ORIGINAL ARTICLE

Surgery for Primary Filum Terminale Ependymomas: Outcome and Prognostic Factors

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SUMMARY

Introduction: Primary filum terminale ependymoma (PFTE) is a unique type of ependymomas and locates on extramedullary site. However, the clinical features and prognostic factors of PFTE are still unknown due to its rarity. **Aim:** This study aimed to evaluate the clinical features, outcomes, and prognostic factors of PFTE in the largest series of cases. **Result:** Thirty-eight patients were included in this study. Gross total removal (GTR) of the tumors was achieved in 33(87%) patients. Five (13%) patients had subtotal resection (STR). For the residual tumors, postoperative radiotherapy increased the interval between the first surgery and tumor regrowth ($P = 0.063$). Six patients had local recurrence/progression. Univariate analysis identified STR($P = 0.001$), unencapsulated tumor ($P = 0.018$), tumor involving more than two vertebral columns ($P = 0.005$), and tumor invading sacral canal($P < 0.001$) as predictors of tumor recurrence. In addition, 36 (95%) patients had stable or improved neurological status directly after surgery. Klekamp–Samii score was better correlated with the symptoms than McCormick scale. **Conclusion:** Extent of surgical removal, tumor size, tumor location, and the integrity of tumor capsule are the prognostic factors of PFTEs, and the intrasacral PFTEs always have a poor prognosis.

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The first two authors contributed equally to this work.

Introduction

Spinal cord ependymomas are rare neoplasms and account for 1–5% of spinal tumors [1,2]. They are mainly intramedullary [2–4]; however, about 35–40% of them originate from the filum terminale and are extramedullary [5–7]. These tumors are known as primary filum terminale ependymomas (PFTEs). Primary filum terminale ependymomas have significantly different surgical outcome, metastasis rate and relapse rate from intramedullary ependymomas. However, most previous studies are focused on PFTEs and intramedullary ependymomas together in a same series due to the rarity of PFTE [3,4,7–10]. Thus, these studies cannot reveal the real outcome of PFTEs. Only few series of pure PFTEs have been studied and the sample size was always small [11–14], and the clinical features and prognostic factors are unclear and controversial in some aspects.

Unlike intramedullary ependymomas, the most common histological type of PFTE, is myxopapillary ependymomas (MPE). According to the classification of World Health Organization (WHO), MPEs belong to grade I tumors [15], which are usually histologically benign and slow-growing tumors. However, in some

cases, the outcomes are not so benign [4,16]. Therefore, some investigators recommended surgery and adjuvant radiotherapy (RT), whereas others advocated gross total resection (GTR) alone might achieve good clinical outcomes [4,17,18]. Prognosis of filum terminale ependymomas is related to the length of clinical history and the extent of tumor resection [14]. However, there might be some other potential prognostic factors, such as the tumor location, the histology and the integrity of the tumor capsule. The objective of this study is to evaluate the clinical features, outcome and prognostic factors of PFTE in a series of 38 patients, which is the largest series ever been reported. In this series, a minimally invasive technique was also introduced for some PFTEs.

Materials and Methods

Patient Population and Clinical Data

One hundred and seventy-eight patients received surgical treatment in Changzheng hospital for spinal cord ependymomas from 2001 to 2012. Of these 178 patients, 38 (21%) had tumors originating from the filum terminale. Patients with ependymomas

Table 1 Klekamp–Samii clinical scoring system [19]

Score	Sensory deficits, pain, dysesthesias	Motor weakness	Gait ataxia	Bladder function	Bowel function
5	No symptom	Full power	Normal	Normal	Normal
4	Present, not significant	Movement against resistance	Unsteady, no aid	Slight disturbance, no catheter	Slight disturbance, full control
3	Significant, function not restricted	Movement against gravity	Mobile with aid	Residual, no catheter	Laxatives, full control
2	Some restriction of function	Movement without gravity	Few steps with aid	Sometimes catheter	Sometimes loss of control
1	Severe restriction of function	Contraction without movement	Standing with aid	Often catheter	Often loss of control
0	Incapacitation of function	Plegia	Wheel chair	Permanent catheter	No control

Table 2 McCormick classification [5]

Grade	Definition
I	Neurologically normal; mild focal deficit insignificantly affecting the function of the involved limb; mild spasticity; normal gait
II	Presence of sensorimotor deficit affecting function of involved limb; Mild to moderate gait difficulty; Severe pain or dysesthetic syndrome impairs quality of life; Independent function and ambulation maintained
III	More severe neurological deficit; Requires cane and/or brace for ambulation or maintains significant bilateral upper-extremity impairment; May or may not function independently
IV	Severe neurological deficit; Requires wheelchair or cane and/or brace with bilateral upper-extremity impairment; Usually not independent

arising from the conus medullaris were excluded from this study. All patients' charts, including medical records, radiological findings, pathological findings, surgical reports, and follow-up examinations, were studied retrospectively by the same junior physician. The following data were recorded from the charts: age at surgery; sex; presenting symptoms; duration of symptoms before diagnosis; radiological findings; tumor location; extent of surgery (gross total resection [GTR] vs. subtotal resection [STR]); histological findings; postoperative radiotherapy; postoperative neurological outcome; recurrence; and treatment for recurrence. Standardized telephone interviews were performed if necessary.

Both Klekamp–Samii (KS) scores [19] and McCormick (McC) scale [5] were applied to assess the neurological function of patients (Tables 1 and 2). The assessment was performed before surgery, at discharge, at 3 months after surgery, and at the last follow-up (>9 months). By comparing the pre-operative neurological status with the status during the follow-up time, the neurological

outcomes were classified into “improved,” “unchanged,” and “worse.” Tumor recurrence and progression were defined as the presence of new symptoms related to tumor growth and/or tumor regrowth on follow-up MRI.

Surgical Treatment

No patients had previously received surgical or nonsurgical treatment. In the present study, 32 patients underwent laminectomy, three unilateral interlaminar fenestration, and three laminoplasty. Unilateral interlaminar fenestration is a minimally invasive approach and can be used in selective cases (Figure 1A–E). The intraoperative neuro-physiological monitoring system has been introduced to our department since 2007, and somatosensory-evoked potentials (SSEP) and motor-evoked potentials (MEPs) were monitored in the recent 13 of 38 (34%) patients in the surgical process.

Figure 1 Radiological images showed an E11 ependymoma undergoing unilateral interlaminar fenestration. The contrast-enhanced sagittal (A) and coronal (B) magnetic resonance images demonstrated an intradural extramedullary tumor. Postoperative three-dimensional computed tomography (CT) scan demonstrated left interlaminar fenestration (arrow) at L2 (C). Axial CT scan showed a hemilaminectomy (D). The postoperative sagittal T1-weighted magnetic resonance images obtained 9 months after the surgery showed no residual tumor (E).

Figure 2 Radiological images and histology of an EII ependymoma of the filum terminale at L2-4. Preoperative sagittal T2-weighted MRI (A) showed a well-demarcated intradural extramedullary tumor at L2-3, and the patients refused the surgical intervention. Two months after the MRI of A, the sagittal T2-weighted MRI (B) showed the tumors enlarged significantly. Then the patients received the surgery. Three months after operation, MRI (C) showed no residual tumor. But MRI (D) Ten months after the surgery showed recurrent tumor, and the patient received a second surgery. MRI (E) that obtained 3 months after the second surgery showed no obvious residual tumor. Twenty months after the second surgery, the MRI showed CSF dissemination in the spinal canal (F, G) and possible cranial metastasis (H, white arrow). Histopathology showed monomorphic tumor cells forming perivascular pseudorosettes (I) ($\times 200$). The Ki-67 immunostaining showed a high positive rate of 13% in this case (J) ($\times 200$).

Histopathological Analysis

Pathological specimens were fixed in formalin overnight and embedded in paraffin. Two neuro-pathologists independently reviewed all pathological specimens. According to the WHO classification, tumors were classified as MPE and ependymoma WHO grade II (EII). Typical examples are shown in Figures 2I and 3C.

Statistical Analysis

Progression-free survival (PFS) was estimated using the Kaplan–Meier method, measuring survival from time of surgery to time of progression. Univariate and multivariate (logistic and Cox regression) analyses were performed to assess correlation between possible prognostic factors and postoperative outcome (functional outcome and recurrence). Fisher's exact test was used in the analysis of qualitative data among groups. Correlation between the McC scale and the KS score was tested by Wilcoxon. The Mann–Whitney *U* test was used to clarify which symptoms have an impact on the McC scale and KS score. Statistical analysis was supported by commercially available software (SPSS version 16.0; SPSS Inc., Chicago, IL, USA). A value of $P < 0.05$ was considered as statistically significant.

Factors that were tested included age (<40 years vs. ≥ 40 years), gender (male vs. female), symptoms duration (≤ 2 months vs. >2 months), location of tumor site (sacral canal invaded vs. sacral canal not invaded), extent of tumor resection (GTR vs. STR), capsule of the tumor (encapsulated vs. unencapsulated), tumor size (≤ 2 vertebral columns vs. >2 vertebral columns), histology (MPE vs. E II), preoperative McC scale (I vs. II or III), and preoperative KS score (≤ 20 vs. >20). These factors were thought to be potential prognostic factors. For logistic regression analysis, functional outcome was converted into a binary outcome: "improved or unchanged" and "worse."

Results

Demographics and Clinical Features

There were 14 men and 24 women. Their mean age was 43.5 years (range, 15–64 years; median 47 years), and the mean duration of their symptoms was 25 months (range, 2 weeks to 144 months)

Figure 3 Radiological images and histology of a myxopapillary ependymoma of the filum terminale at L2. Preoperative sagittal MRI depicted a homogeneous contrast-enhancing tumor with sharp borders filling the entire spinal canal (A). MRI 1 year after surgery revealed no tumor recurrence (B). The histology of myxopapillary ependymoma showed elongated ependymal tumor cells lying in the mucoïd microcystic matrix (C) (×200).

Table 3 Demographic data and treatment characteristics

Patient Characteristics	Value (%)
Age (years)	
Mean	43.5
Range	15–64
Sex	
Female	24 (63.2%)
Male	14 (36.8%)
Presenting symptoms	
Pain	29 (76%)
Paresis	8 (21%)
Sensation disorders	13 (34%)
Bowel disturbance	6 (16%)
Urinary disturbance	7 (18%)
Symptoms	
Average duration, month	25
Duration ≤2 month	8 (21%)
Duration >2 month	30 (79%)
Preoperative McCormick grade	
I	27 (71.1%)
II	9 (23.7%)
III	2 (5%)
Preoperative Klekamp–Samii score	
10–15	2 (5%)
16–20	8 (21%)
21–25	28 (74%)
Tumor location	
Sacral canal	7 (18%)
Lumber spinal canal	31 (82%)
Tumor size	
≤2 levels	27 (71%)
>2 levels	11 (29%)
Capsule of the tumor	
Encapsulated	24 (63%)
Unencapsulated	14 (37%)
Histology	
Myxopapillary ependymoma (WHO grade I)	18 (47%)
Ependymoma (WHO grade II)	20 (53%)
Extent of initial resection	
Gross total resection	33 (87%)
Subtotal resection	5 (13%)
Postoperative radiotherapy	6 (16%)
Recurrence	6 (16%)

(Table 3). Symptom onset was subacute (≤2 months) in eight patients (21%) and insidious (>2 months) in 30 (79%). Rarely, one patient suffered from chronic local back pain and sudden acute cauda equina syndrome owing to spontaneous hemorrhage of the MPE (confirmed by surgery). The most common symptoms were pain ($n = 29$, 76%), including local back pain and radicular pain. Eighteen patients had neurological deficits before the first surgery (motor weakness in eight patients, sensory loss in 13 patients, bladder disturbance in seven patients, and bowel dysfunction in six patients).

Radiological Diagnosis

All the patients underwent MRI scanning of the spine. Tumor invading ≤2 and >2 vertebral columns was found in 27 (71%) and 11 (29%) patients, respectively (Figures 2 and 3). Tumors mainly located at the level of L1–L3 (27, 71%), and only seven tumors (18%) invaded the sacral canal. One male patient had multifocal involvement preoperatively (multiple lesions in thoracic spinal canal and an intracranial lesion). A case of spontaneous bleeding from a L2–3 ependymoma was detected, and the MRI showed a large hyperintense area between L1 and S1 in the subarachnoid space of the spinal canal on T1-weighted images suggestive of hemorrhage.

Treatment and Follow-Up

No spinal malformation was found in the patients during follow-up period (Table 4). Total removal of the tumors was achieved in 33(87%) patients, and 5(13%) patients had subtotal resection. It was the involvement of multiple nerve roots that prevented a complete resection. The tumors involving the sacral canal always were more likely to be larger and severely adherent to the surrounding nerve, and only three of the seven these tumors (43%) had a total resection.

Postoperative radiotherapy was recommended for the five patients, whose removal was subtotal. However, only two patients received local radiotherapy (45–50 Gy) after the first surgery, and tumor regrowth was found in one patient during the follow-up time (68 months after the surgery). Three patients did not receive radiotherapy after the first surgery, and tumor regrowth was found in all of them (18, 34, and 10 months after surgery respectively). They all received radiotherapy after recurrence, and two of them also received a second surgery. For the residual tumors,

Table 4 Univariate analysis of variables possibly associated with tumor recurrence and neurological status

Variables	Recurrence		Functional outcome (early postoperative)		Functional outcome (9 months follow-up)	
	Odds ratio	P-value	Odds ratio	P-value	Odds ratio	P-value
Age (<40 years vs. ≥40 years)	1.20 [0.19–7.57]	1.000	1.64 [1.26–2.12]	0.522	1.17 [0.17–7.995]	1.000
Gender (male vs. female)	1.20 [0.19–7.57]	1.000	1.64 [1.26–2.12]	0.522	1.17 [0.17–7.995]	1.000
Symptoms duration (≤2 months vs. >2 months)	0.75 [0.61–0.91]	0.309	1.29 [1.08–1.53]	1.000	1.32 [1.09–1.60]	0.563
Tumor location (sacral vs. none sacral)	0.01 [0.001–0.176]	<0.001	5.00 [0.27–91.52]	0.339	10.88 [1.37–86.37]	0.035
Tumor size (≤2 levels vs. >2 levels)	21.67 [2.12–221.20]	0.005	0.39 [0.02–6.76]	0.501	0.21 [0.03–1.51]	0.134
Extent of resection (gross total vs. subtotal)	62.0 [4.53–848.70]	0.001	0.13 [0.01–2.41]	0.249	0.15 [0.02–1.28]	0.120
Tumor capsule (encapsulated vs. unencapsulated)	12.78 [1.31–125.07]	0.018	0.57 [0.03–9.81]	1.000	0.33 [0.05–2.30]	0.337
Histology (WHO grade I vs. WHO grade II)	0.88 [0.15–5.05]	1.000	1.12 [0.07–19.28]	1.000	2.00 [0.46–8.70]	0.468
Preoperative KS score (≤20 vs. >20)	3.57 [0.59–21.75]	0.310	0.33 [0.02–5.90]	0.462	0.48 [0.07–3.40]	0.592
Preoperative McC grade (I vs. II or III)	1.28 [0.20–8.24]	1.000	1.44 [1.16–1.79]	1.000	1.74 [0.17–17.59]	1.000
Recurrence (yes vs. no)	–	–	0.16 [0.01–3.02]	0.294	0.02 [0.001–0.221]	0.001

Bold face represents the values which approach statistical significance.

postoperative radiotherapy increased the interval between the first surgery and tumors regrowth, although there was no statistical significance ($P = 0.063$). Two patients received craniospinal radiotherapy. A MPE patient with craniospinal dissemination before surgery received craniospinal radiotherapy. Another E II patient, who was detected with craniospinal dissemination after 1 year follow-up (Figure 2F–H), also received craniospinal radiation. None of the patients in the study received chemotherapy.

The mean follow-up was 81 months (range, 9–141 months; median, 89 months). Six patients had evidence of local recurrence/progression and the median time to recurrence was 34 months (range 10–68 months). In addition, two of 33 cases

(6%) from the GTR group and four of five cases (80%) from the STR group had clinical and radiological recurrence. The recurrence rate showed statistically significant variations by the STR and GTR group ($P = 0.001$) (Table 4). The tumors were completely encapsulated in 24 (63%) cases and unencapsulated adhering to cauda equine in 14 (37%) cases. The encapsulated tumors were all totally removed, while 5 (36%) of the unencapsulated tumors were subtotally removed. The PFS was 80 months for patients with encapsulated tumors and 63 months for those with unencapsulated tumors ($P = 0.011$) (Figure 4). Univariate analysis also identified tumor involving more than two vertebral columns ($P = 0.005$) and tumor involving sacral canal ($P < 0.001$)

Figure 4 Kaplan–Meier survival curves showed differences in progression-free survival depending on tumor histology (A), extent of surgical excision (B), integrity of tumor capsule (C), and tumor location (D).

as predictor of tumor recurrence. Multivariate Cox regression analysis with the variables of extent of resection, tumor size, tumor location, and tumor capsule revealed only tumor location (sacral canal invaded) as an independent risk factor for recurrence ($P = 0.001$).

Histology

Histological examination revealed MPE in 18 (47%) patients and E II in 20 (53%) patients. Craniospinal dissemination was found in both histological types. Three (17%) of the 18 MPE patients endured recurrence, while 3 (15%) of the 20 ependymoma II patients also had recurrence during the follow-up period. Mean PFS was 76 months for MPE patients, and 72 months for EII patients. The progression-free rate was comparable between MPE group and EII group (Figure 4).

In recent years, Ki-67 immunoreactivity was investigated in the specimen of 19 patients. The Ki-67 (MIB-1) labeling index was less than 1% in 12 cases, 1–2% in three cases, 2–3% in two cases, 3–4% in one case, and 13% in one case. The Ki-67 labeling index of MPE was all <2%. The tumor with high positive rate of 13% Ki-67 labeling index grew quickly and relapsed during follow-up time (Figure 2J).

Functional Outcomes

Before surgery, two patients (5%) were classified as McC III, nine patients (24%) as McC II, and 27 patients (71%) as McC I. After surgery, two patients (5%) experienced deterioration immediately after surgery (from McC I to McC II), and at the latest follow-up one returned to McC I while the other deteriorated to McC IV. Thirty-one patients (81.6%) maintained their pretreatment status immediately after surgery, and afterwards two of them achieved improvement at the final follow-up, while two patients experienced deterioration due to the recurrence of the tumor. The McC score was improved from McC II to McC I in three patients (8%). In two patients (5%), the McC score was improved from McC III to McC II immediately after surgery, and afterwards one further improved to McC I, while the other returned to the preoperative status because of recurrence at the final follow-up. (Table 5).

According to the KS score, the functional outcome was verified as 31 (81.6%) improved, 5 (13.2%) unchanged, 2 (5.3%) deteriorated at early postoperative time, and at the latest follow-up the outcome changed to 28 (73.7%) improved, 5 (13.2%) unchanged and 5 (13.2%) deteriorated. Preoperative averaged KS score (21.29 ± 0.43 points) had significantly improved at 1 week (23.16 ± 0.36 points) and at final follow-up (23.18 ± 0.43) ($P < 0.01$). Correlation between the McC scale and the KS score was weak ($P < 0.001$, Wilcoxon test) (Table 5).

Univariate analysis revealed tumor involving sacral canal ($P = 0.035$) and recurrence ($P = 0.001$) as predictors of poor functional outcome at the long-term follow-up (Table 4). No factors were identified as predictors of functional outcome in multivariate analysis.

The clinical complaints of the patients were motor function, sensibility, gait function, bladder and bowel symptoms as well as pain. To clarify which symptoms have an impact on the score, we used the Mann–Whitney U test to investigate whether presence or absence of the above symptoms show a significant difference in the heights of the score (Table 6). Results showed the KS score correlated well with bladder symptoms, bowel symptoms and pain, while McCormick scale reflected none of the above symptoms.

Discussion

Primary filum terminale ependymoma, which originates from the ependymal cells of the filum terminale [20], is a unique type of ependymomas and mainly locates on extramedullary site. Its clinical features are heterogeneous as compared to intramedullary ependymomas.

Surgical Results and Progression-Free Survival

In our center, the goal of PFTE treatment is GTR with good long-term functional outcome, which can be achieved in most cases. In cases that GTR is not applicable, patients are usually recommended to receive adjuvant radiotherapy for the residual tumor. Previous studies, both about intramedullary ependymomas and PFTE, have demonstrated that patients with GTR have a signifi-

Table 5 Preoperative, early postoperative, and latest follow-up scale/score according to the McC scale/KS score

	Preoperative	Early postoperative				Latest follow-up (>1 year)			
	Mean score/scale	Mean score/scale	Improved	Unchanged	Worse	Mean score/scale	Improved	Unchanged	Worse
McC scale	1.34 ± 0.09	1.26 ± 0.07	5 (13.2%)	31 (81.6%)	2 (5.3%)	1.26 ± 0.11	7 (18.4%)	27 (71.1%)	4 (10.5%)
KS score	21.29 ± 0.43	23.16 ± 0.36	31 (81.6%)	5 (13.2%)	2 (5.3%)	23.18 ± 0.43	28 (73.7%)	5 (13.2%)	5 (13.2%)

Table 6 Correlation between McC scale/KS score and clinical symptoms

	Paresis	Paraesthesia	Gait function	Bladder symptoms	Bowel symptoms	Increased muscle tone	Pain
McC scale	+	+	+	–	–	–	–
KS score	+	+	+	+	+	–	+

“+” If symptom is positive, the score is significantly worse ($P < 0.05$). “–” No significant correlation between presence or absence of symptoms and the height of the score.

cantly longer PFS compared with those who receive STR and post-radiotherapy [4,8,14,21–23]. This coincides with our data. The mean PFS was 77 months in GTR group, while 53 months in STR group (Figure 4, $P < 0.001$).

Unlike intramedullary ependymomas, univariate analysis identified tumor size (≤ 2 vertebral columns), tumor location (sacral not involved), and tumor capsule (encapsulated) as survival status predictors of PFTEs. The three factors are thought to have an influence on the extent of surgical removal. Most PFTEs are encapsulated well. However, once the encapsulation breaks down, the tumors may adhere to the nerve roots of cauda equine. Consequently, these tumors will be hard to be totally removed and associated with a high recurrence rate. In our series, 5(36%) of the unencapsulated tumors were subtotally removed and all the 5 patients were found recurrence during the follow-up period. Celli *et al.* [14] and Sakai *et al.* [24] also came up with the similar results.

Intradural ependymomas seldom invade the sacrum [25]. However, once the tumors invade the sacral canal, the treatment will be a challenge. Quraishi *et al.* [26] and Gupta *et al.* [27] both reported cases of sacral ependymomas that were difficult to be totally removed. In our series, the intrasacral ependymomas were always huge and destructive, and they can also present as extensive bony destruction (Figure 5A–C). During the surgery, these tumors were frequently unencapsulated and infiltrated to the surrounding nerve roots and even bone. The surgeries were usually extremely difficult due to the invasiveness of the tumor and the GTR rate was extremely low. Four of seven (57%) sacral ependymomas were subtotally removed and recurrence were found in 5 (71%) during the follow-up time.

Cerebrospinal fluid (CSF) dissemination is not uncommon due to the extramedullary location of PFTEs, while it is rare for intramedullary ependymomas. The CSF dissemination rate for PFTEs was 5% in our series.

A minimal Invasive Approach for PFTE

Laminectomy is the traditional approach for the surgery of intradural tumors, but it is easy for patients to acquire delayed spinal instability. So in recent years, interlaminar fenestration and laminoplasty were used in our department to prevent the potential spinal instability. Interlaminar fenestration is a minimal invasive approach and has been considered to have great advantages in preserving spinal stability [28,29]. The rationale for interlaminar

fenestration is to try to prevent future spinal instability. In our series, three patients received unilateral interlaminar fenestration during the operation, and tumors were all totally removed without recurrence during follow-up time. Although none of the patients developed spinal deformity in our series, the long-term spinal stability was the predominant advantage of this approach, especially for children and young adults.

However, we should highlight that this procedure is suitable for selective tumors, such as tumor size smaller than two vertebral columns and encapsulated tumor, and otherwise tumors may be difficult to be totally resected.

Neurological Function

Functional outcome after surgery was good in the majority of PFTE patients. In our study, 36 patients (95%) had stable or improved neurological status directly after surgery. The late deterioration in KS score or McC scale was always due to the regrowth of the tumor. The outcomes were better than that of intramedullary ependymomas. Postoperative dysesthesia was common after surgery of intramedullary ependymomas due to the posterior midline myelotomy, and deteriorated functional outcome was seen in 10–46% patients [2,21,23].

Unlike intramedullary ependymomas, the preoperative status and other prognostic factors were not associated with functional outcome. This can be explained by the fact that the majority of patients suffered from pain first over the course of many years rather than neurological deficit. Some patients may have their lumbar inspected with MRI when they are in pain, while others may not ask for MRI until the onset of neurological deficit.

In our study, pain is the most frequent symptom of PFTE patients. Besides, bowel and bladder symptom is also common due to the lumbosacral location of PFTEs. However, there is no clear information for evaluating pain, bowel symptom, and bladder symptom of patients in McC scale [5]. The presence of pain or bowel and bladder symptom, whatever the degree is, does not modify the grade measured by McCormick scale. For example, a patient with improved bowel and bladder symptom may be classified as the same grade on McCormick scale both pre- and postoperatively. Samii and Klekamp [19] proposed a new scoring system, but it remains being infrequently used. This system contains five subgroups: “Sensory deficits, pain, dysesthesias,” “Motor weakness,” “Gait ataxia,” “Bladder function,” and “Bowel function”, so this system can better reflect the functional outcome of

Figure 5 Radiological images of an intrasacral MPE of the filum terminale before the second surgery. The contrast-enhanced sagittal MRI (A) depicted a huge MPE extending from L4 to S2. Lumbosacral pelvic stabilization had been performed in the first surgery. Axial contrast-enhanced MRI (B) and CT (C) depicted the intrasacral MPE with extensive bony destruction.

the patients. Our research revealed that the functional outcome is significantly different when it was evaluated by KS score and McC scale respectively (Table 5), and the KS score correlated better with the symptoms (Table 6). Thus, KS score system is more suitable for the functional evaluation of PFTEs patients.

Role of Pathological Grading on Prognosis

The WHO classification [15] distinguishes four different types of ependymal tumors: subependymoma WHO grade I, myxopapillary ependymomas WHO grade I (MPE), ependymoma WHO grade II (EII), and anaplastic ependymoma WHO grade III (AE III). MPE and EII are two common histological types of PFTEs. MPE occurs almost exclusively within the region of the conus medullaris and filum terminale.

Many existing results confirmed that MPEs are associated with a deteriorated outcome as compared to EII and AE III [4,7,30]. Boström *et al.* [4] reviewed 57 patients with spinal cord ependymomas and indicated that MPE has a relatively higher recurrence rate than E II/AE III (19% vs. 5%). However, intramedullary ependymomas were also included these studies, because MPE mainly locates on extramedullary site, and the recurrence rate may differ because of different tumor locations. All PFTEs were extramedullary, and thus the two histological types could be investigated after eliminating the bias due to different tumor location. Our results showed that both MPE and E II have similar recurrence rates (17% vs. 15%, $P > 0.05$) and functional outcome, and metastasis was found in both types of tumors during follow-up period.

The prognostic value of Ki-67 immunostaining associated with cell proliferation in central nervous system neoplasms has been generally accepted. Iwata *et al.* [31] investigated the Ki-67 labeling index (LI) in spinal cord tumors and found that the proliferation index of ependymoma was $0.12 \pm 5.53\%$. In our series, the Ki-67 LI was analyzed in 19 recent cases, and the LI was 0–4% in 18 cases, 13% in one case. The tumor with high positive rate of 13% Ki-67 LI grew with a remarkable speed and recurrence and metastasis were found during follow-up time. Thus, the Ki-67 LI is expected to become a useful indicator for predicting the outcome of PFTE.

Radiotherapy

It is controversial regarding the role of radiotherapy in the treatment of spinal ependymomas. Akyurek *et al.* [32] indicated that radiotherapy after surgery for MPE conferred significantly better

PFS rates than surgery alone ($P = 0.04$) and advocated that adjuvant radiotherapy to the primary disease site appears to significantly reduce the rate of tumor progression regardless of the extent of resection. However, most reports advocated GTR as the sole treatment, because the risk of recurrence is usually very low that the benefits of adjuvant radiation may be limited after GTR. Post-radiotherapy was only recommended for patients treated with STR, and it appeared to lengthen the survival of these patients [5,8,33–35]. In our study, the recurrence rate was low as 6% for the GTR group, and thus few patients of GTR can benefit from the adjuvant radiation. So we also reserved radiotherapy for STR and disseminated cases. In this series, the patients who received radiotherapy appeared to acquire long interval between the first surgery and the detection of regrowth, although there was no marked difference.

Conclusion

In this retrospective analysis of PFTE treated at a single institution, results showed PFTE has significantly different outcome from intramedullary ependymomas, and following conclusions may be drawn:

- 1 A complete removal is the preferred surgical treatment for PFTE, because it is usually surgically resectable.
- 2 Univariate analysis revealed that the prognostic factors of disease progression-free rate include tumor size, tumor location, extent of surgical removal, and the integrity of tumor capsule.
- 3 Tumor location was identified as the only significant factor in multivariate analysis. The intrasacral ependymomas are more likely to be huge and destructive, and its surgical intervention is usually extremely difficult. These tumors have a high risk of recurrence.
- 4 KS scoring system is more suitable for the functional evaluation of PFTE patients than McC scale.

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Conflict of Interest

The authors declare no conflict of interest.

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