

Spinal hemangiopericytoma: an institutional experience and review of literature

Amitabha Das · Pankaj Kumar Singh ·
Vaishali Suri · Mukund N. Sable · Bhawani Shankar Sharma

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Abstract

Purpose Hemangiopericytoma is a rare tumor of CNS with potential for recurrence and widespread metastasis, even outside CNS with even rare involvement of spinal cord. This case series presents five patients to evaluate the clinical presentation, radiological features, management, pathology and outcome of spinal hemangiopericytomas.

Methods Between 2004 and 2013, five patients underwent surgery for spinal hemangiopericytoma. Histopathological data were reviewed in all cases and clinical and follow-up details were collected from the data available in our department.

Results There were three males and two females, including one pediatric patient. Three patients had dorsal spine involvement and two patients had involvement of cervical spine. There were two patients with intradural extramedullary tumors, one patient each with pure intramedullary tumor, pure extradural tumor and both intra and extradural tumor. All of them presented with motor weakness. Gross total resection of the tumor was done in three patients. Four patients received post-operative radiotherapy. Histopathology showed anaplastic tumor in four cases with high MIB-1 LI. Most of them were positive for CD34, mic-2 and bcl-2. Three patients who underwent gross total resection improved significantly in the follow-up period. Two patients who underwent subtotal resection expired due to spread of their disease.

Conclusion Spinal hemangiopericytoma is a rare tumor. Strong clinical suspicion is required to diagnose it pre-operatively. Gross total resection is the goal and radiotherapy should be given in case of residual tumor or high-grade tumors.

Keywords Hemangiopericytoma · Spine · Surgery · Histopathology · Radiotherapy

Introduction

Hemangiopericytoma is a rare tumor of central nervous system that has the potential to escape from the CNS and metastasize widely [1]. Initially, it was characterized as angioblastic meningioma and later termed as hemangiopericytoma by Stout and Murray in 1942 [2]. However, in 2007, they were classified as tumors of meninges of mesenchymal origin in ‘WHO classification of CNS tumors’. They account for 1 % of all CNS tumors and represent 2–4 % of all meningeal tumors [1, 3–6]. Brain is the commonest location for these tumors and spinal occurrence is a rare event [1]. Till date, only 80 cases of spinal hemangiopericytoma have been reported and most of them are intradural–extramedullary tumors [4, 7–36]. Intramedullary spinal hemangiopericytoma is extremely rare and only five cases have been reported so far [4, 12, 17, 18]. Liu et al. [18] classified spinal hemangiopericytomas in three types and five subtypes—type I is extradural tumor (IA—intracanal, IB—extracanal), type II is intradural type (IIA—extramedullary, IIB—intramedullary) and type III is intradural tumor with extension into extradural and paravertebral area. In our center, we have found five cases of spinal hemangiopericytoma in last 10 years which includes both adult and pediatric patients. In this paper, we have

A. Das · P. K. Singh (✉) · B. S. Sharma
Department of Neurosurgery, All India Institute of Medical Sciences, New Delhi, India
e-mail: drpankajsingh11@gmail.com; amithedoc@yahoo.co.in

V. Suri · M. N. Sable
Department of Neuropathology, All India Institute of Medical Sciences, New Delhi, India

evaluated their clinical presentation, radiological features, management, pathology and outcome.

Methodology

In this retrospective review, patients were identified from the biopsy reports of spinal tumors operated between 2004 and 2013. Five patients with spinal hemangiopericytoma were found. Details of the patients were then obtained from the discharge summary and also from the available follow-up data.

Results

From 2004 to 2013, five patients with spinal hemangiopericytoma underwent treatment in our institute. There were three males and two female patients with a mean age at diagnosis of 34 years (12–50 years). Cervical tumors were found in two patients, while dorsal tumors were present in three. Both the cervical tumors were located in the subaxial cervical spine, while in the dorsal level all three tumors were located below D7. All dorsal spine tumors arise de novo as primary tumors. One patient presented with primary cervical hemangiopericytoma, while another patient presented with recurrence of cervical tumor who underwent surgery, in a peripheral hospital 5 years back (Table 1).

All patients presented with motor weakness of variable duration. In four adult patients, the presentation was gradual; while in the pediatric patient, the onset was sudden. Sensory loss was present in one patient. Two of them presented with bladder and bowel involvement. The mean duration of symptoms before presentation was 5.62 months (3 days–12 months) (Table 1).

Pre-operative contrast-enhanced MRI scans were evaluated in all cases. Tumors were found in extradural, intradural–extramedullary and intramedullary locations. The average length of the tumors was 4.3 cm. The MRI of

the patient with intramedullary tumor showed intensely enhancing soft tissue mass with cord expansion and proximal syrinx formation. Three IDEM tumors had variable contrast enhancement, well defined plane between tumor and cord parenchyma with variable extension into the neural foramina. One patient presented with extensive involvement of the posterior elements.

All patients underwent surgery as primary treatment. Although imaging features were suggestive of vascular nature of the tumor, pre-operative embolization was not used in any of these tumors. The tumors were approached from posterior aspect either by laminectomy or laminoplasty. Gross total resection was achieved in three cases. Two patients underwent subtotal resections because of high vascularity and cord invasion (Table 1).

Histopathological evaluation shows hemangiopericytoma in all cases. Four of them were anaplastic type. One patient had grade 1 tumor. Frequent mitoses were noticed in all specimens. Rate of mitoses was around 7.6 per 10 HPF. MIB-1 labeling index was very high in all anaplastic cases. Mean MIB-1 labeling index was 16.5 % with a range of 4–35 %. Tumor necrosis was not a common finding in the tumor specimens (Table 2).

Molecular studies revealed immunopositivity for CD34 in four out of five tumors. Similarly bcl-2 was also seen in four patients. Immunopositivity for mic-2 was found in three patients. Vimentin was present in one tumor (Table 2).

The post-operative period was uneventful in four patients. One patient with cervical tumor developed wound infection and CSF leak. He was managed conservatively with antibiotics and discharged after resolution of infection. Post-operative contrast-enhanced MRI was done in all patients. Small residual tumor was found in one patient, even after gross total excision, in the post-operative MRI scan. Patients who underwent subtotal resection also had residual disease in follow-up scans.

Four patients, including patients with residual diseases, who had anaplastic hemangiopericytoma, were given

Table 1 Clinical and radiological characteristics of patients

Case	Age/sex	Location	Type [19]	Presentation	Surgery	Primary/ recurrent	Adjuvant	Follow-up (months)	Outcome ASIA preop/postop
1	50/M	C4–5	IIA	Quadriparesis, numbness in bilateral upper limbs × 4 months	GTR	Primary	RT and CT	23	D/E
2	34/M	D8–10	IIB	Paraparesis, bladder dysfunction × 6 months	STR	Primary	RT and CT	24	D/expired
3	37/F	D7–9	III	Paraparesis, bladder dysfunction × 6 months	GTR	Primary	Nil	12	B/E
4	37/M	C5–6	IA	Quadriparesis × 1 year	STR	Recurrent	RT and CT	60	D/expired
5	12/M	D11–L1	IIA	Para paresis × 3 days	GTR	Primary	RT	9	B/E

Table 2 Histopathological details of patients

Case	WHO grade	Mitoses/10 HPF	Necrosis	MIB-1 LI (%)	Molecular markers
1	Anaplastic, grade III	7	Nil	16	CD34, mic2, bcl2
2	Anaplastic, grade III	7–8	Nil	17	CD34, mic2, bcl2, vimentin
3	Grade I	Rare	Nil	4	CD34, mic2, bcl2
4	Anaplastic, grade III	3–4	Focal	12	CD34
5	Anaplastic, grade III	13	Nil	35	Bcl2

external beam radiotherapy. Chemotherapy was also given to three patients. After adjuvant treatment, patients were routinely followed up after 6 months and then annually. Mean duration of follow-up was 25.4 months (range 9–60 months). At the last follow-up, three patients who underwent gross total excision were healthy and ambulatory and had significant neurological improvement. Contrast MRI done at last follow-up did not reveal any tumor in those patients. Unfortunately, two patients who underwent subtotal resection expired due to spread of their disease (Table 1).

Case 1

A male patient of 50 years presented with slowly progressive ascending quadriparesis for 4 months. Contrast-enhanced MRI showed an enhancing mass lesion at C4–5 level.

C4–5 laminectomy and durotomy were done. A moderately vascular well-encapsulated tumor was found intradurally. The cord parenchyma was not involved. The tumor was adherent to the dura matter. Gross total removal of the tumor along with involved dura was done. Post-operatively, he developed CSF leak which was managed conservatively.

Histomorphological features were suggestive of grade III anaplastic hemangiopericytoma. Immunohistochemical analysis was positive for CD34, bcl-2 and mic-2. The MIB-1 LI was 16 %.

Considering the high grade of the lesion, he received both chemo and radiotherapy as adjuvant treatment. He was regularly followed up for nearly 2 years after surgery. Till the last follow-up, he had significant neurological improvement and was ambulatory. There was no recurrence of the disease in that period.

Case 2

Another male patient of 34 years presented with slow onset progressive paraparesis for 6 months with early onset involvement of sphincter. MR scan with contrast revealed lower dorsal (D8–10) intramedullary tumor with enhancement (Type 2B).

He underwent dorsal laminectomy at D8 and D9 levels. The tumor was highly vascular and had infiltrating margins. It was not easily separable from cord parenchyma and removed subtotally.

Histopathology was suggestive of grade III anaplastic hemangiopericytoma with MIB-1 LI of 17 %. The tumor tissue was positive for CD34, mic-2, bcl-2 and vimentin.

Patient received both chemo and radiotherapy as adjuvant treatment. He was under close follow-up for 24 months. Although he showed neurological improvement initially; he started deteriorating after around 2 years of surgery and died due to extensive spread of the disease.

Case 3

A 37-year-old female patient presented with progressive ascending spastic paraparesis for 6 months and became bed ridden. Pre-operative MRI revealed a well defined tumor with both intradural extramedullary and extradural components at D7–9 level on right side and extending into the D8–9 neural foramina. Cord was pushed to the left side. The lesion was $1.4 \times 1.9 \times 4.3$ cc in size (Fig. 1a, b).

She underwent D7–8 laminoplasty approach and gross total excision of the tumor. The tumor was primarily extradural in location with small intradural and intra foraminal extension at D8–9 level. The tumor was moderately vascular and firm in consistency.

On histopathological evaluation, the tumor specimen was diagnosed as a WHO grade II hemangiopericytoma with a MIB-1 labeling index of 4 %. The tumor cells were positive for CD34, Bcl-2 and Mic2 (Fig. 2).

No adjuvant treatment was given to the patient and she was kept under regular neurosurgical follow-up. Post-operative MRI revealed complete excision of the tumor without any evidence of tumor residual (Fig. 3a, b). At the last follow-up 6 months post-surgery, she improved significantly with normalization of motor power in both lower limbs.

Case 4

A male patient of 37 years who was a known case of cervical hemangiopericytoma presented with recurrence of

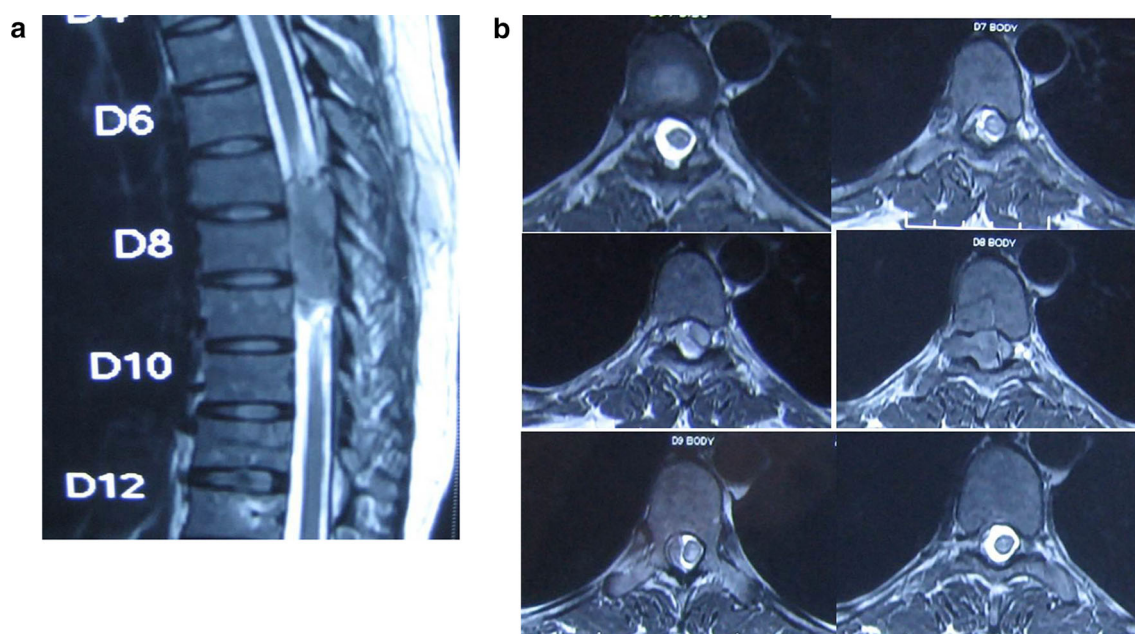


Fig. 1 **a** Pre-operative midsagittal T2WI MRI image of D7–9 intradural extramedullary hemangiopericytoma with extradural extension. **b** Pre-operative axial T2WI MRI image at D7–9 level

showing intradural extramedullary hemangiopericytoma with extradural extension extending into D8–9 foramina on the *right side*. Cord pushed towards *left side*

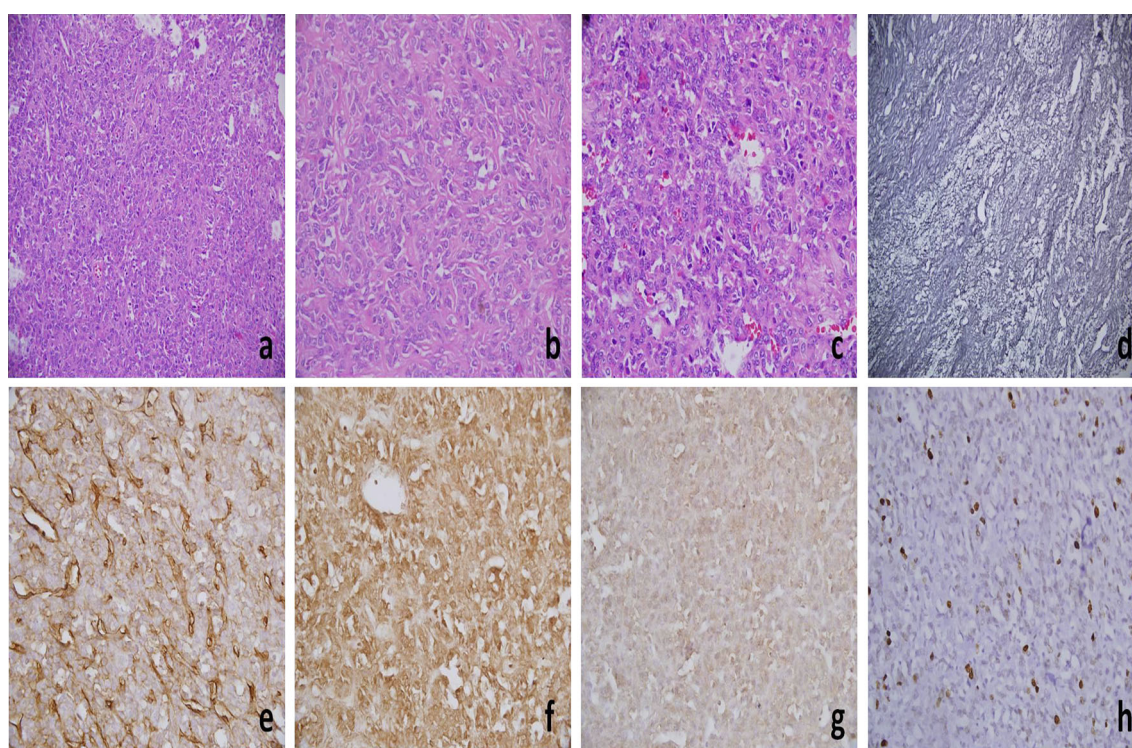


Fig. 2 Histological and immunohistochemical features of hemangiopericytoma **a** highly cellular tumor with monomorphic cells, staghorn vessels (H&E, $\times 200$), **b** higher power showing intervening fibrosis (H&E, $\times 400$), **c** Bizzare spindle cells and an occasional mitotic figure (H&E, $\times 400$), **d** reticulin rich network (special stain,

$\times 200$), **e** CD 34 immunopositivity in tumor cells and endothelial cells (IHC, $\times 400$), **f** Bcl2 immunopositivity in tumor cells (IHC, $\times 400$), **g** focal immunopositivity for Mic2 (IHC, $\times 400$), **h** MIB-1 labeling index (IHC, $\times 400$)

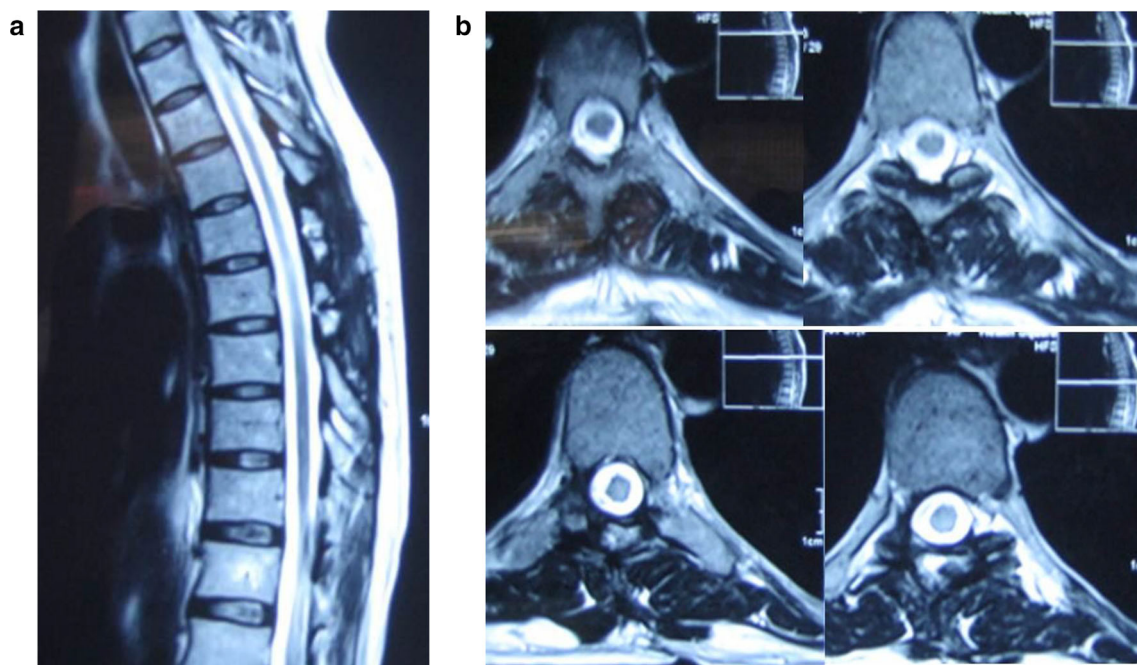


Fig. 3 **a** Post-operative midsagittal T2WI MRI image of the same patient showing complete excision of tumor. **b** Post-operative axial T2WI MRI image at D7–9 level of the same patient showing complete excision of tumor

symptoms with spastic quadriparesis. Initially, he underwent surgery 5 years back and gross total removal of tumor was done. However, no adjuvant therapy was done.

His MRI showed regrowth of tumor at C5–6 level with enhancement. Majority of the tumor was lying inside the intervertebral foramen on the left side.

Surgical intervention was done in this patient with a posterior approach following previous route. The tumor was removed subtotally because of dense scarring from previous surgery and high vascularity.

Histopathology was suggestive of anaplastic hemangiopericytoma in both ancestral and recurrent tumor samples. The recurrent sample was positive for CD34 and had a MIB-1LI of 12 %.

He received chemo and radiotherapy after second surgery and was kept in follow-up for 5 years. However, there was regrowth of the tumor with extensive spread including into the brain and he succumbed to that.

Case 5

Another female patient of 12 years presented with sudden onset paraplegia for 3 days. Pre-operative MRI of spine showed an intradural extramedullary (Type IIA) lesion at D11 to L1 level. It was enhancing on contrast injection.

She underwent D11 to L1 laminectomy. Intraoperative findings were confirmatory to that of MRI. The tumor was

moderately vascular and there was no cord invasion. Gross total excision of the mass was done.

Histopathological and immunohistochemical analysis were suggestive of anaplastic hemangiopericytoma grade III with MIB-1LI of 35 % and Bcl-2 positivity.

Considering the anaplastic nature patient was sent for adjuvant radiotherapy and she tolerated that well.

At the last follow-up, patient had significant neurological improvement with normalization of lower limb power. Follow-up MRI did not show any residual disease.

Discussion

Spinal hemangiopericytoma is a rare entity [1]. Until now, not more than 80 cases have been reported in the literature [4, 7–36]. Hemangiopericytomas are aggressive tumors with the potential for widespread metastasis [1]. Although it is considered to arise from mesenchymal cells controversy exists regarding its cell of origin [37, 38]. While some consider pericytes, which are modified smooth muscle cells found around post capillary venules, as the source of hemangiopericytomas; others think that they are more fibroblastic in nature [37, 38]. This tumor is more commonly found in males [1, 18]. Although hemangiopericytomas have been reported in all parts of spinal column, cervico-dorsal region is the commonest site involved (Table 3) [1, 7–36]. Hemangiopericytomas of spine

commonly presents with motor weakness, pain and sensory symptoms (Table 3). Sphincter involvement is relatively rare and late [11, 14, 16–18]. Data from our series also show the similar findings.

Radiologic findings in case of spinal hemangiopericytomas are often non-specific and they share similarities with other tumors [17, 18]. They are usually intradural extramedullary (type IIA), dural based, well circumscribed lesions [17, 18]. Pure intramedullary (type IIB) and pure extradural (type I) tumors are rare [4, 12, 17, 18]. On contrast-enhanced MRI, they usually enhance heterogeneously [7–9, 12, 13, 16–18]. Flow voids are frequent suggesting highly vascular nature of the lesion [17]. They are often misdiagnosed pre-operatively as meningiomas or schwannomas [17, 18]. Rarely, intramedullary hemangiopericytomas are confused with ependymomas and hemangioblastomas [18]. Angiography can be used especially when pre-operative embolization is planned. However, findings are often non-specific and pre-operative embolization in reducing intraoperative bleeding is not very helpful [17, 35].

Surgery is the primary mode of treatment for spinal hemangiopericytoma [18]. Gross total resection should be the goal [8, 35, 39–42, 45]. Some studies have shown better recurrence-free and overall survival after gross total resection of central nervous system hemangiopericytomas [17, 41, 42]. Similar findings were also seen in our study—both the patient who underwent subtotal resection died due to systemic spread of their disease. However, some other studies did not found any clinical benefit or overall and recurrence-free survival benefit after complete resection [18, 31, 35]. Liu et al. [18] cautioned against total resection of spinal hemangiopericytomas in high risk patients especially those with type IB and III tumors.

Radiotherapy, as an adjuvant treatment for CNS hemangiopericytoma, has been found to improve local control and overall survival [35, 39–45]. However, beneficial role of post-operative radiotherapy in spinal hemangiopericytoma is yet to be proven [17, 18]. Effective radiation dose that has been found by most studies is more than 50 Gy [35, 39–41, 45]. In our study, four patients received radiotherapy in the post-operative period. All of them had anaplastic tumor and two of them underwent subtotal resection. Although stereotactic radiosurgery has been used for intracranial hemangiopericytomas, its use in spinal hemangiopericytomas is sporadic and no conclusion can be drawn from the present reports [18, 39, 46]. Use of chemotherapy is rare in such tumors and available literature failed to show any benefit [35, 43, 47].

Hemangiopericytomas once considered as a type of meningioma were grouped as mesenchymal tumors in 2007 WHO classification [7]. They are of two types—grade II or low grade and grade III or anaplastic tumors [7]. These are

Table 3 Summary of previous and present case series of spinal hemangiopericytomas

References	No. of cases	Sex		Site		Type [19]					Surgery			Adjuvant therapy		Follow-up (years)			
		M	F	Cervical	Thoracic	Lumbar	Sacral	IA	IB	2A	2B	3	GTR	STR	NA				
RT	CT	SRS																	
Pitlyk et al. [14]	3	2	1	2	1	0	0	–	–	–	–	3	0	0	0	0	10–18 years		
Harris et al. [23]	2	1	1	2	0	0	0	–	–	–	–	–	–	2	2	0	0	4–5 years	
Cappabianca et al. [25]	2	0	2	2	0	0	0	–	–	–	–	–	–	2	0	0	0	Up to 2 years	
Muraszko et al. [26]	3	1	2	0	2	1	0	2	0	1	0	0	1	2	0	2	0	0	Up to 6 years
McMaster et al.[34]	5	–	–	0	4	0	1	–	–	–	–	–	–	–	–	–	–	–	–
Ecker et al. [35]	3	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Zhao and Zhao [16] and Liu et al. [18] ^a	26	14	12	10	9	7	0	5	5	8	2	6	14	12	0	22	2	2	6.6 ± 6 years
Dufour et al. [11]	4	2	2	1	3	0	0	–	–	–	–	–	3	1	0	1	0	0	2–12.6 years
Wu et al. [32]	3	2	1	2	1	0	0	–	–	–	–	–	–	–	3	0	0	0	–
Shirzadi et al. [17]	4	3	1	1	3	0	0	0	0	2	1	1	3	1	0	2	0	1	1.5–3
Present study (2014)	5	3	2	2	3	0	0	1	0	2	1	1	3	2	0	4	3	0	Mean 2 years

^a Both studies were from same institute between 1987 and 2010

GTR gross total resection, STR subtotal resection, NA not available, RT radiotherapy, CT chemotherapy, SRS stereotactic radiosurgery

most commonly intradural–extramedullary tumors with high vascularity and adherence to dura but without involvement of underlying neural tissue [1, 17, 18]. Extradural and intramedullary forms are rare [17]. Microscopically, they display high cellularity with frequent mitoses, loss of architecture, nuclear pleomorphism, and necrosis [1, 5, 18]. Sometimes ‘staghorn’ vascular channels can also be found in them [18]. Hemangiopericytomas can express a wide variety of markers of mesenchymal tissues like, HLA-DR, CD34, Leu-7, vimentin, S-100 protein, CD99, BCL-2 and factor XIIIa [48, 49]. In the present series CD34 and BCL2 were found in 80 % and MIC-2 in 60 % patients and all the tumor specimens were uniformly negative for epithelial tissue markers like EMA. Unlike meningiomas biologic behavior of hemangiopericytomas cannot be predicted from the MIB-1 LI or DNA ploidy but, we have found a high MIB1-LI level in most of the cases.

Because of its rarity, effective treatment plan and further surveillance program are yet to be decided. Studies have shown a 5-year survival rate and local tumor control rate of 76 % [18, 39, 50]. However, even after surgery and adjuvant treatment, 29 % tumors recur within 2–18 years [14, 16, 18, 50]. Three factors that are thought to be associated with good prognosis are low tumor grade, post-operative radiotherapy and gross total resection of tumor [8, 35, 39–42, 45].

Current recommendation for spinal hemangiopericytoma is gross total resection of tumor, when possible. Although its role is not well established, radiotherapy can be used in the post-operative settings in case of residual or high-grade tumors. Long-term follow-up is required because recurrences are common even after complete resection.

Conclusion

Spinal hemangiopericytomas are rare tumor and are difficult to diagnose and treat, with high recurrence rate. Strong clinical suspicion and increased awareness can help in pre-operative diagnosis. Gross total resection should be the goal. Radiotherapy should be given to the patients with high-grade tumors and with residual disease. Recurrences are common even after complete resection and hence long-term follow-up is required.

Conflict of interest None of the authors has any potential conflict of interest.

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