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Clinical Study

Progression free survival and functional outcome after surgical resection of intramedullary ependymomas

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ABSTRACT

We present a 15 year institutional analysis of the factors affecting progression free survival (PFS) and overall survival (OS) in patients undergoing attempted resection of adult intramedullary spinal cord ependymomas. Intramedullary spinal cord tumors are rare but important clinical entities, and ependymomas are the most commonly encountered intramedullary tumor. In total, 53 adult patients over the span of 15 years were analyzed for OS, PFS, and the effects of plane of dissection (POD) and gross total resection (GTR) on functional and long term outcomes. The mean age was 45 years and median follow-up was 54 months. The follow-up neurological outcome and modified McCormick scale were used to determine the functional outcome. Kaplan–Meier curves were used to calculate progression and survival. The overall ability to achieve GTR was significantly correlated to identification of an intraoperative POD ($p < 0.001$). There was a trend towards increased PFS with the ability to achieve a GTR. There was no significant difference in the pre- and postoperative functional outcome scores. The ability to achieve a GTR is strongly correlated to the identification of a POD in ependymomas. There is a trend towards an increased probability of PFS in intramedullary spinal cord tumors when GTR is achieved. The resection of these tumors is likely to halt, but not reverse, neurological deterioration.

1. Introduction

Intramedullary spinal cord tumors are uncommon but important pathological entities, of which ependymomas are the most commonly encountered tumor. Several recent studies have highlighted the difficulties in identifying the factors that are associated with treating and prognosticating the long term clinical outcomes of these patients after resection [1–11]. The impact of histology and plane of dissection (POD) have been implicated, among others, including the significant influence of the appropriate extent of resection, adjunctive therapy, and progression free survival (PFS) [1,2]. We present an analysis of 15 years of institutional experience with adult patients who underwent attempted gross total resections (GTR) of intramedullary spinal cord ependymomas.

2. Methods

2.1. Evaluation and demographics

The clinical, operative, pathological, and relevant radiographic reports of all available patients with intramedullary spinal cord tumors, with a histological diagnosis of ependymoma and attempted resection between 1998 and 2013, were reviewed. Patients who presented after a previous resection at another institution, with metastatic disease, who were less than 18 years of age at the time of presentation, or those with von Hippel Lindau disease, were excluded. The patients for whom a biopsy-only was performed were excluded. The modified McCormick scale (MMS) [12], a simplified ordinal 1–5 scale of descending functional status, was applied to all patients both preoperatively and at the last available follow-up (Table 1) [12]. The preoperative and postoperative status was further measured by the presence or absence of motor, sensory, or bowel function. These were compared to the postoperative functional outcomes of better, worse, or unchanged for each

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neurological symptom, as defined by the postoperative clinic notes and patient interviews. Demographic factors such as age, sex, and distance from the medical center were also recorded.

Postoperatively, recurrence, revision surgery, and OS were recorded. GTR was defined as a complete resection of all visible tumor during surgery, confirmed via a postoperative contrast-enhanced MRI, and POD was based on the primary surgeon's intraoperative notes. Recurrence was recorded from radiographic or clinical evidence of a tumor burden either increasing in size from the previous subtotal resection (STR), or with new evidence of a neoplasm after GTR.

2.2. Operative and perioperative course

Based on the operative notes, the following variables were recorded: the number of levels spanned by the lesion, the presence or absence of POD, the use of evoked potentials and associated changes in amplitude, and frozen section results. Perioperative clinical documentation was reviewed to determine any complications, including evidence of non-resolving neurological deterioration, deep vein thrombosis, pulmonary embolism, cerebral ischemic event, cerebrospinal fluid leak, epidural hematoma, syrinx formation, or wound infection. The length of hospital stay and disposition at discharge were also recorded.

2.3. Statistical analyses

All data were analyzed using JMP statistical software (version 11.0; SAS Institute, Cary, NC, USA). The descriptive statistics summarizing the patient demographics were presented as medians and interquartile ranges for continuous characteristics, and counts and percentages for categorical characteristics. Kaplan–Meier curves present the OS and PFS by tumor type. The association between POD and GTR was investigated with a Fisher's exact test. p values $\leqslant 0.05$ were considered significant.

3. Results

3.1. Demographics and clinical presentation

In total, 53 consecutive adult patients who underwent resection for intramedullary ependymoma were identified during the study period. The median age was 45 years, 55% were men, and the mean follow-up period was 54 months. The demographic and clinical characteristics are presented in Table 2. Tumors were most common in the cervical region (42%), followed by a relatively even distribution among the thoracic (21%), conus (11%), and cervicothoracic regions (17%). The most common presenting symptom was sensory dysfunction (89%), followed by motor dysfunction (62%), and bowel or bladder dysfunction (28%). The symptoms were often concurrent, and had been present for a mean of 26 months before presentation for surgical evaluation.

Table 1
Modified McCormick scale

Grade	Modified McCormick scale[a]
1	Intact neurologically with minimal sensory change
2	Mild motor or sensory deficit, still functionally independent
3	Moderate deficit, functionally limited, independent with assistance
4	Severe motor/sensory deficit, functionally limited, dependent
5	Paraplegia or quadriplegia, severe functional limitation

[a] Adapted from McCormick and Stein [12].

3.2. POD and GTR

Among all tumor types, the ability to identify a POD was significantly associated with the potential for a GTR ($p < 0.001$; Table 3). The ability to obtain a GTR was also associated with the ability to identify a POD (Fig. 1). PFS was not statistically associated with GTR (Fig. 2).

3.3. OS and PFS

OS and PFS probability curves were plotted (Fig. 3, 4). The probability of PFS for ependymomas was 60% at 3 years, and 40% at 5 years. The probability of OS was 98% at 3 and 5 years, 87% at 10 years, and 53% at 15 years.

3.4. Functional outcome and neurological status

There was no statistical difference between the preoperative and postoperative neurological outcome status (Fig. 5). Among the patients with ependymomas, angiomas, and gliomas, there were no significant differences between the pre- and postoperative MMS grades (Fig. 6).

4. Discussion

Intramedullary spinal cord tumors are uncommon, and few modern studies have characterized their natural history. Of the currently available studies, most include children and patients with von Hippel Lindau syndrome, which may obscure the natural course of disease in adult patients who present with an isolated lesion. The epidemiology of intramedullary spinal cord tumors leads to difficulties when surgeons attempt to counsel patients on their long term survival and recurrence probabilities.

In 2009, Garces-Ambrossi et al. examined the outcomes of 101 consecutive patients, adults and children, and found that the POD (Fig. 7) and GTR were likely to increase PFS in patients with ependymomas and hemangioblastomas, but not gliomas [1]. In

Table 2
Demographics and clinical presentations of patients undergoing resection for intramedullary ependymoma

Characteristic	n = 53
Age, mean years (range)	45 (20–76)
Male, n (%)	29 (55)
Follow-up, mean months (range)	54 (16–205)
Tumor location, n (%)	
Cervical	22 (42)
Thoracic	11 (21)
Conus	11 (21)
Cervicothoracic	9 (17)
Presenting symptoms, n (%)	
Motor weakness	22 (62)
Sensory change	47 (89)
Bladder or bowel dysfunction	15 (28)
Symptom duration, mean months (range)	26 (1–123)
Incidentally discovered, n (%)	2 (4)

Table 3
The overall relationship between plane of dissection and gross total resection for intramedullary ependymoma

		Gross total resection*	
		Yes	No
Plane of dissection	Yes	39 (74%)	5
	No	3(6%)	6

* $p < 0.001$.