Cushing syndrome' or 'disease'. (3) He was the first person who associated pituitary adenoma with Cushing syndrome.

He used the transsphenoidal approach in 227 patients with a mortality of 5.2%. (4)

One of Cushing's important contributions is in the area of neuroradiology. He immediately understood the importance of Professor Roentgen's discovery, and he managed to bring a Crooke tube to the Massachusetts General Hospital to generate X-rays at approximately five months after the discovery. After he insisted that the Boston hospital have a radiology service. After a few months Cushing left with the tube to the Johns Hopkins Hospital, to the bewilderment of his colleagues. (4)

In November 1896 he used X-rays to investigate a spine after a gunshot. The female patient had Brown-Secquard syndrome. It was for the first time that a neurologic syndrome to benefit of this investigation. The exposure lasted 35 minutes. Cushing was not the first person to appreciate X-rays. In 1987 alone, more than 1,000 articles were published on their role in medicine. (4)

Together with Ernest Amory Codeman, he developed the predecessor of the modern anaesthesia machine, monitoring temperature, heart rate, and blood pressure during surgical interventions. (4)

Among other innovations initiated by Cushing are cortical stimulation, understanding of the natural evolution of the central nervous system, and understanding of increases in intracranial pressure. He collaborated with W.T. Bovie in the development of the electrocautery with the same name, leading in 1925 to the resection of a brain tumour, and to wide-scale use since 1928. (4)

Cushing's scientific activities included those of his resident, Walter E. Dandy, with whom he worked on hydrocephaly. Dandy discovered ventriculography, but Cushing was upset that he experimented on children with hydrocephaly and not on dogs, as there was a risk of secondary herniation of the amygdalae. (4) On the other hand Dandy did not agree with Cushing on using metallic clamps in aneurysm surgery. (4)

The relationship between Cushing and Dandy was tense, as Dandy was quite aggressive. (4)

When they are talking about the competition between Harvey Cushing and Walter Dandy, other authors think that the first did not have an elegant behaviour. (7)

When the composer George Gershwin was discovered with a brain tumour and went into a coma, Cushing was sought immediately. As he retired several years before, he recommended Dr. Walter Dandy, who was on the ocean with the governor of the state of Maryland. The White House sent a Coast Guard ship to fetch Dandy as quick as possible.

He published 13 books and over 300 articles during his career. The best known books are "*Surgery of the Head*" (1910)*, "The Pituitary Body and its Disorders"* (1912)*, and "Meningiomas"* (1938).

At Cushing's suggestion in 1919, the "Society of Neurological Surgery" was formed, and in 1931, with Cushing's permission, a group of young neurosurgeons founded the "Harvey Cushing Society". (1)

He donated his collection of books and magazines to the Yale Medical Library near the end of his career. (1)

The destroyer "USS Cushing", named to honour the achievements of Harvey Cushing, was launched on December 31, 1935. In 1988 he was honoured with a stamp issued as part of the "Great Americans" series. (1)

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Anatomical localization of intracranial grade II meningiomas in North-Eastern Romania. Our 25-years experience

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Keywords
atypical meningioma, grade II WHO meningioma, meningiomas localization

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ABSTRACT

Objective. Our research aims to assess a possible connection between tumour localization and histological subtypes of grade II meningiomas.

Material and methods. 143 patients with grade II WHO meningiomas underwent surgical resection in "Prof. Dr. N. Oblu" Emergency Clinical Hospital Iași between 1990 and 2015. The collected data included: patient age, gender, tumour localization and histopathological diagnosis (atypical, clear cells and chordoid meningioma).

Results. 135 (94.4%) of all 143 patients with grade II meningiomas were atypical meningiomas, 6 (4.2%) were cell clear meningiomas and only 2 (1.4%) were chordoid meningiomas. As concerns their distribution by gender, 79 (55.2%) were female and 64 (44.8%) were male. Grade II meningiomas were most commonly located at convexity 49.7% (n=71), followed by skull base in 30.8% (n=44) of the cases and parasagittal/falcine in 14.7% (n=21) of the patients.

Conclusions. The most common localization of grade II meningiomas was convexity, followed by skull base, parasagittal/falcine and intraventricular areas. We have also noticed that convexity meningiomas are more frequent in women, unlike the other anatomical localizations in which the male-female ratio is almost equal. Therefore, further research is necessary to determine the role of embryological, anatomopathological and genetic factors in underlying the connection between meningioma grade and anatomical localization.

INTRODUCTION

Meningiomas makes up about one third of all primary central nervous system tumours, being the most common brain tumour in adults over the age of 35 (1), with an incidence that has increased in recent years (2, 3). As far as Romania is concerned, an increase in the number of intracranial meningiomas was noted in its North-Eastern region (where this research was conducted) over the 1990-2015 period (4).

Although meningiomas are usually benign slow-growing tumours, their

histological aggressiveness may classify them in grade II or III tumours, according to the WHO classification (5, 6). Whereas grade II meningiomas only made up 5-7% of all types of meningiomas before the 2007 WHO classification (7), they currently make up more that 20% of all meningiomas (7, 8, 9). Grade II meningiomas include three histological subtypes: atypical, the most common, and also chordoid and clear cell meningiomas, the occurrence rate of which is considerably lower (10).

Among the multiple prognostic factors that can predict meningioma grade prior to tissue diagnosis (11, 12), several studies also found the anatomical localization (13, 14). Thus, several authors noticed the predisposition of grade II meningiomas for cerebral convexity (13, 15, 16) (Figure 1).

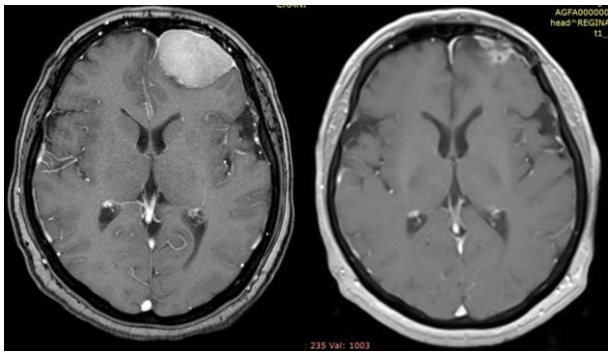

Figure 1. Preoperative and postoperative axial T1-weighted images with contrast of an atypical meningioma (Professor Poeata's personal collection)

The goal of our research was to analyze grade II meningiomas distribution in North-Eastern Romania over a 25-year period (1990-2015). The patients underwent surgery in "Prof. Dr. N. Oblu" Emergency Clinical Hospital of Iasi, the advantage of this hospital being the fact that it services the whole of North-Eastern Romania, a region with a population of about 4 million inhabitants (17) (Figure 2).

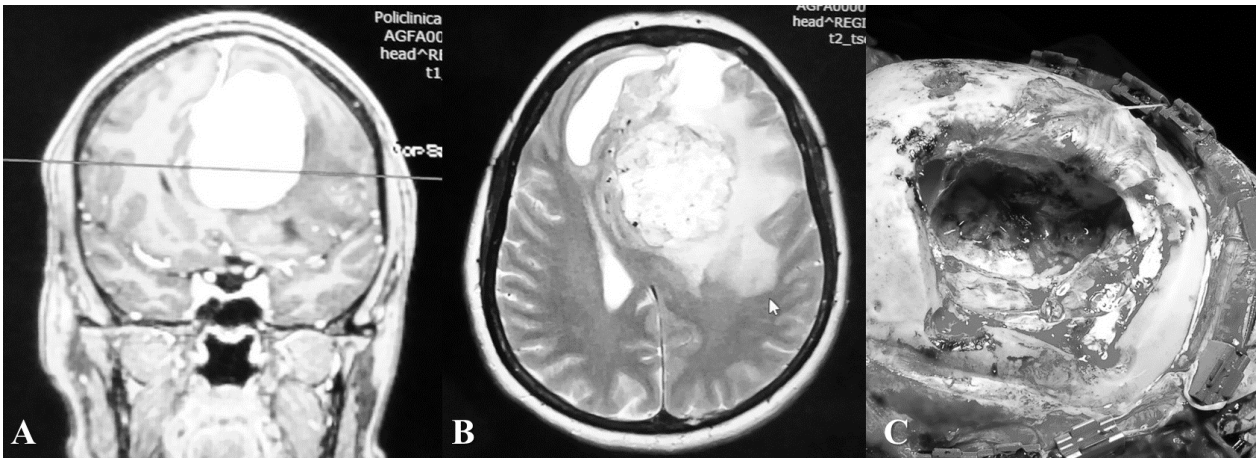

Figure 2. Preoperative coronal (A) and axial (B) T1-weighted images with contrast showing a left falcine meningioma. Postoperative images showing tumour bed after gross total resection (C) (Assoc. Professor Turliuc's personal collection)

Material and methods

We have evaluated 143 patients hospitalized in "Prof. Dr. N. Oblu" Emergency Clinical Hospital of Iași between 1990 and 2015, with histologically proven grade II meningiomas (atypical, clear cells and chordoid). Also, the histological samples have been reviewed according to the current WHO 2016 criteria (18). We have excluded all patients with type 2 neurofibromatosis (2 patients) and those for whom we were unable to collect full information about tumors (16 patients). The collected data included: gender, age, anatomical localization and histopathological diagnosis (Table I). In order to confirm the anatomical localization of grade II meningiomas, the surgeon's operative notes were taken into consideration. As concerns the intracranial localization of meningiomas, they were divided into four main categories: (1) convexity, (2) parasagittal/falcine, (3) skull base and (4) intraventricular.

Results

Of all 143 patients with meningiomas, 79 (55.2%) were female patients and 64 (44.8%) were male

patients. The male: female ratio was 1:1.2. As concerns patients distribution on demographic groups, more than half of them were in the 50-69 year age group (58.1%, n=83). As for the distribution of meningiomas according to anatomical localization, they occurred mostly: 49.7% (n=71) at convexity, 30.8% (n=44) at skull base, 14.7% (n=21) in the parasagittal/falcine area and 4.9% (n=7) intraventricular. Most meningiomas were atypical (94.4%, n=135), followed by clear cell meningiomas (4.2%, n=6) and only 1.4% (n=2) were chordoid. All patient characteristics are shown in Table I.

Characteristics		Grade II n (%)
No. of patients		143
Gender	female	79 (55.2)
	male	64 (44.8)
Age groups (years)	20-29	3 (2.1)
	30-39	9 (6.3)
	40-49	23 (16.1)
	50-59	42 (29.4)
	60-69	41 (28.7)
	70-79	22 (15.4)
	80-89	3 (2.1)
Tumor localization	Convexity	71 (49.7)
	Skull base	44 (30.8)
	Parasagittal/falcine	21 (14.7)
	Intraventricular	7 (4.9)
Histological subtypes	Atypical meningioma	135 (94.4)
	Clear cell meningioma	6 (4.2)
	Chordoid meningioma	2 (1.4)

Table 1. Characteristics of 143 patients with grade II meningioma

Discussion

Our research revealed a predilection of grade II meningiomas for the convexity, as 49.7% (n=71) of them occurred in this area, which is consistent with similar studies (10, 14, 19, 20, 21, 22). Skull base meningiomas ranked second 30.8% (n=44), followed by the parasagittal/falcine and intraventricular localization (Table 1, Figure 3). The distribution of the anatomical localization of tumors on age groups was similar in both women and men.

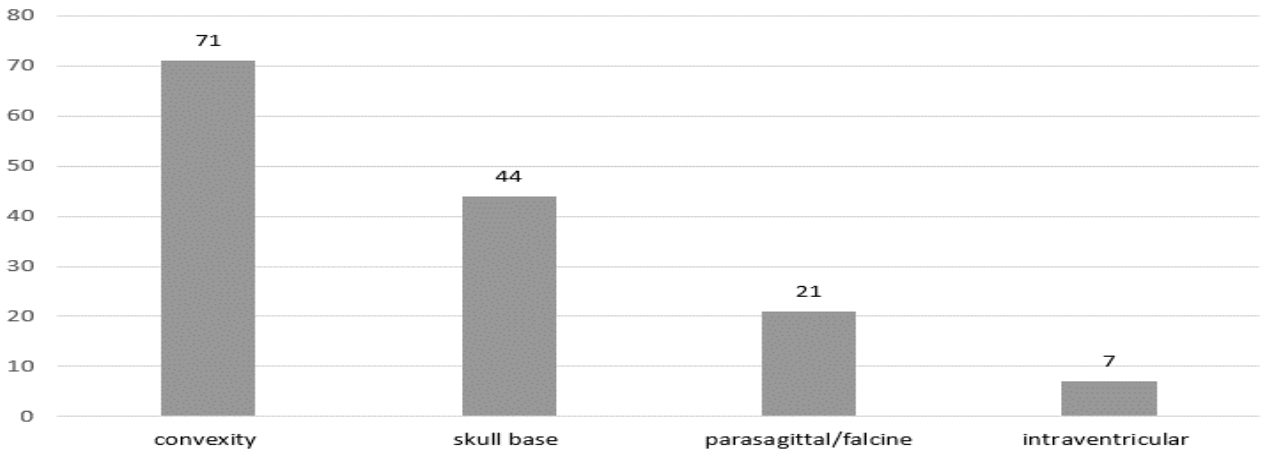

Figure 3. Incidence of Grade II meningiomas according to anatomical localization

Although previous studies have demonstrated a predilection of grade II meningiomas for cerebral convexity (13, 15, 16), a clear etiological connection between a particular meningioma grade and its anatomical localization could not be established. However, some authors consider that the histological grade of the tumor may be related to the meninges' complex embryological origin, which has a variable neoplastic potential (23, 24, 25, 26).

Among the first studies that demonstrated the predilection of grade II meningiomas for cerebral convexity were those conducted by Mahmood *et al.* and Maier *et al.* (27, 28). Also, Kane *et al.* later demonstrated that non-skull base tumors would have an increased risk for grade II meningiomas compared to skull base tumors (13). On the other hand, Zhou *et al.* noted that meningiomas located at the median line of the skull base are the least likely to be grade II or III (6), similar to other studies that have revealed that skull base meningiomas are more frequently meningothelial (29, 30) and are also lower grade at initial resection (15). This predilection of meningiomas for various anatomical localizations in the intracranial space could be explained by the distinct embryological origins of non-skull and skull-base dura (14, 15, 30, 31). In this respect, various authors have demonstrated that meninges around the brainstem would arise from cephalic mesoderm, whereas telencephalic meninges arise from neural crest cells (25, 29, 32, 33). This differential meningeal embryogenesis resulted in the predominance of one arachnoid cell type over the other location, which accounts for the aggressive behavior of some meningiomas as compared to others in some anatomical localizations (15). However, genomic studies have shed light on intracranial locations and mutational patterns, as well as on the potential embryonic cancer stem cell-like origin (34).

In a study on 110 patients with incidentally discovered meningiomas, Hashimoto *et al.* also noticed that non-skull base meningiomas have a more aggressive behavior and that skull base meningiomas do not tend to grow when compared to non-skull base meningiomas (35). Moreover, even when these tumors grow, the growth rate was significantly lower in terms of annual growth rate and percentage (35). Also, the same authors demonstrated that 60% of the skull base incidental meningiomas had an exponential pattern of growth, unlike non-skull base incidental meningiomas characterized by a 33% growth percentage (35). In conclusion, the authors recommend non-skull base meningioma follow-up by magnetic resonance imaging at shorter intervals. The authors mention that the results must be interpreted as most meningiomas fit both exponential and linear patterns statistically (35).

In 2003, the same authors suggested that a loss of 1p was shown to be significantly correlated with malignant progression of meningiomas, analyzing 72 grade II and III meningiomas, with fluorescence in situ hybridization and loss of heterozygosity analyses (35, 36). The authors also pointed out that skull base meningiomas had a significantly lower percentage of cells with 1p loss (20.31%) compared to non-skull base meningiomas (37.87%), suggesting that skull base tumors would have fewer genetic alterations and consequently would have less aggressive biological behavior (35). Similarly, Murphy *et al.* showed in their study that meningiomas originating at the convexity had more chromosomal abnormalities than those arise from skull base (37).

In terms of histopathology, there have been studies that have shown its importance in the prediction of some types of meningiomas for certain intracranial localizations. Thus, McGovern *et al.*, in a study of 216 patients with grade I, II and III meningiomas, claimed that grade I non-skull base meningiomas had a higher MIB-1 labeling index than grade I skull base meningiomas, suggesting that non-skull base tumors may have a more aggressive biology (16). As concerns their recurrence, the same author noted that non-skull base meningiomas, when they recur, have a higher WHO grades than skull base meningiomas (16). Also, in 2018, Turk *et al.* concluded in a study of 40 grade I and II meningiomas that the skull base group had significantly higher CD34 levels than the non-skull base group, suggesting that skull base meningiomas tend to have higher microvascular density and are better vascularized than non-skull base tumors (38).

As regards the distribution of meningiomas on genders in the overall number of patients, we revealed a male: female ratio of 1:1.2, with a slight predominance in females, in agreement with other literature studies (14, 19, 39). On the other hand, whereas in the skull base, intraventricular and parasagittal/falcine localizations the male: female ratio was approximately 1:1, location at convexity level was dominated by women, with a male: female

ratio of 1:1.5 (43/28) (Figure 4). In order to justify this predominance of women, research has shown that grade I meningiomas have a high level of progesterone receptor expression relative to grade II and III meningiomas, which seem to have a lower frequency of estrogen and androgen receptors (13, 40, 41, 42), which means close male-female ratios.

On the other hand, Morokoff *et al.* in a study of 163 convexity meningiomas (grades I, II and III) noted a prevalence of the female sex, with a male: female ratio of 1:2.7 (43). In higher-grade meningiomas, Morokoff *et al.* found a male: female ratio of 1:1, much lower than our ratio of 1:1.5.

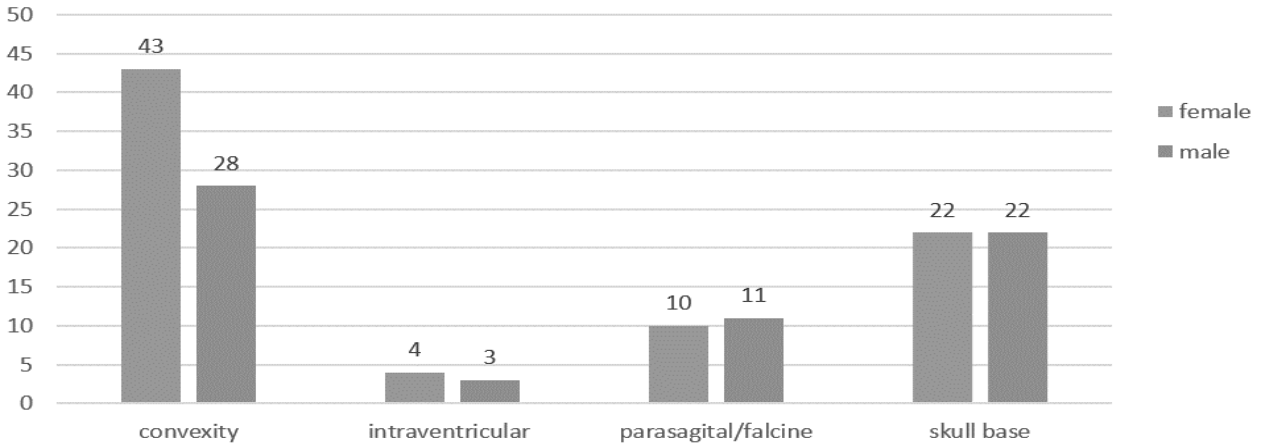

FIGURE 4. Incidence of grade II meningioma according to gender

With regard to the distribution of histological subtypes of grade II meningiomas, atypical meningiomas prevailed in our research (94.4%), followed by clear cell and chordoid meningiomas in a much lower percentage, as there are rare types of tumors (Table 1).

Of all grade II meningiomas, atypical meningiomas are the most common, their percentage increasing to 20-30% of all meningiomas after the introduction of the WHO classification in 2000 and 2007 (2, 8, 9). Like grade I or III meningiomas, atypical meningiomas may develop anywhere in the intracranial space, with some studies reporting a higher frequency of atypical meningiomas at the level of cerebral convexity (8, 27, 44, 45).

Clear cell meningioma is a rare disorder, as it makes up less than 1% of all meningiomas, and English-language literature reports 218 intracranial tumors (46). This percentage is also low in our research, with an incidence rate of this type of meningioma only 4.2% (n=6) over the 25-year period (Table I). Whereas previous studies revealed that the most common localization for clear cell meningioma was the cerebellopontine angle (47, 48, 49), all clear cell meningiomas in our group were located in the parasagittal/falcine area (n = 6). From this point of view, the results of the studies differ from each other: some studies show that the most affected location is convexity (46), whereas others point to skull base (50), particularly cerebellopontine angle, parasagittal tumors having lower occurrence rates (47).

Chordoid meningiomas are also rare types of meningiomas, as only a little more than 100 cases are reported in literature (51, 52, 53, 54, 55, 56). Rare neoplasia with a unique chordoid appearance, chordoid meningioma has a predilection for the supratentorial localization (1, 57), similar to our study in which the two chordoid meningiomas had parasagittal/falcine localization.

CONCLUSIONS

Our study has shown a predominance of grade II meningiomas for cerebral convexity, which is the most common location in the intracranial space, followed by the skull base, parasagittal/falcine and intraventricular locations. We also noticed that convexity meningiomas predominate especially in women. Further research is needed to highlight the role of genetic, embryological and anatomopathological factors in highlighting the

connection between meningioma grade and anatomical localization

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Syringobulbia and syringomyelia in a case with Chiari 0 malformation successfully treated by posterior fossa reconstruction. Case presentation and literature review

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ABSTRACT

"Chiari zero malformation" is a rare and a relatively new described condition which associates syringohydromyelia without caudal displacement of the cerebellar tonsils through the foramen magnum. We present a case of a 40 years old woman with Chiari zero malformation with both syringomyelia and syringobulbia and a good clinical and radiological outcome after posterior fossa decompression. The presence of associated syringomyelia and syringobulbia in this condition is less frequent and it usually occurs in younger patients. In our case we considered syringobulbia as being an extension of syringomyelia.

Keywords
Chiari zero malformation, syryngomyelia, syringobulbia, cerebellar tonsils

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INTRODUCTION

The Chiari malformations were first described by Hans Chiari in terms of the cerebellar tonsils herniating out of the skull and he identified four different types, of which the type I and II are more common (4). Nowadays, most people define Chiari I as tonsillar herniation of greater than 3-5 mm, measured as the distance below the foramen magnum and the condition is often associated with syryngomyelia (1). But patients with syringohydromyelia without hindbrain herniation that respond to posterior fossa decompression have been described and the condition was named "Chiari zero malformation" (7). Conversely, many patients can have herniations greater than 3-5 mm, but with no symptoms, so tonsillar herniation identified radiographically is of limited prognostic value and requires clinical correlation (5). The association with syringobulbia is even a rarer situation, with only a few cases in the literature and especially in children (19,20). Hereby we present a case of a women with Chiari zero malformation and the presence of both syringomyelia and syringobulbia who was treated surgically in our department.

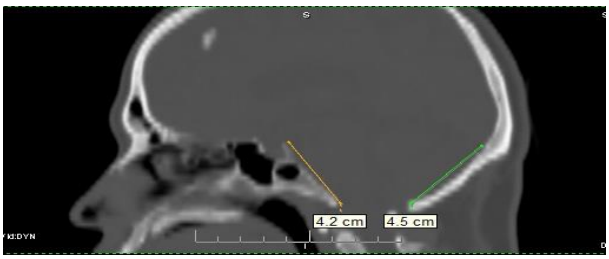
CASE REPORT

A 40-year-old woman was admitted to our hospital with a 2-years history of progressive proximal left-sided upper limb weakness. At admission she had a decreased sensitivity to painful stimuli associated with decreased temperature sensation as well in the upper limbs and swallowing difficulties. She also presented kypho-scoliosis developed during the childhood.

The patient was investigated with a head computed tomography (CT) and a 1.5T IRM of the cranio-cervical junction, cervical and thoracic spine.
On the preoperative images, we made some linear measurements for posterior fossa dimensions: the length of the clivus defined as the distance from the top of the dorsum sellae to the basion, and the length of the supraocciput measured between the internal occipital protuberance and the opisthion. We also calculated the spheroidal posterior fossa volume (PFV) based on the spheroidal formula (6):
PFV=4/3 x π x (X/2 x Y/2 x Z/2), where: X is the anteroposterior measurement from the posterior clinoid process to the torcula; Y is the height of the posterior fossa measured from the basion to the peak of the tentorium cerebelli; and Z is the maximum width of the posterior fossa. (6)

To assess the syrinx characteristics, we noted the cranial and caudal extent and we measured on the pre and postoperative images the ratio between the syrinx and the spinal cord diameter at the level of the maximum expansion. In addition, we calculated the ratio of the surface area of syrinx to spinal cord using the formula πr^2 for surface area, with r being the radius (7).

The clival length of our patient was 4,2 cm and the length of the supraocciput was 4,5 cm. The width of the posterior cranial fossa was 9,9 cm (Z=9,9 cm), and the anterior-posterior dimension was 8,3 cm (X=8,3 cm). The height from the basion to tentorium cerebelli was 5,3 cm (Y=5,3 cm). The calculated spheroidal posterior fossa volume was 227,9 cm^3. These measurements are consistent with a small posterior fosa.



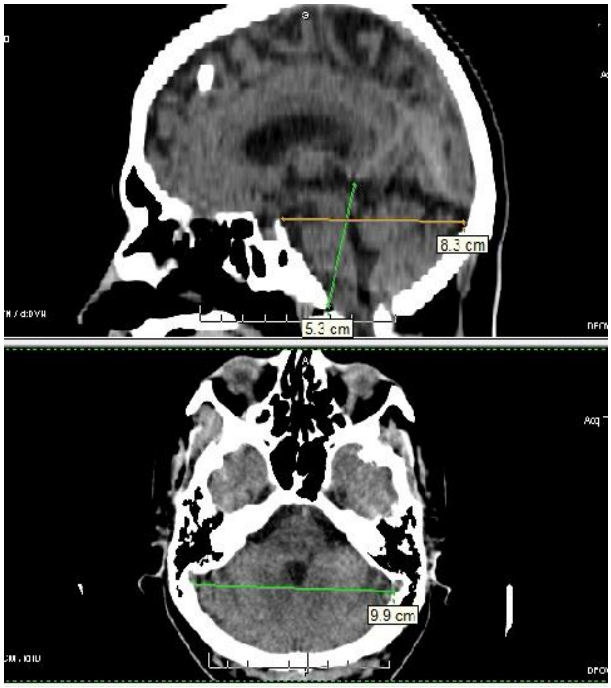
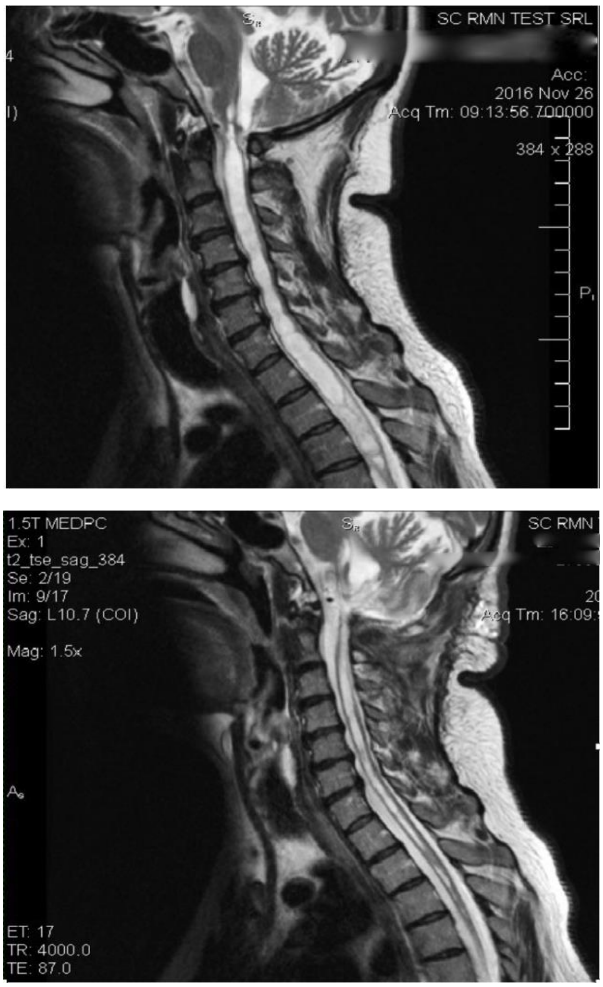


FIGURE 1. Posterior fossa measurements

FIGURE 2. Pre and post-operatively MRI images



The cranial extent of the syrinx was at the level of the medulla oblongata and the caudal extent was at the level of T4 vertebral body. We measured the maximum expansion of the syrinx cavity at the level of the T1 vertebral body and compared the pre and 3 months postop values. The ratio of the preoperative syrinx/spinal cord diameter at the level of greatest expansion (T1 vertebral body) was 0.81 (9mm/11mm). The ratio of the postoperative syrinx/spinal cord diameter at the same vertebral level was 0.37 (3mm/8mm). The ratio of the preoperative syrinx/spinal cord surface at the level of greatest expansion (T1 vertebral body) was 0.67, and 3 months postoperatively was 0.14

The patient was surgically treated by performing a craniocervical decompression which consisted of a suboccipital craniectomy, C1 laminectomy, intradural lysis of the arachnoidal adhesions that occluded the foramen of Magendie and duraplasty. She had a good post-operative evolution with the progressive remission of the symptoms.

Discussion

Chiari 0 malformation is a rare and a relatively new described condition which associates syringohydromyelia without caudal displacement of the cerebellar tonsils through the foramen magnum, of which clinical symptoms and radiological aspect can be ameliorated after posterior fossa decompression. (7,18). While Chiari II and III malformations can be explained by a maldevelopment of the posterior fossa neural structures, more and more evidence point to an underdevelopment of the bony structures of posterior fossa, leading to a smaller p-fossa that contain a normal developed neural tissue as an explanation for Chiari I and Chiari 0 malformations (2,8,10,11,12,13,14,15,16).

Syringomyelia may be associated with many conditions such as Chiari malformations, spinal trauma, spinal tumours, tethered cord or spinal dysraphism. In a study of Strahle et al, the authors identified a number of 271 patients with a syrinx out of 14118 patients who undergone brain or spine imaging during a period of 11 years. The Chiari malformation type I was the most common associated condition with syringomyelia and the syrinx was more likely to have the cranial extent in the cervical spine and to have a width greater than 5 mm compared with other conditions. They found only 4 patients with Chiari 0 malformation but the syrinx in these cases had the big-gest width and length, bigger than syrinx associated with Chiari type I and II malformations. Al-so the Chiari type 0 patients had a more superior cranial extent of their syrinx. (17).

We considered that the characteristics of our patient are consistent with the Chiari 0 malformation. The measurements corresponded with a small posterior fossa and the MRI revealed syringomyelobulbia without tonsillar herniation. Three months postoperatively, the symptomatology improved, the algesthesia and temperature sensation in the upper limbs were better than preoperatively, the swallowing difficulties disappeared and the abduction of both upper limbs obviously improved. The MRI performed 3 months postop showed that syringomyelia diminished semnificatively compared with that before surgery.

Conclusion

The presence of associated syringobulbia with syringomyelia in the Chiari zero malformation is a condition rarely described in the literature and in the most of the cases the patients are younger. (19,20). In our case we considered syringobulbia as being an extension of syringomyelia.

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Learning curve in rat dissection for experimental sciatic nerve repair

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Keywords
learning curve, operation times, sciatic nerve rat, nerve defect

ABSTRACT
The baseline for any key research in nerve regeneration is an experimental model and the sciatic nerve in the rat model is the workhorse in this field. Although physically resistant to external traumas, a surgical intervention constitutes a major distress even for a rat. In the following presentation, we will analyse the learning curves for different stages in the rat sciatic nerve surgery as well as possible factors which influence these times.

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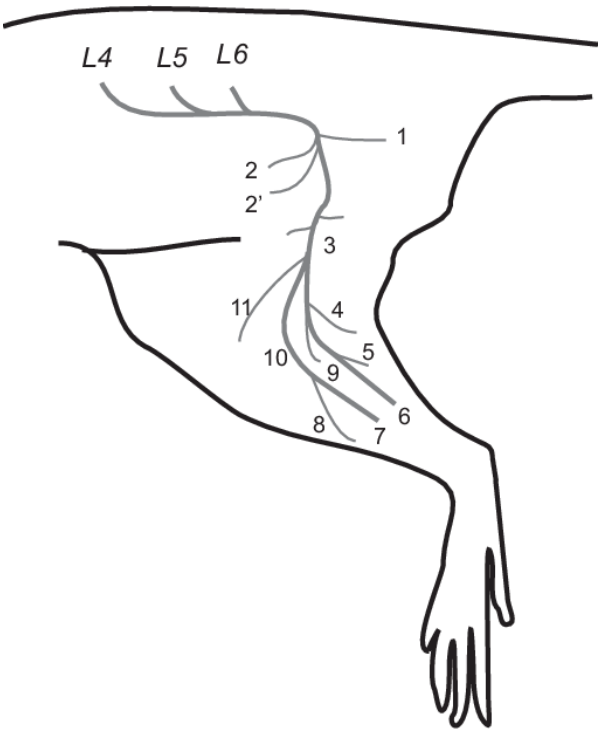
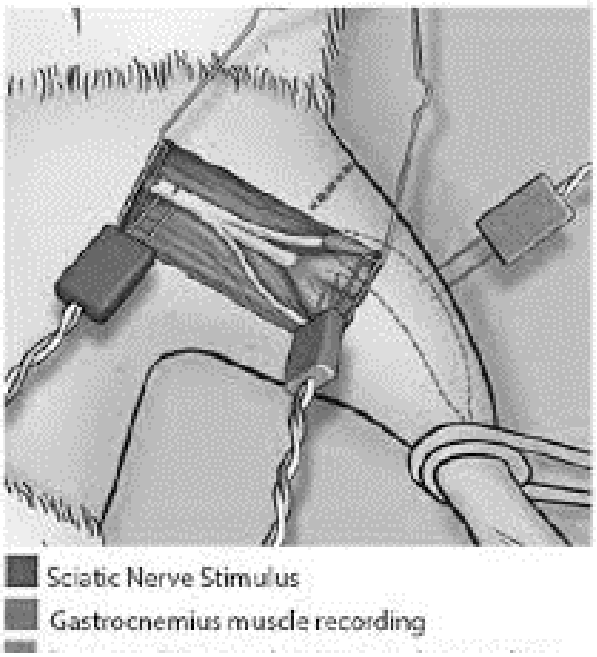
INTRODUCTION

Every major breakthrough discovery starts from research. In surgery, it is immoral, unethical and sometimes even illegal for experiments which can be performed on animals to be done directly on humans. For this reason, animal experiments in the field of modern medicine are a necessity and they constitute the starting point for most of the innovative techniques in the surgical field. When it comes to nerve regeneration, the preferred choice is the sciatic nerve in the rat model.

The reason for this choice is that the sciatic nerve has a reasonable size (1-3mm in diameter), is fairly easily accessible (being located underneath the gluteus maximus, at the intersection between this muscle and the biceps femuri muscle, running its course between the knee joint and the ischial tuberosity) and because it divides towards the knee joint into its 3 main branches (common peroneal nerve, tibial nerve and sural nerve).

These 3 branches can be large enough for individual repair, but the sciatic nerve has proximal to this division sufficient length for different types of operations (grafts, nerve conducts), where an artificial gap can be created.





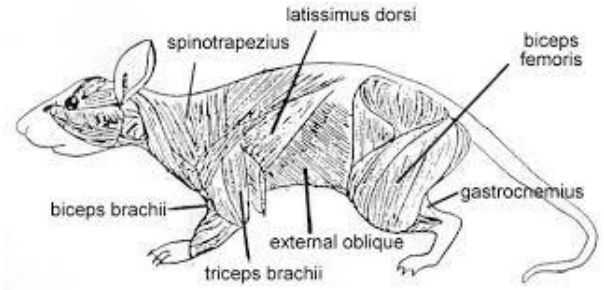
Sciatic nerve and its divisions right leg of a rat: [1], [2]

Material and method

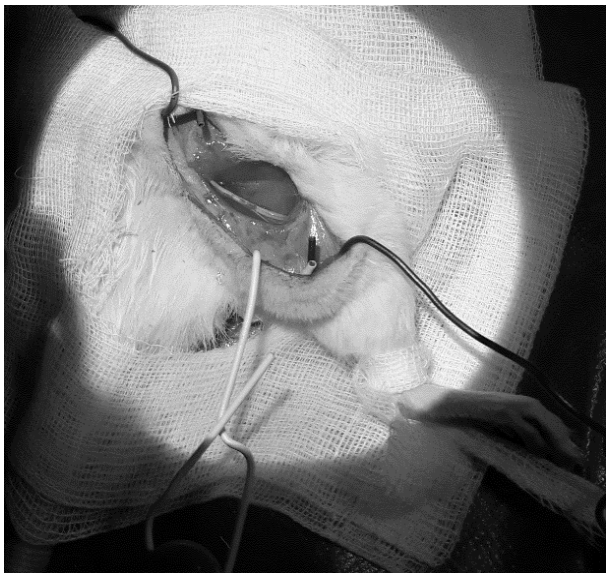
For the experiment 42 Wistar male rats were used. All rats weighed between 240g and 310g and were 50-62 days of age at the time of surgery. All conditions regarding the safety and the well-being of the animals have been met. 2 rats were sacrificed to harvest vascular conducts and blood for PRP processing and the other 40 rats were divided into 4 batches of 10. The learning curve presented in this article was designed for the first 2 batches (20 rats).

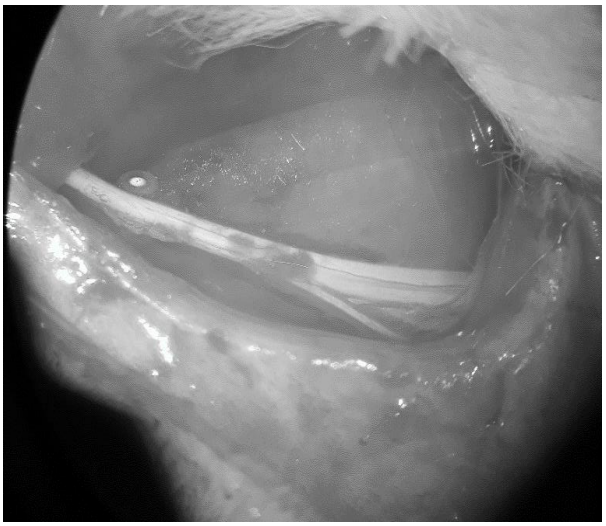
The operations were performed under general anaesthesia. The rat was positioned in supine position and an incision on the right posterior gluteal-thigh region was performed, followed by an incision of the biceps femuri muscle with sciatic nerve exposure. In the first batch, a distal section of the nerve was created, followed by nerve repair, proximal section of the sciatic with nerve anastomosis (by doing so, a controlled nerve graft of 0,5cm in size was created in each rat, which was then sutured back into its original place). A 5th grade Sunderland lesion – neurotmesis was created at 2 different sites and then repaired. [3]

In the 2nd batch, a 0,5cm nerve defect was created and then solved using a vascular conduct. Batches 3 and 4 are part of a different study and involve adding PRP (platelet rich plasma) or human stem cells from the umbilical cord in the vascular conduct. [4],[5],[6].



[7] Rat leg anatomy





Sciatic nerve exposure

All interventions were performed in sterile conditions. An assistant was present for the duration of every operation to ensure the sterile conditions. All microsurgical anastomosis were performed using 10.0 Nylon suture under the microscope using a 10x magnification. The rats received 3 subcutaneous doses of meloxicam 0,04ml and 3 doses of enroxil 0,02ml (1 immediately after the operation, and one for each of the next 2 days). Each rat was marked with circles on the tail and put in a separate cage.

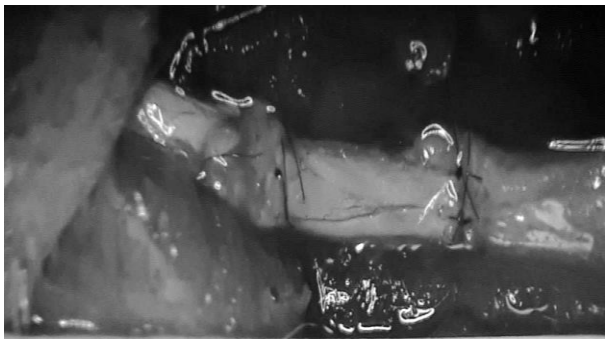
Every procedure was recorded using a chronometer from the moment of the intraperitoneal injection till the skin suture. We observed the rat preparation times, the nerve exposure times and the anastomosis times.

The rat preparation time (T1) represents the time from the first doses of anaesthesia till the moment of incision and involves the time needed to shave the area which will be operated as well as time needed for setting the sterile field and the disinfection time. The nerve exposure time has 2 components: a macroscopic time for skin incision and muscle dissection till the nerve can be visualized (T2) and a microscopic time consisting in proper nerve dissection (T3). The 4rd registered time is the anastomosis time (T4)– the distal anastomosis followed by the proximal anastomosis. Once the nerve was completely repaired, muscle repair and skin suture finalized the intervention (T5). TT – total time – represents the sum of T1-T5.

The anaesthesia protocol consisted of using a mixture of ketamine 75mg/kg and xylazine 10mg/kg injected intraperitoneal. The anaesthesia normally worked in 5 minutes and one dose lasted between 20 and 50 minutes, when a new dose may have been required. Before the nerve dissection, as well as before nerve section, drops of lidocaine were supplementary used at the dissection site. The time for every anaesthesia dose administered was recorded and correlated to one of the 4 above mentioned times.

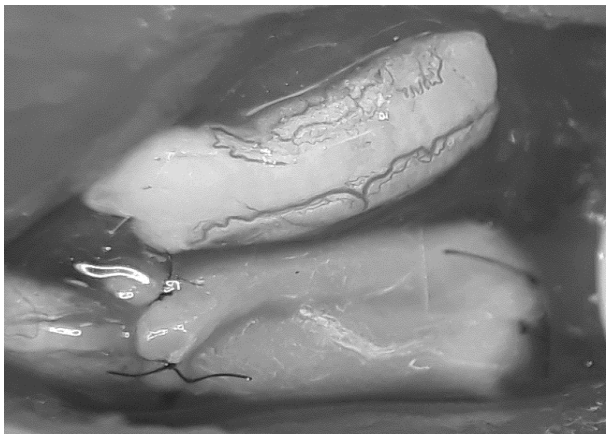
The rats in the 1st batch were operated in 3 separate days during the first week of the experiment (1 rat the first day, 4 rats the second day and 5 rats the 4th day of the week). The rats in the second batch were operated in 4 separate days over the second week of the experiment (2 rats the first day, 2 rats the 4th day, 4 rats the 5th day and 2 rats the 6th day).

Files for every operation were created in order to record all the data and for the assistant to remember the steps in the operations which they needed to fulfil (preparing the operating area, disinfection, adding lidocaine directly on the nerve once exposed, dropping saline solution in the eyes to prevent eye dryness and noting down all the previously mentioned times).



First batch – autograft

2nd batch – Vascular conduct

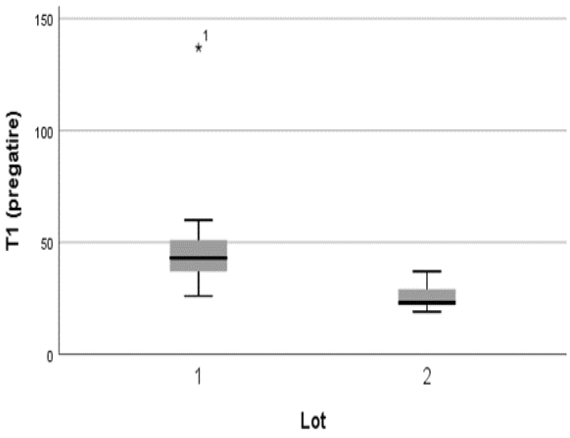


RESULTS

There is no statistical meaning between the 2 batches when referring to the median of age (p=0.148) or weight (p=0.264). Batch 1 ranged between 50-61 days of age at the time of the operation, while the weight ranged between 246-300g. In the second batch, the age varied between 50 and 53 days and the weight between 235-268g.

Variable	Batch 1 Median (IQR)	Batch 2 Median (IQR)	Total Median (IQR)
Age (days)	52 (4)	51 (1)	55 (2)
Weight (gram)	269 (28)	245 (18)	258.5 (25)
T1 (min)	43 (17)	23 (9)	35 (21)
T2 (min)	5.5 (2)	7 (8)	6 (5)
T3 (min)	9 (4)	8 (6)	8.5 (5)
T4 (min)	37 (9)	29 (16)	35 (11)
TT (min)	93 (43)	71.5 (30)	86 (31)
No. anesthesia	2 (1)	2 (1)	2 (1)
No. sutures	6.5 (2)	8 (3)	7 (3)

There was a statistically significant difference between the preparation times (T1) in the 2 batches p=0.005 (the second batch having shorter preparation times compared to the first one). In the first batch, the T1 times improved from 136 minutes to 26 minutes, while the second batch had T1 times ranging from 37 to 19 minutes.



An overview of the variables recorded for the operations in the 2 batches shows:

1. number of doses of anaesthesia administered:

- batch 1 – median=2 (IQR:1), with minimum 2 and a maximum of 6 doses
- batch 2 – median=2 (IQR:1), with a minimum of 1 and a maximum of 3 doses

2. number of sutures for both proximal and distal anastomosis

- batch 1 – median = 6,5 (IQR:2), with a minimum of 4 and a maximum of 9 sutures
- batch 2 – median = 8 (IQR:3), with a minimum of 7 and a maximum of 12 sutures

After the statistical analysis (Pearson correlation), 2 positive correlation with statistical meaning were observed: on the one hand between the number of doses of anaesthesia administered and the total time of the operation for the 2 batches (r=0.59, p= 0,007) – diagram A and on the other hand between the number of doses of anaesthesia and the anastomosis time T4 (r=0.65, p=0.002) –diagram B.

The T4 times recorded for the 2 batches varied. For the first batch, there was a median of 37 minutes for the 2 anastomosis performed (with a maximum of 63 minutes and a minimum of 29 minutes), while in the second batch the median was at 29 minutes for 2 anastomoses (with a maximum of 60 minutes and a minimum of 13 minutes).

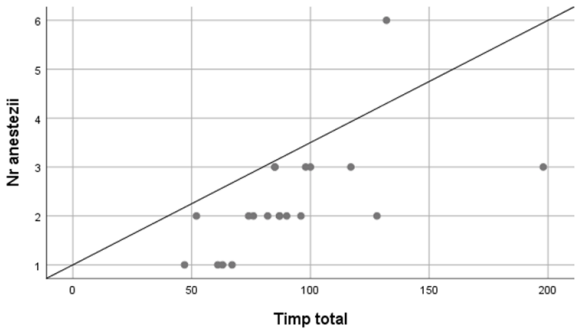
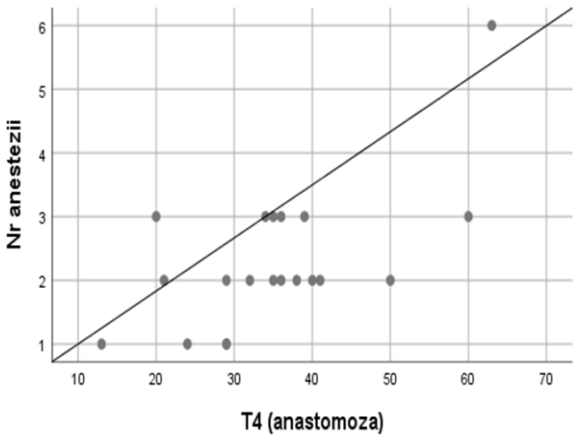


Diagram A

Diagram B



Correlation	Batch 1 Correlation coef (r)	p	Batch 2 Correlation coef (r)	p	Total (batch1 + batch2) Correlation coef (r)	p
T4 – no. of anaesthesia	0.74	**0.014**	0.52	0.12	0.65	**0.002**
T4 – no. of sutures	0.29	0.41	0.68	**0.03**	0.24	0.31
TT – no. of anaesthesia	0.43	0.21	0.8	**0.005**	0.59	**0.007**
TT – no. of suturi	0.19	0.59	0.46	0.18	0.18	0.43
No. of sutures – no. of anaesthesia	0.18	0.6	0.45	0.19	0.12	0.62

No statistically significant correlations were established between the number of sutures and the anastomosis time T4 (r= 0.24, p=0.31), number of doses of anaesthesia administered (r=0,12, p=0.62) or total time (r=0.18, p=0.43).

Discussions

There are no scientific data regarding operation times in sciatic nerve surgery performed in the rat model. The correlation between the number of doses of anaesthesia administered and the total time of the operation is reasonable, taking into consideration that administrating a new dose of anaesthesia requires extra time; this is due to the fact that the rat was placed in supine position, while the anaesthesia was administered intraperitoneal (on the ventral side) by elevating the opposite inferior limb under sterile conditions.

The correlation between the number of doses of anaesthesia and the anastomosis time T4 can also be explained by the fact that the 2nd or 3rd dose of anaesthesia administered occurred mostly during T4, thus prolonging the anastomosis time.

Subjective factors may also influence the T2, T3 and T4 operation times (the overwork of the operator prolong the operating times) and resulted in fewer rats operated in a single day over the second week of the experiment.

The assistant who was partially in charge of shaving the rat after anaesthesia was able to considerably reduce the T1 time by improving his technique, as well as the operator who prepared simultaneously the sterile draping and suitable placed pins and retractors for the operation. This is how the rat preparation time was considerably reduced in the second batch.

The number of sutures might not have been correlated with the anastomosis time T4 because in the second batch this number was higher compared to the number of sutures performed in the first batch and while having similar or even faster times of execution. Therefore, when performing a higher number of sutures in similar times shows that the learning curve improved the timing of these anastomoses.

The only longer T4 time in the second batch of 60 minutes was in the case of the first rat, in which a new element was introduced – the bridging of the defect using the aortic conduct. All the other T4 times were under 40 minutes (compared to the first batch were 6/10 T4 times were under 40 minutes). This shows an improvement in the learning curve for the anastomosis, although no statistical difference was found. (p=0,31).

Conclusions

The learning curve improved in the preparation time in the second batch compared to the first one, existing a statistical difference between the 2 batches. T4 – anastomosis times also improved in the second batch compared to the first one but this result wasn't statistically different.

Prolonged overall times were observed when a second or 3rd dose of anaesthesia was needed during the intervention. The anastomosis time and total operation time is directly proportional with the number of anaesthesia's performed for the anastomosis.

The learning curve also improved when referring to the anastomoses of the nerves, since a higher number of sutures was performed in similar or even shorter times. However, the number of sutures

performed does not appear to influence the anastomosis time or the overall time in the given experiment.

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Neurosurgery in the elderly patient

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Motto:
"Love and respect old age people because you are aging too"
Aparna Verma

ABSTRACT

Objective. For government officials and health providers, elderly population - aged 65 and over, especially neurosurgical patient, represent a larger concern, an increasing problem not only for socio-economic reasons related to the medical act, but also for additional care requirements which should be done by the family and society, including rehabilitation facilities, occupational & physical therapy, speech therapists, visiting nurses, to insure an effective recuperation after hospital discharge. A retrospective study with 325 "elderly" patients cohort, aged 65 and over, admitted in the Neurosurgery Department undergoing common neurosurgical procedures, in the last five years offer an evaluation for neurosurgical procedures, outcomes, comorbidities, anaesthetic and analgesic requirements, outcome.

Material and method. This study was performed on patients aged 65 years or older, with neurosurgical diseases, admitted to the Neurosurgery or the Intensive Care Unit of our hospital, between 2014-2019. An analysis was made on variables such as age, pathology, comorbidities, length of hospital stay especially in the ICU unit, type of cranio-cerebral or spinal procedures performed, anaesthesia protocols, complications, performance status, re-admissions and mortality.

Results. Patients age were divided into three categories: between 65-70 years old there were 152 patients (46,76%), between 70-85 years old 93 patients (28.61%) and over 85 years old 80 patients (24,61%). 173 patients were females (53,23%), 152 were males (46.76 %). The admission Glasgow Coma Scale (GCS) score to those over 85 years old was between 3-12 in 29 cases (8.02%) with early death in 13 patients. Several comorbidities were noticed in 294 patients (90.15%): cardiac, pulmonary, hematologic especially coumarinic overdose, hepatic and renal failures, psychiatric illnesses, concomitant systemic disease or immunosuppressed patients by decompensated diabetes, primitive cancers affecting various organs, infectious diseases, also severe osteoporosis, chronic ethylic intoxication, limiting surgical attitude, also obtaining the informed consent for surgery. There were 154 (47,38%) patients with cerebral pathology and 171 (52,61%) patients with spinal pathology. Most common surgical procedures performed were: craniotomies for tumours and hematoma removal, minimal invasive procedures for spine, endovascular and vertebroplasty. The median length of stay for emergency patients was significantly longer than that of elective patients (13 vs. 8 days). For 215 (66.15%) patients general anaesthesia was performed, local anaesthesia in 97 (29.84%) patients, 13 patients (4%) were not operated. Good quality of life results appreciated by patients and relatives were recorded in 236 cases (72.61%) in the first and second category; less better results to those over 85 years old; same symptoms especially pain 63 patients (19.38%), complications to 47 patients (14,46%) especially cardiac, renal and

Keywords
geriatric neurosurgical patient,
anaesthetic and analgesic requirements to aged people,
concomitant diseases,
minim invasive neurosurgical procedures,
pre-and postoperative care,
life quality

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respiratory failures, also motor deficits, seizures, CSF fistula, mortality in 26 cases (8%), re-admissions in 45 cases (13.84%) less than 1 month after discharge.

Conclusions. Old prejudices that old age is a contraindication for surgery have to be removed. Clinical and surgical decisions for neurosurgical procedures in the elderly are decisive for limiting reported morbidity and mortality rates. For life quality, realistic family and society expectations, several aspects should be considered for safe and effective results: careful patient selection on patient status, comorbidities and physiological reserve; neurosurgical pathology, urgency of the surgical procedure, the strategy of neurosurgical management based on advances in imaging and interventional radiology, minimal invasive neurosurgical procedures with significant preoperative and postoperative care. Good results could be obtained even in elderly people for chronic subdural hematoma, simple brain or spinal tumour, good grade aneurysm, trigeminal pain, vertebroplasty in spinal vertebral fractures, etc.

Introduction

Aging means concomitant a physiological process but also structural degeneration, a graded loss of functional capacity of all organs and tissues (1)(2). The number of elderly patients is increasing worldwide, generating a larger concern (3-7), an increasing problem regarding socio-economic reasons related to the medical act, morbidity and additional care requirements, perioperative adverse events (8-10). It is estimated that between 2000 and 2050, the proportion of the world's population over 60 years will double, and the number of people aged 80 and older will quadruple (7)(11). For neurosurgical patient, beyond the age of 65 years, both chronic or in emergency, all measures should be institute to maintain quality of life, to avoid perioperative mortality and morbidity (10). In Romania the share of people over 65 years of age, was 18% of the total population on January 1, 2018, respectively 3,559,957 persons out of 19,523,621. According to the NIS data, among the elderly, the men numbered 1,433,412 persons (15% of the total number of men in Romania of 9,543,228 persons) and the women 2,117,495 (21% of the total number of women residing in Romania of 9,980,393 persons)(12).

Material and method

This retrospective study was performed on 325 patients aged 65 years or older, with neurosurgical diseases, admitted to the Neurosurgery or the Intensive Care Unit of our hospital, between 2014-2019. An analysis was made on variables such as: age, pathology, the admission Glasgow Coma Scale (GCS) score, both chronic or in emergency, comorbidities - using Charlson Comorbidity Index (13)(14), length of hospital stay especially in the ICU unit, type of cranio-cerebral or spinal procedures performed, anaesthesia protocols, complications, performance status, re-admissions morbidity and mortality. 45.8% of patients had neurosurgical cranial pathology and 54,2% had neurosurgical spinal diseases. Patients age were divided into three categories: between 65-70 years old there were 152 patients (46,76%), between 70-85 years old 93 patients (28.61%) and over 85 years old 80 patients (24,61%). 173 patients were females (53,23%), 152 were males (46.76 %). The admission Glasgow Coma Scale (GCS) score was between 3-15, worse: between 3-5 especially to those over 85 years old in 29 cases (8.02%) with early death in 13 patients. A CGS score between 7-14 was recorded to 89 patients (27,38%): 12 cases (3.69%) in the first category, 42 cases (12.95%) cases in the second and 35 cases (10.76%) in the third. Several combined comorbidities were encountered in 294 patients (90.15%), limiting surgical attitude, also obtaining the informed consent for surgery: cardiac insufficiency, several cardiac diseases with damage to the ejection fraction (myocardial infarction, arrhythmias, valvular stenosis or insufficiency, untreated hypertension); chronic pulmonary disease, bronchial asthma; previous strokes with hemiplegia; severe haematological diseases (lymphoma, leukemia, myeloma, coagulation disorders with thrombocytopenia or coumarinic overdose); hepatopathy (cirrhosis, portal hypertension with variceal bleeding history, chronic hepatitis); kidney failure - patients submitted in the dialysis program; peptic ulcer disease; connective tissue disease; peripheral vascular disease (intermittent claudication, chronic arterial insufficiency with by-pass, untreated thoracic or abdominal aneurysm), psychiatric illnesses (dementia); concomitant systemic disease or immunosuppressed patients by diabetes, primitive and metastatic cancers affecting various organs, chemotherapies, transplant patients, infectious diseases even AIDS; severe osteoporosis, chronic ethylic intoxication, drug allergies.

Neurosurgical pathologies varied alone or concurrently: 154 (47,38%) patients with cerebral pathology and 171 (52,61%) patients with spinal pathology: cranio-cerebral and spinal trauma

(hematomas: epidural, subdural, intracerebral, posttraumatic subarachnoid haemorrhage, cerebral and spinal contusions, DAI, cerebral lacerations, CSF fistula, Schneider syndrome, hematomyelia); cerebral tumours: extraaxial meningioma, metastasis, gliomas especially glioblastoma, schwanomas, pituitary and spinal tumours: extradural, intradural, intramedullary, frequent metastasis in lung, breast, prostate cancer; cerebral aneurysm, carotid-cavernous fistula, MAV, spinal degenerative myeloradiculopathy, mielopathy with cervical and lumbar canal stenosis, spinal instability with osteoporotic vertebral changes, vertebral fractures; Arnold neuralgia, trigeminal, atypical facial pain, spinal neuropathic pain; tremor (Parkinson's syndroms & disease, dystonic movements), blepharospasm even Meige syndrome, spasmodic torticollis. All patients were carefully neurologic, biologic, neuro-imagistic, multidisciplinary evaluated; neurosurgical surgical indication, anaesthesia protocol, informed consent to be used to each patient were supported with accuracy. Several procedures have been performed: craniotomies for tumours and hematoma removal, minimal invasive procedures for spine, endovascular, vertebroplasty, nerve block, neuro-vascular decompression or Gamma-Knife for pain procedures have been performed.

Results

The median length of stay for emergency patients was significantly longer than that of elective patients ranged between 13 vs.8 days, and in the ICU unit vary from 1 to 63 days.

For 215 (66.15%) patients general anaesthesia was performed, local anaesthesia in 97 (29.84%) patients, 13 patients (4%) were not operated. Good quality of life results appreciated by patients and relatives were recorded in 236 cases (72.61%) in the first and second category; less better results to those over 85 years old; same symptoms especially pain 63 patients (19.38%), complications to 47 patients (14,46%) especially cardiac, renal and respiratory failures, also motor deficits, seizures, CSF fistula, mortality in 26 cases (8%), re-admissions in 45 cases (13.84%) less than 1 month after discharge. For old patients physical therapists may improve strength and balance, safely walk ability, climb stairs before being released from the hospital. Occupational therapists may help such patients to be able to do personal hygiene using the bathroom, to get dressed; speech language pathologists could help patients with speech, language or thinking.

Discussion

The elderly patient - defined as an individual 65 years of age and over, still represent all around world in general, a fragile population, a great concern, with higher costs of health care, a difficult issue for the health systems struggling with limited resources (3-7)(9)(10). For each aging person there are a personal rate of degeneration of CNS as like as the whole body, in anatomy, in mental and physical activity, also in higher costs of living, lifestyle change, loneliness, possible dependence of specific medication for medical associated illnesses - such as diabetes and cardiovascular disease (3)(6). It's also a reality that the elderly population represent the fastest growing segment of the world's population; the world's population over 60 years will double between 2000 and 2050 and the number of people aged 80 and older will quadruple (7). 47,8 million the number of people age 65 and older in the United States on July 1,2015; this group accounted for 14,9 per cent of the total population (15). 98,2 million - the projected population of people age 65 and older in 2060; of this number 9,7 million will be age 85 or older (16). Such growing proportion affect also the neurosurgical admissions both in emergency surgeries or classical presentations for every group of persons on age “young-old” - 65-74, “middle-old” - 75-84 and “old-old” > 85 (17). There are several changes involved in different degree with age, with neurosurgical interest too (1)(2)(18-23):

-*cerebral atrophy* affecting especially the frontal and temporal lobes, decline in brain weight, increase in ventricular size, thickening of meninges, decrease in width of gyri, deep sulci, cortical neurons, myelinated axons, the number of synapses per neuron, loss of Nissl substance, nuclear atrophy; intracellular deposits, granulation or fragmentation of mitochondria. These aspects are generating tolerance in front of any expansive process, clinical onset delay in case of tumours, intracranial hematoma, facilitates surgical approach, allows intracranial expansive processes removal.

-*cerebral fragility* with decreased cerebral compliance that induces the brain's difficulty to resume its

anterior position, able to generate hematoma recurrence, hydrocephalus, etc.

-decreased cerebral blood flow, loss of vascular autoregulation and responsiveness to neuronal demand, hypercapnia, heterogeneous regional variations with decreased cellular oxygen, glucose and oxidative metabolism, altered sodium, potassium and calcium homeostasis with reduced axoplasmatic transport, calcium mediated and synaptic neurotransmitter release. There are also general decrease in excitability, peripheral nerve conduction velocity, altered reflex responses and increased latency of evoked potential, a disorganization of highly coordinated activities, with autonomic and homeostatic changes: reduced temperature regulation, orthostatic hypotension, chronic constipation, slowed hear rate, decreased blood pressure.

-leukoaraiosis (gr."leuko-" = white, meaning white matter and the adjective «araios" ="thin."- Hachinski V. 1987) are typically generated by: lacunar stroke/transient ischemic attack (TIA), dementia of both vascular and non-vascular etiologies (hypertension, degenerative, in Alzheimer's disease), sporadic cerebral amyloid angiopathy, diabetes; the precise pathogenic mechanisms remain unclear. Recent genetic results strongly supported that leukoaraiosis is associated with immune response and neuroinflammation (23). Pathologically, leukoaraiosis is characterized by white matter gliosis, axonal and myelin loss, increased perivascular spaces, patchy demyelination, hyaline thickening and arteriosclerosis of small vessels that can evolve to lipohyalinosis, fibrinoid necrosis, and denudation of ependyma. Main clinical manifestations are cognitive and executive troubles (memory loss especially short-term memory, visual and hearing loss, declining endurance, verbal intelligence, processing speech dysfunction in learning and language skills, depression), ankle jerks decreased or absent, increased primitive reflexes (glabella, palmo-mental), slowed forward flexed, altered gait, tremor with loss of fine motor coordination bladder instability. There are hypo-dense areas to cerebral CT scan, diffuse, heterogeneous, imprecisely delimited, primarily interesting the centre of the white substance or the immediate subcortical areas. The MRI examination in weighted T_1 sequences shows hypointense areas and the weighted T_2 sequences show hyperintense areas; sometimes without correlation as number, localization. MRI findings are commonly seen to elderly people with prevalence ranging from 50% to 100%. Leukoaraiosis may explain poor clinical outcomes and increases the risk of disability, dementia, depression, stroke, and the overall morbidity and mortality.

-amyloid angiopathy **>** 70 years: explains the difficulties of hemostasis, haemorrhagic recurrences, preanesthetic assessment, informed consent, perioperative evaluation, risk issues especially for those people identified with ASA physical status of III or IV. and care are magnified in older patient, anaesthetic management, efficient surgical skills procedures - especially functional neurosurgery, radiosurgery, planned postoperative management may contribute to successful outcomes also to ameliorate quality of life related to neurosurgical diseases, also to a specific neurosurgical pathology, especially pain (3)(5)(7)(8)(10)(11)(24-29). There are medical factors affecting anaesthesia: multiple medical comorbidities including sepsis, metabolic disturbances severe obesity or poor nutritional status, alcohol and/or drug abuse, history of cardiac failure or myocardial infarction ≤ 1 year with low ejection fraction (EF) on echocardiography, severe uncontrolled hypertension, severe respiratory dysfunction, hepato-renal failures, neurovascular, psychiatric disease, history of CVA or TIA, peripheral vascular disease, immuno-compromised patients by diabetes, tuberculosis, etc; severe coagulopathy status with trombocytemia, haemophilia, antiplatelet agents even help syndrome (to old patients even a normal coagulogram may coexist with difficult hemostasis), cognitive function at risk especially at advanced age > 70 years: cognitive impairment, acute confusional state, delirium. There are also surgical factors affecting anaesthesia in all such high-risk geriatric patients which should be discussed in detail for optimizing the outcome with the anaesthesiologist and cardiologist (28)(29):

-surgical position: prone, sitting, Concorde position have always cardio-respiratory implications, Wilson Frame or similar with varying degrees of inclination, neck stabilization, spine traction, requirement of elective ventilation, head up to 10 degree and reverse Trendelenburg may avoid perioperative blindness by direct/indirect eye pressure, ischemic

optic neuropathy, central retinal artery occlusion (CRAO), cortical blindness. Also a severe spinal trauma or an important scoliosis, osteoporosis, osteomyelitis, severe obesity or undernourished people.

-plan of surgical excision, anticipated duration (in general surgery should never exceed 6.5 h in older patient), anticipated blood loss, neurophysiologic monitoring, postoperative ventilation. The anaesthetic regimen has to be tailored according to the physiological reserve: local or general anaesthesia. For general anaesthesia there are several remarks:

-before induction the invasive monitoring for arterial blood pressure - ABP and central venous pressure - CVP should be instituted under local anaesthesia.

-induction should be performed with fentanyl, etomidate (etomidate requirement beyond the age of 80 years may decrease by 50%,), non depolarisant muscular blockade agents intravenously. Propofol produces an exaggerated fall in blood pressure especially to old patients, dehydrated, midazolam has increased duration and potency, neuromuscular blocking agents are unchanged oral intubation.

-anaesthesia should be maintained with 50% oxygen, air, sevoflurane in minimum alveolar concentration - MAC of 0.5 (MAC requirement for volatiles also decreases in the elderly, though the onset may be delayed due to decreased cardiac output). Monitoring should be performed by pulse oximetry: SpO_2, arterial blood pressure ABP avoiding acidosis, hyper or hypotension - 84 mm systolic minimum, Hct > 28%/, Hb > 9.4 with cardiac index (stroke volume) ↓ 24%; blood loss > 45%, heart rate HR, electrocardiogram ECG, end-tidal carbon dioxide, hourly urine output, temperature. To maintain hemodynamics and to avoid cerebral perfusion pressure crash crystalloids and noradrenaline should be infused intraoperatively.

-even in case with normal coagulation test, haemostasis could be laborious in the confined space of the cranial cavity or the spinal canal presenting as the surgical field; in case of bleeding diathesis (due to prescribed medications in the form of clopidogrel, warfarin, etc., alone or more often in combination) especially in emergency this is dangerous. For such situations there are several costly, time consuming, delaying procedures: red blood cell transfusion, donor platelet, frozen plasma, Novoseven, Pronative, Hemocompletan, recombinant factor VIIa, all of this are costly, time consuming, delay procedures.

-postop. Slowly awakening, extubated and closely watched in neurosurgical intensive care unit to improve resource utilization, decreased in-hospital mortality (26). The effect of depth of anaesthesia on outcomes is still a grey area. Perioperative cardiac - maintaining volume status, pulmonary evaluation are reliable predictors of complications, (ex. unoptimized pulmonary diseases, increased closing volumes and decreased expiratory flow rates, tracheostomy, postoperative mechanical ventilation) predispose older patients to complications and death, also renal status avoiding nephrotoxic drugs, prevention of hyperglycemia or hypoglycemia, adequate prophylaxis for deep venous thrombosis - even with pneumatic compression devices, multiple medications for other co-morbidities. Mental status should be assessed preoperatively because dementia is a predictor of poor outcome perioperatively, increasing mortality by 50% (25). Nutritional deficiencies should be corrected because they play a role in wound healing and recovery - albumin levels of < 3.2 g/dl in hospitalized elderly patients increased perioperative mortality (28), also pain should be treated.

Most common geriatric pathology are:
-*traumatic brain injuries*, more common: subdural uni or bilateral hematoma - a common pathology (11)(30-35), mainly affecting elderly patients, " not a benign disease" (34) In patients over 80 years old chronic subdural hematoma incidence is reported 127.1/100.000/year, with a mortality of less than 10%, a history of head injury is not always admitted, several cases could be under anticoagulant treatment because of cardiac pathologies or ictus cerebri, arterial hypertension, diabetes mellitus with severe thrombocytopenia, high INR, even with a normal coagulogramm haemostasis may be difficult. The most common clinical presentation include hemiparesis, disphasia/ aphasia, disorientation, hemianopsia. Diagnosis is sustained on CT scan. Anaesthesia should be local or general, to correct a severe coagulopathy may be necessary: thrombocytes, Novoseven-factor VII, Pronativ, Hemocompletan in case of fibrinolysis. Several

surgical techniques could be used: *craniotomy* centred on the thickest portion of the clot (useful in clots that can't be evacuated through a simple trepan hole, allows brain to resume its anterior position, to evacuate a concomitant intracerebral hematoma, to monitor intracranial pressure in those with CGS <9 Bullock et al, allows haemostasis), *craniotomy*, useful when intracranial pressure is maintained, requiring removal of the bone, *trephination* or two - several trepan holes in the thickest parts of the hematoma (for example, frontal and parietal that may be needed to be incorporated into a fronto-temporo-parietal craniotomy in case of relapse, hematoma consistency, thick membranes), *the subdural evacuating port system (SEPS)*: the minimally invasive technique, a safe method, effective in subacute and chronic subdural hematoma in elderly patients, easy to perform with local or general anaesthesia, it takes less than 10 minutes, without irrigation, aspiration, catheter (36). Postop complications are: recurrences, persistence of preop. brain position by decreased cerebral compliance, parenchymal haemorrhages in the same hemisphere or controlateral. Outcome are measured with Glasgow outcome scale (GOS) or Markwalder grading system (MGS) to evaluate improvement in neurological function in general a good GOS in 86.1% of patients older than 80 years (11), the discharge disposition to return to an independent life, to rehabilitation or nursing home. There are also cerebral contusions and lacerations, rare extradural hematoma with late shift effect of cerebral parenchima, veins ruptures and haemorrhagic events, dimished recovery capacity.

-cerebral aneurysm and less frequent cerebral arterio-venos malformation with subarahnoidian haemorrhage, *ischemic & haemorrhagic strokes supra and infratentorial*, associated with *hydrocephalus and occlusive cerebrovascular disease* 40% (3)(37).

-epilepsy to older patients is are more frequent (the annual incidence is 85.9 per 100,000 for people aged 65-69 years and 135 per 100,000 for those aged over 80 years (38); similar status epilepticus appears to occur more frequently with significantly greater morbidity and mortality in this age group (39). There are focal seizures, automatisms without generalisation or with secondary generalisation, the postictal phase is prolonged with confusion and memory problems corresponding with focal changes on electroencephalograph (EEG) and neuroimaging epileptogenic lesion (40). Epilepsy are more common encountered with stroke - the risk of epilepsy increases up to 20-fold in the first year after a stroke, hypertensive encephalopathy, cerebral vasculitis, tumours (gliomas, meningiomas and metastases), trauma, dementia, Alzheimer's disease - are up to 10 times more likely to develop epilepsy than those without the condition (38). To older patients there are: side-effects, toxicity, increased susceptibility to anti-epileptic drug, a mortality rate 2-3 times higher than the general population, a very variable prognosis depending on the epilepsy syndrome, the frequency of seizures, the response to treatment - an inadequate seizure control raise the suspicion of poor adherence or progressive neurodegenerative disease; social difficulties, multidisciplinary service requirements in the community (41).

-cerebral tumours:
meningiomas: are 12.8/100,000 incidence to those of ≥ 65 years of age, increasing with age (42)
In the elderly, meningiomas are diagnosed small, slow growing, asymptomatic extraaxial tumours without brain edema, even calcified, occurring more frequently in women than men (43). For such tumours therapeutic attitude are conservative clinical observation and radiologic follow-up (44-46). For clinically symptomatic and fast growing meningioma, especially atypical or malignant, to elderly patients with limited physiological capacities and comorbidities, surgery after a careful consideration should be the mainstay of treatment for local tumour control (47-52), to realise genetic and histological diagnosis (it's possible to the same patient to see meningiomatosis with different genetic and histologic behaviour: benign and malignant meningiomas), but also stereotactic radiotherapy (SRT), Gamma knife, Linac-based stereotactic radiosurgery effective in terms of tumour control and survival, safe with regard to toxicity - the overall rates of complications ranged from 2.7% to 29.8%, and the overall incidence of complications 20% (range, 3–61%)(53-59).

Metastasis are increasing to the majority of cancer patients over the age of 65, not only cerebral or intradural spinal metastasis, but more frequent bone metastasis, involving the spine in approx. 50% (60). Elderly survivors of breast cancer, lung cancer, and melanoma face risk of brain metastasis later in life; rates of synchronous brain metastases incidence

proportions in lung, breast, and melanoma cancers were 9.6%, 0.3%, and 1.1%, respectively; such tumours may require extra surveillance in the years following initial cancer treatment. Non-small cell lung cancer made up the majority of lung cancer SBM IP, at 13.4%, and small-cell lung cancer made up the majority of lung cancer - lifetime brain metastases at 23.1%. The most frequent spinal metastases (60%) are from breast, lung, or prostate cancer (61). The chance that an elderly patient (60–79 years old) is affected by bony metastases is four times higher in men and three times higher in women than a middle-aged patient (40–59 years old). Pain, neural compression with motor deficits, pathological fracture, and instability are the most common surgery indication. For cervical area: the occipito-cervical junction can generally be treated by posterior resection and stabilization, in the middle and lower cervical spine the anterior approach with anterior decompression and anterior column reconstruction; in the thoraco-lumbar spine a posterior decompression and postero-lateral vertebral body resection through a posterior approach only, with a concomitant reconstruction and stabilization. There are also for paleative cases different treatment modalities—irradiation, chemotherapy, steroids, biphosphonates, morphine pump. Since prospective randomized studies comparing different treatment modalities for spinal metastases including surgery are not available and are ethically difficult to achieve, each case remains an interdisciplinary, shared decision-making process for what is considered best for a patient or elderly patient. However, whenever surgery is an option, it should be planned before irradiation since surgery after irradiation has a significant higher complication rate.

Glioblastoma multiforme are at old age a high incidence, also most significant associated with poor prognosis, even after the introduction of temozolomide (TMZ) in 2006, without any clear borderline (62). After published statistics from the Japan Brain Tumour Registry from 2001 to 2004 (63), patients aged > 65 years and > 75 years accounting for 42% and 11.4%, respectively; the most frequent age group of patients was 65–69 years, which accounted for 17% of the cases, median overall survival was 15 months. GBMs are subdivided according to their molecular phenotype see WHO classification of central nervous system (CNS) tumour 2016 (64), namely, CpG island methylator phenotype (G-CIMP) and isocitrate dehydrogenase (IDH) mutation: IDH wild type and IDH mutant - absence of IDH mutation, is the most predominant GBM in the elderly. Also MGMT promoter methylation is independent of age, with 47% in the elderly, epidermal growth factor receptor - EGFR, p53, CDKN2A, PTEN were not prognostic factors (65), vascular endothelial growth factor (VEGF) was higher in GBM in the elderly than in young patients, also the prognostic value of telomerase reverse transcriptase (TERT) promoter mutation in GBM has been debated (66). Although age is a poor prognostic factor, old age alone is suggested to have no association with poor prognosis, an aggressive treatment should not be withheld because of old age (67). Multimodal treatment in elderly patients with GBM aged > 65 years should include:

-surgical resection: achieving maximal tumour cytoreduction within the safety margin, brain decompression, histopathological and genetic diagnosis especially for *IDH* mutation and *MGMT* methylation status. Such aggressive attitude may prolonge survival by 2.8 times than biopsy (median OS: 171 days after the craniotomy versus 85 days after the biopsy), also for aged patients ≥75 years may extend survival by 2 months, delayed tumour progression and improved functional prognosis (68-76).

-radiotherapy - hypofractionated radiotherapy (Hypo-RT 40 Gy/15 Fr) alone can be considered if the tumour has an unmethylated *MGMT* promoter (77-80)

-with concurrent and adjuvant TMZ - in elderly patients with MGMT methylated tumours monotherapy with TMZ can expect prolonged survival (78-82); clinical benefits of bevacizumab use in remain unclear (83)(84), also lack of evidence regarding the efficacy of carmustine wafer (85)(86).
another cerebral tumor: schwanoma, pituitary adenoma (87)

-*spinal pathology* means for old patients a wide range of neurosurgical procedures to solve:
spinal degenerative myeloradiculopathy, mielopathy with cervical canal stenosis, lumbar spinal stenosis (it's important to clarify that surgery will not give another spine, also surgery is better to be done in a

only surgical procedure); spinal tumours: extra/intra dural, intramedullary and more frequent vertebral metastasis in lung, brest or prostate cancers; spinal instability and osteoporotic vertebral changes.

-chronic geriatric pain defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage", is a longstanding pain that persists beyond the usual recovery period or occurs along with a chronic health condition, for greater than 3 months is a more frequent neuropathic, persistent, recurrent, underreported; much more difficult to treat especially for those with long-lasting pain compared to young people, justified by pain corticalisation (88). Such condition is impairing activities of daily living, ambulation, quality of life; more difficult to be understood especially to those patients with cognitive or language impairments; also may generate polypharmacy with concomitant medication, but also responsive for poor health, accidents, gait abnormalities, cognitive decline, denial, depression, psychosocial concerns, with direct and indirect estimated treatments costs close to $50 billion a year (89). There are several types of chronic pain, complex, multifactorial in older population, very debilitating and painful: trigeminal neuralgia, atypical facial pain, occipital neuralgia, postherpetic neuralgia, headache, stroke and phantom limb pain, failed spinal surgery, referred or pain related to cancer; also pain perception is more difficult to be treated. For such patients a multidisciplinary approach needs to be conceived: pharmacotherapy, psychological support, psychological support, also interventional procedures. A wide range of procedures (88) should be wisely proposed taking into account life expectancy, comorbidities, the patient's desire focusing on neuromodular rather than lesional techniques, also risks for each procedure: microvascular decompression, chemical neurolysis, radiofrequency and glycerol rhizotomy, stereotactic radiation, deep brain & spinal cord stimulation, motor cortex stimulation and neuraxial drug delivery.

-tremor (Parkinson's syndrome & disease and dystonic movements) treated especially by medication, DBS, motor cortex stimulation (90).

-neuro-infections especially to immunocompromise patients: diabetes, TB, HIV, etc.

-multiple sclerosis

-dementia

Conclusions

This study is a plea argue that in elderly patients, which is likely to continue to grow (6), risk factors should be adequately managed even in emergency (3), with correct preoperative evaluation, appropriate perioperative care (8), titrated anesthetic management, efficient surgical skills. Planned postoperative management may improve neurological status (30)(91), outcomes, reduce mortality rates, reduce length of intensive care stay, improved resource utilisation, fiscal benefits (7)(9). Further studies in the elderly are mandatory to be performed to improve clinical decisions on risk benefit ratios pending on new technologies.

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"The Silk Road" via subarachnoid cisterns. Cerebrospinal fluid dissemination of meningiomas

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Keywords
meningioma, metastatic spread, CSF disseminated meningioma

ABSTRACT
Meningiomas are generally slow-growing extra-axial benign tumours and in rare cases they can metastasize both neural and extra-neural. Intracranial meningiomas with leptomeningeal dissemination are extremely rare and the exact pathogenesis still remains unknown. The aim of this review is to analyse the pathways of intracranial and spinal metastatic spread of intracranial meningiomas and to discuss their particular clinical and pathological features. We highlight the fact that there is a possibility of leptomeningeal dissemination, even if cerebrospinal fluid cytology is negative, in patients with a medical history of a resected meningioma. We identified three possible ways of dissemination: haematogenous, through the CSF, or during surgery. From a histopathological point of view, the more malignant the meningioma, the more likely its leptomeningeal dissemination.

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INTRODUCTION

Meningiomas are generally benign intracranial tumours and represent approximately 30% of all primary central nervous system tumours, with an incidence that has increased in recent years (1, 2, 3, 4, 5). Usually occurring on the surface of the brain as they originate in the arachnoid cells, meningiomas are generally slow-growing extra-axial benign tumours. In very rare cases, especially when the tumours become malignant, meningiomas can metastasize both in neural and extra-neural sites (6).

Only 0.1% of meningiomas are thought to metastasize (7), and usually these cases were atypical and anaplastic meningiomas (8, 9, 10), also known for their tendency to relapse after surgery (2, 11, 12, 13). Ather Enam et al. report an overall metastatic risk of 5% for atypical meningiomas and of 30% for anaplastic meningiomas (8), although

other authors consider these percentages to be overestimated (11, 14, 15).

Meningiomas can metastasize in various organs (lung, liver, spleen, adrenal gland, thyroid, parotid gland) or bones, skin and deep soft tissue (16), but also in the intracranial or spinal space through cerebrospinal fluid (CSF) pathways. According to the existing literature, metastatic dissemination of meningiomas through CSF is a rare presentation (17, 18, 19, 20, 21) and, since 1950, only 45 cases have been reported (22). Nevertheless, different other authors consider that the CSF dissemination risk of meningiomas is an uncommon event, as it may occur in 4% of metastasizing meningiomas (17, 23).

However, the first historical description of leptomeningeal metastasis was made by Oliver in 1837, followed by Eberth in 1870 (24, 25) Also, the first description of carcinoma cells in the CSF was realized by Dufour (26) and, in 1912, Berman was the first who used the term "meningeal carcinomatosis" (27). However, Kalm, in 1950, was the first who published a case of a malignant tentorium tumour, i.e. an anaplastic meningioma that metastasized in the medulla oblongata and in the leptomeningeal space (28).

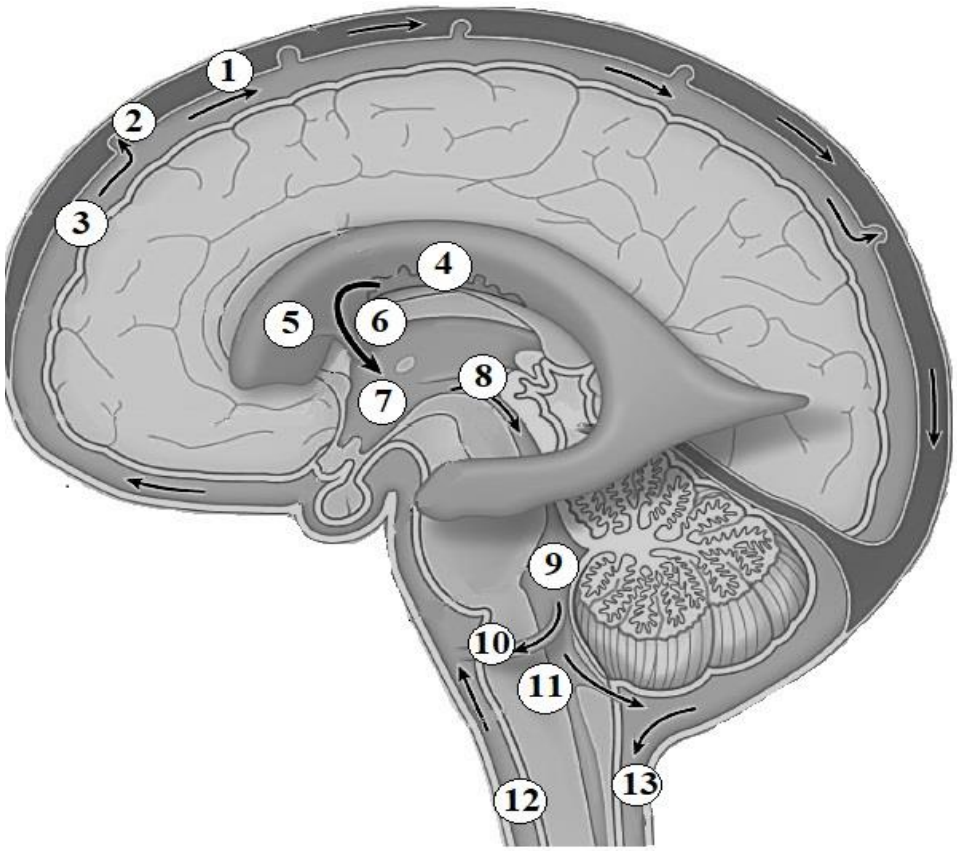

Figure 1. Cerebrospinal fluid circulation: (1) superior sagittal sinus, (2) arachnoid granulation, (3) convexity subarachnoid space, (4) choroid plexus (site of CSF production), (5) lateral ventricle, (6) interventricular foramen (Monro), (7) third ventricle, (8) cerebral aqueduct (Sylvius), (9) fourth ventricle, (10) lateral aperture (foramen of Luschka), (11) median aperture (foramen of Magendie), (12) ventral subarachnoid space, (13) dorsal subarachnoid space. (Adapted after Ropper AH et al., Adams and Victor's Principles of Neurology, 11th Edition)

Pathways of metastatic spread in meningiomas

Meningioma cells gain access to the subarachnoid space in several ways: haematogenous pathway, through the CSF, or during surgery. More frequently, the spread is haematogenous via the venous system and tumour cells gain access to the CSF through the dural sinuses or epidural plexus, especially in meningiomas that invade dural sinuses (29, 30). A

second route of dissemination is by CSF with the tumour spreading throughout the neuroaxis (Figure 1).

In a review, Rawat et al. highlighted the fact that approximately 75% of patients with meningiomatous metastasis regardless of the route they followed have had previous operation for the primary tumour (31). Also, it was hypothesized that tumour cells gain access to the vascular channels and meningeal surface by seeding during surgery (32). Although this theory has earlier been rejected (33, 34), now it is accepted that surgical manipulation may release tumour cells into the CSF (30, 31).

Metastatic spread during or after surgery exists theoretically, even though this theory is unlikely. But the incidence of leptomeningeal dissemination after meningiomas surgery is low and there are also cases with leptomeningeal dissemination through CSF without surgical intervention (35). Regarding malignant transformation of meningiomas after surgical resection, there is also the theoretical one (22). Koenig et al. reported that at the site of surgical injury, the growth factors can promote malignant changes inside the meningeal tumour (36) and this event was observed by Morantz and Shain in an experimental rat model (37).

Intracranial and spinal cord dissemination through CSF pathways

There are variable sites of meningioma metastasis through CSF pathways. The metastasis occurred due to leptomeningeal seeding from the neighboring meningioma, and the spinal canal is the second most common site (17) (Table 1).

In literature, spinal metastasizing meningiomas are rarely reported (17, 38, 39, 40, 41). In spinal intradural dissemination, the tumour cells have a tendency to accumulate more frequently at dorsal nerve root level, especially in the medullary cone and cauda equine, probably due to directional active flowing of the CSF throughout the neuroaxis, and also to the effect of gravity (42, 43). In a large study on 200 consecutive meningiomas, of WHO grade I, which were followed prospectively during a median time of 8.5 years, Chamberlain and Glantz reported that 4 patients (2%) were diagnosed with spinal metastasis (21). Vries et al. also reported CSF or drop metastasis in 5% of non-benign meningiomas (44).

Meningioma metastasis may be simultaneous, both in the intracranial space and in the spinal cord (17, 45). In 1992, Akimura et al. reported a malignant meningioma metastasizing through the CSF pathways, both in the cerebellopontine angle cistern and in the thoracic spinal cord. The primary tumour was a parasagittal malignant meningioma two-times operated, the second time for recurrence. At the first surgery, the frontal horn of the lateral ventricle was opened because the meningioma infiltrated into the deep frontal brain. The authors concluded that this artificial communication between the meningioma cavity and the CSF pathways enhanced the probability for tumour metastasis into cerebellopontine angle cistern and thoracic spinal cord (17).

Neoplastic meningitis

It is well known that neoplastic meningitis is more common with solid carcinoma such as lung, breast and gastrointestinal cancer (46), but literature also reported few malignant meningioma cases with CSF dissemination into the brain ventricles (47). There were only eight cases (47, 48) with intracranial or intraspinal malignant meningioma arising from low-grade meningiomas, which disseminated throughout the CSF (47). In neoplastic meningitis, CSF dissemination of malignant meningioma cells may cause a variety of neurological symptoms such as disturbances of multiple cranial nerves, hydrocephalus, cerebellar dysfunction and multiple spinal nerve roots or cauda equine symptoms (49).

Brainstem damage by CSF dissemination of malignant cell is rare, literature reporting a few cases with central hyperventilation, Wallenberg syndrome and diplopia, facial nerve palsy and unsteadiness of gait secondary of CSF dissemination of malignant tumour cells (20, 47, 50).

It is important to mention, in terms of diagnosis, that only 54% of all cases with leptomeningeal meningiomatous dissemination revealed malignant cells in the CSF on initial lumbar puncture, and only 8% of these cases remained negative, even after repeated examinations (51). The reason for this low specificity of the lumbar puncture remains unclear, although Fujimaki et al. speculate the fact that malignant cells adhere rather than float freely in the CSF (47). Although identification of malignant cells by CSF cytology has been considered the diagnostic gold standard, these paradigms have changed nowadays due to limited sensitivity of cytology.

Histopathology of CSF-disseminated meningiomas

Even though the pathogenesis of CSF - disseminated meningiomas is not completely understood, over time researchers have issued various theories. In this regard, Engelhard proposed three different pathways of dissemination: (1) tumour cells could be "shed" away directly into the CSF due to direct contact between an anaplastic meningioma and CSF pathways; (2) tumour cells might invade the leptomeningeal space during its progression; 3) the tumour cells might be inoculated within the CSF at the time of the surgery (52).

Other authors, such as Russel and Rubinstein, considered that tumour friability may play an important role in meningioma dissemination within CSF (42). However, considering that meningiomas arise from arachnoid cells and are naturally exposed to CSF during their growth, it is difficult to explain the scarcity of meningioma dissemination through CSF (22) as Chamberlain and Glantz reported that only 4% of the meningiomas could present leptomeningeal dissemination and positive CSF cytology at the time of the diagnosis (21).

More theoretically, the risk of intraventricular meningiomas to metastasize through CSF pathways should be high, but literature reports only nine cases of intraventricular meningiomas (22). As an explanation, Miller and Ramsden considered that the dynamics of the CSF pathways might prevent fragment formation and deposition of tumour cells (22, 53). However, in a review of 45 cases of meningioma with leptomeningeal dissemination through CSF, Park et al. noticed that the period of time needed for leptomeningeal dissemination in cases with intraventricular meningiomas is the shortest when compared to other intracranial and spinal meningiomas (22).

All histological subtypes of meningiomas can metastasize (Table 1), even benign meningiomas (45, 54, 55, 56, 57, 58), but meningeal tumours with clearly malignant features have a higher metastatic rate (59). Metastatic meningiomas are associated more frequently with aggressive meningiomas (WHO grade 2, and WHO grade 3), with a range of occurrence of 10-25% (21), i.e. the more malignant the meningioma, the more likely its leptomeningeal dissemination (9, 17, 41, 60).

According to literature, from a histological point of view, several factors are predictive of meningioma metastasis, including high cellularity, nuclear pleomorphism (Figure 2), high mitosis rate, tumour necrosis, and invasion of blood vessels (7, 8). On the other hand, other authors consider that the metastasizing behaviour of these tumours is not correlated with their histological features (30, 31).

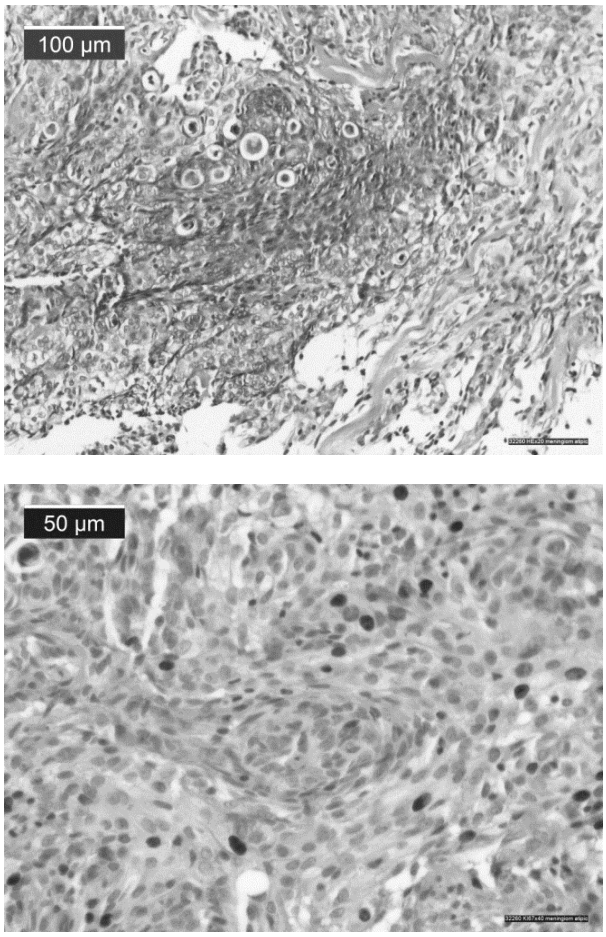

Figure 2. Microphotographs of atypical meningioma, WHO grade II. A. A tumour made up of meningothelial cells arranged in a sheet-like pattern, with increased cellularity, pleomorphism, and areas with small cells having high Nucleus/Cytoplasm ratio (HE staining, x20); B. Ki67 labelling index has high values and indicates a malignant neoplasia (Anti-Ki67 antibody immunohistochemical staining, X40).

Conclusion

Intracranial meningiomas with CSF dissemination are extremely rare and, despite reports from literature, their pathogenesis remains unknown. In the case of a patient with a resected meningioma, the possibility of CSF dissemination of tumour cells should be borne in mind, even if CSF cytology is negative. Also, a spinal MRI should be performed, especially when spinal signs and symptoms are present.

TABLE 1. Literature review of meningioma cases with CSF- dissemination

Year of publication, Author	Primary site of meningioma	WHO Grade	Intracranial metastasis	Spinal metastasis	Time to CSF disseminated disease
2013, Tsuda et al. (43)	T10-11 intradural	I →II	-	+	12 years
2011, Wu et al. (61)	Convexity	III	+	-	1.7 years
2011, Kim et al. (62)	Posterior fossa	III	+	-	0
2011, Peng et al. (63)	Medial temporal	III	+	-	2 years
2009, Kuroda et al. (64)	Skull base	I→II→III	+	+	6.3 years
2009, Eom et al. (6)	Lateral ventricle	II→III	-	+	1.3 years
2008, Erkutlu et al. (65)	Posterior fossa	III	-	+	2.7 years
2008, Santhosh et al. (65)	Convexity	III	+	+	9 months
2007, Shintaku et al. (67)	Lateral ventricle	I→III	+	-	4.3 years
2006, Chuang et al. (68)	Convexity	III	-	+	3 months
2005, Cramer et al. (60)	C1-C3 intradural	II	-	+	1.4 years
2005, Al-Habib et al. (69)	Not mentioned	III	+	+	2 months
2005, Chamberlain and Glantz (21)	Not mentioned, 8 cases	I	+ (8 cases)	+ (6 cases)	-
2005, Wakabayashi et al. (70)	Frontal convexity	III	+	-	13 years
2005, Koenig et al. (36)	Temporal lobe	III	-	+	1 month
2005, Darwish et al. (71)	Lateral ventricle	II→III	+	+	7 months
2002, Ramakrishnamurthy et al. (35)	Lateral ventricle	I	+	-	4 years
2001, Conrad et al. (72)	Convexity	I→II→III	+	+	6.4 years
2000, Meinsma-VdTuin et al. (73)	C2-C4 intradural	III	+	+	6 months
2000, Lee et al. (74)	Convexity	III	+	+	9 years
1998, Lee and Landy (41)	Convexity Skull base Convexity	III I III	+ + -	+ + +	1.5 years 3.8 years 8.5 years

1995, Peh and Fan (39)	Lateral ventricle	III	+	+	5 years
1993, Greenberg et al. (75)	Lateral ventricle	III	+	+	2 months
1992, Satoh et al. (18)	Skull base	I	+	+	0
1992, Akimura et al. (17)	Convexity	III	+	+	1.8 years
1989, Kamiya et al. (76)	Lateral ventricle	III	-	+	6 months
1987, Strenger et al. (77)	Third ventricle	III	+	-	1.5 months
1985, Kleinschmidt-DeMasters and Avakian (20)	Lateral ventricle	III	+	+	1.7 years
1975, Ludwin and Conley (78)	Convexity	III	+	+	10 months
1972, Miller and Ramsden (53)	Convexity	III	+	-	-
1971, Riley et al. (22, 78)	Convexity	I→III	-	+	-
1970, Shuanghoti et al. (22, 78)	Convexity	III	-	+	-
1963, Russell et al. (22, 78)	Skull base	I	+	-	-
1960, Hoffman et al. (22, 78)	Convexity	I→III	+	+	-
1954, Winkelman (22, 78)	Skull base	I	+	-	-
1950, Kalm (22, 78)	Posterior fossa	III	+	-	-

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A rare case of metastatic esthesioneuroblastoma

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ABSTRACT

Olfactory neuroblastoma, also known as esthesioneuroblastoma (ENB), is a rare malignant tumour of the basal layer of the olfactory epithelium, which originally develops unilaterally, accounting for 3-6% of all intranasal tumours. We present the case of a patient with a voluminous ethmoidal lesion that invaded the left basal frontal lobe and left orbit. The biopsy revealed a stage C KADISH, grade III neuroblastoma. The patient followed a multimodal treatment with chemotherapy and radiation therapy to which he responded partially, then returned after 11 months for sphincter disorder and bilateral sciatic type pain. An MRI showed metastasis of the filum terminale, the anatomopathological exam identifying also neuroblastoma. CT and MRI imaging are required for a correct assessment of the regional extension of olfactory neuroblastoma, response to oncological treatment but also for the detection of secondary lesions found in a small number of cases.

Keywords
neuroblastoma,
olfactory,
spinal metastasis

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INTRODUCTION

ENB is a rare malignancy, includes 3% of all intranasal tumours (1), was first described in 1924 (2), and it develops from the olfactory epithelium of the cribriform plate. These tumours are initially located unilaterally, and then invades orbit, nasal fossa, skull base, and intracranial space. The risk factors are unknown and there is a bimodal incidence at 10-15 years and 40-50 years. The most common symptoms are nasal congestion, anosmia, epistaxis, headache, and diplopia. These tumours have a high potential for regional and distance extension and multimodal treatment may help patients and increase their survival rate (3).

CASE PRESENTATION

A 33-year-old patient presented to the emergency room with headache and vomiting. CT exploration was recommended which showed hydrocephalus and a lesion that occupied the ethmoidal air cells, an extension in the nasal fossa, the anterior cranial fossa with bone lysis. A gadolinium enhanced MRI was performed that showed a 33/34/23

mm (AP/CC/T) lesion, with a heterogeneous enhancement, with calcified areas, occupying mostly of the nasal fossa and all ethmoid cells, most likely developing from the cribriform plate, invading the orbit (with mass effect on the internal muscles) and frontal lobes, more evident in the left side (Fig. 1, Fig. 2, Fig. 3, Fig. 4).

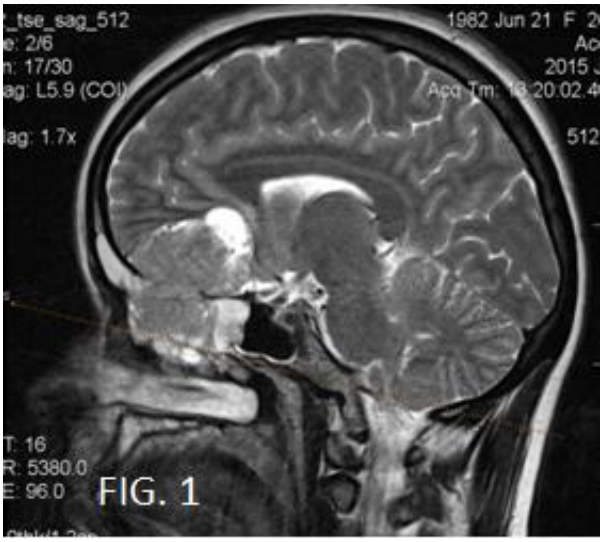

Figure 1. Sag T2WI. The tumour occupying the nasal fosa, originating from cribriform blade with superior extension.

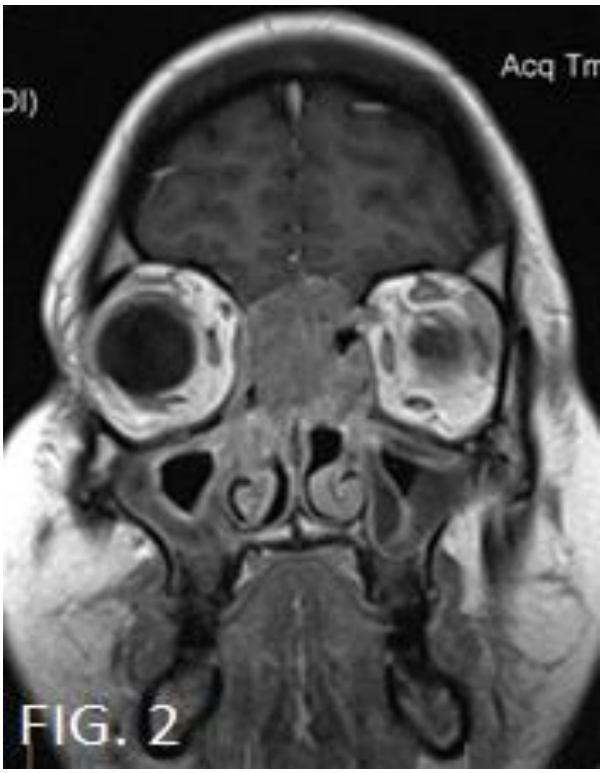

Figure 2. MRI Cor Gd-T1WI.

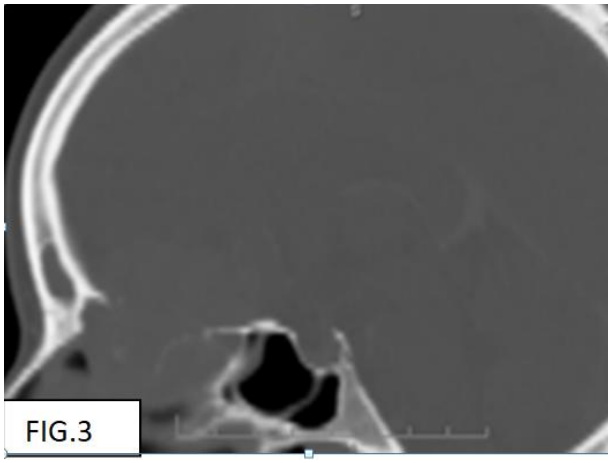

Figure 3. Sag CT (bone window): bone lysis.

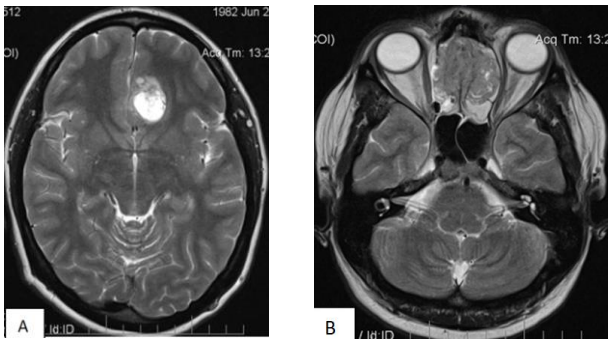

Figure 4. (**A**) Axial T2WI-extension of the frontal lobe; (**B**) Axial T2WI - mass effect on the internal muscles in the left orbit.

After the biopsy, the anatomopathological exam concluded stage III Kadish group C neuroblastoma. In this case the patient followed two chemotherapy cycles but abandoned it later because he was known to have hepatitis B and the viremia level was increasing. Therefore, he continued only with radiotherapy.

The patient returned to control after six months when the MRI scan showed a decrease in tumour size, with the same characteristics as before, and was kept under control for one year. After one year the patient came back with bilateral sciatica and major sphincter dysfunctions. The MRI exam of lumbar region highlighted a hyperintense T1 and T2, hypointense STIR lesion in the S1 vertebral body and a nodular vivid enhancing lesions of cauda equina in S1 and S2 region, suggestive of secondary lesion (Fig. 5, Fig. 6); the anatomopathological examination confirmed the diagnosis of metastasis from neuroblastoma.

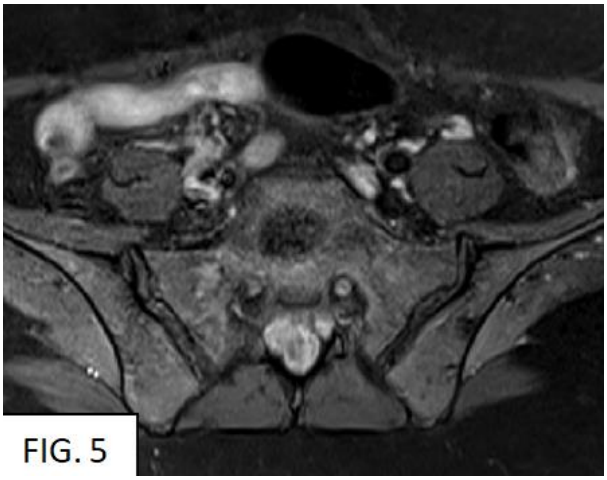

FIGURE 5. MRI Axial STIR - S1 vertebral body level.

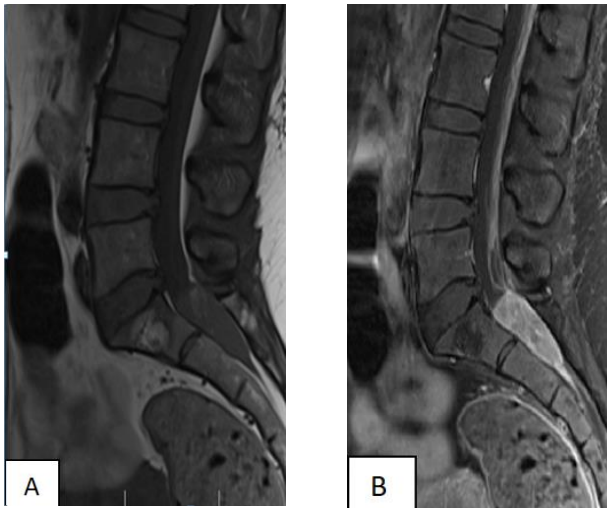

FIGURE 6. S1 secondary lesion (**A** – T1WI; **B** – Gd enhanced-T1WI))

After 10 episodes of lumbar radiotherapy, the patient returned accusing headache, diplopia and diffuse cervico-lumbar pain. MRI exploration revealed a stationary aspect of the tumor compared to the previous exam. The patient wanted to be discharged and unfortunately, he died shortly afterwards.

DISCUSSIONS

Olfactory neuroblastoma is a tumour which originates from the olfactory cells of the cribriform blade and, although it develops initially in an unilateral manner, it invades afterwards the bilateral intracranial spaces. Kadish classifies these tumours in three classes (4): A - limited to the nasal cavity, B - infiltrated into the nasal cavity and paranasal and C - extended beyond the nasal and paranasal cavity. Our case was classified in stage C and histologically in class III. There are four histological classes that divide this type of tumour by histological cellularity and histochemical analysis. According to some authors, ENB it is most likely congenital, and it develops even in intrauterine life (5).

The role of imaging in the staging of ENB is very important. In 40% of cases, it extends in the paranasal sinuses, in 30% extension is intracranial, and in 30% extension is orbital (6). MRI is the most used technique in staging because the report on the extension of the tumour in the adjacent tissues can be very thorough.

Very important are the CECT and PET-CT exams of lymph nodes because esthesioneuroblastoma disseminates in cervical and laterocervical lymph nodes which are asymptomatic and undetectable on physical exam. CECT and PET-CT can highlight these lymph nodes by marked contrast enhancement on CECT and moderate to highly avid of FDG on PET/CT.

Some studies highlight a cervical dissemination in the lymph nodes in 30% of cases and the presence of secondary lesions are rare and very rare for spine (7). In our case there was secondary involvement of vertebral body of S1 and also a metastasis of cauda equina in S1 and S2 region.

Many studies show that patients treated with surgery have a 5-year survival rate of about 50%, while surgery combined with chemotherapy prolong survival to 65% at 5 years in the case of local esthesioneuroblastoma (8,9).

In local advanced ENB, resection of the cervical lymph nodes is performed to reduce the risk of recurrences. Postoperative chemotherapy and radiotherapy in patient with lymph nodes metastasis have decreased recurrences and the survival rate at 10 years was 80%.

Chemotherapy combined with radiotherapy is widely accepted recently, with a survival rate of 35%. Despite lymph node resection, radiotherapy and chemotherapy, in most cases of advanced ENB lymph node recurrence is detected 12 months after completion of treatment.

Currently, radiotherapy in ENB is used in combination with surgery and chemotherapy because there are no randomized trials to guide radiotherapy treatment, but radiotherapy plays an important role in the treatment plan in early stages with definitive cure and good tumour control. The

doses used are 50-60 Gy with intensity-modulated radiation therapy to minimize doses to the optic structures, pituitary gland and brain (10).

Conclusions

Olfactory neuroblastoma is a rare tumour that originates from olfactory epithelium and extends into the orbit, nasal fossa, skull base and intracranial space. The combined use of CT and MRI techniques is excellent in providing necessary information for treatment planning. Recognizing the limitation of current data, surgical resection and postoperative radiation therapy for resectable lesions is the most commonly used management approach. For unresectable tumours, radiation alone or chemoradiation therapy are also viable treatment options. Palliative chemotherapy has not shown a clear survival benefit in patients with recurrent and/or metastatic disease.

Considering the metastatic potential of this type of tumour, a rigorous imaging examination is required for an early diagnosis and a more effective treatment.

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Idiopathic normal pressure hydrocephalus. A brief review

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ABSTRACT
Idiopathic normal pressure hydrocephalus (INPH) is a neurodegenerative disease which affects the elderly, with a significant prevalence in the general population (0,2% - 5,9%), thus a common pathology encountered by neurologists and neurosurgeons, alike. Although the widespread availability of modern imaging techniques has facilitated the diagnosis of this disorder, the clinical manifestations can often be misleading. Also, an overlap with other degenerative or psychiatric diseases can make the differential diagnosis even more challenging. Cerebrospinal fluid (CSF) diversion procedures are the first line of treatment for INPH. Nowadays, there are several shunting options available, including: ventriculoperitoneal (the most commonly used), ventriculoatrial, ventriculopleural, ventriculosternal, lumboperitoneal, endoscopic third ventriculostomy. Choosing a procedure tailored to the individual patient is essential for therapeutic success. Although they are generally straightforward surgical interventions, they associate a high rate of failure, regardless of procedure used, which emphasizes the need for regular clinical and imagistic follow-up. Thus, INPH remains a disease where there is significant room for improvement, both in diagnosis and treatment.

Keywords
idiopathic normal pressure, hydrocephalus, CSF shunting

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DEFINITIONS

Hydrocephalus is produced by an excessive accumulation of cerebrospinal fluid (CSF) at the level of the ventricular system that determines a specific clinical picture (depending on the patient's age) and enlargement of ventricles on imaging studies.

Normal pressure hydrocephalus, also known as chronic adult hydrocephalus, is clinically characterized by the classic triad: gait, urinary and cognitive dysfunction, associated with ventriculomegaly.

Normal pressure hydrocephalus can be idiopathic or secondary.

Idiopathic normal pressure hydrocephalus (INPH) is a neurodegenerative disease which affects the elderly, representing a treatable cause of dementia with a prevalence of 0,2% up to 5,9%1,2.

CLINICAL PICTURE

In 1965, Hakim and Adams described the clinical picture of this disease, characterized by walking, urinary and cognitive dysfunction (3).

The patients present an ataxic gait, bradykinetic, with small steps and low cadence, as well as balance disorders. They have difficulty in ascending or descending stairs, in getting up from a sitting position or turning around. In advanced stages, patients become hypertonic, bradykinetic.

Urinary disfunctions generally manifest as incontinence. In the early stages of the disease, the urinary symptoms consist of urgency in emptying the bladder, but subsequently it is replaced by urinary incontinence, more frequently than fecal incontinence. In advanced stages, patients become indifferent to their urinary disorders.

Cognitive disorders consist of memory impairment, slow ideation, attention deficits, apathy, depression and aggressiveness.

It is important to obtain a correct diagnosis because other diseases present a similar clinical picture. INPH symptoms are also encountered in other disorders that must be included in the differential diagnosis, such as: Parkinson's disease, Alzheimer's disease and vascular dementia. Similar cognitive impairment can be encountered in schizophrenic patients and the two conditions can also coexist. In Vanhala's opinion, INPH is three times more frequent in this category of patients4.A list of other disorders that must be differentiated from INPH is presented by Bech- Azeddine5.

According to Israelsson et al, the prevalence of depression is four times higher in patients with INPH compared to the elder population without INPH2.

Imagistic diagnosis

Modern imagistic methods reveal ventriculomegaly. The size and span of ventricles can be appreciated by calculating certain indices:

- Evans index (bifrontal index) is the distance between the lateral walls of the frontal horns of the ventricle divided by the internal diameter of the skull at the same level. In INPH, the value of this index is ≥ 3
- Bicaudate index is equal to the ratio between a line drawn between the two ends of the caudate nuclei and the internal diameter of the skull at the same level
- Fronto-occipital horn index represents the ratio between the sum of the distances between the lateral walls of the frontal horns and occipital horns of the ventricles respectively and twice the largest internal diameter of the calvaria in the horizontal plane

CSF physiology and INPH physiopathology

Briefly, it is known that CSF is produced at the level of the choroid plexus located in the ventricular system with a rate of 0,3 - 0,5 ml/min, representing approximately 500 ml every 24 hours.

CSF travels from the lateral ventricles to the fourth ventricle through the aqueduct of Sylvius and subsequently, through the Magendie foramen reaches the subarachnoid spinal space and cerebral convexities.

CSF is reabsorbed at the level of Pacchioni's granulations located parasagitally on the cerebral convexities and afterwards reaches the superior sagittal sinus, entering the blood stream.

In the case of INPH, one hypothesis suggests that enlargement of ventricles compresses or deforms the axons of the central motor neurons that pass through the medial portion of the corona radiata.

Parkinson's disease type symptoms of INPH patients are caused by the dysfunction of the nigrostriatal dopaminergic pathways caused by abnormal CSF pulsations which affect the substantia nigra and determine the disorder of motor planning.6

The cognitive disorders are produced by involvement of the frontostriatal system, of the projection fibers which pass in the proximity of the lateral ventricles.

Treatment

The majority of INPH patients benefit from surgical treatment of CSF diversion.

Preoperatively, there must be a careful selection of patients that respond to this treatment. In order to do so, there are multiple methods to evaluate potential responsiveness and tests which evaluate the degree of clinical improvement:

1) CSF pressure: is measured during a lumbar puncture, with the patient positioned in left lateral decubitus, with the help of a manometer. In healthy individuals, the opening pressure is 122 mmH2O, while in INPH patients, the pressure varies between 60 – 240 mmH2O, with a mean of 150 mmH2O. This pressure is not constant, a value higher than 245 mm mmH2O indicating secondary noncommunication hydrocephalus, not INPH1,7.

2) Alleviation of symptoms after repeated

lumbar punctures with removal of 40 ml CSF is a common method for estimating responsiveness, but nonetheless a subjective one.

3) External CSF drainage for 72 hours, which determines clinical improvement. It is carried out by inserting an intrathecal catheter in the lumbar area and drainage of 10 ml CSF every hour for 72 hours8.

4) Postoperative clinical improvement can be evaluated by comparing results of several tests:

- Timed Up and Go (TUG)
- Timed Up and Go Cognition (TUG-C)
- Berg Balance Scale (BBS)
- Performance Oriented Mobility Assessment (Tinetti)
- Mini Mental Status Examination (MMSE)
- NPH Japanese Scale
- Minimal Clinically Important difference (MCID)
- Geriatric Depression Scale 15

Surgical treatment is not risk free. Therefore, a risk-benefit evaluation must be carried out for each patient. Patients under anticoagulant treatment associate a high risk for intracranial haemorrhage. Those with cerebrovascular disease have a low rate of response to CSF drainage.

Types of CSF drainage

- Ventriculoperitoneal (VP) shunt is the most frequently used.
  There are however other shunt options, each with its advantages and disadvantages:
- Ventriculoatrial (VA)
- Ventriculopleural
- Ventriculosternal
- Lumboperitoneal (LP)
- Endoscopic third ventriculostomy (ETV)

Ventriculoperitoneal shunting is not recommended for patients with a history of multiple abdominal surgery or peritonitis, due to the presence of adhesions and low CSF absorption. Also, VP shunting is difficult to perform in obese patients.

Ventriculoatrial shunting can be associated with chronic infections, which if undiagnosed, can lead to shunt nephritis.

Lumboperitoneal shunt has a similar efficiency compared to ventriculoperitoneal shunt in INPH treatment. It is indicated for INPH patients who are not ideal candidates for intracranial procedures. LP shunts are technically more difficult to perform in obese patients, in ones with spinal deformity (kyphosis, scoliosis), degenerative lumbar stenosis. In these patients, repeated lumbar dural sac punctures may be necessary, which can lead to venous plexus lesions with blood-stained CSF and also radicular lesions.9

Endoscopic third ventriculostomy can be performed "d'emblée" or in the case of VP shunt malfunction. A rigid neuroendoscope is introduced through a burr hole placed in the right Kocher point (10-13 cm posterior from the nasion and 2-3 cm lateral from the median line) up to the third ventricle, through Monro's foramen. The floor of the third ventricle is entered between the mammillary bodies and the infundibular recess and the fenestration is enlarged by inflating a Fogarty catheter's balloon, thus creating a communication between the third ventricle and the prepontine cistern, representing a 4-6 mm diameter ventriculostomy. The patients who, intraoperatively, immediately after ETV present no pulsations on the floor of the third ventricle ("flag signal"), will not improve after ETV and need immediate VP shunting10.

Ventriculosternal shunting

In critical situations, when vascular access cannot be performed, intraosseous fluid infusion is a procedure that has been performed for many years11.

From this technique, Tubbs conceived ventriculosternal shunting. The distal catheter is implanted in the sternal manubrium, after a 4 cm tunnelization. From this point, CSF is drained through the internal mammary veins and the azygos vein12.

The ventriculosternal shunt represents an alternative to other types of shunting, when they are contraindicated. Risks of fat embolism, sternal iatrogenic fracture, brachiocephalic vein injury or vagus nerve injury are disadvantages of this method13.

Types of valves

CSF pressure must be measured intraoperatively and a valve corresponding to that pressure must be chosen or in the case of a programmable valve, the opening pressure will be adjusted to the measured pressure.

There are low, median and high pressure valves with a range of opening pressure of 20 - 40 mmH2O, 50 - 90 mmH2O and 100 – 140 mmH2O, respectively.

CSF overdrainage can occur in the case of VP shunts because of the hydrostatic pressure of the liquid column, when the patient is standing. Anti-siphon systems, placed distally from the valve, prevent overdrainage and intracranial pressure decrease.

In the case of programmable valves, pressure values can be adjusted noninvasively, thus avoiding revision surgery to replace the existing valve with a different pressure one.

Postoperative course

Preoperatively, patients that will benefit from the shunting procedure must be selected and the surgery must be tailored to the patient's particularities (type of shunting/valve). In the postoperative period, all patients need clinical and imagistic follow-up in order to evaluate their response to surgical treatment and to obtain an early diagnosis of shunt system malfunction or possible complications.

Out of the cardinal symptoms of INPH, gait disturbances are the first to improve. Evaluation of the cognitive component requires psychometric testing. Stein and Laughfitt scale, Black scale or Rankin scale can be used14,15.

Approximatively ¼ of operated patients experience shunt malfunction in the first year after surgery and up to 60% require shunt revision during the next years. The rate of shunt failure in the first year is 20 - 50%, with a mean of 40%16. Two causes contribute to shunt malfunction: inadequate catheter placement and infection. In order to prevent proximal catheter malposition, when the catheter is located paraventricularly or partially intraventricular, adequate placement of ventricular catheter can be achieved with the help of image guidance, stereotaxis, neuronavigation or endoscopy. A correctly placed catheter must float at equal distance from the ventricular walls, far from the choroid plexus and must have a straight trajectory from the burr hole. All catheter perforations must be located intraventricularly in order to prevent its obstruction with paraventricular tissue16.

Recently, the concept of prevention of readmission and reoperation has been introduced in neurosurgery, from which Preventable Shunt Revision Rate was derived and introduced in the US in 2016. The fact that a part of shunt failures are caused by intraventricular catheter malposition was noted. Therefore, at the end of each operation a control of catheter position with imagistic guidance is recommended.

The rate of shunt infection reported in the literature varies between 1% and 15%. This rate is lower when: antibiotic impregnated catheters are used, 2 layers of gloves are worn by the operators, the number of medical personnel in the operating room is limited, prophylactic antibiotherapy is administered, antibiotics are applied in the surgical wound (Bacitracine) etc. All these aforementioned measures can prevent bacterial inoculation during surgery.

In the case of febrile patients (temperature > 38oC) with meningeal irritation signs, CSF must be obtained through lumbar puncture in order to obtain cultures and determine the microorganisms that are present as well as their antibiotic sensitivity.

Overdrainage, which occurs more frequently in standing position, in the case of an inadequate valve can determine the formation of a subdural fluid collection, followed by the development of subdural hematoma. In other patients, the drainage is insufficient and the valve must be replaced with a low pressure one.

Conclusions

INPH is a frequently encountered condition that is still challenging to diagnose and treat despite significant progress in imaging diagnosis and development of different surgical techniques. Although surgical treatment consists of generally straightforward procedures, it associates a high rate of failure, regardless of technique used, which emphasizes the need for regular clinical and imagistic follow-up. Thus, INPH remains a disease where there is significant room for improvement, both in diagnosis and treatment.

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3D patient specific implants for cranioplasty. A multicentre study

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Keywords
3d printing, Cnc milling and drilling, cranioplasty, Peek, titanium, Bioverit, trauma, tumour, decompression, neurosurgery, reconstruction, patient specific implant

ABSTRACT
This article presents a multi-centre study cohort study on 50 patients with cranial defects of multiple etiologies (trauma, decompression, tumour surgery, etc.) operated in 10 hospitals. In all patients the neurosurgeon repaired the cranial defect using 3D printed and CNC milling and drilling grafts or Patient Specific Implants, from two world known manufacturers, custom made in accordance with the data obtained from the patient's 3D CT reconstruction.

INTRODUCTION

Cranioplasty is defined as the surgical intervention performed to repair cranial defects following trauma, surgical decompression, tumour surgery, congenital anomalies or growing skull fractures. The implications of cranioplasty are psychological, aesthetic and functional. The history of cranioplasty dates back to 7000 BC. with archeologic evidence (1, 2) supporting the use of both inorganic and organic materials. Although many methods have been described there is little consensus regarding the optimal solution for such cases.

MATERIALS AND METHODS

We started a multicentre cohort study on patients with cranial defects of multiple etiologies (trauma, decompression, tumour surgery, etc.) operated in 10 hospitals having enrolled in study a total of 50 patient from which 16 were female 34 were male, 22 from urban , 28 from rural area of Romania, age between 5-68 years old. Regarding etiologies: 31 were trauma, 16 were decompression and 3 were tumour. In all patients during the surgery were repaired the cranial defects using Patient Specific Implants made by 3D printing and Cad Cam manufacturing (Cnc milling and drilling) methods using specific data obtained from the patient's 3D CT reconstruction using a very clear scanning protocol.

✉
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CT – scan protocol

Algorithm	optimised for bone
Contrast material	no
Matrix	at least 512 x 512 Pixel
Gantry Tilt	no
Change of thickness	no
Change of spacing	no
Patient Position	back position preferred
Patient Orientation	head first
Thickness Orientation	axial preferred
Slice thickness (Z)	1 mm (reconstructed)
Pixel resolution (X,Y)	0.5 – 0.7 mm
Field of View	quadratic
Table feed (Spiral CT)	<3 mm per Rotation

Figure 1. CT scan protocol used to create specific data to be converted in a 3D dynamic precise model.

Centres and Hospitals involved in this study were as follows: 1. Sanador Clinic Hospital, 2. Emergency Hospital " Bagdasar - Arseni" , 3. Emergency Clinical Hospital " Floreasca", 4. University Emergency Clinical Hospital, 5. " M.S. Curie" Clinical Emergency Hospital for Children, 6. "Grigore Alexandrescu" Emergency Hospital for Children ,7. Medlife Metropolitan Hospital, 8. Elias Emergency University Hospital, 9. "Sf.Pantelimon" Emergency Hospital, Bucharest, Romania and "Prof. Dr. Nicolae Oblu" Emergency Clinic Hospital, Iasi, Romania.

The follow up varies from 1 to 9 years. Materials used for implants: Peek, Titanium Alloy and Bioverit (ceramic glass). Distribution of implant materials from our study was: 45 cases with Peek, 4 cases with Titanium Alloy, 1 case with Bioverit.

Procedure: In almost all cases, the procedure is the same. DICOM data files are collected and archived into a zip file and sent encrypted, through a secure transfer platform, with a dynamic password, that has to be communicated each time, to recipients and that is internet safe and keeps all info strictly confidential.

Files are extracted, verified if scanning protocol was respected and if they are qualified to be transformed in ".stl" extension files or other software extension used to see bone defect, compare it with standard anatomic models, with contra-lateral side of the same patient and create a 3D dynamic model of cranium with all defects and of patient specific implant that has to fit perfectly into that defect. The 3D model (pdf file with 3D media option activated) is sent and presented by manufacturer directly to the surgeon with several comments regarding: surrounding soft tissue, sizes, distances, thickness and a lot of other parameters, including material together with an approval letter that has to be stamped and signed by the surgeon. The surgeon will reply (in written) to the manufacturer with its comments regarding all of the above and in some steps will conclude if he agrees or not, on the proposed 3D model. If the response is affirmative and all legal and financial issues are agreed upon by all parts, the manufacturer will start to produce the implant, respecting all safety and regulations of EU, regarding Patient Specific Implants. That will be delivered in the country of the surgeon, directly to its hospital OR during a period of 5-15 days. In some emergency cases, the implant can be delivered within 48 hours, with a set of legal documents and a passport for the implant; the passport contains all of the important info that patient has to have, after surgery. If the Implant came unsterile and very well packaged, it will be sterilized to 134 °, 1-2 cicles 20 minutes, 24-48 hours prior the day of surgery.

Depending on the size of bone defect, anatomical area, position on cranium and risk of infection (frontal, sinus, zygomatic area) the surgeon will decide upon the best material for the implant (Titanium alloy, Peek or ceramic glass) and what fixation systems are best for the implant. The most common and used materials are: non-resorbable

suture 2.0, Titanium, Peek or bio-resorbable craniofix type implants that use a special tool for anchoring and fixation, Titanium 2-4-6 holes plate 1.3/1.6/2.0 mm and 1.3/1.6/2.0 mm, different designs (straight, double-Y plate, adjustable mesh or pre-contoured) screws locking or non-locking 3-5 mm length.

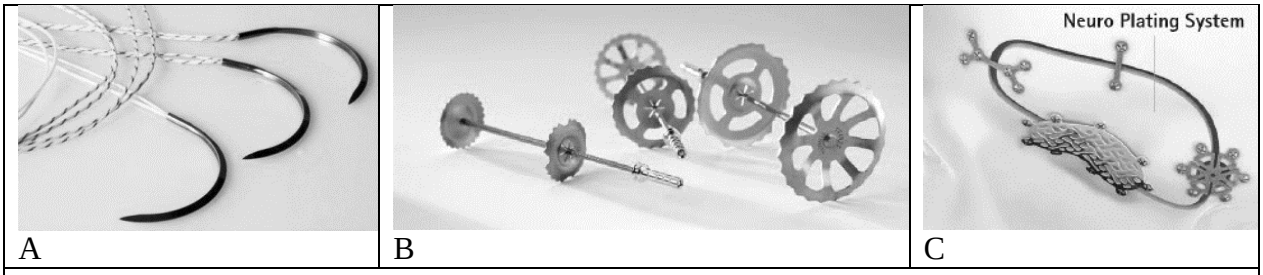

FIGURE 2. (**A**) suture; (**B**) Titanium or resorbable craniofix fixation type system; (**C**) plates; mesh different designs and screws (11)

CASE REPORT

Female, 23 years old. Event that caused trauma: Car accident 28.11.2018;

At the time of the arrival at the Clinical Emergency Hospital, the patient had intracranial pressure with a peak of 80 mmHg (standard values: 20 mmHg) Glasgow score 3 (GCS) state of coma;

Procedure: The surgeon opted for cranial resection with dural plasty (optional: can be done with artificial dura);

Observation: Cerebral edema post-trauma malign, with progressive values 32-46-62-80 mmHg in spite of conservative treatment;

Secondary, a large craniectomy FTPO (fontal-temporal-parietal-occipital) and dural plasty with temporal muscle and periosteum is performed. The craniectomy was performed in the 3rd day after the car accident;

The cranioplasty surgery was performed in 14.01.2019 (47 days after car accident and 44 days after craniectomy), that means a short term cranioplasty.

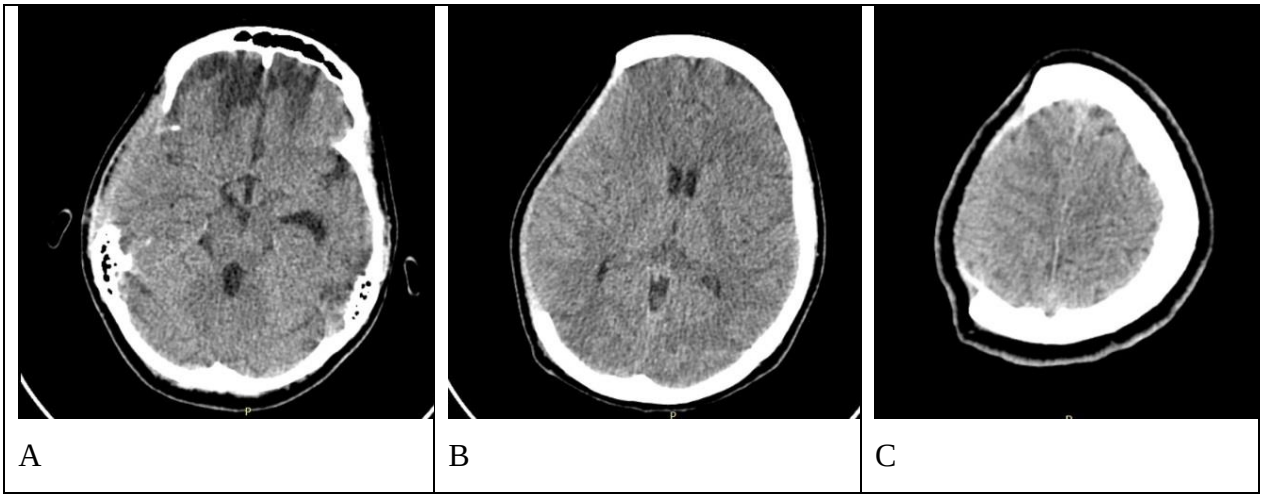

FIGURE 3. (A, B, C): CT scan images done respecting above scanning protocol.

CT DICOM files are sent, analysed by the manufacturer and result is a 3D model that is sent directly to the surgeon for discussion and legal approval. There are cases when CT DICOM files are rejected, because they are not done as required by the protocol and they are not accurate enough and cannot be used for 3D model and also for implant construction.

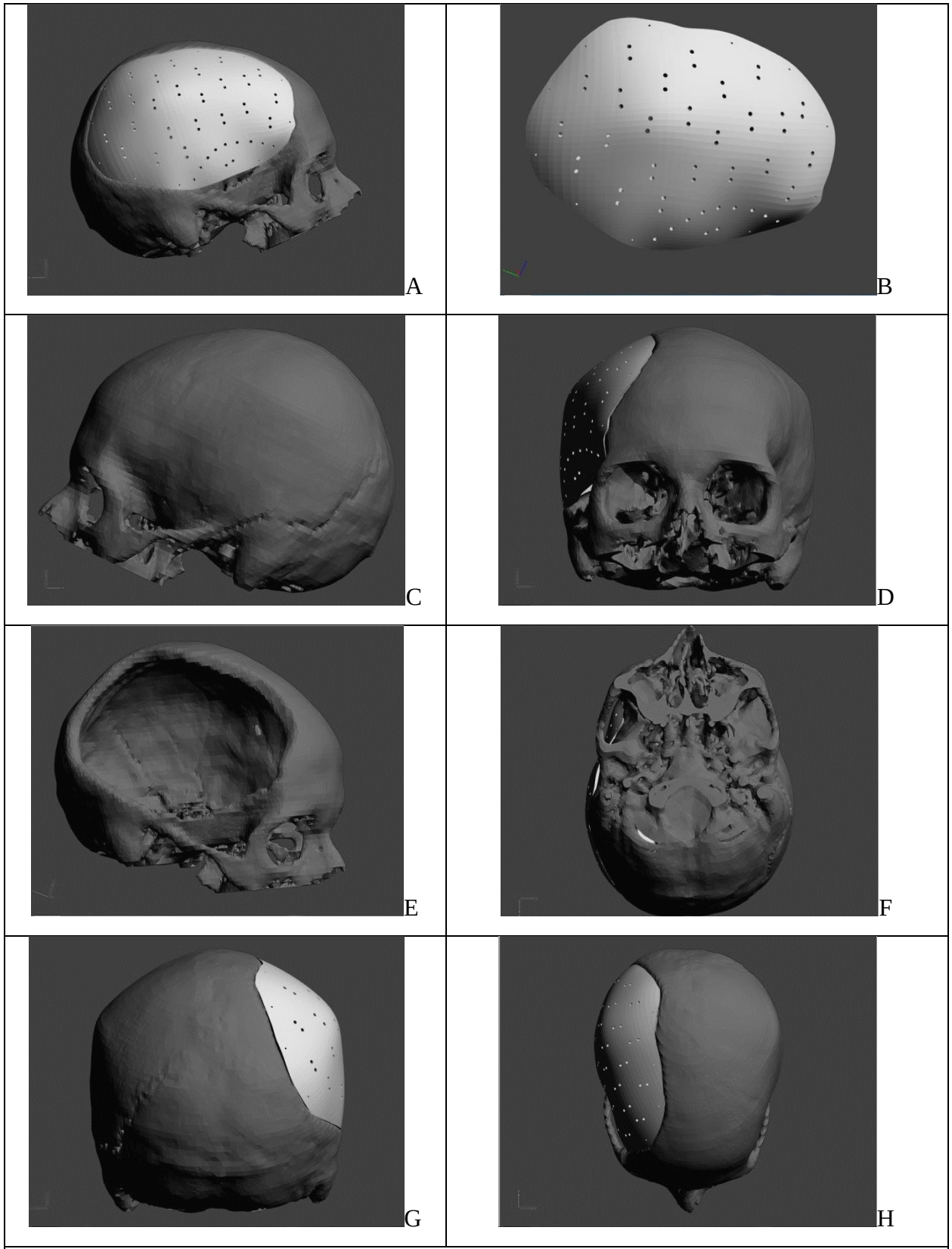

Figure 4. Presentation for surgeon of a 3D model proposed by manufacturer using Adobe Acrobat 3D pdf. file where model can be visualized dynamic, 3d in motion. Are presented screenshots as follows: (**A**) right view with implant; (**B**) proposed model of implant; (**C**) left view; (**D**) frontal view with implant into defect; (**E**) right view without implant; (**F**) below view; (**G**) rear view with implant; (**H**) above view with implant in place.

A team of specialists in cranial reconstruction communicate to the surgeon (in writing): any possible complications, details regarding sizes of implants, remaining bone, distances and surrounding soft tissues, options for manufacturing materials, fixation systems (Titanium Alloy, Peek, Bioverit – ceramic glass) (9,10) to help him take the most efficient decision. (Figure 4)

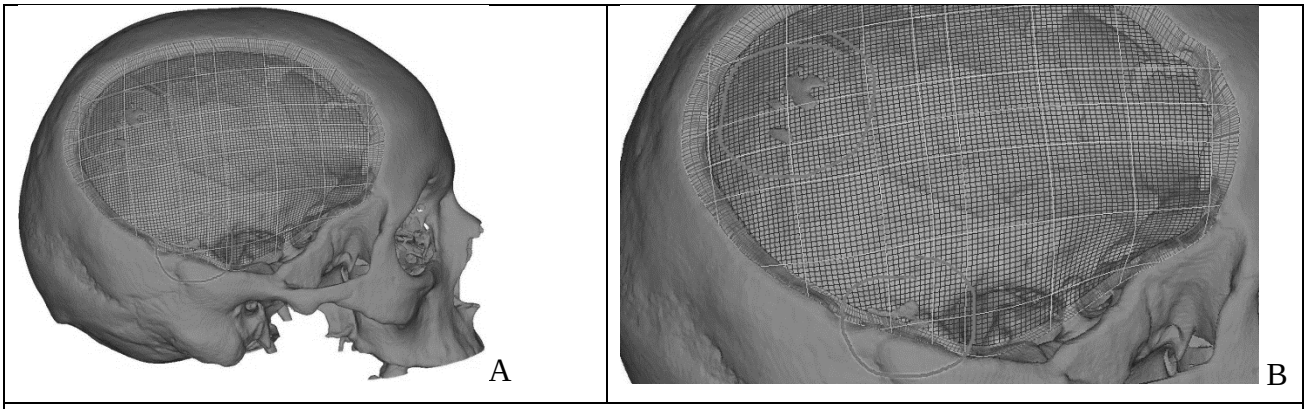

FIGURE 5. Observation of small islands of ossification are sent in attention of surgeon. (**A**) Large right view; (**B**) right detailed view.

The surgeon requested that the implant had to be made from Peek –Optima®(polyether-ether –ketone) as being optimal (weight, strength, hardness) in case he needs to make small adjustments intra-op; he also requested suture holes, each 1 cm on implant margin, assuming that the fixation systems could be suture and craniofix type systems. (Figure 3, 4)

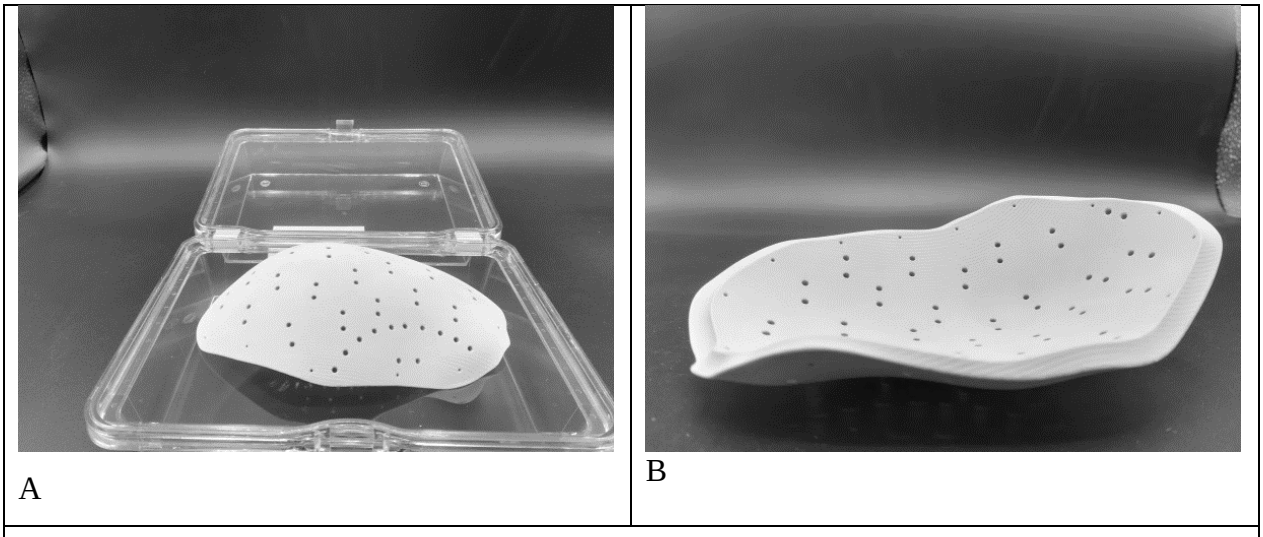

FIGURE 6. Above view of Patient Specific Implant made from PEEK in protective case; (**B**) Inferior image of implant

The method of implant manufacturing: Cad Cam manufacturing (Cnc milling and drilling) from an initial reclangular block of Peek. The final volume of implant was 548 cm3.

In the case presented above, for fixation of the implant, non-resorbable sutures were used and small drills of 1-2 mm on perimeter of cranial defect at equal distances were performed, in order to allow the insertion of titanium craniofix type fixation system (with a 20mm diameter). The patient received its own passport of implant (with all the important details in it: data of production and surgery, surgeon details, sizes in mm ad weight & material of implant). (Figure 6)

Results and discussion

In the presented case, the cranioplasty surgery was performed with a Patient Specific Implant from Peek, respecting all sizes and anatomy of the patient; the implant fitted perfect into the defect and the surgery was shorter (with about 1-2 hours) because the cranioplasty solution was already created beforehand for that specific patient and implemented in only 1 step; there were no complications after the surgery and a visible aesthetic result for a female patient.

Regarding the general study: There were a total of 50 patients treated with Patient Specific Implant that proved significant aesthetic, functional and psychological improvements after the cranioplasty surgery. Minor complications occurred in several cases, that were related to cranioplasty fixation systems and scalp complications (related to initial trauma), and two cases of wound infection (one related to the type of suture used and the other wound contamination without suture defect). There were no fatalities and no long-term complications.

Conclusion

- Custom 3D implants for cranial reconstruction are a safe and viable solution that has been available for some time;
- Superior aesthetics and good functional outcomes can be achieved with a 3D patient specific implant (where other common methods fail: cement, PMMA broken implants, etc.);
- A Patient Specific Implant is made 1 time for 1 single Patient and involves multiple parties, each with their own responsibilities: the patient ant his family, the surgeon, the hospital, the manufacturer, the project manager;
- Our study proves the fact that this method can be safely implemented even in surgical centres with no prior experience, using 3D custom made implants;
- Nevertheless, the financial aspect of using such an implant is the main factor that negatively influences the addressability of such a technique to the general public. At this time Patient Specific Implants in Romania are paid by patients and are expensive, but very reliable and effective at the same time;
- We can appreciate that the number of cranioplasty cases done with PSI (Patient Specific Implants) would be 10 times more in Romania , if a National Program for Neurosurgery would cover the costs of such implants;
- This method would also increase the economy of the Ministry of Health's budgets, due to a reduced period of post-op recovery and minimal rate of re-interventions and complications.

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Our experience with a single stage bilateral approach for treatment of bilateral middle cerebral artery aneurysms

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ABSTRACT

Surgical management of bilateral middle cerebral artery (MCA) aneurysms is particular challenging clinical situation. For these patients various options of surgical treatment are available as unilateral approach, single stage bilateral craniotomy or two stage bilateral craniotomy. We report our experience with a case of bilateral MCA aneurysm which was managed by single stage bilateral pterional craniotomy.

Keywords
middle cerebral artery aneurysm,
single stage,
bilateral approach

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INTRODUCTION

Surgical management of bilateral intracranial aneurysms is still difficult especially when it involves bilateral middle cerebral artery aneurysms. Even though endovascular treatment is widely accepted as the first option in the treatment of intracranial aneurysms, the middle cerebral artery aneurysms remained with quite high addressability for microsurgical clipping due to its special predisposition to have a broad neck that incorporate the parent vessels and frequent association with massive intracranial haemorrhages. Depending on some anatomical features, experience and preference of the neurosurgeon, these lesions can be operated in single or two separate sessions by unilateral or bilateral approach. Therefore, direct clipping of both ruptured and unruptured aneurysm in a single-stage operation, is more preferred today, if technically possible. The risk and worry about rupture of an untreated associated aneurysm is not insignificant during the early or late postoperative period when aggressive management against vasospasm is fundamental.

We report upon our experience with a single stage bilateral craniotomy approach for clipping the bilateral middle cerebral artery aneurysms.

CASE REPORT

A 49-year-old woman addressed to the emergency room with spontaneous severe headache, photophobia and few episodes of vomiting form one day. At clinical examination she was conscious with no motor deficits only slight nuchal rigidity. The cerebral CT-scan showed features of acute subarachnoid haemorrhage at basal cisterns

and both Sylvain fissure. The patient was classified as Fisher grade III and Hunt and Hess grade 1. CT angiography was performed and revealed bilateral MCA bifurcation aneurysms (Figure 1). The presence of a nipple on aneurysmal sac and the slight prevalent SAH in left Sylvian fissure suggested that the left was the ruptured aneurysm. Because the unruptured aneurysms at the contralateral MCA were not negligible and concerning represented by necessity of an aggressive triple H therapy a single-stage operation was decided. Single stage bilateral craniotomy and microsurgical clipping of the aneurysms was done in the same day of admission.

The procedure was performed with the patient under the general anaesthesia. A bilateral small sized pterional approach was performed in consecutive steps. The rupture side was approached first. The head is positioned on the operating table without being fixed in the frame with pins. The head is slightly rotated to the contralateral side and extended enough to minimize the frontal lobe retraction.

A curvilinear skin incision was made inside the hairline starting in front of the tragus (5 mm approx.) to the level of the midline. The incision on the attachment of the muscle to the superior temporal line is made with monopolar cut in order to detachment and retraction of the muscle posteriorly and inferiorly with hooks. A classic pterional craniotomy by tow blur holes is performed. By bone flap removal pterion bone and a prominent sphenoid wing are smoothed using a high-speed drill. Dura is C-like shape incised and reflected toward the cranial base. After minimal opening of the sylvian fissure, the optic, chiasmatic, and lamina terminalis cisterns are opened with gradually cerebrospinal fluid aspiration to obtain a slack brain and avoiding excessive retraction. With the highlighting of the internal carotid artery and its terminal bifurcation, microdissection is continued with widely opening of the sylvian fissure. A good exposure of the M1 segment is obtained. This segment is followed up to the bifurcation with careful microdissection of the aneurysmal neck to prevent the aneurysm rupture. After the clear exposure of the neck and the origins of the M2 branches a clip is applied with aneurysm exclusion. After carefully haemostasis and dura closure, the bone was fixed in two or three points. Finally the wound is closed as the usual fashion.

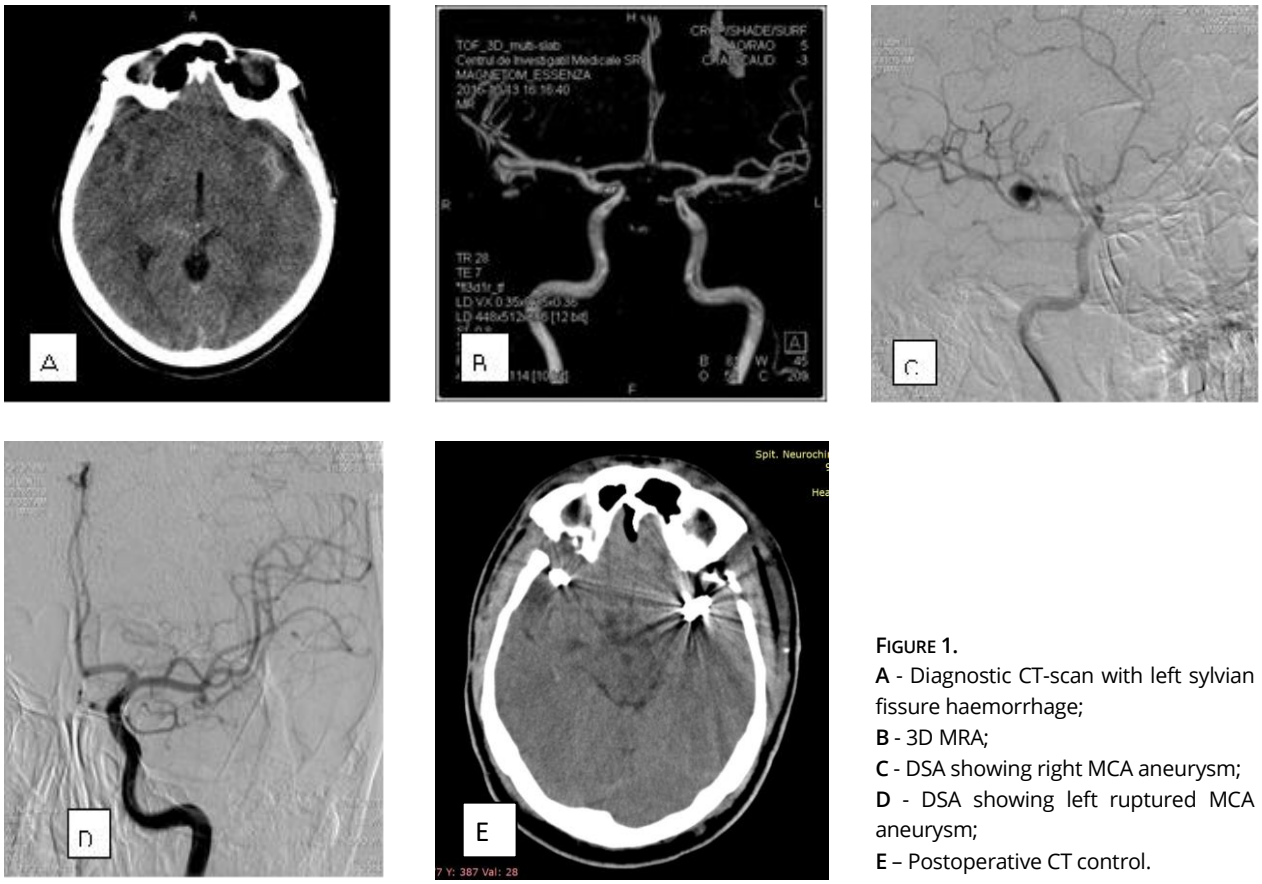

Figure 1.
A - Diagnostic CT-scan with left sylvian fissure haemorrhage;
B - 3D MRA;
C - DSA showing right MCA aneurysm;
D - DSA showing left ruptured MCA aneurysm;
E – Postoperative CT control.

A total of three clips were used with two on the right side to preserve the bifurcation anatomy. The total time for surgery was four and a half hours. There was no intraoperative complication. Triple-H therapy was started immediately postoperatively. Control CT scan was performed 24 hours later. The patient evolution was favourable accompanied only by mild episode of headache. She was discharged home on the 21th day.

Discussion

The clinical status regarding the incidence of bilateral aneurysm of MCA was mentioned in the literature around 1.18%. For bilateral MCA aneurysms, several surgical treatment options such as unilateral approach, single-stage bilateral craniotomy, or two-sided bilateral craniotomy have been reported. For each type of approach it is extremely important to pay attention to several preconditions in order to perform them safely and effectively.[3,4,6,7]

Single stage surgery has the advantages of removing a new risk of bleeding, curative treatment with one-time risk of general anaesthesia, shorter hospital stay and reduced cost in terms of bed charge, investigations and operative expenditure.[3,4,6,7]

The most important reason for single stage surgery by bilateral approach is to eliminate the risk of bleeding from unruptured aneurysm in the early or late postoperative period. Two important large studies have showed that associated aneurysm in patients with SAH due to another ruptured aneurysm presents a higher risk for future bleeding than makes aneurysms of similar size with no SAH history [3,4,6]. Furthermore, the necessity of an aggressive hypertensive treatment for fighting with cerebral vasospasm may carry a potential risk of rupturing for associated untreated aneurysm in the postoperative period. [4,6]

Optimal selection of the patient with bilateral MCA aneurysm for a single stage surgery by unilateral or bilateral approach is dependent on a number of parameters such as severity of brain edema, the length of contralateral M1 segment, configuration and projection of the contralateral aneurysm. Presence of an important brain swelling, correlated with recent severe SAH is usually associated with very difficult microdisection and an excessive brain retraction that leads to a single stage bilateral approach choice. Longer contralateral M1 segment and a complex or large associated unruptured aneurysm are also condition this type of approach. If the anterior projection of the associated contralateral aneurysm is an indication for a unilateral single stage approach, the posterior or along the axis of the MCA projections are condition more favourable for a bilateral single stage approach.

Another important factor in bilateral MCA aneurysms surgery is represented by correct determining the side of ruptured aneurysm, because surgery should always be started from the ruptured side. In case of the misdiagnosed of ruptured bilateral MCA aneurysm with first clipping of unruptured one, the contralateral (ruptured) MCA aneurysm should always be clipped via a second contralateral craniotomy. A good clinical grade presentation can also be a factor favourable for a single stage bilateral surgery.

Conclusions

Challenging for a single stage bilateral approach should be considered in suitable cases of bilateral MCA aneurysm in all centres with experienced vascular neurosurgeons. A careful analysis based on clearly defined parameters will help the neurosurgeon in patient selection for this particular type of approach. This particular approach is more indicated in a patient with bilateral middle cerebral artery aneurysms presenting with bleeding and the ruptured side is not easily identifiable.

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Primary central nervous system sarcomas. Clinical, radiological and pathological features in our institution

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ABSTRACT

Objective: Primary CNS sarcomas are very rare tumours with no defined standard of care.

Patients and methods: This study was a retrospective review of seven patients diagnosed with a primary CNS sarcoma at neurosurgery department, Mansoura university hospital between 2006 and 2018. We reviewed the clinical, radiological, and pathological data of these patients. There were 2 female (28.6%) and 5 male (71.4%) with age ranged from 8 years to 73 years (mean age 25.4 years). Three patients (42.9%) had an intracranial sarcoma, and four (57.1%) had intraspinal tumours. All intracranial tumours located in supratentorial region.

Results: we have characteristic imaging findings inform of osteolytic bony erosion in 3 patients and marked enhancement of the tumour in 5 (71.4%) patients. We operated upon all patients to remove the tumour surgically with our aim is gross tumour resection. Tumour was totally resected in 5 patients (71.4%) and subtotal in another 2 patients (28.6%). Tumour has dural attachment in 5 cases (71.4%) and brain invasion was present in all intracranial 3 patients (42.9%). Postoperative radiotherapy was used in 5 patients and postoperative chemotherapy was used in all patients. We used immunohistochemical studies for all patients with the most consistent finding being strong Desmin positivity. The mean length of patients survival was 4.6 years (range from 3 month to 8 years).

Conclusions: Primary CNS sarcomas are very rare CNS tumours, total surgical resection and post-operative radio and chemotherapy provided encouraging outcomes.

Keywords
Primary CNS, sarcoma

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INTRODUCTION

Primary CNS sarcomas are rare tumours. There are many theories of the cell of origin of these tumour. Tumour may arise from pluripotential primitive mesenchymal cells which located in the dura, or originated from the leptomeningial cells or their extensions via the pia into the brain and the spinal cord along the stroma of the choroid plexus, the tela choroidea, or the periadventitial spaces and these considered as widely accepted theory.

We can defined sarcomas that have originated from metastases of soft tissue or bone sarcomas to the CNS as Secondary CNS sarcomas. These tumours result from direct extension of sarcoma located at places neighbouring the CNS.

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PATIENTS AND METHODS

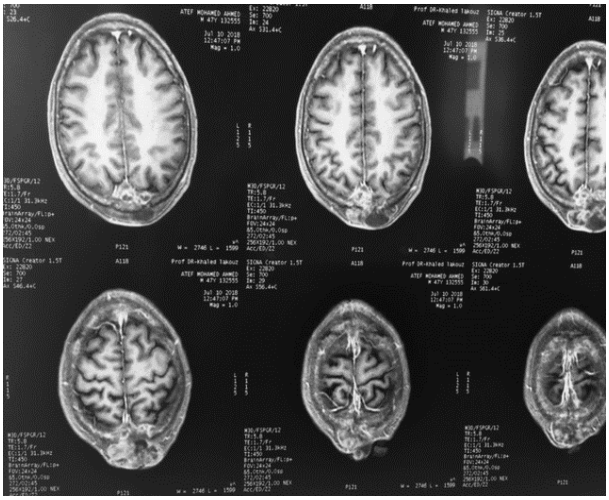
We looking for all types of primary CNS sarcomas between 2006-2018 at Mansoura university hospital through retrospective analysis of our CNS tumor database which archived in our neurosurgery department in these period. The Research Ethical committee at Mansoura medical school give us permission to use these patients' data. In this study, we defined primary CNS sarcomas as tumours that originated primary in the CNS from non-neuronal, non-glial, and non-reticular elements, and we not include any previously diagnosed benign tumour with sarcomatous transformation.

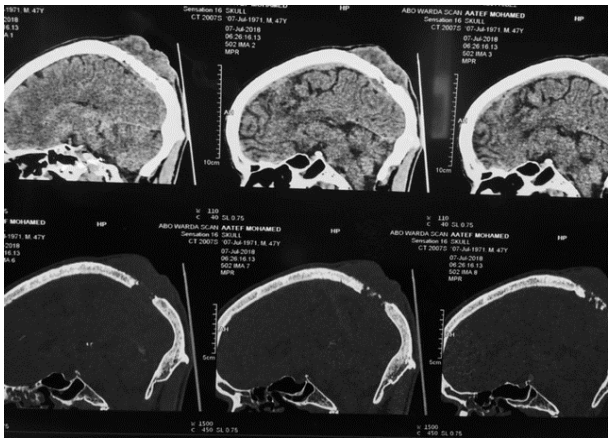
The medical data of these patients included in our definition of a primary CNS sarcoma were then analysed for clinical, radiological and pathological features.

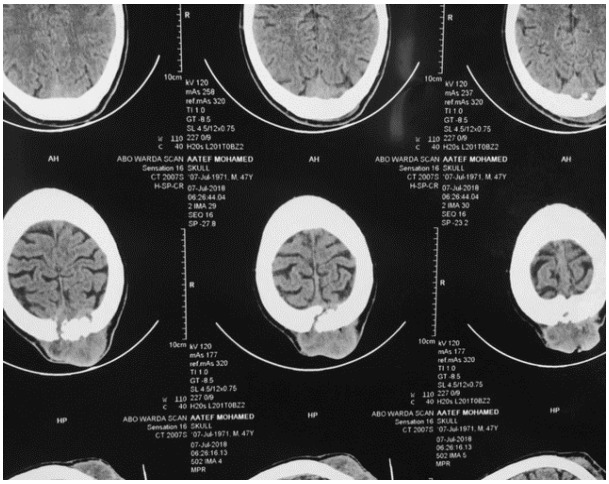
All primary CNS sarcoma were investigated for any possibility of the presence of extra CNS sarcomas at the time of study. The work-up study were chest X-ray, chest CT, abdominal and pelvic CT, and abdominal ultrasound.

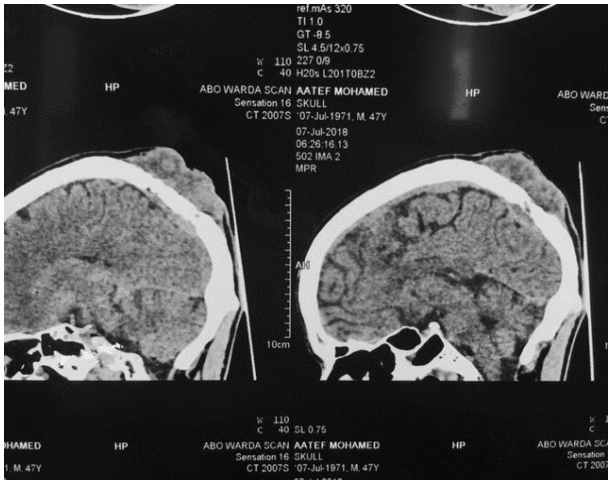
All cases surgical specimens were examined in pathology department by light microscopy using eosin and hematoxylin stain, periodic acid-Schiff, and reticulin. We used immune histochemical studies in all cases.

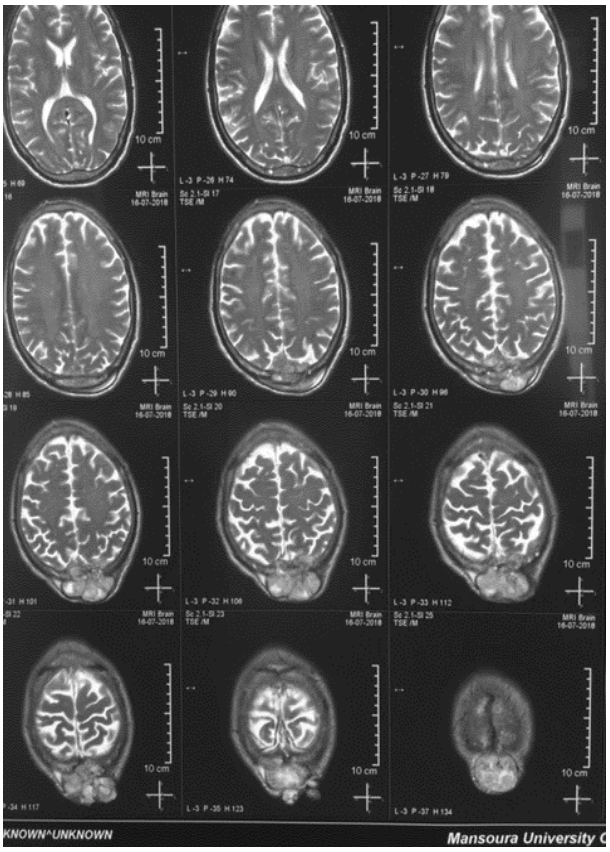
The range of follow up varied from 3 month to 8 years (mean 2.9 years). We calculated the length of survival from the date of diagnosis of the disease and the end points were the patient death day or the last follow-up visit.

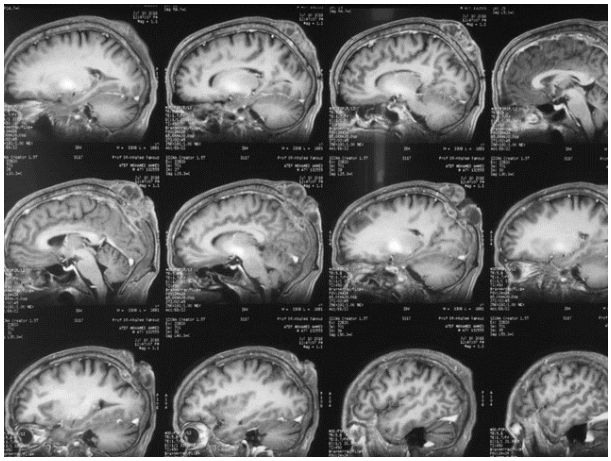


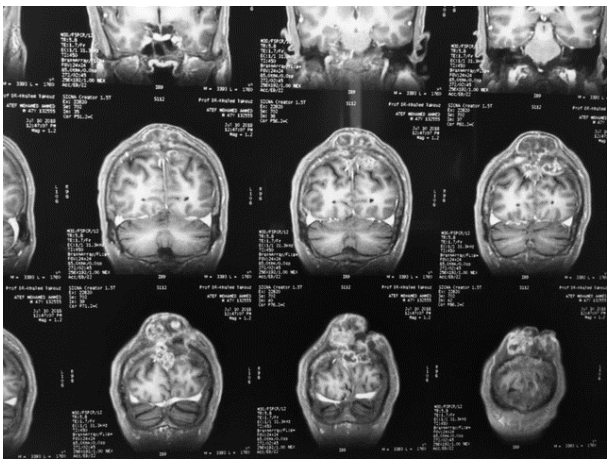


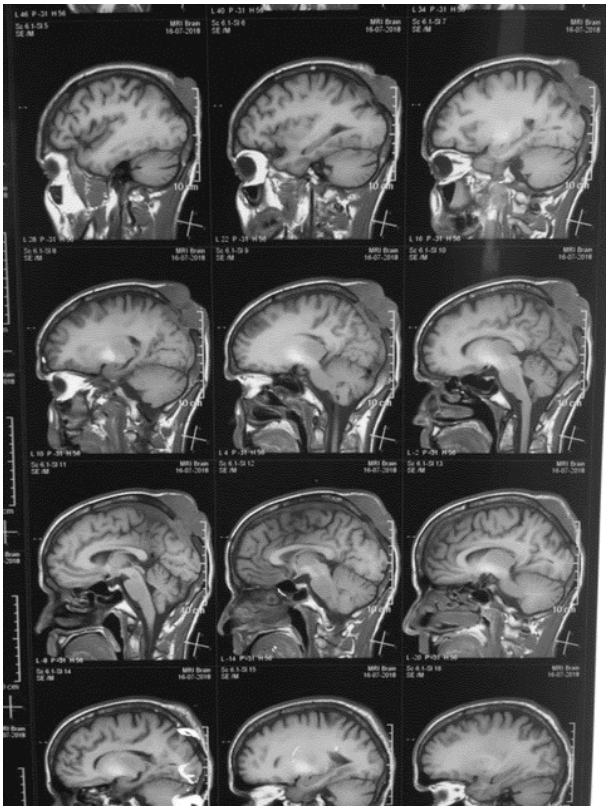


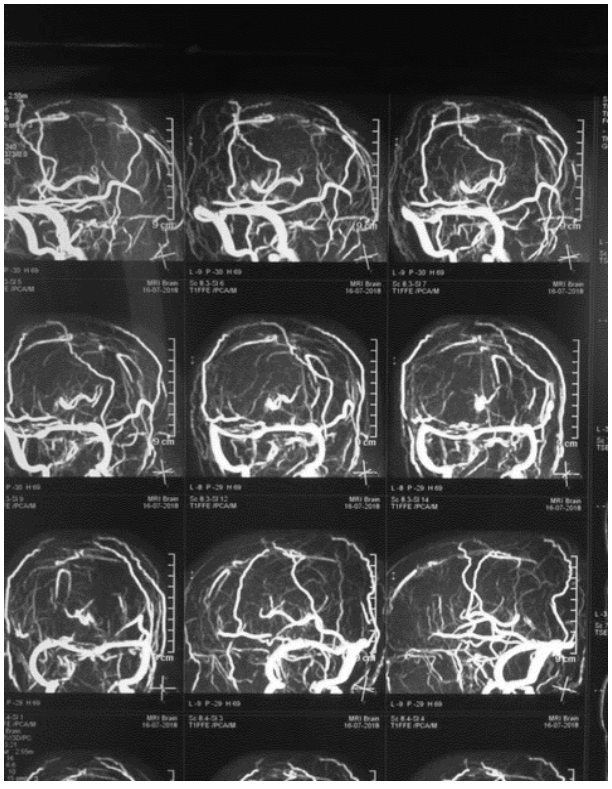












PATIENT	Age/ sex	location	CT	MRI	Extent of resection	Radio-therapy	Chemo-therapy	Dural attachment	Brain invasion	survival
1	73/f	D10	Enhancement ++, bone destruction		Total	Yes	Yes	No	No	Alive 1 years then absent
2	8/f	D11-12	Enhancement +++, cystic		Near total	No	Yes	Yes	No	Alive 1years 6 months
3	8/m	Frontal lobe	Enhancement +++, bone destruction		Total	Yes	Yes	Yes	No	Alive 8years
4	47/ m	Occipital lobe	Cystic, enhancement++,bone destruction		Total	Yes	Yes	Yes	Yes	Alive 3months
5	8/m	L2-5	Enhancement +++, bone destruction ,cystic		Total	No	Yes	No	No	Alive 7years
6	18/ m	Bifrontal lobe	Cystic, enhancement++,		Near total	Yes	Yes	Yes	Yes	Alive 7months
7	16/ m	D4-6	Enhancement +++, bone destruction		Total	Yes	Yes	Yes	No	Alive 2years

RESULTS

Clinical pictures

We summarized the clinical pictures in this study in Table 1. There were 2 female (28.6%) and 5 male (71.4%) ranged in age from 8 years to 47 years (mean age 19.4 years). Three patients in this study (42.9%) were in the first decade of life. Three sarcoma patients (42,9%) were intracranial and 4 patients (57.1%) were intraspinal. All intracranial sarcomas in this series were supratentorial in location, two of them presented bilaterally either in frontal or occipital lobes. Three of intraspinal tumours (75%) were located in the dorsal area and the remaining presented in the lumbar region.

The clinical presentation of these patients varied from symptoms and signs of ICP as vomiting, headache and papillodema and other presentation as focal neurological deficit such as dysphasia, fits, hemiparesis for intra cranial tumours and paraparesis for the intra spinal tumours.

Radiological features

We summarized the radiological data in Table 1. CT and MRI used for investigation (Fig. 1). CT was performed in all patients, tumour enhancement with contrast had been obtained. All intracranial tumours patients in this study showing osteolytic bony destruction. 5 patients (71.4%) showed marked humoral enhancement. Magnetic resonance imaging in selected cases revealed increased signal on T2 images on these lesions, and irregularly enhancement after contrast study (Fig. 2).

Surgery

All patients in these series underwent at least one surgical procedure with the aim of surgery is gross tumoural resection; only 2 cases underwent another surgical operation due to recurrence of the tumour. Surgical tumoural resection was total in 5 cases (71.4%) and subtotal in the remaining 2 patients (28.6%). We performed true cut needle biopsy in just a patient of intracranial tumour with extra cranial extension prior to surgical excision. Postoperative radiotherapy was used in 5 patients (71.4%) and postoperative chemotherapeutic agents were used in all patients (100%).

TABLE 1 showed the operative details of the patients included in this series. At surgery, we found dural attachment of the tumour in 5 patients (71.4%) and parenchymal invasion of the tumour in 2 patients (28.6%). We found a well-defined demarcation plane of dissection around the lesion in four patients, two of them were intracranial sarcoma and the other were intra spinal.

Pathological features

In this series, we found similar histological characters of the different intracranial and extra cranial sarcomas. We did immunohistochemical studies for all cases (Table 2). The most consistent data in immunohistochemical studies were strong positive results of vimentin and general negative results for both neuronal and glial markers. All patients showed positive Desmin with more rhabdomyoblastic differentiation.

All patients tumour examined by Electron microscopic studies. There are many feature as the spindle shape of the cells, lack of well-developed junctions, dilated rough endoplasmic reticulum, and absence of microvilli and neurosecretory granules.

The final pathological diagnosis in these series was a ewing's sarcoma in 2 (28.6%) patients, a embryonal rhabdomyosarcoma in 2 (28.6%), an otherwise low grade chodrosarcoma (14.3%), synovial sarcoma and an undifferinated sarcoma in the remaining three patients alternatively.

Patient No	desmin	neurone specific enolase	BDL-2	LCA,CD3,CD99
1	negative	positive	negative	NA
2	negative	negative	positive	NA
3	positive	negative	NA	NA
4	negative	negative	NA	negative
5	negative	positive	NA	NA
6	NA	NA	NA	NA
7	positive	NA	NA	negative

Survival

We calculate the length of survival from the day of the diagnosis of the disease (Table 1). We have data on survival for 6 patients and lack information in just one patient.

The longest survival time in these study was eight years and the shortest survival time was three month (mean 3.2 years).

The durations of patient survival in intracranial tumours ranged from three months to eight years (mean 2.9 years), while the intraspinal tumours ranged from 18 months to 7 years (mean 3.5 years).

Three months to 8 years (mean 4 years) was the length of survival in the cases with gross surgical resection of the lesion; and the range of length of survival in cases with subtotal tumour resection was 18 months to 2 years (mean 1, 8 years).

Adjuvant therapy

We used Postoperative radiation in 5 patients; with a radiation dose ranged from 4,500–5,900 Gy.

On the other hand we used Postoperative chemotherapy in all patients. The most used chemotherapeutic agents were ifosfamide, carboplatin, vincristine and cyclophosphamide.

DISCUSSION

The occurrence of a primary CNS sarcoma described firstly by Bailey in 1929.2 CNS sarcoma with all forms considered as rare tumours.[6–14–30]the survival in sarcoma patients increased than in the past due to advances technique in chemotherapy. [6–26–45]In different studies, we found variation in the incidence of primary CNS sarcomas which ranged from 0.1% to 4.3%.[3–19–27–31–33–36]

This variation happened due to the term of a primary CNS sarcoma were inconsistent in different series. Previous reported studies included different forms such as giant cell sarcoma, circumscribed sarcoma of the posterior fossa, reticulum cell sarcoma, and hemangiopericytoma, and this gave a false result in high incidence of these tumour type.[7–20–21–25–35] In other series, they considered cases of primary glial, neuronal, neuroectodermal, and/or previously diagnoesd benign meningeal tumours with. sarcomatous features as sarcomas and this lead to falsely high incidence of these tumour type .[23–31]finally, many studies not used immunohistochemistry that could be helpful to resolve diagnostic issues for many examined sarcomatous tumors.[23–33–36–43]

The origin of sarcoma have many theories, the most accepted theory assumed the origin of these

tumour to pluripotential primitive mesenchymal cells, the leptomeninges or their extension into the brain and the spinal cord via the pia along the. periadventitial spaces, the stroma of the choroid plexus and the tela choroidea.[2–4–1–24–25–31–3–35–45]

The causes for occurrence of the primary CNS sarcoma is not known yet well accepted inciting agent of sarcoma in the literature is radiation therapy[19–23–27–34–5–38–44]. There are another predisposing factor as trauma[17–19–27–28–29–31], genetic and familial factors[19–31] and viruses such as RSV.[8–21–27–31]

Primary CNS sarcomas may happen at any life decade, with high incidence in children [23–31–44]. In these series sarcomas were exist in the age range 8–73 years, with the youngest case was 8 years old.

Primary intracranial sarcoma clinically presented as other intracranial tumours. However, it can present with intracranial hemorrhage due to their extreme vascularity[1–15–27–30]. The clinical presentation of primary intraspinal sarcoma had the same clinical presentation of other intraspinal tumours.

There are nonspecific image of primary CNS sarcomas on radiology as CT or MRI. In our series, tumour was large and with different heterogeneous density, cystic (hypodense), or solid and in one patient presented bilaterally in intracranial. Two of the 7 tumours had both solid and cystic components.

MRI of sarcoma was available with an inhomogeneous signal. Solid parts of the tumour usually enhanced after administration of intravenous contrast. Enhancement of the tumour after contrast in the MRI has been a feature of sarcomas in the many series in literature [34–35]. An important characteristic feature of sarcoma is the location near to the surface of the brain or the meninges, and it existed in four patients in our studies `. CNS sarcoma have high incidence of leptomeningeal spread [11–13–45]. There are many differential diagnosis of primary CNS sarcoma on radiology as CT and MRI includes glioma, medulloblastoma in posterior fossa, cranial and spinal meningioma, and ependymoma [19–27–32–36].

In current study, our paients tumor are located in supratentorial region with the most common sites of origin is the frontal lobes which is not match with other studies in literature [13–22–23–32–36–45]. None of our patients presented with their tumour in intraventricular region, although in many series reported intraventricular sarcomas which originated from the choroid plexus[23–26–28–40–4145]. A common feature of primary CNS sarcoma is dural involvement[5–17–36–44–45–47]. We have dural involvement of the tumour in 3 patients which considered as a half of the cases in our study. We did not report any malignant glial tumour within or adjacent to the primary sarcoma on our series. Although some series document that reactive glioma can be happened in a primary CNS sarcoma [16–23–29–46].

Primary sarcomas of CNS has the ability to send metastasis outside the central nervous system, as the liver, bone, and lung with a poor prognosis[3–12–13–2]. It is difficult to determine the incidence of the different histological subtypes of these tumour. This is due rare incidence of the lesion, and the deficient criteria for including specific subtypes in the patients who documented in study [3–40]. We have frequent changes happened in the classification system for primary CNS sarcomas due to appearance of new histological subtypes such as malignant fibrous histiocytoma, and in the literature its considered as most common soft tissue sarcoma[4–5–16–27–38] .

Undifferentiated sarcoma considered as the most common pathological type in our study, and this not matched with others series [7–45]. Other series reported fibrosarcomas and MFH as the most pathological tumoural subtype [1–2–9–36].

Primary CNS sarcomas characteristic with a bad prognosis, although the long duration of postoperative survival is well reported in many series in literature[13–31–32–34–40–45].

Many studies in the literature reported that gross surgical resection is considered as the best treatment of choice. We can use postoperative radiation or chemotherapy for prolonged the patient survival [1–3–11–13–17–16–36–40–45–46].

In Our study, we found that maximal surgical resection of the tumour followed by post-operative radiotherapy help the patient to receive his best choice of management. Although, There are many side effects of radiation on young patient category. The aim of postoperative chemotherapy could not be exactly reported in our study.

Conclusion

The primary central nervous system sarcoma is a rare tumour that mainly originated in the

supratentorial region with ability to be exist in the intraspinal region. CSF dissemination and dural attachment of the tumour are frequently exist. Metastases outside the CNS associated with bad prognosis. For long term survival we advised gross surgical resection followed by postoperative radiotherapy. Chemotherapy regimens may be considered as one of the factor that prolong the survival if they are tolerated by the patient. Future studies should be focused to understand the histopathological subtypes of primary CNS sarcoma to use different chemotherapeutic agents which be helpful to give patients long survival and best choice of treatment.

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Tentorial dural arteriovenous fistulae presenting as transient ischemic attack. Case illustration

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ABSTRACT
Dural arteriovenous fistulae are vascular lesions of the dura mater, usually acquired, consisting of abnormal connections between the dural arteries with the venous sinuses or the cortical veins. A case report presents a case with an unusual form of presentation of the dural (tentorial) arterio-venous fistula simulating a transient ischemic attack in a 60-year-old male patient.

Abbreviations
DAVFs: Dural arteriovenous fistulas, tDAVFs: tentorial Dural arteriovenous fistulas
MRI: Magnetic resonance Imaging, MRA: Magnetic resonance Arteriography
CT: Computerized Tomography.

INTRODUCTION

As described and characterized angiographically, dural arteriovenous fistulas (DAVFs) are lesions generally acquired and progressive with an

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incidence of 10 to 15% Of all cerebral vascular lesions (1-3). They are divided into two main types: DAVFs that drain into a venous sinus with direct reflux to a cortical vein, or not of the venous sinus type (3).

The first type includes those that drain into the cavernous sinus, the sigmoid-transverse sinus, the sinuses confluence, superior sagittal sinus, and petrous sinuses. The Second type, include tentorial, ethmoidal, cranio-cervical DAVFs (4-9).

The most frequent DAVFs is at the transverse-sigmoid junction (38%), and the cavernous sinus, followed by deep veins, the Superior sagittal sinus, superior petrous sinus, ethmoidal sinus, inferior petrous sinus and ethmoidal DAVFs (2,10). The etiology is controversial and the location of the DAVFs in very specific sites, and not throughout the dura mater.

Case report

A 60-year-old male patient came to the emergency department with the complaint of acute onset of slurred speech that started 15 minutes prior to his arrival. He denied any associated headache or visual, motor, balance, sensory symptoms, or any previous similar episode, and his family denied witnessing any loss of consciousness, abnormal body movement or odd behavior when inquired. Relevant history included hypertension for 10 years for which the patient was prescribed a Lisinopril 10 mg once daily taken regularly as the patient emphasized.

The initial evaluation demonstrated a conscious, oriented patient with a blood pressure of 130/85, afebrile, with dysarthria. Other aspects of the neurologic examination were normal. The routine investigation showed normal blood sugar, electro-cardiography showed sinus rhythm and native brain CT-scan.

Meanwhile, the patient reported complete resolution of his speech difficulty and requested if he can go home. His initial ABCD2 score was 3 (1 for age, 1 for his dysarthria & 1 for less than 60 minutes duration of symptoms), and was deemed low risk for recurrent TIA (Transient Ischemic Attack) or stroke within the next 48 hrs., kept on antiplatelet and statin tablets, sent for full stroke workup including cardiac telemetry, given MRI/MRA appointment and was discharged home.

36 hours later, he presented again with disorientation that soon evolved into a stupor with a blood pressure of 200/110 mm Hg, and was suspected to have suffered from a hemorrhagic stroke. Aspirin was stopped and urgent CT scan was done, it showed left tempo-occipital hematoma. Evaluated by neurosurgeon and neuro-endovascular specialist. MRI/MRA and CT- Angiography were performed (Figure. 1 and 2), suggested the presence of tentorial vascular malformation.

The next day, Cerebral Digital Subtraction Angiography was performed, showed the dural arteriovenous fistula of the tentorium. During the procedure, histoacryl embolization was performed without any complications (Figure. 3). The patient was transferred to an intensive care unit. He was discharged after 15 days without neurological deficit.

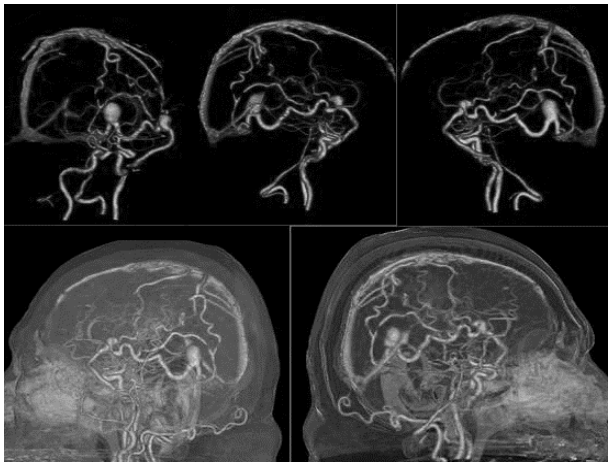

Figure 1. CT angiography 3D reconstruction study showed Tentorial DAVF, the fistulous connection was between the middle meningeal artery, tentorial branches of the meningohypophysial trunk of the Internal Carotid Artery with the transvers-sigmoid sinuses junction and the straight sinus, with venous varices that render the lesion as a high risk for haemorrhage DAVFs.

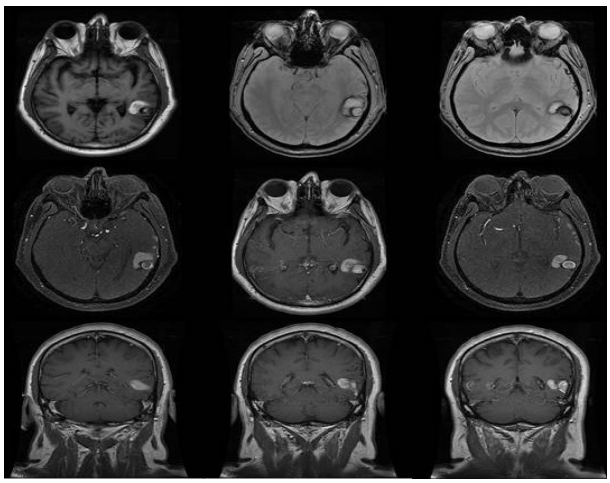

Figure 2. Cerebral MRI showing posterior left temporal intraparenchymal hematoma.

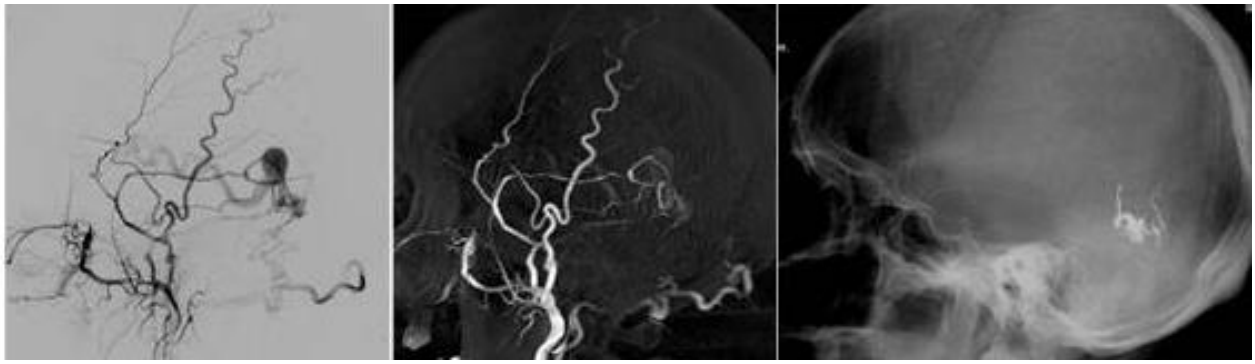

Figure 3. (**A, B**) Cerebral Digital Subtraction Angiography (DSA) of the left external carotid artery showing the medial tentorial DAVF supplied by the middle meningeal artery and drained into the transverse-sigmoid junction and the the straight sinus, with the venous varices. (**C**) Post embolization image showing the histoacryl used in relatively large amount due to multiple fistulous connections.

Discussion

Dural arteriovenous fistulas (DAVFs) are relatively rare, representing 10% to 15% of intracranial vascular malformations. Their usual locations are tentorium (26%), cavernous sinus (26%), transverse/sigmoid sinus (25%), convexity and superior sagittal sinus (11%), and frontal cranial vault (9%). The tentorial dural arteriovenous fistulas (tDAVF) clinically present with hemorrhage, with reported rates from 58% to 92%, and neurological deficits in 79% to 92% of patients. The pathophysiology is retrograde leptomeningeal venous drainage with ensuing venous congestion (1, 2, 11-13).

Common presentations include intracranial hemorrhage, urinary incontinence, paresis, and sensory loss affecting the extremities (14,15). Transarterial endovascular treatment of DAVFs showed symptomatic improvement in about 78% of the cases, with a complication rate of 5% (16).

In our patient, digital subtraction angiography revealed a fistulous connection located at the medial tentorium draining directly into cerebellar veins and finally into the straight sinus. DAVFs clinical presentation includes specific and nonspecific neurological symptoms. Non-specific manifestations such as headache are usually attributed to cerebrospinal fluid malabsorption due to increased pressure in the superior sagittal sinus, venous sinus thrombosis or meningeal scarring due to repeated small subarachnoid hemorrhages. Cranial nerve deficits are probably related to arterial steal phenomena. Specific neurological manifestations may be the result of venous ischemia, venous mass effect, venous rupture or venous thrombosis due to passive venous hypertension, congestion or both (17-20). Many non-hemorrhagic neurological deficits due to tDAVFs have been reported, including gait instability, bruit, personality changes, depression, trigeminal neuralgia, syncopal events, slurred speech, cranial nerve VII weakness (3), visual symptoms. (including bilateral proptosis, bilateral episcleral and retinal venous congestion, optic disc pallor, quadrantanopia and concentric narrowing of the visual field) (10), hemifacial spasm (3), progressive myelopathy, hemisensory disturbance, brainstem dysfunction and obstructive hydrocephalus (4). The mechanism of brainstem dysfunction may be related to arterial steal phenomena, brainstem venous congestion or compression due to dilated veins or cerebellar edema (15). The vast majority of these lesions can be successfully treated with selective endovascular embolization (3,17,21).

Conclusion

The clinical symptoms of DAVFs depend on the location and pattern of the venous drainage. The transient ischemic attack should be kept in mind as an uncommon presentation of tentorial DAVFs. Endovascular, surgical, radiosurgery, and even observation in certain cases are valid options in the treatment of different grades DAVFs.

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Quality and reliability of information available on YouTube videos pertaining to transforaminal lumbar epidural steroid injections

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Keywords
YouTube, videos, transforaminal lumbar epidural steroid injections, discern, global quality index

ABSTRACT

Background. This study analyses the transforaminal lumbar steroid injection videos that have the highest views and likes on YouTube, and attempts to reveal the video qualities in order to contribute to the literature.

Methods. For review, "transforaminal lumbar steroid injection" was written to the standard YouTube search bar, and the videos with the highest views were ranked using advanced search preferences. The 50 most widely viewed videos were watched and scored by 2 physicians.

Results. The mean Modified DISCERN Score of the videos was 2,66+/-1,032 (the lowest: 1; the highest: 4) while the mean GQS score was 2,876+/-1,06 (the lowest: 1; the highest:4). In addition, the mean DISCERN score and the mean GQS value were 3,51 and 3,82, respectively, for the informational videos that were uploaded by health professionals but did not contain actual surgery.

Conclusion. We think that medical associations and state authorities in medicine should check the validity and accuracy of the information on the internet and should support the society in access to the most correct information.

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INTRODUCTION

In daily practice, internet search rates have increased in almost every subject due to developing information technologies that are used more and more every day. In health practices, professionals and patients make internet researches in order to get information and gain experience. Among these sources of application, YouTube is the biggest video archive website in the world and attracts 95% of internet users with 30 million active users every day (1). There are also many health-related videos in the archive. Generally, patients apply to a physician and get detailed information about recommended treatments but they are also inclined to watch on YouTube the operation to be carried out.

Therefore; the quality of a video, the persons who shot it and whether such video contains correct information are matters of great importance.

Lumbar disc herniation is frequently observed among people. Recently, fluoroscopy injections have been increasingly applied with success for nerve roots that cause pressure on patients whose pains do not regress with medical treatment and rehabilitation programs and who are not appropriate for operation (11).

This study analyses the transforaminal lumbar steroid injection videos that have the highest views and likes on YouTube, and attempts to reveal the video qualities in order to contribute to the literature.

MATERIAL AND METHODS

Search Strategy and Data Collection

For review, "transforaminal lumbar steroid injection" was written to the standard YouTube search bar, and the videos with the highest views were ranked using advanced search preferences. The 50 most widely viewed videos were watched and scored by 2 physicians.

Inclusion and Exclusion Criteria

The videos that were not in English language or did not have subtitles or speech or that did not explain the operation were eliminated.

Variables Extracted

Views, upload dates, like rates, uploaders, video lengths, comment numbers, like numbers and dislike numbers were identified as well as whether they were actual or animated videos.

In addition, video power index (VPI) values [(number of likes / number of likes þ number of dislikes) 100] were calculated to evaluate the popularity of the videos.

Assessment of Usefulness

All videos were independently evaluated by two physicians for usefulness and categorized into the following mutual exclusive categories.

1. Useful information: Videos designated as useful information were mainly focused on information delivery. They contained accurate information and were useful for learning how to do transforaminal lumbar steroid injection.
2. Misleading information: The videos contained in correctin formation or did not contain useful information about transforaminal lumbar steroid injection.
3. Useful patient opinion: The videos in this group have the DISCERN and GQS scores as 3 or above and clearly explain the patient experiences, the performance of operations, and preoperational and post operational pain scores.
4. Misleading patient opinion: The videos in this group have the DISCERN and GQS scores as 2 or lower and do not clearly explain patient experiences.

Scoring System

Video reliability was scored using a modified five-point DISCERN tool (2), which was adapted from the original DISCERN tool for the assessment of written health information by Charnock et al. (3).

The overall quality of each video was rate during the five-point Global QualityScale (GQS). The GQS was developed as an evaluation tool for website resources and it assesses the flow and ease of use of the information presented online, and the quality of video (Table 1) [4].

Statistical analysis

The results were statistically analysed during a non-parametric Kruskal–Wallis test. A p value of 0.05 or less was considered significant. The Statistical Package forth eSocial.

Sciencesversion 23 software (SPSS, Chicago, IL, USA) was used for all statistical analyses.

RESULTS

60 videos with the highest views were analyzed while 10 videos were later excluded from the analysis for they were neither in English language nor contained subtitles. Among these, 10 videos were animations while 32 consisted of actual images. There were 22 surgery, 10 patient view and 13 technically-narrated animated and actual videos. On the other hand, 6 videos were uploaded by physicians and gave theoretical information about the processes they applied (Figure 2). The oldest video was uploaded in 2007 while the newest one was added to the system in 2017. The videos were uploaded by hospitals (27 videos), health professionals and physicians (13 videos), and personal accounts (10 videos) (Figure 1).

The mean time of the video lengths was 4.22 sec (the shortest: 0,20 sec; the longest: 12,08 sec), and the mean view was 88,293+/-9,75 (the least viewed: 4075; the most viewed: 825.731). The daily mean

view of the videos was 42,975+/-4,442 (the least viewed: 4,45; the most viewed: 323,8). The mean like rate was 53,6+/-3,52 (the most liked:3000; the least liked: 0), and the mean dislike rate was 28+/-2,21 (the most disliked: 758; the least disliked: 0).As for the comments, the mean number was 42,8 (the least commented: 0; the most commented: 423).Similarly, video power index (VPI) analyses showed that the mean VPI value of the 50 videos was 82,557+/-9,766 (the lowest VPI: 60,1; the highest VPI: 95,8).

The mean Modified DISCERN Score of the videos was 2,66+/-1,032 (the lowest: 1; the highest: 4) while the mean GQS score was 2,876+/-1,06 (the lowest: 1; the highest:4). In addition, the mean DISCERN score and the mean GQS value were 3,51 and 3,82, respectively, for the informational videos that were uploaded by health professionals but did not contain actual surgery. Similarly, the mean DISCERN score and the mean GQS value were 1,08 and 1,29, respectively, for the patient videos in which personal experiences were shared. No statistically significant correlation was found between the GQS and DISCERN scores according to both researchers and VPI values (P > 0.05).

Table 1. Analyses of video characteristics by usefulness category

	Useful İnformation (Gr1)	Misleading İnformation (Gr2)	Useful Patient Opinion (Gr3)	Misleading Patient Opinion (Gr4)
Video Number	n:16(32%)	n:24(48%)	n:4(8%)	n:6(12%)
Views peer day	35,2+/-7,31	53,7+/-8,1	40,3+/-4,55	42,7+/-8,3
Video Lenght	4,01 min (2,04-5,91 min)	3,50 min (0,20-8,17 min)	6,03 min (5,02-8,54 min)	7,25 min (4,01-12,08 min)
Like	216+/-24	27,14+/-2,1	43,08+/-2,01	33,4+/-3,33
Dislike	189,5+/-24,5	46,3+/-4,44	20,2+/-1,35	15,2+/-1,56
Comments	26,8+/-2,33	27,2+/-1,33	92,1+/-7,41	113,4+/-11,2
Discern Score	3,4	2,2	3,2	0,5
GQS Score	4,1	2,3	4,2	1,6

Table 2. Pairwise comparisons of video groups according to usefulness

	Gr1-Gr2	Gr1-3	Gr1-4	Gr2-3	Gr2-4	Gr3-4
Discern Score p value	0,518	0,708	0,001	0,652	0,332	**0,0018**
GQS Score p value	0,125	1,00	**0,001**	0,069	0,852	**0,001**

Values of p 0,05 was accepted

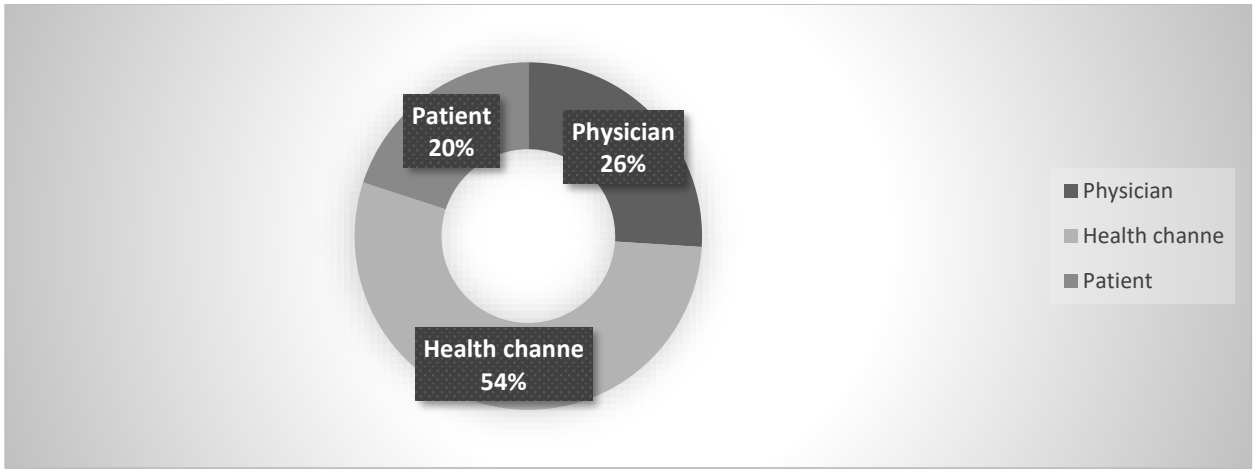

Figure 1. Video disseminator

Modify Discern (1 point per question answered yes)

1. Is the video clear, concise, and understandable?
2. 2. Are valid sources cited? (from valid studies, physiatrists or rheumatologists)
3. 3. Is the information provided balanced and unbiased?
4. 4. Are additional sources of information listed for patient reference?
5. 5. Does the video address areas of controversy/uncertainty?

Global quality scale

1. Poor quality, poor flow, most information missing, not helpful for patients
2. Generally poor, some information given but of limited use to patients
3. Moderate quality, some important information is adequately discussed
4. Good quality good flow, most relevant information is covered, useful for patients
5. Excellent quality and excellent flow, very useful for patients

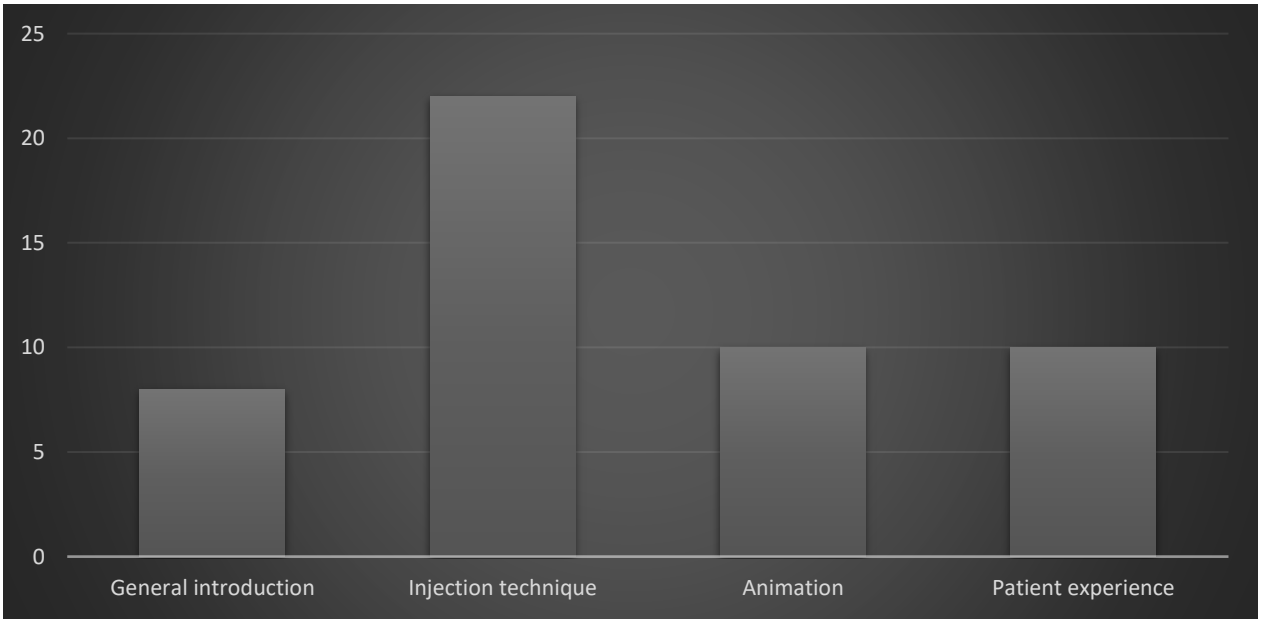

Figure 2. Video contents

Discussion

YouTube is a video sharing website based in San Bruno, California, the USA. The website was founded in 2005 and was later acquired by Google in 2006. The primary purpose of the website is that the users can upload and share any video in any subject free-of-charge (5).

The first video uploaded to the website was the video showing Jawed Karim, one of the founders of the website, in which he appears in a zoo (5). Concerning medical subjects; health professionals, hospitals and patients have a heavier traffic of video uploading activity. Patients and patient relatives refer to these videos in order to see treatment methods and possible risks and to make inferences from the experiences of cases. On the other hand, health professionals use operation videos to learn by watching (10). However, there may also be incorrect, low-quality and prejudiced videos on this platform where everyone can upload videos free-of-charge without being subject to any inspection. PubMed reviews reveal 1089 studies that measure the quality of YouTube videos on health issues (8,9). The first of these is a study from 2007 that evaluate the training of health professionals (6).

The first publication concerning transforaminal steroid application with fluoroscopy was made by Lutz GE in 1998. The study follows up 69 cases for about 80 weeks and describes the results thereto. The study was described as an effective attempt on cases with radiculopathy due to non-surgical disc herniation (7). After the article, PubMed also

published a paper indicating that the attempt was a positive one. Many physicians who deal with pain studied this attempt and applied the same to their patients.

In this sense, the purpose of the present study is to find out whether patients can get reliable information from YouTube channels prior to their transforaminal operations applied to lumbar disc herniation cases that do not require or are not recommended surgery. The second purpose is to evaluate the quality of the theoretical and visual information health professionals can get from such videos. The literature review we made did not produce any study concerning the subject in question. There are various scales and measures to evaluate the quality of the information in videos and on the internet. In this study, 2 researchers assess the videos using modified DISCERN scoring system, Global Quality Index and Video Power Index (VPI). According to the analysis of the 50 videos with the highest views and VPIs, it was found out that the videos presented weak and poor-quality information to patients, patient relatives and professionals who desire to learn the narrated operation.

However, it was also observed that 80% of the videos were uploaded by health professionals and institutions. In 16 (32%) videos with actual surgeries, it was seen that the average time was 3,44 seconds, the operators did not satisfactorily explain the methods before and after the operations, they did not clearly specify alternative treatments and effects and possible complications, and the videos were not supported with subtitles. It was observed that the videos did not explain the operations in simple language to convey the processes to patients and patient relatives but only the course was expressed, and that there were dialogs with patients during operations. Furthermore, it was revealed that 6 (12%) videos with the highest results of evaluation were animated or notional surgery videos, made theoretical PowerPoint presentations and were supported with anatomic cross-sections.

Although 6 of 10 videos with patient experiences contained information about pain statuses in post-op early stage and the post-op 2nd day, these were not found sufficient in terms of quality. The most-viewed 5 videos had approximately 300 views every day, on average, and 3 of these were actual surgeries while the other 2 were about patient experiences. The videos with the highest VPI values but had 2 or below in DISCERN and GQS scoring were found to convey inadequate information. In contrast with the foregoing, the videos with the highest scores had 60 views every day, on average, and did not appear on the first page when searched on YouTube. However, the videos that had the highest views but contained insufficient information appeared on top in YouTube searches. Apart from these, the video comment analyses demonstrated thatthe highest number of comments were entered to the uploads with patient experiences. The comments notably asked the regression rate of complaints, the length of the period without complaints and whether the operations were painful. Accordingly, the videos with the highest like numbers were those that contained patient remarks.

The videos were divided into 4 groups in terms of usefulness, and only 16 videos were found to contain useful and valid information. All these were uploaded by health professionals and were generally about physician remarks. The mean time of these videos was 2,44 seconds. Useful patient remarks were identified only in 4 videos, and their mean view time was 2,31 seconds.

The limitations of this study include the cross-sectional design (popularity based on number of views changes constantly), and the inclusion of only the 50 most widely viewed videos (an arbitrary cut point).

Conclusion

As a result, it may not always be accurate to believe that the medical videos with high view, comment and like numbers on YouTube contain reliable, comprehensible and correct information. Although the access to information and videos on medical subjects is very easy in today's world, it is more appropriate to apply to experienced health professionals in order to get information. We think that medical associations and state authorities in medicine should check the validity and accuracy of the information on the internet and should support the society in access to the most correct information.

Compliance with ethical standards

This study does not include any human participants or animals. Videos that were available to everyone were evaluated for this study. Therefore, ethics committee approval was not required.

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Spontaneous cerebrospinal fluid rhinorrhea in a patient with Pallister–Hall syndrome

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Abstract

Pallister-Hall syndrome (PHS) is extremely rare autosomal dominant disorder with typical clinical features such as presence of polydactyly, hypothalamic hamartoma, bifid epiglottis, anal, renal, genitourinary and pulmonary abnormalities, mainly located in the midline of the body. Spontaneous cerebrospinal fluid (CSF) rhinorrhea is also a rare condition, and it is used to describe nasal discharge of CSF unrelated to previous trauma, localized tumour, surgery, or previous radiation therapy. The exact cause is not yet fully understood.

We report a case of adult female patient previously diagnosed with PHS and late onset of spontaneous nasal liquorrhea, due to defect in the anterior skull base. Although it can be incidental finding, we believe that described defect in the body midline can be another presentation of congenital craniofacial abnormality which are common in PHS.

Keywords
Pallister-Hall syndrome, Spontaneous CSF rhinorrhea, nasal liquorrhea

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Introduction

Pallister Hall syndrome (PHS) is extremely rare autosomal dominant disorder usually diagnosed in infants and children, but it can be seldomly seen in adulthood (1). In 1980, Judith Hall and Philip Pallister described 6 cases of infants with a neonatally lethal malformation syndrome of hypothalamic hamartoblastoma, postaxial polydactyly, and imperforate anus, and after several simmilar cases were described by other authors, this syndrome was named after Pallister and Hall (2, 3). Typical clinical features of PHS are presence of polydactyly and hypothalamic hamartoma, however, in recent years, many patients were reported expanding the phenotype, and more rare features may also be seen, such as bifid epiglottis, anal, renal, genitourinary, and pulmonary abnormalities, nonpolydactyly skeletal anomalies, and developmental delay. Even rearly epilepsy, hypopituitarism, aganglonosis of colon, congenital cardiac defect, and adrenal abnormalities can also be found (4). Clinical suspicion of PHS is confirmed by genetic testing of the GLI3 zinc finger transcription factor

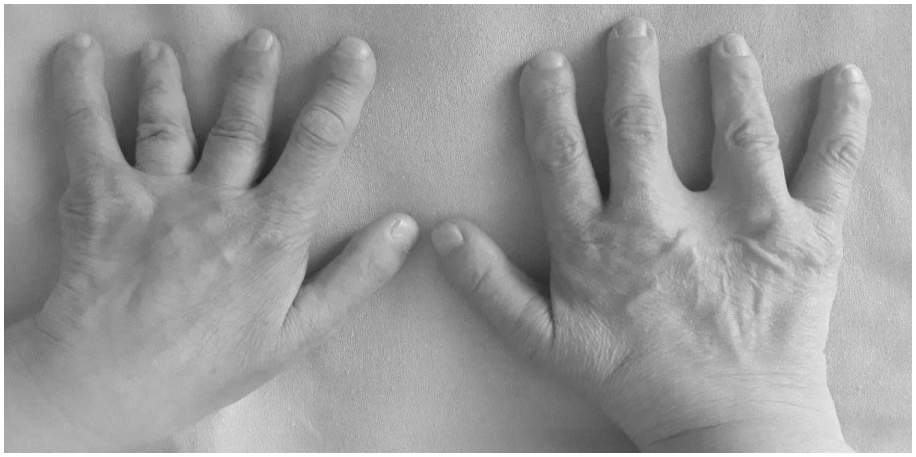
gene on 7p14 (2). The importance of this gene located on chromosome 7 is that it regulates downstream genes of the hedgehog pathway important to the formation of the neural tube, otic vesicles, craniofacial structures, and distal limb buds (4).

We report a case of adult female patient previously diagnosed with PHS and late onset of spontaneous nasal liquorrhea.

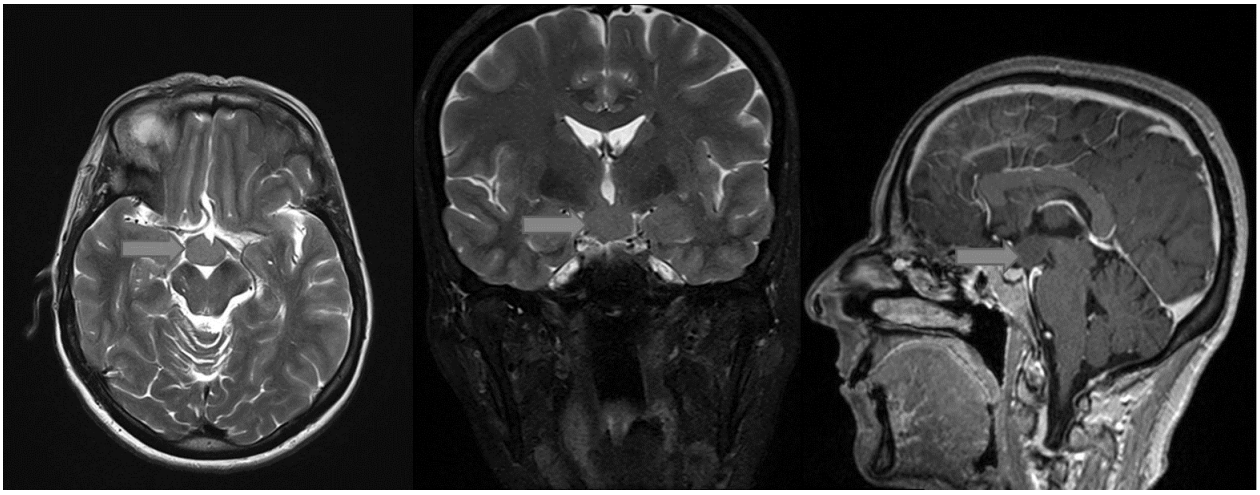
Case report

We present a case of a 56-year-old woman admitted to the Neurosurgery Clinic of the Clinical Center of Serbia, with signs of spontaneous nasal liquorrhea. She was born from healthy and non-consanguineous parents after normal pregnancy and delivery. On birth examination, she was found to have polysyndactyly on both hands. At the age of 2, she was operated, and ablation of redundant fingers and soft tissue was performed with surgical reconstruction and good appearance in size and shape of both hands was achieved (Picture 1). After few years, in early childhood, patient developed epilepsy with laughing, gelastic seizures, and she was placed on two antiepileptic drugs after which seizures resolved. Later on, during fertility testing she was found to have bilateral renal hypoplasia, as well as uterine hypoplasia. In the late 40's, during the clinical testing due to signs of polyneuropathy, suspicion of PHS was made by attending neurologist, and brain magnetic resonance imaging (MRI) showed typical hypothalamic hamartoma (Picture 2). Patient underwent genetic testing, and mutation of GLI3 gene in the short arm of chromosome 7 was found.

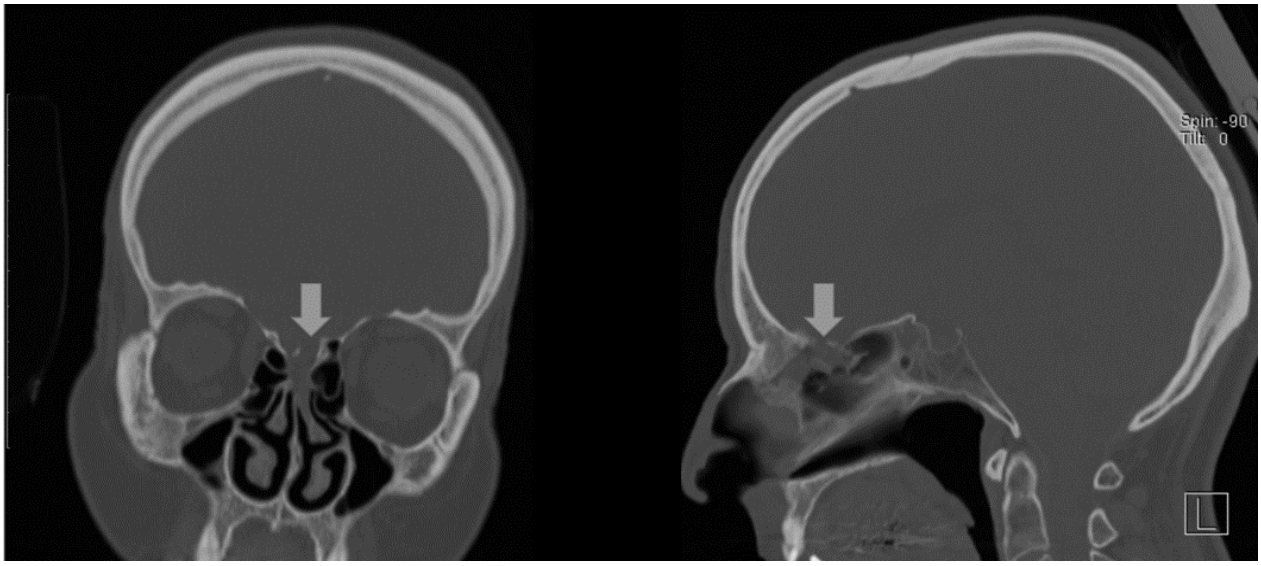
At the age of 50, the patient noticed spontaneous watery discharge from left nostril, and occasional sweet taste in her mouth, usually in the morning or after a long bed rest. There was no history of head trauma. After 4 years of neglecting this symptom patient was referred to our hospital. At admission her neurologic exam was indicative of distal polineuropathy without signs of motor weakness. High glucose concentration, and detection of β-2-transferrin in clear fluid collected from left nostril confirmed the diagnosis of cerebrospinal fluid rhinorrhea. Head MRI was performed and communication of the frontobasal liquor space with the upper nasal corridor at the level of the left olfactory nerve was found. Also, presence of hypothalamic hamartoma in the projection of tuber cinereum, 19 x 13 mm in diameter was confirmed. A non-contrast CT scan with bone window revealed mucosal thickening in the left cribriform plate in conjunction with the olfactory fila presenting possible defect in the adjacent skull base (Picture 3). We performed endonasal endoscopic repair of CSF rhinorrhoea under general anaesthesia. Operatively identified bone defect in the left cribriform plate with signs of CSF leak was closed by dura matter, fascia lata, and tissue glue. The mucosa of middle turbinate and adjacent septum was made raw and bolgerisation was performed. Valsalva manoeuvre did not show signs of CSF leakage. After haemostasis was achieved nose was bagged for five days. Avoidance of coughing or sneezing, the use of stool softeners, elevation of the head, and bed-rest were given in the post-operative period. Patient was on prophylactic antibiotics for one week. On the 5th post-operative day patient was discharged from the hospital. At 2 year follow-up patient is asymptomatic, without signs of nasal liquorrhea. Also, nasal cavities healed well, with no breathing difficulties.



Picture 1. Present look of patient's hands, 54 years, after ablation of redundant fingers and soft tissue due to polysyndactyly.



Picture 2. Brain MRI showing hypothalamic hamartoma in our patient



Picture 3. CT scan (bone window) showing mucosal thickening in the left cribriform plate in conjunction with the olfactory fila presenting defect in the adjacent skull base

Discussion

PHS is extremely rare autosomal dominant disorder usually diagnosed in infants and children, but it can be seldomly seen in adulthood (1). Dramatic beginning of PHS started in 1980, when Judith Hall and Philip Pallister described 6 lethal cases of infants with typical combination of hypothalamic hamartoblastoma, postaxial polydactyly, and imperforate anus (2, 3). Today, this clinical features of PHS in the terms of the clinical findings are considered to be just a tip of the iceberg, since many others rare features may also be seen, such as bifid epiglotis, polydactyly, dysmorphic face in the form of small ears pointing backwards, small retroverted nose, flat nasal bridge, and small tongue. Also, different cardiac, anal, renal, adrenal, genitourinary, and pulmonary abnormalities can be found. Hypothalamic hamartomas are typically found, and can be asymptomatic or in the origin of epilepsy, hypopituitarism, lethargy, hypoglycaemia, electrolyte dysfunction, and metabolic acidosis. So far, about 100 cases of PHS with variable manifestations are reported in literature (4-6). We reported a case of adult female patient previously diagnosed with PHS and late onset of spontaneous nasal CSF rhinorrhoea. To our knowledge this is a

first case of PHS patient with skull base bone defect, presented with spontaneous cerebrospinal fluid rhinorrhoea. Also, this is the first described case of PHS in Serbian population according to our knowledge. Our patient is a 56-year-old woman with previously operated polysyndactyly on both hands, well controlled epilepsy with typical gelastic seizures, bilateral renal and uterine hypoplasia, and hypothalamic hamartoma. These are usual signs and symptoms found in PHS. About ninety-five percent of PHS patients have GLI3 gene mutation in the short arm of chromosome 7 (6). This was also case in our patient, since definite diagnosis was confirmed after molecular testing showing mutation of GLI3 gene.

Hypothalamic hamartoma represents a benign tumour of the hypothalamus and does not need treatment from a tumour biological perspective. However, other problems can be associated with hypothalamic hamartoma such as pharmaco-resistant epilepsy, behavioural problems, and endocrine disturbances (7). An MRI of the brain in our patient revealed presence of hypothalamic hamartoma in the projection of tuber cinereum, 19 x 13 mm in diameter. In presented case patient developed epilepsy with laughing, gelastic seizures. After introduction of two different antiepileptic drugs, our patient was in total remission.

The term spontaneous CSF rhinorrhoea has been used to describe nasal discharge of CSF unrelated to previous trauma, localized tumour, surgery, or previous radiation therapy, and it represents a rare medical condition (8). Our patient had first onset of watery discharge from left nostril at the age of 50, without history of previous trauma, and after neglecting symptoms for about 4 years, patients was referred to our hospital. Also, other possible causes of spontaneous CSF rhinorrhoea were excluded in our patient.

In the study of Schuknecht et al, more than 70% of patients with spontaneous CSF leak had osteodural interruption at the site of cribriform plate leading into the olfactory cleft (8). This was also a case in our patient.

In the case of osteodural interruption surgical repair is recommended to prevent complications such as meningitis. Endonasal endoscopy is the preferred and minimally invasive approach and it has been accepted worldwide as the method of choice. The advantages of this approach are: excellent visualization, precise placement of graft, minimal surrounding tissue damage, preservation of olfactory nerves and their function, shortened operating time, and faster recovery. This approach has a high success rate up to 97% (9, 10). We performed surgical endonasal endoscopic repair of previously found osteodural deffect along the cribriform plate leading into the left olfactory cleft. On two years fallow-up, patient is without signs of CFS rhinorrhoea recurrence.

PHS is a rare, autosomal dominant, genetic disorder with a mutation in the GLI3 gene on the short arm of chromosome 7. This gene regulates pathways important for the formation of the neural tube, craniofacial structures, otic vesicles, and limbs (11). Many different congenital abnormalities are found in patients with PHS, and hypothalamic hamartoblastoma, bifid epiglottis, polydactyly, epilepsy, imperforate anus and other genital anomalies being most common, with predominance of anomalies in the midline of the body (4, 12). About 100 case reports of PHS are found in the literature, but to our knowledge this is the first case of PHS with spontaneous CSF rhinorrhoea, due to defect in the anterior skull base. Although it can be incidental finding, we believe that described defect in the body midline can be another presentation of congenital craniofacial abnormality which are common in PHS. Endoscopic endonasal approach is minimally invasive and successful treatment approach for described congenital osteodural defect.

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Bilateral traumatic basal ganglia haemorrhage, a rare entity. Experience at single institute with review of literature

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Keywords
basal ganglia, trauma, bilateral, haemorrhage

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ABSTRACT

Aims. Traumatic basal ganglia haemorrhage is rare entity but post traumatic bilateral basal ganglia hematoma is even extremely rare and was earlier presented as case reports. Its incidence is about 3% after a closed head injury however, the incidence is higher in post mortem studies.

Material & Methods. Out of 1485 head injury patients admitted to our institute from January 2012 to January 2019, there were 9 cases of traumatic bilateral basal ganglia haemorrhage. The incidence of traumatic bilateral basal ganglia Haemorrhage in our series is 0.61% which is very less compared to previous literature.

Results. There were 6 males and 3 females; age ranging from 19 to 50 years (average 32 years). Patients with hypertension, history of drugs abuse, history of coagulopathy, with doubtful history of trauma or unknown mode of injury were excluded from the study. The mode of injury in all the patients was road traffic accidents. Average follow up was 9.54 months. Outcome was assessed by Glasgow outcome Score. In 8 out of 9 patients, outcome was good. One patient died. All the nine cases were managed conservatively.

Conclusion. We report nine cases from a single institute which to the best of our knowledge is the largest series in world literature. Prognosis is variable and dependent on many factors. The prognosis of TBGH is favourable if not associated with other disorders like hypertension, diabetes mellitus, and coagulation disorders or diffuse axonal injury.

INTRODUCTION

Traumatic basal ganglia haemorrhage (TBGH), are a rare entity and reported in only 3% of closed head injuries. [1] However autopsy series indicate a higher incidence ranging between 10%to 12%.[2,3] It is defined as a haemorrhagic lesion located in the basal ganglia or neighbouring structures, such as the internal capsule and the thalamus, It can be classified as “large,” if it is more than 2cm in diameter or as “small” if it measures <2 cm in diameter.[2] Bilateral basal ganglia hematoma after trauma is extremely rare and is limited to case reports. The mechanism of TBGH is unclear but is thought to be due to shearing

of lenticulostriate or anterior choroidal blood vessels due to the violent acceleration deceleration brought about by a high velocity injury. [2,4] Since Basal ganglia hematoma can be due to trauma and thus takes importance in the medico legal cases where bleeding may be attributed to a non-traumatic cause. Thus, the identification of TBGH is of prime relevance.

Material and methods

Out of the 1485 traumatic head injury patients, the study group comprised of nine patients of TBGH identified on the basis of initial Noncontrast CT (NCCT) head, admitted from January 2012 to January 2019 in the Department of Neurosurgery at R.N.T. Medical College and M.B. Hospital, Udaipur, Rajasthan. A written informed consent was taken from all patients, as applicable. Hypertensive patients, drugs abuse history, history of coagulopathy with doubtful history of trauma or unknown mode of injury was excluded from the study. The diagnosis of TBGH was made on the basis on NCCT head and Outcome was assessed by Glasgow outcome score.

Results

Total head injury patients admitted to the hospital were1485 among which nine patients of Traumatic bilateral basal ganglia Hemorrhage were identified and thus incidence of Bilateral TBGH in our series is 0.61% (nine patients) which is very less as compared to previous literature. There were 6 males and 3 females; age ranging from 19 to 50 years (average 32 years (Table1). All patients had sustained road traffic accidents. NCCT head was done in all the patients [Figure -1, 2, 3, 4 & 5] after initial resuscitation. GCS at admission were 7 to 12 (mean 10.0). (Table 1)All the patients were managed conservatively .Outcome was assessed by Glasgow outcome Score (Table 2). Outcome were labeled as good (GOS-5, 4) and poor (GOS1-3).The average follow up was 9.54 months. In 8 out of 9 patients the outcome was good. One patient had poor outcome and died.

Table 1. Demographic analysis, management and outcome of all patients

S.no	Age (yr)	Gender	Mode of injury	GCS at admisson	Focal neurological deficit	Management	Outcome measured by GOS
1	19	Male	RTA	12	No	Conservative	5
2	45	Female	RTA	9	Left sided hemiparesis	Conservative	4
3	24	Male	RTA	10	Left sided hemiparesis	Conservative	5
4	50	Male	RTA	7	Left sided hemiparesis	Conservative	1
5	20	Male	RTA	9	Right sided hemiparesis	Conservative	5
6	40	Male	RTA	9	Left sided hemiparesis	Conservative	5
7	35	Female	RTA	10	No	Conservative	5
8	25	Female	RTA	12	No	Conservative	5
9	30	Male	RTA	12	No	Conservative	5

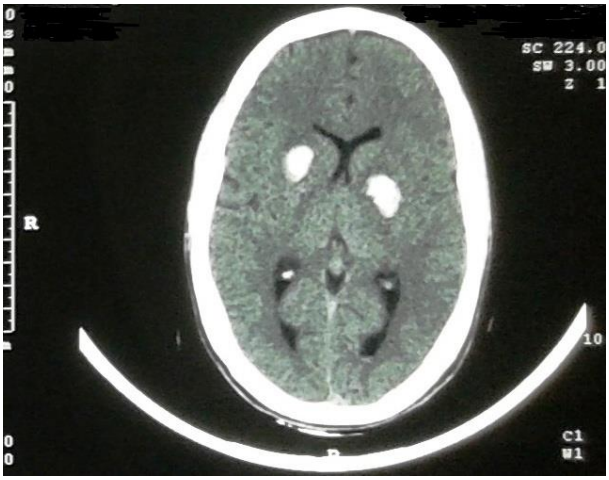

Image 1. NCCT head shows hemorrhage in bilateral basal ganglia region, with involvement of right anterior limb of internal capsule.

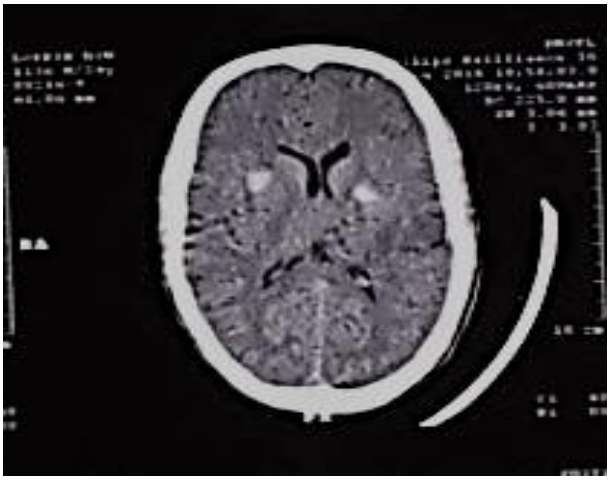

Image 2. NCCT head shows hemorrhage in bilateral basal ganglia, with left frontal depressed fracture with underlying small left frontal contusion.

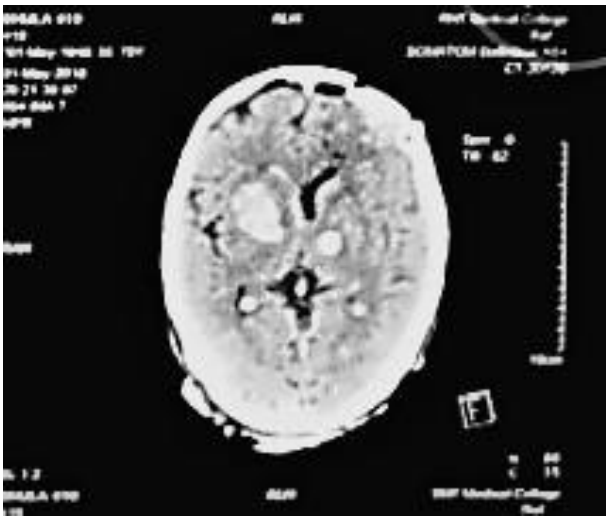

Image 4 & 5. NCCT head shows hemorrhage in bilateral basal ganglia region with subdural hemorrhage in right frontotemporoparietal region and subarachnoid hemorrhage along right frontal and temporal sulci and gyri.

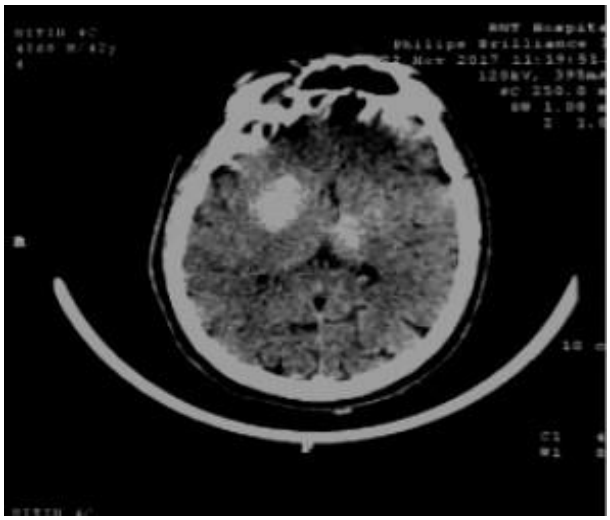

Image 3. NCCT head shows hemorrhage in bilateral basal ganglia region with fracture of outer table of right frontal sinus.

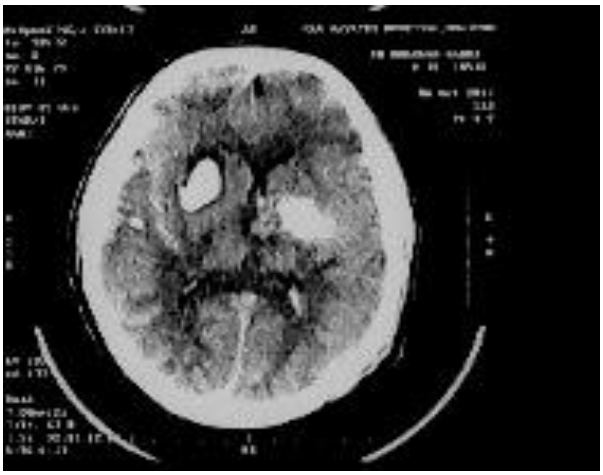

Table 2: Glasgow outcome score (GOS)

GOS Score	Functional status
5	Resumption of normal life, there may be minor neurological and or psychological deficit
4	Able to work in a shattered environment and travel by public transportation
3	Dependent for daily support by reason of mental or physical disability or both

2	Unresponsive for weeks or months or until death
1	Death

Discussion

The TBGH is a rare entity with an incidence rate of about 3% in closed head injuries. The exact pathogenesis of basal ganglia hematoma is unclear; however, it is suggested that a strong impact over the vertex, forehead, or occipital region, then shearing force causes the brain to be displaced through the tentorial notch. This results in stretching and tearing of the vessels resulting in hematoma. [2] The sudden acceleration/deceleration forces at the time of injury result in shearing strain over the lenticulostriate and anterior choroidal vessels leading to bleeding. Mosberg and Lindenberg, in an autopsy of fatal head injury patient, demonstrated massive hematoma in the pallidium and ruptured twig of the anterior choroidal artery. [4]

Since basal ganglia region is predisposed to hypertensive bleed, at times, it becomes difficult to distinguish between hypertensive and traumatic hemorrhage. It has been suggested that the TBGHs are small, multiple, rarely bilateral, located in the zone of lentiform nucleus and external capsule, whereas spontaneous hemorrhages are large, solitary, and located mainly in the region of thalamus and internal capsule. [5, 6] In a known hypertensive patient with head injury and findings of basal ganglia bleed, it is imperative to ascertain the sequence of events. This may be a medico legal issue; as to whether the patient had spontaneous basal ganglia bleed leading to the subsequent head injury or it was the head injury, which caused the basal ganglia hematoma.

In all our patients, there was a definite history of trauma with no antecedent history of preexisting medical illnesses and bleeding diathesis, thus the bilateral basal ganglia bleed seen on CT/MRI scans was traumatic in nature. As our patients had small bilateral TBGH with volume <25 mL and showed gradual improvement of GCS with medical management, they were managed conservatively.

Treatment is based on protocol as for intracranial hematoma taking into account the neurological status, presence of mass effect and response to other means of controlling intracranial pressure. Treatment options for TBGH include conservative, open surgery, CT guided stereotactic or ultrasound guided aspiration. Katz et al [1], Bhargava et al [6], Jang et al [7] and Kimura et al,[8] have reported favorable outcomes for TBGH with conservative management. Boto et al advised surgical evacuation of all lesions with volume >25 ml; however, poor outcome was noted in most of these patients. [3] Boto et al noted that 84% of surgically managed patients had an unfavorable outcome. Surgical evacuation entails approach to the hematoma via the thalamo-ganglionic region, leading to further damage of the eloquent areas resulting in possible poor outcome. Surgical management was done in patient described in case report by Yanaka etal.[9] Craniotomy was performed in patients reported by Pandey et al [10],Jain et al[11] and Calderon et al [12].

The outcome of TBGH has been found to be variable. Amongst 37 patients studied by Boto et al.59%died, 5% were vegetative, 19% experienced severe disabilities, and 16% made a favorable recovery.[3] Katz et al.[1], Bhargava et al [6], Kaushal et al [13] and Zhang et al [14] have also reported good prognosis for TBGH. Kankane et al reported bilateral traumatic basal ganglia bleed and both the patient managed conservatively and outcome was good and no focal neurological deficit. [15] Zhang YX, et al reported single case of 45year female of traumatic bilateral traumatic basal ganglia bleed and patient managed conservatively and outcome was good. [14]In our study, all the patients were managed conservatively and in 8 out of 9 patients the outcome was good. One patient had poor outcome and died. Large size, associated coagulation disorders, DAI, presence of other bleeds like intraventricular of brain stem hemorrhage, age >60, abnormal pupillary response, abnormal motor response to pain, and severe head injury are reported to be indicators for poor prognosis.[1,2,5,16,17]

This rare entity has been previously reported in literature by Yanaka et al (2 cases), Jang et al (1 case), Kaushal et al (1 case), Bhargava et al. 1 (1 case), Jain et al (1 case), Pandey et al (1 case), Calderon et al (1 case), Kankane et al (2 cases) and Zhang et al (1 case). (Table 3)

TABLE 3. Review of literature with previously reported cases

No	author	Year	Totalc ase	Age	Gender	Diagnosis	Management	Out come
1	Yanaka et al	1991	2	17 75	Male Male	TBBGH TBBGH	Surgical	Good
2	Jang et al	2007	1	50	Male	TBBGH with SAH	Conservative	Good
3	Kaushal et al	2011	1	42	Male	TBBGH	Conservative	Good
4	Bhargava et al	2012	2	25 50	Male Male	TBBGH TBBGH	Conservative	Good
5	Jain et al	2013	1	38	Male	TBBGH with epidural hematoma	Craniotomy	Good
6	Pandey et al	2014	1	37	Male	TBBGH with subdural hematoma	Craniotomy	Poor
7	Calderon et al	2014	1	28	Male	TBBGH with epidural hematoma	Craniotomy	Death
8	Kankane et al	2016	2	20 40	Male Male	TBBGH with hemiparesis	Conservative	Good
9	Zhang et al	2016	1	45	Female	TBBGH	Conservative	Good
10	Present study	2019	9	19-50 (range)	6-males 3-females	4-TBBGH 5- TBBGH with hemiparesis	9--Conservative	8-Good 1-Death

CONCLUSION

Traumatic BGH is uncommon, and bilateral BGH is very rare entity with only few cases reported in world's literature. We report nine cases from a single institute which to the best of our knowledge is the largest series in world literature. Prognosis is variable and dependent on many factors. The prognosis of TBGH is favorable if not associated with other disorders like hypertension, diabetes mellitus, and coagulation disorders or diffuse axonal injury. TBGHs are compatible with a favorable recovery if present in isolation and not associated with damage to other cortical and sub cortical structures. Patients with isolated TBGH do well with conservative management.

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Risk factors for preoperative and postoperative late seizure in supratentorial meningiomas. A retrospective analysis of 63 patients

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Keywords
epilepsy, meningioma, postoperative, preoperative, seizure

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ABSTRACT

Introduction. Seizure following meningioma surgery is common and management may be challenging. Identifying risk factors may help physicians to initiate optimal medical management. The aim of this study is to report seizure outcome and risk factors for perioperative seizure.

Materials and Methods. Sixty-three adult patients who underwent supratentorial meningioma resection were included, and perioperative data and long-term follow-up were provided in this retrospective study. Binary logistic regression analysis was used to identify the risk factors for perioperative seizure and postoperative late seizure.

Results. The results showed that 20 (37.1 %) patients had preoperative seizure and 10 (50 %) patients were seizure free at the long-term follow-up. Absence of headache was associated with preoperative seizure (p=0.002) while presence of early seizure was significant predictor for postoperative late seizure (p=0.03). Although not significant, occurrence of surgical complications (p=0.08) and non-skull base location (p=0.06) tended toward being a significant risk factor for postoperative late seizure.

Conclusion. Presence of early seizures, surgical complications and locations out of skull base may direct postoperative anti-epileptic treatment to decrease seizure incidence which, indeed, increases quality of life for patients with meningioma.

INTRODUCTION

Meningioma is the most common form of benign intracranial neoplasms and surgery is the first-line treatment. Epileptic seizure, as the first symptom, is one of the most common manifestations of supratentorial meningiomas, occurring up to 60% (5, 14). Surgical resection results in complete cessation of seizure in the majority of patients, but new-onset seizures can develop following surgery in the patients who are seizure free preoperatively.

Leaving a proportion of patients with seizure even after total tumor removal significantly decreases quality of life and patients have to use

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anti-epileptic drugs (AED) for long-term, which also affects patients' life adversely (8). Predicting preoperative and postoperative risk factors for seizures in patients with meningioma have become the focus of recent studies and accumulating evidence showed that younger age, presence of preoperative peritumoral edema, and tumour location are the strongest predictors for either preoperative or postoperative seizure (3, 9, 10, 13). Prediction of risk factors is of utmost importance which guides physicians to decide whether or not AED should be started (1, 4, 12, 15, 16). More importantly, informing patients or next of their kin about seizure outcome makes the follow-up period easier for both patients and treating physicians.

In this paper, we aimed to share our experience related to preoperative and postoperative seizures in patients who underwent meningioma resection and to find out which patients are under risk of seizure after surgery.

Material and Methods

Patient selection

This retrospective study included the patients operated on supratentorial meningiomas between 2010 and 2017. Patients who had infratentorial meningioma, multiple meningioma, and previous intracranial meningioma surgery were excluded from the study. To provide a homogeneous population, patients who were younger than 18 were excluded from the study. The remaining 63 patients were enrolled in this study. The research was conducted in accordance with the principles of Helsinki Declaration.

Data retrieval

Perioperative clinical, radiological, and pathological data were retrieved from the patients' files. All patients were followed-up clinically and radiologically at regular intervals. Clinical, radiological, seizure and AED outcomes were noted.

Statistical analysis

Statistical analysis was performed by using SPSS, version 22.0 (IBM, Chicago, IL). Independent sample t test and chi-square test were used in appropriate comparisons. Binary logistic regression analysis was used for multivariate testing of factors associated with preoperative and postoperative seizures. The differences were accepted significant if p value was < 0.05.

Results

Demographic and clinical characteristics

45 (71.4%) females and 18 (28.6%) males were enrolled in the study with a mean age of 51.9±14.2 years (range: 20-76 years). Headache was found in 35 (55.6%) patients at admission and 20 patients (31.7%) suffered from preoperative seizure. Of the 20 patients with preoperative seizure, 10 had single (50%) and the other 10 had multiple seizures. The majority of seizure type was generalized tonic-clonic (n=12; 60%), followed by focal motor (n=5; 25%) and focal sensory (n=3; 15%) seizures. Neurological examination demonstrated that 22 patients (34.9%) had neurological deficit ranging from cranial nerve dysfunction to paresis. Before surgery, 24 patients (38.1%) were on AED monotherapy. Nineteen patients with preoperative seizure (19/20; 95 %) and 5 patients with no seizure (5/43; 11.6%) were on AED. The difference regarding use of AED between patients with and without preoperative seizure was significant (p=0.00001). Demographic features of the patients are presented in Table 1.

Table 1. Demographic and radiological characteristics. GTC: generalized tonic-clonic, R: right, L: left, M: male, F: female.

	Patient number	(%)
Sex (M/F)	18/45	28.6%/71.4%
Age	51.9±14.2 years	-
Preoperative seizure	20	31.7%
GTC	12	60%
Focal motor	5	25%
Focal sensory	3	15%
Preoperative AED therapy		
with seizure	19/20	95%
without seizure	5/43	11.6%
Tumour side (R/L/midline)	24/36/3	38/57.1/4.7
Tumour location		

Skull-base	15	23.8%
Non-skull base	48	76.2%

Radiological characteristics

All patients were evaluated by cranial magnetic resonance imaging (MRI). Peritumoral edema (PTE) was determined on T_2-weighted images. Anterior-posterior diameter was measured on post-contrast axial MR images. The location was divided into 2 groups: skull base and non-skull base. Non-skull base group included tumors located on convexity or parasagittal/falx region. MRI showed that 36 patients (57.1%) had tumor on the left side, followed by the right side (n=24; 38.1%) and midline (n=3; 4.8%). The difference with respect to the side of location was significant (p=0.00001). But side was not significant between the patients with and without preoperative seizure (p=0.41). Skull base and non-skull base location were noted in 15 (23.8%) and 48 (76.2%) patients respectively. The difference was significant (p=0.00001). However, the difference did not reach a significant level between patients with and without preoperative seizure related to skull base and non-skull base location (p=0.62). Convexity was significantly the most common location (30 patients; 47.6%) (p=0.00001). Second common location was the parasagittal/falx region (18; 28.6%). Six patients (9.5%) had anterior clinoid and 4 patients (6.3%) had sphenoid wing meningiomas. Two olfactory groove, 2 tuberculum sellae, and 1 petroclival meningioma were observed. Comparing patients with and without preoperative seizures, no significant difference was found regarding the site (p=0.60). PTE on preoperative MRI was present in 37 (58.7%) patients. The difference between presence or absence of PTE was insignificant in the whole group (p=0.16). Fifteen out of 20 patients (75%) with preoperative seizures and 22 of 43 patients (51.16%) without preoperative seizure had PTE on preoperative MRI and the difference was not significant (p=0.07). None of the 12 patients diagnosed with atypical meningioma showed PTE. The mean anterior-posterior (A-P) diameter was found to be 37.6 ± 14.4 mm (range: 10-72 mm). Twenty patients with and 38 patients without preoperative seizure had a mean A-P diameter of 40.8 ± 10.5 mm and 36.2 ± 15.7 mm, respectively. The difference was not significant (p=0.17).

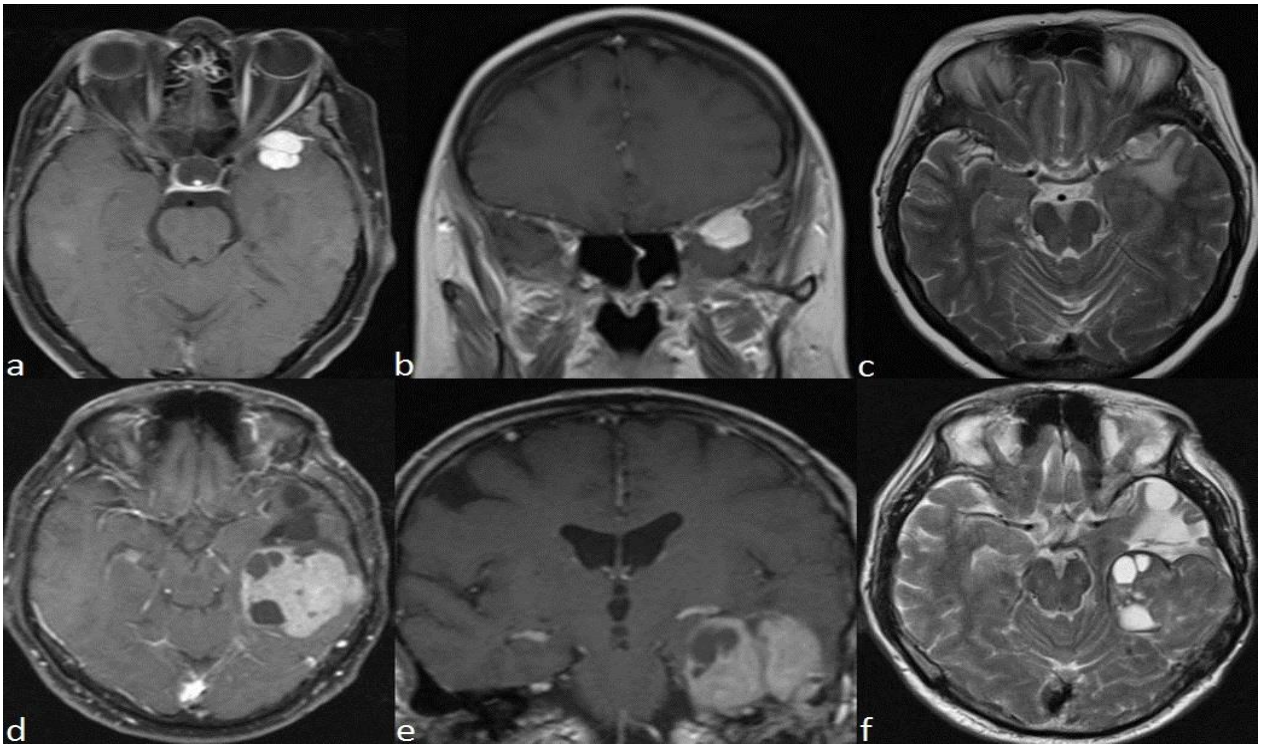

Figure 1. A left temporal Grade 1 secretory meningioma presenting with seizure shows homogeneous contrast enhancement (**a** and **b**) and PTE on T2 weighted (**c**) MR images. A Grade 1 fibrous meningioma which also shows contrast enhancement with cyst formation (**d** and **e**) and PTE on T2 weighted images (**f**) without preoperative epileptic seizure. PTE: peritumoral edema.

Surgical and histopathological characteristics

Informed consent form was obtained from all patients undergoing surgical resection. Extent of surgery was categorized as gross total resection (GTR) and subtotal resection (STR) depending on the findings on postoperative MRI. GTR was defined as absence of contrast enhancement on postoperative MRI. GTR was achieved in 54 (85.7%) patients and STR in 9 (14.3%) patients. Histopathological diagnosis was grade-I in 51 (81%) and grade-II (atypical) in 12 (16.9%) patients. GTR was achieved in all grade-I meningiomas, and all STRs were noted in the atypical group. Considering grade-I meningiomas, transitional type was the most common subtype (n=24; 38.1%).

Follow-up

The mean follow-up period was 46.87 ± 29.4 months (range: 12-96 months). No new neurological deficit was noted early after surgery. Nonetheless, 16 patients (25.4%) in the whole group continued to have neurological deficits. Of the 22 patients with preoperative neurological deficit, 6 patients recovered after surgery (27.2%). Postoperative seizures were divided into two groups: 1) Early seizure and 2) late seizure were defined as a seizure occurring within 7 days and after 7 days following surgery respectively. Five (7.9%) patients in the whole group showed early seizures and 10 (15.9%) exhibited late seizures. Two (4.65%) and 5 patients (11.62%) without seizure before surgery had early and late seizures respectively. Three patients who showed early seizure had late seizure at the last follow-up. Of the 10 patients with late seizure, 5 (50%) had single and the rest had multiple seizures. Focal motor, generalized tonic-clonic, and focal sensory seizures were seen in 5 (50%), 3 (30%), and 2 (20%) patients, respectively. Eight patients (8/10; 80%) with persistent seizure at the last follow-up had convexity meningiomas. Interestingly most of the patients with late seizure (8/10) had GTR. Although the number of patients with seizure decreased from 20 (31.7%) to 10 (15.9%) at the last follow-up, the difference was not significant (p=0.26). Overall, seizure free rate of patients with preoperative seizure was 50% at the last follow-up.

Five patients (7.9%) showed surgery-related complications. Two had hematoma within the resection cavity. Two other patients developed hydrocephalus which required ventriculo-peritoneal shunting. All patients were put on AED therapy after surgery. At the last follow-up, 10 patients (15.9%) with late seizure were still using AED monotherapy. Comparing the number of patients who were on AED before surgery (n=24; 38.1%) and at the last follow-up showed no significant difference although there was a trend to decrease in the number of patients using AED (p=0.48). The continuation of AED in these 10 patients depended on the clinical and electrophysiological findings.

Early MRI was obtained from all patients during their stay in the hospital. The first follow-up MRI was obtained at the 3rd month of surgery. Patients with atypical meningioma had MRI every 3 months. In contrast, it was performed in patients with grade-1 meningiomas at the 1st year, then every 2 years until 5 years after surgery. No patient showed new tumor formation or progression of residual tumor on the follow-up MRIs.

Predictors of preoperative seizure

In this study, 6 categorical risk factors were introduced in logistic regression analysis to find out predictors for preoperative seizure. The risk factors included *gender* (female/male), *edema* on MRI (present/absent), *headache* (present/absent), *neurological deficit* (present/absent), *location* (skull base/non-skull base), and *side* (right/left/midline). Binary logistic regression analysis (log likelihood=60.697; chi square=18.045; p=0.012) showed that among the 6 risk factors, only absence of *headache* (OR 8.295, 95% CI 2.105-32.68, p=0.002)) was found to be a significant and strong predictor for preoperative seizure.

Predictors of postoperative late seizure

For identification of risk factors for late seizure, 10 categorical variables were analyzed. The factors included *gender* (female/male), *preoperative seizure* (yes/no), use of *preoperative AED* (yes/no), *postoperative early seizure* (yes/no), *side* (right/left/midline), *edema* on preoperative MRI (present/absent), *location* (skull base/non-skull base), *extent of resection* (gross total/subtotal), *surgical complication* (present/absent), *pathological grade* (grade-I/grade-II). Binary logistic regression analysis (log likelihood = 36.571; chi square = 18.561; p=0.06) showed that among the variables above, presence of postoperative *early seizure* (OR 0.045; 95% CI 0.009-0.864; p=0.03) was a risk factor for postoperative late seizures. Although regression analysis did not show non-skull base location (p=0.06) and occurrence of

surgical complication (p=0.08) to be a significant risk factor postoperative late seizure, they tended toward.

Discussion

Seizure is a common symptom adversely affecting the quality of life after intracranial tumor surgery (8). In case of meningiomas, seizure even after total removal of the tumor may require collaboration of epileptologists to figure out the epileptogenic area. Preoperative and postoperative seizure outcomes after glioma surgery have been studied extensively and risk factors have been defined (6, 11). However, this issue has not been well-studied for meningioma.

Depending on the limited number of studies, it was shown that nearly 30% of patients present with seizure in supratentorial meningioma (1, 3, 4, 9, 10, 12, 13, 15, 16). However, type of seizure differs among the papers so that either generalized tonic-clonic seizures (GTC) or focal tonic seizures can be encountered as the most common type (1, 4, 13, 16). In fact, GTC seizure is expected to be more common given that meningioma generally presents with seizure after reaching a certain size compressing larger cortical zone.

Following surgery, about 50 to 70% of patients become seizure free but new seizures can be seen in almost 12% (9, 14). Previous studies suggested that prophylactic AEDs should be used depending on the risk factors which are associated with seizures (8, 12, 15). The rate with respect to prophylactic AED use in the present paper is comparable to previous studies which do not support routine use of prophylaxis without seizure despite of peritumoral edema (5, 14).

Almost all previous studies showed that the left side was more commonly involved similar to our findings (1, 4, 9,13, 15). Different from other series, non-skull base location was more common in the present paper which may be due to smaller number of patients (3, 10, 13). Convexity region is noted as the most common site besides the other frequent locations such as tuberculum sellae, sphenoid wing or parasagittal/falx region (3, 4, 10, 12, 13, 16). In the current literature, convexity meningiomas have been shown to be more epileptogenic (3, 9), nevertheless some authors found that parasagittal/falx meningiomas present with seizure more common than other locations (1). Side and site of locations were not different between the patients with and without preoperative/postoperative seizures in our study.

Atypical and malignant meningiomas are generally associated with PTE which may explain higher occurrence of seizure in these types. Glutamate, an amino acid which decreases electrical threshold of surrounding cortex and aggravate seizure, has been found to be higher in peritumoral edematous tissue (2). Furthermore, PTE is shown to be related to angiogenesis, increased pial blood supply, and increased vascular endothelial growth factor (7). All these factors give PTE an epileptogenic potential and AED is preferred to start upon detection of edema on MRI. We found PTE in 58.7% of the patients. However, no difference was found regarding presence of PTE and preoperative seizure. Interestingly, no PTE was detected on MRI in 12 patients with atypical meningioma. Concerning the size of tumor, >3-3.5 cm diameter was associated with either preoperative or postoperative seizure (3, 13). Mean diameter did not show difference between the patients with and without preoperative seizure in our study suggesting that location and/or size of PTE may be more important than size of meningioma itself.

Our overall seizure free rate at the last follow-up was 50% similar to previous reports (50-70%; 5, 14). Besides, our early and late seizure rates are comparable with the current literature (3, 10, 16) so that 50% of patients with preoperative seizure have become seizure free after surgery. Complex-partial seizure is the seizure type that responds to surgery well. Almost 80% of patients with late seizure had surgery on convexity meningiomas and again majority had GTR. Concerning these results, we support the notion that GTR may result in seizure more commonly due to increased damage to surrounding cortex.

Predictors of preoperative and postoperative late seizures

When the limited number of retrospective studies are reviewed, only the number of variables included in statistical analysis differs while the negative and/or positive predictors before and after surgery are almost similar (5, 14). Male gender, convexity or falx location, absence of headache, tumor diameter >3-3.5 cm, presence of peritumoral edema, younger age were found to be predictors of preoperative seizures. On the other hand, male gender, convexity or falx location, tumor size >3- 3.5 cm diameter,

presence of edema, presence of preoperative seizure, use of postoperative AED, location of the left side and higher grade were associated with postoperative seizure (4, 12, 15, 16).

The present study demonstrated that among the variables which we introduced into regression analysis, occurrence of postoperative early seizure was a significant risk factor for postoperative seizure. Existence of postoperative surgical complications and non-skull base location showed a tendency to be postoperative late risk factor.

Study Limitations

The small patient group and retrospective nature of our study are two major limitations.

Conclusion

Depending on our results, absence of headache in the preoperative period and presence of postoperative early seizure are associated with seizure outcome. Occurrence of surgical complication(s) and non-skull base locations tend toward to be a predictor for postoperative late seizure. Identifying risk factors in the perioperative period may lead treating physician to start timely AED and decrease seizure incidence which, indeed, improves quality of life in patients with meningiomas.

Conflicts of Interest: The authors inform that there is no conflict of interest in this study.

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A case report of retrograde suction decompression of a large paraclinoid aneurysm

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Keywords
paraclinoidal, proximal aneurysm control, retrograde suction decompression (RSD)

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ABSTRACT

Surgical clipping of large Paraclinoidal IC (Internal carotid) aneurysm pose a great challenge as there are adhesions hindering exposure of aneurysm dome and parent artery . Obtaining adequate visualization of the aneurysm neck is very difficult in these aneurysms, also in the access of proximal control. There are many methods to obtain a proximal control in these aneurysms. Retrograde suction decompression provides adequate visualization of the aneurysm neck and its relation with the optic apparatus. Retrograde suction decompression can be done by many methods. The technique done via open catheterization of superior thyroid artery is readily accessible and provides adequate relaxation of the aneurysm dome enabling complete dissection of the aneurysm from the surrounding important neurovascular structures. In this report of a case of left Paraclinoidal ICA aneurysm which was clipped applying this method, we elaborate on the technique and discuss other methods available for proximal control in these difficult aneurysms.

INTRODUCTION

Microsurgical treatment for paraclinoid aneurysms continue to pose severe challenges to vascular neurosurgeons because of attaining difficulty in proximal control of the parent artery and obtaining adequate visualization of the aneurysm neck. (1)

Microsurgical treatment of large paraclinoid aneurysms often requires the use of the one or the other methods of attaining proximal control. These can vary from exposure of internal carotid artery in the neck, Adenosine induced cardiac arrest, Rapid ventricular pacing (RVP), and Retrograde suction decompression (RSD). These, in addition to anterior clinoidectomy facilitate safe and complete clipping in these difficult aneurysms. (2,3)

RSD can be in the form of both open as well as endovascular approach. In both variants it provides adequate relaxation of the

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aneurysm dome, enabling the surgeon to dissect the aneurysmal complex from the surrounding structures such as optic apparatus and dural ring allowing adequate visualization of the aneurysm neck and reconstruction of the parent artery. (1, 4, 5, 6)

We present a case and discuss the surgical nuances of retrograde suction decompression of a large left Paraclinoidal IC aneurysm in Banbuntane Hotokukai Hospital, Fujita Health University, Japan. Haemorrhages or eponymously Duret haemorrhages are a feared consequence of a transtentorial brain herniation or of a decompression of the intracranial space by means of craniectomy or by removal of an intracranial mass lesions. (16, 21, 22).

CASE REPORT

A 49-year-old woman was admitted to our hospital with incidentally detected, no history of headache, dizziness or blurring of vision. Magnetic resonance angiography showed a left Paraclinoidal aneurysm. Three-dimensional computed tomography (CT) angiography (3D-CTA) and digital subtraction angiography revealed a left Paraclinoidal aneurysm with a fundus height 8.2 mm in size, neck width 8.5mm (Figure 1) .We also performed computational fluid dynamics (CFD) which showed wall pressure to be high, wall shear stress was low and vectors were divergent at the base of neck as it impend rupture (Figure 2).

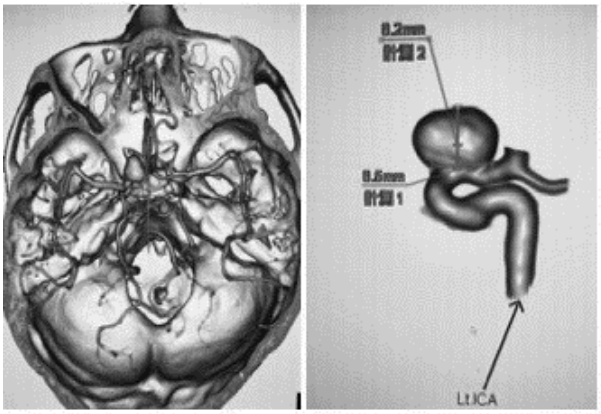

FIGURE 1. 3D-CTA Show left Paraclinoidal aneurysm with fundus height 8.2 mm, neck width 8.5 mm

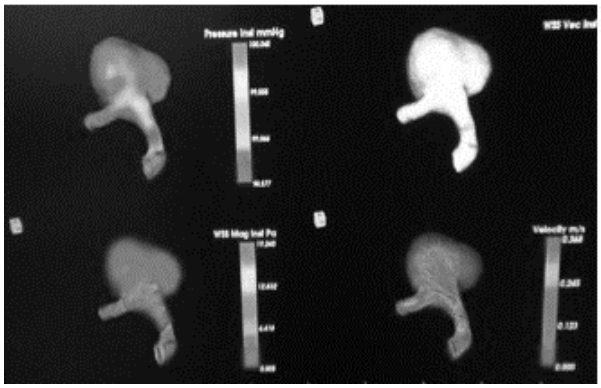

FIGURE 2: CFD of our left Paraclinoidal aneurysmthese

OPERATIVE PROCEDURE

The patient was placed in supine position with head rotated 30 degrees and neck slightly extended to facilitate cervical incision. Intraoperative monitoring MEP was used. A curvilinear incision of about 10 cm was made in the neck. Deeper layers were exposed in succession to dissect out the common carotid, external and internal carotid artery. The superior thyroid artery was dissected and secured with a loop. A standard left pterional craniotomy in addition to anterior clinoidectomy (extradural) was done. The sylvian fissure was widely split for minimal retraction of the frontal lobe to expose the internal carotid artery and the optic nerve. The large aneurysm arising from the medial wall of the carotid was visualized. The posterior communicating artery, anterior choroid artery (Ach), and their branches were also defined. The common carotid, external carotid distal to superior thyroid artery and internal carotid artery distal to the aneurysm were clamped. The superior thyroid artery was opened and a 5F feeding tube was introduced in the direction of the internal carotid artery. Retrograde suction decompression (RSD) was performed with the help of 10cc syringe. The aneurysm was effectively deflated following which a definitive clipping of aneurysm was performed with two permanent clips (Figure 3). Post clipping dual injection video angiography (DIVA) showed complete occlusion of the aneurysm (Figure 4). The postoperative was uneventful and patient recovered well without any deficits.

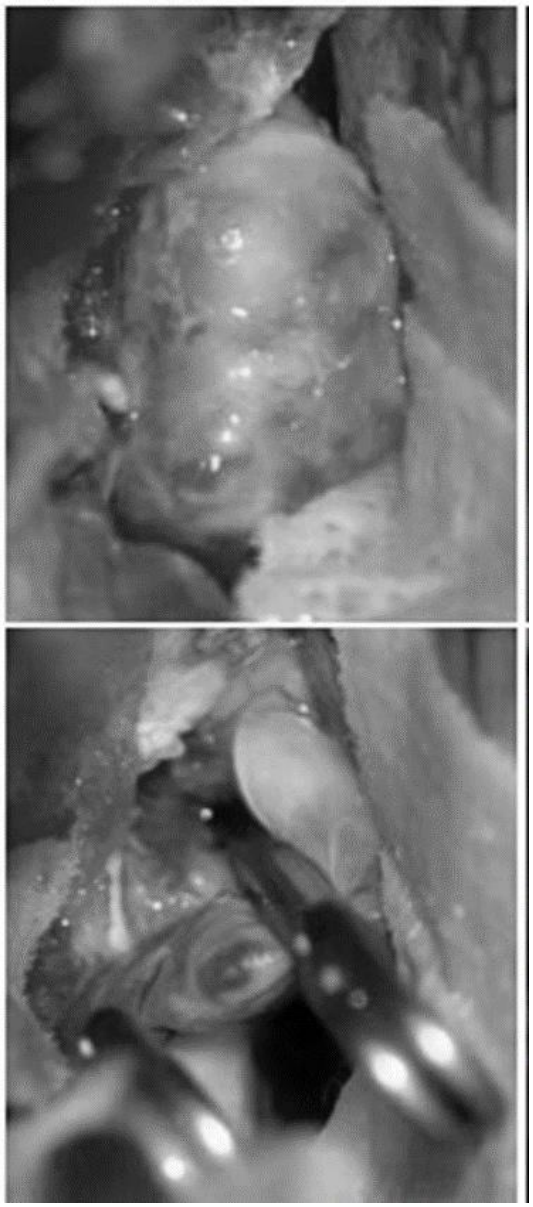

FIGURE 3: show defensive clipping of left Paraclinoidal aneurysm with 2 permanent clips

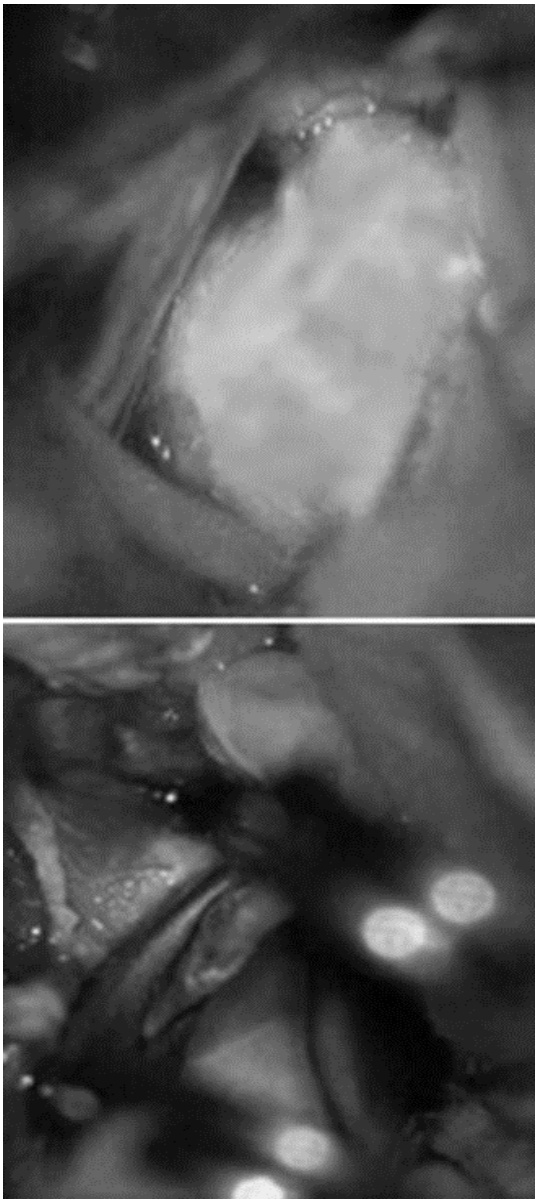

FIGURE 4. DIVA showed complete occlusion of aneurysm

DISCUSSION

Paraclinoidal aneurysms are surrounded by many important osseous and neurovascular structures, which continue to present great difficulties in achieving proximal control of the parent artery and obtaining adequate visualization of the aneurysm neck because of adhesion to surrounding anatomical components (7, 8). Therefore, anterior clinoidectomy and dissection of the neurovascular components from the aneurysm dome are the key steps to safe and successful clipping surgery for these aneurysms. In this scenario, the importance of proximal control of the aneurysm becomes indispensable. Among the several options for this RSD technique provides adequate relaxation of the aneurysm dome enabling complete dissection of the aneurysm from the surrounding important neurovascular structures (1, 4, and 6)

Retrograde suction aspiration was first described by Bather and Samson, who inserted an angiocatheter into the cervical ICA and treated over 40 cases with giant paraclinoid aneurysms using this technique. Carotid artery dissection developed in a case in their series, which required emergency endarterectomy. (7) Tamaki, et al reported the use of the RSD technique under the name of 'trapping-

evacuation.' They deflated aneurysms by aspirating intra-aneurysmal blood through the ICA via the superior thyroid artery (8).

In our case, we use RSD via catheterization of superior thyroid artery with clamping common carotid artery, external carotid distal to it and internal carotid artery distal to Paraclinoidal aneurysm. So, it allowed dissection, definitive clipping and reconstruction of internal carotid artery.

This measure can be done using endovascular balloon but it had a risk of embolization and dissection of internal carotid artery. It has its advantages in that, it avoid neck incision and also allows performing intra-operative angiography (9, 10).

Other measures described for the proximal control of aneurysms are adenosine assisted cardiac arrest, Rapid ventricular pacing. Adenosine induced arrest allows temporary flow arrest into the parent vessel, facilitating the circumferential exposure of the aneurysm and decreasing the risk of premature rupture during the dissection, and finally safe clip placement but it had drawbacks like causing atrial fibrillation ,bronchospasm and can be perilous in medically ill patient(11,12).Also, Rapid ventricular placing (RVP) was to induce hypotension in the face of sudden intraoperative hemorrhage which could not be controlled with conventional means during intracranial aneurysm surgery. Unlike adenosine, the consideration to use RVP is not affected by patient factors including allergies or medical conditions such as asthma and heart blocks (13).

Conclusion

The RSD technique viacatheterization of superior thyroid artery provides adequate relaxation of the aneurysm dome enabling complete dissection of the aneurysm from the surrounding important neurovascular structures and also avoids dissection of internal carotid artery and frequent embolization, so it is an important surgical tool in the surgery for large paraclinoid aneurysms.

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Spinal epidural angiolipoma causing spinal cord compression. A case report

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Abstract

Background. Spinal angiolipoma (SAL) is a rare tumour with double component mature adipose tissue and proliferating abnormal blood vessels, which result in spinal cord compression requiring an urgent surgical removal. We report a case of woman with spinal angiolipoma.

Case presentation. The patient is a 26 years old woman with past medical history of a low grade urothelial bladder carcinoma removed 4 months before she consults at our department, 2 months later the patient presented a lower limbs weakness. The clinical exam at the admission found a patient with paraparesis, hypoesthesia at the level of Th4 and urinary urgency. The spinal MRI objectified a spinal cord compression by a lesion located at the epidural space from Th2 to Th4. The patient was operated and a fatty well vascularized tumour distinct from the epidural fat was removed through a Th2 to Th4 laminectomy. The pathology study was in favour of an angiolipoma. Days after the operation the patient recovered totally, the weakness and the urinary urgency disappeared. The patient is flowed since 24 months she got pregnant.

Conclusion. Spinal angiolipoma is a rare tumour with a clinic of spinal cord compression, MRI is the gold standard in diagnosis it shows a fatty lesion with a large enhancement, surgery is the perfect treatment with good outcome and exceptional recurrence.

Keywords
angiolipoma,
epidural tumour,
spinal cord compression

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Introduction

Spinal angiolipoma (SAL) is a rare tumour with double component mature adipose tissue and proliferating abnormal blood vessels, which result in spinal cord compression requiring an urgent surgical removal. We report a case of woman with spinal angiolipoma.

Case presentation

The patient is a 26 years old woman with past medical history of a low grade urothelial bladder carcinoma removed 4 months before she consults at our department, 2 months later the patient presented a lower limbs weakness. The clinical exam at the admission found a patient with paraparesis, hypoesthesia at the level of Th4 and urinary urgency. The spinal MRI objectified a spinal cord compression by a lesion located at the epidural space from Th2 to Th4 fusiform measuring 83 x 12

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mm, hyper intense on T1 and T2 weighted images (Figure 1) there was a homogenous enhancement after gadolinium injection with persistence of the signal on T1 SPIR injected and in STIR sequences (Figure 2). The patient was operated and a fatty well vascularized tumour distinct from the epidural fat was removed through a Th2 to Th4 laminectomy. The pathology study was in favour of an angiolipoma. Days after the operation the patient recovered totally, the weakness and the urinary urgency disappeared. The patient is flowed since 24 months she got pregnant.

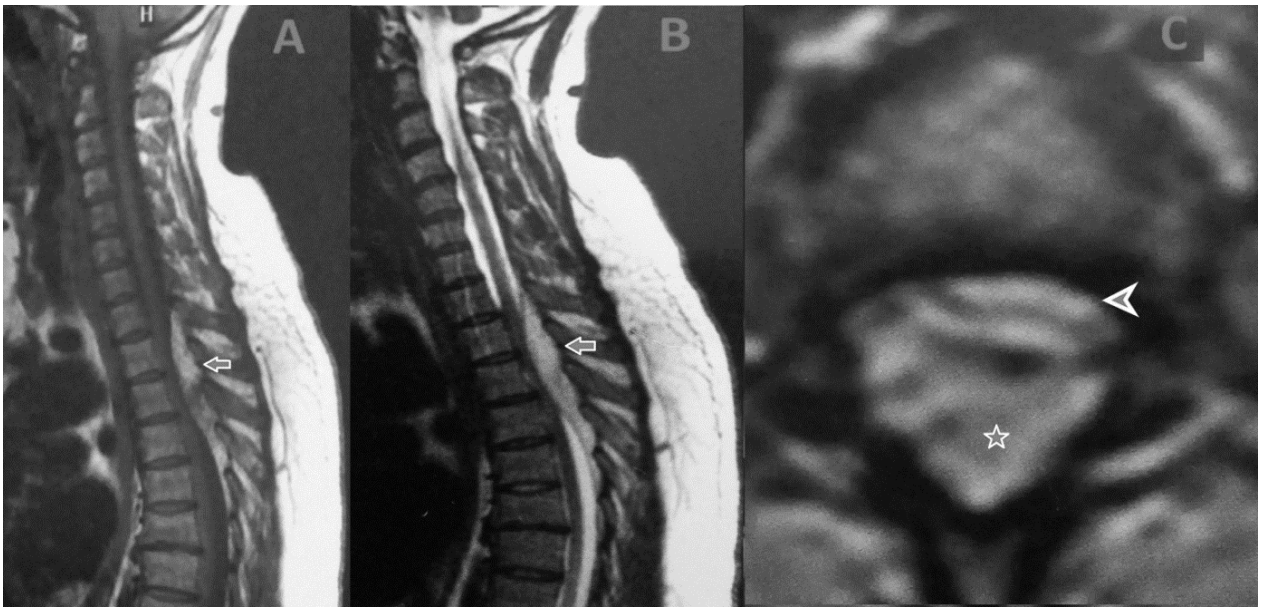

Figure 1. Spinal MRI. **A**: sagittal T1 weighted image; **B**: sagittal T2 weighted image; **C**: axial T2 weighted image; showing hyperintense T1 and T2 lesion (arrows and the star) causing spinal cord compression (head of the arrow).

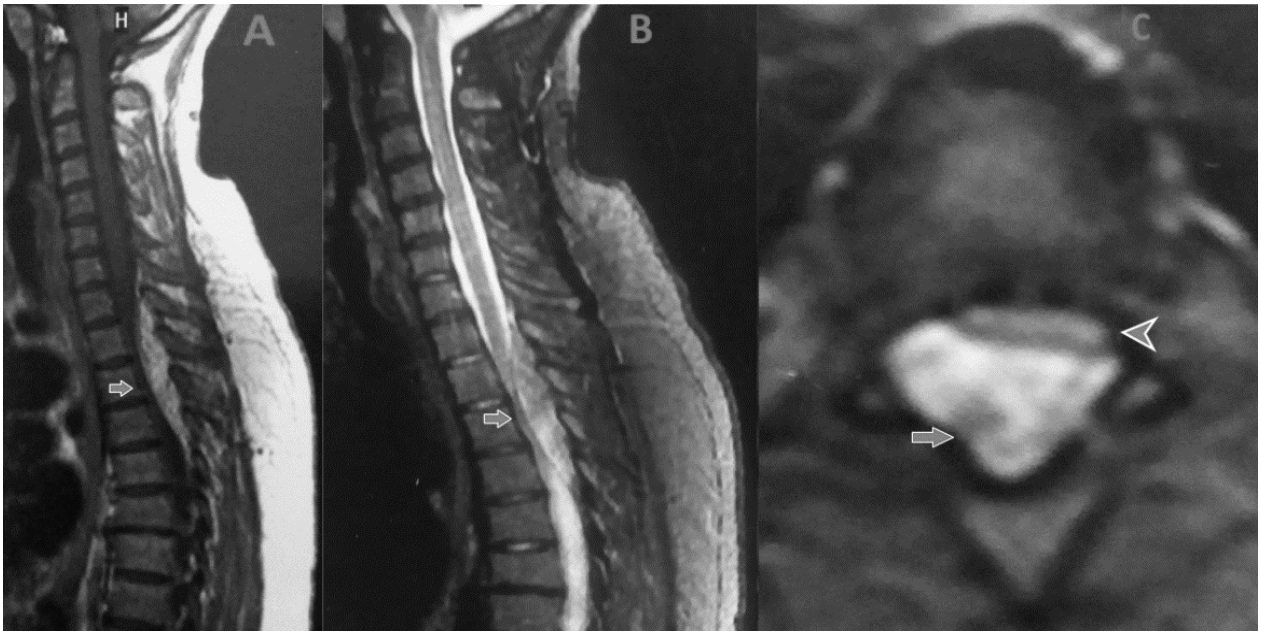

Figure 2. Spinal MRI. **A**: sagittal injected sequence; **B**: sagittal STIR sequence; **C**: STIR injected sequence; showing a homogenous enhancement of the lesion after gadolinium injection with persistence of the signal after the suppression of the fat signal (the arrows). The head of the arrow shows the situation of the spinal cord.

Discussion

SAL are tumours with double component mature adipose tissue and proliferating abnormal blood vessels (1,2,3,4,5,6,7,8), they are rare, 177cases are found in the literature from 1890 where the first case was reported by Berenbruchto to June 2015 (2). Some studies suggest that it represent 0.04% to 1.2% of spinal tumours, 2% to 3% of epidural spinal tumors (1,3,5,6,8) and 16 % to 35 % of spinal lipomas (5,8). It has a female predominance (1,2,3,4,5,7,8) with a sex ratio of 3/2 (8), with an average age between 40 and 60 years(2,3,4,7) and mostly located in thoracic spine (1,2,3,4,5,6,7,8) in 78 % of cases (8), mostly between Th2 and Th5 (6), other location are less common, it occurs in 10 % in the lumbar spine and in 1 % in the cervical spine (8).SAL can be infiltrating or non-infiltrating, In the majority of cases it is non infiltrating encapsulated and limited in the epidural space(3,7,8).The clinical presentation include back pain and signs of spinal cord compression (1,2,3,4,5,6,7,8), although the symptoms evolves slowly some cases of acute paraplegia were described (4).MRI is the imaging of choice for SAL diagnosis(1,2,3,4,5,6,7,8) ,commonly the tumour has a fusiform shape located in the posterior epidural space (2,4,5), the signal of the lesion is the reflect of its two components: lipomatose and angiomatose, so SAL is usually hyperintense in T1 and T2 weighted images with loss of the signal in fat suppression sequences which could be regained after injection of gadolinium (1,2,3,6,8).Surgery is the reasonable treatment modality (1,2,3,4,6,7,8), usually the lesion is reached by a posterior approach through a suitable laminectomy, total resection is possible for the non-infiltrating lesions with good outcome and exceptional cases of recurrence are reported (1,2,3,4,5,8,7).

Conclusion

Spinal angiolipoma is a rare tumour with a clinical presentation of spinal cord compression, MRI is the gold standard in diagnosis it shows a fatty lesion with a large enhancement, surgery is the perfect treatment with good outcome and exceptional recurrence.

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Overview of neurosurgical capacity in St. Lucia

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Keywords
Caribbean neurosurgery, neurosurgery capacity in lmics

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ABSTRACT

When we talk about the most scenic Caribbean islands, St. Lucia is one of those islands that certainly come into our mind. It is a beautiful tourist destination and the place of post-volcanic paradise on earth. However, just like many remote Caribbean islands, St. Lucians (name for local population) used to have its own difficulties of obtaining on demand basic neurosurgical services in their homeland. This beautiful Caribbean island, socioeconomically falls in the same category as most low-and middle-income countries (LMICs) and unfortunately echoes the same unmet surgical and anaesthesia needs as the rest of them.

INTRODUCTION

Out of any specialized medical professions, neurosurgery requires diversely prepared physicians and specialized operating rooms and experienced staff, who can handle variety of cranial and spinal cases on demand. In this paper we provided an overview of current neurosurgical capacity in St. Lucia, a Caribbean island that recently defined its neurosurgical scope of work. Our research included a systematic survey, in-person data mining and observation of neurosurgical capacity on the island from 2018 to 2019.

THE STATE OF NEUROSURGERY SERVICES ON THE ISLAND

As of 2019 population census reported a count of 180,287 St. Lucians living on the island [1]. It's very hard to imagine that population which is getting closer to 200,000 people didn't have an adequate access to

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the lifesaving specialized surgical procedures. Up until august 2016 St. Lucian's population who suffered from complex neurosurgical diseases or traumas, had to be evacuated by air to the nearest and more medically developed island such as Barbados, in order to receive a competent neurosurgical care. With this model in mind, it's not hard to figure out that majority of critical patients who needed an immediate intervention, simply didn't make pass the receiving hospital's doors.

Presently, St. Lucia has 2 fully functioning board certified neurosurgeons, namely Dr. Curby Dwaine Sydney who is native St. Lucian and Dr. Esteban Roig Fabré – a distinguished professor from Cuba. Both neurosurgeons provide a broad (general) spectrum of adult and paediatric neurosurgical services on the island (Figure 1), which are not limited to [2]:

1. Brain and spine microsurgical procedures
2. Craniotomy and cranioplasty for traumatic brain injuries
3. Cerebrovascular accident treatments.
4. Ventriculostomy and ventriculoperitoneal shunt placements.
5. Spinal procedures include: discectomy, microdiscectomy and laminectomy.

On the diagnostic/imaging side, the following equipment is utilized:

- Computed Tomography (CT).
- Magnetic Resonance Imaging (MRI).
- Electroencephalogram (EEG).
- Intracranial pressure (ICP) monitoring.
- 3D volume rendering and multi-planar reconstruction software.

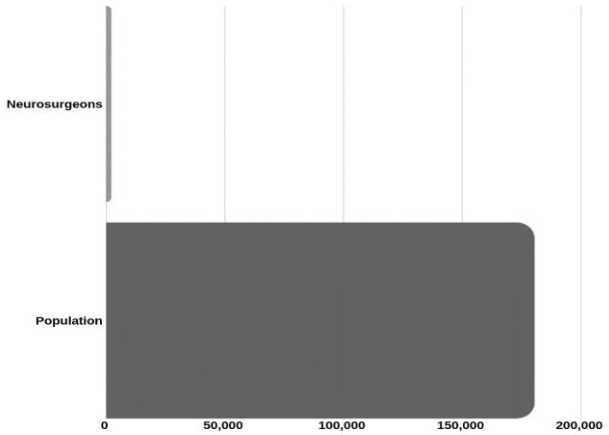

Figure 1. Proportion of available neurosurgeons to population of St. Lucia

Due to a scarce nature of neurosurgeons on the island, both neurosurgeons also cover neuro-consult services in public Victoria and private Tapion hospitals for referred emergency patients. Both hospitals function as level 1 trauma centres and are equipped with generalist physicians in the emergency room. Additionally the ministry of health of St. Lucia is working with U.S non-profit organization "WPP" which stands for World Paediatric Project. The WPP organization provides volunteer specialized paediatric surgeons from U.S to address the need of surgically sick children in the Caribbean islands. The majority of ongoing WPP surgeries in St. Lucia were addressing congenital scoliosis. Those children with more complex spinal deformities have an opportunity to be flown to U.S for ongoing treatment and monitoring.

Prevalence of neurosurgical disease

Upon our discovery, St. Lucia along with other LMICs such as Haiti has the same prevalence of neurosurgical disorders [3]. The number one spot takes traumatic brain injury (TBI) followed by cerebrovascular accidents (CVA) [4][5], spinal deformities and congenital pediatric cases (Figure 2).

During our research findings it was interesting to note that St. Lucia has low percentage of tumour prevalence in both adult and paediatric patients.

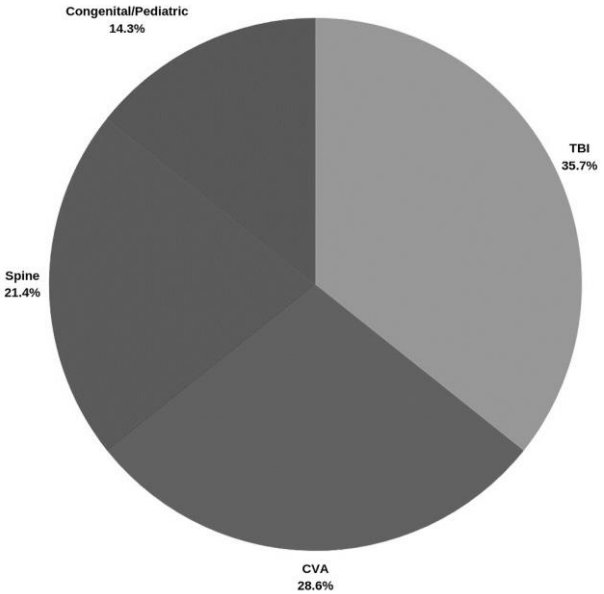

Figure 2. Graphical representation of neurosurgical cases in St. Lucia

The most obvious reason for high incidence of traumatic brain injury prevalence is uncoordinated

and unstructured road infrastructure. There is no evidence of dedicated traffic police or clear markings on the pavement for traffic to flow on some major highways (figure 3). Therefore every driver and pedestrian is guided according to his/her own intuition.

The second largest prevalence of neurosurgical disease is cerebrovascular accidents. The cerebrovascular accidents in St. Lucia directly correlate to lack of primary care screening. Even though shortage of primary care doctors is not evident, citizens are not exposed to ongoing physical check-up or simply neglect doctor's visits. Our findings showcased that majority of St. Lucian population older than 50 years old are found to have diabetes mellitus or uncontrolled hypertension; which can explain why it contributes to CVA and makes up to 28.6% of all neurosurgery related diseases.

Figure 3. St. Jude highway in Vieux Fort

Conclusion

This paper showcased an overview of current state of neurological surgery that could be used as a guidance to further neurosurgical development in St. Lucia. As St. Lucian government in collaboration with World Bank continues to invest capital in public healthcare [6], further studies are suggested to assess advancement of neurosurgical care from this point on.

Declarations

Consent for publication

The consent for publication is not applicable for this review article.

Competing interests

Authors declared no competing interests to declare.

Availability of data and material

Data sharing is not applicable for this review article.

Funding

Funding is not applicable to this study.

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Ethics approval and consent to participate

The approval and consent is not applicable to this study.

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Ewing's sarcoma of the mobile spine. Three unusual observations

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Abstract

Background. Ewing's sarcoma is a bony highly malignant tumour, it occurs most frequently in the second decade of life. Ewing's sarcoma is a rare affection, located usually in the pelvis, the femur, the humerus, the ribs, the mandible and clavicle, other location are rare especially in the spine. We report three cases of spinal Ewing's sarcoma, two primary spine locations and one on young adult with unusual clinical presentation.

Cases presentation

Case 1. The first patient is a girl of 14 years old without past medical history. She presented initially two months before consultation a neck pain followed days after by a weakness of the left upper limb; the spine imaging performed objectified a destructive process of C2 with a spinal cord compression. The patient was operated beneficiating of a spinal cord decompression and a subtotal removal of the tumour. The pathologist's results were in favour of Ewing's sarcoma and the patient was oriented to oncology.

Case 2. The second patient is a man of 31 years old operated five years before he consulted for shoulder Ewing's sarcoma followed by chemotherapy and radiotherapy, he presented two months before consultation a cauda equina syndrome. Spine MRI objectified a double location of an epidural tumour at T3-T4 and S1-S2 levels. The patient was operated beneficiating of subtotal removal of the tumour. The laboratory exam results were in favour of Ewing's sarcoma and the patient was oriented to oncology.

Case 3. The third patient is a 6 years old boy who presented a 1 month history of low back pain followed by a rapidly deteriorating weakness of both lower limbs over a weak. On examination there was bilateral spastic paraplegia, hypoesthesia below the level of Th10 and a urinary retention. The MRI imaging revealed a lesion on the levels Th8, Th9 and Th10 vertebras involving the body, pedicle, lamina, and the transverse process on the left side with an epidural invasion compressing the spinal cord. The tumour was radically removed. Pathology report was in favour of Ewing's sarcoma. Two weeks after surgery the patient was able to walk. He was referred for adjuvant systemic chemotherapy.

Conclusion. Ewing's sarcoma is rare malignant tumour. The location in the spine exposes the patient to more complications because of the neurostructures compression. The surgical total removal followed by radio and chemotherapy is the only option with the best prognostic and guaranties an acceptable life quality.

Keywords
Ewing's sarcoma, spinal cord compression, child malignancy

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Introduction

Ewing's sarcoma is a bony highly malignant tumour, it occurs most frequently in the second decade of life (1,3,4,5,7,8,10). Ewing's sarcoma is a rare affection (4), located usually in the pelvis, the femur, the humerus, the ribs, the mandible and clavicle (7), other location are rare especially in the spine(4,8). We report three cases of spinal Ewing's sarcoma two primary spine locations and one on young adult with unusual clinical presentation.

Case presentation

Case 1

The first patient is a girl of 14 years old without past medical history. She presented initially two months before she consults a neck pain followed days after by a weakness of the left upper limb; the spine CT and MRI performed objectified a destructive process of C2 with a spinal cord compression (Figure 1). The patient was operated beneficiating of a spinal cord decompression and a subtotal removal of the tumour, the lesion is considered to cause a spinal instability so an occiptocevical fixation was put. The pathologist's results were in favour of Ewing's sarcoma and the patient was oriented to oncology for adjuvant treatment.

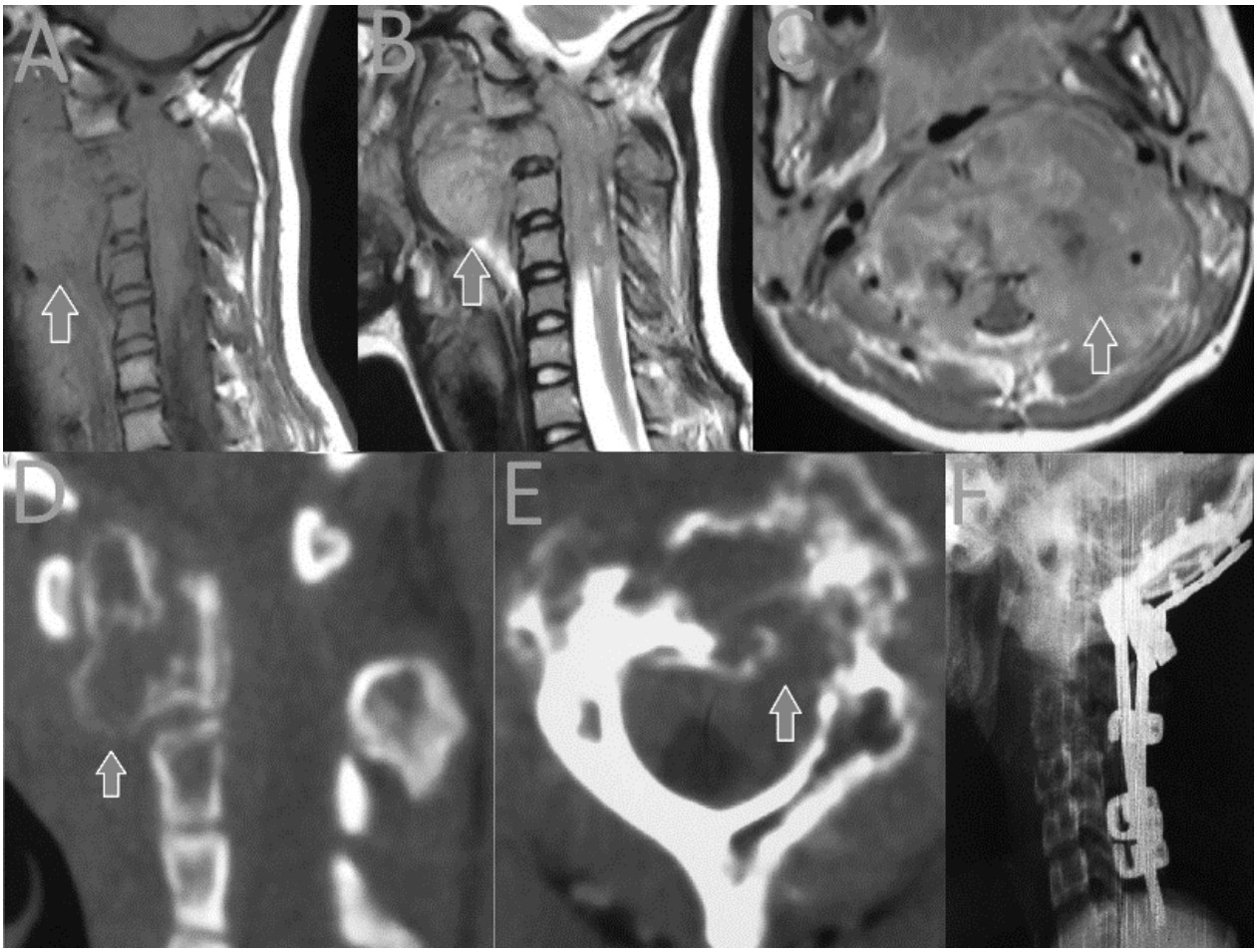

Figure 1 Patient 1 imaging. **A**: sagittal T1 WI sequence cervical MRI; **B**: sagittal T2 WI sequence; **C**: axial T2 WI sequence; **D**: sagittal bone window CT; **E**: axial bone window CT; **F**: post-operative x rays.

Case 2

The second patient is a man of 31 years old operated five years before for shoulder Ewing's sarcoma followed by chemotherapy and radiotherapy, he presented two months before consultation a cauda equina syndrome. Spine CT and MRI objectified a double location of an epidural tumour at T3-T4 and S1-S2 levels (Figure 2). The patient was operated beneficiating of subtotal removal of the both lesions through Th3 and Th4 then S1 and S2 lamenectomy. The laboratory exam results were in favor of Ewing's sarcoma and the patient was oriented to oncology.

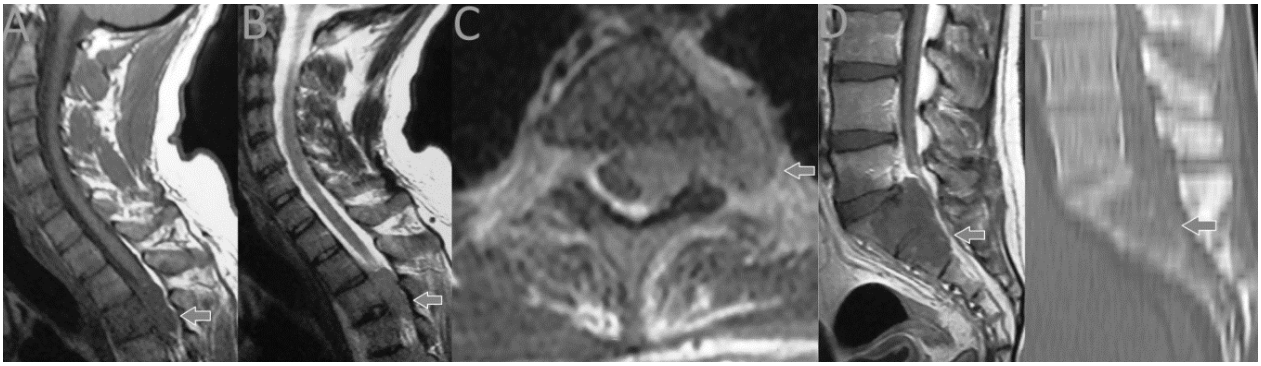

Figure 2. Patient 2 imaging. **A**: sagittal cervical T1 WI MRI; **B**: sagittal cervical T2 WI MRI; **C**: axial cervical T2 WI MRI; **D**: sagittal lumbosacral T2 WI MRI; **E**: sagittal lumbosacral bone window CT.

Case 3

The third patient is a 6 years old boy who presented a 1 month history of low back pain followed by a rapidly deteriorating weakness of both lower limbs over a weak. On examination there was bilateral spastic paraplegia, hypoesthesia below the level of Th10 and a urinary retention. The MRI imaging revealed a lesion on the levels Th8, Th9 and Th10 vertebras involving the body, pedicle, lamina, and the transverse process on the left side with an epidural invasion compressing the spinal cord (Figure 3). The tumour was radically removed. Pathology report was in favour of Ewing's sarcoma. Two weeks after surgery the patient was able to walk. He was referred for adjuvant systemic chemotherapy.

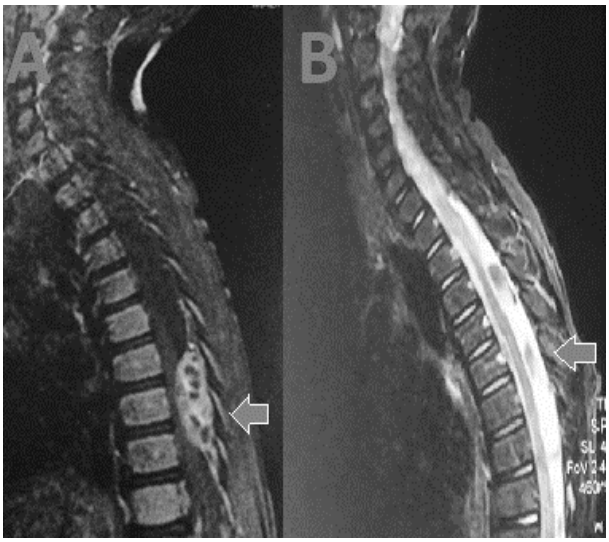

Figure 3. Patient 3 spine MRI. **A**: preoperative T1 injected sequence; **B**: postoperative T2 WI.

Discussion

Ewing Sarcoma (ES) was first described by James Ewing in 1921(2,6). It is a small round blue neoplastic cells (1,2,3,4,5,6,7,8,9) with clear to lightly eosinophilic cytoplasm, evenly dispersed chromatin, and indistinct nucleoli (3,7). ES is found in bones or in the surrounding soft tissues (1,3,4,5,6,7,8). ES is usually diagnosed in the second decade of life (1,3,4,5,7,8,10), the occurrence in adulthood is sporadic (1,6,3,8). Ewing's sarcoma present 4% of paediatric malignant tumours (4), It arises mostly in the long bones in 47% of cases, pelvis in 19%, and on ribs in 12% of cases (7), vertebral location is seen in less than 6% of cases (4,8), and mostly located in sacrococcygeal region (5,6,7), its presence on non-sacral spine is found in only 0.9% of all cases (7) with extremely rare involvement of the cervical spine (5,7). The primary location on the spine is unusual (4,6,7). Being a primary bone tumour, extra osseous locations are rare in a review between 1969 and 2015 only 119 cases of extra osseous ES was reported among them 76 cases of epidural ES (3). The clinic is summarized in the triad of local pain, palpable mass and neurologic deficit depending on the site of compression (1,7). Radiographic exams in spinal ES are not specific (3,6,8). Mostly it is a lytic lesion, sclerotic changes are rarely seen (7,8,9) especially in primary lesions(8). Spinal ES is located on posterior elements in 70% of cases and on the body in 30% of cases which could lead to vertebral collapse (8), extraossous location is limited to some reported cases (3,8). Plain radiography shows the lytic lesions tardively (7,9) usually after the neurological signs became obvious (9). CT is very helpful to assess the amount of destruction of the vertebral body and posterior element (7,9). Soft tissue lesions are better

outlined by MRI, ES have hypo or isointense signal on T1 weighted imaging and a hyperintense signal on T2 weighted imaging with heterogeneous enhancement after gadolinium injection (3,8). There is no standard management described for the spinal ES and no difference between child and adult treatment strategy (1,6). Usually it associates surgery chemotherapy and radiotherapy. The surgery assures biopsy, the local control of the tumour, spinal cord decompression and spinal stabilization. Because of the intimate relationship with neurological structures some surgeons prefer intralesional excision or debulking of the tumour in order to prevent long term morbidity (4) but many studies suggest that gross total resection is associated with better outcome (1,2,3,4,6,9). Tumours excised with 2 cm of normal tissue are considered to have safe surgical margins (2) otherwise radiotherapy is highly indicated (1,2,3,4,5,6,7,9). Radiation doses could not exceed 45 Gy (3,4,9). Radiotherapy could be used alone to assure the local control of the tumour (2,3,4,6), but with high risk of deterioration and less overall survival (2,3,4). When surgery and radiotherapy assure the local control of the tumour, chemotherapy is indicated to eradicate systemic micro metastasis (1,2,3,4,5,9). With patients who have no neurological deterioration and If the diagnosis is made before by needle biopsy a neoadjuvant chemotherapy could be proposed in order to shrink the tumour which could facilitate its removal (1,2,6,7,9). The classical chemotherapy protocol of ES is VACA (vincristine, actinomycin, cyclophosphamide and doxorubicin) (3,9) many other drugs have been added like ifosfamide and or etoposide (VAC/IE) which improved the outcome (1,2,3). Prognosis is poor in the spinal ES compared to other locations (1,4), other factors are related to a bad prognosis like the presence of metastasis (1,5,7) the adult age (3,7) and extra osseous location (3). In the other hand tumours located in the sacrum are associated with a poor prognosis due to the late stage diagnosis (4) and those located in cervical spine due to the difficulties of the total resection (7). The local control of the tumour with en bloc resection is associated with the best survival outcome (1,3,4,6,9). Overall median survival in spinal ES is 26 months, the survival rates for 5-year is at 41% and for 10-year 34% (4,10).

Conclusion

Ewing's sarcoma is rare malignant tumor. The location in the spine exposes the patient to more complications because of the neurostructures compression. The surgical total removal followed by radio and chemotherapy is the only option with the best prognostic and guaranties an acceptable life quality.

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Supratentorial hemangioblastoma without von Hippel-Lindau syndrome in an adult. A rare case report

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Keywords
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ABSTRACT
Hemangioblastomas (HBLs) are highly vascular and cystic benign neoplasms. They form very small part of intracranial tumours and are often localized in the posterior fossa. Although most of them are sporadic, a significant group is accompanied with von Hippel-Lindau (VHL) syndrome.
This case report presents a 57-year-old woman treated with total resection using micro-surgical technique and was diagnosed as HBL based on histopathologic findings. Contrast-enhanced cranial MRI of the patient with the complaints of spasms in the right side of body showed a right paracentral mass that caused midline shift.
In literature, the previously reported cases of supratentorial HBL unaccompanied with VHL syndrome were searched in PUBMED, compiled and presented. It should be borne in mind that rare HBLs manifesting with various neurological symptoms may occur in the supratentorial region, and may not accompany with VHL syndrome.

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INTRODUCTION

Hemangioblastoma (HBL) is a benign vascular tumour of the central nervous system consisting of veins and neoplastic stromal cells (1). It usually occurs after the third decade (2). It may arise sporadically (66-80%) or along with von Hippel-Lindau (VHL) syndrome (20-33%), a familial neoplasia syndrome. Although HBLs are located in infratentorial site, rare supratentorial cases are present. (3). The most common infratentorial localizations in order of decreasing frequency are cerebellum, brain stem, and spinal cord, and less frequently in the cerebral hemispheres along the optical pathways in supratentorial region (4). Although they have benign histology, HBLs can cause symptoms such as peritumoral edema, cyst formation, and as a result of the mass effect occurring in adjacent structures due to tumour growth (5).

Our case was a 57-year-old female patient and was worth of reporting due to the presence of HBL manifesting supratentorial localization without an accompanying VHL syndrome. The current literature mostly consists of case reports and series of HBL associated with VHL disease. Due to its rarity, detailed information on the clinical features, treatment, and prognosis of supratentorial HBL is limited.

Case Report

A 57-year-old female patient was admitted to our clinic with complaints of spasms in the left side of her body that began about a month ago, frequent awakenings that lasted for about ten minutes. Neurological examination revealed left 3/5 hemiparesis. Her medical history revealed no known comorbidities and medication use, but a previous surgery for varicose veins. Upon conducting contrast-enhanced cranial MRI, a mass lesion in the right paracentral region with dense contrast enhancement of 6x5.5x5.5cm causing a midline shift (Figures 1 and 2). Patient was operated upon a provisional diagnosis of meningioma, and lesion was observed to be hypervascularized. The lesion was totally resected without any complication utilizing microsurgical technique. Histopathologic examination showed a tumour rich in vascular framework harbouring granular cells in where some nuclei revealing "degenerative atypia. Immuno-histochemical examination, showed certain pathognomonic findings with specific antibodies verifying HBL. The reactivities for EGFR and inhibin were significant, while the GFAP reactivity was dubious. Although it is not a general rule, mast cell tryptase activity used to reveal the presence of mast cells embedded in tumour tissue for supporting the diagnosis. Furthermore, rare nuclear progesterone reactivity is a finding that helps with the diagnosis of HBL (Figure 3). In the post-operative examination of the patient, neurological deficit diminished. In the early post-operative period, contrast-enhanced cranial MRI revealed total removal of the lesion. Additional tests showed no stigmata consistent with VHL syndrome after the discharge of the patient.

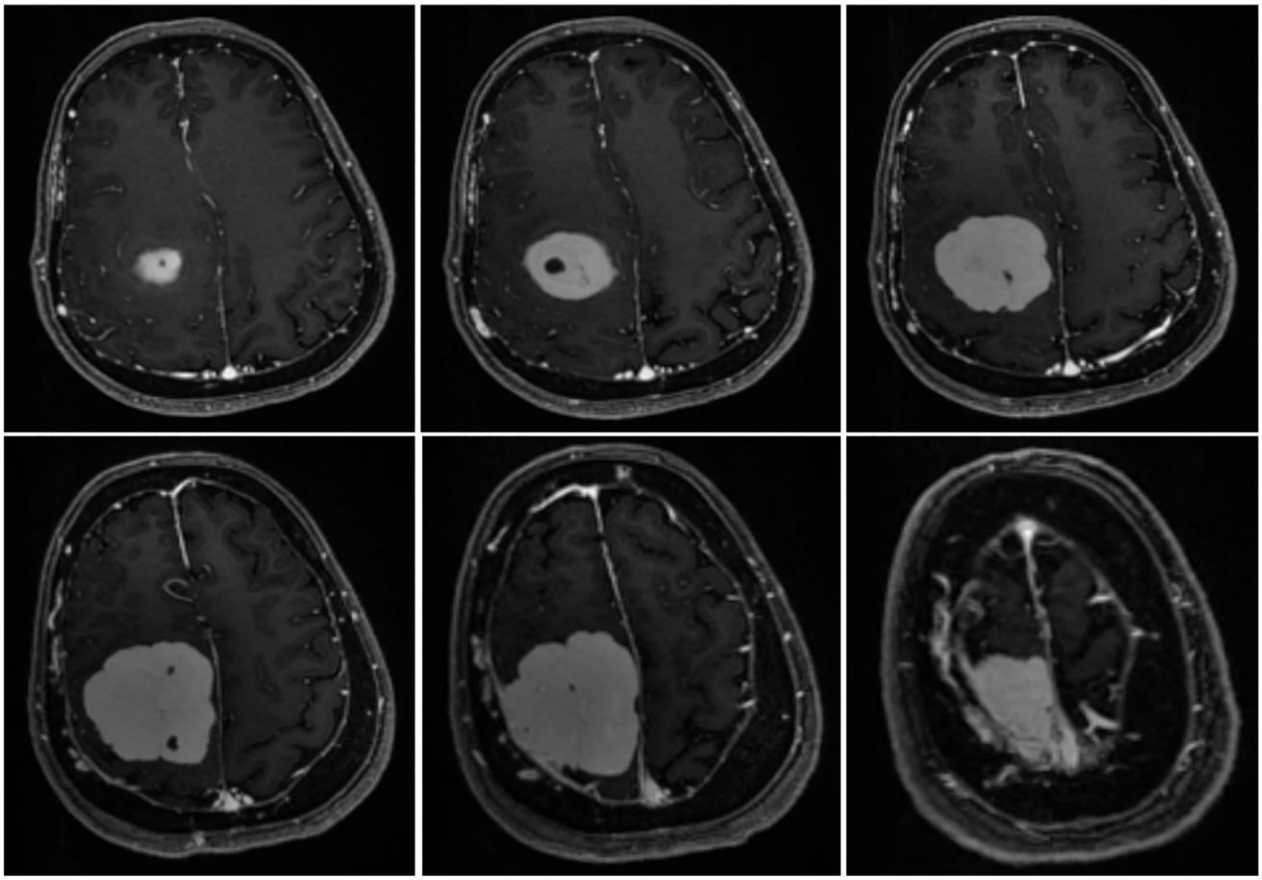

Figure 1. In preoperative axial contrast enhanced cranial MRI sections, a mass lesion with dense contrast enhancement that caused edema in the periphery of paracentral region and a shift in midline is observed.

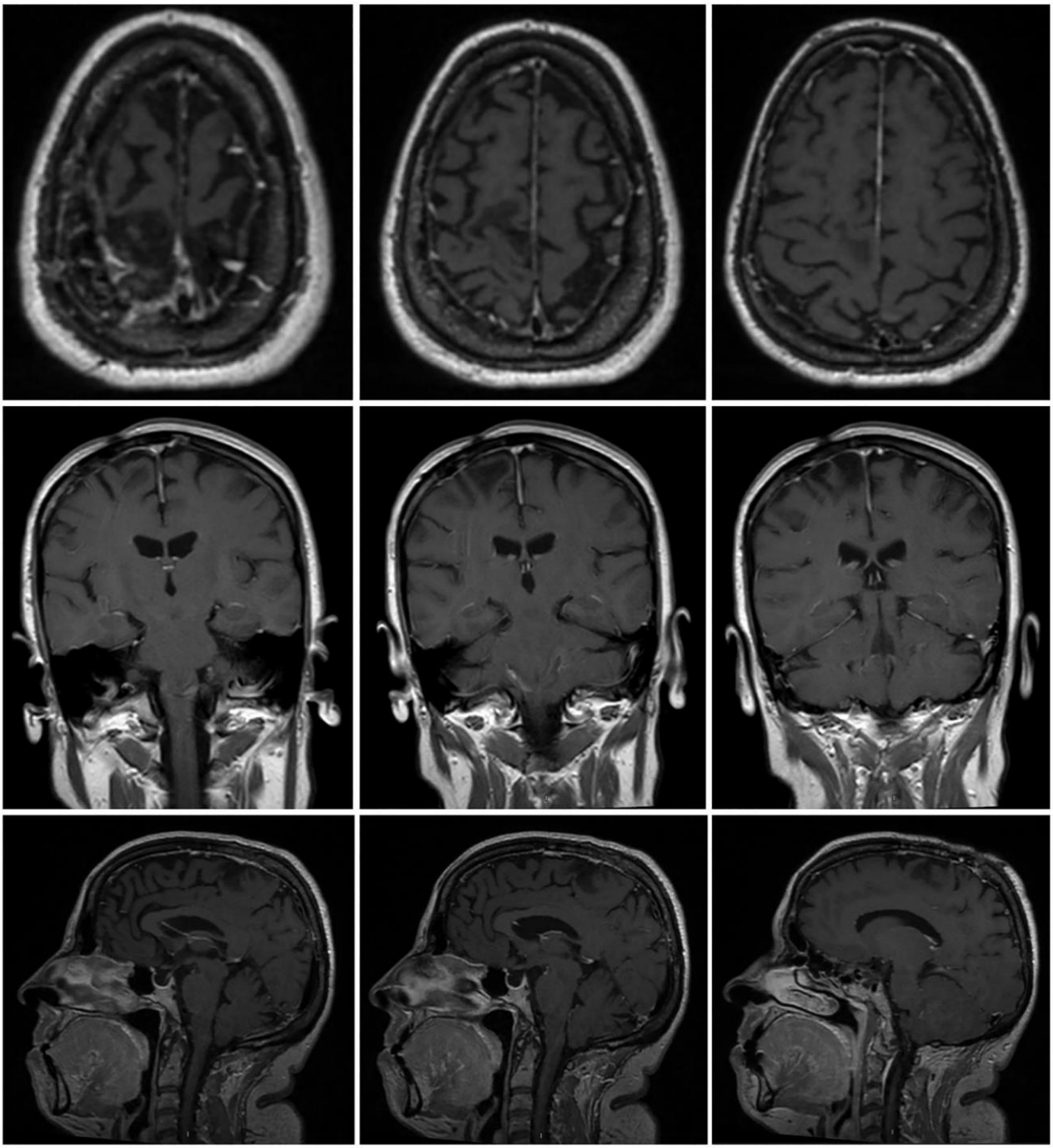

Figure 2. In cranial MRI sections with postoperative contrast, the lesion is observed to have been totally resected.

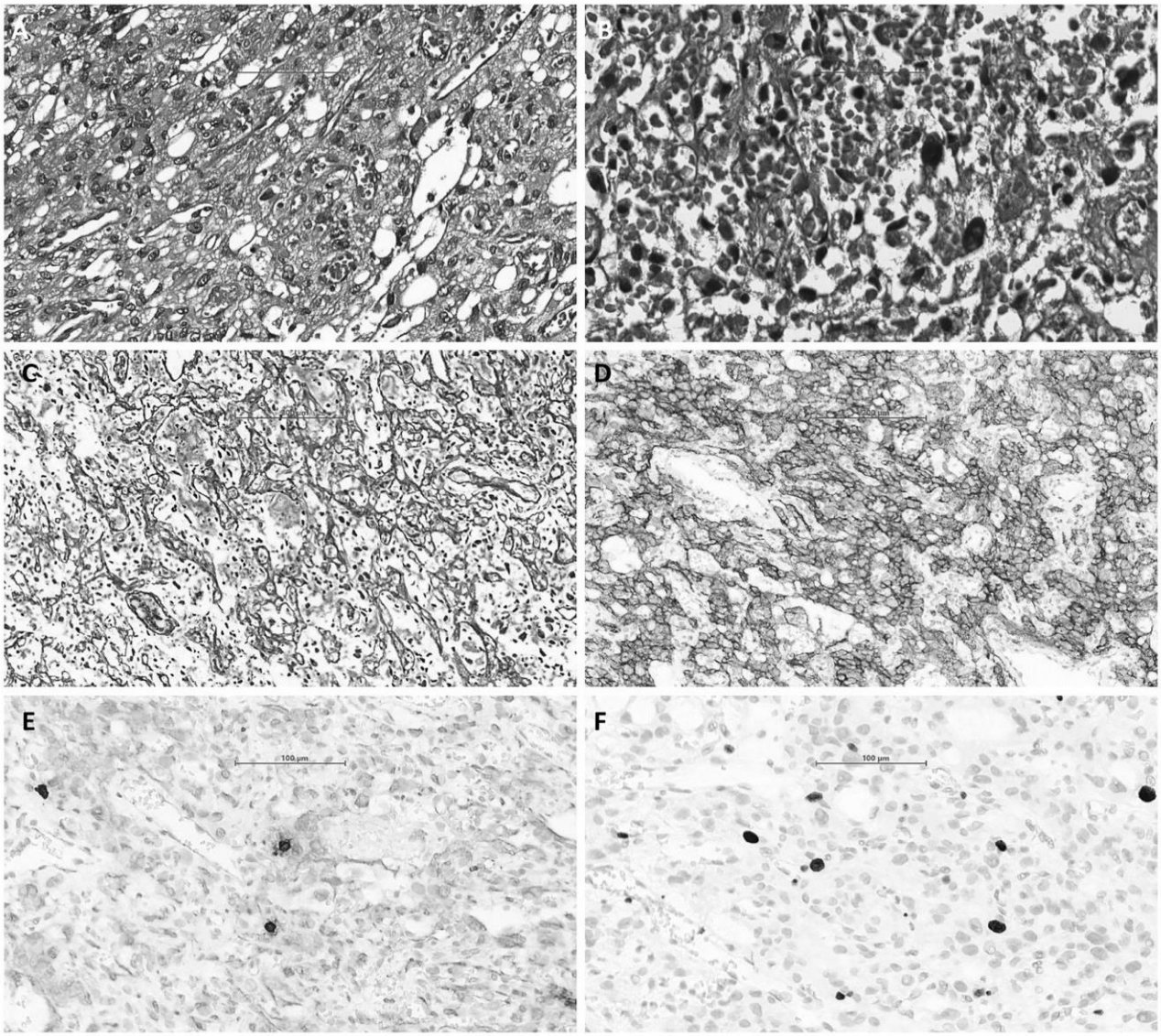

Figure 2. (**A**) Tumour consisting of capillaries surrounded by atypical cells bearing nuclei with rough chromatin pattern and granular cytoplasm typical for hemangioblastoma. (Hematoxylin-eosin, x200).
(**B**) Higher magnification reveals cells with "atypical nuclei" consistent with "degenerative atypia" with no effect on prognosis. (Hematoxylin-eosin, x400).
(**C**) A dense reticulin framework surrounding tumour cells as clusters typical for hemangioblastoma, reticular variant. (x100, reticulin stain).
(**D**) An intense cytoplasmic EGFR reactivity. (EGFR, streptavidin biotinylated complement, x100).
(**E**). Eye-catching mast cells randomly distributed in tumour tissue (Mast cell tryptase [MTC], streptavidin biotinylated complement, x100).
(**F**). Ki-67/MIB-1 labeling index is low (4%). (Ki-67/MIB-1, streptavidin biotinylated complement, x200).

Discussion

HBLs of the central nervous system are rare, benign and vascularized neoplasms of unknown origin (6). Most of the HBLs that are generally macroscopically well limited, are cystic in nature, however, can be 20% solid. For this reason, they mostly show cystic mural nodule adjacent to tumour tissue (7). HBL is generally considered as a non-metastatic tumour, and in many cases, diagnosis is delayed due to the absence of clinical findings (8). They account for approximately 1.5-2.5% of all primary intracranial tumours and 7-10% of primary posterior fossa tumours (9). This is observed in both sexes at approximately equal ratios and most often at the age

of 35-45 years. They are most commonly observed in the cerebellum, less frequently in the brain stem and in the spinal cord, and rarely in the supratentorial region (2,4).

The uncommon supratentorial HBL was first defined by Bielschowsky in 1902 (10). The frontal lobe of the cerebrum is followed by the parietal and temporal lobes according to the incidence (8). The clinical presentation of supratentorial HBLs is anatomically dependent on the site and growth pattern. In some cases, the endothelia of the vascular component of the tumour secrete erythropoietin-like substance, and correspondingly, such paraneoplastic syndromes as polycythemia may be observed (11). In general, supratentorial HBLs have long-term minor symptoms or symptoms may not appear at all. In most cases, sudden exacerbations requiring urgent surgical intervention may occur (12).

It is reported that 5-31% of cerebellar HBL cases, 11% of supratentorial cases, and 80% of spinal cord cases are associated with VHL disease. Rare supratentorial HBLs account for 1-6% of HBLs that accompany VHL disease (6). HBLs are macroscopically well-circumscribed neoplasms with solid and varying sizes containing cystic components. Due to its ability to manifest cystic mural nodules, a differential diagnosis specifically from pilocytic astrocytomas is mandatory (13).

HBL is usually observed frequently in the form of enhancing mural nodule accompanied by cystic component in computed tomography. MRI is the gold standard imaging method in the differential diagnosis. In contrast-enhanced T1-weighted sections, the tumour nodule is prominent and hyperintense in homogeneous form However, in T2-weighted images, the cystic area is displayed as hyperintense. HBL is characteristically of a highly vascular tumour and is located in the avascular cyst, and is directly fed from the vessels originating from dural arteries (14).

Histological features of HBL are distinctive. Vessels of various sizes are important components of tumour tissue and are furnished with a single row of endothelial cells. Stromal cells in the interstitial area contain lipid droplets and glycogen in varying proportions (6). Stromal cells constituting the main component of the tumour show pleomorphism and diverse levels of nuclear hyperchromasia. Mastocytes may be found and mitosis is very rare. In “reticular” variant the stromal cells are dominantly located around the veins whereas wider groups are formed in “cellular” variant (15).

If there is evidence of the progression of the lesion, due to bleeding or mass effect, then surgery is primary choice of treatment. Removal of nodules in cystic lesions during surgical resection is vital (9). For solid lesions, procedures similar to the management of arteriovenous malformation should be performed. Surgical treatment is considered certainly curative (16).

In the relevant literature, there are infrequent supratentorial HBL cases those of which are unaccompanied VHL. Concisely, Table 1 shows a compilation of HBL cases reported in the medical literature.

Author (year)	Age	Sex	Supratentorial location	Gross
Bielschowsky (1902) (10)	24 y	F	Frontal	Solid
Berger and Guleke (1927) (17)	24 y	M	Parietal	Cystic
Schley (1927) (18)	48 y	F	Occipital	Cystic
Marrioti (1936) (19)	N/A	N/A	Posterior part of the corpus callosum	Solid
Zeitlin (1942) (20)	54 y	M	Meningeal parasaggital	Solid
Kautzky and Vierdt (1953) (21)	55 y	M	Right cerebrum-occupied thalamus, globus pallidus, basal surface of brain	Solid
Floris et al. (1954) (22)	32 y	M	Frontal	Solid
Grattarola (1955) (23)	18 y	M	Temporal	Cystic
Morello and Bianchi (1958) (24)	10 y	M	Temporal	Solid
Stein et al. (1960) (25)	49 y	M	Temporal	Solid
Stein et al. (1960) (25)	12 y	F	Frontal	Cystic
Morello and Bianchi (1960) (24)	27 y	M	Parieto-occipital	Solid
Papo et al. (1961) (26)	N/A	N/A	Frontal	N/A

Morello and Bianchi (1960) (24)	27 y	M	Parieto-occipital	Solid
Rivera and Chason (1966) (27)	16 y	M	Meningeal parietal	Solid
Ishwar et al. (1971) (28)	62 y	F	Meningeal falx, occipital	Solid
Perks et al. (1976) (29)	21 y	F	Frontal	Highly vascular
Grisoli et al. (1984) (30)	28 y	F	Pituitary stalk	N/A
Katayama et al. (1987) (31)	N/A	N/A	Third ventricle	N/A
Neuman et al. (1989) (32)	35 y	F	Pituitary stalk	N/A
Black et al. (1991) (33)	15 y	M	Third ventricle	Solid
Sharma et al. (1995) (34)	72 y	M	Meningeal Parietal	Solid
Kachhara et al. (1998) (35)	57 y	F	Sella sphenoid sinus	N/A
Choi et al. (1998) (36)	26 y	F	Meningeal parietal	Solid
Isaka et al. (1999) (5)	47 y	F	Third ventricle	Solid
Tarantino et al. (2000) (37)	N/A	F	Cerebral	N/A
Yamakawa et al. (2000) (38)	17 y	M	Parietal	Cystic
Kim et al. (2001) (39)	45 y	M	Meningeal convexity, frontal	Solid
Ikeda et al. (2001) (16)	62 y	M	Suprasellar	N/A
Ozveren et al. (2001) (40)	40 y	F	Right supratentorial lesion near the splenium	Solid-cystic
Acikalin et al. (2003) (4)	43 y	M	Frontal	Cystic
Rumboldt et al. (2003) (14)	60 y	M	Sellar suprasellar	N/A
Agostinelli et al. (2004) (41)	10 y	F	Meningeal convexity, frontal	Solid
Iyigun et al. (2004) (13)	61 y	M	Meningeal convexity, frontal	Solid
Peker et al. (2005) (42)	54 y	M	Suprasellar	N/A
Tekkök and Sav (2006) (43)	18 m	F	Lateral ventricle	Cystic
Cosar et al. (2006) (44)	50 y	M	Meningeal parasaggital, parietal	Solid
Ohata et al. (2006) (11)	27 y	F	Hippocampus	Solid
Murali et al. (2007) (12)	57 y	M	Meningeal parasaggital	Solid
Sherman et al. (2007) (3)	52 y	F	Meningeal convexity, frontal	Solid
Jang (2007) (45)	68 y	F	Meningeal convexity, frontal	Solid
Takeuchi et al. (2008) (8)	58 y	M	Meningeal parasaggital, frontal	Solid
Jaggi et al. (2009) (46)	30 y	M	Third ventricle	Solid
Peyre et al. (2009) (47)	3 m	M	Lateral ventricle	Cystic
Elguezabal et al. (2010) (48)	67 y	F	Meningeal falx frontal	Solid-cystic
Crisi et al. (2010) (49)	N/A	N/A	Hippocampus	N/A
Schär et al. (2011) (50)	80 y	F	Pituitary	N/A
Yang et al. (2011) (2)	19 y	F	Temporal-occipital lobe	Solid-cystic
Kaloostian and Taylor (2012) (7)	49 y	F	Meningeal falx frontal	Solid
Sarkari and Agrawal (2012) (51)	45 y	F	Midline basifrontal	Solid
She et al. (2013) (9)	60 y	F	Cerebral falx	Solid-cystic
She et al. (2013) (9)	24 y	M	Temporal, choroidal fissure	Solid
She et al. (2013) (9)	21 y	M	Frontal	Cystic
Kishore et al. (2013) (15)	50 y	M	Parietal	Solid-cystic
Al-Najar et al. (2013) (52)	N/A	N/A	Lateral ventricle	N/A
Xie et al. (2013) (53)	64 y	F	Suprasellar	Solid

Raghava et al. (2014) (1)	50 y	M	Frontal	Solid
Pandey et al. (2016) (6)	39 y	M	Parietal	Cystic
Baran et al. (2019)	57 y	F	Right paracentral region	Solid

Table 1. Reported cases of supratentorial hemangioblastoma without VHL.

Conclusions

Infratentorial hemangioblastoma cases are inherently observed at high rates along with von Hippel-Lindau disease. However, it should be borne in mind that a small percentage of supratentorial hemangioblastoma cases may be presented with various neurological symptoms due to mass in imaging studies. Hemangioblastoma should be considered as an entity among other possible tumorous masses occupying supratentorial area.

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The manuscript sent for publishing must be submitted in English. The manuscript will be typed without formatting, with a 1-line space. Please enclose 1 copy of the manuscript, tables, graphics and photos. After publishing, the paper and pictures become the property of Romanian Neurosurgery.

There are no article processing charges (NO APCs) and no article submission charges.

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Paper sent for publishing should be in accordance with international standards of manuscript submittance. These standards are mentioned in "British Medical Journal" 1988; 296: 404-405 or in "Annals of Internal Medicine" 1988; 108:258-265. The authors are responsible for the accuracy of the information contained in the essay.

4.1. The title page should contain the whole title of the essay and complete names of authors with their academical degrees. If it is necessary, the department, the hospital or the institution where the search has been undertaken, should be also mentioned.

4.2. Please include an additional page containing the title of the essay and the author responsible for correcting of any and of all mistakes and for maintaining correspondence. The address, phone and fax number should be included (e-mail be available).

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

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Manuscripts should be sent to the Editor:

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Romanian Neurosurgery

"Gr.T. Popa" University of Medicine and Pharmacy Universitatii Street, No. 16, 700115, Iasi, Romania or by e-mail to ***mirceasteffan@yahoo.com***.

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After the manuscript submission, the peer review process is broken down into the following steps:

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2. The Reviewers review the manuscript.
3. The Editor drafts a decision to be sent to the author/authors.

The review process takes between three weeks and two months.