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ORIGINAL ARTICLE

Surgical treatment of intramedullary spinal cord tumors: prognosis and complications

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Study design: Retrospective case series.
Objective: To evaluate our recent treatment strategy for intramedullary spinal cord tumors.
Setting: Department of Orthopaedic Surgery, Keio University, Japan.
Methods: We reviewed 68 cases of intramedullary tumors (ependymoma, 33; astrocytoma, 23; hemangioblastoma, 12), treated surgically between 1994 and 2003. There were 42 males and 26 females whose mean age at the time of surgery was 43 years. The mean follow-up period was 6.2 years. The tumor malignancy grade according to the WHO classification was astrocytoma grade I, 3; grade II, 8 (low-grade: 11 cases); grade III, 10; grade IV, 2 (high-grade: 12 cases). All ependymomas were grade II. Three of the 12 hemangioblastomas were associated with von Hippel–Lindau disease.
Results: Total excision was achieved in 90% of the ependymomas and functional improvement was obtained when the preoperative neurological deficit was mild. Approximately 50% of low-grade astrocytomas could be totally excised with favorable survival outcomes, suggesting that total excision should be attempted for low-grade astrocytomas. However, total excision of high-grade tumors was difficult and the functional outcomes were poor. Cordotomy should be considered in patients with a thoracic high-grade astrocytoma. Total resection was possible in 92% of hemangioblastoma, and the functional outcomes were good, however, more attention should be paid for tumors with feeding arteries on the ventral side and for those associated with von Hippel–Lindau disease.
Conclusions: Predictors of good surgical outcome for intramedullary spinal cord tumors were histological grades of the tumors, surgical margins, and neurological status of the patient before surgery.
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Keywords: intramedullary spinal cord tumor; surgical outcome; prognosis

Introduction

In recent years, there has been a remarkable improvement in the surgical outcomes of patients with intramedullary spinal cord tumors, due to advances in diagnostic imaging and microsurgical techniques, and the introductions of ultrasonic surgical aspirators and intraoperative monitoring. Although, there have been several reports on the surgical outcomes of intramedullary tumors, because these tumors are not encountered frequently, old cases from the past were often included in the assessments to increase the statistical power, thus making it impossible to exclude the possibility of biases from changes in the treatment strategy, diagnostic imaging technologies, surgical techniques and so on in a long term.[1,2] The purpose of this study was to retrospectively review the results of surgery for ependymomas, astrocytomas and hemangioblastomas, the three most common intramedullary tumors of the spinal cord, that were treated surgically at our hospital during the recent 10 years, to elucidate the problems associated with surgery, and to validate our treatment strategy for intramedullary spinal cord tumors.

Patients and methods

We reviewed clinical results in 68 cases including 33 cases of ependymoma, 23 cases of astrocytoma and 12 cases of hemangioblastoma, the three most common tumors among the 81 cases of intramedullary tumors treated surgically at Keio University Hospital between 1994 and 2003. There were 42 males and 26 females whose age at the time of surgery ranged from 3 to 76 years (mean: 43 years). The postoperative follow-up period ranged from 2.5 to 11.4 years (mean: 6.2 years). The tumor malignancy grade according to the WHO classification[3] was astrocytoma grade I, three cases, grade II, eight cases (low-grade group: 11 cases); grade III, 10

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Table 1 Localization of the intramedullary spinal cord tumors

Localization	*Number of patients*
Cervical	30
Cervicothoracic	19
Thoracic	16
Conus medullaris	3

cases, grade IV, two cases (high-grade group: 12 cases). All ependymomas were grade II. Three of the 12 hemangioblastomas were associated with von Hippel–Lindau disease. In all the cases, the histological diagnoses were confirmed by two neuropathologists at the Department of Pathology of our university hospital. The most frequently involved localization was the cervical region followed by the cervicothoracic and thoracic regions and the medullar conus (Table 1).

Following laminoplasty in the cases of cervical tumors or laminectomy in both thoracic and thoraco-lumbar tumors, we approached the tumors through the midline in all cases except for some hemangioblastomas, the part of which appeared from the spinal cord surface. In such cases, we directly developed the plane between the tumor and the spinal cord. During the past 10 years, our treatment policy has been to attempt total resection for all intramedullary tumors, except for grade IV astrocytomas. However, in cases, in which the boundary between the tumor and the spinal cord was indistinct or the spinal evoked potentials decreased markedly and/or frequently during surgery, we abandoned total resection and removed the tumor as much as possible or in some cases, ended up in a biopsy alone. For astrocytomas or residual ependymomas, adjuvant postoperative radiation therapy was administered to the extent allowed by the patient's general condition. In the present study, the impacts of the severity of preoperative paralysis, the level of the tumor, the pathological grade and the surgical procedure employed on the survival and functional outcomes of the patients were analyzed. Survival was calculated as the period from the time of the initial surgery to the date of death or of the last follow-up. Survival rates were drawn using the Kaplan–Meier method and assessed using Wilcoxon's test. The functional status of each patient was determined using the modified Frankel classification before surgery and at the time of the final examination.[4]

Results

Ependymoma

Total resection was achieved in 30 (91%) of the 33 cases of ependymoma. In two of the three remaining cases, only subtotal resection (more than 90%) could be performed because the boundary between the tumor and the spinal cord was indistinct. In the last case, partial resection (more than 50%) was performed because the intraoperative pathological diagnosis was astrocytoma and the intraoperative spinal evoked potential decreased frequently. In this case, the tumor was confirmed to be an ependymoma by the final histological examination, (Table 2).

Table 2 Type of tumor and surgical procedures

	Total	*Subtotal*	*Partial*	*Biopsy*	*Cardiotomy*
Ependymoma (33)	30	2	1		
Astrocytoma					
Low grade (11)	6		1	4	
High grade (12)	1	1	1	7	2
Hemangioblastoma (12)	11	1			

		Final				
		A	B	C	D	E
Pre-operative	A	1				
	B	1	1		2	
	C		2	1	5	
	D			1	5	9
	E					5

Figure 1 Functional outcomes of the patients with ependymoma. Changes in the severity of paralysis by the modified Frankel grade before surgery and at the final examination.

The prognosis of ependymomas thus appears to be favorable, with 32 (97%) of the 33 patients still surviving. One patient had underlying pulmonary fibrosis and developed pneumonia and died of respiratory failure 3 months postoperatively.

Functional improvement was obtained in 16 cases of total tumor resection. Among these cases, the preoperative modified Frankel grade was B in two cases, C in five cases and D in nine cases. Total resection was also achieved in all five cases of grade E preoperatively, and no deterioration was observed postoperatively. Thus, the functional outcome in the cases of ependymoma was favorable if the preoperative paralysis was mild. On the other hand, among four cases in which the paralysis became worse postoperatively, the surgical procedures were partial resection in one case, and total resection of thoracic tumors in the other three cases (Figure 1). An investigation of the impact of the level of the tumor on the postoperative functional recovery revealed that there was improvement in 18 of the 23 cervical cases, whereas only three of the 10 thoracic cases showed improvement.

Astrocytoma

Total resection was achieved in six of the 11 cases of low-grade astrocytomas. Total resection could not be performed in one case because of frequent decreases in intraoperative spinal evoked potentials, and biopsy alone was performed in other four cases, because the boundary between the tumor and the spinal cord was indistinct (Table 2). In the high-grade group, on the other hand, total, subtotal and partial

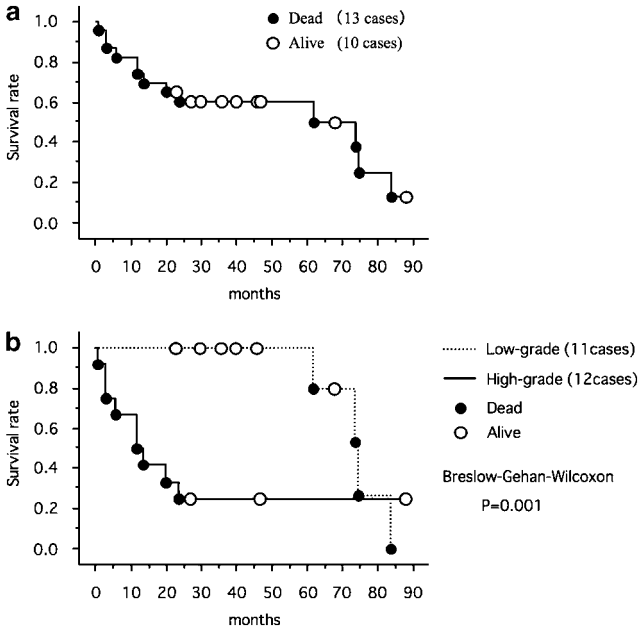

Figure 2 (**a**) Cumulative survival curve of the patients with astrocytoma. (**b**) Impact of the tumor pathological grade on the survival of the patients with astrocytomas: there was a significant difference in survival between patients with the low-grade and high-grade astrocytomas (Breslow–Gehan–Wilcoxon's test, $P=0.001$).

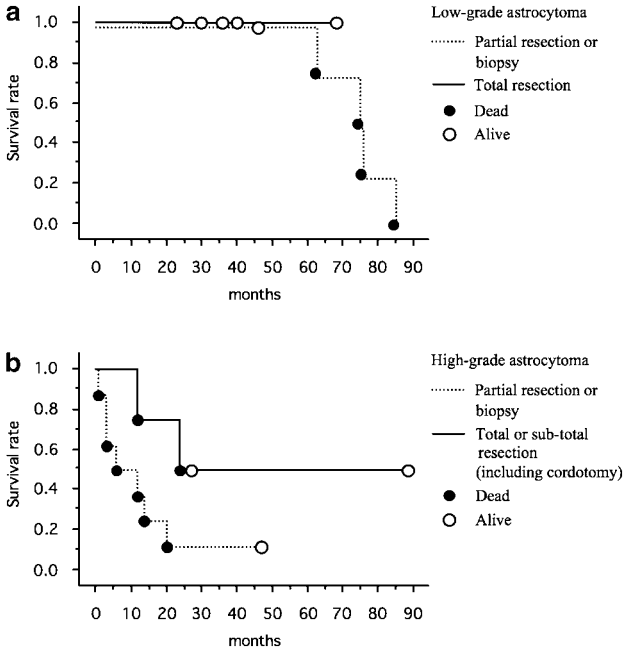

Figure 3 Impact of the surgical procedure on the survival of the patients with astrocytoma: (**a**) low malignancy group, (**b**) high malignancy group.

resections were performed in one case each, and biopsy in seven cases. Spinal cord transection was supplemented in a two-stage manner in two patients with a thoracic astrocytoma, who initially had partial resection or biopsy of the tumor.

Of the 23 astrocytoma patients, 13 had died by the time of the final survey. The 5-year survival rate was 60% (Figure 2a). However, assessment by the pathological grade revealed that there were seven survivors (64%) among the 11 patients in the low-grade group, and three survivors (25%) among 12 patients in the high-grade group. The prognosis in the low-grade group was significantly better than that in the high-grade group (Figure 2b). Because of the small number of cases, assessment of the impact of the differences in the surgical procedures on the prognosis failed to detect any statistical significance. However, it is noteworthy that all six patients in the low-grade group whose tumors were totally removed survived (Figure 3a). On the other hand, even in the high-grade group, the prognosis in the cases of total and subtotal resection, including two cases of spinal cord transection, tended to be longer than that in the cases of biopsy and partial resection. The three patients who survived in the high-grade group consisted of a patient whose tumor was totally removed, a patient who had a spinal cord transection, and a patient in whom a dramatic response to radiotherapy was obtained after a biopsy. Except for three patients, all died within 2 years regardless of the surgical procedure employed (Figure 3b). Assessment of the impact of the level of the tumor on the survival did not reveal any significant difference between the cases of cervical and thoracic astrocytoma ($P=0.8$, Figure 4).

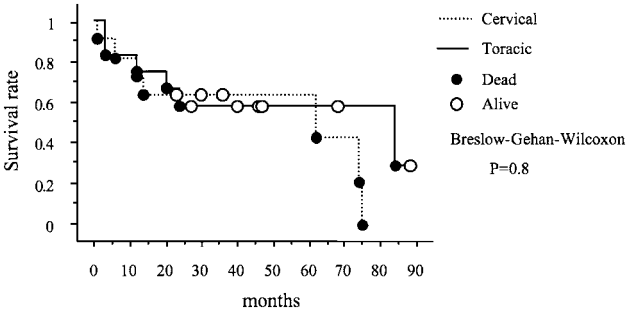

Figure 4 Impact of the level of astrocytomas on survival: there was no significant difference in the survivals between patients with cervical cord and thoracic cord astrocytomas.

The functional outcomes were poorer in the astrocytoma cases than in the ependymoma cases, and postoperative improvement of paralysis was found in only three of the 23 astrocytoma cases (Figure 5). The preoperative Frankel grades in these three cases that showed improvement were D, and they consisted of two cases of total tumor resection in the low-grade group and one case that responded dramatically to radiotherapy in the high-grade group as mentioned above. There were five cases in which the neurological function was maintained at D and E. All five cases belonged to the low-grade group, and total resection was accomplished in four cases and biopsy in one case. In the 12 cases in the high-grade group, the paralysis aggravated postoperatively, regardless of the preoperative Frankel grades or the surgical procedures employed (Figure 5).

Pre-operative	Final A	B	C	D	E
A	2				
B	1				
C	3	1	1		
D	5	1	1	3	3
E					2

Figure 5 Functional outcomes in the patients with astrocytoma: change in the severity of paralysis by the modified Frankel grade before surgery and at the final examination.

Hemangioblastoma

Total resection was possible in 11 of the 12 cases (Table 2). In the remaining case, because there were multiple feeder vessels in the ventral aspect of the tumor, it was difficult to control intraoperative bleeding, which resulted in partial resection despite two operations.

The preoperative paralysis in the hemangioblastoma patients was mild, and their functional outcomes were better than those in the patients with ependymomas or astrocytomas (Figure 6a). However, a detailed assessment of the pre- and postoperative symptoms revealed that in 7 of the 9 patients who had paresthesia and 3 of the 10 patients who had pain preoperatively, the symptoms persisted postoperatively (Figure 6b). In addition, no postoperative improvement of the Frankel grade was observed in four of the 12 cases, which consisted of one case each of partial resection and thoracic cord tumor in an elderly patient and one case each of multiple surgeries for von Hippel–Lindau disease and adhesive arachnoiditis that developed after initial surgery.

Complications

Early-onset complications developed in eight patients (12%). Five patients developed major early-onset complications. Two patients had a cerebrospinal fluid leak, which were treated successfully by lumbar drainage. Two patients developed aspiration pneumonia requiring intravenous antibiotics, and in one patient with a high cervical tumor, postoperative extubation was unsuccessful requiring a tracheostomy. Urinary tract infection developed in three patients as minor early-onset complications and were treated with oral antibiotics. Adherent arachnoiditis developed in one patient (1.5%) with hemangioblastoma as a late-onset complication and was treated surgically.

Discussion

Previous reports have indicated that the surgical outcomes of intramedullary spinal cord tumors vary greatly depending on

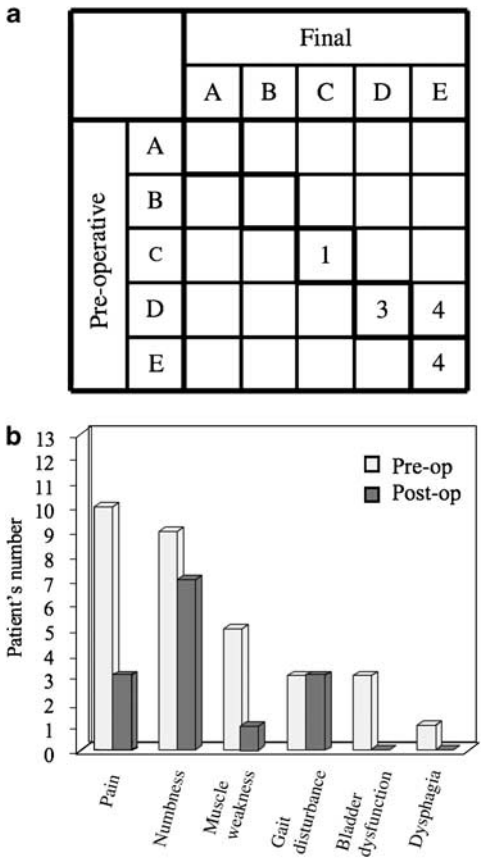

Figure 6 Functional outcome of hemangioblastomas. (**a**) Change in the severity of paralysis by the modified Frankel grade before surgery and at the final examination. (**b**) Changes in clinical symptoms before surgery and at the final examination.

the histology of the tumor.[5,6] Ependymomas can usually be resected completely under a microscope; however, the rate of total resection in past reports has been approximately 70%.[5,6] In recent years,[4,7,8] however, the rate has improved to approximately 90%, as in the present report. These higher percentages appear to be attributable to advances in diagnostic imaging and improvements in the surgical techniques in recent years. Nevertheless, functional prognosis is still poor in patients with severe preoperative paralysis and in those with a tumor arising in the thoracic cord. This could be attributable to irreversible changes in the spinal cord caused by prolonged tumor compression and to poor microcirculation within the thoracic spinal cord both increasing the vulnerability of the spinal cord against intraoperative maneuvers.[9] It is, therefore, concluded that early diagnosis and early surgery, before the paralysis becomes severe, are important to obtain good functional outcomes in cases of ependymomas. Early surgery may be particularly important in cases with the tumors arising in the thoracic cord, even if the neurological deficit is mild.

On the other hand, the prognosis was much worse in the astrocytoma cases than in the ependymoma cases, but still significantly better in the low-grade group than the high-grade group; this difference in the outcome by the tumor

pathological grade was consistent with previous reports.[1,2,10] Reports regarding the selection of the surgical procedure varied from those encouraging aggressive resection[11,12] to those claiming that a biopsy may result in a better functional outcome;[1,2,10,13] and this issue remains controversial. During the past 10 years, we have attempted vigorously to totally remove astrocytomas whenever possible. We think that total resection should be attempted in low-grade astrocytomas while the paralysis is still mild because total resection was possible and the prognosis was favorable in such cases in the present study, and four of five patients who underwent biopsy or partial resection ultimately died. On the other hand, since 75% of the patients with a high-grade astrocytoma died within 2 years regardless of the surgical procedures employed, it must be concluded that the prognosis of high-grade astrocytomas is still very poor, despite the recent advances in the diagnostic imagings and surgical techniques. Nevertheless, since three patients who survived consisted of the patient with total tumor resection, the patient who underwent spinal cord transection, and the patient who responded dramatically to radiation therapy, we think, total resection should be attempted even for high-grade astrocytomas. However, because it is often extremely difficult to distinguish the tumor from the spinal cord, we also consider the administration of postoperative radiation therapy in such occasions. Saving the patient's life by spinal cord transection would be a reasonable choice for high-grade thoracic cord astrocytomas, even if the lower limb function must be sacrificed, because cerebrospinal fluid metastasis of malignant spinal cord tumors is rare. It is important to perform spinal cord transection with wide margin, otherwise tumor infiltration at the cut end could occur.[14]

The prognosis of the hemangioblastoma patients was very good, and there were no deaths in our series. Previous studies have also reported high total tumor resection rates, in the range of 80–100%,[15–17] and total resection was possible in 11 (92%) of the 12 cases in our own series. The functional outcomes were also much better than those in the patients with ependymomas or astrocytomas, but because of the high possibility of persistent paresthesia and pain after surgery, it is most important to obtain preoperative informed consent. Moreover, when a hemangioblastoma is associated with von Hippel–Lindau disease, it is important to exercise care to prevent the development of adhesive arachnoiditis due to repeated surgeries to prevent aggravation of paralysis.

In conclusions, predictors of good surgical outcome for intramedullary spinal cord tumors were histological grades of the tumors, surgical margins and neurological status of the patient before surgery. In cases of intramedullary spinal cord tumors, early diagnosis and early surgery, before the paralysis becomes severe, are important to obtain good functional outcomes. Surgery for intramedullary spinal cord tumors should aim at complete removal of ependymomas, low-grade astrocytomas and hemangioblastomas. Because radical surgery is extremely difficult for high-grade astrocytoma, saving the patient's life by spinal cord transection would be a reasonable choice for high-grade thoracic cord astrocytomas.

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