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Original Article

Management and Outcome Analysis of Conus and Filum ependymoma: A Tertiary Center Study

Manoharan Dwark Sudhan, Guru Dutta Satyarthee, Leve Joseph[1], Mehar Chand Sharma[2], Aanchal Kakkar[2], Bhawani Shankar Sharma

Departments of Neurosurgery, [1]Neuroradiology and [2]Neuropathology, All India Institute of Medical Sciences, New Delhi, India

Abstract

Background: Spinal ependymomas constitute approximately 2%–8% of primary adult central nervous system tumors. Authors analyzed demographic, clinical, radiological, surgical, and histopathological factors which correlated with the postoperative neurological outcome of patients who underwent surgery for conus and filum ependymoma (CFE). **Materials and Methods:** A retrospective analysis of 31 patients regarding clinical feature, imaging study, surgical management, and McCormick grading system for assessing functional neurological status was carried out, who underwent surgical management for CFE between January 2009 and April 2014. Final neurological outcome at follow-up period was correlated with various factors in search to find out probable prognostic factors affecting final neurological outcome following surgical management. **Results:** The myxopapillary ependymoma was observed in 55% of cases (n = 17), while 39% cases (n = 12) had Grade II ependymoma and rest 6% (n = 2) cases had anaplastic ependymomas. The mean age was 30 years (range 7–60 years) with male to female ratio of 1:0.82. Patients predominantly presented with pain (80.65%); mean duration of symptoms was 28.61 months. Only, the preoperative McCormick grade was found to be the statistically significant prognostic factor (P = 0.045), affecting neurological outcome however, the age, sex, duration of symptoms, location of the tumor, extent of the tumor, extradural spread, degree of surgical excision, vascularity of tumor, and histopathological World Health Organization grades were not found to be significant prognostic factors in the current study. **Conclusion:** The preoperative McCormick score was found to be the only statistically significant factor predicting the functional and neurological outcome after surgery, so surgical treatment should be offered early in the course of the disease to provide chance of preservation and good neurological recovery.

Keywords: *Conus medullaris, filum terminale, intradural lesion, myxopapillary ependymoma, postoperative neurological outcome, prognostic factors*

Introduction

Spinal ependymoma is considered as rare neoplasm, constituting approximately 15% of all the primary intradural spinal tumors and accounting for about 2%–8% of primary adult central nervous system (CNS) tumors.[1,2] It originates from ependymal lining, filum terminale, and embryonic nest cells.[3,4] In lumbosacral region, ependymoma is commonly located intradurally at conus medullaris and filum terminale. However, sporadic cases of extradural ependymomas are also reported.[5] The conus and filum ependymoma (CFE) is categorized as a distinct clinical entity as both share similar clinical presentations, histopathological, surgical management, and prognostic outcomes.

According to the histopathology, the ependymoma is categorized by the World Health Organization (WHO) into three grades. The Grade I include subependymoma and myxopapillary ependymoma (MPE), while the classic ependymoma corresponds to the WHO Grade II and anaplastic tumors designated as Grade III.[6] Most of the CFE is myxopapillary representing the WHO Grade I tumors. In 1932, Kernohan was first to describe MPE located in the lumbosacral region. With the advancement in the fields of spinal neuroimagings, immunohistology, intraoperative spinal monitoring uses, and practice of microneurosurgical techniques, the surgery of spinal ependymomas has evolved considerably over the periods. However, there exists a paucity of published literature, barring a few, analyzing the various prognostic factors affecting the postsurgical functional and neurological outcome of CFE.

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Address for correspondence:
Dr. Guru Dutta Satyarthee, Department of Neurosurgery, All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110 029, India. E-mail: drguruduttaaiims@gmail.com

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The aim of the current study was to retrospectively analyze the clinical presentation, neuroimaging feature, operative management, and neurological outcome in cases with CFE managed by surgery at our center. Various predicting factors that lead to improved neurological functional outcome in these patients were also analyzed.

Materials and Methods

Study design

All consecutive patients undergoing surgery for CFE at our tertiary care center over a 6-year period from 2009 to 2014 were included in the study. However, patients with <3 months of follow-up were excluded from the current study. The consent of the patients for enrollment in the study was not possible as it was a retrospective study; however, the study was initiated after getting approval of ethics clearance from the Institutional Ethics Committee and also permission sought for institutional approval of the study and publication.

Data collection

Hospital records including case sheets, operative notes, neuroradiology records, discharge summaries, and outpatient follow-up notes were used to collect the requisite data, after obtaining ethical clearance.

Study protocols and definitions

The functional status of the patients was recorded using McCormick grading system. A decrease in McCormick grade or subjective improvement in symptoms was taken as improvement.

The institutional protocol for spinal tumors included a gadolinium-enhanced magnetic resonance imaging (MRI) in the preoperative period and postoperatively at 3 and 9 months following surgery during the follow-up period. The assessment of extent of surgical excision was based on the neurosurgeon's intraoperative assessment and postoperative imaging studies. All cases were categorized pathologically in accordance with the fourth edition, WHO classification of tumors of the CNS, 2007. For the sake of statistical analysis, Grade III and IV tumors were combined as high-grade tumors. Reappearance of symptoms attributable to tumor growth and radiological evidence was used to define the recurrence of lesion.

Statistical analysis

Age, sex, preoperative McCormick grade, duration of symptoms, location of the tumor, and extent of the tumor measured as the number of corresponding vertebral levels, extradural spread, extent of excision, vascularity of tumor, and the WHO grades were correlated with the functional outcome of the patient at the last follow-up. Functional outcome was dichotomized into two categories: improved and not improved. Statistical Package for the Social Sciences version 11.0 (SPSS, Chicago, IL, USA) was used for statistical analysis. Pearson's Chi-square test and Fisher's exact test were applied for univariate analysis; multivariate analysis was done using logistic regression method. A $P < 0.05$ value was considered statistically significant.

Results

Demographic parameters

Out of the 31 patients, 17 were males with the male to female ratio being 1:0.82. Mean age of the patients was 30.23 years (range 7–60 years). Majority (54.84%) of the cases were in their third to fourth decades of life.

Clinical presentation

Mean duration of symptoms before admission was 28.61 months (range, 3–120 months). [Table 1] Pain was the most common symptom in 80.65% (n = 23) and also represented the most common initial symptom (74%). However, the most common causes for seeking medical consultation included appearance of the bladder symptoms (42%) and motor weakness of limbs (38%) [Table 2].

Radiological features

In MRI study, 80.65% of ependymomas (n = 25) exhibited isointense signal on T1-weighted (T1W) image and rest were hypointense; [Figures 1 and 2] however, all cases exhibited hyperintense signal on T2W image with evidence of occasional heterogeneous areas in the matrix, probably

Table 1: Age distribution of conus filum ependymoma

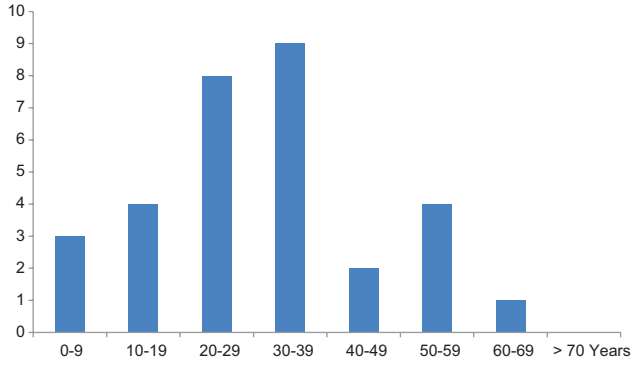

Table 2: Demographic profile and symptomatology

Demographic profile		
Mean age (years)	30.23	Range - 7-60
Sex (male:female ratio)	1:0.82	17:14
Duration of symptoms (months)	28.61	Range - 3-120
Symptomatology		***n* (%)**
Symptoms		
Pain		25 (80.65)
Paresthesia		4 (12.90)
Sensory loss		14 (45.16)
Motor deficit		25 (80.65)
Bowel involvement		15 (48.39)
Bladder involvement		19 (61.29)

Table 3: Functional outcome predictors conus filum ependymoma

	Not improved (*n*=15)	Improved (*n*=16)	*P*	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age	28.13±15.56	32.18±15.4	0.539		
Sex					
Male	7 (46.67)	10 (62.50)	0.376	1.0	1.0
Female	8 (53.33)	6 (37.50)		0.52 (0.12-2.20)	0.32 (0.39-2.72)
Duration of symptoms					
<6 months	3 (20.00)	4 (25.00)	0.718	2.22 (0.28-17.63)	
6 months-2 years	7 (46.67)	9 (56.25)		2.14 (0.37-12.19)	
>2 years	5 (33.33)	3 (18.75)		1.0	
Preoperative McCormick scale					
Good (I, II)	8 (53.33)	11 (68.75)	0.045	8.5 (0.82-82.66)	1.80
Moderate (III)	1 (6.67)	4 (25.00)		24 (1.14-505.19)	5.71
Poor (IV, V)	6 (40.00)	1 (6.25)		1.0	1.0
Location					
Lumbar	15 (100)	16 (100)			
Extent (segments)					
1	0	1 (6.25)	1.00		
2-4	6 (40.00)	7 (43.75)		1.31 (0.30-5.58)	0.83 (0.11-6.31)
>4	9 (60.00)	8 (50.00)		1.00	1.00
Extradural spread					
Present	0	0			
Absent	15 (100)	16 (100)			
Excision					
Gross total	13 (86.67)	14 (87.50)	1.000	1.07 (0.06-19.04)	2.63
Near total	1 (6.67)	1 (6.25)		1 (1.00-0.19)	6.78
Sub total	1 (6.67)	1 (6.25)		1.0	1.0
Vascularity					
High	8 (53.33)	4 (25.00)	0.149	1.0	1.0
Moderate	7 (46.67)	12 (75.00)		3.42 (0.75-15.67)	5.00 (0.51-48.94)
Low	0	0			
WHO grade					
Grade I	8 (53.33)	10 (62.50)	0.851	1.25 (0.06-23.25)	2.46 (0.33-179.78)
Grade II	6 (40.00)	5 (31.25)		0.83 (0.04-16.99)	1.06 (0.01-111.40)
Grade III, IV	1 (6.67)	1 (6.25)		1.0	1.0

CI – Confidence interval; WHO – World Health Organization; OR – Odds ratio

representing hemorrhage or calcification. All tumors showed intense enhancement on MRI contrast study.

CFE had a mean spread of the vertical extent of 4.5 vertebral segments (range 1–9 spinal segments). [Table 3] Associated widening of spinal canal, scalloping of posterior surface of the vertebral bodies, was observed in 63.64% cases. Areas of calcification in the tumor matrix were evident in 25% and evidence of intratumor hemorrhage was observed in 45.16 (n = 14) cases. Five cases had associated the presence of syrinx (16.13%).

Surgery

All cases underwent surgical resection utilizing posterior approach; 18 cases had laminoplasty (58.06%) and remaining 13 had laminectomy with microsurgical removal of the tumor. A gross total excision (GTE) was carried out in 87%. However, in the remaining cases, subtotal (n = 2) or near-total excision (n = 2) was carried out, due to intraoperative factors such as poor surgical plane due to dense adherence of the tumor to nerve roots or extensive lesion causing risk to injury to the conus or nerve roots.

Recurrence and adjuvant therapy

The two cases who had subtotal excision were subjected to adjuvant radiotherapy. Recurrence was observed in three cases (10%). Recurrent cases were managed with surgery and radiotherapy in two cases, and surgical intervention alone in one case.

Metastasis

Drop metastases were detected in 9.68% (n = 3) of cases at initial presentation, during preoperative workup with contrast-enhanced MRI studies and located intradurally in the sacral region and treated with surgically. The histopathological findings were Grade II ependymoma in two cases and rest one had MPE.

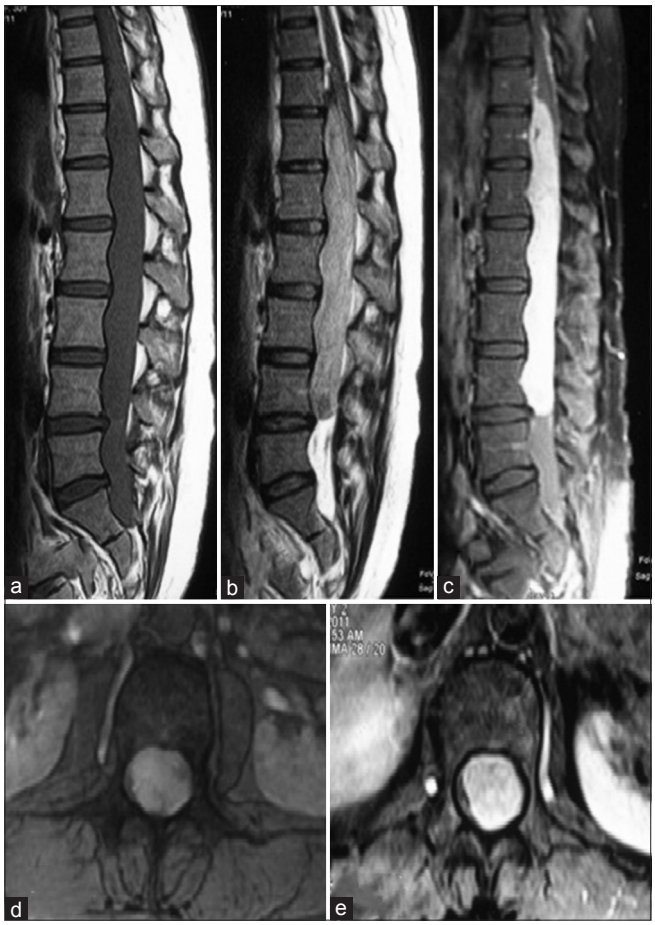

Figure 1: Magnetic resonance imaging dorsolumbar spine of a 32-year-old female, sagittal section image, showing conus ependymoma extending over D11 to L4 vertebral level (preoperative). (a) T1-weighted image showing an isointense lesion extending from lower border of T11 to L4, (b) T2-weighted image showing a predominantly hyperintense lesion with hypointense foci at the superior and inferior margins of the lesion representing hemorrhage, (c) contrast-enhanced magnetic resonance imaging showing an almost homogenously enhancing lesion; and axial section (d) contrast-enhanced magnetic resonance imaging, image showing homogeneously enhancing intradural lesion, and (e) T2-weighted image showing a predominantly hyperintense lesion

Histopathology

On histopathological examination, 54.83% (n = 17) cases had MPE, 38.71% cases (n = 12) had Grade II including two tanycytic ependymomas, and 6.46% (n = 2) had anaplastic (Grade III) ependymomas. A total of 16 out of 17 MPE exhibited typical morphological features, with tumor cells arranged in papillary architecture around vascularized stromal cores containing myxoid matrix [Figure 3a]. MIB-1 labeling index ranged from 1% to 8%, with a mean of 2.8%. One MPE, a recurrent tumor, showed the presence of anaplastic features, including areas of necrosis and an MIB-1 labeling index of approximately 8% in highest proliferating areas. The Grade II ependymomas were composed of small, monomorphic cells having uniform nuclei with salt-and-pepper chromatin. The tumor cells were arranged in perivascular rosettes [Figure 3b]. However, true ependymal rosettes were scanty with infrequent mitoses.

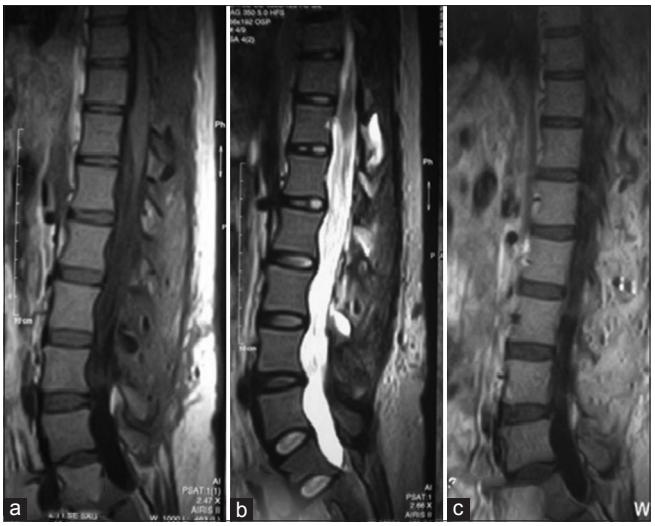

Figure 2: Postoperative magnetic resonance imaging dorsolumbar spine of a 32-year-old female, sagittal sections image showing complete resection of conus ependymoma, which was extending over D11 to L4 vertebral level (same case in Figure 1). (a) T1-weighted image, (b) T2-weighted image, and (c) gadolinium contrast-enhanced image

Mean MIB-1 labeling index was 2.4% (range = 2%–4%). Two tanycytic ependymomas included showed elongated cells in fascicles. Anaplastic (Grade III) ependymomas (n = 2) showed increased cellularity, frequent mitoses, microvascular proliferation [Figure 3c], and high MIB-1 labeling indices of 10% and 40% each.

Outcome and follow-up

The mean follow-up duration was 26.03 months with a range of 3–48 months. Based on McCormick grade and patient symptomatology, an improvement observed in 52% cases following surgical resection and neurological status remained unchanged in 29% cases. However, deterioration in neurological status was observed in 19.35% cases in our study. There was one mortality, who had anaplastic ependymoma, following surgery, and after receiving adjuvant radiotherapy.

Predictors of favorable outcome

Only preoperative functional status evaluated by McCormick grade was found to be the statistically significant (P = 0.045) prognostic factor affecting outcome following surgical management. Other factors analyzed including extradural spread, age, sex, duration of symptoms, location, extent of the tumor, degree of surgical resection, vascularity of tumor, and WHO grade were found not to be statistically significant.

Discussion

Conus and filum terminale ependymoma is a rare tumor, which poses a challenge in early diagnosis, surgical excision with preservation of neurological function. Management is debated, further the rarity of makes difficulty in a formulating a consensus. Although CFE

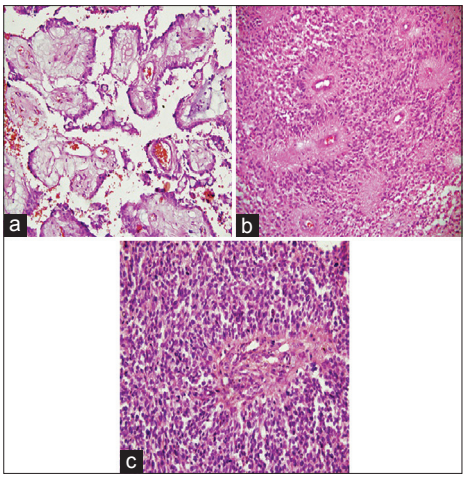

Figure 3: Photomicrograph of myxopapillary ependymoma. (a) microscopic appearance of the World Health Organization Grade I myxopapillary ependymoma (H and E, ×200), (b) microscopic appearance of classical World Health Organization Grade II, and (c) microscopic appearance of the World Health Organization Grade III anaplastic ependymoma showing presence of areas of necrosis (H and E, ×400)

forms a significant proportion of spinal ependymomas, there is a lack of consensus in standard surgical management protocols, role of adjuvant therapy as only few small studies are available[2,5,7,8] and prognostic factors affecting CFE.[9-11] Further, these studies analyzed either ependymomas occurring along the whole spine or only spinal MPE.

CFE can occur over a wide range of age groups; Sonneland *et al*. reported a mean age of 36.4 years in the study analyzing MPE.[7] However, mean age can vary between 30 and 45 years in literature;[3,10,12,13] however, it mostly occurred in young adults with a mean age of 30.23 years in the current study. Male predominance was noted in our study (male: female 1:0.82), but similar gender predilection has not been observed previously.[7,10,12] In the current study, the sex and age were not significant statistical outcome predictors ($P = 0.376$, $P = 0.539$).

CFE usually tends to have a long latency period before seek medical advice following onset of initial symptoms, and the mean duration of symptoms was 28.61 months in the current study; back pain with or without associated radiation was usually the most common symptom and also constituted the most common initial symptom.[14,15] However, patients usually neglected initial symptoms and only sought medical advice following the development of bladder symptoms or weakness in lower limbs. More than half of the patients presented with bladder symptoms (61%); probably, this can be attributed to their lumbosacral location. However, the duration of symptoms was also not statistically significant.

MRI with gadolinium contrast is considered as the investigation of choice, and all our cases had preoperative MRI. Most CFE showed iso- or hypo-intense on T1W and hyperintense on T2W images and usually demonstrated heterogeneous or homogenous enhancement with gadolinium contrast. However, MPE can also be hyperintense on T1W due to the presence of mucinous content or previous hemorrhage and blood degradation product. Further, cystic degeneration and hemorrhage may cause change in appearance with areas of signal heterogeneity. The tumor was located in the conus or filum and extended to an average of 4.52 segments either cranially or caudally (range 1–9 segments) in the present study; in contrast, de Jong *et al*. observed more than two vertebral segments involvement in about 59% of cases.[16] MRI in the follow-up period is also used to assess the degree of resection [Figure 2] and also pick up recurrence.

The goal of surgical resection is *en bloc* tumor removal along with preservation of neurovascular structures.[7,12,16] With meticulous planning and diligent surgery using microneurosurgical techniques, it is possible to achieve gross total resection in most cases of CFE; all cases were operated using a posterior approach either through a laminectomy or a laminoplasty. Celli *et al*. noted that gross total resection could be carried out in 43% of cases.[8] However, GTE was possible in 87.10% cases in the current study. A subtotal resection only was possible in two cases, who had due to dense adherence of the tumor to nerve roots. However, the extent of excision did not have significance as a neurological outcome predictor ($P = 0.851$). Kucia *et al*. also noted no difference in the outcome between patients, who underwent either GTE or subtotal resection augmented with adjuvant radiotherapy.[17]

Recurrence tends to occur in 4%–43% of cases, despite meticulous surgical excision, developing after a time interval of 2–9 years following the initial surgery.[7,8,16,18,19] In present study, recurrence was observed in 12.5% cases. Recurrence rates of 19% were reported by Sonneland *et al*., whereas Chao *et al*. noted a recurrence rate of 43.2%.[7,20] Various factors such as piece meal excision, subtotal excision, volume of tumor, and histological grade of the tumor have been attributed to recurrence.[7,18] Recurrence involving a small number of segments can be treated by surgery alone.

The role of radiotherapy in the management of CFE remains undefined due to paucity of published larger studies. Most authors recommend adjuvant radiotherapy if surgical resection is subtotal or biopsy of the lesion was carried out. Radiotherapy is also advocated in case of recurrence and even for piecemeal excision; however, these indications remain controversial.[3,7,8,13,16,19,20] In 2011, Chao *et al*. observed postoperative radiotherapy delayed recurrence in their study involving 37 cases myxopapillary[20] radiation therapy also been used in CNS metastasis; however, this is another area of controversy. Anecdotal reports of chemotherapy are available for cases of ependymomas in those nonoperable or recurrent cases and refractory to radiation therapy; however, most authors do not advocate chemotherapy as a routine.[3,7,21] In our study, two patients with recurrence received radiotherapy.

The exact incidence of metastasis in CFE is still debated. A complete evaluation with MRI brain and whole spine is indicated in all cases of ependymoma. CFE has a propensity to disseminate along the neural axis, especially in those involving piecemeal tumor excisions.[22-24] Although drop metastasis is more common, proximal spread and intracranial dissemination are also been reported.[3,25] Very rarely, even extraneuraxial spread can occur.[26] Metastatic disease can be treated with surgery with or without adjuvant radiotherapy. In our study, three cases had drop metastasis which was treated with surgery.

MPE is the predominant histotype among CFE tumors.[7,27,28] In our study, MPE was found in 54.83% cases, while Grade II ependymoma occurred in 38.71% and anaplastic variety in 6.45% cases.

Two cases developed recurrence in MPE and one case of Grade II ependymoma in the current study, and there was no correlation between recurrence and histological grade of tumor. Further, multivariate analysis did not show any association between the WHO grading and the functional outcome. Oh *et al*. in literature review and analysis of 175 spinal cord ependymomas correlated tumor grade with recurrence and concluded that overall survival was not influenced by tumor grade and further observed progression-free survival was significantly improved by GTE in Grade II tumors but not in Grade I.[29]

Sonneland *et al*. reported clinicopathological and immunocytochemical findings in 77 cases of MPE in 1985; however, analysis of prognostic factors was not made.[7] Pica *et al*. analyzed 45 cases of lumbosacral MPE and concluded that age >36 years, absence of neurological symptoms at diagnosis, tumor size >25 mm, and adjuvant high-dose radiotherapy were independent predictive factors of progression-free survival.[19] However, authors failed to analyze CFE separately.

Halvosen *et al*. analyzed a subset of 58 patients of CFE out of total 86 spinal ependymoma and observed that preoperative neurological function was a predictor of outcome.[9] However, Kucia *et al*. in a study involving 34 patients of MPE noted no correlation between the extent of resection and neurological outcome.[17] Bostrom *et al*. analyzed 57 patients with ependymoma, out of which 19 were CFE and deduced that preoperative McCormick grade was an independent predictor of functional outcome.[10]

Among the various factors analyzed, only preoperative functional status evaluation by McCormick grade was found to be statistically significant (P = 0.045) in predicting the functional outcome after surgery. However, other factors including age, sex, duration of symptoms, location of the tumor, extradural spread, extent of excision, vascularity of tumor, length of the tumor measured as the number of corresponding vertebral levels, and WHO grade were not found to be significant predictors in the current study. Limitation of the present study includes relatively small sample size and comparatively short duration of follow-up.

Conclusion

CFE forms a distinct clinicopathological entity. MPE represented the most common histopathological variety of ependymoma. Gross total microsurgical excision is the treatment of choice and can be safely achieved in a majority of cases. The preoperative McCormick score was found to be the only significant factor in predicting the functional outcome following surgery for conus and filum terminale ependymoma, implying that surgery should be offered very early in the course of the disease to provide good functional and neurological outcome. However, further studies with larger sample size or meta-analysis is required to address the role of adjuvant therapy, issues of management of recurrence of ependymoma, and other prognostic factors predicting outcome.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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