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Intraspinal hemangioblastomas: analysis of 92 cases in a single institution

Clinical article

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Object. Intraspinal hemangioblastomas are relatively uncommon benign tumors. The surgical strategies remain controversial, and the risk factors with regard to clinical outcome are unclear. The purpose of this study was to analyze the clinical characteristics, imaging findings, surgical strategies, and functional outcomes associated with intraspinal hemangioblastomas.

Methods. A series of 92 patients who underwent 102 operations for resection of 116 intraspinal hemangioblastomas at a single institution during 2007–2011 were consecutively enrolled in this study. Of these, 60 patients (65.2%) had sporadic hemangioblastomas and 32 (34.8%) had von Hippel-Lindau disease. Preoperatively, 13 patients underwent digital subtraction angiography (DSA), 15 patients underwent 3D CT angiography (3D CTA), and none underwent preoperative embolization. Clinical characteristics, imaging findings, and operative records were analyzed. The advantages and disadvantages of DSA and 3D CTA were compared. For identification of risk factors that affect prognosis, logistic analysis was performed.

Results. The male/female patient ratio was 1.8:1.0 (59 male and 33 female patients). Of the tumors, 41% were intramedullary, 37% were intramedullary-extramedullary, and 22% were primarily extramedullary. Three-dimensional CTA and DSA did not differ significantly in the ability to identify the feeding arteries ($p = 1.000$) and image qualities ($p = 0.367$). However, compared with 3D CTA, the effective x-ray dose of spinal DSA was 2.73 times higher and the mean amount of contrast media injected was 1.88 times higher. Spinal DSA was more time consuming (mean 120 minutes) than 3D CTA (scanning time < 1 minute). No complications were observed after 3D CTA; acute paraparesis developed in 1 patient after DSA.

Gross-total resection was achieved for 109 tumors (94.0%), and resection was subtotal for 7 tumors. Mean duration of follow-up was 50 months (range 24–78 months). At the most recent follow-up visit, the functional outcome was improved for 38 patients (41.3%), remained stable for 40 (43.5%), and deteriorated for 14 (15.2%). Logistic analysis showed that subtotal resection was a risk factor affecting prognosis ($p = 0.003$, OR 12.833, 95% CI 2.429–67.806).

Conclusions. The authors' study suggests that safe and effective treatment of intraspinal hemangioblastomas can be achieved for most patients, even without preoperative embolization. Gross-total resection, when safe to perform, leads to better outcomes. Compared with spinal DSA, 3D CTA is a promising technique because it is noninvasive, takes less time to perform, requires lower x-ray doses and less contrast media, results in fewer complications, and offers high accuracy for delineating the feeding arteries.
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Key Words • **hemangioblastoma** • **spinal** • **microsurgery** • **von Hippel-Lindau disease** • **oncology**

Hemangioblastomas are highly vascularized, histologically benign tumors that occur throughout the CNS. They can develop either sporadically or as part of von Hippel-Lindau (VHL) disease, a multicentric disorder of autosomal dominance. The association with VHL disease is well recognized and occurs in 20%–38% of patients.[1,24] Spinal hemangioblastomas are relatively rare; they constitute 2%–15% of all spinal cord neoplasms,[2,4,5,13] predominate in young men, and more than 50% are associated with syringomyelia.[1]

Because of the rarity of this tumor, the management

Abbreviations used in this paper: DLP = dose length product; DSA = digital subtraction angiography; DSP = dose surface product; VHL = von Hippel-Lindau disease; 3D CTA = 3D CT angiography.

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strategies, clinical outcomes, and risk factors that affect prognosis remain controversial. We reviewed our data for 92 patients consecutively admitted to a single institution with respect to preoperative angiography, management strategies, and clinical outcomes.

Methods

After the study was approved by the Institutional Review Board of Beijing Tiantan Hospital, Capital Medical University, we retrospectively reviewed the medical records and radiological studies of 92 patients with intraspinal hemangioblastomas, who had been referred to our department (Department of Neurosurgery, Beijing Tiantan Hospital) from January 2007 through July 2011. We then analyzed the clinical characteristics, imaging studies, management strategies, complications, and short-term and long-term outcomes.

Clinical Evaluation

Neurological function was evaluated according to the classification of McCormick (Table 1)[16] at 4 times: before surgery, immediately (1–4 weeks) after surgery, at short-term follow-up (3–6 months after surgery), and at long-term follow-up (2–6 years after surgery, most recent follow-up). Follow-up data were obtained from medical records and by telephone and outpatient interviews.

Imaging Evaluation

All patients underwent preoperative and postoperative contrast-enhanced T1-weighted MRI (Figs. 1A and C; 2A and B; and 3A, B, E, and F). Radiographically, each tumor was classified as either dorsal or ventral. In addition, each tumor was characterized as completely intramedullary, intramedullary-extramedullary (≤ 50% of the tumor was extramedullary), or primarily extramedullary (> 50% of the tumor was extramedullary). Tumor volume was determined using the following equation: greatest anteroposterior dimension × greatest mediolateral dimension × greatest craniocaudal dimension × 0.5.[17] Gross-total resection was defined as complete tumor removal according to operative microscopic findings and postoperative contrast-enhanced T1-weighted MR images.

A total of 28 patients (30.4%) underwent diagnostic angiography before surgery, and 13 (14.1%) underwent digital subtraction angiography (DSA) (Fig. 1B), which was indicated for large-volume lesions and tumors involving the medulla oblongata. Radiographic parameters were 80 kV, 400 mA, and matrix 1024 × 1024. Anteroposterior and lateral views of each vessel were obtained by manual injection of 3–5 ml nonionic contrast media at a flow rate of 3 ml per second (iodine concentration 300 mg/ml). The total amount of contrast media used ranged from 70 to 132 ml (mean 94 ± 17 ml). The mean duration of the DSA procedure was 120 minutes (range 100–150 minutes).

Three-dimensional CT angiography (3D CTA) was performed for 15 patients both before and after surgery (Figs. 2C and D, and 3C, D, G, and H) by a 64-multidetector row CT scanner (Discovery CT750 HD, GE Healthcare). The scanning parameters were 120 kV, 500 mA, table speed 3.5 mm per rotation, scanning time 0.5 sec per rotation; slice thickness was 1 mm, and reconstruction increments were 0.5 mm. A power injector was used to deliver a total volume of 50 ml nonionic contrast medium (iodine concentration 370 mg/ml) through a 20-gauge needle into the antecubital vein at a rate of 6 ml per second; subsequently, a 40-ml bolus of saline solution was delivered at the same rate. A real-time computer-assisted bolus tracking system was applied. The region of interest was placed at the vertebral artery, and the scanning was started at 110–140 HU. A scan delay of 16 seconds was normally used. The mean scanning time was 18 seconds (range 14–20 seconds). Acquired data were transferred to a GE Advantage workstation–Mozilla and processed with maximum intensity projection and volume-rendering technique methods. For each patient, 250–513 axial images were generated. If necessary, further thin maximum intensity projection images were generated by an experienced neuroradiologist, and the axial source images (raw data) were also reviewed.

Two independent readers, blinded to the aim of the study, evaluated the entire series of DSA and 3D CTA images on a picture archiving and communication system (PACS) workstation with respect to visualization of the feeding arteries and quality of the images. The visualization of the feeding arteries was defined as the presence of a branching artery with connection to the tumor. The image quality was divided into 3 grades, and the criteria were as follows: 0 (poor), the shape of the tumor is not clear or the feeding artery is not visible; 1 (adequate), the shape of the tumor is clear, the feeding artery is visible but not continuous, or the vessel wall is not smooth; and 2 (good), the shape of the tumor is clear and the feeding artery is visible and continuous, and the vessel wall is smooth (Fig. 2C, and 3C and D).

TABLE 1: McCormick clinical grading scale for neurological function*

Grade	Grade Definition
I	neurologically normal; mild focal deficit not significantly affecting function of involved limb; mild spasticity or reflex abnormality; normal gait
II	presence of sensorimotor deficit affecting function of 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

* Reproduced with permission From McCormick et al.: *J Neurosurg 72*:523–532, 1990.

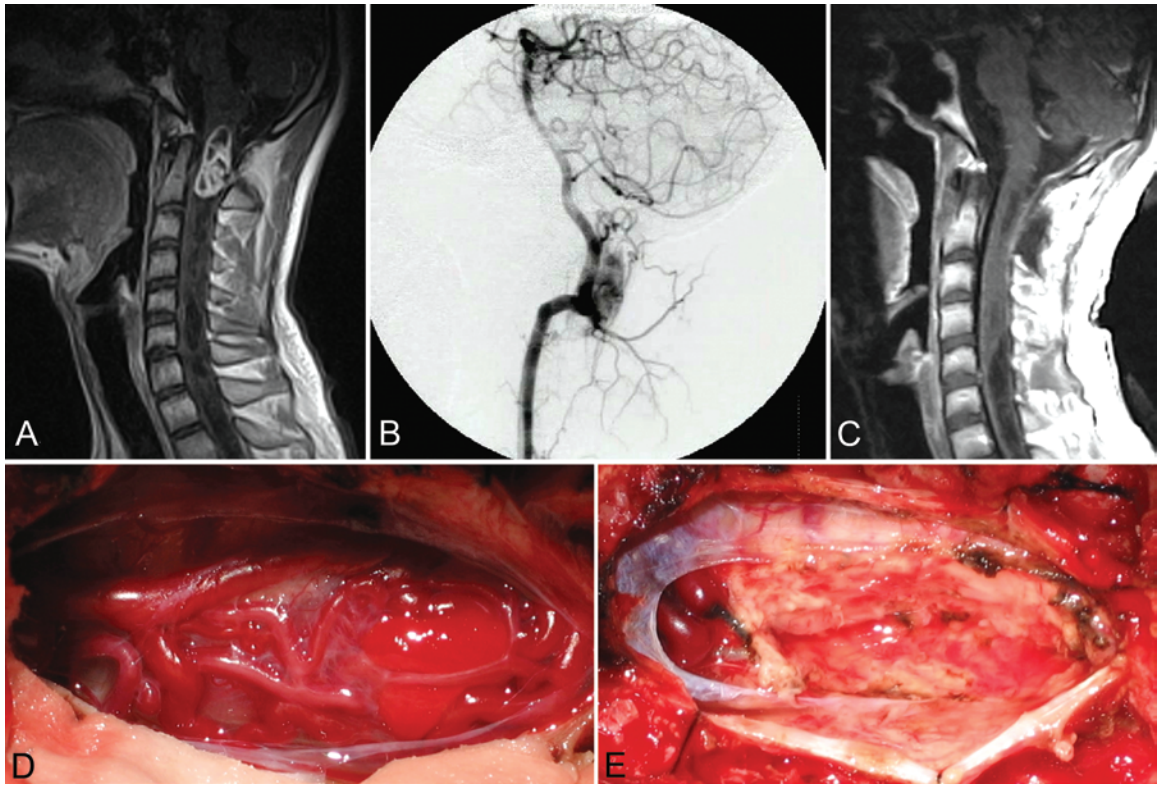

Fig. 1. Contrast-enhanced sagittal MR images, DSA images, and intraoperative photographs **A:** Preoperative MR image revealing a heterogeneous enhancing mass at the C1–2 level. **B:** Preoperative left vertebral artery DSA image demonstrating a hypervascular tumor fed by the anterior spinal artery. **C:** Postoperative MR image showing no evidence of residual tumor. **D:** Intraoperative photograph demonstrating a dorsal midline hemangioblastoma. **E:** Intraoperative photograph after gross-total resection of the tumor.

Evaluation of X-Ray Exposure

To compare the x-ray dose delivered by the spinal DSA (dose surface product [DSP] expressed in micrograys per square meter [$\mu Gy.m^2$]) with the dose delivered by the 3D CTA (dose length product [DLP] expressed in milligrays per centimeter [mGy.cm]), we converted DSP and DLP into effective dose (E) (expressed in millisieverts [mSv]) by using the following formulae[3]:

Effective dose (mSv) = DLP (mGy.cm) × k (mSv/mGy.cm) (k = generalized E/DLP coefficient, ≈0.015 for thoracoabdominal acquisition)

Effective dose (mSv) = DSP ($\mu Gy.m^2$) × 10^{-2} × k (mSv/$\mu Gy.m^2$) (k = generalized E/DSP coefficient, ≈0.20 for thoracoabdominal x-ray acquisition)

Surgical Procedures

No patient underwent preoperative embolization or radiosurgery. All patients underwent laminotomy and microsurgical tumor removal via a posterior approach. Most feeding arteries were located at the pial surface (Figs. 1D and 4A). First, the feeding arteries were coagulated, and then the tumor was exposed by circumferential incision at the tumor-pial margin. The well-defined plane between the tumor and the spinal cord was progressively developed by applying traction to the tumor with a microdissector or suction tip (Fig. 4B). Every attempt was made to resect the tumor en bloc (Fig. 4C) because piecemeal removal could lead to extensive bleeding. The major draining veins were left intact until the end of the tumor resection. For dorsolateral tumors, the dorsal root fascicles always partially obscured the surface of the tumor (Fig. 4A). These dorsal root fascicles usually needed to be mobilized and divided to facilitate tumor removal. The associated syringes were not manipulated directly.

For 7 patients, indocyanine green videoangiography was performed during surgery to reveal the feeding arteries, abnormal venous drainage, and the border of lesions and after resection to demonstrate absence of residual tumor.[8]

For patients with VHL disease, the goal was to remove the main lesions; adjacent tumors were also resected if possible (Fig. 3). Moreover, surgery was recommended as soon as practical if symptomatic tumor growth was observed on MR images.

Postoperatively, none of the patients received adjuvant therapies, such as external-beam radiation therapy and stereotactic radiosurgery.

Statistical Analysis

All statistical analyses were performed by using SPSS Windows version 18.0 (IBM). Concordance between the 2 observers for 3D CTA, with respect to the visualization of the feeding arteries and quality of the images, was determined by calculating the κ coefficient[18] (κ < 0.20, poor agreement; κ = 0.21–0.40, fair; κ = 0.41–0.60, moderate;

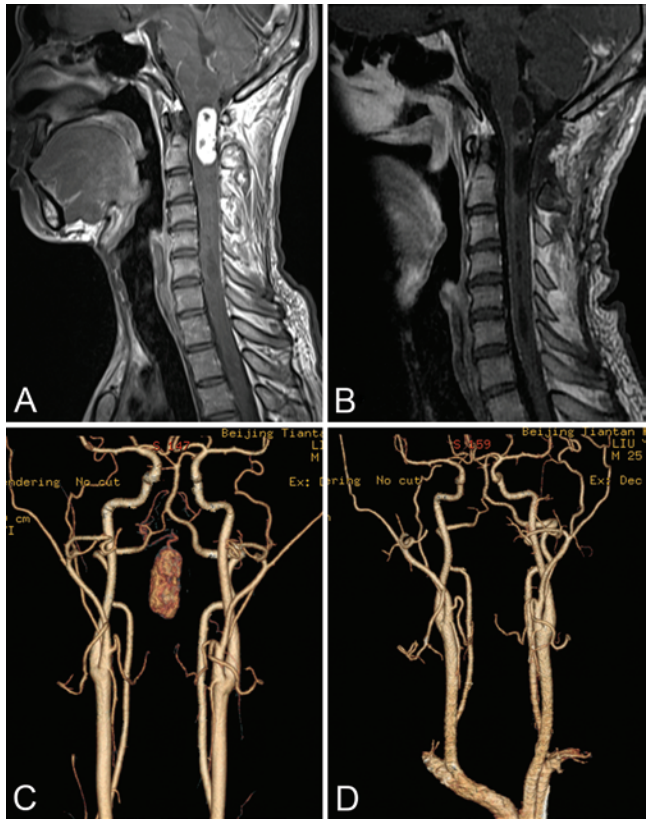

Fig. 2. Contrast-enhanced sagittal MR images and 3D CTA images of a patient with a single intraspinal hemangioblastoma. **A:** Preoperative MR image revealing a heterogeneous enhancing mass at the C1–2 level. **B:** Postoperative MR image demonstrating no evidence of residual tumor. **C:** Preoperative 3D CTA image revealing a hypervascular tumor fed by the right posterior inferior cerebellar artery. **D:** Postoperative 3D CTA image demonstrating complete resection of the tumor.

$\kappa = 0.61–0.80$, good; and $\kappa > 0.80$, excellent). The visualization of the feeding arteries and image qualities of 3D CTA and DSA studies were also compared by use of the Fisher exact and Wilcoxon rank-sum tests, respectively. Logistic regression analyses were performed to investigate risk factors associated with clinical outcome, including patient sex, age, duration of symptoms, syrinx, VHL disease, largest tumor volume, ventral tumor, intramedullary tumor, blood loss, and subtotal resection. Odds ratios with 95% CIs were determined. Clinical outcomes were based on neurological status at the long-term follow-up visit and were categorized as 1) improvement or stabilization or 2) aggravation. A probability value < 0.05 was considered statistically significant.

Results

Patient Population

From January 2007 through July 2011, a total of 92 patients underwent microsurgical treatment for intraspinal hemangioblastomas in our department. During the same period, intraspinal tumors were diagnosed for 1624 patients and CNS hemangioblastomas for 383. Therefore, intraspinal hemangioblastomas accounted for 5.67% of all intraspinal tumors and 24.02% of all CNS hemangioblastomas. Of the 92 patients, 59 were male and 33 were female (ratio 1.8:1.0), average age at first laminotomy was 32.5 years (range 10–73 years), and average age at first clinical signs was 30.3 years (range 9.6–71.5 years). At the most recent follow-up evaluation of the data, a total of 102 operations had been performed and 116 intraspinal hemangioblastomas had been removed.

Clinical Characteristics

The main clinical characteristics were sensory changes in 60 patients (65.2%), pain in 49 (53.2%), motor deficit in 35 (38.0%), and bladder dysfunction in 8 (8.7%). Clinical progression was relatively slow, and the mean duration of symptoms was 26 months (range 2–204 months). Preoperative neurological status is shown in Table 2. Status in a total of 32 patients (34.8%) met the criteria of VHL disease, including 22 patients with multiple CNS hemangioblastomas, 8 with a family history of VHL disease, 8 with pancreas cysts, 4 with multiple kidney cysts, 1 with pheochromocytoma, 1 with retinal hemangioblastoma, and 1 with both renal cell carcinoma and polycythemia; some patients met more than 1 criterion.

Radiological Features

Among the 60 patients with sporadic hemangioblastoma, the most common location was the cervical spine (28 [46.7%]), followed by the thoracic spine (26 [43.3%]) and the lumbar spine (6 [10.0%]) (Table 3). Among those with VHL disease, a total of 56 intraspinal hemangioblastomas were removed; the tumors were located in the cervical spine (30 [53.6%]), thoracic spine (23 [41.1%]), and lumbar spine (3 [5.3%]). Overall, the most common locations were the cervical (58 [50.0%]) and thoracic (49 [42.2%]) spine.

Out of the 116 tumors, 41.4% were intramedullary, 37.1% were intramedullary-extramedullary, and 21.5% were primarily extramedullary (Table 4). Most tumors (92.2%) were located dorsally. The volume of the largest tumor resected in each operation ranged from 0.05 to 10.25 cm^3 (1.8 ± 1.4 cm^3). Tumors were accompanied by peritumoral edema in 63 (68.5%) and by syringomyelia in 71 (77.2%).

Angiography

According to the aforementioned criteria, the feeding arteries could be identified in all 13 patients who underwent DSA (Fig. 1B) and in 14 of the 15 patients (93.3%, consensus of 2 observers) who underwent 3D CTA (Figs. 2C, and 3C and D). The feeding arteries were the posterior inferior cerebellar artery in 7 patients, the anterior spinal artery in 10, the posterior spinal artery in 3, and both the anterior and posterior spinal arteries in 7.

Both observers agreed on the visualization of the feeding arteries in 14 (93.3%) of 15 studies; interobserver agreement was good ($\kappa = 0.63$, $p = 0.008$) (Table 5). In 13 (86.7%) of 15 studies, both readers agreed on the quality of 3D CTA images; interobserver agreement was also good ($\kappa = 0.75$, $p = 0.000$). When the ability to identify the feeding arteries and the image qualities of 3D CTA

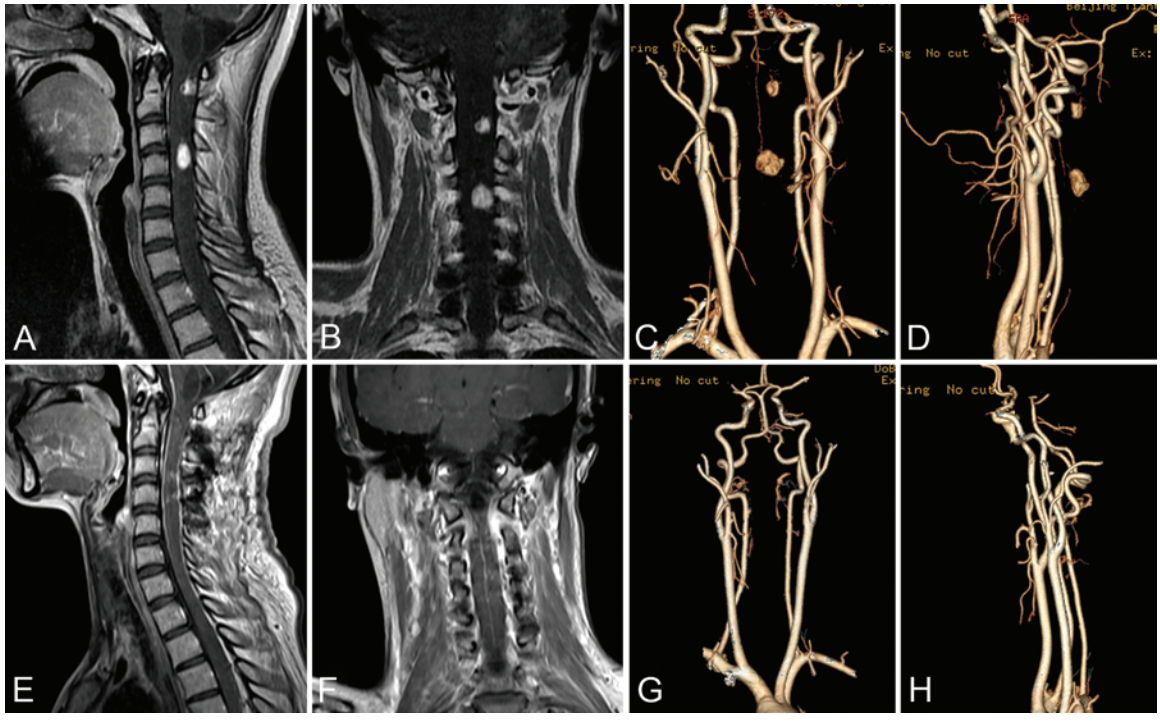

Fig. 3. Contrast-enhanced MR images and 3D CTA images of a patient with VHL disease with 2 intraspinal hemangioblastomas. Preoperative sagittal **(A)** and coronal **(B)** MR images revealed 2 enhancing masses at the C-2 and C3–4 levels. Preoperative 3D CTA images **(C and D)** detected 2 hypervascular tumors fed by the branches of the anterior spinal artery and posterior spinal artery. The 2 tumors were completely removed during a single operation. Postoperative sagittal **(E)** and coronal **(F)** MR images demonstrated no evidence of residual tumor, and postoperative 3D CTA images **(G and H)** revealed complete resection of the 2 tumors.

and DSA studies were compared, results showed no significant difference between the 2 techniques ($p = 1.000$ and 0.367, respectively) (Table 6).

The mean DLP of 3D CTA was 2413 ± 242 mGy.cm (range 2010–3123 mGy.cm). After conversion by the aforementioned formula, the mean equivalent dose of 3D CTA was 36.2 ± 3.6 mSv (range 30.2–46.5 mSv). The mean DSP of DSA was 49,332 ± 35,443 μGy.m^2 (range 9865–212,953 μGy.m^2), and the mean equivalent dose was 98.7 ± 70.9 mSv after conversion (range 19.7–425.9 mSv). Thus, the x-ray dose was 2.73 times higher for spinal DSA than for 3D CTA. Moreover, compared with 3D CTA, spinal DSA required more contrast medium (1.88 times higher) and was much more time consuming (120 minutes versus < 1 minute).

No renal failure was observed after DSA and 3D CTA. Acute paraparesis developed in 1 patient after DSA; muscle power in both lower limbs changed from UK Medical Research Council Grade 5 to Grade 3, and muscle power was recovered after 2 days of conservative treatment.

Intraoperative Findings

Most hemangioblastomas were located on the dorsal or dorsolateral surface of the spinal cord and were readily seen during initial inspection after dural opening. Most arterial feeders (90.2%) were located at the pial surface (Figs. 1D and 4A). In 79 patients (85.9%), there was a well-developed capsule against the pia of the spinal cord. The average blood loss was 267 ml (range 50–800 ml); blood loss was 253 ± 187 ml in those who underwent gross-total resection and 442 ± 257 ml in those who underwent subtotal resection; the difference between the 2 groups was significant ($p = 0.014$). Of the 7 patients who underwent indocyanine green videoangiography, the feeding arteries, abnormal venous drainage, and the borders of lesions were revealed for 5.

Gross-Total and Subtotal Resection

Of the 60 patients with sporadic hemangioblastomas, each patient underwent 1 operation, and gross-total resection was achieved in 58 (96.7%). The other 2 patients (3.3%) underwent subtotal resection because of severe adhesion to the surrounding spinal cord tissues; more than 60% of the tumor was removed, which was confirmed by postoperative contrast-enhanced MR images.

For the 32 patients with VHL disease, 46 tumors were removed at the first surgery, and second operations were performed for 8 patients; the time between the 2 operations ranged from 5 months to 2 years (mean 14 months). One patient underwent 3 surgeries for 3 symptomatic tumors. Thus, 42 operations were performed in 32 patients with VHL disease and 56 intraspinal hemangioblastomas were removed, including gross-total resection of 51 tumors and subtotal resection of 5 tumors.

Therefore, a total of 102 operations were performed in 92 patients for resection of 116 intraspinal hemangioblastomas. Gross-total resection of 109 tumors (94.0%)

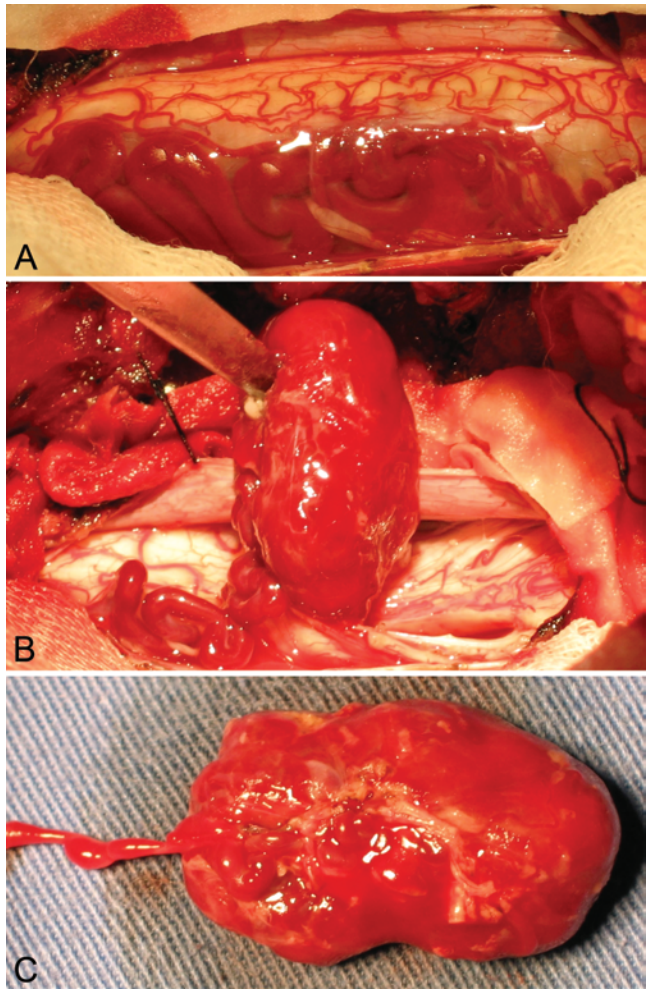

Fig. 4. Photographs of intraoperative findings **A:** A large cervical hemangioblastoma arising from the left dorsolateral pia. Note the dorsal root fascicles coursing over the surface of the tumor. **B:** After circumferential dissection of the tumor was complete, the caudal pole of the tumor was reflected to expose the deep surface. **C:** The tumor was resected en bloc.

was achieved, and subtotal resection of 7 tumors was performed. No significant correlation was observed between gross-total resection and tumor location (ventral or dorsal; $p = 0.138$, Fisher exact test) or between gross-total resection and tumor classification (intramedullary, intramedullary-extramedullary or primarily extramedullary; chi-square = 3.246, $p = 0.078$).

TABLE 3: Distribution of the 116 resected intraspinal hemangioblastomas

Location	No. of Tumors	
	Sporadic (n = 60)	Associated w/ VHL (n = 56)
C-1	2	9
C-2	9	8
C-3	6	3
C-4	3	5
C-5	4	2
C-6	1	2
C-7	3	1
total cervical	28	30
T-1	1	4
T-2	2	3
T-3	3	2
T-4	2	2
T-5	0	1
T-6	4	3
T-7	1	1
T-8	2	2
T-9	3	1
T-10	2	1
T-11	2	1
T-12	4	2
total thoracic	26	23
L-1	5	3
L-2	1	0
total lumbar	6	3

Follow-Up

All patients underwent follow-up examinations. The duration of follow-up ranged from 24 to 78 months (average 50 months). The neurological recovery data are summarized in Table 2.

Immediate Outcome (1–4 Weeks After Surgery). Neurological status was maintained in most patients (64.1%) and deteriorated 1 neurological grade in the immediate postoperative period in 7 (7.6%). New or worsened symptoms included hypesthesia (9.8%), weakness of lower limbs (6.5%), bowel and bladder dysfunctions (3.3%), and dysphagia (1.1%). Neurological status improved 1 neurological grade in 23 patients and 2 grades in 3 patients.

TABLE 2: Preoperative neurological status and neurological recovery data at different follow-up periods according to McCormick grade

Grade	No. of Patients			
	Before Surgery	Immediate Outcome (1–4 wks postop)	Short-Term Outcome (3–6 mos postop)	Long-Term Outcome (2–6 yrs postop)
I	22	34	42	43
II	47	46	33	32
III	19	7	12	12
IV	4	5	5	5

TABLE 4: Clinical and imaging characteristics of 92 patients with 116 resected intraspinal hemangioblastomas*

Characteristic	Value
male patient, no. (%)	59 (64.1)
mean age at 1st laminotomy (yrs)	32.5 ± 6.4
mean duration of symptoms (mos)	26.0 ± 7.3
VHL	32 (34.8)
tumor location, no. (%)	
ventral	9 (7.8)
dorsal	107 (92.2)
tumor relation to spinal cord, no. (%)	
intramedullary	48 (41.4)
intramedullary-extramedullary	43 (37.1)
primarily extramedullary	25 (21.5)
mean largest tumor vol (cm^3)	1.8 ± 1.4
syrinx	71 (77.2)
mean blood loss (ml)	267 ± 198
resection, no. (%)	
gross-total	109 (94.0)
subtotal	7 (6.0)

* Mean values are presented ± SD.

Short-Term Outcome (3–6 Months After Surgery). Functional outcome was improved in 35 patients (38.0%, including 32 patients with improvement of 1 grade and 3 patients with improvement of 2 grades), remained stable in 47 (51.1%) and deteriorated in 10 (10.9%, including deterioration of 1 grade for 7 patients and 2 grades for 3 patients). Another symptomatic intraspinal hemangioblastoma developed in 1 patient, and a second operation was performed 5 months after the first laminotomy. All patients underwent contrast-enhanced MRI 3–6 months after surgery. Evidence of residual tumor was observed in 7 patients, but no operation was recommended because they stayed clinically stationary. Of the 71 patients with syringomyelia, syrinx resolution was observed for 59 (83.1%).

Long-Term Outcome (2–6 Years After Surgery, the Most Recent Follow-Up). At the most recent follow-up visit, according to McCormick grade the functional outcome had improved in 38 patients (41.3%), remained stable in 40 (43.5%), and deteriorated in 14 (15.2%) (Table 7). Patients with improvement at the last follow-up visit experienced a median change of 1 grade (range 1–2 grades).

TABLE 5: Diagnostic results for 3D CTA of 15 patients assessed by 2 neuroradiologists

Observer	Feeding Arteries		Image Quality		
	Positive	Negative	Poor	Adequate	Good
Observer 1	13	2	3	3	9
Observer 2	14	1	2	3	10
interobserver agreement	κ = 0.634, p = 0.008		κ = 0.750, p = 0.000		

TABLE 6: Comparison of 3D CTA and DSA

Modality	Feeding Arteries		Image Quality		
	Positive	Negative	Poor	Adequate	Good
3D CTA (n = 15)*	14	1	2	3	10
DSA (n = 13)*	13	0	1	1	11
intermodality difference	p = 1.000†		p = 0.367‡		

* Results indicate consensus of the 2 observers.
† According to the Fisher exact test.
‡ According to the Wilcoxon rank-sum test.

Deterioration of 1 neurological grade was documented in 11 patients and deterioration of 2 grades was documented in 3. During this period, new symptomatic tumors developed in 8 patients with VHL disease and second operations were performed. One of these patients underwent a third surgery 2 years after his initial operation.

Complications

In 1 patient a CSF leak occurred and was treated successfully with lumbar drainage. Meningitis occurred in 6 patients after surgery, and all were successfully managed with conservative strategies. An extradural hematoma developed in 1 patient, who underwent reoperation for its removal. The total rate of complications was 8.7%. No patient in this series died.

Risk Factors Affecting Prognosis

Outcomes were significantly better for patients who underwent gross-total resection than for patients who underwent subtotal resection (p = 0.005, Fisher exact test). Logistic analyses demonstrated that subtotal resection was a predictor of poor clinical prognosis (p = 0.003, OR = 12.833, 95% CI 2.429–67.806) (Table 8). The other factors (patient sex, age, duration of symptoms, syrinx, VHL disease, largest tumor volume, ventral tumor, intramedullary tumor, and blood loss) were not significantly associated with long-term clinical outcome.

Discussion

Epidemiology and Clinical Characteristics

Intraspinal hemangioblastoma is a relatively rare entity; it accounts for 2%–15% of all spinal cord tumors and 13%–26% of all hemangioblastomas.[10,12] It predominates

TABLE 7: Neurological status before surgery and at last follow-up visit

Preop McCormick Grade	McCormick Grade at Last Follow-Up			
	I (n = 43)	II (n = 32)	III (n = 12)	IV (n = 5)
I (n = 22)	18	4	0	0
II (n = 47)	21	17	6	3
III (n = 19)	4	10	4	1
IV (n = 4)	0	1	2	1

TABLE 8: Probability of factors affecting clinical outcomes

Factor	p Value
patient sex	0.15
patient age at 1st surgery	0.31
duration of symptoms	0.35
presence of syrinx	0.75
VHL disease	0.13
largest tumor volume	0.42
ventral tumor	0.16
intramedullary tumor	0.39
blood loss	0.63
subtotal resection	0.003

in male patients; reported male/female ratios range from 1.6:1 to 5.5:1.[2,4,15] On average, presentation is during an individual's 4th decade of life; and 20%–38% of patients have associated VHL disease.[6,12,19] Most tumors occur in the thoracic spinal cord, most commonly in the intramedullary location.[15]

In the study reported here, intraspinal hemangioblastoma constituted 5.67% of all intraspinal tumors and 24.02% of all CNS hemangioblastomas. There was a predominance of male patients (male/female ratio 1.8:1.0), and patient age at presentation (30.3 years) was in the expected range. The most common location was intramedullary (intramedullary/intramedullary-extramedullary/extramedullary = 48:43:25); VHL disease was present in 32 (34.8%) patients. All of these findings correspond to the findings of previous studies. However, the predominance of the cervical location (50.0%) differed from that previously reported in the literature.[14,15,17]

It has been reported that the most common clinical manifestations are pain (50%–80%) and sensory changes (39%–69%), followed by motor deficits (7%–40%) and autonomic involvement (0%–26%).[6,10,20,22] In this series, the most common clinical manifestations were sensory changes (65.2%) and pain (53.2%), which might result from the fact that most tumors were located in the dorsal area of the spinal cord. Motor deficit occurred in 35 patients (38.0%) and bladder dysfunction in 8 (8.7%). The mean duration of symptoms was 26 months (range 2–204 months), which reflected the slow growth of the tumor. No patient exhibited acute symptoms suggestive of tumor hemorrhage.

Angiography

Contrast-enhanced MRI is the diagnostic method of choice for intraspinal hemangioblastomas (Figs. 1A, 2A, and 3A and B). In addition, most authors recommend a preoperative DSA study to delineate the feeding arteries.[1,12] We agree that angiography is useful for operative planning and resection. However, spinal DSA is an invasive procedure, and complications such as cerebral ischemia or even paraparesis and paraplegia occur in 1.2%–4.6% of patients.[7] In the series reported here, acute paraparesis developed in 1 patient. Moreover, there are many arteries that supply the spinal cord, including bilateral vertebral arteries, thyrocervical trunk, costocervical trunk, intercostal arteries, lumbar arteries, and internal iliac arteries. Most of these arteries need enhanced examination, which makes this procedure more difficult and time consuming and requires injection of a high volume of contrast medium and heavier doses of radiation. In this study, the mean duration of spinal DSA was 120 minutes; the scanning time of 3D CTA was less than 1 minute. Compared with 3D CTA, the effective x-ray dose for spinal DSA was 2.73 times higher and the mean amount of contrast medium was 1.88 times higher.

Different from medulla oblongata hemangioblastomas, however, the blood supply of intraspinal hemangioblastomas is not as rich, and the feeding arteries can be easily identified intraoperatively for most tumors because most (90.2%) arterial feeders are located at the pial surface (Figs. 1D and 4A). Therefore, at our institution, before 3D CTA was available, spinal DSA was performed only in patients with large tumors or with tumors involving the medulla oblongata.

Since October 2010, in our department, spinal 3D CTA has been performed for intraspinal hemangioblastomas. In this series, 15 patients underwent 3D CTA both before and after surgery. No associated complications were noted. In our experience, this simple and noninvasive technique could delineate the feeding arteries clearly in most (14 of 15) patients (Figs. 2C and 3C and D), although it is not dynamic. Compared with DSA, 3D CTA could reveal 3D anatomy between the tumors and the feeding arteries as well as vertebrae. This capability is especially useful for patients with VHL disease with multiple intraspinal hemangioblastomas because 3D CTA could simultaneously demonstrate all the intraspinal tumors and their feeding arteries in 1 picture, and this offers a clearer picture of the 3D anatomy between the tumors and the artery feeders (Fig. 3C and D). Moreover, no significant difference was observed between 3D CTA and DSA images with regard to identifying the feeding arteries ($p = 1.000$) and image qualities ($p = 0.367$). Compared with spinal DSA, 3D CTA takes less time (real scanning time is < 1 minute), is well tolerated by most patients so it is also convenient for postoperative examination (Figs. 2D and 3G and H), requires less contrast medium (about half), and delivers a lower x-ray dose (about one-third). Because of these advantages, in our department 3D CTA is recommended instead of DSA.

To our knowledge, ours is the first study that describes the application of 3D CTA in intraspinal hemangioblastomas for a large series of cases. Although the sensitivity and specificity of this procedure for detecting feeding arteries cannot be evaluated (because no patient in this series underwent both techniques), 3D CTA seems to be promising because of its advantages. Moreover, as a supplement to 3D CTA, indocyanine green videoangiography can be used intraoperatively to reveal the feeding arteries, abnormal venous drainage, and the borders of lesions.

Embolization

Preoperative embolization remains controversial. It is emphasized and recommended by most authors be-

cause embolization of feeding arteries can reduce tumor blood supply and make resection of the tumor easier.[1,12,20] However, different from embolization for the feeding arteries of intracranial hemangioblastomas, this procedure requires complicated superselective catheterization; some complications have been reported, such as intradural hemorrhage, exacerbation of hydrocephalus, and deterioration of neurological functions.[15,24] Therefore, some authors are not in favor of this procedure, and they believe that it is usually unnecessary for complete resection.[21,24] None of the 92 patients reported here underwent preoperative embolization, and the rate of gross-total resection was high (94.0%). We therefore speculate that for most patients, a safe and effective treatment can be conducted even without preoperative embolization. Bleeding can usually be controlled if careful microsurgery is performed. Subsequently, the risks associated with diagnostic DSA and selective embolization can be avoided.

Meanwhile, although treatment for most of the patients reported here was successful without preoperative embolization, we need to clarify that we do not oppose its use. Because we failed to achieve gross-total resection of 7 tumors despite having performed careful microsurgeries, we believe that preoperative embolization might be helpful for some patients. However, the indications for embolization need to be further studied, and we hold the opinion that it is unnecessary and unreasonable to perform preoperative embolization for all patients with intraspinal hemangioblastoma.

Surgical Procedures

Although stereotactic radiosurgery has recently been proposed,[11,23] microsurgery is still the treatment of choice for intraspinal hemangioblastomas. In our experience, several steps should be followed when removing hemangioblastomas. First, the principle of dissection of arteriovenous malformations should be adhered to. That is, manipulation of feeding arteries should be done first, followed by resection of the tumor and occlusion of draining veins. Second, en bloc removal should be emphasized because piecemeal removal would probably lead to uncontrollable bleeding, which prevents gross-total resection of the tumor. In the case series reported here, every attempt was made to achieve en bloc removal. However, because of severe adhesion to the surrounding spinal cord tissues, piecemeal dissection was conducted in 7 patients. Extensive bleeding was encountered and gross-total resection was not achieved for those 7 patients. The blood loss was significantly more for patients in the subtotal resection group (442 ± 257 ml) than for those in the gross-total resection group (253 ± 187 ml, $p = 0.014$).

We avoided entering or draining the syrinx during resection because the syrinx would collapse after tumor removal. Among the 71 patients with syringomyelia, syrinx reduction was observed postoperatively in 59 (83.1%). It has also been reported that syrinx resolution is not influenced by whether the syrinx cavity is entered.[14]

Clinical Outcome and Risk Predictors Affecting Prognosis

The results of this study confirm that microsurgery of intraspinal hemangioblastomas yields high rates of clinical improvement and low rates of complications over a long period. The functional outcome was improved for 38 (41.3%) patients, remained stable for 40 (43.5%), and deteriorated for 14 (15.2%); these rates are similar to those reported in the literature.[1,6,12,14,15,20]

However, the predictors of poor clinical outcome remain controversial. Some authors believe that gross-total resection leads to a better outcome than does subtotal resection.[6,20] Some authors have pointed out that neurological impairment is more likely to be minimal for patients with preoperative neurological dysfunction, small tumor size, and dorsal lesions.[14] Other authors found no correlation between the deterioration and the size of tumor or the syrinx.[6] In our large series of 92 patients who consecutively underwent microsurgery at a single institution, multivariate analysis of 10 suspected risk factors showed that subtotal resection was the only significant risk factor affecting clinical prognosis ($p = 0.003$, OR 12.833, 95% CI 2.429–67.806). Therefore, every attempt should be made to achieve gross-total resection of intraspinal hemangioblastomas.

One study,[17] which enrolled 108 patients with VHL disease for resection of 218 intraspinal hemangioblastomas, reported a higher rate of gross-total resection (99.5%) and found that ventral tumors and completely intramedullary tumors were associated with an increased risk for worsened postoperative function. However, in the study reported here, subtotal resection was found to be the only significant risk factor affecting clinical outcome. The ability to achieve gross-total resection did not correlate with the location (ventral or dorsal) or classification of the tumor (intramedullary or exophytic). In our experience, the probable reason is that the main factor that prevents gross-total resection is the adhesion to the surrounding spinal cord tissues, which may not be associated with ventral or intramedullary locations.

Limitations

Our study has several limitations. First, it is retrospective research with limitations inherent to the study design. Second, because none of the patients underwent embolization, we had no control group. Third, gene analysis was not performed for patients with VHL disease. Last, although we favor 3D CTA, data are insufficient for validating the superiority of this technique over DSA because no patient underwent both 3D CTA and DSA. For clarification of the role of 3D CTA in the clinical setting, further studies with larger series of patients undergoing both techniques are needed.

Conclusions

Complete resection is the treatment of choice for intraspinal hemangioblastomas. Our study suggests that for most patients, safe and effective treatment can be achieved even without preoperative embolization. Gross-total resection, when safe to perform, led to better outcomes; subtotal resection was identified as a risk factor on prognosis. Compared with DSA, 3D CTA is noninvasive, takes less time, delivers a lower x-ray dose, requires less

contrast medium, results in fewer complications, and offers high accuracy for feeding artery delineation. Therefore, we believe that 3D CTA is a promising technique for delineating the feeding arteries of spinal hemangioblastomas.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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