



Original Article

Myxopapillary ependymomas; proximity to the conus and its effect on presentation and outcomes

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ABSTRACT

Background: Myxopapillary ependymomas (MPE) are intradural spinal tumors with a predilection to the filum terminale. Damage to conus medullaris during surgery can result in sphincteric and sexual dysfunction. The purpose of this study is to determine how myxopapillary ependymoma proximity to the conus impacts patient presentation, extent of resection, and clinical outcomes.

Methods: Fifty-one patients who underwent surgical resection of pathologically confirmed myxopapillary ependymoma with at least 1 year of follow-up were included in the study. We collected initial presenting symptoms, distance of the tumor from the conus, extent of resection, and postoperative clinical outcomes including bladder dysfunction.

Results: Average age was 38 years (range 7–75 years) with a male to female ratio of 1.43:1. Patients most commonly presented with pain symptoms (88%), and 12 patients (23.5%) had urologic symptoms on presentation. The mean tumor distance from the tip of the conus was 1.60 cm (10 cm above to 21 cm below the tip of the conus). Patients with tumors in contact with the conus had a significantly higher rate of preoperative urinary symptoms and were more likely (32% vs. 14%) to suffer postoperative urinary sphincteric disturbances. Tumors with direct invasion of the conus medullaris were more likely to require intralesional resection and fail to achieve a gross total resection (GTR).

Conclusion: Patients with MPE in close proximity to the conus were more likely to suffer from long-term morbidity related to urologic issues following surgical resection. Adjuvant radiotherapy may be a viable option for patients who fail to achieve GTR.

Keywords: Conus, Ependymoma, Myxopapillary, Outcome, Predictors

INTRODUCTION

Spinal cord ependymomas comprise 35–40% of all primary spinal cord tumors and can be classified into a number of different subtypes, including myxopapillary ependymomas (MPE).^[7] MPE are a distinct type of grade one ependymomas with a predilection to the conus medullaris and filum terminale.^[9,16] Despite their benign nature, MPEs can invade locally and metastasize within and outside the central nervous system.^[8,17] There is no current standard of care in the management of MPEs, but a complete resection without capsular violation, so called *en bloc* gross total resection (GTR), has been suggested as the is the primary goal of surgery and can

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be curative without further adjuvant therapy.^[1] In cases, where *en bloc* GTR cannot be achieved, a patient may require radiation therapy. In this study, we aim to better define the role tumor proximity to the conus in determining extent of resection and clinical outcomes.

MATERIALS AND METHODS

This study was approved by the Mayo Clinic institutional review board (IRB); all patients provided informed consent for using clinical data for research purposes. A retrospective chart review was performed from 1995 to 2019 to identify patients with pathologically proven MPE. Patients without a preoperative MRI, sufficient operative detail, or <12 months of follow-up were excluded from the study. Baseline demographic data including age, gender, and clinical presentation details were collected. Preoperative MRI was used to determine tumor location, tumor size, distance between the superior- and inferior-most poles of the tumor, presence or absence of CSF metastases, and proximity to the conus. Proximity the conus was defined on MRI as the distance between the superior pole of the tumor and the inferior tip of the conus. Tumors in which the superior pole of the tumor was at or above the tip of the conus were considered to be in contact with the conus and were further subdivided depending on whether they appeared to be invading or displacing the conus on imaging.

Operative notes were used to determine extent of resection, whether an *en bloc* resection, piece meal GTR, in which a complete resection was performed with violation of tumor capsule, or a sub-total resection (STR). In lesions involving the conus, drop metastases of the *cul-de-sac* were considered separately with regard to technique and extent of resection. Postoperative MRI was evaluated to confirm extent of resection. There was no discrepancy between intra-operative findings and postoperative MRI in our series. Follow-up data included any adjuvant therapy, clinical performance at last follow-up, and details regarding recurrence. Preoperative and postoperative urinary disturbances were collected including retention, urgency, hesitancy, as well as any form of incontinence.

Statistical analysis was performed using JMP software version 14 (SAS Institute Inc., Cary, North Carolina, USA). Chi-square test and Fischer exact test compared preoperative, intra-operative, and postoperative variables and outcomes including urinary sphincteric disturbances, technique of resection, extent of resection, and recurrence rates.

RESULTS

We identified 51 patients who met all inclusion criteria for our study. Average patient age at time of surgery was 38 ± 17.9 years with a male to female ratio of 1.4:1.

Initial presenting symptoms included low back pain or radiculopathy (88%), urinary sphincteric disturbances (24%), lower extremity paresthesias (12%), and lower extremity weakness (12%). Average tumor size was 4.7 ± 4.4 cm and was located at the level of the conus in 22 (43%) patients, cauda equina in 28 (55%) patients and at the level of the thoracic cord in one patient (2%). The average distance from the superior portion of the tumor and the inferior tip of the conus was 1.6 ± 4.6 cm. CSF seeding was evident in 6 (12%) patients at the time of diagnosis, equally distributed between the two groups. The one patient with a tumor involving the thoracic cord had a drop metastasis at the level of S1. Of the 22 patients with lesions in contact with the conus, 18 were found to be displacing and four were invading the conus as seen on preoperative MRI and confirmed intraoperatively [Table 1].

Fifty-seven tumors were surgically resected from the 51 patients in this study. *En bloc* resection was achieved in 32 lesions (56%), intralesional GTR in 11 lesions (19.3%), and partial resection of 14 lesions (25%). Of the 51 patients, GTR of all lesions, present at time of diagnosis, was possible in 39 (76.5%) patients. Pathologically, 46 (90.2%) tumors had classical features of MPE, 4 (7.8%) showed signs of atypia, and 1 (2%) tumor was extensively calcified. Adjuvant postoperative radiation therapy was given to six patients, all of which had partial resections. In all six patients radiation therapy was administered to the surgical bed with adequate margins, using intensity modulated radiotherapy techniques when available [Table 2].

Average follow-up was 57 months with a range of 12–165 months. Only 2 (4%) patients in our cohort developed new postoperative lower extremity weakness. A good outcome, defined by an mRs score of 0–2, was achieved in all but one patient who died after multiple systemic metastases. Eight patients developed tumor recurrence at an average of 18.1 ± 12.8 months from surgery. There were four patients with isolated local recurrence, three with concomitant

Table 1: Baseline patient characteristics.

Age	38.0±17.9
Gender M:F	1.41:1
Presentation	
Low back pain/Radiculopathy	45 (88.3%)
Sensory symptoms	6 (12%)
Urinary disturbances	12 (24%)
Motor weakness	6 (12%)
Size	4.7±4.4
Location of 1ry lesion	
At the level of the conus	22 (43%)
At the level of the cauda	28 (55%)
Thoracic cord	1 (2%)
Distance from conus of primary lesion	1.6±4.6
CSF Seeding on initial presentation	6 (12%)

spread along the craniospinal axis, and one patient with associated extra-neural metastasis. One of six patients who received postoperative radiation therapy after partial resection developed recurrence at 9 month post radiation therapy. In comparison, four recurrences, at a mean 20.8 ± 18.1 months from surgery, occurred in the remaining six patients who underwent partial resection but did not undergo postoperative radiation therapy. Of the eight patients who developed recurrence, five went on to receive local radiation therapy after first recurrence. Of these, two patients developed recurrence at 41 and 48 months post radiation therapy, two were stable at last follow-up, and one was lost to follow-up.

After excluding tumors with pathological features of atypia, there was a statistically significant difference in recurrence rate between *en bloc* GTR and intralesional GTR, $P = 0.0444$, with no recurrences occurring in the *en bloc* resection group with MPE with classic pathological features. When comparing clinical presentation and outcome of patients with MPE in contact with the conus versus those not in direct contact to the conus, there was a statistically significant difference in rate of urinary symptoms at presentation (40.9% vs. 10.7%, respectively, $P = 0.0123$). Preoperative urinary symptoms improved in six patients (five in the conus group and one in the nonconus group) after surgical resection. Patients with tumors contacting the conus had more than twice the incidence of postoperative long-term urinary disturbances

compared to patients with MPE not contacting the conus (32% vs. 14%) but the difference did not reach statistical significance, this difference was evident even after excluding patients with urinary disturbances at baseline [Figure 1]. There was no statistically significant difference in technique or extent of resection among lesions involving the conus versus those that did not [Table 3]. However, when considering lesions involving the conus, *en bloc* resection was possible in 61% of lesions displacing the conus while all patients with tumors invading the conus underwent intralesional resection ($P = 0.0451$). GTR was achieved in 83.3% of lesions displacing the conus but only 25% of lesions invading the conus ($P = 0.0458$) [Table 4]. [Figure 2] shows an example of varying tumor location in relation to the conus.

DISCUSSION

Myxopapillary ependymoma proximity to the conus medullaris is associated with higher rates of preoperative and postoperative urinary dysfunction compared to MPE that does not directly contact the conus. Invasion of the conus is an important preoperative predictor of technique and extent of resection. Patients who had an *en bloc* GTR were less likely to develop a recurrence than those with intralesional GTR.

There is limited literature assessing the role of anatomical location in prediction of surgical outcomes of MPE.^[3] This study is the first to highlight the role of conus involvement in determining the risk of preoperative and postoperative urinary dysfunction. Our data did not show a significant difference in extent of resection according to location, we believe that this may be a result of the fact that a large proportion of tumors in proximity to the conus displaced rather than invaded the conus, allowing GTR. The presence of concurrent drop metastases in the *cul-de-sac* may be a potential confounder for our results regarding urinary

Table 2: Surgical outcomes.

	n=51
Extent of resection	
GTR	39 (76%)
En bloc	31
Intralesional	8
NTR/STR	12 (24%)
Pathology	
Classical	46 (90%)
W/Atypia	4 (8%)
Calcified	1 (2%)
Adjuvant therapy	6
Recurrence	8 (16%)
Local	6 (12%)
Intradural	4 (8%)
Extra-axial	1 (2%)
Treatment of recurrence	
RT	3
Surgery	1
RT+Surgery	2
Follow-up	1
Unknown	1
Time to 1 st recurrence (Months)	18.1±12.8
Duration of follow-up (Months)	57.3 (12-165)
GTR: Gross total resection, STR: Sub-total resection, RT: Radiation therapy	

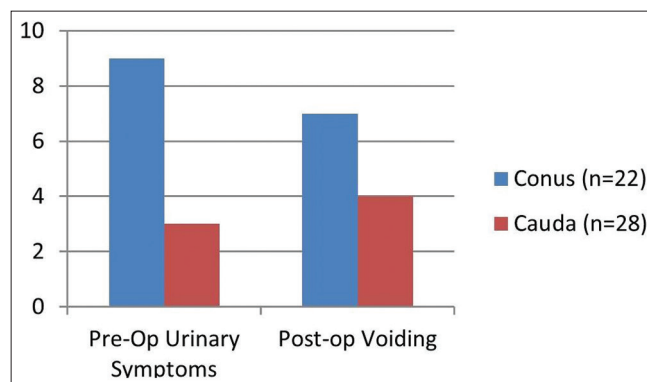


Figure 1: Comparison of tumors according to location with regard to clinical presentation and outcomes. *One Patient had a primary tumor involving the thoracic cord, thus was excluded from the comparison.

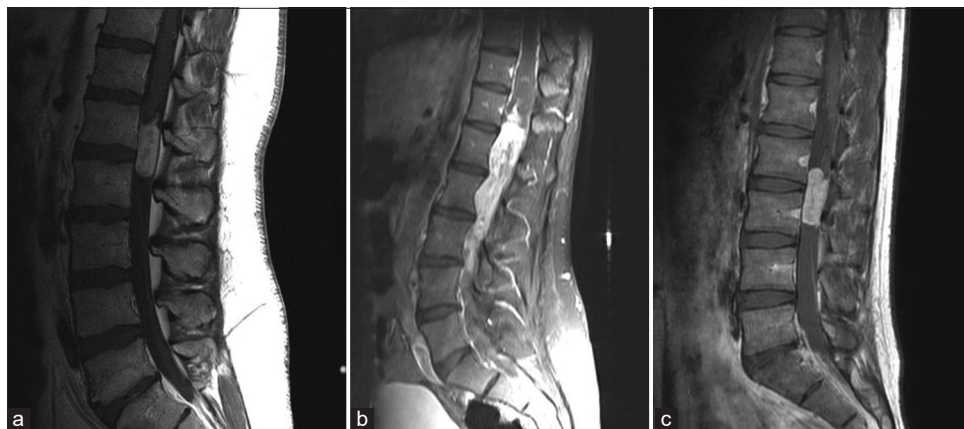


Figure 2: Sagittal T1W postcontrast MR Images showing tumor (a) displacing conus (b) invading conus (c) not in contact with conus.

Table 3: Comparison of resected lesions according to location with regard to operative outcomes.

	Conus (n=22)	Cauda (n=33)	P-value
Type of resection			
<i>En bloc</i>	11 (50%)	21 (63.6%)	0.3157
Intralesional	11 (50%)	12 (36.4%)	
Extent of resection			
GTR	16 (72.7%)	25 (75.8%)	0.8009
NTR/STR	6 (27.3%)	8 (24.2%)	

GTR: Gross total resection, STR: Sub-total resection. *Two lesions were at the level of the thoracic cord, thus were excluded from this comparison

Table 4: Comparison of tumors at the level of the conus with regard to surgical outcomes.

	Displacing (n=18)	Involving (n=4)	P-value
Type of resection			
<i>En bloc</i>	11 (61%)	0	0.0451
Intralesional	7 (39%)	4 (100%)	
Extent of resection			
GTR	15 (83%)	1 (25%)	0.0458
STR	3 (17%)	3 (75%)	

GTR: Gross total resection, STR: Sub-total resection.

dysfunction; however, this is unlikely given the equal distribution of drop metastases between the two groups.

While many prior studies assessing MPE outcomes have failed to distinguish *en bloc* GTR versus intralesional GTR, our study demonstrates the importance of maintaining tumor capsule integrity in lowering recurrence rate. We found zero recurrences in patients who underwent *en bloc* GTR versus 25% for patients with intralesional GTR. Similar results have been published in prior studies.^[14] Extent of resection was found to be independently associated with tumor recurrence in a recent multi-institutional series again highlighting the value of achieving GTR.^[13]

The role of postoperative radiation therapy in patients with partially resected MPE has not been fully established in the literature. While many authors believe that adjuvant therapy is warranted to decrease the risk of cranio-spinal axis and extra-axial spread, others believe that close follow-up should suffice given the benign nature of these tumors.^[2,4,6,10,11] Our data suggest that adjuvant therapy for patients with partially resected MPE may decrease recurrence risk. This is consistent with a study by Kukreja *et al.*, the rare cancer network, and others.^[2,11,15] However, a number of other studies including a large systematic analysis by Feldman *et al.* have found that adjuvant radiotherapy did not improve overall survival.^[6] In favor of delaying radiation therapy, Kotecha *et al.* have found a significant improvement in postrecurrence progression free survival in patients receiving salvage radiation therapy.^[10] Similarly a recent study by Montero *et al.* showed successful tumor control after salvage therapy for initial recurrence.^[13] Inconsistencies in the role of adjuvant radiation therapy may be attributed to the limited number of patients as well as the lack of standardization in the extent and dosing of radiation therapy. Due to the limited number of patients receiving adjuvant or salvage radiation therapy in our cohort it was not possible to perform further analysis to determine the superiority of one treatment paradigm over the other. With the introduction of more conformal techniques for radiation therapy and especially proton beam therapy acute and late toxicities have become minimal to negligible thus advocating for upfront adjuvant radiation therapy in patients with sub-total tumor resection.^[12] Furthermore, the previous studies have shown a paradoxical improvement in progression free survival and worsening of overall survival with the use of radiation therapy, this may be attributed to a selection bias, where patients with higher disease burden are selected for adjuvant therapy.^[5] However, given the lack of consensus, it is our current practice to employ shared decision-making for patients with STR to determine the optimal fields and timing of radiation therapy. Given the proposed safety and efficacy of more conformal radiation therapy, planned radiation

therapy following a more conservative resection may be a more suitable option to minimize morbidity in patients with MPE invading the conus.

Our study is limited by its retrospective nature. Furthermore, given the rare nature of these tumors, outcomes such as recurrence were of limited numbers and thus the study is underpowered for more detailed analysis. This study was performed at a single institution, which may limit its application across other practices.

CONCLUSION

Patients with MPE in contact with the conus are more likely to suffer from urinary sphincteric disturbances both in the pre and postoperative setting. Regardless of tumor location *en bloc* resection is feasible and should be attempted given the lower risk of recurrence achieved. *En bloc* GTR is less feasible and urinary morbidity is higher when tumors invade the conus medullaris. Our data support the utility of postoperative adjuvant radiotherapy in patient who fail to attain a GTR. For tumors invading the conus, efforts to minimize morbidity, such as more conservative resection followed by adjuvant radiation therapy, are worthy of further evaluation.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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