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ORIGINAL PAPER

The clinical features and surgical outcomes of pediatric patients with primary spinal cord tumor

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Abstract
Background Primary spinal cord tumors (PSCTs) in pediatric patients are rare, with a reported overall incidence rate of 1–2.6 per one million children. We reviewed our experience of surgically treated 27 pediatric patients with PSCT and discussed the clinical features, radiological findings, surgical outcomes, and prognostic factors.
Methods Between March 1999 and March 2010, a total of 27 pediatric patients with PSCT were surgically treated in a single institution. We retrospectively analyzed their data.
Results There were 13 females and 14 males, and their ages ranged from 6 months to 19 years (mean age, 12.1 years). The most common presenting symptom was motor weakness, and the histologic type of the tumors were mainly schwannoma, astrocytoma, and ependymoma. The tumor was completely resected in 17 patients, subtotally resected in 7 patients, and partial resection or biopsy was performed in 3 patients. Adjuvant chemotherapy was performed in 9 patients, and radiotherapy in 12 patients, respectively. The average follow-up period was 33.5 months (1.17–129). Five patients experienced the progression of disease, and three of them expired. The mean time for disease progression was 19.0 months (4.5–48.7).
Conclusions PSCT in pediatric patients can be surgically removed with an acceptable low surgical morbidity. Progression-free survival was found to be related to the grade of tumor and the extent of tumor resection. Early diagnosis and treatment anticipate good functional neurologic outcome.

Keywords Primary spinal cord tumor · Spinal cord · Pediatric · Prognostic factors

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Introduction

Primary spinal cord tumors (PSCTs) comprise 4–8% of all tumors from the central nervous system. While they are not uncommon, it is rarely found in pediatric patients with a reported overall incidence rate of 1–2.6 per one million children [1–3].

Traditionally, the treatment method of PSCT was conservative dural decompression surgery followed by adjuvant treatment including radiation therapy for the purpose of preventing iatrogenic neural injury. With the advent of modern neuroimaging equipment, operating microscopy, intraoperative neurophysiologic monitoring, and microsurgical techniques, more aggressive resection of PSCT became

feasible and resulted in long-term survival of the patients [4–6].

Unlike many studies involving adult patients, there are only a handful of studies about prognostic factors associated with survival and functional outcome of PSCT in pediatric ages [7–11].

In this study, we retrospectively reviewed a series of 27 pediatric patients with surgically treated PSCT in a single institution and discussed the clinical features, radiological findings, surgical outcomes, and prognostic factors.

Methods and materials

Patient population

Between March 1999 and March 2010, a total of 27 consecutive pediatric patients with PSCT were surgically treated in a single institution, and their charts were retrospectively reviewed. The clinical presentation, magnetic resonance imaging (MRI) characteristics, intraoperative findings, and pathological results were recorded.

Neurological scoring

Patients' preoperative and postoperative neurological statuses were classified using the modified McCormick scale (MMCS; Table 1) [12].

Surgery

The surgery was performed under the standard microsurgical conditions using the conventional laminectomy in early days and osteoplastic laminotomy in recent years. The extent of tumor resection was classified into three groups as total, subtotal, and partial or biopsy. Tumor removal was defined as a total resection if at least 95% of the tumor was removed based on postoperative MRI. If the resection was less than 50%, the removal was defined as a partial resection. Otherwise, the resection was classified as a subtotal resection.

Table 1 Modified McCormick scale for functional classification of patients

Grade	Definition
1	Neurologically intact, ambulates normally, may have minimal dysesthesia
2	Mild motor or sensory deficit, maintains functional independence
3	Moderate deficit, limitation in function, independent with external aid
4	Severe motor or sensory deficit, dependent with external aid
5	Paraplegia or quadriplegia

Follow-up

The follow-up of patients was performed via clinic visits. Standard follow-up consisted of clinic visits after postoperative 1, 2, 3, and 6 months, and then every 6 months thereafter. The average follow-up period was 33.5 months (1.17–129 months). Recurrence-free period was defined as the interval between the operation and the last follow-up without clinical and radiological evidence of tumor regrowth. Time to tumor progression was defined as the time interval between the operation and follow-up MRI demonstrating tumor regrowth or time to death due to disease progression.

Statistical analysis

Statistical analysis was carried out using Kruskal–Wallis test and Mann–Whitney U test for intergroup comparison, and recurrence-free survival was analyzed using the Kaplan–Meier analysis with the use of the log rank test. Statistical Package for Social Science for Windows Release 14.0 was used, and a p value less than 0.05 was considered significant.

Results

The patients' data are summarized in Table 2.

Clinical presentation

There were 13 female and 14 male patients, and their age ranged from 6 months to 19 years (mean age, 12.1 years). The most common presenting symptom was motor weakness followed by axial pain and sensory change. The mean duration of symptoms was 7.3 months (0.25–36) before the time of operation. The type of motor weakness was paraparesis (12 patients, 44%), followed by monoparesis (six patients, 22%), and quadriparesis (three patients, 11%). Among nine patients who complained of pain before diagnosis, seven patients had axial pain, and the remaining two patients suffered both axial pain and limb pain.

Imaging study findings

The spinal location of the tumor was cervical in 7 patients, thoracic in 20 patients, lumbosacral in 1 patient, and multilevel region in 5 patients. Eleven patients had an intramedullary

Table 2 Clinical characteristics of patients

Case no.	Age (years)	Sex	Symptoms	Duration (months)	Pathology	Treatment			MMCS			Outcome	F/u (months)
						Resection	CTx	RTx	Preop	Postop	Last		
1	5	F	Paraparesis	1.5	Neuroblastoma	T	Y	Y	5	5	4	↑	129.20
2	0.9	M	Scoliosis	8	Ganglioglioma	T	N	N	5	5	5	0	112.97
3	16	M	Both buttocks pain	9	Schwannoma	T	N	N	2	1	1	↑	30.07
4	14	M	Incidental	no	Schwannoma	T	N	N	1	1	1	0	24.47
5	13	M	Quadriparesis	8	Schwannoma	T	N	N	4	3	2	↑	76.63
6	6	F	Paraparesis, gait disturbance	1	Astrocytoma, pilocytic	ST	Y	Y	3	1	5	Progress	72.40
7	17	M	Paraparesis	18	PNET	T	Y	Y	3	3	3	Dead	19.30
8	14	M	Paraparesis, foot sensory change	1	Schwannoma	T	N	N	2	1	1	↑	48.10
9	10	M	Monoparesis, Rt L/Ex	1	Astrocytoma, diffuse	P	Y	Y	4	5	5	Dead	8.43
10	17	M	Lt hemiparesis	2	Schwannoma	T	N	N	2	1	1	↑	75.40
11	6	M	LBP, B/B symptom, paraparesis	11	Astrocytoma, pilocytic	T	N	N	4	3	2	↑	52.10
12	19	M	Rt L/Ex sensory change, weakness	12	Astrocytoma, pilocytic	ST	N	Y	2	1	1	↑	40.00
13	14	F	LBP, abdominal pain, Lt L/Ex weakness, urinary incontinence	5	Astrocytoma, anaplastic	ST	Y	Y	3	4	2	Progress	48.77
14	13	F	Lt arm weakness	3	Schwannoma	T	N	N	2	1	1	↑	35.67
15	16	F	Sacral area pain	36	Schwannoma	T	N	N	1	1	1	0	4.00
16	18	M	Quadriparesis, all Ex sensory change	6	Astrocytoma, pilocytic	T	N	N	2	5	2	0	22.43
17	15	F	Rt hand tingling, weakness	12	Schwannoma	ST	N	N	2	2	1	↑	14.00
18	15	F	Paraparesis	0.5	Ependymoma, myxopapillary	B	N	Y	1	2	4	↓	20.13
19	19	M	Lt shoulder, arm numbness	12	Ependymoma	T	N	N	1	1	1	0	12.17
20	19	F	PNP, Lt arm pain and paresthesia, both hand numbness	6	Hemangioblastoma	T	N	N	2	3	1	↑	6.33
21	5	F	PNP, subjective quadriparesis	6	PNET	T	Y	Y	1	1	1	0	3.97
22	3	M	Gait disturbance, urinary difficulty	0.5	ATRT	ST	Y	Y	5	5	5	0	2.13
23	10	F	LBP	1	Ependymoma, myxopapillary	T	N	N	2	1	1	↑	1.27
24	12	F	PNP, Rt shoulder pain	0.75	Glioblastoma	P	Y	Y	1	1	1	0	5.93
25	12	F	Paraparesis	4	Schwannoma	T	N	N	3	3	1	↑	1.17
26	16	M	LBP, both leg pain	24	Ependymoma, myxopapillary	ST	N	Y	2	2	1	↑	17.53
27	0.6	F	Paraparesis, urinary incontinence	0.25	ATRT	ST	Y	Y	4	4	5	Dead	7.50

CTx chemotherapy, *RTx* radiotheray, *Preop* preoperative, *Postop* postoperative, *F/u* follow-up, *Lt* left, *Rt* right, *L/Ex* lower extremity, *LBP* lower back pain, *B/B* bladder/bowel, *PNP* posterior neck pain, *PNET* primitive neuroectodermal tumor, *ATRT* atypical teratoid/rhabdoid tumor, *T* total, *ST* subtotal, *B* biopsy, *P* partial, ↑ improved, ↓ deteriorated

tumor, 12 patients had an intradural extramedullary tumor, 3 patients had an extradural tumor, and 1 patient had a tumor located in both intradural extramedullary and extradural areas. The mean vertebral level for the size of the lesion was 4.5 levels (1–17 levels). MRI data were available for 26 patients, and contrast enhanced images were available for 25 patients. On T1-weighted image, all except one patient showed an isointense signal. T2-weighted images showed high signal intensity for 19 patients and an isointense signal for 7 patients. Twelve patients demonstrated homogeneous enhancement, and 11 patients demonstrated heterogeneous enhancement after contrast administration. Five patients showed cystic

portion inside the tumor and seven patients had tumor-associated syrinx (Table 3; Fig. 1).

Treatment

Surgical treatment was performed in all patients. For the surgical approach, 12 patients underwent osteoplastic laminotomy, and 1 patient underwent additional laminectomy of atlas. Twelve patients underwent conventional laminectomy, and the remaining two patients underwent simultaneous fusion procedures. Complete resection of the tumor was performed in 17 patients, and 7 patients underwent subtotal resection. Partial resection or biopsy only was achieved in the remaining three patients. We observed no major complications related to the surgical procedures. Adjuvant chemotherapy was performed in 9 and radiotherapy in 12 patients, respectively.

Histopathologic findings

Histopathological examination showed an astrocytoma in six patients, ependymoma in four patients, and schwannoma in nine patients. There were two patients with primitive neuroectodermal tumor, and two patients with atypical teratoid/rhabdoid tumor. The remaining four patients were diagnosed with hemangioblastoma, glioblastoma, gangliglioma, and neuroblastoma, respectively. According to the WHO classification system, 18 tumors were grade 1, 2 tumors grade 2, 1 tumor grade 3, and 4 tumors grade 4 (Table 4).

Outcomes and prognostic factors

Postoperatively, 5 of 27 patients suffered progression of the disease, and 3 of them expired. The mean time for disease progression was 19.0 months (4.5–48.7). The cumulative

Table 3 Summary of radiologic findings

Case no.	Level	Location	Pathology	MRI findings					
				T1	T2	Enhancement	No of involved level	Cyst	Syrinx
1	C7–T5	ED	Neuroblastoma	NA	NA	NA	6	NA	NA
2	T1–L3	IM	Ganglioglioma	↔	↔	I	15	N	N
3	L5/S1	IDEM	Schwannoma	↔	↑	H	2	Y	N
4	T9/10	IDEM	Schwannoma	↔	↑	I	2	N	N
5	C2/3	IDEM	Schwannoma	↔	↔	H	2	N	N
6	T5–12	IM	Astrocytoma, pilocytic	↔	↑	I	8	Y	Y
7	T9	IM	PNET	↔	↑	N	1	N	N
8	T8	IDEM	Schwannoma	↔	↑	H	1	N	N
9	C6–T4	IM	Astrocytoma, diffuse	↔	↔	I	6	N	Y
10	FM	IDEM	Schwannoma	↔	↑	H	2	N	N
11	T10	IM	Astrocytoma, pilocytic	↔	↑	H	1	Y	Y
12	C6/7	IM	Astrocytoma, pilocytic	↔	↑	I	2	N	N
13	T5–T10	IM	Astrocytoma, anaplastic	↔	↑	I	6	Y	Y
14	C5/6	IDEM	Schwannoma	↔	↑	H	1	N	N
15	L5–S3	IDEM	Schwannoma	↔	↔	H	4	N	N
16	T5–T8	IM	Astrocytoma, pilocytic	↔	↔	N	4	N	Y
17	C5/6	ED	Schwannoma	↔	↔	H	2	N	N
18	T2–S1	IDEM	Ependymoma, myxopapillary	↔	↑	H	17	N	N
19	T3/4	IM	Ependymoma	↔	↑	I	2	N	Y
20	C0–C2	IM	Hemangioblastoma	↔	↑	I	3	Y	Y
21	C2–C4	ED	PNET	↔	↔	H	3	N	N
22	T6–T12	IDEM	ATRT	↔	↑	I	7	N	N
23	L1–3	IDEM	Ependymoma, myxopapillary	↔	↑	H	3	N	N
24	C4–C7	IM	Glioblastoma	↔	↑	I	5	N	N
25	T4/5	IDEM + ED	Schwannoma	↑	↑	NA	2	N	N
26	L2–S1	IDEM	Ependymoma, myxopapillary	↔	↑	H	5	N	N
27	T11–S2	ED	ATRT	↔	↑	I	9	N	N

ED extradural, *IM* intramedullary, *IDEM* intradural extramedullary, *NA* not available, ↑ hyperintense, ↓ hypointense, ↔ isointense, *H* homogeneous, *I* inhomogeneous

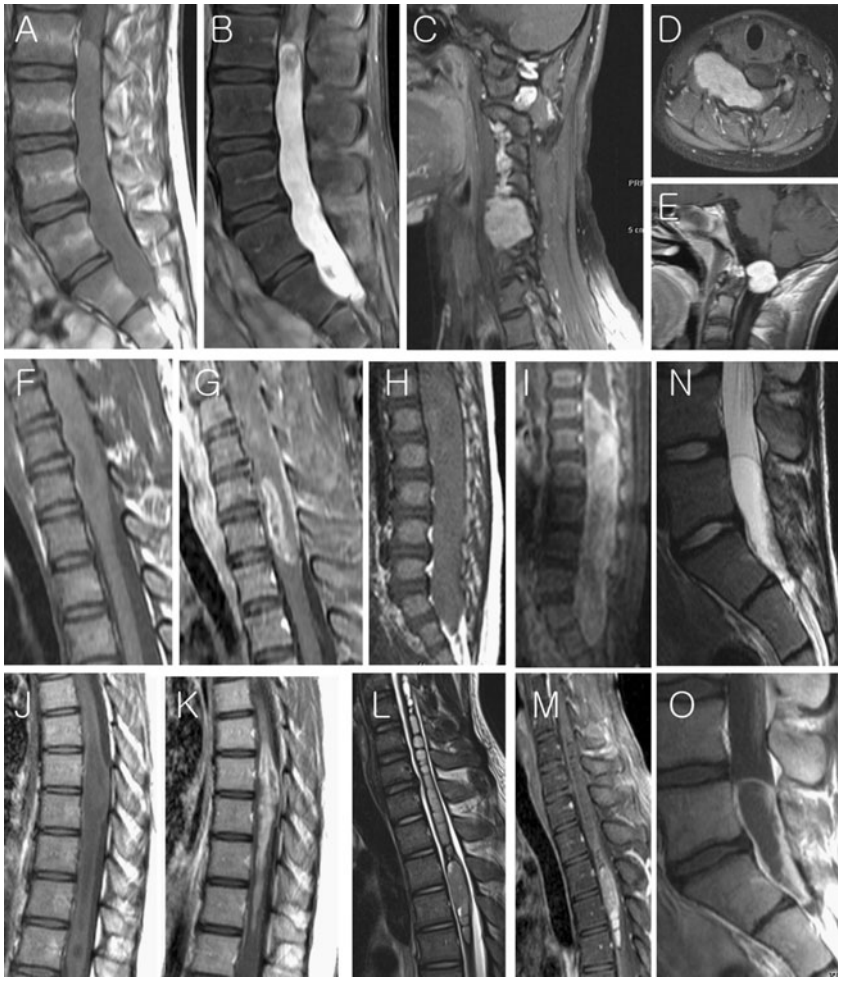

Fig. 1 MRI findings of pediatric spinal cord tumors. **a**–**b** Myxopapillary ependymoma with homogeneous enhancement. **c**–**d** Schwannoma at C5 and C6 level with foraminal extension. **e** Homogeneously enhancing schwannoma at the foramen magnum. **f**–**g** Glioblastoma with peritumoral edema and heterogeneous enhancement at midcervical level. **h**–**i** Heterogeneously enhancing ATRT in the lumbosacral area. **j**–**k** Heterogeneously enhancing anaplastic astrocytoma with syrinx and edema at the midthoracic level. **l**–**m** Ependymoma with profound tumor-associated syrinx. **n**–**o** Schwannoma containing a cyst inside the tumor

Table 4 Summary of clinical characteristics of patients

Variables	
Mean age	12.1 (0.6–19) years
M/F	14:13
Mean symptom duration	7.3 months
Level	
Cervical	7
Thoracic	10
Lumbosacral	4
Foramen magnum	1
Multilevel	5
WHO grade of pathology	10
1	18
2	2
3	1
4	6
Progression of disease	5 (21%)
Long-term MMCS outcome	
Improved	13 (59%)
Unchanged	8 (36)
Worsened	1 (5%)

survival rate was significantly higher in total tumor resection group compared to subtotal and partial or biopsy groups (p=0.044; Fig. 2) and in low-grade (grades 1 and 2) tumor group than high-grade (grades 3 and 4) tumor group (p=0.030; Fig. 3).

Clinical predictors for tumor grade were enhancement pattern and patient age. That is, high-grade tumor was more common in younger patients (<6 years; p=0.005) and in patients showing heterogeneous contrast enhancement on MRI (p=0.005). Other variables including sex, duration of symptom, number of involved vertebral levels, associated cyst, and syrinx did not correlate with tumor grade with statistical significance.

In terms of functional neurologic outcomes of 22 patients with well-controlled disease, 13 patients experienced improvement in the neurological state on the MMCS compared to their preoperative status, and eight patients remained unchanged. There was one patient who experienced postoperative worsening of neurological state (case 18; Fig. 4). She presented with subjective paraparesis of her lower extremities, and her MR images demonstrated an extensive IDEM tumor from T2 to S1 with diffuse leptomeningeal seeding.

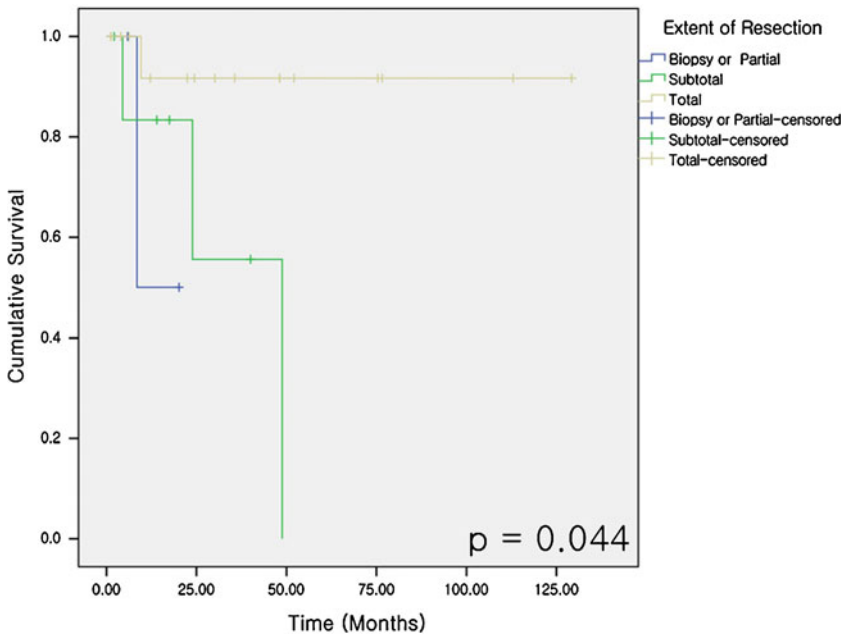

Fig. 2 The effect of the degree of tumor resection on progression-free survival. The cumulative survival rate was significantly higher in total tumor resection group

Biopsy was done, and the pathologic examination revealed myxopapillary ependymoma. She underwent radiotherapy, but her motor strength gradually worsened to grade 2 at the last follow-up. The only statistically significant prognostic factor related to long-term functional outcome was the preoperative neurologic state (p=0.014; Table 5).

Discussion

The spinal cord tumors can be classified into three groups based on the location. The extradural tumors, which were located between the bony structures and the dura, represent approximately 30% of all spinal cord tumors in children. The most common histologic types have been reported as neuroblastoma and sarcoma [13]. Two of our patients belonged to these histologic types except one schwannoma patient.

Intradural extramedullary tumors account for approximately 25% in children [8]. Unlike most previous studies reporting the relatively rare incidence of meningioma, schwannoma, and neurofibroma in children than those in adults, schwannoma was the most common type of tumor (58%), followed by myxopapillary ependymoma (25%) and atypical teratoid/rhabdoid tumor (17%) in the present series.

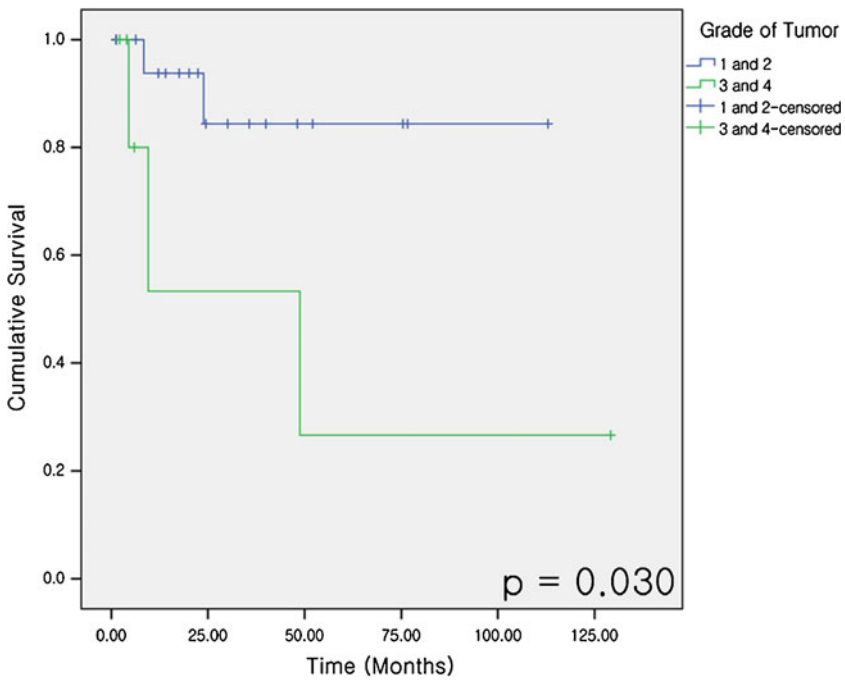

Fig. 3 The effect of tumor grade on progression-free survival. The cumulative survival rate was significantly higher in patients with low-grade (grades 1 and 2) tumor

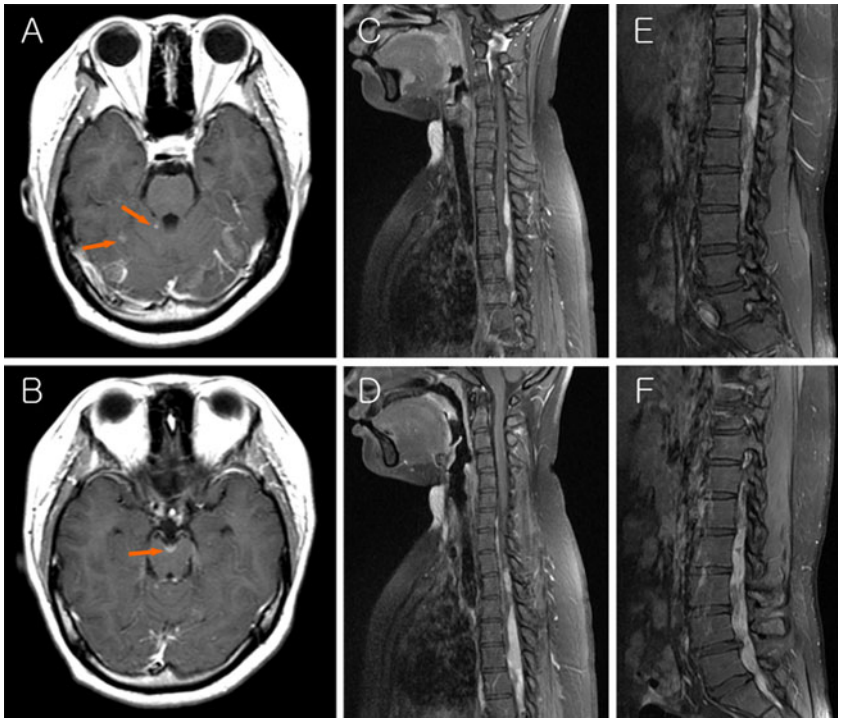

Fig. 4 Case 18. Myxopapillary ependymoma. **a**–**b** Intracranial tumor spreading to the cerebellar folia and around the midbrain. **c**–**f** A homogeneously enhancing tumor with disseminated CSF seeding at T2–S1 level

Intramedullary tumors are known to comprise 25–35% of intraspinal tumors in children [4, 14, 15]. The most common histologic type is low-grade astrocytoma followed by ependymoma and ganglioglioma, which is similar with our series.

Symptom presentations in pediatric patients with intraspinal tumors are somewhat different from those of adults. Unlike adult patients who usually present with sensory changes, pain, or myelopathy, pediatric patients often present with vague, nonspecific, generalized symptoms, which often leads to delayed diagnosis of tumor with progressed motor weakness. Indeed, 21 of 27 (78%) patients had motor weakness, and only 6 patients (22%) had no motor weakness at the time of diagnosis in this series. Furthermore, most patients who presented with pain or sensory changes (85%) were adolescents.

Table 5 Preoperative neurological status and postoperative outcome (MMCS)

Preop grade	Long-term outcome					Total
	1	2	3	4	5	
1	5	0	0	10	0	6
2	9	1	0	0	0	10
3	1	0	0	0	0	1
4	0	2	0	0	0	2
5	0	0	0	1	2	3
Total	15	3	1	2	2	22

P=0.014

MRI is the imaging modality of choice for the diagnosis of spinal cord tumor in pediatric patients as well. Many tumors (19/27, 70%) showed discrete hyperintense signal on T2-weighted images, and most tumors (23/25, 92%) showed contrast enhancement with gadolinium administration. In addition, the pattern of contrast enhancement was closely related to tumor grade as mentioned above. Five patients showed a cystic portion inside the tumor, and seven patients were found with tumor-associated syrinx, but these findings did not correlate with tumor grade nor survival and functional outcomes.

Due to the paucity of large case series of pediatric patients with PSCT, an optimal therapeutic modality remains unclear and should to be elucidated. In our series, the most important prognostic factors affecting progression-free survival of pediatric patients with PSCT were the extent of resection and tumor grade, which is consistent with numerous previous reports [3, 5, 16]. Moreover, except for patients with disease progression, 21 of 22 patients did not at least deteriorate in condition compared with their preoperative conditions. In this regard, complete surgical resection should be aimed in pediatric patients with PSCT too, if feasible. Radiotherapy and chemotherapy would be reserved for high-grade tumors, tumors with extensive cerebrospinal fluid seeding at the time of diagnosis, and unresectable tumors without significant neurological deterioration.

The only factor related to postoperative functional outcome was preoperative neurologic state. To expect good functional outcome, it is crucial to diagnose and treat the patient as soon as possible before the development of serious preoperative neurologic impairments.

Limitations of this study include the retrospective study design, a small number of cases, relatively short follow-up periods, and nonuniform chemotherapy and radiotherapy regimens. However, we investigated postoperative functional outcome as well as survival and clinical predictors of tumor grade for the first time to our knowledge.

In conclusion, PSCT of pediatric patients can be surgically removed with acceptable low surgical morbidity. Progression-free survival was found to be related to tumor grade and the extent of tumor resection. Early diagnosis and treatment are important for good functional neurologic outcome.

Ethical standards All human studies have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All persons gave their informed consent prior to inclusion in this study.

Conflicts of interest The authors declare that they have no conflicts of interest.

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