Surgical Technique and Outcomes in the Treatment of Spinal Cord Ependymomas, Part 1: Intramedullary Ependymomas

BACKGROUND: Intramedullary spinal ependymomas are rare tumors. OBJECTIVE: To provide a large retrospective review in the modern neuroimaging era from a tertiary center where aggressive surgical resection is favored.

METHODS: Charts of intramedullary spinal ependymomas treated between 1983 and 2006 were reviewed.

RESULTS: Sixty-seven cases were reviewed. The mean age was 45.6 years (range, 11-78 years) with a male-to-female ratio of 2:1. The most common location was the cervical spine, followed by the thoracic and lumbar spine. The average duration of symptoms was 33 months, with the most common symptom being pain and/or dysesthesias, followed by weakness, numbness, and urinary or sexual symptoms. Gross total resection was achieved in 55 patients and a subtotal resection was performed in 12 patients; 9 patients were treated with adjuvant radiation therapy. Mean follow-up was 32 months. The mean McCormick neurological grade at last follow-up was 2.0. The preoperative outcome correlated significantly with postoperative outcome (\( P < .001 \)). A significant number of patients who initially worsened improved at their 3-month follow-up examination. Outcomes were significantly worse in patients undergoing subtotal resection with or without radiation therapy (\( P < .05 \)). There were 3 recurrences. The overall complication rate was 34%. The primary complications were wound infections or cerebrospinal fluid leaks.

CONCLUSION: Spinal cord ependymomas are difficult lesions to treat. Aggressive surgical resection is associated with a high overall complication rate. However, when gross total resection can be achieved, overall outcomes are excellent and the recurrence rate is low.

KEY WORDS: Ependymomas, Hemangioblastomas, Intramedullary, Primary glial tumors, Spinal cord

Intradural spinal tumors account for 10% to 20% of primary central nervous system neoplasms in adults.\(^1,2\) This percentage is higher in children and young adults, approaching 35%.\(^3\) Approximately two-thirds of these lesions are extramedullary and one-third are intramedullary. Primary glial tumors and hemangioblastomas represent > 90% of intramedullary spinal cord tumors, with ependymomas accounting for 35% to 40% of these lesions.\(^4-11\)

Ependymomas are lesions that arise from the ependymal cells lining the ventricles or central canal of the spinal cord. They account for 4% to 6% of primary central nervous system tumors, with one-third being intraspinal. Ependymomas are unencapsulated lesions but are usually well circumcised with smooth, regular margins. Consequently, gross total removal of these benign lesions is possible in most cases. We retrospectively reviewed a consecutive series of patients who underwent the removal of an intramedullary spinal ependymoma at the Barrow Neurological Institute.

ABBREVIATIONS: GTR, gross total resection; MEP, motor evoked potential; SSEP, somatosensory evoked potential; STR, subtotal resection
METHODS

The neuropathology and surgical databases at the Barrow Neurological Institute were searched for patients who underwent resection of a spinal cord ependymoma from January 1983 to May 2006. Their charts were reviewed retrospectively for age, gender, tumor location, symptoms at diagnosis, duration of symptoms before diagnosis, and treatment before presentation at the Barrow Neurological Institute. Results of the neurological examination at presentation, immediately after surgery, and at last follow-up were recorded. The extent of surgical resection, use of any adjuvant therapy, length of follow-up, evidence of recurrence, and complications were also noted.

The neurological examinations of each patient at presentation, immediately after surgery, and at last follow-up were graded according to the McCormick grading scale developed for assessment of patients with spinal cord tumors (grade I, neurologically normal; grade II, sensorimotor deficit, gait difficulties, dysesthetic pain, ambulates independently; grade III, severe deficit, cane/brace for ambulation, may or may not function independently; and grade IV, severe deficit, requires wheelchair, not independent).²

Neurological grade at presentation was compared with grade at last follow-up, and neurological grades of patients who underwent subtotal resection (STR) were compared with those who underwent gross total resection (GTR) at presentation and at final follow-up. All comparisons were evaluated for significant differences with \( \chi^2 \) analysis. A value of \( P < .05 \) was considered significant.

Surgical Technique

After general endotracheal intubation, the patient was placed on the operating table in the prone position. Spinal cord somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs) were monitored. A standard midline incision was made. The muscles were elevated subperiosteally from the spinous processes and lamina at the appropriate levels. With a curette, all ligamentous attachments were cleared from the most inferior lamina. The lamina was then cut bilaterally using a high-speed drill with a pediatric footplate, beginning at the most inferior level and moving superiorly (Figure 1A). Typically, a minimum of 3 spinal levels were exposed. The lamina and spinal processes were removed as a single unit by lifting the spinal processes with an instrument and separating all ligamentous connections with either a curette or small Kerrison rongeur. A Microvac (PMT Corp, Chanhassen, Minnesota) suction was placed lateral to the laminotomy and stapled in place. The dura was opened in the midline with a No. 15 scalpel blade and tacked away from the spinal cord with 4-0 Nurolon stitches.

The remainder of the procedure was performed microsurgically. A No. 11 scalpel blade was used to make a midline myelotomy, and careful dissection with microforceps deepened the myelotomy to the depth of the tumor. Although intraoperative ultrasonography and dorsal cord mapping have been useful adjuncts for localization, they were not used routinely in this series.⁷,¹²,¹³ Once the tumor was identified, the myelotomy was lengthened to identify the most rostral and caudal aspects of the lesion. Round dissectors and microforceps were used to develop the plane between the tumor and normal spinal cord. Pial retraction stitches were not used routinely because they can increase the tension exerted on the normal spinal cord. A well-defined plane was usually present. The dissection then proceeded circumferentially (Figure 1B). Sharp dissection with microscissors was often necessary to separate the tumor anteriorly. Feeding vessels from the anterior spinal artery were cauterized and cut sharply. When possible, the tumor was removed en bloc. If the tumor was especially large, the middle of the tumor was entered and debulked via ultrasonic aspiration.

Hemostasis was obtained using bipolar electrocautery, with the addition of a hemostatic agent if necessary. The dura was closed with a running 5-0 Prolene stitch. Tisseel (Baxter, Vienna, Austria) or another
dural closure agent was applied to the dural repair. The wound was irrigated copiously. The laminae were replaced with multiple small plates and screws (Figure 1C). Care was taken to ensure that there was no pressure on the spinal cord. The muscle and fascial layers were reapproximated, and the wound was closed in a standard fashion.

RESULTS

One hundred four patients with spinal cord ependymomas were identified during the database search. Seventy patients had intramedullary lesions, and 34 patients had lesions of the conus medullaris or filum terminale consistent with the myxopapillary variant of ependymoma. The patients with myxopapillary ependymomas are reviewed in part 2.14 Three of the remaining 70 charts were unavailable for review; therefore, this review was completed on 67 patients.

The age range was 11 to 78 years (mean, 45.6 years). The male-to-female ratio was 2:1 (45 males and 22 females). The tumor location was cervical or cervicothoracic in 51 patients (76%), thoracic in 15 patients (22%), and lumbar in 1 patient (1%). The patient with the lumbar ependymoma had a lesion without an extramedullary component that showed a typical fibrillary pattern on histopathology. The mean duration of symptoms before diagnosis was 33 months. The most common symptom was pain or paresthesias in 47 patients (70%), followed by weakness in 41 patients (61%), numbness in 29 patients (43%), and bowel or bladder deficits in 21 patients (31%) (Table). Four patients had neurofibromatosis 2.

Fifty-five patients (82%) underwent GTR. Two of these patients demonstrated enhancement on postoperative magnetic resonance imaging (MRI). One of these patients underwent immediate reoperation. MRI after the second procedure showed no enhancement. The other patient was followed up for 4 years and then underwent a second procedure, after which MRI showed no further enhancement. The remaining 53 patients had no evidence of residual tumor.

At the time of their initial treatment, 12 patients (18%) underwent STR. Seven of these patients were initially treated at an outside hospital and underwent radiation therapy after STR. Two of these patients also underwent a regimen of chemotherapy. All 7 patients subsequently underwent GTR at our institution. One patient underwent STR twice at an outside hospital before undergoing a third attempt at resection. Four patients were initially treated with STR or biopsy. In 1 case, resection was nearly total and stopped secondary to a loss of SSEPs in the left lower extremity. One elderly patient had a very extensive lesion and was completely paraplegic at presentation. Because of his age and because it was not thought that he would regain function after resection, this patient opted to undergo a biopsy and radiation rather than radical resection.

The third patient was originally diagnosed with a syrinx before MRI was available. A syringe-subarachnoid shunt was placed, and a biopsy was obtained because of the suspicious appearance of the spinal cord at the time of shunt placement. Soon thereafter, MRI was available and revealed the tumor, which was then removed. The reason for STR in the final patient was not well documented. Altogether, 3 of these patients underwent radiation therapy, and 1 patient underwent GTR.

The mean follow-up was 32.2 months. Thirteen patients were followed up for > 5 years, and 6 patients were followed up for > 10 years.

At presentation, 35 patients were McCormick neurologic grade I, 24 patients were grade II, 5 patients were grade III, and 3 patients were grade IV. Twenty-four patients remained a grade I, 8 patients remained a grade II, 1 patient remained a grade III, and 3 patients remained a grade IV. Six patients who were originally a grade II improved, and 1 patient who was originally a grade III improved; none of the grade IV patients changed grades. Eleven patients who were originally a grade I worsened; 10 patients who were originally a grade II worsened; and 3 patients who were originally a grade III worsened.

Forty-seven patients were classified as having no deficit or only a minor deficit (grade I or II) at presentation and remained so at final follow-up. Twelve patients were classified as having no deficit or only a minor deficit at presentation and had a major deficit (grade III or IV) postoperatively or at final follow-up. One patient who had a major preoperative deficit had only a minor deficit at final follow-up, whereas 7 patients with major preoperative deficits continued to have major deficits at final follow-up. Patients with minor deficits at presentation had a high likelihood of having only minor deficits at final outcome, whereas patients with major deficits at presentation had a high likelihood of remaining so at final outcome (P < .001; Figure 2).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
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<tr>
<td>Age, y</td>
<td>46</td>
</tr>
<tr>
<td>Range</td>
<td>11-78</td>
</tr>
<tr>
<td>Sex, n</td>
<td>M 45; F 22</td>
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<tr>
<td>Location, n</td>
<td>Cervical/cervicothoracic 51; Thoracic 15; Lumbar/conus (no extramedullary component) 1</td>
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<td>Symptoms</td>
<td>Average duration before diagnosis, mo 33</td>
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<tr>
<td>Symptoms at diagnosis, n</td>
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</tr>
<tr>
<td>Treatment, n</td>
<td>GTR 55; STR 12</td>
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*GTR, gross total resection; STR, subtotal resection.*
Of the patients with follow-up > 3 months, 1 improved immediately after surgery, 18 were unchanged, and 26 worsened. However, at 3 months, 6 patients were neurologically improved, 26 patients were unchanged, and only 13 patients had worsened. Although patients showed less improvement in the immediate postoperative phase, a large number of patients returned to baseline or improved on long-term follow-up.

The presentation and outcomes of patients who underwent STR at initial presentation were compared with those who underwent GTR. There was no significant difference in neurological grade between the 2 groups at presentation; however, there was a significant difference between their outcomes. The patients who underwent STR at the time of initial presentation had a worse outcome \((P \leq .001; \text{Figure 3})\).

Documentation of SSEP recordings and MEP recordings was found in 61 and 9 charts, respectively. Of the 61 cases in which SSEP monitoring could be reviewed, 28 cases revealed no change in monitoring, but new postoperative deficits were recognized. In 8 of these cases, the SSEP recordings were considered unreliable at the start of the procedure. In 3 cases, the SSEP recording worsened; however, the patients awoke with no new deficits. In 11 cases, there was no change in the SSEPs, and the patients awoke with no new deficits. In 19 cases, the SSEP recordings worsened during the procedure, and the patients awoke with new deficits. SSEP recordings accurately predicted neurological status in only 30 of the 61 cases.

Of the 9 cases in which MEP monitoring could be reviewed, none of the MEP recordings accurately predicted neurologic status. In 7 cases, the MEP recordings did not change, but the patients awoke with new deficits. In 2 cases, the MEP recordings worsened, but patients awoke with no new deficits. Documentation of a halt of surgical resection related to a change in monitoring could be found in only 1 case in which the SSEP was lost in the left lower extremity of a patient. The resection was thought to be nearly total and was therefore halted at that time. This patient awoke with weakness in the left lower extremity and never fully recovered. Furthermore, his lesion recurred.

Three recurrences followed definitive treatment (average time to recurrence, 3.9 years; range, 2.2 to 5.6 years). Two of these patients underwent GTR at presentation. One patient had a recurrence at the original site; the other had a recurrence above the original site. Both underwent GTR at the time of recurrence. One patient underwent nearly total resection at presentation and experienced regrowth of the tumor. This patient underwent STR at the time of recurrence with postoperative radiation therapy.

Twenty-three patients had complications related to surgical resection. Six patients had postoperative wound infections that were treated with antibiotics and wound debridement when needed. Nine patients had a cerebrospinal fluid leak or pseudomeningocele. Four of these patients underwent multiple procedures for resection of their lesions; the cerebrospinal fluid leak occurred during the repeat procedure. These patients were treated with lumbar drainage, wound revision, and lumboperitoneal shunting when necessary.

Postoperatively, 3 patients had spinal instability. At the time of their initial surgical intervention, 27 patients underwent a laminectomy and 40 patients underwent laminoplasty. Of the patients who experienced spinal instability, 2 underwent laminectomy and 1 had a laminoplasty. Instability occurred in 1 patient who initially had a thoracolumbar laminectomy. Follow-up imaging revealed a recurrent lesion above the existing operative site 2 years after the initial procedure and anterolysisis at L1-2. A second procedure was performed with extension of the laminectomy for resection of the lesion, as well as thoracolumbar fusion to treat the instability. A second patient experienced instability after a laminectomy at C4-7. Approximately 7 years after the initial procedure, this patient began to experience chronic neck pain and weakness in all 4 extremities. Follow-up imaging revealed no tumor recurrence; however, instability with a kyphotic deformity was found at C6-7. The patient underwent an anterior cervical disectomy, interbody fusion, and placement of an anterior plate at C4-T1.
An 11-year-old child who originally underwent a laminoplasty at C1-7 also experienced instability. Approximately 1 year after initial treatment, the patient began to experience triceps and hand weakness bilaterally. Imaging studies revealed no tumor recurrence; however, a cervical kyphotic deformity was found. The child underwent traction followed by an anterior cervical disectomy, interbody fusion, and placement of an anterior plate at C2-4. This was the only complication associated with laminoplasty in this series.

Two patients developed deep venous thrombosis or pulmonary embolism. On long-term follow-up, 2 other patients had a tethered spinal cord that led to neurological deficits. One patient had a postoperative hematoma 11 days after a laminectomy for biopsy was performed. The patient presented with neck swelling and bilateral upper extremity paresthesias at the time the hematoma was discovered and underwent emergent evacuation of the hematoma. At discharge, the patient had improved.

**DISCUSSION**

As early as 1911, Elsberg and Beer succeeded in removing an intramedullary spinal cord tumor. However, high morbidity and mortality rates prevented widespread operative treatment of intramedullary spinal cord tumors until Greenwood used bipolar electrocautery and loupe magnification in 1954. With the introduction of contrast-enhanced MRI to localize tumors and the use of an operative microscope and microscopic techniques, the removal of intramedullary spinal cord tumors has become associated with even lower morbidity and mortality rates, making GTR the primary goal in the treatment of spinal cord ependymomas. The present series is the largest such series incorporating contemporary microsurgical techniques and MRI.

Our series confirms multiple aspects important to the treatment of intramedullary spinal cord ependymomas. GTR with neurological preservation remains the surgical goal. Although these lesions are not encapsulated, they have well-defined planes that allow GTR to be the goal of surgery in most cases. Even when the tumor has reduced the remaining spinal cord to a thin ribbon of normal spinal cord, GTR is possible. In our review, patients who had undergone only STR at their first presentation had a worse outcome at final follow-up. Repeat resection in these patients was associated with an increased complication rate and was less likely to result in GTR. GTR at the time of initial surgery should be the primary goal in the removal of these lesions.

Patients who had only minor deficits at presentation had a statistically significant chance of having only minor deficits at long-term follow-up, whereas patients with major deficits at presentation rarely made a meaningful recovery. Therefore, it is important to have a high index of suspicion when evaluating a patient for neurological complaints so that lesions can be found and resected before major neurological deficits develop. The present series supports the finding by Epstein and colleagues that postoperative neurological deterioration is rare and, if present, almost always temporary.

Nonetheless, patients should be counseled before surgery about possible proprioceptive deficits related to the posterior midline approach and other deficits that may occur immediately after surgery but that will most likely resolve with physical therapy and time. In this retrospective series, review of physical examination documentation did not always reveal a comment on dorsal column function. However, in 26 cases, there was documentation of a new dorsal column deficit after surgery. At final follow-up, 23 of these patients were either McCormick grade I or II, indicating that most of these patients did well neurologically and were able to ambulate independently despite the postoperative dorsal column dysfunction. Despite this positive outcome and given that many additional patients in our series could have suffered from a more long-lasting dorsal column dysfunction that simply was not well documented, it is important to identify midline as precisely as possible before the myelotomy is made to minimize these deficits. Our institution relies primarily on the anatomic landmarks of the posterior spinal arteries visualized on exposed normal spinal cord above and below the lesion. Other institutions have reported the use of ultrasonography and dorsal cord mapping to assist in this vital portion of the procedure.

Additionally, it is felt that avoiding pial retraction stitches as described above decreases tension and damage to the dorsal columns during tumor resection. With regard to other sensory deficits, they are often subjective and decrease over a 3-month period. Hanbali and colleagues evaluated a timeline for recovery of neurological deficits after aggressive resection of spinal cord ependymomas. Neurological recovery tended to occur 4 to 12 weeks after surgery, with recovery continuing in the first year. Postoperative dysesthesias began to improve within 1 month of surgery, with significant improvement at 1 year.

The use of SSEPs and MEPs during surgical resection of spinal cord tumors is the standard of care. However, in this series, SSEPs only reliably predicted the patients’ postoperative neurological status about half of the time. Furthermore, our retrospective findings suggest that a large majority of patients will recover from deficits incurred at surgery and that GTR leads to better long-term outcome than STR. MEPs were only beginning to be used at our institution and proved highly unreliable over the course of the series. Although no sound conclusions can be drawn from the review of SSEPs and MEPs in this series, we believe that they should be monitored routinely during surgery. If a surgical maneuver correlates with a change in evoked potentials, the dissection should be modified, but the goal should still be GTR of the lesion.

In this series, 40 patients underwent a laminoplasty vs a simple laminectomy at the time of tumor resection. The senior author (R.F.S.) prefers that all patients undergo laminoplasty regardless of their age. It is well known that laminoplasty for spinal cord tumor resection helps prevent spinal instability in the pediatric population compared with a laminectomy. Almost all cases in
which a laminectomy was performed either were originally done by another surgeon at an outside institution or were done by another surgeon at our institution. The rationale for a laminoplasty is to try to prevent future spinal instability and to increase the ease of reoperation should the need present itself. Of 27 adults who underwent a laminectomy, 2 developed spinal instability at a later date, whereas this problem occurred in none of the adult patients in the laminoplasty group. All 3 pediatric patients in this series underwent a laminoplasty. As described above, 1 patient developed spinal instability despite the laminoplasty procedure. Although postoperative compression of the spinal cord by misplaced or mobile bone could occur after a laminoplasty, it was not seen in this series.

Radiation therapy has been used as adjuvant therapy after GTR and STR of intramedullary ependymomas. Because of the relative rarity of the disease and the long-term, relatively benign nature of residual disease, evidence to support postoperative adjuvant treatment with radiation cannot readily be interpreted. In a retrospective cohort of 26 patients, Quigley and colleagues could not demonstrate a statistical difference in progression-free survival in the portion of their cohort who underwent STR with radiotherapy. This was despite excellent results regarding improved functional outcome, which compared favorably with patients in whom GTR was achieved (79% vs 75%). Chang and colleagues reported that patients with GTR have a significantly longer progression-free survival than those who underwent incomplete excision and adjuvant radiotherapy. Wahab and colleagues reviewed 22 patients treated with postoperative radiation and concluded that progression-free survival is excellent (80% at 15 years). However, this review included 9 patients with myxopapillary ependymomas, which were not analyzed separately. Therefore, the results for the 14 intramedullary ependymomas can only be interpreted from summary data. Furthermore, 27% of the patients in their series demonstrated progression of neurological deficits after treatment. Whitaker and colleagues reviewed 50 patients over 37 years and proposed that radiotherapy may achieve long-term tumor control in more than half of patients with residual spinal ependymoma. This series, however, highlights a major deficiency of such reviews in that only 1 patient underwent preoperative MRI.

The present series, the largest in the MRI and microsurgical era, does not span the decades during which rapid improvements in diagnostic imaging used for follow-up and in surgical techniques and radiotherapy were developed. Thus, analysis of follow-up data is improved, and such variables are controlled within the limits of a retrospective review. In our series, no patients who underwent GTR received postoperative radiation therapy, whereas all patients who underwent STR received postoperative radiation therapy. Although 1 weakness of this series is the brevity of long-term follow-up, we still recommend following this course of action given the benign, slow-growing nature of these lesions, the lack of definitive evidence to support or dispute the use of radiation therapy, and the low number of recurrences in our series. In our 67 patients, there were only 3 recurrences. In these 3 patients, a second surgery was attempted and was successful in 2 cases. We advocate repeat resection at the time of recurrence with the goal of GTR when possible.

CONCLUSION

Intramedullary spinal cord ependymomas are best treated before major neurological deficits appear, with GTR being the primary aim of treatment. Preoperative neurological status remains the best predictor of postoperative function. The use of adjuvant radiotherapy is an option when GTR cannot be achieved.

Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES


**COMMENT**

This is one of the largest groups of intramedullary spinal ependymoma patients presented. The follow-up is not excessively long, but outcomes are defined. It is interesting that 20% (12 of 60) preoperative grade I or II patients were grade III or IV postoperatively when operated on by a very experienced team. This is important information for surgeons counseling patients before surgery on potential outcomes.

I agree with the authors that early surgery, before there is significant deficit, is advised and that total removal is far superior to subtotal resection. I would prefer to reoperate for residual or recurrence rather than offer radiation therapy.

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