

Clinical characteristics and surgical strategy of sporadic cerebellar hemangioblastomas

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Abstract. Hemangioblastoma is a rare benign vascular tumor that occurs mostly in the cerebellum. The aim of the present study was to analyze the clinical characteristics of sporadic cerebellar hemangioblastoma and its surgical strategy. A total of 76 cases of sporadic cerebellar hemangioblastoma (42 males and 34 females; age, 46.4±13.9 years; age range, 23-72 years) admitted to the Department of Neurosurgery of the General Hospital of Northern Theater Command (Shenyang, China) from July 2012 to April 2021 were retrospectively analyzed. All patients had only one isolated tumor and underwent surgical resection. Their basic characteristics, serial radiographic examinations, surgical records and follow-up were analyzed. A total of 57 patients with cystic hemangioblastoma and eight patients with cystic solid hemangioblastoma directly underwent resection treatment. Of 11 patients with solid hemangioblastoma, 8 underwent vascular embolization prior to surgical resection. Furthermore, 3 patients with solid hemangioblastoma who were not embolized prior to surgery had intraoperative hemorrhage and poor prognosis. In addition, 3 patients underwent partial resection of the tumor and all of them suffered recurrence after the surgery. A total of 71 patients achieved good neurologic improvement. However, 5 patients had a poor prognosis after the initial surgery. In conclusion, total microsurgical resection is essential to improve the health status of patients with sporadic cerebellar cystic hemangioblastoma. In addition, preoperative embolization of arteries supplying solid hemangioblastomas can reduce intraoperative bleeding and improve prognosis.

Introduction

Hemangioblastomas are rare and vascular-rich benign tumors of the central nervous system that account for 2% of all intracranial tumors (1,2). Hemangioblastomas frequently occur in the posterior cranial fossa, most commonly in the cerebellum (3). Based on the radiological features examined by magnetic resonance imaging (MRI), most hemangioblastomas are classified into three categories: i) Large cysts with reinforcing cystic walls or small nodules, ii) a combination of solid and cystic features and iii) completely solid tumors (4,5). Despite the progressive development of neurosurgical techniques, surgical resection of solid hemangioblastomas remains a great challenge (6). How to reduce the risk of intraoperative hemorrhage, postoperative complications and high mortality remains a concern.

Recent advancements in imaging techniques and preoperative planning have improved the identification and characterization of hemangioblastomas, allowing for more precise surgical interventions (7,8). The integration of intraoperative MRI and neuronavigation systems has enhanced the surgeon's ability to achieve complete resection while minimizing damage to surrounding brain tissue (9,10). Additionally, the use of functional MRI and tractography has helped in preserving critical neurological functions by mapping out vital brain structures and their relationship to the tumor (11).

However, the highly vascular nature of these tumors continues to pose significant challenges, particularly in managing intraoperative bleeding (12). Preoperative embolization has been employed as a strategy to reduce intraoperative blood loss by decreasing the blood supply to the tumor (13). This technique, coupled with advanced anesthetic management and meticulous surgical techniques, has contributed to improved surgical outcomes (14).

Moreover, understanding the molecular and genetic underpinnings of hemangioblastomas has opened new avenues for targeted therapies (15). For instance, studies have identified mutations in the VHL gene associated with sporadic hemangioblastomas, suggesting potential therapeutic targets (16). The VHL protein plays a crucial role in regulating hypoxia-inducible factors (HIFs), and disruptions in this pathway can lead to tumor development (17). Targeted therapies aimed at this pathway are being explored, offering hope for non-surgical treatment options (18).

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These advancements underscore the importance of a multidisciplinary approach, combining neurosurgery, neuro-oncology and genetics, to optimize patient outcomes (19). Collaborative efforts involving neurosurgeons, radiologists, pathologists and geneticists are essential in developing personalized treatment plans that address the unique characteristics of each tumor and patient (20).

Therefore, in the present study, the clinical data of patients with sporadic cerebellar hemangioblastoma were collected and retrospectively analyzed, including clinical characteristics, radiographic features, postoperative recurrence and prognosis, in order to determine the appropriate surgical treatment strategy for sporadic cerebellar hemangioblastoma. This comprehensive analysis aims to provide insight into improving surgical techniques, reducing complications and enhancing long-term prognosis for patients with this challenging condition. By identifying factors associated with favorable outcomes and potential complications, the study seeks to refine surgical approaches and inform clinical decision-making, ultimately leading to better management of sporadic cerebellar hemangioblastomas.

Patients and methods

Patients. The cases of patients with sporadic cerebellar hemangioblastoma were collected. The study was approved by the Ethics Committee of the General Hospital of Northern Theater Command (Shenyang, China; approval no. 2021-135) on August 2nd, 2021. The patient selection criteria were as follows: i) All patients had been diagnosed with sporadic cerebellar hemangioblastoma after preoperative computed tomography (CT) and MRI examinations of the brain, as well as postoperative pathologic examinations; ii) detailed information about the patients' hospitalization had been stored and multiple clinical manifestations had been accurately recorded; iii) the patient had no previous specific neurological disease or severe neurological dysfunction.

Imaging examination. All patients underwent preoperative CT and MRI. A total of 37 patients underwent CT angiography and 10 underwent concurrent digital subtraction angiography (DSA). The preoperative MRI data of the brains of the patients were analyzed in detail, including T1 and T2 scanning sequences and T1 enhancement sequences. The size, location and texture of the tumor were measured and evaluated by MRI. Tumor sites were divided into the left cerebellar hemisphere, right cerebellar hemisphere and cerebellar vermis.

Tumors were classified as completely solid, a combination of solid and cystic (<50% of the tumor mass was cystic) or predominantly cystic ($\geq 50\%$ of the tumor mass was cystic) (21). The size of the tumor was indicated by the maximum diameter of the lesion, including the cystic portion surrounding the tumor. The diagnosis of preoperative hydrocephalus was determined by measurement of bilateral frontal horn diameters or intracranial diameters (Evans index) after CT or MRI. Postoperatively, patients were routinely followed up and regularly underwent imaging examinations, and CT or MRI of the brain could be performed at any time if the patient had any particular conditions.

Surgical procedure. A total of 76 patients with sporadic cerebellar hemangioblastoma underwent microsurgical resection of the tumor under general anesthesia. Different surgical approaches were chosen according to different parts of the tumor. The suboccipital ipsilateral approach, suboccipital midline approach or suboccipital supracerebellar approach were chosen mainly according to the location of the solid part of the tumor. Ventricular drainage was performed in 20 patients with obstructive hydrocephalus before surgery.

For tumors located in the superior vermis or inferior vermis, a prone position and suboccipital midline approach was used. For tumors located in the cerebellar hemispheres and extending toward the cerebellopontine angle, a lateral position and suboccipital lateral approach were used. A total of 13 patients were treated with a suboccipital midline approach and 63 patients with a suboccipital lateral approach. The extent of surgery was divided into gross total and partial excision. A total of 73 patients had gross total resection and 3 patients had partial resections. Furthermore, 8 patients underwent vascular embolization prior to tumor resection, and the others underwent direct craniotomy.

Tumor recurrence and prognosis were determined by the clinical presentation and imaging of the patients. The patients' clinical status was assessed using the modified Rankin scale (mRS) (22) (neurosurgeons followed patients up by telephone or outpatient appointments). Poor functional outcome was defined as mRS ≥ 2 .

Statistical analysis. Statistical analyses were performed using SPSS version 27 (IBM Corp.). Continuous variables were described as the mean \pm standard deviation and median with interquartile range, and count variables as incidence (percentage).

Results

Patient characteristics. From July 2012 to April 2021, 76 patients with sporadic cerebellar hemangioblastoma underwent one-stage surgical treatment at the Department of Neurosurgery, General Hospital of Northern Theater Command (Shenyang, China). From an initially considered 86 patients, 7 patients with von Hippel-Lindau (VHL) disease and 3 patients with incomplete medical records were excluded. Finally, 76 patients diagnosed with sporadic cerebellar hemangioblastoma were included in the present study. The clinical characteristics and various imaging features of the 76 patients with sporadic cerebellar hemangioblastoma are presented in Table I.

There were 76 patients in this study, including 42 males and 34 females. The age ranged from 23 to 72 years with a mean age of 46.4 ± 13.9 years. The median follow-up time was 52.5 (interquartile range, 20.0-74.5) months (range, 2-111 months). The time from the date of microsurgery or interventional embolization to the most recent clinical investigation was regarded as the follow-up period. Detailed information of the 76 patients is provided in Table SI.

The duration of clinical symptoms ranged from a minimum of 0.3 months to a maximum of 24 months before admission to hospital for diagnosis and the average was 3.1 ± 4.4 months.

Table I. Clinical manifestations and a variety of imaging features of the patients with sporadic cerebellar hemangioblastomas (n=76).

Item	Value
Mean symptom duration, months	3.1±4.4
Symptomatic presentations	
Headache	51 (67.1)
Dizziness/vertigo	50 (65.8)
Cerebellar ataxia	45 (59.2)
Nausea or vomiting	29 (38.2)
Blurred vision	9 (11.8)
Hearing disturbances	5 (6.6)
Extremities numbness	4 (5.3)
Diplopia	3 (3.9)
Movement disorder	1 (1.3)
Extremity paresis	1 (1.3)
Conscious disturbance	1 (1.3)
MRI features	
Obstructive hydrocephalus	20 (26.3)
Location of tumor	
Left cerebellar hemisphere	41 (53.9)
Right cerebellar hemisphere	22 (28.9)
Vermis	13 (17.1)
Composition of tumor	
Completely solid	11 (14.5)
Combined solid and cystic	22 (28.9)
Primarily cystic	44 (57.9)
Mean size of whole tumor, mm	37.9±11.1
Mean size of solid tumor, mm	13.6±12.5

Values are expressed as the mean ± standard deviation or n (%).

The difference in tumor size and location resulted in a variety of clinical symptoms, mainly including increased intracranial pressure, cerebellar dysfunction and cranial nerve damage. The most common symptoms were headache in 51 patients (67.1%), dizziness/vertigo in 50 patients (65.8%) and cerebellar ataxia in 45 patients (59.2%). Nausea or vomiting was the main complaint, which was reported in 29 patients (38.2%), followed by blurred vision (11.8%). Other neurologic deficits included hearing disturbances (6.6%), numbness of extremities (5.3%), diplopia (3.9%), movement disorder (1.3%), extremity paresis (1.3%) and conscious disturbance (1.3%).

Imaging manifestations. Of the 76 patients, 41 had lesions located in the left cerebellar hemisphere, 23 in the right cerebellar hemisphere and 13 in the vermis. Among 57 patients with cystic tumors, enhancement scans revealed small nodular enhancement at the margins of the cyst wall in 53 cases and ring-like enhancement of the cyst wall in 4 cases. A total of 11 patients had solid tumors, which were markedly enhanced on enhancement scans. DSA was performed in 11 patients prior to surgery and the major arteries of blood supply included the superior cerebellar artery, the anterior inferior

cerebellar artery, the posterior inferior cerebellar artery and the cerebromedial branch of the occipital artery. The tumor size was based on the maximum tumor diameter. In the present study, the maximum tumor diameter was 62.0 mm, the minimum tumor diameter was 15.0 mm and the average diameter was 37.9±11.1 mm. Prior to surgery, 20 of the 76 patients were found to have symptoms of hydrocephalus, which were confirmed by imaging.

Surgery and adjuvant therapy. A total of 73 patients (96.1%) underwent gross total resection. Furthermore, three patients underwent partial resection for a variety of reasons, including i) uncontrolled intraoperative hemorrhage, ii) to protect important neurologic function of the brainstem, and iii) a deep lesion that was difficult to detect even through a microscope. A comparison of preoperative and postoperative imaging in two cases is provided in Figs. 1 and 2. Of the 11 patients with cerebellar solid hemangioblastoma, 8 patients were treated with endovascular embolization followed by tumor resection 3 days later.

Follow-up. A total of 71 patients (83.1%) had a good prognosis (mRS <2) after the first surgery. However, 5 patients (6.6%) had significant neurological deficits (mRS ≥2) after surgery. Furthermore, 3 partially resected patients underwent postoperative radiotherapy and tumor recurrence in the original location was observed at 24, 41 and 20 months after surgery, respectively. Of these patients, 2 underwent a second surgery to completely remove the recurrent tumor. After the second surgery, their symptoms improved without permanent neurological deficits. The 2 patients continued to receive radiotherapy, which resulted in a reduction in tumor size and a resolution of symptoms, and therefore, observation was recommended. A total of 8 patients with preoperative embolization had no serious complications. Of these patients, two developed mild postoperative headache, which gradually resolved the next day (data not shown).

After several follow-ups, 8 cases were free of complications and recurrence. However, in three solid cases without preoperative endovascular embolization, postoperative cranial CT examination after complete tumor resection showed peripheral hemorrhage of 15-20 ml around the fourth ventricle (data not shown). No other patient showed any recurrence during the follow-up period.

Discussion

Hemangioblastomas are benign tumors of the central nervous system that frequently occur in the posterior cranial fossa, particularly the cerebellum. Hemangioblastomas tend to be sporadic and the clinical presentation and treatment strategy differ from those of patients with combined VLH disease (23-25). In addition, the composition of the tumor has been reported to be an important factor affecting the postoperative prognosis of hemangioblastoma (5). Solid hemangioblastomas have a higher risk of intraoperative hemorrhage and postoperative complications compared to cystic hemangioblastomas (26). Studies have indicated that patients with solid hemangioblastoma have a worse prognosis than patients with cystic hemangioblastoma (26,27).

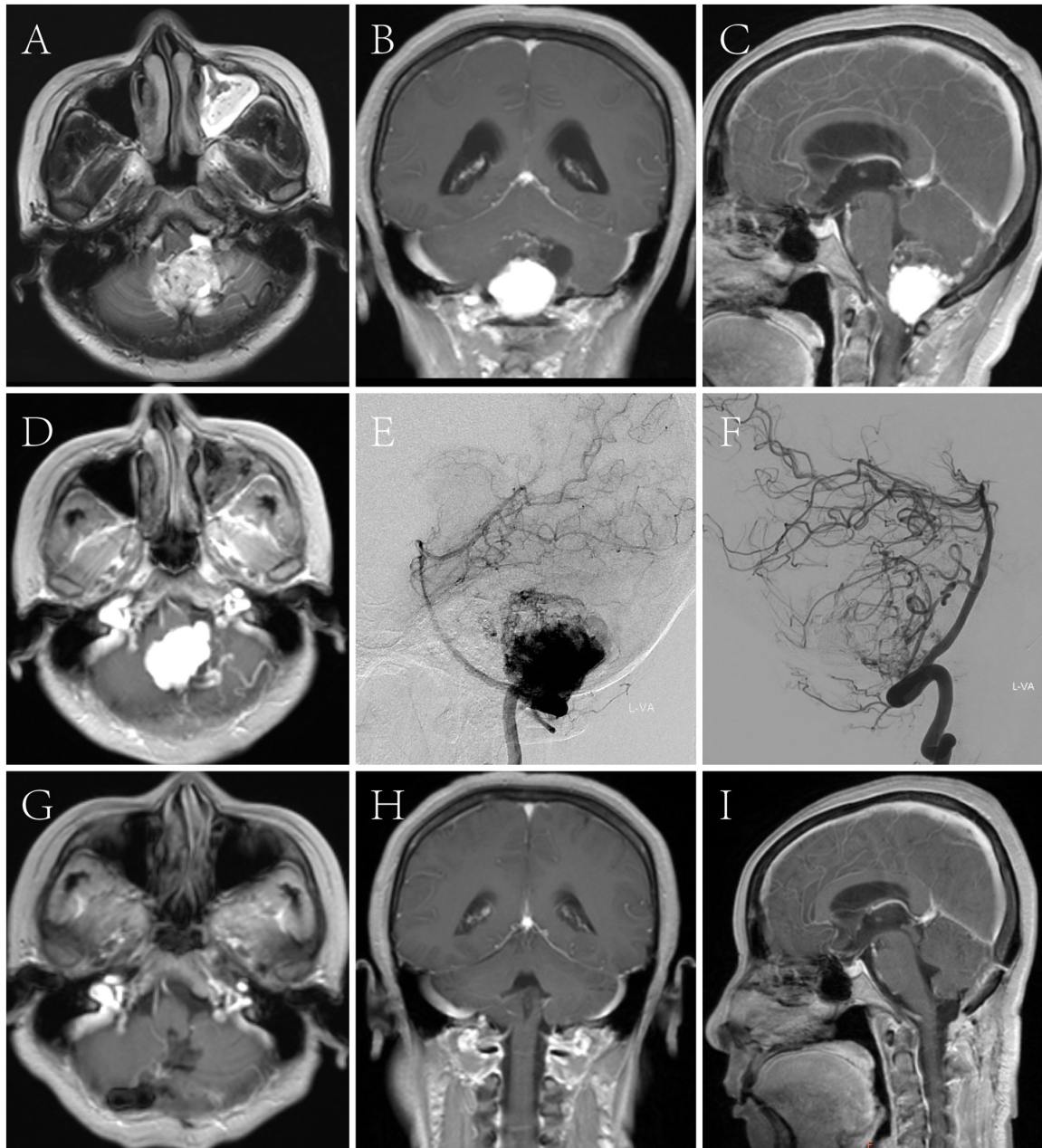


Figure 1. Imaging of a 45-year-old female with hemangioblastoma of the posterior cranial fossa. (A) Axial T2-weighted MR images showing a slightly longer T2 signal in the cerebellar vermis. Preoperative (B) coronal, (C) sagittal and (D) axial post-contrast T1-weighted MR images revealing a large, solid hemangioblastoma with significant reinforcement performance. (E and F) Digital subtraction angiography comparison (E) before and (F) after endovascular embolization of tumor-feeding arteries of solid hemangioblastoma. (H) Axial, (I) coronal and (G) sagittal post-contrast T1-weighted MR images demonstrated total resection of the tumor and no recurrence for two months of follow-up.

Due to the lack of characteristic clinical manifestations, CT and MRI examinations have become the main diagnostic methods for hemangioblastoma. According to the imaging features of sporadic cerebellar hemangioblastomas, it can be categorized into three types: Large cysts with reinforcing cystic walls or small nodules, a combination of solid and cystic, and completely solid tumors (5). Among them, the type of cyst with small nodules was the most common. Of the 76 cases included in the present study, 57 patients had cystic tumors confirmed by MIR imaging, accounting for 75.0% of all cases.

In the present study, the diameter of cystic hemangioblastomas was measured by combining the respective lengths of the cysts and nodules. Studies have indicated that

the size of the tumor correlates with the clinical presentation of the patient (22,28). In the present study, the mean diameter of the lesion was 37.9 ± 11.1 mm and it produced a significant mass effect in the posterior cranial fossa, leading to preoperative hydrocephalus. Among the 57 patients with cystic tumor, 16 patients presented with obstructive hydrocephalus, whose clinical symptoms included headache, vertigo, cerebellar ataxia and nausea or vomiting. In the present study, 54 cystic tumors were completely resected and the clinical symptoms of these patients improved significantly after surgery. A total of three cases of cystic tumors were partially resected and underwent postoperative radiotherapy; however, all of them recurred at different

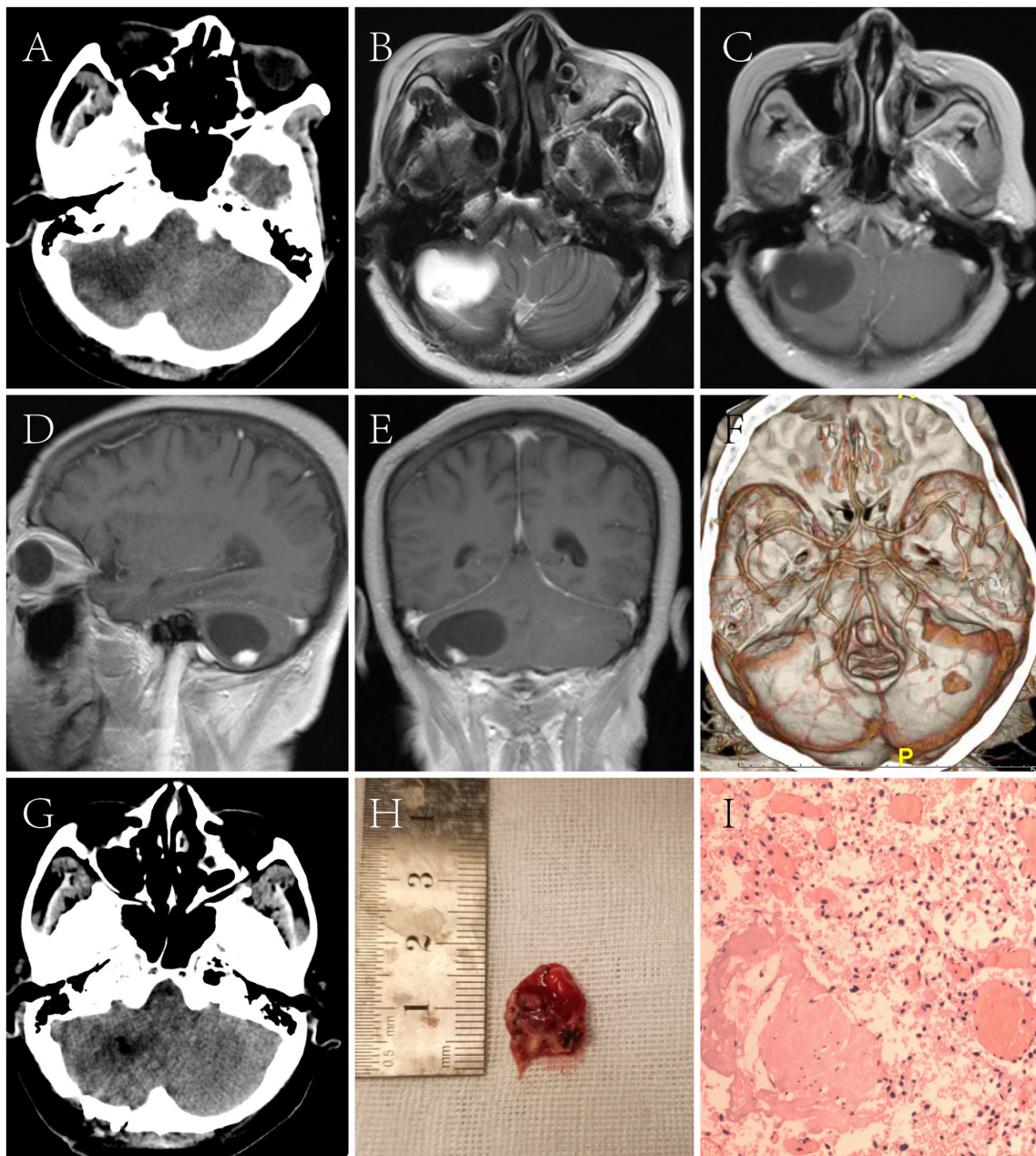


Figure 2. Imaging of a 50-year-old male with hemangioblastoma of the posterior cranial fossa. (A) Preoperative computed tomography demonstrating a large low-density area in the right cerebellar hemisphere. (B) Axial T2-weighted MR images showing a slightly longer T2 signal. Preoperative (C) axial, (D) sagittal and (E) sagittal post-contrast T1-weighted MR images showing a small hemangioblastoma tumor nodule with a large peritumoral cyst. (F) Preoperative CT angiography showing tumor nodules with rich blood supply. (G) Postoperative computed tomography demonstrating total resection of the tumor. (H) Gross appearance of excised tumor nodule with a round and red appearance. (I) Hematoxylin and eosin staining of the enhanced tumor nodules revealed a vascular tumor consisting of vacuolated stromal cells and thin-walled blood vessels, which supported the diagnosis of hemangioblastomas (magnification, x400).

time-points. Therefore, it was concluded that in cases of cystic hemangioblastoma, complete resection significantly reduces the rate of tumor recurrence. Drainage of cystic fluid and removal of reinforcing tumor nodules have also been shown to be the most appropriate treatment for cystic hemangioblastoma (22). As long as the tumor can be completely removed, most patients' symptoms will remain stable or ameliorative (29). Failure to completely resect the tumor usually leads to tumor recurrence (30). Therefore, the present analysis suggests that complete resection of the tumor at the time of initial surgery is essential to reduce the incidence of tumor recurrence and complications.

In addition, the present study included four cystic cases, which showed large non-enhancing cysts and surrounding enhancing cystic walls on enhanced MRI scans. Since intra-operative pathology confirmed that the reinforcing walls of the cystic tumors also contained tumor tissue, it was ultimately decided to carefully separate the tumor walls from the surrounding brain tissue and resect them completely, while preserving the critical neurological functional areas surrounding the cystic tumors as much as possible. Previous studies have also reported that the resection strategy for such cystic cases should be modified and refer to the surgical access for solid tumors, and that all components of the tumor, including

the wall nodules and the cyst itself, must be removed (4,31,32). In addition, because the significantly enhanced cystic tumor wall may be rich in capillaries, it has been suggested that preoperative needle aspiration biopsy should be avoided due to concerns about tumor hemorrhage (33,34). Therefore, it is vital in the surgical management of such cystic tumors to perform intraoperative pathology to determine clear tumor boundaries and thereby completely resect the enhanced cystic wall.

Solid hemangioblastomas show marked enhancement on MRI enhancement scans, which is the distinguishing imaging feature of solid cases. Therefore, the diagnosis of solid hemangioblastoma is not particularly difficult. However, the specific surgical treatment strategy for this type of tumor is still controversial.

Certain studies have argued that surgical outcomes for patients with solid hemangioblastomas are poor regardless of whether they have VHL or not (3,20). However, other studies have shown that surgical outcomes in patients with solid hemangioblastomas are not significantly different from those in cystic patients (35,36). In the present study, the majority of patients with solid hemangioblastomas achieved favorable clinical outcomes without serious complications or progression. Of the 11 patients with solid hemangioblastomas, 8 underwent endovascular embolization prior to surgical resection. During embolization, first, the primary tumor-supplying artery was carefully identified by multi-angle microangiography. Furthermore, it was ensured that the arteries selected for embolization would not affect the blood supply to important functional brain areas. The materials used for solid tumor embolization included a variety of substances, such as Onxy-18, flocculated sponge fragments and filament segments. Consistent with previous reports, we have made preliminary observations that the operative time for removal of solid hemangioblastoma was significantly shortened and intraoperative bleeding was more easily controlled after preoperative endovascular embolization (37). After several follow-ups, 8 cases were free of complications and recurrence. However, in three solid cases without preoperative endovascular embolization, postoperative cranial CT examination after complete tumor resection showed peripheral hemorrhage of 15-20 ml around the fourth ventricle. We believe that one of the most important reasons for the poor prognosis of these three patients may have been inadequate intraoperative hemostasis, which made intraoperative bleeding difficult to control in the absence of preoperative vascular embolization.

The safety and necessity of preoperative interventional embolization of solid hemangioblastomas is still controversial (35). Certain studies have shown that preoperative embolization is associated with high intracranial pressure and cerebral infarction (7,8). However, in the present study, eight patients with preoperative embolization had no serious complications. Of these patients, two developed mild postoperative headache, which gradually resolved the next day. During tumor resection, the numerous surgical techniques available appear to influence patient prognosis. First, the blood-supplying artery, the passing artery and the draining vein must be correctly determined. In general, the supplying artery and draining vein can be identified by looking at the vessel diameter, color, pulse or intraoperative ultrasound. In difficult cases, temporary closure clips are used to close the vessel to determine the nature of the vessel. If there is swelling

of the tumor, it is a draining vein; otherwise, it is a supplying artery. In cases of solid tumor adjacent to the brainstem, separation of the tumor-brainstem interface is critical to the success of the procedure. Since there is often a thin layer of edematous brain tissue between the tumor and the brainstem, the tumor should be cauterized along the brain tissue interface with low-power bipolar electrocoagulation under neurophysiological monitoring and the operative field should be continuously irrigated to minimize heat conduction injury. Furthermore, the movements should be gentle so as to not cause brainstem displacement by excessive intraoperative pulling of the tumor. Most importantly, it was required to perform complete tumor resection instead of removing the tumor piece by piece, which could lead to intraoperative bleeding and unpredictable consequences. The conclusion of the present study is consistent with those of previous studies, namely that preoperative embolization of solid hemangioblastomas is safe and necessary, and complete tumor resection results in a good prognosis (37,38).

In the present study, there were only 76 patients. Next, multicenter case reports should be collected and a detailed prognostic analysis for each type of case should be performed.

In conclusion, total microsurgical resection is essential to improve the health status of patients with sporadic cerebellar cystic hemangioblastoma. In addition, as the safety of vascular intervention techniques continues to improve, preoperative embolization of arteries supplying solid hemangioblastomas can reduce intraoperative bleeding and improve prognosis.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

GH: Conceptualization, data curation, editing/drafting/writing the manuscript, revising the manuscript (for intellectual content), language editing; BZ and YL: Data curation, software, visualization, obtaining materials, checking and confirming the authenticity of raw data, language editing; YW: Software, visualization, language editing, confirming the authenticity of raw data, providing general supervision; YH: Adjustment of conceptualization and study design, writing and critical revision of the manuscript; XC: Data review, collation and proofreading, data analysis and further processing, work coordination. All of the authors have read and agreed to the final version of the manuscript.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the General Hospital of Northern Theater Command (Shenyang,

China; approval no. 2021-135; August 2, 2021). All processes were performed in accordance with the Declaration of Helsinki and local ethical policies.

Patient consent for publication

Consent for publication was obtained from the two patients whose images are shown in Figs. 1 and 2.

Competing interests

The authors declare that they have no competing interests.

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