Neurosurgical Review (2020) 43:1351–1356
https://doi.org/10.1007/s10143-019-01150-z

ORIGINAL ARTICLE

Clinical characteristics and surgical outcomes of spinal myxopapillary ependymomas

Tie Liu[1,2] · Chenlong Yang[3] · Xiaofeng Deng[1,2] · Anqi Li[1,2] · Yu Xin[1,2] · Jun Yang[1,2] · Yulun Xu[1,2]

Received: 21 December 2018 / Revised: 19 June 2019 / Accepted: 24 July 2019 / Published online: 31 August 2019

Abstract

Spinal myxopapillary ependymoma (SME) is a rare pathological variant of ependymoma, which most commonly occurs in the cauda equina and filum terminale of the spinal cord. Although SME is considered as a benign entity, histologically corresponding to WHO grade I, local recurrence and metastasis have been reported in many cases. The purpose of this large-scale, single-center study was to investigate the clinical characteristics and surgical outcomes of SME. A total of 34 consecutive patients diagnosed with SME were enrolled in this retrospective study. All patients underwent magnetic resonance imaging (MRI) and were treated with surgical resection. Individual clinical data were collected, and surgical outcomes were evaluated during the follow-up period. There were 21 males and 13 females, with an average age of 29.97 years. Clinical symptoms included back pain (82.4%), weakness (44.1%) and numbness (20.6%) in extremities, and sphincter dysfunction (26.5%). The tumor locations included lumbar segments (52.9%), thoracolumbar segments (23.5%), lumbosacral segments (17.6%), and thoraco-lumbosacral segments (5.9%). On MRI, all SMEs appeared hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging, with remarkable enhancement. Gross total resection was achieved in 18 patients, and subtotal resection (STR) was achieved in 16 patients. After an average follow-up period of 41.5 months, recurrence was noted in 5 patients (5 of 16) who underwent STR. SMEs have some characteristic features on MRI which can facilitate the preoperative diagnosis. Complete surgical resection is the best treatment of choice with a favorable outcome. In cases of incomplete resection, postoperative radiotherapy may be an effective alternative.

Keywords Myxopapillary ependymoma · Spinal tumor · MRI · Surgical resection · Prognosis

Introduction

Spinal myxopapillary ependymoma (SME) refers to a rare pathological variant of ependymoma, which is predominantly located in the cauda equina and filum terminale regions of the spinal cord. Although SME is generally considered as a benign entity with a slow-growing nature, histologically corresponding to WHO grade I, local recurrence, metastasis, and even cerebrospinal fluid (CSF) dissemination have been reported in many cases [9, 15, 22]. According to previous reports, the overall recurrence rate of SME ranged from 7 to 37% [14]. The optimal therapeutic strategy for SMEs remains controversial. The surgical outcomes have not been well established, and some scholars recommend adjuvant radiotherapy and/or chemotherapy [3, 4, 21]. Nakamura et al. proposed that radiation on the whole brain and spine may be helpful to prevent the local recurrence and CSF dissemination, when the tumor capsule is ruptured intraoperatively [21]. Moreover, sparse case reports demonstrated that temozolomide had a certain efficacy for controlling the recurrent SME [7, 9]. In literatures, studies regarding SMEs were limited to single-case reports or small case series. The purpose of this large-scale, single-center study was to investigate the clinicoradiological characteristics and surgical outcomes of SMEs.

Tie Liu and Chenlong Yang contributed to the work equally and should be regarded as co-first authors.

✉ Yulun Xu
xuhuxi@sina.com

[1] Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

[2] China National Clinical Research Center for Neurological Diseases (NCRC-ND), Beijing, China

[3] Department of Orthopedics, Peking University Third Hospital, Beijing, China

Materials and methods

Patients

This retrospective study enrolled a total of 34 consecutive patients diagnosed with SME between Jan 2007 and June 2016. SME was diagnosed based on pathological evidence, and the histopathological slides were reassessed by two neuropathologists independently. Individual demographic and clinical data were collected, including sex, age at diagnosis, onset symptoms, duration of symptoms, and physical signs.

The study was approved by the Institutional Review Board and Ethics Committee of Beijing Tiantan Hospital.

Radiological evaluation

Magnetic resonance imaging (MRI) with gadolinium-contrast enhancement was performed as the standard radiological examination pre- and postoperatively in all cases. The radiological features, including tumor location (spinal segment), size (the maximum diameter), cystic or solid appearance, signal intensity, tumor margins, and contrast enhancement, were analyzed independently by two neurosurgeons.

Treatment

All patients underwent laminotomy and microsurgical removal via the posterior median approach, with intraoperative neurophysiologic monitoring of somatosensory- and motor-evoked potentials. No patients received preoperative radiotherapy. Gross total resection (GTR) was defined as gross macroscopical removal of the tumor and no evidence of a residual tumor on postoperative MRI. Subtotal resection (STR) was defined as resection of the majority of the tumor with a small residual portion. Postoperatively, none of the patients received adjuvant chemotherapy. Among the patients undergoing STR, 8 of them received postoperative adjuvant radiotherapy which was delivered for 35 days with daily fractions of 115–150 cGy (total dose range, 40–52 Gy). Radiation fields included the tumor plus one to two vertebral bodies above and below the tumor.

Prognostic assessment

Follow-up data for all patients were obtained during individual office visits, with a mean follow-up time of 41.5 months (standard deviation = 19.9, range 21–85). The patients' postoperative status was investigated by physical examination and gadolinium-enhanced MRI, and McCormick classification was applied to assess neurological function [1, 19]. Radiological and functional assessments were performed preoperatively, at discharge, at 3 months postoperatively, and annually thereafter.

Statistical analysis

SPSS 24.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analyses. Fisher's exact test was used for the comparison of categorical variables. Probability (p) values ≤ 0.05 were considered significant.

Results

Clinical features

There were 21 males and 13 females, yielding a male-to-female ratio of 1.6:1. The average age at diagnosis was 29.97 ± 12.46 years (range 8–59 years); there were 9 pediatric patients (26.5%) and 25 adult patients (73.5%). The clinical onset symptoms included pain (28/34 cases; 82.4%), weakness (15/34; 44.1%) and numbness (7/34; 20.6%) in extremities, and sphincter dysfunction (9/34; 26.5%). The duration of symptoms preceding the initial diagnosis ranged from 1 month to 6 years (mean, 20.7 ± 16.5 months). The demographic and clinical profiles were summarized in Table 1.

Radiological characteristics

The tumor locations included lumbar segments (18/34 cases; 52.9%), thoracolumbar segments (8/34; 23.5%), lumbosacral segments (6/34; 17.6%), and thoraco-lumbo-sacral segments (2/34; 5.9%). On MRI, all SMEs appeared heterogeneously hypointense on T1-weighted imaging and heterogeneously hyperintense on T2-weighted imaging. After Gd-diethylenetriaminepentaacetic acid (Gd-DTPA) administration, all tumors showed heterogeneously remarkable enhancement. All of these tumors were solid and well-demarcated, and no remarkable cystic component was noted. Rostral or caudal syringomyelia was noted in 20 cases (58.8%). The preoperative suspected diagnoses included spinal ependymomas, dermoid cysts, schwannomas, and teratomas. The radiological images of representative cases were presented in Fig. 1.

Intraoperative findings and surgical outcomes

According to the operative documents, no evoked potentials were lost during the surgery. The SMEs were grayish-red in color and soft in texture, with a rich blood supply. The tumors were encapsulated, with close adhesion to the surrounding cauda equina and/or filum terminale. Macroscopically, the SMEs showed a sausage-like appearance (Fig. 2). GTR was achieved in 18 patients (52.9%), and STR was achieved in 16 patients (47.1%).

Postoperatively, all the patients were uneventful. After an average follow-up period of 41.5 months, radiological recurrence was noted on MRI in 5 of the 8 patients (62.5%) who

Table 1 Demographic and clinical characteristics

Variable	Number (%)
Number of patients	34 (100%)
Age at diagnosis (years)	
Pediatric	9 (26.5%)
Adult	25 (73.5%)
Gender	
Male	21 (61.8%)
Female	13 (38.2%)
Symptoms	
Pain	28 (82.4%)
Extremity weakness	15 (44.1%)
Extremity numbness	7 (20.6%)
Sphincter dysfunction	9 (26.5%)
Tumor location	
Thoracolumbar	8 (23.5%)
Lumbar	18 (52.9%)
Lumbosacral	6 (17.6%)
Thoraco-lumbo-sacral	2 (5.9%)
Tumor size	
1–5 cm	21 (61.8%)
6–10 cm	7 (20.5%)
≥ 10 cm	6 (17.7%)
Extent of resection	
Gross total resection	18 (52.9%)
Subtotal resection	16 (47.1%)
Radiotherapy	
Yes	8 (23.5%)
No	26 (76.5%)
Recurrence	5 (14.7%)

underwent STR but no adjuvant radiotherapy. The age of patients with recurrence was 8, 17, 18, 18, and 29 years, respectively. The time interval between operation and recurrence was 37, 41, 50, 62, and 71 months, respectively. The sizes of recurrent tumors were all less than 2 cm. There was no tumor progression in the patients who underwent GTR ($n = 18$) or combined STR and radiotherapy ($n = 8$) (Fig. 3a). Fisher's exact test showed incomplete resection (STR) was significantly associated with tumor recurrence ($p < 0.05$).

Regarding the neurological function, preoperatively, 12 patients were at grade I of the McCormick classification (neurologically normal or mild deficits), 20 at grade II, and 2 at grade III (grades II and III represent moderate to severe neurological deficits); during the follow-up period, 31 patients were at grade I, 2 at grade II, and 1 at grade III (Fig. 3b). Fisher's exact test showed surgical treatment can significantly improve the neurological function of patients with SMEs ($p < 0.05$).

Discussion

Ependymomas are tumors of glial origin arising from the ependymocytes, which line the CSF-filled ventricles in the brain and the central canal of the spinal cord. Ependymomas are the most common primary tumors of the spinal cord, occupying approximately 60% of all spinal neuroepithelial neoplasms [15]. Pathologically, spinal ependymomas can be divided into four subtypes: conventional ependymomas (cellular, papillary, clear cell, and tanycytic), subependymomas, myxopapillary ependymomas, and anaplastic ependymomas. According to the 2007 and 2016 CNS WHO classifications, myxopapillary ependymomas are classified as grade I low-grade tumors [17, 25]. SME was firstly designated as a distinct clinicopathological entity by Kernohan in 1932 [13]. As reported, SMEs were estimated to account for about 27% of all spinal ependymomas [23].

In literatures, SMEs were found most commonly in the fourth decade of life with a male preference, and 8–20% of them occurred in pediatric patients [10, 23]. In the current study, our demographic results were consistent with previous findings. Due to its slow-growing nature, SME usually has a long clinical course [5]. The average symptom duration of ependymomas was reported to be about 1 year [27]; in our

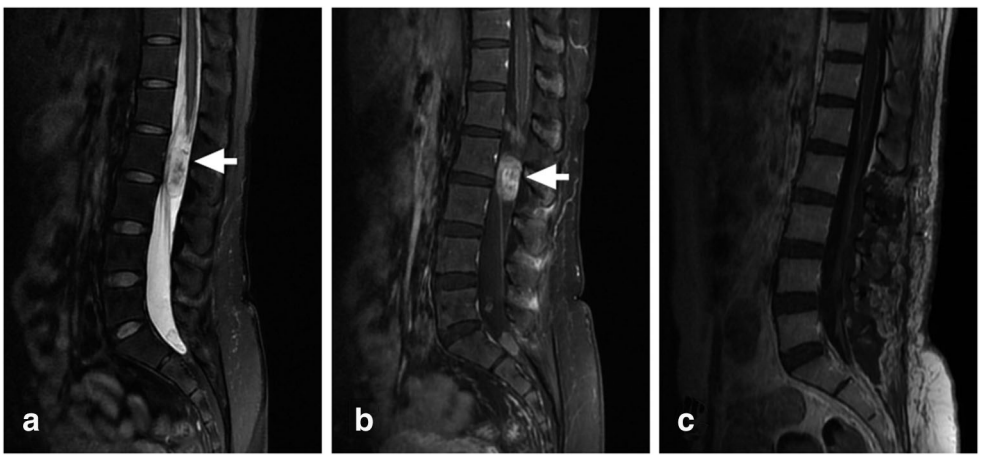

Fig. 1 Magnetic resonance images of a representative case with SME. Magnetic resonance imaging revealed an intraspinal lesion (arrow) at the L2 level, which was heterogeneously hyperintense on T2-weighted imaging (**a**) and heterogeneously enhanced on T1-weighted contrast-enhanced imaging (**b**). Postoperative imaging showed the lesion was completely removed (**c**)

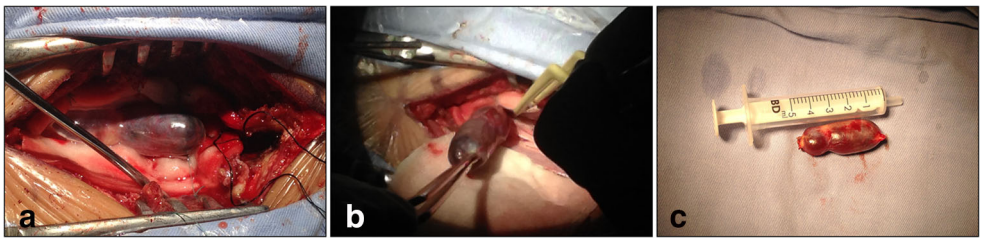

Fig. 2 Intraoperative findings. Intraoperatively, we found the SME was grayish-red with complete capsule, and it showed a sausage-like appearance

study, the mean symptom duration of SMEs was much longer (20.7 months). Clinical manifestations of SMEs are nonspecific, including local pain, sensorimotor disturbance, and sphincter dysfunction. As SMEs most frequently occur in the cauda equina and filum terminale regions of the spinal cord, hypoesthesia in the saddle area (perineum and anus) and bladder-rectal dysfunction as well as sexual dysfunctions are quite common. Once the nerve root is affected, the patients can manifest as intractable lumbosacral or lower-extremity pain. In the late stage of the disease, the patients can develop flaccid paralysis [27]. In the current series, pain is the most common onset symptom, which may be related to the involvement of surrounding nerves [24].

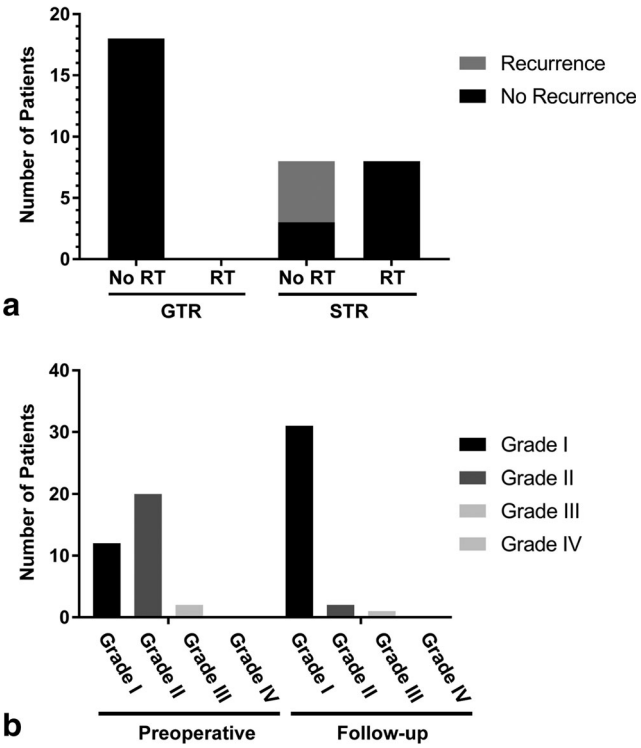

Fig. 3 Follow-up data. **a** Eighteen patients underwent gross total resection (GTR) and none of them received postoperative radiotherapy (RT); among these patients, no tumor recurrence was noted during the follow-up period. Sixteen patients underwent subtotal resection (STR) and 8 of them received postoperative RT; during the follow-up period, tumor recurrence was noted in 5 of the 8 patients who underwent STR but no RT. **b** Preoperatively, 12 patients were at grade I of the McCormick classification, 20 at grade II, and 2 at grade III; during the follow-up period, 31 patients were at grade I, 2 at grade II, and 1 at grade III

In fact, almost all the previously described SMEs as well as SMEs in our study were located in the lumbar spinal canal, and some scholars hypothesized that these entities arise from the lumbar thecal sac in proximity to the conus medullaris, cauda equina, and filum terminale [15, 20]; nevertheless, some intracerebral counterparts have also been reported [16, 18, 26, 28]. Considering myxopapillary ependymomas have a potential for metastasis and CSF dissemination, the diagnosis of primary intracerebral myxopapillary ependymomas should be differentiated from metastatic or disseminated tumors. Noteworthily, on MRI, SMEs are well-demarcated unlike conventional ependymomas. This radiological feature was consistent with macroscopical findings that SMEs were encapsulated with a sausage-like appearance.

Currently, surgical resection is the mainstream modality for the treatment of SMEs. The goal of surgery is decompression of the spinal cord and maximal safe resection of the tumor. In the previous literature, few studies analyzed the functional outcomes after surgical resection. Herein, we found surgical treatment could significantly improve the neurological function of patients with SMEs. Therefore, timely surgical decompression should be highlighted for the functional rehabilitation. With the development of neurophysiological monitoring and microneurosurgical techniques, the rate of total resection has been significantly increased with a lower incidence of complications. However, due to the close adhesion to surrounding nerves, complete removal of SMEs may still be challenging. In our study, only 52.9% of the patients gained GTR. Previous studies indicated that the extent of resection in the initial surgery is a prognostic factor for spinal cord ependymomas [12]. Feldman et al. performed a systematic review which enrolled 28 articles describing 475 patients, and they found that the overall recurrence rate after GTR (15.5%) was significantly lower than that after STR (32.6%); additionally, they also noted significantly higher recurrence rates in pediatric patients compared with adults (40.5% vs 23.4%) [8]. Consistently, in our study, all the five patients with recurrence were treated by STR, and four of them were pediatric. The role of radiotherapy for treating SMEs remains controversial. Feldman's systematic review found that adjuvant radiotherapy was not associated with a decrease in recurrence rates [8], while the experience from M.D. Anderson Cancer Center showed that the addition of postoperative radiotherapy to surgery was associated with

significantly higher 10-year progression-free survival rates (75% for surgery and postoperative radiotherapy vs. 37% for surgery alone) and 10-year local tumor control rates (86% for surgery and postoperative radiotherapy vs. 46% for surgery alone) [2]. Our results also support that tumor recurrences may occur late (> 10 years) with adjuvant radiotherapy. The optimal dose of radiation for SMEs is under debate as well. In previous studies, a dose of 40–50 Gy has been widely used [6, 29], and a dose-response effect has been reported by Garcia [11]. Akyurek et al. proposed that doses greater than 40 Gy had significant efficacy in improving progression-free survival rates [2]. In our study, there was no tumor progression in the patients who underwent STR with postoperative radiotherapy (40–52 Gy). The definitive role of radiotherapy still needs further research. However, considering the potential risk of recurrence and metastasis, radiotherapy should be recommended for patients who undergo incomplete resection.

Conclusions

SMEs have some characteristic features on MRI which can facilitate the preoperative diagnosis. Surgical resection can significantly improve the clinical symptoms. Complete surgical resection is the best treatment of choice with a favorable outcome. In cases of incomplete resection, postoperative radiotherapy should be highlighted.

Acknowledgments We thank all of the patients and their families who trusted us, and all of the physicians and staff members who helped in this study.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Aghakhani N, David P, Parker F, Lacroix C, Benoudiba F, Tadie M (2008) Intramedullary spinal ependymomas: analysis of a consecutive series of 82 adult cases with particular attention to patients with no preoperative neurological deficit. Neurosurgery 62:1279–1285; discussion 1285-1276. https://doi.org/10.1227/01.neu.0000333299.26566.15
2. Akyurek S, Chang EL, Yu TK, Little D, Allen PK, McCutcheon I, Mahajan A, Maor MH, Woo SY (2006) Spinal myxopapillary ependymoma outcomes in patients treated with surgery and radiotherapy at M.D. Anderson Cancer Center. J Neuro-Oncol 80:177–183. https://doi.org/10.1007/s11060-006-9169-2
3. Bagley CA, Kothbauer KF, Wilson S, Bookland MJ, Epstein FJ, Jallo GI (2007) Resection of myxopapillary ependymomas in children. J Neurosurg 106:261–267. https://doi.org/10.3171/ped.2007.106.4.261
4. Bagley CA, Wilson S, Kothbauer KF, Bookland MJ, Epstein F, Jallo GI (2009) Long term outcomes following surgical resection of myxopapillary ependymomas. Neurosurg Rev 32:321–334; discussion 334. https://doi.org/10.1007/s10143-009-0190-8
5. Chan MD, McMullen KP (2012) Multidisciplinary management of intracranial ependymoma. Curr Probl Cancer 36:6–19. https://doi.org/10.1016/j.currproblcancer.2011.10.013
6. Clover LL, Hazuka MB, Kinzie JJ (1993) Spinal cord ependymomas treated with surgery and radiation therapy. A review of 11 cases. Am J Clin Oncol 16:350–353
7. Fegerl G, Marosi C (2012) Stabilization of metastatic myxopapillary ependymoma with sorafenib. Rare Tumors 4:e42. https://doi.org/10.4081/rt.2012.e42
8. Feldman WB, Clark AJ, Safaee M, Ames CP, Parsa AT (2013) Tumor control after surgery for spinal myxopapillary ependymomas: distinct outcomes in adults versus children: a systematic review. J Neurosurg Spine 19:471–476. https://doi.org/10.3171/2013.6.SPINE12927
9. Fujiwara Y, Manabe H, Izumi B, Shima T, Adachi N (2018) Remarkable efficacy of temozolomide for relapsed spinal myxopapillary ependymoma with multiple recurrence and cerebrospinal dissemination: a case report and literature review. Eur Spine J 27:421–425. https://doi.org/10.1007/s00586-017-5413-z
10. Gagliardi FM, Cervoni L, Domenicucci M, Celli P, Salvati M (1993) Ependymomas of the filum terminale in childhood: report of four cases and review of the literature. Childs Nerv Syst 9:3–6
11. Garcia DM (1985) Primary spinal cord tumors treated with surgery and postoperative irradiation. Int J Radiat Oncol Biol Phys 11:1933–1939
12. Hanbali F, Fourney DR, Marmor E, Suki D, Rhines LD, Weinberg JS, McCutcheon IE, Suk I, Gokaslan ZL (2002) Spinal cord ependymoma: radical surgical resection and outcome. Neurosurgery 51:1162–1172 discussion 1172-1164
13. Kernohan J (1932) Primary tumors of the spinal cord and intradural filum terminale. Cytol Cell Pathol Nervous Syst 3
14. Klekamp J (2015) Spinal ependymomas. Part 2: Ependymomas of the filum terminale. Neurosurg Focus 39:E7. https://doi.org/10.3171/2015.5.FOCUS15151
15. Kraetzig T, McLaughlin L, Bilsky MH, Laufer I (2018) Metastases of spinal myxopapillary ependymoma: unique characteristics and clinical management. J Neurosurg Spine 28:201–208. https://doi.org/10.3171/2017.5.SPINE161164
16. Lim SC, Jang SJ (2006) Myxopapillary ependymoma of the fourth ventricle. Clin Neurol Neurosurg 108:211–214
17. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW (2016) The 2016 World Health Organization classification of tumors of the central nervous system: a summary. Acta Neuropathol 131:803–820. https://doi.org/10.1007/s00401-016-1545-1
18. Maruyama R, Koga K, Nakahara T, Kishida K, Nabeshima K (1992) Cerebral myxopapillary ependymoma. Hum Pathol 23:960–962
19. McCormick PC, Torres R, Post KD, Stein BM (1990) Intramedullary ependymoma of the spinal cord. J Neurosurg 72:523–532. https://doi.org/10.3171/jns.1990.72.4.0523
20. Mork SJ, Loken AC (1977) Ependymoma: a follow-up study of 101 cases. Cancer 40:907–915

21. Nakamura M, Ishii K, Watanabe K, Tsuji T, Matsumoto M, Toyama Y, Chiba K (2009) Long-term surgical outcomes for myxopapillary ependymomas of the cauda equina. Spine (Phila Pa 1976) 34: E756–E760. https://doi.org/10.1097/BRS.0b013e3181b34d16
22. Rege SV, Narayan S, Patil H, Songara A (2016) Spinal myxopapillary ependymoma with interval drop metastasis presenting as cauda equina syndrome: case report and review of literature. J Spine Surg 2:216–221. https://doi.org/10.21037/jss.2016.08.06
23. Sonneland PR, Scheithauer BW, Onofrio BM (2015) Myxopapillary ependymoma. A clinicopathologic and immunocytochemical study of 77 cases. Cancer 56:883–893
24. Thoriya PJ, Watal P, Bahri NU, Rathod K (2015) Primary spinal primitive neuroectodermal tumor on MR imaging. Indian J Radiol Imaging 25:459–463. https://doi.org/10.4103/0971-3026.169451
25. Thurnher MM (2009) 2007 World Health Organization classification of tumours of the central nervous system. Cancer Imaging 9(A):S1–S3. https://doi.org/10.1102/1470-7330.2009.9001
26. Tseng YC, Hsu HL, Jung SM, Chen CJ (2004) Primary intracranial myxopapillary ependymomas: report of two cases and review of the literature. Acta Radiol 45:344–347
27. Verstegen MJ, Bosch DA, Troost D (1997) Treatment of ependymomas. Clinical and non-clinical factors influencing prognosis: a review. Br J Neurosurg 11:542–553
28. Warnick RE, Raisanen J, Adornato BT, Prados MD, Davis RL, Larson DA, Gutin PH (1993) Intracranial myxopapillary ependymoma: case report. J Neuro-Oncol 15:251–256
29. Whitaker SJ, Bessell EM, Ashley SE, Bloom HJ, Bell BA, Brada M (1991) Postoperative radiotherapy in the management of spinal cord ependymoma. J Neurosurg 74:720–728. https://doi.org/10.3171/jns.1991.74.5.0720