Original Article

En Bloc Resection for Spinal Cord Hemangioblastomas: Surgical Technique and Clinical Outcomes

Xiaofeng Chen[1,2,3,*] Hua Guo[1,*] Jianli Zhang[4,*] Junyi Ye[5] Shurong Wang[6] Haiping Jiang, PhD, MD[7] Qingchun Mu, PhD, MD[8] Xiaoxiong Wang, PhD, MD[1,2,3]

[1] Department of Neurosurgery, The First Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang, China
[2] Institute of Brain Science, Harbin Medical University, Harbin, Heilongjiang, China
[3] Institute of Neuroscience, Sino-Russian Medical Research Center, Harbin Medical University, Harbin, Heilongjiang, China
[4] Department of Neurology, Xiamen Fifth Hospital, Xiamen, Fujian, China
[5] Department of Neurosurgery, The Affiliated Lihuili Hospital of Ningbo University, Ningbo, Zhejiang, China
[6] Department of Neurology, Hainan Medical University, Haikou, Hainan, China
[7] Department of Neurosurgery, The Affiliated Hospital of Guangdong Medical University, Zhanjiang, Guangdong, China
[8] Department of Neurosurgery, The People's Hospital of Gaozhou of Guangdong Medical University, Maoming, Guangdong, China

Address for correspondence Xiaoxiong Wang, PhD, MD, Department of Neurosurgery, The First Affiliated Hospital of Harbin Medical University; Institute of Brain Science and Institute of Neuroscience, Sino-Russian Medical Research Center, Harbin Medical University, No. 23 Youzheng Street, Nangang District, Harbin 150001, China (e-mail: steven_xiaoxiong@yeah.net).
Haiping Jiang, PhD, MD, Department of Neurosurgery, The Affiliated Hospital of Guangdong Medical University, Zhanjiang 524001, Guangdong, China (e-mail: 1404266177@qq.com).
Qingchun Mu, PhD, MD, Department of Neurosurgery, The People's Hospital of Gaozhou of Guangdong Medical University, Maoming 525299, Guangdong, China (e-mail: muq@hainmc.edu.cn).

J Neurol Surg A Cent Eur Neurosurg

Abstract

Background Spinal cord hemangioblastomas are rare benign and highly vascular tumors that develop either sporadically or as part of von Hippel–Lindau (VHL) disease. Generally, complete resection without significant neurologic deficit remains considerably challenging due to the risk of massive bleeding. The current study therefore aimed to describe en bloc resection of spinal cord hemangioblastomas according to the typical anatomical structures of peripheral lesions and evaluate the neurofunctional prognosis of this technique.

Methods A total of 39 spinal cord hemangioblastomas from a series of 19 patients who underwent en bloc resection were retrospectively analyzed. In all cases, clinical and radiologic characteristics, as well as surgical tenets, were retrospectively determined and analyzed. Short- and long-term outcomes were analyzed using the McCormick grade and Odom's criteria. Factors significantly associated with poor neurologic function after en bloc resection were also determined.

Results All 39 spinal cord hemangioblastomas, including 28 intramedullary, 2 intramedullary–extramedullary, and 9 extramedullary lesions, were located dorsally or dorsolaterally (100.0%). The most common lesion location was the thoracic segment (53.8%), with most of the lesions being accompanied by syringomyelia (94.7%). Long-term follow-up (mean: 103 ± 50.4 months) for prognosis determination revealed that

Keywords
- spinal cord hemangioblastomas
- en bloc resection
- surgical technique
- prognosis
- retrospective analysis

* *These authors contributed equally to this work.*

received
March 24, 2023
accepted after revision
August 31, 2023

DOI https://doi.org/10.1055/s-0043-1776707.
ISSN 2193-6315.

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

88.2% (15/17) of all cases had stable or improved neurofunctional outcomes according to the McCormick grade and Odom's criteria. Only one case with VHL disease developed recurrence 4 years after surgery. Additionally, statistical analysis showed that VHL disease was an independent prognostic factor associated with deteriorating neurologic function ($p = 0.015$).

Conclusions En bloc resection facilitated satisfactory long-term functional outcomes in patients with spinal cord hemangioblastomas. Given that VHL disease was identified as a predictor of poor long-term outcomes, regular long-term follow-up of patients with VHL-associated spinal cord hemangioblastoma seems necessary.

Introduction

Spinal cord hemangioblastomas are uncommon benign tumors that are highly vascularized. They account for 2 to 15% of intramedullary spinal cord tumors.[1] They can occur as sporadic lesions or as part of von Hippel–Lindau (VHL) disease,[1,2] a multicentric disease caused by an autosomal dominant tumor suppressor gene mutation on chromosome 3p25.3.[3] The loss of VHL protein (pVHL) induces the development of various tumors or cysts, including central nervous system lesions, renal cysts, renal cell carcinomas, pheochromocytomas, pancreatic tumors, and epididymal cystadenoma.[4,5] Sporadic tumors account for 70 to 80% of spinal cord hemangioblastomas in the cases with VHL-associated central nervous system disease.[6,7] Despite being histologically benign, spinal hemangioblastomas can cause significant neurologic morbidity given its highly brittle and vascularized pathology.[8]

The optimal management strategy for spinal cord hemangioblastomas is gross total surgical resection without significant neurologic deficit through the microsurgical procedures. Although a few studies have reported on the surgical treatment of spinal cord hemangioblastomas,[6,8] the relationship between surgical techniques and clinical outcomes has been rarely described in the literature considering the rarity of the disease. To address these issues, 19 consecutive patients with spinal cord hemangioblastoma who underwent en bloc resection in a single institute were retrospectively evaluated, focusing on the clinical presentations, preoperative imaging, surgical management strategies, and functional outcomes.

Materials and Methods

Clinical Case Selection

This study retrospectively collected data from 19 consecutive cases of spinal cord hemangioblastomas at the Neurosurgery department of the First Affiliated Hospital of Harbin Medical University from January 2006 to December 2022. We evaluated the clinical data of all 19 cases, including clinical features, preoperative and postoperative McCormick classification, postoperative neurologic outcomes, and recurrence rates. Moreover, cases with VHL syndrome were diagnosed using the Melmon criteria.[9] Patients who received surgical treatment for spinal hemangioblastomas and had sufficient pathologic material and clinical information were included in the study, whereas those who underwent preoperative embolization or were followed up for less than 6 months were excluded from the study.

Clinical Evaluation

Neurologic function was examined according to the preoperative and postoperative McCormick classification (grades I–IV), which is presented in ►**Table 1**. We compared the pre- and postoperative neurofunctional outcomes (improved, stabilized, and worsened), including new or worsened motor or sensory deficits and bladder/bowel dysfunction. Odom's criteria were used to evaluate the general postoperative clinical outcomes of each patient (excellent, good, fair, and poor). Of the 19 cases of spinal cord hemangioblastomas included in the study, long-term follow-up for symptoms and functional outcomes was performed in 17 (2 cases who were lost to follow-up) cases through telephonic interviews and outpatient clinical records.

Table 1 McCormick's clinical grading scale for neurologic function

Grade	Definition
I	Neurologically normal; mild focal deficit not significantly affecting function of the involved limb; mild spasticity or reflex abnormality; normal gait
II	Presence of sensorimotor deficit affecting function of the involved limb; mild to moderate gait difficulty; severe pain or dysesthetic syndrome impairing patient's quality of life; still functions and ambulates independently
III	More severe neurologic deficit; requires cane/brace for ambulation or has significant bilateral upper extremity impairment; may or may not function independently
IV	Severe deficit; requires wheelchair or cane/brace with bilateral upper extremity impairment; usually not independent

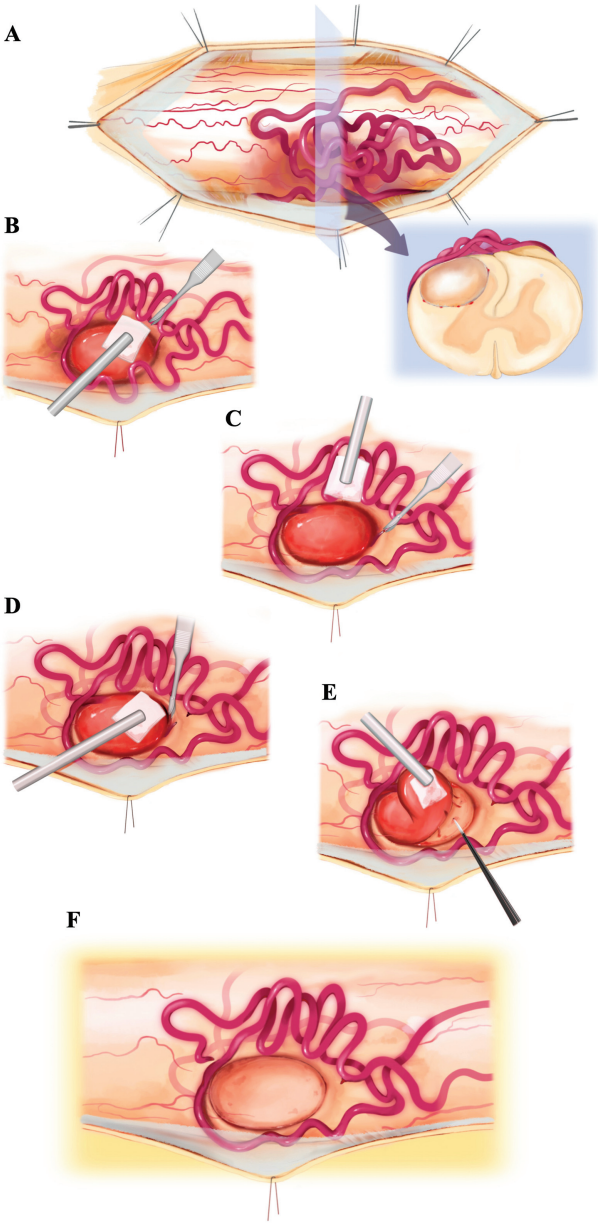

Fig. 1 Schematic steps for the en bloc resection of spinal cord hemangioblastomas. This schematic pattern describes the intradural steps. (**A**) Under the operating microscope, the surface component of the hemangioblastoma is identified. (**B**) The tumor is exposed by reflecting the overlying vessels with gentle traction. The junction between the pia and the tumor capsule is identified and incised using microscissors. (**C**) Small draining veins are cauterized and divided, leaving one or two major draining veins intact until the end of the tumor resection. (**D**) Dissection of the tumor is continued deeper and circumferentially at the tumor capsule–spinal cord interface using bipolar microforceps. (**E**) After completing the circumferential dissection of the tumor margin, the inferior pole to the hemangioblastoma is reflected with gentle suction on cotton pieces to expose the underlying vessels. (**F**) Finally, en bloc resection of the tumor was performed.

Imaging Evaluation

In all 19 cases, pre- and postoperative contrast-enhanced magnetic resonance imaging (MRI) and sagittal T2-weighted MRI sequences were used to evaluate the location of the tumor. The lesions were classified as intramedullary, intramedullary–extramedullary, or extramedullary based on the intraoperative observations.[10,11] Existing syringomyelias were evaluated using T2-weighted MRI sequences. En bloc resection was defined as complete tumor resection based on intraoperative observations combined with postoperative contrast-enhanced MRI.

Surgical Procedure for en Bloc Resection

All 19 cases underwent conventional laminoplasty via the median posterior approach. All the tumors were removed via microscopic en bloc resection after a midline incision of the spinal dura. The arachnoid was opened and secured to the edges of the dura. The methods used for spinal cord hemangioblastoma resection differed from those used in common intramedullary spinal cord tumor resection (e.g. astrocytomas or ependymomas) via dorsal midline myelotomy. Given that a majority of the tumors derived from the spinal pia mater were located on the dorsal or dorsolateral surface of the spinal cord, the anatomical structures of the tumors were the fundamental basis of the en bloc resection strategy and technique. Based on these characteristics, en bloc resection was performed through careful microsurgical dissection with minimal blood loss. The key steps in en bloc resection of spinal cord hemangioblastoma include the following: (1) separating the overlying veins of the surface of the tumor and protecting the major draining veins during microsurgical dissection; (2) cauterizing the feeding vessels and small draining veins crossing the well-defined plane between the tumor and the surrounding normal pia and dividing them using a microdissector; (3) using microscissors to incise tumor capsules apart from the surrounding normal pial interface; (4) separating the tumor–spinal cord interface with microscissors or bipolar forceps; (5) exposing, coagulating, and transecting each feeding artery passing through and from the tumor capsule before surgical resection; and (6) preserving the main draining veins until the end of the whole progression of en bloc resection. The spinal dura was surgically sutured in a watertight fashion with a running locked 6–0 silk suture (►**Fig. 1**).

Statistical Analysis

Prognostic factors associated with neurologic outcomes, including sex, age at surgery, symptom duration, syringomyelia, VHL disease, preoperative McCormick grade, and intramedullary tumor location, were investigated through multivariable logistic regression analysis and Fisher's exact test using SPSS 19.0 (International Business Machines Crop.), with a p value of <0.05 indicating statistical significance.

Results

Clinical Characteristics

Nineteen patients, including 12 males and 7 females (ratio 1.7:1), underwent microsurgical en bloc resection for spinal cord hemangioblastomas. The mean preoperative age was 43.3 ± 16.8 years (range: 19–74 years). The mean follow-up duration was 103 ± 50.4 months (range: 6–192 months). A

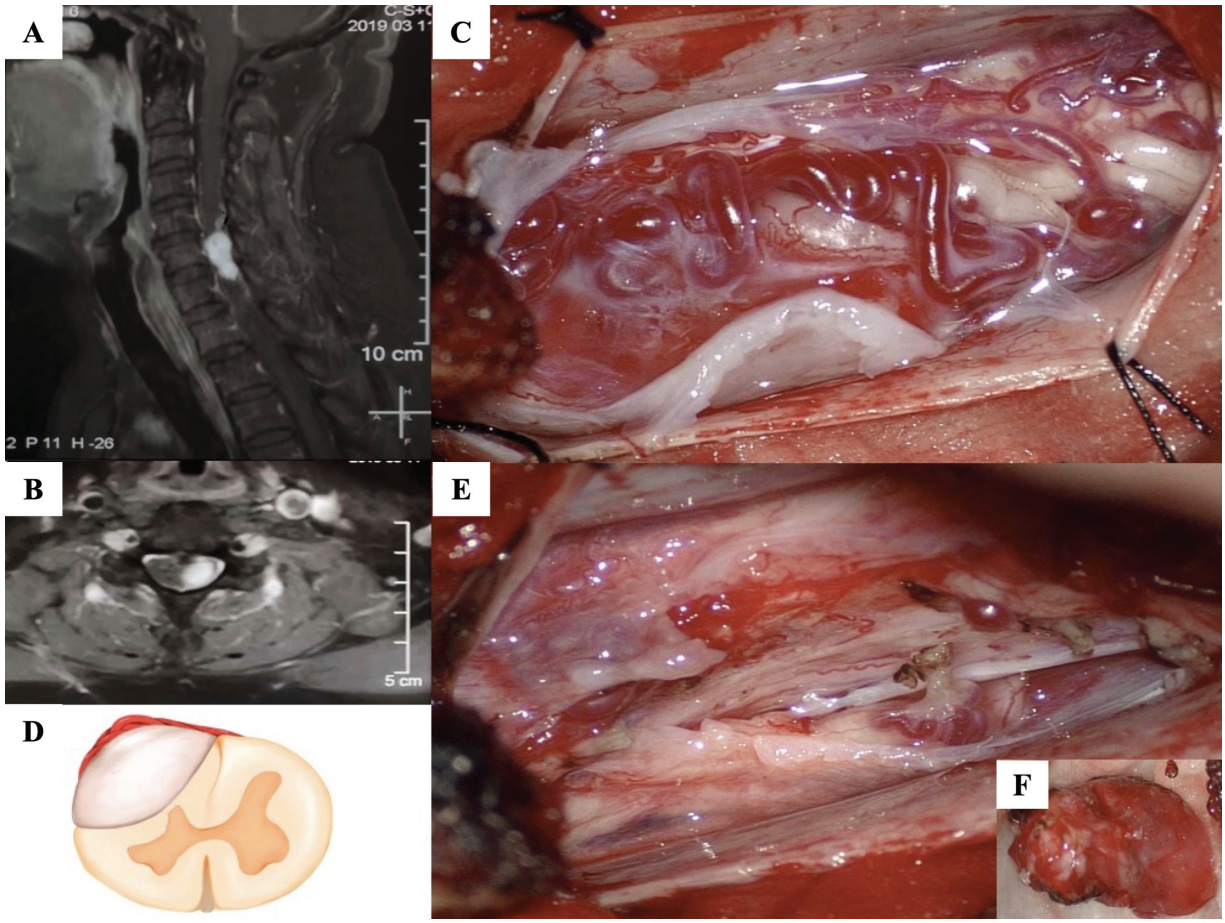

Fig. 2 En bloc resection of a cervical spinal cord hemangioblastoma. Contrast-enhanced T1-weighted sagittal (**A**) and axial (**B**) magnetic resonance imaging (MRI) demonstrating a densely enhancing dorsolateral spinal cord lesion at the C6–C7 level. (**C**) Axial MR images of the extramedullary hemangioblastoma. (**D**) Intraoperative image showing a well-circumscribed, superficially dorsolateral hemangioblastoma localized in the extramedullary part. (**E**) Intraoperative image after the removal of the hemangioblastoma. (**F**) The whole tumor is removed via en bloc resection.

total of 27 en bloc resections for 39 spinal cord hemangioblastomas were performed (►**Figs. 2** and **3**). Eight of 19 (42.1%) patients with tumors located in the thoracic segments satisfied the diagnostic criteria for VHL disease. The tumors in these patients were associated with pancreatic tumors, renal cysts, pheochromocytomas, and renal cell carcinomas. Of the eight cases, two had a positive family history of VHL disease. The most common locations of these hemangioblastomas were the thoracic segments (21/39, 53.8%), followed by the cervical segments (16/39, 41.0%) and lumbar segments (2/39, 5.1%), as shown in ►**Fig. 4**. All these tumors were located dorsally or dorsolaterally. Of the 39 resected tumors, 28 (71.7%) were completely intramedullary, 2 (5.1%) were intramedullary–extramedullary, and 9 (23.1%) were primarily extramedullary (►**Table 2**). Of the 19 patients who underwent microsurgical en bloc resection for spinal cord hemangioblastomas, 18 (94.7%) were accompanied by obvious syringomyelia on T2-weighted MRI sequences (►**Table 2**).

Short-Term Clinical Outcome Evaluation

The postoperative neurologic function of all 19 patients were evaluated and compared to the preoperative findings. Among the 12 patients whose neurologic function could be classified as McCormick's grade II, 4 improved their neurologic function to McCormick's grade I after surgery, 7 showed no improvements in neurologic function, and 1 showed a deterioration in neurologic function to McCormick's grade III (►**Table 3**). Based on Odom's criteria, 4/19 cases (21.1%) had excellent immediate clinical outcomes, whereas 11/19 cases (57.8%) showed fair outcomes. Nevertheless, 4/19 cases (21.1%) showed poor outcomes (►**Table 4**).

Long-Term Clinical Outcome Evaluation

Among the 19 cases studied, 17 cases (2 cases were lost to follow-up) were followed up for the long term. During the long-term follow-up, neurologic function improved in 8/17 cases (47.05%), remained stable in 7/17 cases (41.1%), and deteriorated in 2/17 cases (11.7%). Overall, the median long-term follow-up McCormick grade (mean: 103 ± 50.4 months after surgery) was grade I (ranging from grade I to IV) as seen in ►**Table3**. Meanwhile, 2/17 cases (11.7%) showed excellent clinical outcomes, 8/17 cases (47.1%) exhibited good clinical outcomes, and 5/17 cases (29.4%) had fair outcomes. Poor clinical outcomes were observed in 2/17 cases (11.7%), as seen in ►**Table 4**.

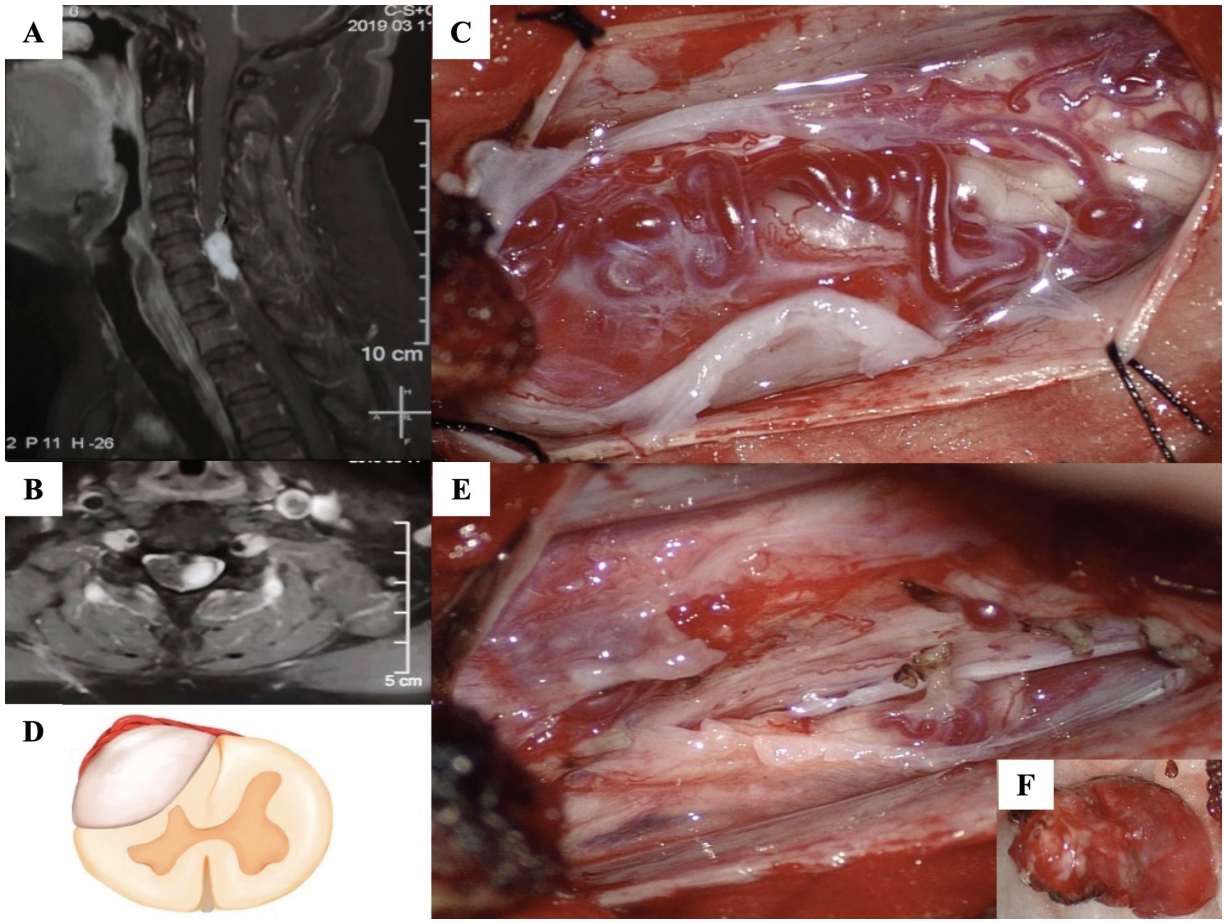

Fig. 3 En bloc resection of a thoracic spinal cord hemangioblastoma. Contrast-enhanced T1-weighted sagittal (**A**) and axial (**B**) magnetic resonance imaging (MRI) demonstrating a small densely enhancing dorsal spinal cord lesion at the T5–T6 level. (**C**) Axial MR images for the intramedullary hemangioblastoma. (**D**) Intraoperative image showing only a small proportion of the tumor localized on the surface of the spinal cord and the large tumor proportion localized in the intramedullary part. (**E**) Intraoperative image showing complete T5–T6 level tumor resection after circumscribed pial detachment and polar myelotomies. (**F**) The whole tumor is removed via en bloc resection.

Tumor Recurrence and Risk Factors

Tumor recurrence was evaluated at the last follow-up using contrast-enhanced T1-weighted MRI sequences. Postoperative recurrence was observed in one case within 4 years after surgery. This patient had VHL disease with multiple lesions and underwent a total of seven surgeries. Long-term neurologic function was significantly diminished in our VHL disease cases ($p = 0.015$), as seen in ►**Table 5**. According to the multivariable logistic regression analysis, other factors, including sex, age, duration of symptom, presence of syringomyelia, preoperative McCormick grade, and intramedullary tumor type, did not predict the long-term neurologic outcomes.

Discussion

Epidemiology and Clinical Features

Spinal cord hemangioblastomas are rare, benign neoplasms consisting of stromal cells and abundant capillaries.[12] Unfortunately, recent reports regarding their clinical features, surgical procedures, and neurologic function outcomes have been limited. These tumors are more common among male patients, with an average age of symptom onset of around 40 years.[1,8,13] In our study, the sex deviation and the average age of our patients were consistent with previous reports.[8] Approximately 20 to 45% of these tumors were associated with VHL disease,[6] and in our study, eight cases (42.1%) met the criteria for VHL disease. Although these tumors can occur anywhere in the spinal cord, the most common locations in our study were the thoracic segments (21/39, 53.8%), followed by the cervical segments (16/39, 41.0%),[11,14] which is consistent with previous reports.[11,14,15] Kanno et al found that tumors associated with VHL diseases were more frequently located in the thoracic segments.[13] In our study, spinal cord hemangioblastomas associated with VHL syndromes also tended to occur at the thoracic segments. Consistent with published results, most of the lesions (71.7%) in our study were intramedullary tumors associated with syringomyelia (94.7%).[7,15] The predominant symptoms were preoperative sensory abnormalities (14/19, 73.6%), pain (6/19, 31.6%), and motor deficits (15/19, 78.9%), with bladder/bowel dysfunctions occurring less frequently (2/19, 10.5%). All clinical findings were consistent with previous studies.[1,13]

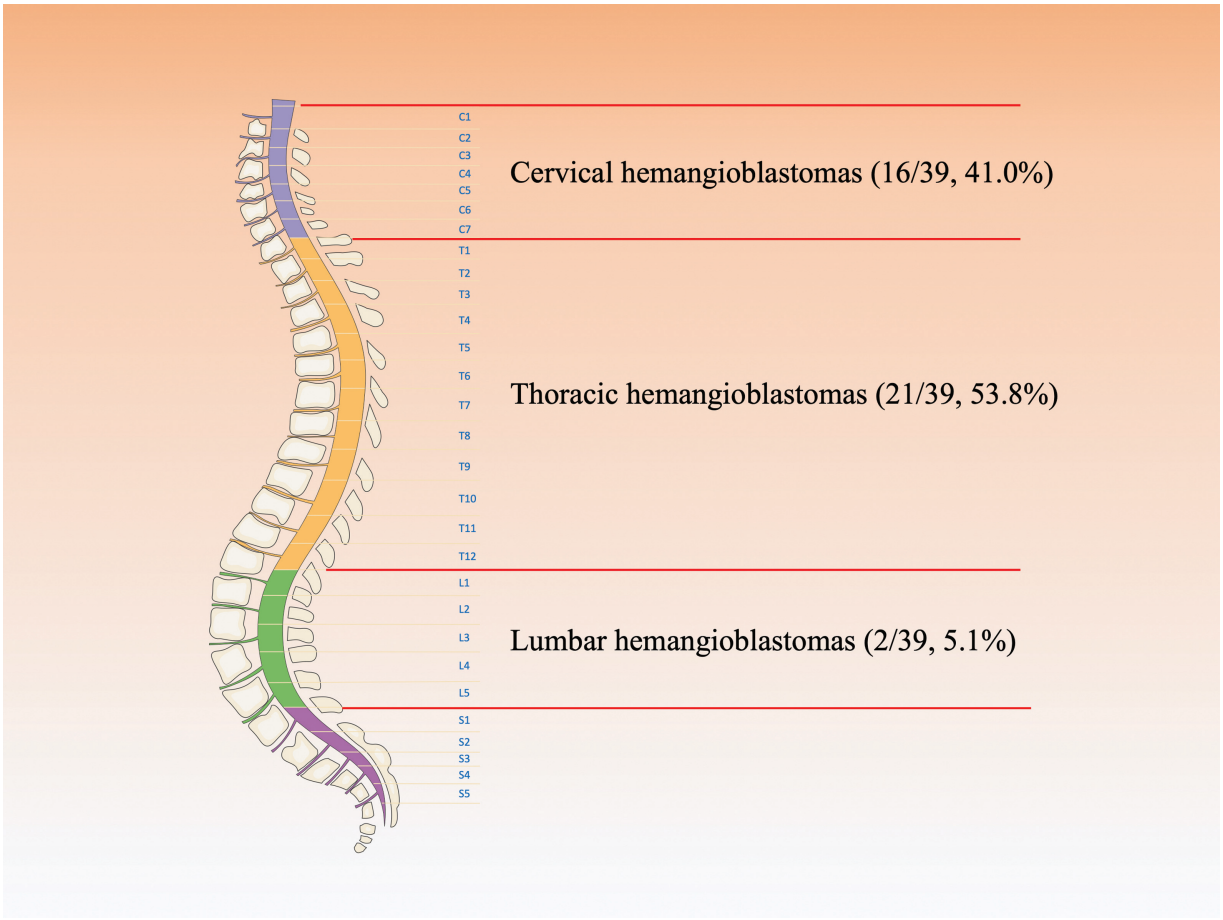

Fig. 4 Distribution of the spinal cord hemangioblastomas according to the spinal segments. The cervical segments (16/39, 41.0%), thoracic segments (21/39, 53.8%), and lumbar segments (2/39, 5.1%).

Surgical Procedures and Outcomes

In general, spinal cord hemangioblastomas are encapsulated, noninvasive, benign tumors for which complete resection is considered the optimal treatment in most cases. However, gross resection of these tumors without significant neurologic dysfunctions remains challenging given the massive intraoperative bleeding. The principal reason for profuse intraoperative bleeding includes the delicate capsule around the lesions and improper handling of the feeding arteries and draining veins.[6,16] In a recent study, Lonser et al recommended gross resection of spinal cord hemangioblastomas.[5] Given our surgical experience, surgical techniques for these tumors differ from those used for other intramedullary spinal cord tumors such as astrocytomas or ependymomas. Gross resection of these tumors should be handled just like arteriovenous malformations: clean separation of the tumor–tissue interface, preservation of venous drainage, and complete resection. We emphasize two critical intraoperative points. First, some major draining veins must be protected until the end of lesion resection. Early venous transection may cause lesion rupture and unnecessary bleeding. Second, to prevent intraoperative bleeding and develop the tumor–spinal cord interface plane, the spinal cord hemangioblastoma capsule must be protected until the end of the lesion resection. We develop this cleavage plane between the tumor and the spinal cord using bipolar forceps, thereby preventing coagulation of the capsule. En bloc resection is the optimal therapeutic option for spinal cord hemangioblastomas given that incomplete removal or piecemeal resection of lesions may promote significant morbidity and mortality. Above all, massive intraoperative bleeding remains the main threat and can lead to significant reduction in postoperative neurologic function due to damage to the surrounding normal tissues caused by obscuration of the intraoperative area. Minimizing intraoperative bleeding and preserving the hemangioblastoma capsule are two key factors affecting successful en bloc resection.

Previous studies have reported poor neurologic outcomes in up to 42.3% of cases in the short-term postoperative period, with a permanent neurologic dysfunction rate of 16.7%.[1,8,11] In our study, the incidence of new and worsened neurologic problems was 21.1 and 11.7% during the short- and long-term postoperative follow-up, respectively. We found that 88.2% of the patients were stable or showed improved clinical outcomes according to Odom's criteria (the mean follow-up of 103 ± 50.4 months). Tumor recurrence has been reported in approximately 20% of cases, particularly in younger patients with VHL syndrome.[2]

Table 2 Clinical and imaging characteristics of 19 cases with 39 resected spinal cord hemangioblastomas

Clinical characteristics	No. (%)
M/F	12 (63.2%)/7 (36.8%)
Mean age (y)	43.3 ± 16.8
Symptoms	
Sensory dysfunction	14 (73.6%)
Pain	6 (31.6%)
Motor deficit	15 (78.9%)
Bladder/bowel dysfunction	2 (10.5%)
VHL disease	8 (42.1%)
Tumors at the spinal segments	
Cervical segment	16 (41.0%)
Thoracic segment	21 (53.8%)
Lumbar segment	2 (5.1%)
Tumor relation to the spinal cord	
Completely intramedullary	28 (71.7%)
Intramedullary–extramedullary	2 (5.1%)
Primarily extramedullary	9 (23.1%)
Tumor location	
Dorsal or dorsolateral	39 (100.0%)
With syringomyelia	18 (94.7%)
Mean follow-up (mo)	103 ± 50.4

In our study, we performed circumferential surgical dissection in all cases allowing for en bloc resection as described. The participants included in the current study had a mean follow-up duration of 10 years. Tumor recurrence was observed in only one patient with VHL syndrome. This patient developed new recurrent lesions after en bloc resection, leading to a recurrence rate of 5.3% at a median follow-up duration of 4 years. As such, our study showed that en bloc resection was associated with prolonged and desirable clinical outcomes.

Prognostic Factors of Postoperative Neurologic Outcomes

Prognostic factors for postoperative neurologic outcomes in patients with spinal cord hemangioblastomas are still unclear. Previous studies have suggested that lesion volume, lesion location, and peritumoral edema may be associated with poor clinical outcomes,[1,7] whereas others have found that subtotal resection may result in worse outcomes due to extensive bleeding.[8,17] Parker et al showed that patients with VHL disease tended to have more unfavorable neurologic function than those without VHL during follow-up.[11,18] In our study, 50% of the patients with VHL-associated spinal cord hemangioblastomas showed a deterioration in McCormick's grade, whereas all cases of sporadic spinal cord hemangioblastoma had a stable or improved postoperative McCormick grade. Multivariable logistic regression analysis revealed that VHL disease was an independent predictor for poor long-term neurologic functions.

Table 3 The evaluation of short- and long-term clinical outcomes in preoperative and postoperative neurologic status according to the McCormick classification

Parameters	No. of patients		
	Before surgery	Short-term outcomes	Long-term outcomes
No. of patients	19	19	17
McCormick's grade			
Grade I	6	7	12
Grade II	12	9	3
Grade III	0	2	1
Grade IV	1	1	1

Table 4 Clinical outcomes at different follow-up periods based on Odom's criteria

Outcomes	No. of patients (%)	
	Short-term outcomes (1 wk post-op, $n = 19$)	Long-term outcomes (1–16 y post-op, $n = 17$)
Excellent	0 (0.0%)	2 (11.7%)
Good	4 (21.1%)	8 (47.1%)
Fair	11 (57.8%)	5 (29.4%)
Poor	4 (21.1%)	2 (11.7%)

Note: Excellent: All preoperative symptoms relieved and abnormal findings improved.
Good: There was minimal persistence of preoperative symptoms, and abnormal findings were unchanged or improved.
Fair: There was definite relief of some preoperative symptoms; other symptoms were unchanged or slightly improved.
Poor: Symptoms and signs were unchanged or worse.

Table 5 Factors associated with clinical outcomes following en bloc resection

Factors	*p* value
Sex	0.800
Ages	0.982
Duration of symptoms	0.963
Presence of syrinx	0.923
VHL disease	0.015
Complete intramedullary tumors	0.389
Preoperative McCormick grade	0.672

Abbreviation: VHL, von Hippel–Lindau.
Note: Categorized functional outcomes according to McCormick's score: 0 = improved or stable; 1 = deteriorated.

Conclusion

In conclusion, we advocate radical en bloc resection for spinal cord hemangioblastomas considering the relatively favorable clinical prognosis observed in the current study. En bloc resection is beneficial for reducing intraoperative bleeding and completing gross total tumor resection. However, given the risk of tumor recurrence, we recommend regular long-term follow-up among patients with VHL disease.

Ethics approval

The study was approved by the ethics committee of the First Affiliated Hospital of Harbin Medical University. All procedures performed in studies involving human participants were in accordance with the ethical standards of the First Affiliated Hospital of Harbin Medical University and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Author Contributions

X.C., H.G., and J.Z. contributed to the conceptualization, design, methodology, and writing and editing of the manuscript. S.W. and J.Y. were responsible for formal analysis and provided administrative, technical, or material support. X. W., H.J., and Q.M. contributed to the methodology and supervision of the study. They also contributed to writing, reviewing, editing, and revision of the manuscript.

Funding

This work was supported by the National Natural Science Foundation of China (81902554), Postdoctoral Science Foundation of Heilongjiang Province (LBH-Z19076 and LBHZ19190), Heilongjiang Welfare Fund Organization of Disabled Persons (HJ2022-1), Youth Foundation of the First Affiliated Hospital of Harbin Medical University (HYD2020YQ0018), Fujian Provincial Department of Science and Technology Guidance Program (No. 2022D031).

Conflict of Interest

None declared.

References

1 Mehta GU, Asthagiri AR, Bakhtian KD, Auh S, Oldfield EH, Lonser RR. Functional outcome after resection of spinal cord hemangioblastomas associated with von Hippel-Lindau disease. J Neurosurg Spine 2010;12(03):233–242
2 Conway JE, Chou D, Clatterbuck RE, Brem H, Long DM, Rigamonti D. Hemangioblastomas of the central nervous system in von Hippel-Lindau syndrome and sporadic disease. Neurosurgery 2001;48(01):55–62, discussion 62–63
3 Latif F, Tory K, Gnarra J, et al. Identification of the von Hippel-Lindau disease tumor suppressor gene. Science 1993;260(5112):1317–1320
4 Vortmeyer AO, Gnarra JR, Emmert-Buck MR, et al. von Hippel-Lindau gene deletion detected in the stromal cell component of a cerebellar hemangioblastoma associated with von Hippel-Lindau disease. Hum Pathol 1997;28(05):540–543
5 Lonser RR, Glenn GM, Walther M, et al. von Hippel-Lindau disease. Lancet 2003;361(9374):2059–2067
6 Mandigo CE, Ogden AT, Angevine PD, McCormick PC. Operative management of spinal hemangioblastoma. Neurosurgery 2009;65(06):1166–1177
7 Kanno H, Yamamoto I, Nishikawa R, et al; Clinical VHL Research Group in Japan. Spinal cord hemangioblastomas in von Hippel-Lindau disease. Spinal Cord 2009;47(06):447–452
8 Deng X, Wang K, Wu L, et al. Intraspinal hemangioblastomas: analysis of 92 cases in a single institution: clinical article. J Neurosurg Spine 2014;21(02):260–269
9 Melmon KL, Rosen SW. Lindau's disease. review of the literature and study of a large kindred. Am J Med 1964;36:595–617
10 Imagama S, Ito Z, Wakao N, et al. Differentiation of localization of spinal hemangioblastomas based on imaging and pathological findings. Eur Spine J 2011;20(08):1377–1384
11 Siller S, Szelényi A, Herlitz L, Tonn JC, Zausinger S. Spinal cord hemangioblastomas: significance of intraoperative neurophysiological monitoring for resection and long-term outcome. J Neurosurg Spine 2017;26(04):483–493
12 Lee DK, Choe WJ, Chung CK, Kim HJ. Spinal cord hemangioblastoma: surgical strategy and clinical outcome. J Neurooncol 2003;61(01):27–34
13 Roonprapunt C, Silvera VM, Setton A, Freed D, Epstein FJ, Jallo GI. Surgical management of isolated hemangioblastomas of the spinal cord. Neurosurgery 2001;49(02):321–327, discussion 327–328
14 Xu QW, Bao WM, Mao RL, Yang GY. Magnetic resonance imaging and microsurgical treatment of intramedullary hemangioblastoma of the spinal cord. Neurosurgery 1994;35(04):671–675, discussion 675–676
15 Sadashivam S, Abraham M, Kesavapisharady K, Nair SN. Long-term outcome and prognostic factors of intramedullary spinal hemangioblastomas. Neurosurg Rev 2020;43(01):169–175
16 Xie T, Qian J, Zhang L, Luo C. Microsurgical resection of intramedullary spinal cord hemangioblastomas: 3-dimensional operative video. Neurosurgery 2014;10(Suppl 1):160, discussion 160
17 Dwarakanath S, Sharma BS, Mahapatra AK. Intraspinal hemangioblastoma: analysis of 22 cases. J Clin Neurosci 2008;15(12):1366–1369
18 Parker F, Aghakhani N, Ducati LG, et al. Results of microsurgical treatment of medulla oblongata and spinal cord hemangioblastomas: a comparison of two distinct clinical patient groups. J Neurooncol 2009;93(01):133–137

