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ORIGINAL PAPER

Spinal meningioma in childhood: clinical features and treatment

Xiao-Qiang Wang · Xian-Wei Zeng · Bi-Yun Zhang · Ya-Fang Dou · Jin-Song Wu · Cheng-Chuan Jiang · Ping Zhong · Hong Chen

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Abstract
Object The purpose of this retrospective study is to determine the clinical characteristics and the prognosis of the spinal meningioma in childhood (under 18 years of age) based on the treatment at our institution.
Methods Ten spinal meningioma cases in children were treated during the last 9 years. The clinical data was retrospectively analyzed and the results were compared with those in the literature.
Results The series included eight males and two females and the mean age was 13.2 years. The most common initial symptoms were pain (6/10) and the common signs were limb weakness (4/10) and gait disturbance (2/10) and distal paresthesia (1/10) and bladder disturbance (1/10). Four patients had other clinical signs of neurofibromatosis type II (NF-2) such as tumors elsewhere. All the tumors were located in cervical and thoracic vertebrae. Resection according to Simpson Grade I (6/10), II (2/10), III (1/10), and IV (1/10) were performed. Grade II meningiomas accounted for 3/10 in this series. All patients were followed up with mean follow-up period of 43 months. Seven patients had recurrence of the tumor in that period and one had died.
Conclusions Spinal meningioma is an uncommon pediatric neoplasm and has a poor prognosis. It has a male predominance and is inclined to be associated with NF-2, and those that are associated with higher pathologic subtypes and NF-2 have more unfavorable outcome. Every effort should be made to achieve total removal which may decrease the incidence of recurrence.

Keywords Spinal meningioma · Simpson grade · Neurofibromatosis type II · Pediatric neoplasm · Prognosis

Xiao-Qiang Wang and Xian-Wei Zeng contributed equally to this work.

X.-Q. Wang · J.-S. Wu · C.-C. Jiang · P. Zhong (✉)
Department of Neurosurgery, Huashan Hospital,
Fudan University,
Shanghai 200040, China
e-mail: zhongping09@126.com

X.-W. Zeng
Department of Neurosurgery, Affiliated Hospital,
Weifang Medical University,
Shandong 261053, China

B.-Y. Zhang · Y.-F. Dou
Department of Radiology, Huashan Hospital,
Fudan University,
Shanghai 200040, China

H. Chen (✉)
Department of Neuropathology, Huashan Hospital,
Fudan University,
Shanghai 200040, China
e-mail: cherrychen001@126.com

Introduction

Meningioma accounts for approximately 20% of all primary central nervous system (CNS) tumors [1]. Meningioma in childhood accounts for less than 2% of all meningiomas. Spinal meningioma is not as common and accounts for 4.3% of all spinal tumors [2]. Until now about 50 cases of spinal meningiomas in childhood (SMCs) have been reported in the English literature and all of them are described as isolated case reports. The clinical features and prognosis of these types of tumors are somewhat different from those of the adult counterpart. This report provides additional data about the rarity of these types of tumor in childhood and critical review of the relevant literature. To the knowledge of the authors, this is the largest series of cases of SMC being reported that has been found in the spinal canal.

Methods

All patients that had been included in this study were 18 years or younger at the time of investigation. They had all undergone surgical treatment between January 2002 and December 2010. The surgical procedures were conducted under guidelines and the terms of all relevant local legislation of the county in China. Clinical data including age, gender, presenting symptoms, duration of symptoms, location of the lesions, neuroradiological data, and details of resection, histological findings, and adjuvant therapy were extracted from medical records. The diagnosis was verified by two pathologists who had no prior knowledge of the clinical status of these patients. They reexamined the tumor samples by using 2007 World Health Organization (WHO) classification [3]. Immuno-histochemical staining was carried out by Envision technique using monoclonal antibodies to progesterone receptors (PR; 1:100), estrogen receptors (ER; 1:100), B-cell lymphoma 2 (Bcl-2; 1:50), and MIB-1 (monoclonal antibody of cell proliferation associated nuclear antigen) (1:100). All antibodies were obtained from M/S Dako Patts—Denmark. The patients' clinical condition was determined by clinic service notes and telephone calls. The authors reviewed the medical charts of all patients who had been diagnosed with meningioma during the same period to determine the incidence of SMC among all meningiomas, meningiomas in childhood, and spinal meningiomas. In order to clarify the relation of SMC and neurofibromatosis type II (NF-2), any child who was suspected of having meningioma or neurilemmoma on admission had undergone regular detailed clinical examination (skin lesions and slit lamp examination of the lens), audiovestibular testing, and complete cranio-spinal MRI scan evaluation. Any child who was not diagnosed to have the findings of NF-2 during the first hospitalization was not found to have the condition in subsequent follow-up examination by Manchester clinical diagnostic standard [4]. Gene mutation research was not part of the protocol.

Results

Demographics

Six thousand seven hundred and eleven cases of meningiomas were diagnosed during the period from January 2002 to December 2010 at Huashan Hospital. Among these one hundred and eighty-nine (189) tumors were located in the spine. There were ninety-seven (97) patients with meningiomas in CNS who were under 18 years old. Ten patients harboring meningiomas in the spine were under 18 years old with a mean age of 13.2 years (7–18 years). Thus SMC constituted 0.15% of all CNS meningiomas, 5.3% of spinal meningiomas, and 10% of meningiomas in childhood at the institution. This series included eight males and two females.

Symptoms and signs

The most common symptom at the time of presentation was pain (6/10) followed by signs of limb weakness (4/10), gait disturbance (2/10), paresthesia (1/10), and urinary incontinence in one patient. The duration of symptoms before admission ranged from 1 to 18 months (median 4 months). Four patients (cases 3, 4, 7, and 8) had clinical signs of NF-2 during first hospitalization according to Manchester clinical diagnostic criteria [4]; the associated stigmata included schwannoma, neurofibroma, glioma, meningioma in another region, and posterior subcapsular lenticular opacity (Table 1). None of the other patients were diagnosed to be of NF-2 variety during subsequent follow-up screening. Gorlin syndrome was not present in any of the patients.

Location

Cervical spinal canal was the site of highest prevalence (n=5) followed by thoracic canal (n=3) and the other two were in the cervico-thoracic segments of the spinal canal. Nine patients had solitary lesions whereas one patient (case 3) had two tumors in separate segments of the canal. These tumors were predominantly intradural-extramedullary masses (n=8) and the others were extradural masses (n=2). The tumors covered an area of one to four spinal segments.

Radiological findings

On computed tomography (CT) and magnetic resonance (MR) imaging, all tumors were well-circumscribed masses. CT images showed predominantly isoattenuation with the mean CT value of 45 HU. The MR images mostly showed isointense to gray matter on T1-weighted images (n=6) but in others they looked to be hypointense (n=4). On T2-weighted images the tumors were mildly hyperintense or isointense to the spinal cord in equal proportion. On post contrast MR images homogenous strong enhancement was seen in all ten cases. Complete spinal and cerebral MRI scan showed the associated lesions in cases of NF-2: bilateral vestibular schwannomas (cases 3, 4, and 7), unilateral vestibular schwannoma (case 8), cervical vertebrae schwannoma (case 4), neurofibroma (cases 4, 7, and 8), left lateral ventricle meningioma (case 8), and cervical glioma (case 4).

Treatment

Standard spinal laminectomy was carried out using microscopic technique. Simpson grade I resection was achieved

Table 1 Summary of clinical presentation and pathology in the series

Case no.	Sex/age (year)	Clinical history (months)	Location	Clinical features	Tumor size (mm)	NF-2/intercurrent disease	Pathology	PR	ER	Bcl-2	MIB-1 LI (%)
1	M/9	2	C4–5, ED	Upper limb pain	30× 20× 15	N	Atypical	−	−	+	1
			LR	/	20× 10× 10		Atypical	−	−	+	1
			LR	/	30× 20× 20		Atypical	−	−	+	2
2	M/16	18	C1–2, EM	Neck pain	30× 20× 20	N	Atypical	−	−	−	2
3	M/15	5	C7, T1, ED	Upper limb pain, paresthesia	20× 20× 15	Y/ Bilateral vestibular schwannomas, posterior subcapsular lenticular opacities	Meni ngothelial	−	−	+	2
			LR	/	N/A		Meningothelial	N/A	N/A	N/A	N/A
4	M/10	12	T2, EM	Gait disturbance, limbs weakness	15× 12× 12	Y/ Bilateral vestibular schwannomas, C1–4 schwannoma, C3 glioma, T11–L5 neurofibroma	Psammomatous	++	−	+	1
5	M/7	2	C1–2, EM	Neck pain	30× 20× 20	N	Psammomatous	++	−	+	1
			LR	/	15× 10× 10		Psammomatous	+	−	+	1
6	M/18	2	C6-T2, EM	Upper limb pain, weakness	N/A	N	Clear cell	N/A	N/A	N/A	N/A
			LR	/	30× 20× 20		Clear cell	−	−	+	3
			LR	/	20× 20× 15		Clear cell	−	−	+	2
			LR	/	30× 20× 10		Clear cell	−	−	+	2
7	M/12	1	C2–5, EM	Gait disturbance	30× 20× 20	Y/ Bilateral vestibular schwannomas, T11–L5 neurofibroma	Fibro blastic	+	−	+	1

Table 1 (continued)

Case no.	Sex/age (year)	Clinical history (months)	Location	Clinical features	Tumor size (mm)	NF-2/intercurrent disease	Pathology	PR	ER	Bcl-2	MIB-1 LI (%)
8	F/18	3	C1–2, EM	Limbs anest hesia, weakness	20× 10× 10	Y/ Right vestibular schwannomas, left lateral ventricle meningioma, occipital neurofibroma	Fibroblastic	++	–	+	1
9	F/17	6	T10–11, EM	Back pain, lower limbs pain	40× 20× 10	N	Fibroblastic	++	–	+	2
10	M/10	6	T1–2, EM	Lower limbs weakness	25× 15× 10	N	Psammomatous	+	–	+	1

NF-2 neurofibromatosis type II, *PR* progesterone receptor, *ER* estrogen receptor, *Bcl-2* B-cell lymphoma 2, *MIB-1 LI* MIB-1 labeling index, *F* female, *M* male, *Y* yes, *N* no, *EM* intradural-extramedullary, *ED* extradural, *LR* local recurrence, *N/A* not applicable

in six cases, grade II in two cases, and grades III and IV in one case each. External orthosis was provided to all children for 3 weeks after operation. Two patients had developed increased motor deficits after the operations but had improved with rehabilitation therapy. Adjuvant radiotherapy was used in one patient (case 6) after the fourth operation. No patient was treated with any antineoplastic agent.

Pathological findings

Fibroblastic (3/10) and psammomatous (3/10) meningiomas were the most common pathological subtypes in this series, followed by atypical (2/10), meningothelial (1/10), and clear cell meningiomas (1/10, CCM). WHO grade II meningiomas (two atypical meningiomas and one CCM) accounted for 3/10 in this series. There was no grade III (WHO classification) tumor in this series. Bcl-2 positivity was observed in the tumors of nine patients. PR positivity was observed in six patients whereas ER immunoactivity was absent in the series. The mean MIB-1 labeling index (MIB-1 LI) was 1.5% (range 1–3) and the mean MIB-1 LI for non-recurrent meningiomas was 1.3% and it was 1.6% for recurrent meningiomas (Figs. 1 and 2). The second operation for case 3 and the first operation for case 6 were performed in another hospital and immune-histochemical studies were not possible in these two patients' tissues. However, the discharge summary had the pathological subtypes written in the records. Detailed histological characteristics of the tumors are listed in Table 1.

Prognosis

Follow-up data were obtained in all ten patients with a mean follow-up of 43 months (range 14–71 months). Seven out of the ten patients developed recurrent tumors. Two patients (cases 1 and 6) had three recurrences and case 1 had died from the complications of recurrence 20 months after the first operation. One patient had two recurrences (case 5) and the KPS (Karnofsky Performance Scale) score was 90 on the last follow-up. Four patients (cases 3, 4, 7, and 9) had one recurrence. Case 3 had another operation and he was still alive with KPS score of 80, cases 4 and 7 who had numerous associated stigmata of NF-2 had operations on other parts of CNS were in poor condition to undergo further spinal surgery. Follow-up MRI showed that the tumor in case 9 had recurred. However, she preferred further observation for personal reasons. The mean KPS score was 65 in the series in the last follow-up. Six patients were alive with KPS score ≥80 and there was no instability of the spine. Detailed follow-up data is presented in Table 2.

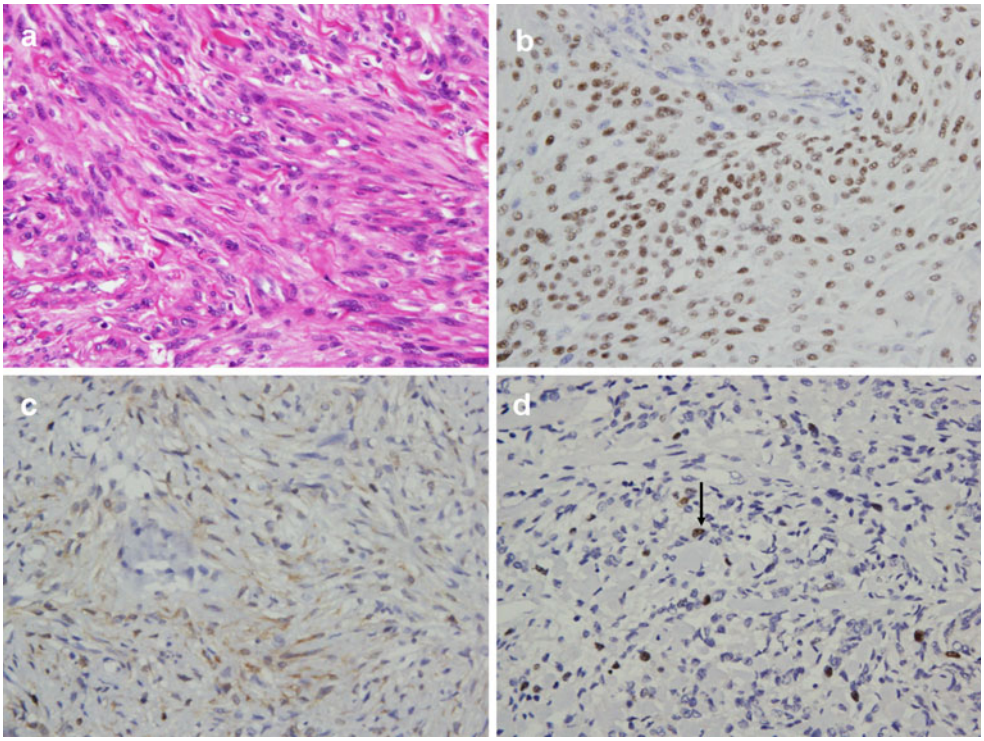

Fig. 1 Case 9. Photomicrograph of the T10–11 lesion under high magnification. **a** Hematoxylin and eosin showing the lesion is composed of sweeping, elongated cells accompanied by abundant intercellular collagen; **b** immunohistochemical stains showing the nucleus of the tumor cell is positive for PR; **c** immunohistochemical stains showing the cytoplasm of the tumor cell is positive for BCL-2; **d** the nucleus of the tumor cell is positive for MIB-1 (*arrow*) and the MIB-1 label index is 2%. (Original magnification, ×400)

Discussion

Etiology and demography

Spinal meningiomas were rare tumors in children and had distinct biological and clinical features. Pediatric meningiomas accounted for less than 5% of brain tumors in children [1]. The annual incidence of pediatric spinal tumors has been reported to be 1 in 100,000 [5, 6]. In this study, SMC constituted to be 0.15% of all CNS meningiomas and 10% of meningiomas of childhood. Spinal meningiomas in infants had been reported in literature [7–10]. The mean age at the time of diagnosis in this series was 13.2 years. The etiology of SMC was not known but some risk factors had been described such as association with NF-2 and history of radiation [6, 11]. None of the patients in this series had received radiation prior to the diagnosis. NF-2 was a multiple neoplasia syndrome with an incidence of 1 in 25,000 live births. It was the result of the mutation of the NF-2 suppressor gene that was on the long arm of the chromosome 22 and was inherited in an autosomal dominant manner [12]. Spinal lesions were frequent in NF-2 (might be as much as 90% of the patients) and included schwannomas, meningiomas, and ependymomas. Non-tumoral features of NF-2 included polyneuropathy, skin, and ophthalmic manifestations. Meningiomas were the second most frequent types of tumor in NF-2 and affected half of NF-2 patients [13]. The prevalence of NF-2 in pediatric meningioma patients was 25–40% [14, 15]. However, they were frequently asymptomatic and many were detected incidentally. They were difficult to distinguish from schwannomas by imaging alone [16]. Patients harboring seemingly isolated multiple meningiomas should be investigated thoroughly for NF-2. In the adult patients described in the literature, the prevalence of meningiomas had been reported to be more in females. The female

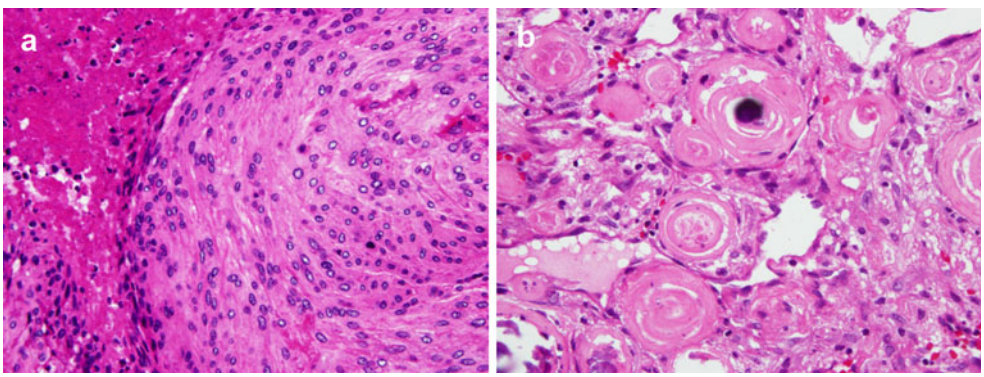

Fig. 2 **a** Case 1: photomicrograph of the C4–5 lesion under high magnification: hematoxylin and eosin showing foci necrosis and increased mitotic activity; **b** case 5: photomicrograph of the C1–2 lesion under high magnification: hematoxylin and eosin showing the lesion with numerous psammoma bodies, some calcified and intervening meningothelial cells. (Original magnification, ×400)

Table 2 Summary of treatment and outcome in the series

Case no.	Sex/age (year)	Treatment	Recurrence (Y/N)	Recurrence time (months)	Follow-up time (months)	KPS score
1	M/9	Simpson IV	Y	3	20	0
		Simpson IV	Y	6	/	/
		Simpson IV	Y	Deceased 11 months later	/	/
2	M/16	Simpson I	N	/	71	90
3	M/15	Simpson II	Y	34	62	80
		N/A	N	/	28	/
4	M/10	Simpson I	Y	12	57	30
5	M/7	Simpson II	Y	4	50	90
		Simpson II	Y	44	/	/
6	M/18	N/A	Y	18	57	80
		Simpson I	Y	19	/	/
		Simpson I	Y	12	/	/
		Simpson I +Radiotherapy	N	/	/	/
7	M/12	Simpson I	Y	15	46	40
8	F/18	Simpson I	N	/	33	80
9	F/17	Simpson III	Y	12	16	70
10	M/10	Simpson I	N	/	14	90

F female, *M* male, *Y* yes, *N* no, *mo* month, *KPS* Karnofsky Performance Scale

predilection had been attributed to the female sex hormones. However, in the pediatric age group male predominance had been reported in most studies and that corroborated with the findings in this series [15]. Some cases showed receptor sensitivity for estrogen and progesterone and in some cases had faster growth in later stages of pregnancy [17]. The exact link between hormones and development of meningiomas was not clear [18].

Clinical presentation

Clinical presentations for SMC were variable in most series. Consistent with the anatomical localization, the most common presenting symptoms were pain and limb weakness. The diagnosis of spinal tumor in a child might be delayed by inattention to these complaints. Pediatric spinal meningiomas commonly presented with back pain, radiculopathy, and gait disturbance [19]. Hearing loss and tinnitus were often the associated symptoms in patients with NF-2 [20]. In this series local pain, paresthesia, limb weakness, and urinary incontinence were the main features among the patients' complaints.

Tumor localization and imaging characteristics

The ratio of intracranial to spinal meningiomas in children was approximately 14:1 or 20:1 [1], [9], and thus the rarity of SMC was obvious. In this series the ratio is 10:1. Colen et al. reviewed 15 cases of SMCs and found that 14 cases were in thoracic and lumbar canal [19]. In this series none of the tumors was in the lumbar area. Most of these tumors were intradural–extramedullary though there were reports of these tumors being more frequently in the epidural space in children and young people [21]. MR imaging was the gold standard for diagnosing SMC. Enhanced MR imaging modality clearly delineated the location of the tumor and its relation to the cord and the different degrees of peritumoral edema which was helpful in planning surgery. When a child was suspected of meningioma or schwannoma, the whole neuraxis should be studied to avoid some lesions to be omitted.

Histopathological findings

Psammomatous and fibroblastic meningiomas were the most common pathological subtypes in this series as had been reported in the literature in cases of spinal meningioma [22]. The former type was firmer and adherent and thus caused the post-operative neurological deficit in one patient of our series. CCM was a rare subtype and accounted for 0.2% of all CNS meningiomas in the reported literature [23]. However, in the pediatric group CCM seemed to be the most common subtype [2, 8, 23–25]. In this series there was only one case of CCM. Meningioma was considered to be potentially hormone sensitive. The preponderance of PR and scarcity of ER was well known [26, 27]. Malignant meningiomas were devoid of PR and ER. There were reports suggesting that progesterone might at least contribute to the growth of PR positive meningiomas and might be responsible for recurrence [17]. In this series PR showed to be negative in all three WHO grade II meningiomas and one WHO grade I meningioma and ER

immunoactivity was absent in all. The results from this series confirmed presence of lower PR values in grade II meningioma. Bcl-2 was the prototype member of a large family of apoptosis regulating proteins and had been shown to have a role in carcinogenesis via inhibition of apoptosis. Bcl-2 immunoreactivity was more frequently observed in the recurrent meningioma than the non-recurrent [28]. In adult meningioma Bcl-2 immunoreactivity varied from 23.3% to 55.9% [29]. However immunoreactivity was 90% in this study. Different pathogenetic factors might account for the occurrence of this type of tumor in children than in adults. SMC had a tendency to have higher Bcl-2 reactivity. Previous reports had suggested that MIB-1 LI could be used to predict the prognosis in patients with meningioma [23, 24, 30]. However, the limited number of patients with SMC made it difficult to assess the value of MIB-1 LI to predict the recurrence rate. In this series the mean MIB-1 LI was 1.6% in the cases with recurrence and it was 1.3% without recurrence. It seemed that the association of MIB-1 LI as a predictor for the risk of recurrence was weak in pediatric meningiomas although MIB-1 LI was a vital prognostic factor in adult cohorts [31, 32]. Gao et al. also reported that the prognostic value of MIB-1 LI was low in pediatric meningiomas on the basis of 54 cases [33]. In adult meningiomas mean MIB-1 LI had been reported to be 4% for grade I, 7% for grade II, and 15% for grade III tumors [23].

Treatment, outcome, and prognosis

Total resection with wide dural clearance should be the goal of treatment. Complete resection could be achieved with good post-operative outcome in most cases [34]. In our series, Simpson grade I resection was achieved in six cases, grade II in two cases, grade III and IV in one case on the first operation, respectively. The extent of resection might be predictive for recurrence. There were many factors that could prevent total resection. Location, size, blood loss, adhesion, and the pathological subtypes (causing severe adhesion) could all be factors that would interfere with total resection. Proper judgment had to be exercised to prevent permanent neurological deficit. SMC had a tendency to be high-grade meningioma [15, 35]. The first operation of case 1 was performed by orthopedist at our hospital (spinal surgery can be performed by either neurosurgeon or orthopedist in China). Because the tumor basal area was broad, the mass had abundant blood supplement and extended to the ventral cord, Simpson IV was attained in order to avoid the secondary lesion. Though post-op radiotherapy was suggested to be performed on the 9-year-old boy with atypical meningioma, the parents did not follow the proposal because of their considerations on the effects of radiotherapy on development of spinal cord. Unfortunately, the mass recurred in a short time. It was difficult for us to reach a total removal because of the extensive adherence on the subsequent operation. Finally, the boy died from the tumor recurrence. In this series the tumor recurred in seven patients (three of these were Simpson grade I). The three patients whose tumors did not recur were considered to have had Simpson grade I resection. Both the patients whose tumors had Simpson grade III and IV resection recurred in 3 and 12 months, respectively. The pathological subtype and the extent of resection seemed to be the important factors in recurrence. Although some SMCs could undergo complete resection and might be grade I meningiomas, but they were apt to be accompanied with NF-2 and thus might harbor multiple lesions. In our series, four patients were confirmed to be associated with NF-2, three of which recurred with a mean recurrence time of 20 months. SMCs with NF-2 were multiple disorders, and the prognosis of patients was not only affected by the spinal meningioma itself, but also by the intercurrent illness, such as vestibular schwannoma, neurofibroma, or glioma. When the patient was in a poor physical condition, he might lose the opportunity of further surgical therapy. Cases 4 and 7 in our series were in poor condition with KPS score 30 and 40 at the last follow-up; both gave up further surgical therapy. Adjuvant radiotherapy had been reported to be beneficial in adults but in children issues of potential hazard to the spinal cord and other organs were to be considered. In the institution of the authors, radiotherapy was considered in cases of high-grade meningioma after incomplete removal in children who were more than 5 years old. All of these might explain for worse prognosis for SMC.

Conclusions

In summary, SMC is a rare neoplasm and has poor prognosis and recurrence rate is high despite efforts to remove completely. Cervical or thoracic tumors seem to be more common in this series and most tumors are intradural–extramedullary. SMC has a male predominance and a higher pathologic subtype, and is inclined to be associated with NF-2. SMC has a more unfavorable outcome, especially in those that are associated with higher pathologic subtypes or NF-2. The prognostic value of MIB-1 LI is low in this group. More data needs to be collected to determine the prognosis adequately.

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Conflict of interest None.

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