

Surgical Results of Intramedullary Spinal Cord Ependymomas in Adults : Retrospective Analysis of 51 Cases

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Objective : The goal of treatment for spinal cord ependymoma is complete removal without postoperative neurological deficit. The authors analyzed the surgical results and factors influencing the postoperative prognosis.

Methods : Fifty-one cases of primary spinal cord ependymoma, surgically treated between 1979 and 2003, were retrospectively analyzed. The mean follow-up period was 44 months.

Results : Gross total removal was achieved in 42 patients and incomplete removal in nine. The proportion of complete surgical removals was influenced by tumor location and histology. Disease progression was observed in five cases (9.8%), the mean progression free interval after surgical removal was 48 months and the 5-year progression free rate was 68%. Disease progression was found in none of the 42 cases who underwent complete removal, and in 5 of 9 cases who had incomplete removal group ($P < 0.001$). Statistically significant disease-progression factors by multivariate analysis were the surgical extent of removal ($P = 0.012$), preoperative functional status ($P = 0.032$), the presence of intratumoral cysts ($P = 0.007$) and postoperative radiation therapy ($P = 0.042$). Of those patients who underwent incomplete removal, radiation therapy was found to significantly improve the clinical result ($P = 0.042$).

Conclusion : In the surgical treatment of spinal cord ependymoma, preoperative functional status, the presence of intratumoral cysts, the extent of removal, and postoperative radiation therapy were found to be significant prognostic factors of postoperative outcome.

KEY WORDS : Spinal cord ependymoma · Surgical extent · Functional status · Radiation therapy · Prognosis.

Introduction

Ependymomas are the most common intramedullary neoplasm of the spinal cord in adults, and account for 15% of all spinal cord tumors^{11,20} and approximately 60% of all intramedullary spinal cord tumors^{1,2,6,13,14,20}.

Nearly all are histologically benign, and slowly growing with little infiltrative potential, and they are usually well circumscribed^{1,2,6,11,13,15,18}. Owing to the relatively well-defined interface between the tumor and the surrounding normal neural tissues², and to the development of microsurgical techniques, these lesions are amenable to complete resection with acceptable postoperative morbidity and a low incidence of recurrence^{1,6}.

The object of this study was to review and analyze our surgical results of spinal cord ependymoma, and to identify those factors influencing surgical resectability and the postoperative prognosis.

Materials and Methods

Patient population

Between May 1979 and May 2003, 51 patients with primary intramedullary spinal cord ependymomas were treated microsurgically at our hospital. The patient population consisted of 31 men and 20 women with the mean age of 38.8 years at the time of diagnosis.

Preoperative evaluations

The most common presenting symptom was pain in 22 (43%), followed by motor weakness in 12 (23%), paresthesia in 10 (20%), hypesthesia in 6 (12%), and dizziness in one (2%) (Table 1). The mean duration of symptoms before diagnosis was 25.3 months. Preoperatively, sensory disturbance was observed in 92% (47/51), motor weakness in 69% (35/51) and bowel or bladder dysfunction in 37% (19/51). According to

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Table 1. Initial presenting symptoms of spinal cord ependymoma

	Number of cases (%)	Mean duration (months)
Pain	22 (43%)	30.3
Weakness	12 (23%)	11.8
Paresthesia	10 (20%)	25.4
Hypesthesia	6 (12%)	36.0
Dizziness	1 (2%)	12.0
	51	25.3

Table 2. Nurick's functional classification of myelopathy (Philips, 1973)

Grade	Description
0	No sign of spinal cord disease
1	Sign of spinal cord disease but no difficulty in walking
2	Slight difficulty in walking but does not prevent full-time employment
3	Difficulty in walking that prevents full-time employment or the ability to do all housework, but is not so severe as to require someone else's help to walk
4	Ability to walk only with someone else's help or with the aid of a frame
5	Chairbound or bedridden

Nurick's functional classification¹⁹⁾ (Table 2), patients were classified by clinical grade. Preoperative functional status by Nurick's grading system at the time of operation showed grade 1 in 20 (39%), followed by grade 3 in 12 (24%), grade 2 in 11 (21%), grade 4 in four (8%) and grade 5 in four (8%).

Of the 51 patients, 1 had a tumor extending from the cervical segments to the medulla oblongata, 17 tumors were exclusively cervical, eight cervico-thoracic, 10 exclusively thoracic, and 13 around the conus medullaris including one tumor mass at the T12-L1 vertebral body level. One patient had more than one focus at the time of diagnosis. Associated syrinx was found in 27 patients (53%) and tumor cysts were observed in 12 (24%) by spinal magnetic resonance imaging(MRI).

Surgical technique

The operation followed routine procedures for intramedullary spinal cord tumors. A wide laminectomy was used, which routinely extended one level above and below the superior and inferior poles of the lesion. The facets were preserved to prevent delayed spinal instability. A midline myelotomy using microdissectors was gently spread both deeper and longer until it reached the surface and both ends of the tumor. Keeping the plane along the lateral surface of the tumor, the dissection was carried out with internal debulking followed by ventral dissection.

Assessment of postoperative outcome

The first postoperative follow-up MRI was performed six months after surgery and was then repeated annually to detect disease progression in cases without symptomatic change. Wh-

en patients experienced symptomatic change, an MRI study was carried out immediately. Disease progression was defined as recurrence in cases that underwent complete removal and regrowth in cases of incomplete removal as demonstrated by radiological study.

Statistical analysis

To compare the two groups, the data was analyzed by cross table studies by generating probability values using either the chi-square test or Fisher's exact probability test. In addition, the Cog Regression method of multivariate analysis was used to predict postoperative disease progression. Data analysis was performed using SPSS for Windows (SPSS Inc., Chicago, IL).

Results

Surgical extent of removal

Gross total or complete removal was achieved in 42 patients (82%), near total removal or subtotal removal in five (10%) and partial removal in four (8%). The causes of incomplete removal were as follows : extensive long segment in the cervicothoracic spinal cord (from C1 to T5) in one case and an indefinite tumor margin in four. The remaining four cases were operated upon with less experience and before the microsurgical technique was adopted, at a time when conservative removal was preferred.

Pathology

All patients were pathologically diagnosed with low-grade ependymoma. Seventeen cases (33%) were of the myxopapillary subtype, and the others (34, 67%) were non-myxopapillary subtype ependymomas. Nine (53%) of the myxopapillary ependymomas were located around the conus medullaris, and 9 of the 13 (69%) cases of ependymomas around the conus medullaris were of the myxopapillary subtype.

Postoperative follow-up results

Postoperative functional status assessed by Nurick's functional classification showed no change in 24 cases (47%), followed by improvement in 20 cases (39%) and aggravation in seven cases (14%). Radiation therapy was adopted in 5 of incomplete removal group and was performed in 3 of complete removal group in our earlier series. Postoperative disease progression was observed in 5 cases of incomplete group (2 with radiotherapy, and 3 without radiotherapy). Disease progression was observed in 5 cases, mean progression free interval after surgical removal was 48 months, and the 5-year progression free rate was 68%. Disease progression was not observed in any of the 42 cases in the complete removal group ($P < 0.001$).

Preoperative functional status ($P=0.032$), the presence of

Table 3. Prognostic factors influencing postoperative disease progression

Factors	P-value
Preoperative functional status	0.032
Intratumoral cyst	0.007
Extent of removal	0.012
Postoperative radiation therapy	0.042
Tumor location	0.086
Histology	0.512
Syrinx	0.139

by multivariate analysis (Table 3). Of those patients that underwent incomplete removal, radiation therapy improved clinical results, and these improvements were statistically significant. Tumor location, pathology or an associated syrinx showed no statistically significant relationship to disease progression ($P > 0.05$).

The likelihood of complete removal depended upon tumor location, histology and the presence of tumor cysts. The proportion of complete surgical removals was influenced by tumor location, 54% in cases around the conus medullaris versus 87% in other regions ($P=0.05$), and by histological subtype, tumors were completely removed in 33 cases (94%) with the 34 non-myxopapillary subtypes, but in only 9 cases (53%) with the 17 myxopapillary subtypes, which was statistically significant ($P < 0.001$).

Discussion

Clinical manifestation

The period between initial symptom presentation and surgery was protracted (mean 25.3 months). Most patients showed a minimal neurological deficit without motor weakness despite the presence of a large mass, as most tumors were benign and demonstrated expansile growth, though a few cases showed infiltrative growth. Patients with a poorer preoperative functional status (Nurick grade 4 and 5) did not show neurologic improvement. Thus, we postulate that once normal plasticity is impaired, surgery provides few benefits in terms of postoperative functional improvement. This evidence justifies the early detection and removal of tumors even in cases of slow growing tumors, such as of spinal cord ependymoma.

intratumoral cysts ($P=0.007$), the extent of the removal ($P=0.012$), and postoperative radiation therapy ($P=0.042$) were identified as statistically significant prognostic factors influencing postoperative disease progression

Radiological findings

It is known that tumor syrinx occurs in more than 50% of cases of intramedullary ependymoma⁹, which is greater than its incidence in spinal astrocytoma.

The presence of syrinx in the intramedullary spinal cord tumors is known to be a good prognostic factor, because it enables the complete resection of the tumor mass and provides an excellent dissection margin between the tumor mass and the normal cord tissue¹⁷. In the present study, a greater probability of complete tumor resection was observed with syrinx (Fig. 1), but this trend did not reach statistical significance ($P=0.139$).

Sometimes low signal intensity was seen in the boundary between the tumor and the cord tissue on T2WI, which suggested repeated tumor bleeding. This finding though specific to spinal ependymomas, was reported to occur only 20% of spinal ependymomas⁴; it was found in 3 of the 51 cases in the present series.

Postoperative outcome

Postoperatively 20 patients improved functionally and 7 patients exhibited aggravated functionality. Of these 7 cases, six had a poor dissection plane around the tumor, the remaining case was due to retraction injury with a large tumor mass and paper-thin cord tissue; all seven cases were managed by complete removal.

Preoperative neurological status has been reported to be another factor of long-term prognosis^{3,7}. Postoperative functional improvement was seen in cases with a Nurick's grade of lower than four, and no improvement was observed in those cases with a Nurick's grade of 4 or 5. This may be because tumor

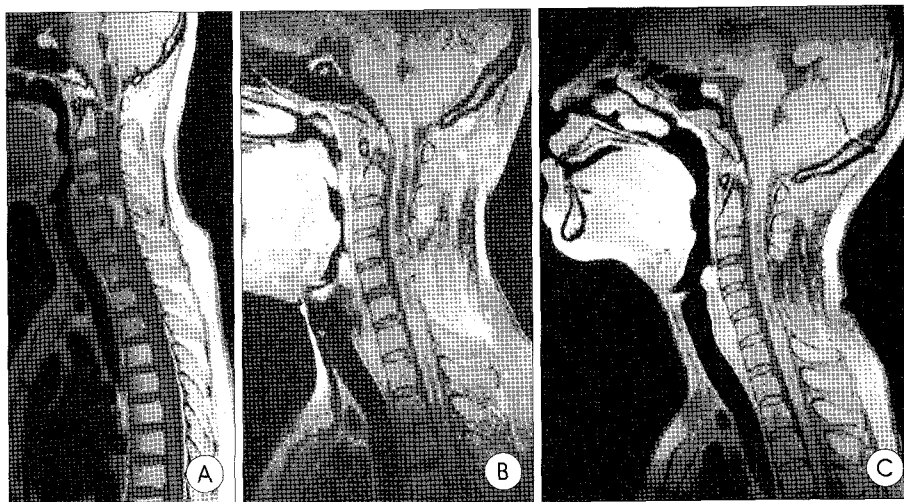


Fig. 1. Pre- and post-operative magnetic resonance images in a 30-year-old woman with right hemiparesis. A : Sagittal T1-weighted cervicothoracic MRI with gadolinium administration reveals a well-enhancing 2.5cm-sized intramedullary mass with syrinx extending from medulla oblongata to the level of T3 vertebra. B : Cervical MRI 6 months after surgery demonstrates no evidence of recurred or residual tumor and decreased syrinx extent. C : Cervical MRI taken after 26 months after surgery shows no evidence of tumor. Compared with preoperative image, this follow-up image shows much decreased volume of syrinx.

mass size is usually large when there is poor and because remaining thin cord tissue is likely to be damaged during dissection.

Follow-up results

When the factors influencing disease progression were analyzed by multivariate analysis, it turned out that the preoperative functional status, the presence of intratumoral cysts, the extent of removal, and postoperative radiation therapy were associated with prognosis. When an analysis was performed using complete removal and incomplete removal as groups, their degrees of disease progression were found to be statistically different. Many authors have reported that the extent of surgical removal is the most important prognostic factor^{3,5)}, which concurs with the author's experience. The preoperative functional status as a statistically significant factor in disease progression may be associated with surgical resectability, but this factor did not show statistically significant relationship to surgical resectability.

The role of radiation therapy

Radiation therapy has been as an adjuvant therapy in cases of incomplete removal, and is known to increase the long-term survival rate^{5,11,16,22)}. Moreover, some authors have suggested a role for postoperative radiotherapy even when a complete surgical removal has been achieved^{4,8,10,20,21)}. However, some authors insist that radiation therapy has no effect on long-term survival or on tumor recurrence^{12,19)}. In recent times, the probability of complete removal has increased due to improved surgical techniques, and re-operations have been recommended for residual tumor regrowth. In our series, radiation therapy was found to be statistically associated with a satisfactory postoperative outcome, but our current strategy is that radiation therapy is reserved for cases of residual tumor even after reoperation.

Conclusion

Early diagnosis and surgical removal of spinal ependymoma is important to achieve sufficient functional improvement. As the tumor is usually surgically resectable, complete removal of the tumor is the preferred initial surgical treatment for spinal ependymoma. Surgical resectability is dependent on the tumor location and on the histological subtype. The statistically significant prognostic factors in disease progression are the extent of surgical removal, the preoperative functional status, the presence of an intratumoral cyst, the extent of removal and postoperative radiation therapy.

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Commentary

The authors have retrospectively analyzed their patients with spinal cord ependymoma to assess the factors associated with final outcome after operation. The authors report 51 patients who underwent surgery for spinal cord ependymoma during a period of 25 years. During the past 25 years,

surgical outcome for intramedullary tumor have been marked improved with excellent microsurgical technique. Therefore this retrospective analysis may be heterogeneous and improper. Although several series larger than the present one have been reported previously, the authors focus on the prognostic factors in disease progression. They found that significant prognostic factors were the extent of surgical removal, preoperative functional status, the presence of intratumoral cyst and postoperative radiotherapy. These analysis is very useful to assess postoperative prognosis before surgery for spinal cord ependymoma.

The authors performed radiation therapy in 5 of incomplete removal group and in 3 of complete removal group. I agree

with the use of radiotherapy in case of recurrent ependymoma, but do not routinely recommend postoperative radiation after gross total resection. Regarding the controversial issue of initiating radiotherapy after incomplete resection, the authors insist that radiotherapy improved postoperative outcome. Recently, reoperation without radiotherapy in case of tumor regrowing is strongly recommended with improved microsurgical technique by some authors.

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