Intramedullary spinal cord tumors in patients older than 50 years of age: management and outcome analysis

RAJ K. SHRIVASTAVA, M.D., FRED J. EPSTEIN, M.D., NOEL I. PERIN, M.D., F.R.C.S., KALMON D. POST, M.D., AND GEORGE I. JALLO, M.D.

Department of Neurosurgery, St. Luke's Roosevelt Hospital Center; Institute of Neurosurgery and Neurology, Beth Israel Medical Center; Department of Neurosurgery, Mount Sinai Medical Center, New York, New York; and Division of Pediatric Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, Maryland

Object. Intramedullary spinal cord tumors (IMSCTs) in the older-age adult population pose complex management issues regarding the extent of resection and functional outcome, especially in terms of quality of life. Historically, IMSCTs in the older adult population were treated with irradiation alone because it was assumed that functional recovery would be poor. The authors examined their IMSCT database and report the first large series of IMSCTs in patients older than 50 years of age.

Methods. In this retrospective clinical and chart review there were 30 cases meeting inclusion criteria drawn from databases at three different institutions. A modified McCormick Scale was used to assess functional levels in all 30 patients pre- and postoperatively. The mean age of patients in this cohort was 59.8 years (range 50–78 years), and the mean follow-up period was 10.6 years (range 2–16 years).

Ependymoma was the most common tumor (83%), and 55% were located in the thoracic spine. The most common presenting symptom was sensory dysesthesia, with rare motor loss. The prodromal period to treatment was 19.4 months. Based on the McCormick Scale score at last follow-up examination 67% of patients were clinically functionally the same, 9% were worse, and 24% were improved after surgery. There were two deaths due tumor progression (both malignant tumors) and one recurrence (anaplastic astrocytoma). All three patients in whom malignant astrocytomas were diagnosed underwent postoperative radiation therapy.

Conclusions. In the population of patients older than age 50 years, thoracic ependymomas are the most common IMSCTs that present characteristically with sensory symptoms. The longer prodromal period in the older adult population may reflect the fact that their diagnosis and workup is inadequate. There was no significant increase in the length of stay in the neurosurgical ward. The authors recommend motor evoked potential–guided aggressive microsurgical resection, because the long-term outcome of benign lesions is excellent (good functional recovery and no tumor recurrence).

KEY WORDS • astrocytoma • ependymoma • intramedullary • outcome • spinal cord

INTRAMEDULLARY spinal cord tumors are relatively rare neoplasms, accounting for only 2 to 4% of central nervous system glial tumors.10,16,17,24 Intramedullary spinal cord tumors are less common in adults than in children10 (20% of all intraspinal neoplasms in the former and 35% in the latter).10,11,31,36 The optimal treatment of these lesions has been controversial in both populations.10,11,31,36 Historically traditional management has indicated (and continues to indicate) the following optimal treatment: 1) examination of a biopsy specimen; 2) dural decompression; and 3) radiation therapy.15,19,33,37,41,42 The problem with the traditional management paradigm has been that the lesions eventually progress neurologically, with patients becoming disabled, suffering significant morbidities, and ultimately dying.6,24,28,46 This traditional management paradigm is further confounded in elderly patients7 in whom too often conservative management without definitive treatment is recommended, especially if there is already evidence of neurological deterioration.10 The belief that the older-age patients suffer more postoperative deficits has led some clinicians to defer radical IMSCT resection. Our protocol, as originally advanced by the senior author (F.J.E.) in 1980, has involved aggressive intraoperative neurophysiological monitoring–guided excision with attempted GTR.6,7,10,11,21,22 Most IMSCTs are low-grade lesions for which resection can provide a cure without the need for postoperative radio- or chemotherapy (and its associated morbidities, especially in the elderly). We initiated this study to investigate the role of aggressive resection in the older adult population (≥ 50 years of age) to assess neurological performance and long-term functional outcome. We report long-term outcome in this first large series of IMSCTs in adult patients older than 50 years of age.
Clinical Material and Methods

Patient Population

The collective patient databases for New York University Medical Center, Beth Israel North Medical Center, and the Mount Sinai Medical Center were pooled and analyzed to determine cases of IMSCTs in patients 50 years old and older. An arbitrary consecutive time period (1985–2002) was analyzed based on the implementation of our computerized database. Patient with cauda equina or terminal filum tumors were excluded. From these patient databases, 30 patients were identified in whom criteria for age and the presence of a complete chart were met. There were 17 men and 13 women who ranged in age from 50 to 78 years of age (mean 59.8 years). In 23% of patients a previous surgery had been performed (88% were biopsy procedures), 5% had undergone previous radiation therapy, and in no case had chemotherapy been conducted. Thus, our analysis involved a retrospective case review consisting of presurgical symptomatology, surgery-related details, and other treatment outcomes. The neurosurgical ward LOS was analyzed when such data were available. All patients or their immediate family subsequently underwent an interview in which a carefully designed questionnaire, as previously used, was administered. Families and their primary care physicians were questioned in detail. All medical records pertaining to follow-up imaging, rehabilitation, and functional status were verified with either verbal or dictated reports on each patient independently of the questionnaire. We used a modified McCormick Scale\(^{11,12}\) to determine functional status, both preand posttreatment (Table 1) (no McCormick Scale Grade V patients [quadriplegic] were included in this study).

Histological Evaluation and Pathological Findings

Senior neuropathologists at each institution reviewed all pathological specimens. Each specimen was reviewed independently and then examined by another neuropathologist at the respective institutions and a consensus was reached when diagnoses differed. We maintained the same histological grading criteria as described previously\(^8,34\) (for example, with diffuse fibrillary astrocytomas categorized into three groups).

Surgical Technique

The details of our surgical technique have been described elsewhere in detail\(^,5,7,11,12\). We have used somatosensory evoked potential monitoring since 1985 and MEP monitoring since 1988 to provide real-time feedback to the operating surgeon.\(^,14,26,27,35\) In all operative cases, GTR was attempted. We used the standard GTR definition: removal of at least 95% of the tumor as evidenced by a microscopically documented clean surgical field at the end of the procedure and an MR imaging–documented clean surgical bed immediately after surgery (within 48 hours). When a small tumor fragment was deliberately left in place, the procedure was considered STR based on the immediate postoperative MR imaging of 80 to 95%. We performed STRs in this series when intraoperative evoked potential monitoring changes heralded impending neurological paralysis. Despite their individual tumor grades, all patients underwent the same intraoperative evoked potential monitoring modality. In our retrospective review of imaging and hospital records an estimate of the extent of excision was found to be subjective and, therefore, variable in the STRs because of postoperative artifact created by contrast-enhanced studies in the operative site.\(^2,6,12,39\)

Statistical Analysis

The determination of PFS and overall survival were estimated using the Kaplan–Meier technique.\(^29\) Progression-free survival was measured from the first operation at each institution to the point of clinical or radiological deterioration (“event”). The last MR imaging study obtained at the most recent examination was used to determine the presence of residual or recurrent tumor. The relationship between each parameter and overall survival and PFS was examined in a series of univariate analyses involving the Mantel–Cox log-rank test to assess the strength of association between the parameters and outcome.\(^29\) For frequency analysis the chi-square test was used.

Results

Preoperative Clinical Function

Age in this series ranged from 50 to 78 years (mean age 59.8 years; Fig. 1 upper). The most common presenting symptoms in our series were sensory deficits (66%), motor loss (23%), and back pain (11%). The preoperative sensory dysfunction included dysesthesia (66%), extremity numbness (50%), myelopathy (40%), gait ataxia (35%), and bladder incontinence (10%). The preoperative motor symptoms consisted of extremity weakness (33%), gait disturbance (23%), hand atrophy (10%), and quadriparesis (3%). The preoperative modified McCormick Scale included Grade I in 10%, Grade II in 50%, and Grade III in 40% of patients. No patient with preoperative Grade IV or V was included.

The mean prodrome time was unexpectedly long (mean 19.4 months, range 1 month–12 years from the beginning of the symptomatology to the first treatment). In the patients with higher-grade tumors (GBM and AA), as can be expected, the prodromal period was shorter. Most patients in this series suffered minimal comorbidities (five cases of hypertension, one of asthma, and one of morbid obesity).

Tumor Location and Associated Cysts

Most patients underwent MR imaging prior to surgery, except those in whom the diagnosis was established before 1987, who underwent computerized tomography myelography. Based on the preoperative imaging (Fig. 1 lower), the tumors were located in the thoracic (40%), cervical (35%), cervicotoracic (15%), and lumbar spine.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Modified McCormick Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>intact neurologically, normal ambulation, minimal dysesthesia</td>
</tr>
<tr>
<td>II</td>
<td>mild motor or sensory deficit, functional independence</td>
</tr>
<tr>
<td>III</td>
<td>moderate deficit, limitation of function, independent w/ external aid</td>
</tr>
<tr>
<td>IV</td>
<td>severe motor or sensory deficit, limited function, dependent</td>
</tr>
<tr>
<td>V</td>
<td>paraplegia or quadriplegia, even w/ flickering movement</td>
</tr>
</tbody>
</table>

TABLE 1

Summary of details in the modified McCormick Scale
Imtramedullary spinal cord tumors in older patients

(10%). Gadolinium enhancement was noted in 80% of tumors and was not correlated to histological composition. Cyst or syrinx formation was found in approximately 30% of tumors and in one case was associated with a tethered cord formation. In cases with associated syringes, 70% were in the thoracic and 30% in the cervical spinal cord. The most recently obtained MR imaging study was defined as that acquired at during the last postoperative visit.

Resection and Tumor Pathological Type

Gross-total resection was achieved in 65% of patients and STR in 35%; there were no partial resections or biopsy procedures performed (Fig. 2 left). The extent of tumor resection was not related to the tumor location, length, presence of cyst, or previous procedure. The distribution of tumor types was ependymoma (83%), subependymoma (7%), AA (7%), and GBM (3%) (Fig. 2 right). In the 23% of patients who had undergone biopsy procedures prior to our surgery, all harbored low-grade lesions that permitted a GTR. In patients who had undergone radiation therapy prior to surgery, both lesions were low-grade tumors that allowed for a GTR at our institutions. Although all syringes were found in cases of low-grade ependymomas, there was no statistically significant correlation between the two to warrant a relationship.

Surgery-Related Outcome and McCormick Scale Grade

There were no surgery-related deaths. Surgery-induced morbidity in this series can best be expressed by the change in the McCormick Scale grade, as has been described by others. In the postoperative period, function in 9% of patients was worse, in 67% it remained the same, and in 24% function improved based on this scale. The mean postoperative McCormick grade was 2.2 compared with a mean preoperative grade of 2.3; thus, there was no significant change in functional grade overall. Of the 9% of patients in whom functional grade worsened, the grade progressed in two to a McCormick Grade IV from a Grade III. There were no cases involving deterioration of function more than one grade. At last follow up, there were no patients with Grade V function (Fig. 3). In most patients in whom deterioration occurred, preoperative deficits had been significant or a malignant tumor had been diagnosed. The mean LOS in the present series was not significantly different or extended from that in other series. Among the 10% of patients with an increased LOS, the reasons were directly related to the perioperative transient morbidities: pneumonia (5%) and pulmonary embolism (3%). In patients suffering perioperative morbidity the McCormick functional grade was more likely to be higher than in other patients. The following variables did not independently affect surgery-related morbidity: previous treatment (of any kind, surgery or radiation), tumor level within the spinal cord, presence/absence of cysts, amount of Gd enhancement, extent of tumor, extent of resection, pathological type, or the patient’s age.

Postoperative Adjuvant Therapy and Recurrence

In all patients, the initial goal of surgery was GTR. All patients with high-grade lesions (AA or GBM) underwent postoperative radiation therapy. The one patient harboring a GBM died within 1 year of disease progression. One of the patients with AA also died within 4.6 years of tumor progression. The other patient with AA continued to suffer from disease progression and associated neurological deterioration. This recurrence developed at the original surgical site. There were no other cases of tumor recurrence in the follow-up period.

Long-Term Follow-Up Results and Functional Grade

All 30 patients underwent long-term follow-up study. The mean follow-up period was 10.6 years (range 2–16 years). At the time of this report, 93% of patients remained alive. Two patients died (one harboring a GBM and the other with an AA). In the surviving patient with AA neurological dysfunction has progressed because of the tumor recurrence. The remaining patients were disease free throughout the long-term follow-up period (the patient harboring an AA was alive despite the tumor’s recurrence after radiation therapy). The main determinant of patient survival and tumor recurrence appeared to be tumor histological composition. Survival was not statistically correlated with age, prior treatment, or MR imaging characteristics (Gd uptake, tumor span, or other factors). Among the low-grade tumors, there was no statistically significant difference between survival according to histological composition. The extent of resection (GTR compared with STR) did not significantly affect long-term survival, although a higher level of GTR achieved among those with low-grade ependymomas.

Of surviving patients (93%) no decrease in McCormick...
Scale grade has occurred during the long-term follow-up period except in the patient with AA. In patients in whom the grade improved after surgery, function has been maintained in the long term. In the 9% of patients with initially decreased McCormick grades, improvement in functional grade during long-term follow up was reported in 33%. Overall, the improvement was one functional grade. In patients whose status remained the same grade after surgery, function improved to levels that were better than those preoperatively. Therefore, in the long term, there was only an improvement of overall function for low-grade tumors.

**Discussion**

The advent of modern microsurgical techniques has yielded a significant change in the approach to IMSCTs. The pioneering work of Epstein and colleagues7,10,11 and the legacy of detailed neurosurgical studies over the last 24 years13,21,22,31,32,43 have dramatically improved the outcome for those patients harboring these tumors, particularly those in the pediatric population. In patients with IMSCTs older than 50 years of age, conservative treatments persist to this day. Many clinicians continue to believe that surgery-associated morbidity and mortality in this population does not justify the assumed risks of surgery compared with conservative treatment (basically, biopsy sampling and/or radiation therapy). The results of nontreatment are no less severe in older patients, with progression toward permanent disability, paralysis, and morbidity-related death occurring in all cases.1,8,16,43 The significantly longer prodrome-to-treatment duration observed (19.4 months compared with 11.6 months8 in older and younger patients, respectively) seems to indicate a failure to establish an appropriate diagnosis of the lesion or a reluctance to initiate an aggressive evaluation. Although there is, no doubt, the additional factor of a patient’s individual compliance with physicians or their own reluctance to seek medical attention for progressive symptoms, almost all patients in our study attended physicians’ office visits during the time of their prodrome. Cases involving treatment of IMSCTs are therefore complex.

We found that surgical treatment of IMSCTs in older patients (> 50 years of age) is associated with low morbidity and mortality rates when it involves MEP-guided monitoring. In our series there was no additional morbidity that was increased by the patients’ age. Itself as a modifier, age did not confer any increased risk either in postoperative function, recurrence, or LOS. Therefore, patients older than 50 years of age should undergo aggressive evaluation and treatment just as the other populations. The protocol of upfront radiotherapy or biopsy sampling combined with radiotherapy did not prevent disease progression, as was observed in this series and, more importantly, led to a preventable deterioration of function in many of these patients. As we have seen, once a GTR or STR was performed in patients who had undergone conservative treatment, the disease recurrence was rare, even in the absence of radiotherapy for most tumors (low-grade lesions). It is important to point out again that we have defined STR as removal of at least 80% of the tumor mass. This quantity alone represents a rather radical surgery20,30,31 and probably accounts for the similarity observed in their respective outcomes after GTR and STR. We therefore strongly believe that there is no role for biopsy sampling alone or combined radiotherapy and biopsy sampling in the treatment of IMSCTs. As we have previously advocated,11,13,17,21,22 one should not wait for the onset of clinical deterioration but rather institute treatment as soon as possible in cases of IMSCTs. The earlier the diagnosis and radical resection of an IMSCT, the greater the likelihood of preserving the patient’s neurological function.

Although the small patient population did provide sev-
eral statistical limitations for the purpose of discussion, we believe that it is important to emphasize that the overall population of 30 patients was derived by combining databases at three different institutions. In the population of patients older than 50 years of age, an IMSCT is a rare clinical entity that has not been addressed separately in previous reports. We have reported the first documented large series of this population with long-term follow-up data. Although a single-center study offers certain statistical advantages regarding variability, we believe that the need to increase the study population outweighed the loss of statistical variability.

In older patients (> 50 years of age) with IMSCTs, thoracic ependymomas are the most common lesion. In this group, 66% of patients most commonly present with sensory dysesthesias, although other symptoms such as gait ataxia and myelopathy can occur. Motor symptoms, although not as common, occur in conjunction with sensory changes and present as motor loss, extremity weakness, and atrophy among other signs. The advent of routine MR imaging in this population was clearly beneficial over other methods of radiographic imaging, as we witnessed during the course of the study period. Clinically low-grade tumors behave the same and have the same immediate- and long-term outcome. Interestingly, in our population we observed no low-grade astrocytomas, which are known to be more common in the pediatric population.

Functional outcome, as measured using a modified McCormick Scale, remained the same or improved in most patients in the immediate postoperative period. Even more encouraging is the fact that we witnessed an improvement in functional grade during the long-term follow-up period that was only dependent on histological grade. The eventual postoperative McCormick Scale grade was defined as the functional status determined at the last clinical examination. Therefore, with an attempt at GTR or even STR, an improved outcome in this population can also be expected, and it is one that seemed only to improve in the long-term period.

The LOS was not increased in the older-age population, with any significance, over the reported LOS for the remaining population. This fact, however, applies only to time on the neurosurgical service and did not encompass inpatient rehabilitation duration. Although methods of patient discharge disposition seemed to be the same for our studied population, this, we believe, may not reflect the total hospital LOS, as the older population may require more rehabilitative time (whether in- or outpatient).

Motor evoked potential–guided resection is clearly superior to that performed with purely somatosensory evoked potential monitoring or no monitoring at all. Since 1988 when we began using MEP monitoring routinely, we have implemented this protocol in all cases and have found it to be crucial in preserving a high level of functional outcome. The importance of MEP monitoring’s real-time feedback during surgery performed by an expert team cannot be underestimated. We undertake resection of IMSCTs in cases in which greater than 50% of the epidural MEPs are maintained, and we routinely stop surgery once substantial changes in the MEPs occurs. This factor, in combination with direct intraoperative observation, allows us to choose between a GTR or STR. We have found that it is almost always preferable to leave a small area of residual tumor rather than to risk neurological morbidity. The residual tumor can then be screened by serial MR imaging for growth, and a repeated operation can be performed if necessary.

Adjuvant postoperative radiotherapy was reserved for cases involving high-grade tumors, such as the AAs and GBMs in our series. We believe that these higher-grade lesions are associated with a significantly higher chance of recurrence and potential leptomeningeal spread. In cases involving high-grade tumors, adjuvant radiotherapy prevented recurrence during the long-term period. More importantly, perhaps, for the long-term outcome is the fact that one cannot safely irradiate a low-grade tumor either after GTR or STR and still maintain a disease-free survival. The role of chemotherapy as an adjuvant therapy for high-grade lesions has not yet been determined; however, there are many reasons to believe that this is a treatment modality that offers hope as more and newer protocols are developed.

**Fig. 3.** Bar graph demonstrating the distribution of modified McCormick grades in patients with an IMSCT.
Conclusions

In the older (> 50 years of age) population with IMSCTs, thalamic ependymomas were the most commonly observed lesion. Most patients typically presented with sensory dysesthesias. Safe GTR or STR can result in low perioperative morbidity and mortality as well as excellent functional outcome during a long-term period (> 10 years). A subtotal resection may confer the same DFS in the long term. Both immediate postoperative and long-term functional grades were improved. Perioperative morbidity and mortality rates seemed to correlate with a higher histological grade alone and not with age, among other variables. Neurosurgical service LOS was not prolonged despite a patient’s age or neurological condition. IMSCTs should be recognized as potentially removable and curable lesions, both at presentation and if they recur, despite a patient’s age or neurological condition.

References

Intramedullary spinal cord tumors in older patients


Manuscript received March 28, 2004.
Accepted in final form July 30, 2004.
Address reprint requests to: George Jallo, M.D., Division of Pediatric Neurosurgery, Johns Hopkins Hospital, Harvey 811, 600 North Wolfe Street, Baltimore, Maryland 21287. email: gjallo1@jhmi.edu.