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Intramedullary Hemangioblastoma – Local Experience of a Tertiary Clinic

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Rezumat

Hemangioblastomul intramedular – experiența proprie din cadrul unei clinici specializate locale

Background: Hemangioblastoamele intramedulare sunt tumori benigne rare, ce apar sporadic sau în cadrul bolii von Hippel-Lindau.
Metode: Sunt prezentate datele clinice, imagistice și operatorii în 5 cazuri de hemangioblastoame intramedulare identificate într-o serie de 59 de pacienți diagnosticați și tratați pentru tumori intramedulare în clinica noastră între 2003-2009.
Resultate: Vârsta medie a pacienților a fost de 39,6 ani (limite 21-56). Toți pacienții au fost simptomatici; în 2 cazuri au fost pacienți cu boala von Hippel-Lindau care aveau și hemangioblastoame de fosa cerebrală posterioară. Examenul RMN preoperator a identificat tumorile intramedulare în toate cazurile. Intervenția chirurgicală a constat în rezecție tumorală completă în 4 cazuri și parțială într-un caz, cu extensie tumorală către porțiunea anterioară a maduvei. Evoluția neurologică ulterioară a fost favorabilă în 4 cazuri, în cel de al 5-lea, complicat cu o hemoragie semnificativă intraoperatorie, înregistrându-se o agravare neurologică temporară, complet reversibilă.
Concluzii: Hemangioblastoamele intramedulare sunt tumori curabile. Rezecția microchirurgicală completă este standardul de tratament și este asociată cu rezultate favorabile în majoritatea cazurilor. Localizarea anterioară a tumorii și hemoragia intraoperatorie sunt parametri asociați cu prognostic negativ.
Cuvinte cheie: hemangioblastoame, boala von Hippel-Lindau, chirurgie

Abstract
Background: Intramedullary hemangioblastomas are rare benign tumors, occurring sporadically or in von Hippel-Lindau disease.
Methods: We describe our local surgical experience with intramedullary hemangioblastomas. Clinical, imaging and surgical data from five consecutive hemangioblastoma cases identified from a series of 59 patients with intramedullary tumors treated between 2003-2009 are reviewed.
Results: The mean age of the patients was 39.6 years (range 21-56). All of them were symptomatic and two patients had von Hippel-Lindau disease with associated posterior fossa hemangioblastomas. All tumors were preoperatively diagnosed as hemangioblastomas based on magnetic resonance findings. All patients underwent surgery with complete removal of the tumor in 4 cases and a partial removal in a case with extension towards the anterior part of the cord. Good neurological outcome was noted in four cases while in the fifth, complicated with a significant intraoperative hemorrhage, a fully reversible aggravation of neurological status occurred.
Conclusions: Spinal cord hemangioblastomas are surgically curable tumors. Microsurgical complete resection is the standard of care and can be performed with good neurological outcome in most of the cases. Ventral tumor location and important intraoperative bleeding are associated with less optimal outcome.

Key words: hemangioblastomas, von Hippel-Lindau disease, surgery

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Introduction

Hemangioblastomas are benign vascular tumors that represent approximately 3% of the tumors in the central nervous system (1). They occur mainly in the posterior cranial fossa. The second most frequent location is the spinal cord (2,3), where the reported frequency in the literature ranges from 2 to 15% in different studies (4,5,6).

Hemangioblastomas can be isolated or multiple, as part of von Hippel-Lindau disease, a heritable multisystem cancer syndrome with autosomal dominant inheritance with high penetrance (7).

While histologically benign, intramedullary hemangioblastomas can lead to significant neurological symptoms related to the size of the tumor, localization, peritumoral edema and syringomyelia (3). The most common reported symptoms are motor and sensitive deficits, pain with a local or radicular distribution or urinary incontinence.

Magnetic resonance imaging (MRI) is currently the imaging modality of choice for intramedullary tumors, including hemangioblastomas. The hemangioblastomas are visualized as low-intensity signals on T1-weighted images with high signal from the cysts on T2-weighted images. On Gd-DTPA enhancement hemangioblastomas appear as bright enhancing lesions on the dorsal part of the spinal cord. MRI can identify multiple tumors and with increasing availability of the imaging modality more asymptomatic tumors are detected, especially in patients with von Hippel-Lindau disease. (1) Before MRI, angiography was the most frequently used imaging modality. Currently its use is limited to visualization of the vascular supply and in some cases to preoperative embolization of the arterial pedicles.

Complete surgical excision is the treatment of choice, with general consensus pointing towards a surgical approach in cases of symptomatic intramedullary hemangioblastomas. In asymptomatic cases the management is still a matter of debate between conservative and operative treatment. (1) This controversy is also favourized by the reduced incidence of this type of tumor. Hemangioblastomas usually have a well-defined cleavage plane and full surgical resection can be employed.

In order to identify the patients' characteristics, surgical outcome and prevalence of hemangioblastomas in our clinic, we prospectively analysed all the patients treated for intramedullary tumors in our neurosurgical center during 6 years, focusing on the hemangioblastoma cases.

Material and Method

Patient selection

We prospectively analysed clinical, imaging and pathological data from all consecutive patients operated for a intramedullary tumor in our department (Neurosurgery I Clinic, Ward II) between January 2003 and August 2009 (80 months). All surgical interventions were performed by the same surgical team. The hemangioblastomas were identified preoperatively based on MRI examination and confirmed histopathologically after surgical removal. The diagnosis of von Hippel-Lindau syndrome was made based on clinical and paraclinical factors combining complete anamnesis with focus on family history, ophthalmological exam, CT scan and MRI examination of the brain, thorax, abdomen and pelvis.

Surgical technique

Surgical interventions were performed under general anesthesia with endotracheal intubation. After laminotomy was performed, dura mater and arahnoid were incised along the midline and retracted laterally. "En bloc" excision was attempted in all cases.

Pre- and postoperative neurological assessment

Neurological assessment was performed before and twice after surgery (once during the first 24 hours and once between days 7-14) using American Spinal Injury Association (ASIA) score (8). Based on the difference between the postoperative and preoperative score the neurological outcome has been classified as: improved (difference > 0), stationary (difference $= 0$) or aggravated (difference < 0).

Results

Patients' characteristics

Fifty-nine patients (mean age 43.5±13.8 years, range 15-70 years old, 60% women) underwent surgery for an intramedullary tumor during the study period. The main pathological diagnosis was: ependymomas (29 cases), astrocytomas (15 cases) and hemangioblastomas (5 cases). *Fig. 1* shows the pathological diagnosis of the intramedullary tumors in our series.

All five hemangioblastomas were identified in women,

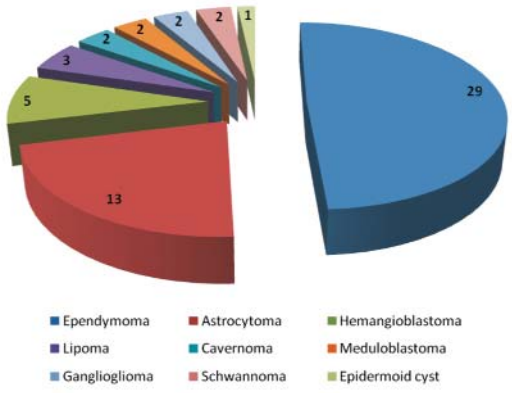

Figure 1. *The pathological diagnosis of the intramedullary tumors in our series. Five hemangioblastomas were identified, corresponding to a prevalence of 8.47%*

Table 1. *Clinical features, tumor localization, surgical complications and outcome in the 5 cases of hemangioblastomas*

Case	Age	Presenting symptoms	Intra-medullary localization	Other associated tumors	vHL syndrome	Surgical resection	Intraoperative significant blood loss	Neurological outcome/ ASIA score difference postOP-preOP
# 1	25	Spinal Cord Compression (SCC)	C2 – C3	Posterior fossa hemangio-blastoma	+	Complete		Good/ stationary
# 2	46	SCC	T2 - T3		-	Complete	500 ml	Good/ stationary
# 3	56	SCC	T5 - T6		-	Partial	800 ml	Good/ stationary
# 4	21	SCC	C2 – C4		-	Complete		Good/ stationary
# 5	50	SCC	T5 – T7	Posterior fossa hemangioblastoma	+	Complete	850 ml	Aggravated motor deficit-reversible after 4 months

vHL - von Hippel-Lindau syndrome; ASIA - American Spinal Injury Association; postOP – postoperative; preOP – preoperative; SCC - spinal cord compression

with a mean age of 39.6 years (range 21-56 years). In three cases solitary intramedullary tumors were present, while in the other two hemangioblastomas in the posterior cranial fossa were also found. These latter cases were previously diagnosed with von Hippel-Lindau syndrome. Beside the presence of hemangioblastoma in two locations (intramedullary and posterior cranial fossa) the two patients with von Hippel – Lindau disease had no other significant pathology.

The localization of the tumors is depicted in *Table 1.* Tumoral extension involved two spinal levels in three patients and three levels in the remaining two cases, with a mean of 2.4 segments.

Clinical and imaging findings

Before surgical intervention all subjects underwent MRI evaluation, which showed typical hemangioblastoma changes. In one case of cervical hemangioblastoma localized at C2-C4 level a preoperative angiography was also performed (*Fig. 2*), in order to better delineate arterial vascularization and drainage vessels.

All patients had symptomatic spinal cord compression, in two cases at C3 cervical level, and in three cases at the thoracic level; the mean duration of symptoms ranged from 2 months to 2 years and 4 months.

Surgical results

Surgical excision was performed in all five cases. In the two cases of von Hippel-Lindau syndrome, the posterior fossa tumors were treated in the first operative stage, followed by intramedullary tumor excision after two months (in both cases).

Complete surgical excision was performed in 4 cases (80%), while in the fifth one, with local extension to the anterior part of the spinal cord, only a partial resection was possible. Two cases were complicated with significant intra-operative blood loss, of 800 ml, respectively 850 ml. No significant postoperative complications occurred, except for the accentuation of the neurological deficit in case #5, with spasticity and motor deficit which slowly recovered in the

Figure 2. *Preoperative selective vertebral artery angiography in a case of cervical hemangioblastoma showing intense tumor blush (arrow) and feeding vessels*

next four months. In all other cases ASIA score showed no postoperative decrease (*Table 1*).

Discussion

Intramedullary hemangioblastomas are rare, benign, highly vascularized tumors, accounting for 2-15% of primary spinal cord tumors (4-6). In our series of 59 patients with intramedullary tumors 8.47% were hemangioblastomas (5 cases, all females), out of which two cases were associated with von Hippel-Lindau syndrome and presented also posterior fossa hemangioblastomas. The exact epidemiology of hemangioblastomas in the general population is unknown and most data come from relatively small surgical series from tertiary centers. While in our data a female preponderance is shown, no gender predilection is seen in some larger series (1,2,9,10) or even a male predominance reported (11), suggesting probably a random effect in a small group of 5 patients.

While hemangioblastomas are benign tumors, (World Health Organization grade I) (12), they can cause significant morbidity due to local edema, extension or cyst formation (11). In our series, all five patients were symptomatic, with spinal cord compression Frankel C in two cases and Frankel D in three cases (*Table 2*)(13).

Complete resection of the tumor is the treatment of choice and it requires careful microsurgical technique in order to allow "en bloc" removal, with optimal neurological outcome. The principles and technique of the removal of hemangioblastomas are different from other intramedullary tumors due to the juxtamedullar location of the former, arising from pia mater in most cases, versus the intramedullary location of the latter (11). Careful circumferential release of the pia attachment from tumor surface and spinal cord, devascularizes the tumor and allows for optimal exposure needed for safely removal of the intramedullary component. Due to the particularities mentioned above myelotomy in hemangioblastomas is called "atypical", in the area of where the tumor expanded at the spinal cord surface, under the pia mater.

After dural opening the spinal cord is inspected in order to identify the surface component of the tumor. Hemangioblastomas always have a cleavage plane between the level of the solid component of the tumor and spinal cord, thus allowing complete dissection and tumoral complete, "en bloc" resection. (4) If preoperative angiography was performed and vascular supply of the tumor is known, the feeding vessels are coagulated and sectioned in the following order: small arteries, drainage veins of small and medium calibre, then large drainage veins. In case of large hemangioblastomas, the tumoral surface can be coagulated in the first step, leading to its progressive shrinkage, and then arterial sources are coagulated and sectioned. In all stages of surgery care should be taken to avoid excessive medulla manipulation and not to enter the tumor, in order to minimize bleeding and damage to nerve vessels.

Most hemangioblastomas are located on the dorsal or postero-lateral surface of the spinal cord (11), as seen in our series in four of the cases. In these cases complete resection is possible. Some authors consider that this predominant localization could explain why hemangioblastomas exhibit sensory symptoms earlier in evolution and more frequently than motor ones.(1) Ventrally located tumors have been associated with worse outcome in some studies. (11) In our series, the case in which complete resection of the hemangioblastoma was not possible, was that of a ventral hemangioblastoma, with arterial sources from the anterior spinal artery. In this patient the tumoral part adherent to the anterior spinal artery was not resected due to the risk of significant irreversible neurological deficits. Some authors suggest that in these cases an anterior approach as opposed to the typical dorsal approach of the intramedullary tumors, might offer better access and lesser risk of neurological damage. (14) Data from different authors suggest that preoperative good neurological status,

Table 2. *Frankel classification grading system. After (13)*

Frankel classification grading system			**Number of patients in our series**
Grade A	"complete"	Complete neurological injury - no motor or sensory function clinically detected below the level of the injury.	None
Grade B	"sensory only"	Preserved sensation only - no motor function clinically detected below the level of the injury; sensory function remains below the level of the injury but may include only partial function	None
Grade C	"motor useless"	Preserved motor non-functional - some motor function observed below the level of the injury, but is of no practical use to the patient.	Two
Grade D	"motor useful"	Preserved motor function - useful motor function below the level of the injury; patient can move lower limbs and walk with or without aid, but does not have a normal gait or strength in all motor groups.	Three
Grade E	"recovery"	Normal motor - no clinically detected abnormality in motor or sensory function with normal sphincter function. Abnormal reflexes and subjective sensory abnormalities may be present.	None

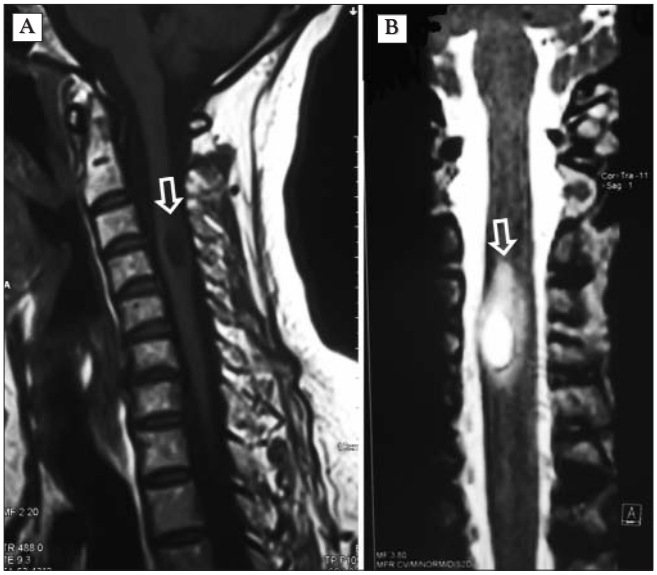

Figure 3. *(A) T1-weighted sagittal MR image in a patient with hemangioblastoma showing hipointense tumor (arrow). (B) T2 - weighted MR image in the same patient showing hiperintens tumor (arrow)*

tumor size less than 500 mm^3 and dorsal tumor localization are all predictors of postoperative status. (15) Moreover, in a series of patients that underwent surgery for intramedullary spinal cord tumors of various types, the presence of a resection plane improved the progression free survival in cases of ependymomas, hemangioblastomas and astrocytomas, being more predictive of event free survival than tumor histology. (16)

Preoperative imaging studies play an important role in surgery planning. All five cases in our series showed typical MRI changes (*Fig. 3*). Hemangioblastomas are hypo- to isointense on T1-weighted sequences and iso- to hyperintense on T2-weighted sequences when compared to normal spinal cord. (17) Gadolinium administration is followed by intense enhancement on T1-weighted images. While large lesions can be identified without contrast, small ones are often isointense and need Gd DTPA enhancement for proper diagnosis (17) and increased sensitivity of the imaging modality. (18)

Different appearances of spinal hemangioblastoma have been described, including hemangioblastoma with diffuse cord enlargement, hemangioblastoma with cyst formation or syrinx, exophytic hemangioblastoma with minimal cord reaction or extramedullary hemangioblastoma. (17) Moreover, the presence of intramedullary T2 high intensity areas spreading toward the cranio-caudal sides of the tumor on saggital MR images can help differentiate intramedullary tumors and intra- and extramedullary tumors from intradural-extramedullary tumors. (19) Nowadays selective angiography is less frequently used for tumor diagnosis. Its use is restricted to cases when knowledge of the exact tumor vascularization is imperative or when tumor embolization, usually performed preoperative in order to facilitate tumor resection in sensitive areas, is taken into consideration. (11, 20)

Careful postoperative neurological examination is mandatory, due to the risk of intramedullary bleeding, more frequent in cases where complete resection is not possible, or epidural hematoma. In von Hippel-Lindau cases, as in other neurosurgical pathologies, neurological examination completed with MRI surveillance should be performed periodically (21).

Conclusions

Spinal cord hemangioblastomas, either sporadically or in von Hippel-Lindau disease, are surgically curable tumors. MR imaging techniques allow accurate preoperative tumor diagnosis. Microsurgical complete resection is the standard of care and can be performed with good neurological outcome in most of the cases. Ventral tumor location and important intraoperative bleeding are associated with less optimal outcome.

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