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Surgical outcomes of intramedullary spinal cord ependymomas

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Abstract

Intramedullary Spinal Cord Ependymomas (ISCE) are uncommon pathologies that need to be aggressively managed before clinical deterioration sets in. Novel application of different therapeutic strategies is being assessed for improving long-term outcomes in patients presenting with these rare neoplasms. In this review, we have discussed the existing literature on ISCEs, and the role of surgery in determining outcomes in terms of neurological status, progression-free survival (PFS) and overall survival (OS).

Keywords: Ependymoma, Spinal cord tumour, Intramedullary tumour.

Introduction

Intramedullary spinal cord tumours account for 4-10% of all primary central nervous system (CNS) neoplasms.[1,2] Approximately 60% of all intramedullary neoplasms are spinal ependymomas, more common in adults than in children.[2,3] The WHO categorizes spinal ependymomas into 3 histological subtypes: grade I myxopapillary ependymoma, usually extramedullary; grade II or classic ependymoma (CE), which includes the cellular, clear cell, tanycytic, and papillary subtypes; and grade III anaplastic ependymoma.[3-6] Despite demonstrating a relatively benign course and a usually well-defined dissection plane in comparison to other intramedullary entities, their tendency towards recurrence, malignant transformation, and metastasising along the neuroaxis frequently results in significant morbidity and mortality.[1,7] Herein, we have reviewed the literature pertaining to the survival outcomes in patients undergoing treatment for intramedullary spinal cord ependymomas.

Review of Literature

Ohata et al., published their series of 18 patients who underwent surgery for intramedullary spinal cord ependymoma ranging from grade I to III. They achieved gross total resection (GTR) in 17 patients, while 1 patient, with a grade II ependymoma, received sub-total resection (STR) followed by adjuvant radiotherapy (RT) of 20 Gy. While there was no surgical mortality, there were either worsening deficits or new onset deficits in 10 cases: transient in 7 cases. Follow-up ranged from 10 months to 249 months, with no evidence of clinical or radiological recurrence. The final neurological outcome was improved in 1 case, remained unchanged in 15 cases, and worse in 2 cases.[8]

Oh et al., reviewed 68 studies in 2012, reporting that 268 (77%) out of the 348 total patients with intramedullary ependymomas received GTR, while the remaining 80 (23%) received STR. Out of the latter, 47 patients also received RT. The authors demonstrated significantly lower GTR rates with lower spinal cord ependymomas and anaplastic pathologies ($p = 0.001$). A significantly longer progression free survival (PFS), with an improvement of 20.2% in the five-year PFS rate, was reported in patients receiving RT with STR, compared to those receiving STR alone. The median PFS time was 48 months in the STR group, which was doubled to 96 months with RT. Although more recurrences were observed in the group with a higher radiation dose (>50 Gy), the results were not statistically significant. However, improved OS was only associated with GTR and benign ependymomas, with the five-year overall survival (OS) for GTR, STR + RT, and STR groups being 98.8%, 79.3%, and 73.7%, respectively.[9]

In their 20 years' experience of treating 24 pediatric patients, Safaee et al., reported similar outcomes between grade I and grade II lesions with respect to PFS; and extent of resection was suggested to be the most important prognostic factor in terms of survival outcomes. A significantly better PFS was reported in patients with GTR. Extent of resection was more variable in grade II lesions. The authors also reported difficulty in achieving GTR in the upper spinal cord, making tumour location another significant prognostic factor. There was no immediate or long-term post-operative mortality.[10]

Klekamp et al., described their experience with 100 patients with intramedullary ependymomas. In their series, thoracic ependymomas demonstrated a relatively worse preoperative clinical course as compared to cervical tumours. They reported increased risk of

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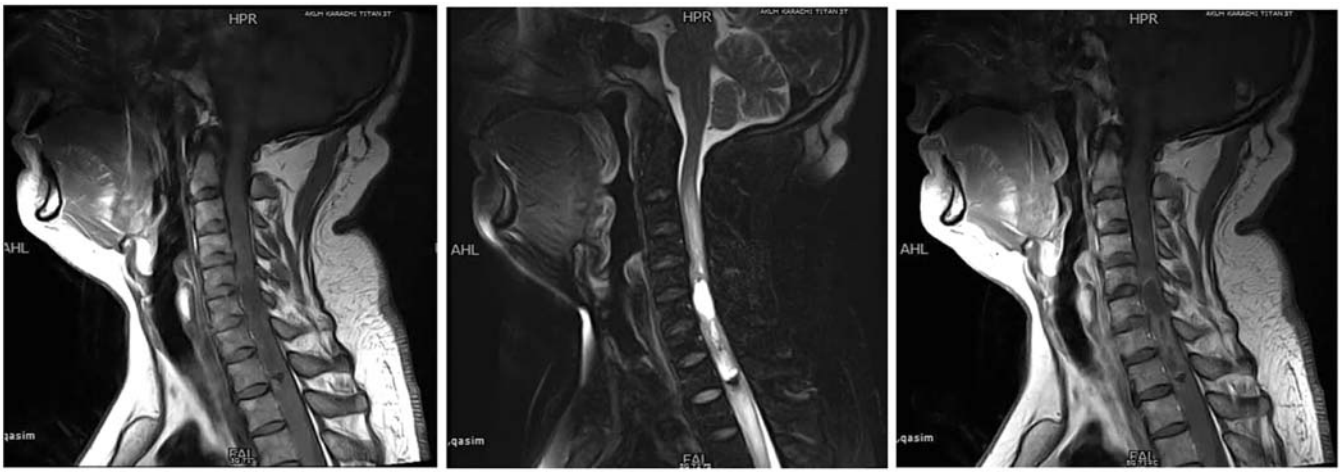

Figure: a) MRI cervical T1WI spine mid-sagittal sections showing C5-T1 iso-intense lesion; b) T2WI (fat-suppressed) of the same patient showing hyper-intense lesion associated with syrinx; I) T1WI with contrast showing heterogeneous contrast enhancement.

permanent morbidity with advanced age, thoracic ependymomas, long clinical history, presence of a tumour bleed, and surgery on a recurrent lesion. Altogether 86.3% patients underwent GTR, with a low preoperative McCormick functional classification grade[8] and first surgery was reported as a strong predictor for complete resection. 67.6% of the patients deteriorated neurologically in the early postoperative period, with the deficit being transient for 40.1% of the patients, and permanent for 27.5%. PFS rates correlated significantly with extent of resection, with the 20-year recurrence rate for GTR and STR being 4.2% and 18.5% respectively. Corresponding OS at 20 years was 92%, with seven deaths during follow-up. Out of these, 3 were unrelated, 2 were related to surgery and happened within six weeks post-operatively, one occurred within a year due to post-operative paraplegia-related complications, and 1 was due to cranial tumours associated with NF-2.[1]

Lin et al., retrospectively analyzed 64 paediatric patients with grade II intramedullary ependymomas. 57% of the subjects underwent GTR. 55 patients were alive at the median follow-up of 9.2 years, while 9 died at a median of 15 months post-operatively. OS at 5 and 10 years was 86% and 83%, respectively. In a multivariate regression model analyzing sex, age at diagnosis, year of diagnosis, radiotherapy, and extent of resection, female sex was found to be an independent predictor of decreased mortality. Tumour progression and recurrence were not reported in the study.[4]

Behmanesh et al., published their series of 28 consecutive patients with intramedullary spinal ependymomas, in which 25 were WHO grade II, and the rest, grade III. GTR was achieved in 93% of patients. Four patients had tumour recurrence, for which they underwent second and third surgeries. While 3 patients experienced minor post-operative complications, there was no mortality within 30 post-operative days. PFS at 5 and 10 was 91% and 85%, respectively, although OS was not reported. An interesting observation was the correlation of permanent unfavourable outcome in 5 out of the 15 (53%) patients, whose radiology showed spinal cord atrophy at the site of resection, at the last follow up.[2]

Svoboda et al., reported 37 patients with intramedullary ependymomas. Most patients presented with the lesion in the cervical region, with either a syrinx formation (49%) or a cyst (32%), seen radiologically. GTR was achieved in 89% of the patients, while 3 patients underwent STR. At a median follow up of 114 months, PFS was 87%, 82%, and 82% at 5, 10, and 15 years, respectively. OS was 97%, 88%, and 63% at 5, 10, and 15 years, respectively. The recurrence rate strongly correlated with the extent of resection, making GTR the most important factor for PFS. OS however was more significantly associated with preoperative clinical status, being significantly better in patients who had McCormick grades 1 and 2 pre-operatively.[5]

Wostrack et al., reported their multicenter retrospective experience of 158 adult patients and concluded that GTR was the most important survival predictor, even with permanent deficits. GTR was obtained in 80% of the patients, with 37% showing worsening of neurological status at discharge. Follow up revealed recovery in majority, whereas 76% showed at least pre-operative status. Transient deficits significantly correlated with cervically located ependymomas and old age. Permanent deficits, observed in 2% of the patients, were only

significantly seen in the older patients. Tumour progression was observed in 15 cases, with the 5-year PFS being 80%. The PFS of 15 patients who underwent RT after first surgery was significantly shorter than those who underwent surgery alone ($p < 0.001$). However, no statistically relevant effects of RT, received by 9 patients in the STR sub-group, were noticed. GTR ($p = 0.037$), WHO grade II ($p = 0.009$), and low Ki-67 index ($p = 0.005$) were significant prognostic variables for PFS. The authors did not report OS in these patients.[7]

Conclusion

Intramedullary spinal cord ependymomas are rare and challenging pathologies. While adjuvant radiotherapy with sub-total resection does prolong progression free survival, gross total resection remains the cornerstone for better outcomes. Overall survival, however, mostly depends upon the pre-operative status and tumour recurrence. Thus, early and active surgical treatment aiming at complete tumour removal optimizes long terms survival outcomes for these patients.

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