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ARTICLE



Surgical management and outcome of adult posterior cranial fossa and spinal hemangioblastoma: a 6-case series and literature review

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ABSTRACT

Objective: Hemangioblastomas of the posterior cranial fossa and spinal cord in adults are excessively vascularized, well-differentiated, and scarce tumors with no metastatic potential. This paper discusses its surgical management and outcome, pointing out their morphological, radiological, and histopathological aspects. This report based on a personal series of six patients and on a literature review.

Methods: A single-institution personal 6-case series of adult patients diagnosed and operated on by a senior neurosurgeon (KIA) due to posterior cranial fossa or spinal cord hemangioblastoma was analyzed. For easier understanding of hemangioblastoma, we have classified them into four different types.

Results: The tumors, which were all surgically treated, were located in the posterior cranial fossa in five patients (4 cerebellar, 1 brain stem) and intramedullary in the thoracic spinal cord in one patient. All patients successfully recovered neurologically after a complete tumor resection, having no post-operative neurological deficit or other complications.

Conclusion: Surgical management of cerebellar and spinal cord hemangioblastoma in adults is highly dependent on its morphological features, as well as on microsurgical technique applied. Since huge differences exist between the cystic/nodular tumor type (Type 1) and the solid type and its two additional variants (Types 2–4), morphology is the most important consideration when deciding surgical approach. Despite significant morphological differences among different subtypes of hemangioblastomas, their histology appears to be relatively similar. Nonetheless, a meticulous and refined surgical technique has to be utilized to achieve a successful outcome.

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Adult hemangioblastoma; posterior fossa; thoracic spinal cord; morphology; microsurgical technique; management outcome

Introduction

Hemangioblastomas are infrequent and benign tumors of the central nervous system (CNS) with no metastatic potential [1] that mostly affect the cerebellum [2], brainstem [3], and spinal cord [4,5]. Sporadic posterior fossa hemangioblastomas tend to occur most often in the fifth decade of life and are more common in males [6,7]. Spinal hemangioblastomas, on the contrary, rarely occur in patients over 65 years of age [8], although the prevalence may be higher than expected [9]. Multiple tumors nearly always occur earlier in life and are associated with Von Hippel–Lindau disease (VHLD) [2,6,10–12], autosomal dominant genetic disorder linked to a defect on chromosome 3, and the mutation of the VHL tumor suppressor gene [10,13,14]. Despite their scarcity, hemangioblastomas of the spinal cord are the third most common intramedullary spinal tumor, representing 2–6% of all intramedullary growths [7], and may appear either sporadically or in association with VHLD [15–17]. The thoracic spinal cord is the predominant location

seen in almost half of the cases (~50%) [18], but only 25% of such tumors are located entirely intramedullary, mainly along the dorsum of the cord [18–20].

Hemangioblastomas may morphologically appear as four different types, which we had classified as Types 1–4: Type 1, large non-enhancing cyst with an enhancing mural nodule (nodular); Type 2, solid (parenchymatous) tumor-enhancing with flow voids; Type 3, cystic with enhancing wall; or Type 4, solid tumor with internal cyst(s) [21]. Nodular and solid types are being more frequent. Such tumors of the spinal cord are commonly associated with syringomyelia [20].

This report is based on a personal 6-case single-institution series of adult hemangioblastomas of the posterior cranial fossa and spinal cord. The authors discuss morphological differences between these tumors, which may have a diverse radiologic appearance, although their histopathology may not differ much. We also discuss how the above-mentioned features may influence surgical management and outcome, emphasizing the importance of planning and tailoring operative technique according to a different

hemangioblastoma subtype classification that we have devised. Finally, we will provide a current literature review of these relatively rare neurosurgical entities.

Material and methods

We analyzed a personal series of 6 adult patients diagnosed with posterior cranial fossa and spinal cord hemangioblastoma who were operated on by the senior author (KIA). The morphological, radiological, and histopathological features of all tumors, as well as surgical operative technique and outcome, are discussed. For the purpose of this paper, the following data were obtained: patient age and gender; disease history; morphological and radiologic appearance of the tumor; histopathological diagnosis; surgical management; and outcome. According to radiologic appearance, tumors were divided into three categories: Types 1–3, which corresponded to their morphological types and were visible on MRI findings.

The following histopathological features were additionally analyzed: overall cell pattern; predominant cell type; vacuolization of cells' predominant pattern; frequency of nuclear degenerative pleomorphism; frequency of intranuclear inclusions; predominance of visible macronucleoli; number of mitoses; and number and size of feeder and small vessels. According to the observed frequency of nuclear degenerative pleomorphism and intranuclear inclusions, the tumors were divided into two groups with high and low frequency, respectively. Immunohistochemical confirmation was done in addition to making a histopathological diagnosis.

Results

Tumor morphology

Four morphological types of hemangioblastomas were defined in the available literature: non-contrast enhancing cyst with mural nodule (nodular) that we classify as Type 1, solid (parenchymatous) that we classify as Type 2, cystic with enhancing wall that we classify as Type 3, and solid (contrast enhancing) containing cyst(s) that we classify as Type 4.

According to the morphological tumor types recorded in our 6-case series, tumors were divided

into three different categories: solid (parenchymatous; Type 2), which accounted for 2 (34%) tumors; cystic with wall enhancement (Type 3), which accounted for 1 tumor (17%), and cystic/nodular (type 1), which accounted for 3 (50%) tumors (Table 1).

Radiologic appearance

Tumor appearance based on specific radiological features is depicted in Table 1. Tumors were divided into three categories that were visible on MRI findings and corresponded to their morphological types (parenchymatous-solid, cystic with enhancing wall, and cystic/nodular-non-enhancing cyst, enhancing mural nodule).

Histopathology and immunohistochemistry

Information concerning hemangioblastoma histopathological diagnosis and tumor-specific histological features (e.g. hypervascularity, vacuolization of stromal cells, mitotic activity, and existence of necrosis) were recorded by developing histological features of resected tissue samples. Immunohistochemical records recognized stromal cells and vascular (reticular) cells as mutually divergent cytological components with no proof of transition between them. There was no difference in immunohistochemical staining (S-100, the glial fibrillar acidic protein [FAP], vimentin, neuron-specific enolase [NSE], epithelial membrane antigen [EMA], CD 34 antibody, cytokeratin, reticulin, CD 56 antibody, inhibin, CD 10 antibody, and vascular endothelial growth factor [VEGF]) between these components in this series. Distribution of tumors according to their histopathological features in the 6-case series is depicted in Table 2.

A 6-case series report

The case series consisted of 6 patients with posterior fossa and spinal cord hemangioblastoma between the ages of 30 and 59 years, who presented with headache and typical cerebellar syndrome or sudden urinary incontinence. The mean age of the group consisting of four men and two women was 46.5 years (median age: 44.5 years). In all patients, a contrast enhancing

Table 1. Gender division, tumor location and morphological/radiological appearance in the 6-case series.

Patients (N)	Mean age	Gender	Tumor location	No.	Morphology	No.	Radiology (MRI)	No.
6	46.5 years	Male: 4	Hemisphere	3	Solid/parenchymatous or solid containing large cyst	3	Diffuse enhancing with flow voids	3
				1	Non-enhancing cyst with enhancing nodule	1	Diffuse enhancing containing large cyst	1
		Female: 2	Hemisphere	1	Non-enhancing cyst with enhancing nodule	1	Non-enhancing cyst/enhancing nodule	2
			Brain stem	1	Non-enhancing cyst with enhancing nodule	1	–	–
			Spinal cord	1	Solid/parenchymatous	1	–	–
Total				6		6		6

Table 2. Tumor histopathological features of the 6-case series.

Characteristics	No.
Cell overall pattern	
Reticular	2
Cellular	4
Predominant cell type	
Epithelioid	2
Undescriptive	2
Mixed	2
Vacuolization of cells	6
Microvacuolization	
Nuclear degenerative pleomorphism	
Frequent	3
Frequent, striking	1
Non-frequent	2
Intranuclear inclusions	
Non-frequent	3
Frequent	3
Macronucleoli	
Absent	6
Mitotic activity	
Scarce	6
No of feeder vessels	
Scarce	6
No. of small vessels	
Abundance	6

brain and/or spine MRI was performed as a main diagnostic tool prior to surgery. Four tumors were situated at the cerebellar hemispheres, one was located at the dorsal brain stem and associated with VHLD, and one was situated intramedullary within the thoracic cord at the T11 level. Sporadic hemangioblastomas were encountered in five out of six patients.

In all the patients, the entire tumor was successfully resected. Patients with posterior fossa tumors underwent midline suboccipital craniectomy, while the one patient with a thoracic spinal cord tumor underwent a dorsal laminectomy and myelotomy. All recovered well and were free of symptoms at 6-month, 1 year, and annual follow-up after surgery. No tumor recurrence was recorded at any follow-up examination.

Patient 1

The first patient was a 58-year-old male with a solid, parenchymatous, partially contrast enhancing, partially flow void, left cerebellar hemisphere hemangioblastoma (Type 2) (Figure 1(a,b)). He presented with severe headache and balance problems. With regard to histopathology, the tumor had a reticular cellular subtype and predominantly epithelioid cell type with frequent nuclear degenerative pleomorphism and non-frequent intra-nuclear inclusions.

Patient 2

The second patient was a 53-year-old female with a solid, parenchymatous, partially enhancing, flow void hemangioblastoma of the right cerebellar hemisphere (Type 2). She presented with severe headache and balance and coordination problems. With regard to histopathology, the tumor had a cellular variant overall pattern, and predominantly epithelioid cell

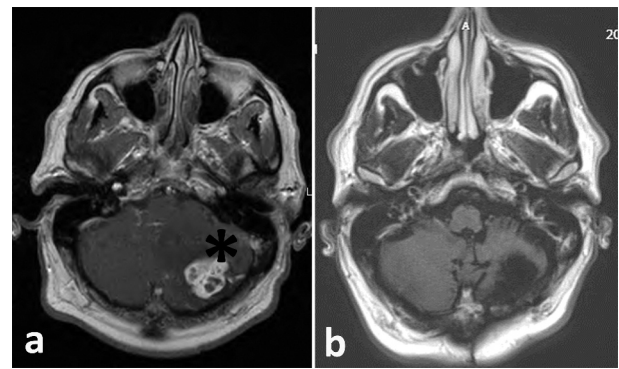


Figure 1. Type 2. An axial T1-weighted postcontrast MRI of a 58-year-old male patient with a solid/parenchymatous, partially contrast enhancing, partially flow void left cerebellar hemisphere hemangioblastoma (a). Axial T1 postcontrast MRI depicting postsurgical gross total tumor resection (b).

type with frequent nuclear degenerative pleomorphism and frequent intra-nuclear inclusions.

Patient 3

The third patient was a 47-year-old male with a cystic/nodular hemangioblastoma of the left cerebellar hemisphere with a non-enhancing cyst and enhancing mural nodule (Type 1) (Figure 2(a,b)). Clinical symptoms and signs included headache, dysmetria, and balance problems. With regard to histopathology, the tumor had a reticular cell variant overall pattern and undescriptive predominant cell type with strikingly frequent nuclear degenerative pleomorphism and frequent intranuclear inclusions.

Patient 4

The fourth patient was a 32-year-old female with a cystic/nodular dorsal brainstem hemangioblastoma (Type 1). Gait disturbances (ataxia), difficulties with swallowing, and VHLD were noticed as clinical signs on hospital admission. MRI of the brain and the entire neural axis showed a cystic lesion with contrast-

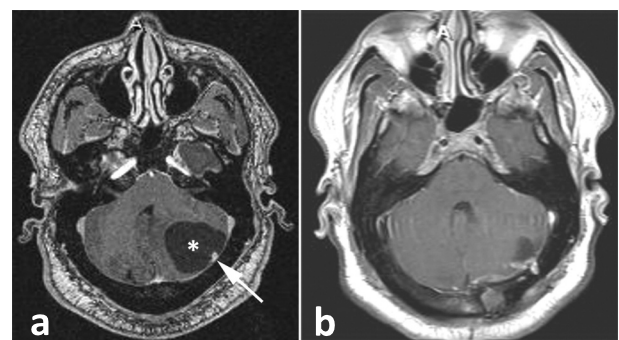


Figure 2. Type 1. A 47-year-old male with a cystic/nodular hemangioblastoma of the left cerebellar hemisphere, non-enhancing cyst, and enhancing mural nodule visible on axial T1-weighted postcontrast MRI (a). Postoperative T1-weighted postcontrast axial MRI showing postsurgical nodule resection (b).

enhancing tumor nodule along the posterior aspect of the lower part of medulla oblongata with an adjacent large non-enhancing cyst (Figure 3(a–c)). With regard to histopathology, the tumor had a reticular cell variant overall pattern with mixed predominant cell types, non-frequent nuclear degenerative pleomorphism and non-frequent intranuclear inclusions.

Patient 5

The fifth patient was a 59-year-old man with hemangioblastoma of left cerebellar hemisphere with a brightly enhancing wall with flow voids containing a large cyst (Type 3) (Figure 4(a)). He presented with headache, dysmetria, and gait disturbances. With regard to histopathology, the tumor had a reticular cell variant overall pattern and mixed predominant cell type with non-frequent nuclear degenerative pleomorphism and non-frequent intra-nuclear inclusions. Postoperative axial MRI depicted complete cyst resolution after microsurgical resection (Figure 4(b)).

Patient 6

The sixth patient was a non-VHLD 30-year-old male who presented with sudden onset of urinary incontinence as a lone symptom. On spinal contrast sagittal MRI scans, sporadic enhancing intramedullary tumor with the adjacent non-enhancing cyst at T11 level (Type 1) and syringomyelia extending to C1 level were seen (Figure 5(a,b)). With regard to histopathology, the tumor had cellular variant overall pattern and undescriptive predominant cell type with non-frequent nuclear degenerative pleomorphism and intranuclear inclusions. During the surgical resection of the tumor, which was detached from the spinal cord, the coagulation of arterial feeders was done while preserving the drainage vein to de-vascularize the tumor [22–27]. After all feeders had been coagulated, the drainage vein was finally coagulated, and tumor

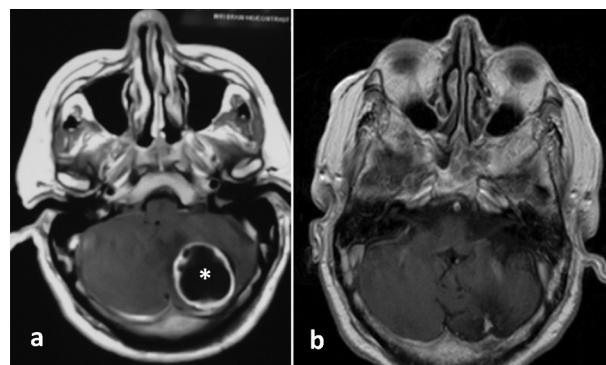


Figure 4. Type 3. Cystic hemangioblastoma of the left cerebellar hemisphere with brightly enhancing cyst wall, visible on an axial T1-weighted MRI of a 59-year-old male (a). Postoperative axial MRI showing complete cyst resolution after microsurgical resection (b).

completely removed [26–28]. The patient's postoperative recovery was complete without incontinence and neurological deficit. A follow-up spinal MRI exposed a marked diminishment of the cervical cord syringomyelia and no signs of tumor recurrence (Figure 5(c,d)).

Discussion

Tumor morphology

Hemangioblastomas are traditionally classified into solid and cystic morphological types [10]; yet, there is no distinct histological differentiation between mainly cystic and solid tumor variants [29]. In contrast to sporadic hemangioblastomas, multiple tumors were frequently seen in the case of VHLD [14].

Different morphological tumor types were described in the literature, of which solid hemangioblastomas were the most common (47.7%) [30]. According to the morphological tumor types recorded in our 6-case series, tumors were divided into three different categories being of solid (parenchymatous), nodular, or cystic with enhancing wall types (Table 1).

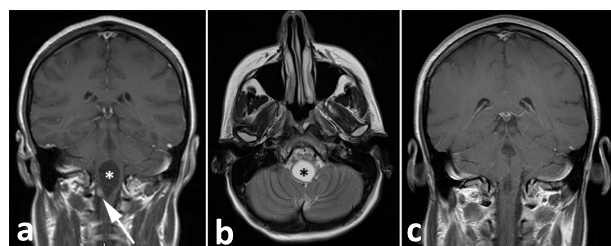


Figure 3. Coronal T1-weighted postcontrast MRI of a 32-year-old female with VHLD and a non-enhancing cyst and enhancing nodular hemangioblastoma of the dorsal brain stem (Type 1) (a). Axial T2-weighted MRI showing the cyst (b). Postoperative coronal postcontrast T1-weighted MRI showing nodule resection and cyst collapse. Coronal T1-weighted postcontrast MRI showing nodule resection and cyst collapse.



Figure 5. Sporadic intramedullary tumor in a 30-year-old male. A nodular hemangioblastoma with adjacent cyst at the T11 level and syringomyelia is shown on sagittal T2-weighted MRI (a). Sagittal T2-weighted MRI showing syrinx extending to C3 (b). Postoperative spinal T2-weighted sagittal MRI demonstrating no signs of tumor recurrence at the T11 level (c), and a marked diminishment of the cervical cord syringomyelia (d).

Radiologic appearance

Cerebral angiography is an important tool in the radiological evaluation of hemangioblastomas, which are highly vascularized that represent as a heterogeneous network of twisted vessels fed by a dilated artery [21]. If present, a cyst may appear as a vascular nodule within an avascular region [31].

Magnetic resonance imaging (MRI) and MR angiography (MRA) deliver the most conclusive diagnosis of hemangioblastomas. They are clearly delineated and bright contrast-enhancing lesions on T1 and T2-weighted scans [14,18,20,21,32] and have a predominantly cystic or solid configuration. Their radiologic appearance correlates well with their typical morphological varieties [21].

According to the radiologic appearance, the tumors in this 6-case series were divided into three categories visible on MRI findings: solid tumor with partial or full flow voids and partial tumor enhancement (Type 2), cystic/nodular with brightly enhancing mural nodule and non-enhancing cyst wall (Type 1), and cystic with enhancing wall (Type 3) (Table 1).

Tumor configuration depicted on preoperative MRI is the essential factor related to postoperative outcome [33]. Accordingly, due to its diffuse spreading, surgery of solid tumors appears to be more complex compared with the cystic tumor type, which is more vascularized and therefore require a more demanding surgical technique. Thus, we believe that tumor morphology is more important than location when management outcome is concerned.

Histopathology and immunohistochemistry

Key histopathological components of hemangioblastoma are made of two distinctive histologic cell overall patterns (cellular and reticular) [34]. A cellular neoplastic pattern (stromal, epithelioid cells) is rare, but a reticular pattern (vascular, mesenchymal type) is more common, which was the case with our patients too. Histogenesis of stromal cells, representing a heterogeneity of differentiating mesenchymal cells, remains questionable [35]. Hence, immunohistochemistry is performed to identify the exact nature of stromal cells [36]. Nevertheless, cytogenetic profiles of cellular (stromal) and reticular (vascular) variants diverge, influencing the recurrence rate and the prognosis of such tumors in different ways [34]. In this 6-case series, the overall pattern of reticular tumor cells was recognized as a principal cellular variant with predominantly epithelioid cell type. Absence of macronucleoli and scarce mitotic activity, a distinctive microvacuolization, scarceness of feeder vessels, and an abundance of smaller vessels in histopathological tumor tissue samples appear to be typical for such kind of tumor. Regarding the frequency of nuclear

degenerative pleomorphism and intranuclear inclusions, more frequent nuclear degenerative pleomorphism but equally frequent intranuclear inclusions were registered in this series (Table 2).

When we correlated the tumors, distinctive histopathological appearance with their characteristic morphology, we did not find any differences that may indicate a specific correlation between these tumor aspects. Therefore, we believe it is not possible to distinguish tumor morphology based on its histopathological form alone.

Microsurgical technique

In spite of being a benign tumor, hemangioblastoma may carry a significant mortality rate if left untreated due to hydrocephalus, tonsillar herniation, and brainstem compression. Complete surgical tumor resection remains the most innocuous management strategy [4,37–47], having a generally favorable prognosis regardless of its location [4,28,30,38,44–47]. However, internal decompression of a solid tumor (Type 2) or its 2 other variants (Type 3 and 4) can be potentially dangerous since such a tumor is highly vascularized. Therefore, outcomes may differ depending on tumor location, morphology, histology, and radiological characteristics, which may make complete resection demanding [3,30,33,48].

When deciding surgical approach, the tumor location and morphology, including its consistency (solid or cystic) and vasculature, have to be taken into consideration. Complete tumor resection can be achieved using a meticulous microsurgical technique and understanding tumor vascular configuration [5,27,47]. Following a detailed preoperative evaluation, a midline suboccipital craniectomy in prone position is the most often used for posterior fossa hemangioblastomas [49], while the brain stem ones could be operated on by a retrosigmoid approach. Dorsal laminectomy and myelotomy is a preferred surgical method for spinal cord growths [50], when accurate microsurgical dissection is obligatory to evade cord damage [51].

Once the tumor becomes symptomatic, a complete resection is the most advantageous mode of management [41,52,53]; however, surgical management differs significantly.

The Type 1 nodular tumor has a non-enhancing cyst and an enhancing nodule; in this type of tumor, resection of the nodule is a simple maneuver that provides gross total resection with immediate cyst collapse and disappearance and cure with a very low risk of recurrence.

Unlike Type 1 tumors, Types 2–4 are extremely vascularized tumors that enhance on MRI scans with contrast, contain flow voids in their enhancing parts, and may contain cysts of different sizes (Types 3 and 4). Surgical management must be

planned in a similar manner as management of arteriovenous malformations due to their extreme tendency for hemorrhaging. Therefore, microsurgical technique has to be planned to circumscribe the tumor and carefully dissect, coagulate, and divide arterial feeders in a systematic fashion [27]. The venous drainage coagulation and interception must be left until the very end of the surgery following elimination of all arterial feeders. For Types 2–4 tumors, preoperative preparation of blood transfusion and close communication with anesthesia are of tremendous importance. Finally, gross total resection should be the goal since leaving tumor parts may lead to significant postoperative hemorrhage and poor clinical outcomes [25–27,33,53].

Postoperative complications – including intracranial hemorrhage, hydrocephalus, and pseudomeningocele formation – were reported in more than half of the reviewed articles dealing with hemangioblastoma surgery [30]. Accordingly, many patients are expected to have some complications postoperatively; they are also predisposed to repeated surgery to avoid permanent neurologic deficits. Because of the propensity for bleeding in morphologically solid tumors, cystic tumors with wall enhancement, and solid tumors with cysts (Types 2–4), it is rational to suggest that such tumor types may be more prone to higher rates of complications. Additionally, in planning surgery of these types of hemangioblastomas, intraoperative blood replacement is of significant importance. Since VHLD patients with multiple tumors are at a greater risk of developing recurrent lesions, their management embodies a more persistent and difficult task [54,55].

All patients in our series were successfully operated on; the entire tumor completely resected from each patient. Because of the success of the techniques we employed, we believe that microsurgical techniques tailored to tumor morphology and preoperative MRI scans are essential to bringing a satisfactory outcome for posterior fossa and spinal cord hemangioblastoma surgery and to avoid postoperative complications.

Conclusion

The management of cerebellar and spinal cord hemangioblastoma in adults is decidedly reliant on its morphological aspects, as well as on applying microsurgical techniques. Substantial differences, therefore, exist between solid and cystic/nodular tumor types with regard to surgical outcome in which solid tumors (Types 2–4) are more morbid, more surgically demanding, and have a less favorable

prognosis compared with cystic/nodular tumors (Type 1), which are easier to treat microsurgically and less prone to complications. Nonetheless, complete surgical tumor resection is the main management option that results in a favorable recovery most of the time. Despite significant morphological differences among different subtypes of hemangioblastomas, their histology appears to be relatively similar.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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