

Original Article

Early microsurgical treatment for spinal hemangioblastomas improves outcome in patients with von Hippel–Lindau disease

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Abstract

Background: Spinal hemangioblastomas (HB) are rare, histologically benign, highly vascularized tumors often associated with von Hippel–Lindau (VHL) disease. The aim of the current study is to demonstrate the benefit of early surgical resection of large spinal HBs in selected asymptomatic patients with VHL.

Methods: Seventeen patients underwent microsurgical resection of 20 spinal HBs at the Department of Neurosurgery at Helsinki University Central Hospital (HUCH). Thirteen tumors were in the cervical spine, five in thoracic and one patient had two lumbar lesions. MRI tumor showed an associated syrinx in 16 patients (94%). Tumor volume ranged from 27 to 2730 mm³. Out of 17 patients, 11 (65%) tested positive for VHL in mutation analysis. Five of these patients with tumors ranging from 55 to 720 mm³ were treated prophylactically.

Results: Complete tumor resection was performed in 16 patients (94%) who were followed up for a median of 57 months (range 2–165 months). No patient had neurological decline on long-term follow-up. Among the patients with VHL, five patients with preoperative sensorimotor deficits showed improvement of their symptoms but never regained full function. One patient who presented with tetraplegia remained the same. Otherwise, all five patients with prophylactic surgery remained neurologically intact.

Conclusion: Although documented growth on serial MRIs and the need for pathological diagnosis have been suggested as indications for surgery in otherwise asymptomatic patients, our series showed that a potentially larger group of asymptomatic patients with spinal HB associated with VHL would benefit from microsurgical resection. Long-term results of the surgical management of spinal HB are generally favorable. Our results suggest staging and early treatment for spinal HB larger than 55 mm³, especially in patients with VHL. Small spinal HBs may be followed up.

Key Words: Spinal cord, spinal hemangioblastoma, McCormick classification, microsurgery, von Hippel–Lindau

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INTRODUCTION

Hemangioblastomas (HBs) are rare, histologically benign, highly vascularized tumors of the central nervous system that can be cured with current microsurgical techniques. Although representing only 2–11% of all spinal cord tumors, 45% of spinal HBs occur with von Hippel–Lindau (VHL) disease. Neurological sequelae of spinal HBs often relate to the development of edema or syrinx.^[32] Spontaneous hemorrhage has also been rarely reported. The average size of hemorrhagic lesions is 2–3 cm, while tumors smaller than 1.5 cm carry virtually no risk of spontaneous hemorrhage.^[9]

The neurological outcome of patients with spinal HB, undergoing microsurgical resection, relates both to preoperative clinical condition and to tumor anatomy. The preoperative functional status, as scored by the McCormick classification, typically correlates with postoperative neurological outcome [Table 1].^[17,18]

Table 1: McCormick classification for intramedullary spinal cord tumors^[17]

Grade 1	Neurologically normal, mild focal deficits, normal gait
Grade 2	Sensorimotor deficits affecting function, severe pain, gait difficulties, can still walk
Grade 3	Moderate neurological deficit, requires cane for ambulation. Minor involvement of arms possible. Patient is partially independent
Grade 4	As grade III with arms affected, usually not independent

Large tumors are associated with both poor pre- and postoperative neurological outcome, whilst long-term recurrence rates depend on whether VHL disease or multicentric lesions are present.^[11,23] Case series with more than 10 patients are presented in Table 2.

Although documented growth on serial MRIs and the need for pathological diagnosis have been indications for surgery in otherwise asymptomatic patients, it has been suggested that a potentially larger group of asymptomatic patients with spinal HB who would benefit from resection.^[1,26] Between December 1997 and March 2011, 17 patients underwent microsurgical resection of 20 spinal HBs at the Neurosurgical Department of the Helsinki University Hospital. Five of these patients with tumors ranging from 55 to 720 mm³ were treated prophylactically. We wanted to evaluate whether these patients benefited from surgery.

MATERIALS AND METHODS

Patients and hemangioblastomas

Between January 1997 and March 2011, 164 patients with HBs of the central nervous system were treated in our department. Ten men and seven women had altogether 20 spinal HBs resected during this period. Patient files and images were reviewed in a retrospective study [Table 3]. The McCormick classification^[17] was used to assess the pre- and postoperative neurological function in the patients [Table 1]. The assessment was performed preoperatively and at the last follow-up. Outcome was

Table 2: Review of case series on spinal hemangioblastoma, with more than 10 cases since 1989

Series	No. of patients	VHL (%)	Syrinx (%)	Average tumor size		Long-term outcome		
				Length in cm	Volume in mm ³	Improved (%)	Same (%)	Worse (%)
Murota and Symon 1989 ^[22]	18	33	50	NA		72	11	17
Lunardi <i>et al.</i> 1993 ^[14]	18	0	20	NA		61	34	0 (5 intraoperative mortality)
Samii and Klekamp 1994 ^[28]	10	NA	80	NA		NA	NA	NA
Xu <i>et al.</i> 1994 ^[34]	12	NA	100	3.3		85	8	7
Cristante and Herrmann 1999 ^[7]	19	32	85	NA		41	50	9
Pietila <i>et al.</i> 2000 ^[26]	15	93	60		650	32	68	0
Conway <i>et al.</i> 2001 ^[15]	10	70	NA	NA		NA	NA	NA
Roonprapunt <i>et al.</i> 2001 ^[27]	19	0	100	2.1		68	32	0
Malis 2002 ^[15]	19	NA	16	NA		100	0	0
Boström <i>et al.</i> 2008 ^[2]	23	35	30	NA		17	79	4
Parker <i>et al.</i> 2009 ^[25]	34	73	32		1600	32	50	18 all VHL
Mandigo <i>et al.</i> 2009 ^[16]	15	27	80	NA		6	88	6
Mehta <i>et al.</i> 2010 ^[18]	108	100	84		800	5	80	15
Clark <i>et al.</i> 2010 ^[4]	20	55	35	NA		25	65	10
Takai <i>et al.</i> 2010 ^[31]	24	33	75		1450	37	53	10
Current series	17	64	94		1000	18	82	0

Table 3: Clinical characteristic of the patients in the current series

Case No.	Age (years), sex	von Hippel-Lindau	Location	Tumor volume (mm ³)	Syrinx	Indication for operation	Pre-op grade	Post-op grade	Follow-up time (months)
1	45, f	Yes	C3	594	Th7-L1	Prophylactic	1	1	10
2	22, f	Yes	C5	55	C5-Th4	Prophylactic	1	1	13
3	16, m	Yes	Th2-3	408	Th2-Th7	Prophylactic	1	1	2
4	37, m	Yes	L2 + L4	2100 + 2448	Th7-L1	Paraparesis	3	2	5
5	42, m	No	C0-C1	27	C0-C3	Hemiparesis right	2	2	12
6	29, m	Yes	Th12-L1	720	Th8-L1	Prophylactic	1	1	31
7	25, m	Yes	C6	180	C4-Th2	Prophylactic	1	1	14
8	52, f	No	C1	238	C0-C6	Hemidysesthesia left	1	1	18
9	50, m	Yes	C5	800	C0-Th4	Sudden tetraplegia	4	4	15
10	36, m	Yes	C6 + Th10	110 + 541	C4-L1	Monoparesis upper limb left	2	1	165
11	28, m	Yes	Th10	1995	C3-L1	Sudden paraplegia	4	2	52
12	78, f	No	C0-C1	2730	C1	Hemiparesis left	1	1	70
13	38, m	Yes	C2	2700	None	Sudden tetraplegia	4	2	64
14	41, f	No	C5-C6	990	C0-Th8	Monoparesis right upper limb	1	1	21
15	63, f	No	C6-Th1	2450	C0-L1	Slow progressive tetraparesis	2	2	100
16	64, f	No	C6	27	C4-C7	Dysesthesia	1	1	146
17	57, m	Yes	C7 + Th12	115 + 250	C4-L1	Dysesthesia	2	2	124

recorded as improved, stable, or worsened, with the initial neurological examination as the baseline.

Imaging

In all patients, pre- and postoperative spinal axis MRI was performed using standard T1- and T2-weighted sequences. All MR images of the head and spine were evaluated separately by two authors (AH and JS). The anatomical site of the lesion in neural axis and the presence of syrinx were recorded. The volume of the tumor was assessed in three planes using the xyz × 0.5 method: [volume = length (x) × width (y) × height (z) × 0.5].^[32]

Surgical techniques

Indications for tumor resection were progressive neurological deterioration or large size. Preoperative embolization was used in only one patient. Intraoperative fluoroscopy was routinely used for planning the incision. A midline incision and a routine subperiosteal dissection of the soft tissues were performed. Either a hemilaminectomy or a laminectomy with preservation of the facet joints was performed. It was not necessary to expose the spinal cord over the rostral and caudal cysts of the solid tumor. After hemilaminectomy, the tumor was approached by sharp incision of the dura and arachnoid and exposure of the affected spinal cord segment. The entire surgical dissection was done under high magnification of the operating microscope (×12). On inspection, the spinal cord usually appeared rotated and distorted, and careful inspection was necessary to identify the normal landmarks before placement of the

myelotomy. Myelotomy was performed at the discolored or bulging medullary surface. Since 2007, indocyanine-green (ICG) videoangiography has routinely been used in our department to identify the tumor and feeding vessels. The interface between the pia and the tumor was identified and then circumferentially detached. In order to control intraoperative hemorrhage, temporary artery occlusion was performed with small aneurysm clips in eight patients. During sharp dissection, surface draining veins were isolated and closed. The dura was closed in a watertight manner to prevent cerebrospinal fluid leak.

Illustrative case reports

Patient 3#

A previously healthy, 16-year-old man with recently diagnosed maternally inherited VHL was referred to our Neurosurgical Department for tumor exclusion. His mother (patient 1#) had been operated for a cervical HB 1 year before. Neurological examination demonstrated diminished visual acuity in the right eye. Thoracocervical MRI showed a 408 mm³ HB at the Th2-3 level [Figure 1]. Selective spinal digital subtraction angiography (DSA) demonstrated the tumor being fed by Th4 segmental artery [Figure 2]. The patient and his parents were willing to go for prophylactic surgery. In surgery, Th2 and Th3 laminectomies were performed to get good view of the tumor. When opening the dura, numerous large veins including the feeding artery were visualized on the dorsal surface of the tumor. The vessels were coagulated and the tumor was removed completely. Histology confirmed the diagnosis of an HB. The patient recovered fully without neurological deficits.

Patient 13#

A previously healthy, 32-year-old man with a known family history of VHL developed back pain, gait instability, spastic

tetraparesis, ataxia, and diminished fine motor functions of both upper and lower extremities (McCormick grade 4). Because of indolence, he presented 6 months after the initial symptoms developed. A contrast-enhanced MR scan of the brain and spinal column and spinal DSA demonstrated a bilobed HB in the cervical spinal cord at the C2-3 level (sized 2700 mm³) and several small HBs in the cerebellum [Figures 3–5]. VHL was confirmed by mutation analysis. The large cervical HB was first embolized with polyvinyl alcohol (PVA) particles and then resected via a C2-3 laminectomy. Postoperatively, the patient's tetraparesis worsened and CT demonstrated a postoperative hematoma, and listhesis at C1/2. The patient underwent evacuation of the hematoma and dorsal craniocervical fusion between C0 and C6. On the 12th postoperative day, the patient was discharged to rehabilitation with a significant tetraparesis. At follow-up at 5 years, the patient is able to walk without assistance (McCormick grade 2).

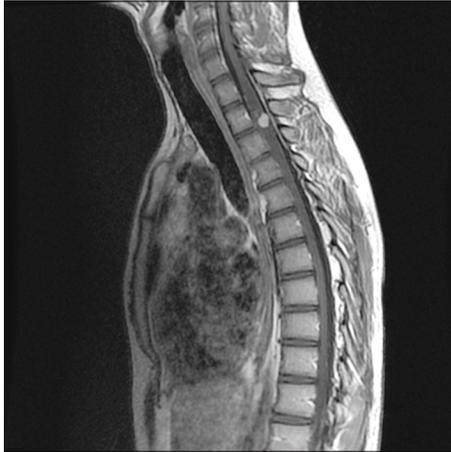


Figure 1: Contrast-enhanced T1-weighted MRI of the thoracic spine in patient #3

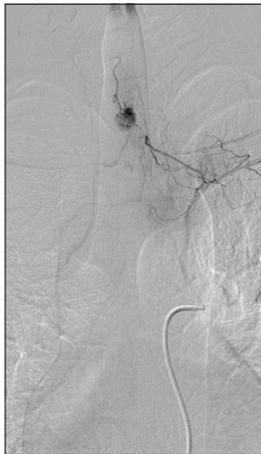


Figure 2: Spinal digital subtraction angiography of patient #3

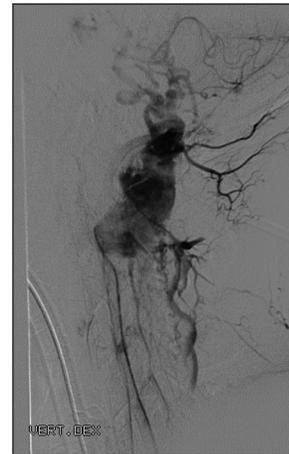


Figure 3: Spinal digital subtraction angiography of patient #13



Figure 4: Contrast-enhanced T1-weighted MRI of the cervical spine in patient #13



Figure 5: MR angiogram of the cervical spine in patient #13

RESULTS

Patients' characteristics

The mean age of the 17 patients was 43 years (range 16–78 years). The mean age was 34 years for the VHL patients and 56 years for non-VHL patients. Multiple lesions occurred in four patients. Overall, 11 patients (65%) tested positive for VHL in mutation analysis. Thirteen lesions were located in the cervical spine, five in thoracic, and one patient had two lumbar lesions. MRI demonstrated an adjoining syrinx to be present in 16 patients (94%). Tumor volume ranged from 27 to 2730 mm³. A tumor volume above 600 mm³ was always associated with neurological deficits. Notably, two patients with tumor volume below 55 mm³ did demonstrate symptoms. Three patients had isolated sensory deficits and back pain as the presenting symptom. Mild progressive sensorimotor deficits were present in five patients, whilst one patient developed sudden paraplegia and one developed tetraplegia without hemorrhage. One patient (illustrative case 2) developed tetraparesis, which progressed into tetraplegia because of indolence. Three patients presenting with tumor regrowth had prior operative treatment at other hospitals. Prophylactic surgery was performed in five patients with VHL.

Operative procedure and postoperative course

Ten patients (59%) underwent hemilaminectomy and seven (41%) underwent laminectomy. Intraoperative ICG was used in five patients to help in identifying the tumor and the feeding vessels. Complete tumor resection was possible in 16 (94%) patients. Due to poor clinical condition, only a biopsy together with decompression of the lumbar spine was performed in one patient (patient #4). He developed postoperative wound infection requiring open revision. However, he recovered from grade 3 to 2. There were two other patients requiring revision surgery. Patient #1 was operated twice since the tumor could not be detected in the first operation; in a second operation with application of ICG, complete tumor removal was achieved. One patient who was embolized and operated on developed progressive tetraparesis, but improved in the long term. There was only one case (6%) of postoperative hematoma and spinal instability requiring fusion in the same patient.

Radiological and clinical long-term follow-up

Patients were followed up for a median of 57 months (range 2–165 months) [Table 3]. Long-term results are presented in Table 4. No patient had neurological decline in long-term follow-up. All patients who had prophylactic surgery remained neurologically intact. Three patients with preoperative sensorimotor deficits showed improvement of their symptoms with respect to their McCormick grade. One of the three patients who presented in our hospital with tetraplegia remained the

Table 4: Long-term results according to Mc Cormick grade^[17] depending on location, association with VHL, tumor volume, and preoperative clinical grade

	Post-op McCormicks` grade			
	Grade 1	Grade 2	Grade 3	Grade 4
Level				
Cervical	7	4	0	1
Thoracic	3	2	0	0
VHL	6	4	0	1
No VHL	4	2	0	0
Tumor volume				
< 51 mm ³	2	1	0	0
51- 1000 mm ³	7	3	0	0
> 1000 mm ³	1	2	0	1
Pre-op McCormicks` grade				
Grade 1	9	0	0	0
Grade 2	1	3	0	0
Grade 3	0	1	0	0
Grade 4	0	2	0	1
Total	10	6	0	1

same despite surgery. All but three patients who came from other countries had control MRI once a year. At the last follow-up, no case of recurrence occurred. During long-term follow-up, one patient died because of chronic alcoholism (patient #4).

DISCUSSION

The present series together with an extensive review of literature showed the importance of staging and early surgery for spinal HBs in patients with VHL. Five asymptomatic VHL patients with tumor volumes from 55 to 720 mm³ did not develop any postoperative neurological sequelae after microsurgical resection and had no residual in long-term follow-up. Otherwise, none of the five VHL patients who presented with neurological deficit fully recovered to McCormick grade 1 despite postoperative improvement during long-term follow-up. The decision to operate on a patient with a spinal HB has historically been reserved for symptomatic patients with progressive deficits, and growth on serial MRIs and histological diagnosis in asymptomatic patients with sporadic occurrence.^[16,24,28] Ammermann *et al.*^[1] have found that HB tumor growth often stutters, so that growth *per se* is not a clear indication for intervention; however, they defined thresholds for size and growth rate above which tumors became symptomatic. They showed in their series that 10% of spinal HBs smaller than 8 mm³ at initial observation had later produced neurological deterioration. After 5 years, 37% of tumors between 8 and 51 mm³ and 90% of tumors larger than 51 mm³ required surgical treatment.^[1] Pietelä *et al.*^[26] showed that none of the operated patients declined while six of the

conservatively managed patients became symptomatic and even with microsurgical resection never regained full function.

Clinical considerations

Symptoms usually range from mild sensory or motor deficits to complete para- or tetraplegia. Occasionally, bulbar symptoms from high cervical tumors or cervicomedullary syrinxes may occur. In concordance with the published literature, sensory dysfunction was the most prevalent initial symptom in our series.^[2,5,7,18,30,31] Hemorrhage from an HB is a rare presenting symptom and did not occur in our series.^[9] Symptoms relate to the location of the tumor and the presence and size of the syrinx. Similar to our results, up to 90% of spinal HBs are associated with a tumor syrinx.^[12,28,33] The majority of tumors including this series were in the cervical spinal cord.^[8,11] In the previous literature, 45% of patients with spinal HBs had VHL and in our series it was 65%.^[5,11,13] Patients with sporadic and VHL-related spinal HBs differ in their average age at presentation and in the number of tumors present.^[3,13] In our series, in concordance with the literature, patients with sporadic tumors typically presented in their fourth decade of life. Those with VHL present earlier, at an average of 30 years, and up to 80% of patients with VHL syndrome have multiple tumors.^[32] Despite these epidemiological differences, sporadic and VHL-related tumors have similar clinical, biological, and histological characteristics.^[12]

Radiographic considerations

Contrast-enhanced MRI is the diagnostic modality of choice for spinal HBs. Most authors have supported the use of angiography to visualize the relevant vasculature preoperatively.^[5,29,34] The adjuvant use of ICG videoangiography for spinal HBs has previously been described in two case reports.^[10,21] In our series, it was used in five cases. In case of recurrence or residual tumors, it was a useful tool to identify the surrounding vasculature of the lesion and facilitate the complete *en bloc* excision (patient #1). ICG may obviate the need of preoperative spinal angiography, depending on the size and depth of the lesion.

Operative techniques

Since the late 1980s, there have been 15 clinical series with more than 10 cases of spinal HB reported in the literature [Table 4].^[2,4,5,7,14-16,18,22,25-28,31,34] Partial resection or biopsy may cause postoperative bleeding and should therefore not be performed. Bleeding during dissection, due to vascularity of HBs, increases the risk of adverse events. Although some investigators recommend preoperative embolization,^[19,35] in our series it was usually not necessary to achieve complete resection. This is in concordance to several other series so that preoperative embolization is generally not recommended.^[6,16,18,24,26] To prevent intraoperative bleeding in selected cases, temporary artery occlusion was performed. This technique

is described in detail by Clark *et al.*^[4] Cyberknife radiosurgery has proven to be safe in the treatment of spinal HBs.^[20] However, as radiographic regression was achieved in only 22%, microsurgical resection remains the gold standard for spinal HBs that are clearly symptomatic or have developed radiographic progression in size, spinal cord edema, or syrinx.^[1,5,28]

Long-term outcome

The long-term surgical outcome of patients with HB depends on preoperative neurological function. Long-term survival also depends on the progress of other lesions, especially in patients with VHL.^[23] Large tumors have been associated with worse pre- and postoperative neurological outcome.^[13] In this series, just one out of three patients who presented with tetraplegia or paraplegia remained the same. One other patient (see case 2, patient #13) recovered after 5 years of rehabilitation from McCormick grade 4 to grade 2. But otherwise, none of the patients who underwent prophylactic resection for an asymptomatic lesion had any neurological deterioration.

CONCLUSION

Long-term results of the surgical management of spinal HB are generally favorable. Improvements in microsurgical techniques, including the addition of intraoperative ICG and temporary arterial occlusion, make complete tumor removal without neurological deterioration feasible. The systematic removal of asymptomatic lesions in the 50-mm³ size range should be considered to improve patient's prognosis in the future.

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