

Conservative Surgery and Radiotherapy for Adult Spinal Astrocytoma: Balanced Strategy for Favorable Outcome

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Abstract

Objective: Spinal cord astrocytomas are considered diffuse infiltrating tumors. The optimal treatment of these lesions has been controversial. The conventional management with partial resection followed by radiotherapy remains. In order to evaluate this traditional and famous strategy, the authors retrospectively review a series of ten consecutive adult patients with spinal cord astrocytoma treated with conservative surgery and radiotherapy. **Methods Results:** A retrospective analysis of ten adult patients (4 men and 6 women) with spinal cord astrocytoma. The mean age was 33 years. Cervical cord was involved in 2 patients, cervicothoracic in 3, thoracic in 5. Seven patients had low grade astrocytoma and 3 high grade (2 anaplastic, 1 glioblastoma). Surgery was subtotal excision in 1 patient, partial excision in 3 and biopsy in 6 patients. All patients received postoperative radiotherapy to a median dose of 45 Gy in 25 fractions over 5 weeks. The follow-up period ranged from 7 to 48 months. Postradiotherapy, local tumor control was achieved in 7 cases (6 low grade, 1 high grade) despite incomplete or no resection. Three patients died, one paraplegic patient of pneumonia, and two patients with high grade astrocytoma from tumor progression or dissemination.

Conclusion: There is no significant effect of the extent of resection on local relapse. We believe that conservative surgery and radiotherapy provide a balanced strategy in the treatment of adult spinal astrocytoma to maintain neurological outcome and prevent tumor recurrence.

INTRODUCTION

Intramedullary spinal cord tumors (IMSCTs) are relatively rare neoplasms, accounting for only 2 to 4% of CNS glial tumors^(6,10) In adults, IMSCTs comprise approximately 20% of all intraspinal neoplasms, whereas in children at least 35% of the tumors are IMSCTs.⁽¹¹⁾ The optimal treatment of these lesions has been controversial in both populations.^(1,2) In general, astrocytomas have to be considered as infiltrating tumors. Therefore, the identification of cleavage planes carries considerable risk and may even be outright impossible.⁽⁴⁾ At surgery, aggressiveness with respect to resection depends on the ability to find and maintain a surgical plane.⁽⁹⁾ Because of the concern for surgical morbidity, many authorities treat adult spinal astrocytoma with conservative debulking from inside out and /or biopsy followed by postoperative radiotherapy.^(7,8) In order to evaluate this traditional and famous strategy, the authors retrospectively review a series of ten consecutive adult patients with spinal cord astrocytoma treated with conservative surgery and radiotherapy.

PATIENTS & METHODS

PATIENT POPULATION

At the department of neurosurgery of Tanta University Hospital, ten patients with intramedullary spinal cord astrocytomas were treated between January, 2001 and December, 2007. There were 4 men and 6 women, ranging from 21 to 60 years. The mean age was 33 years. Signs and symptoms were usually referable to the site of the solid tumor and consisted of posterior midline pain, paresthesias, and sensory and motor deficits below the level of the tumor. Case records were retrospectively examined for preoperative symptomatology, surgical details, postoperative radiotherapy, and outcomes. The details in our records were verified and an up-to-date functional evaluation was obtained. The functional status was graded according to a modified McCormick scale (Table 1).⁽²⁶⁾

Figure 1

Table 1: Modified McCormick scale for functional evaluation of patients with IMSCTs

Grade	Explanation
I	neurologically intact, ambulates normally, may have minimal dysesthesia
II	mild motor or sensory deficit, patient maintains functional independence
III	moderate deficit, limitation of function, independent w/ external aid
IV	severe motor or sensory deficit, limited function, dependent patient
V	paraplegia or quadriplegia, even if there is flickering movement

DIAGNOSTIC IMAGING

Contrast-enhanced MR images were obtained in all patients.

OPERATIVE TECHNIQUE

After induction of general anesthesia, the patient is placed in the prone position with an indwelling bladder catheter. For cervical lesions, the head is immobilized using a Mayfield head holder or equivalent. The abdomen is decompressed to avoid excessive epidural bleeding. A midline incision is made at the appropriate level and extended to the fascia. Subperiosteal dissection of the paraspinal muscles was performed using electrocautry cutting. The level is confirmed by radiograph. A laminectomy is performed over the area of suspected solid tumor at the site of maximal spinal cord widening as defined by preoperative MRI. A durotomy is made in the midline, and the dural edges are tacked to the soft tissues laterally exposing the arachnoid overlying the swollen spinal cord. Through the operating microscope, a midline myelotomy between the dorsal columns is initially performed over a distance of 2 to 3 cm using sharp dissection. The myelotomy is later extended as dictated by the length of the solid tumor. Pial traction sutures are placed to spread the spinal cord open and expose solid tumor which is generally apparent 1-5 mm beneath the dorsal spinal cord surface.

Astrocytomas appear gray, red, and glossy, with a poorly defined plane between tumor and spinal cord. Defining the surgical goal whether biopsy or tumor removal is accomplished by analysis of imaging characteristics and the operative appearance. If the tumor has an exophytic component, this is the initial area of approach. Otherwise the tumor is encountered after the dorsal columns are split. Debulking can be done with tumor forceps, sharp dissection, or ultrasonic aspirator. It is often useful either to debulk internally to facilitate capsule dissection or to perform an inside out resection when no clear plane is identifiable. Gross-total removal of the tumor is defined as removal of at least 95% of the tumor, evidenced both by a clean surgical field under the microscope at the end of the procedure and a clean immediate (within 48 hours) postoperative MR image.

An estimated removal of 80 to 95% is defined as subtotal resection. Partial removal means estimated removal is < 80% of tumor. After tumor resection and hemostasis, the dorsal columns are gently rotated back into position. A primary dural closure is achieved using a running stitch. A dural patch maybe used to expand the thecal sac. A Valsalva confirms a water-tight closure. After meticulous hemostasis , the muscles are loosely approximated with an absorbable suture. A water-tight fascial closure is achieved with an interrupted absorbable suture. The subcutaneous tissues are approximated and the skin is closed.

POSTOPERATIVE RADIOTHERAPY:

Within four weeks of laminectomy, all patients received postoperative radiotherapy to a median dose of 45 Gy in 25 fractions over 5 weeks. Seven patients received treatment to the involved segment of the cord, and three patients had craniospinal treatment (one patient had GM, and two had anaplastic astrocytoma). Length for spinal fields ranged from 10 to 45cm. Field arrangements consisted of the tumor plus a margin of two vertebral bodies.

POSTOPERATIVE OUTCOME AND FOLLOW-UP:

1. Neuroradiological Follow-up : Early MRI with contrast was carried out for all patients inf the very first postoperative days in order to 1. accurately evaluate the residual tumor and serve as a baseline for assessing subsequent progression of the lesion 2. exclude early postoperative hematoma at the operative site or epidural hematoma. Later, an examination at six months was recommended.
2. Immediate postoperative functional outcome: using modified McCormick scale.
3. Long-term follow-up and recurrence: according to modified McCormick scale.⁽²⁶⁾ The follow-up period ranged from 7 to 48 months.

RESULTS

Clinical Presentation of Intramedullary Tumors

A summary of presenting symptoms is provided in Table 2. The most common complaints were sensory deficits and motor weakness.

Figure 2

Table 2: Symptoms at presentation for intramedullary tumors

Symptom	Number
Pain	6 (60%)
Gait ataxia	4 (40%)
Motor weakness	7 (70%)
Sensory deficits	8 (80%)
Dysesthesias	4 (40%)
Neurogenic bladder	3 (30%)

RADIOLOGICAL EVALUATION AND TUMOR CONFIGURATION

The tumors were solid cord expansions (iso/hopintense in T1, hyperintense in T2) in all patients. There were neither cystic parts nor syrinx.

The thoracic spine was the most commonly affected. Enhancement on gadolinium administration occurred in all patients and had no correlation to their histological composition or resectability.

Figure 3

Table 3: Location of tumor site

Spinal level	Number of Patients
cervical	2
cervicothoracic	3
thoracic	5

Figure 4

Table 4: Pattern of contrast enhancement in MRI

Contrast	No. of cases
homogenous	4
heterogenous	6

PATHOLOGICAL FINDINGS

An overview of all pathological diagnoses is presented in Table 5. The pathological entities were divided into three categories. The low grade astrocytoma group was of fibrillary appearance which corresponds to grade II of the WHO classification. Anaplastic astrocytoma and Glioblastoma correspond to grade III & IV of the WHO classification respectively. Two senior neuropathologists reviewed all cases.

Figure 5

Table 5: Pathological Diagnosis

Diagnosis	No. of cases
low grade astrocytoma	7
anaplastic astrocytoma	2
malignant glioblastoma	1

SURGERY

The extent of surgical resection is demonstrated in Table 6. An estimated removal of 80 to 95% is defined as subtotal resection. Partial removal means estimated removal is < 80% of tumor. Biopsies were obtained through a midline dorsal myelotomy from the enhancing regions.

Figure 6

Table 6: Extent of surgical removal

Tumor Removal	Astrocytoma
subtotal	1
partial	3
biopsy	6

MORBIDITY, MORTALITY, AND RECURRENCES

Postoperative complications are listed in Table 7. Severe postoperative motor deterioration means loss of two or more functional grades. It occurred immediately postoperatively in two patients (case 6&9, Table 8.). Of the ten patients , three have died. One patient, a 59-year-old woman who was paraplegic preoperatively, succumbed to pneumonia and died 27 months after surgery (case 10, Table 8.)The other two have died between 4 and 24 months postoperatively from tumor progression and dissemination (case 6&8, Table 8.). Local tumor control was finally achieved in seven cases. No evidence of recurrence was seen in them.

Figure 7

Table 7: Postoperative complications

Complications	No. of Cases
Wound infection	2
Severe postop motor deterioration	2
Increases sensory dysesthesias	3
CSF leakage	1

Figure 8

Table 8: Functional status of patients with intramedullary astrocytoma of the spinal cord

Case No.	Extent of Tumor	Type of Tumor	Preop Grade	Postop Grade	Follow-Up Grade	Tumor Removal
1	C7-T6	low grade	I	I	I	biopsy
2	C7-T4	low grade	I	I	I	biopsy
3	C3-C7	anaplastic	II	II	II	biopsy
4	T5-T7	low grade	II	II	I	partial
5	C3-C6	low grade	II	II	I	biopsy
6	T4-T7	anaplastic	II	IV	died	Partial
7	C6-T1	low grade	III	II	I	biopsy
8	T5-T8	glioblastoma	III	III	died	biopsy
9	T5-T7	low grade	II	V	IV	subtotal
10	T4-T8	low grade	V	V	died	partial

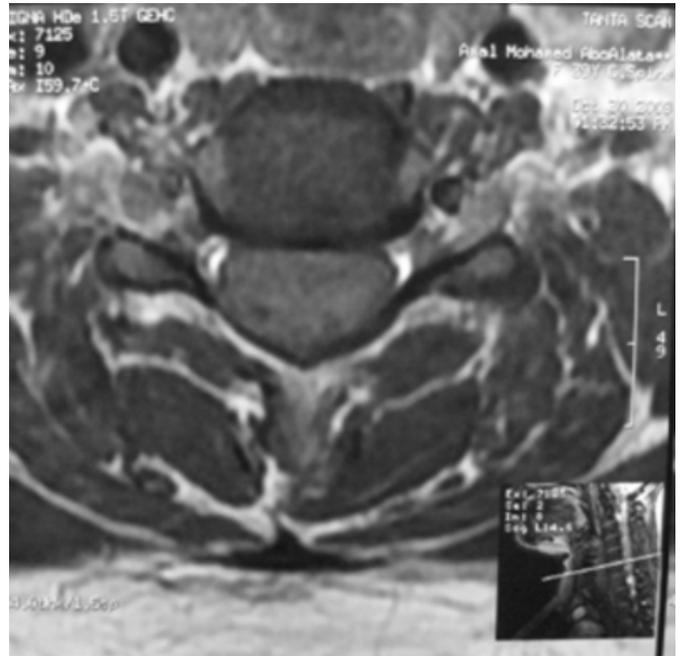
Figure 9

FIG. 1. T1-weighted sagittal MRI of cervical spine of C3-C7 anaplastic astrocytoma with contrast enhancement (case 3, Table 8.).



Figure 10

FIG. 2. T1-weighted axial MRI of the previous case. Note cord expansion with tumor.



DISCUSSION

PREOPERATIVE DIAGNOSTIC FINDINGS:

Without any doubt, MRI has revolutionized our preoperative possibilities to establish the diagnosis, determine the exact extent of the tumor and visualize associated cyst. However, the resectability of an intramedullary tumor cannot be predicted by MRI. In our study four cases took up homogenous contrast on T1-weighted images with clear line of demarcation which obviously encouraged the attending neurosurgeons to embark on resecting the tumors rather than obtaining biopsy. Unfortunately, this was not the case for the tumors turned out to be infiltrative and could be partly resected (Table 6.). Moreover, enhancement on gadolinium administration occurred in all patients and had no correlation to their histological composition which means all the tumors whether low or high grade took up contrast. Authorities have mentioned that inhomogenous uptake of contrast may also be a feature of anaplastic or malignant tumors⁽³⁾, Yet, one case of malignant anaplastic astrocytoma took up homogenous contrast in our series.

TREATMENT PARADIGM:

Intramedullary spinal cord astrocytomas are less common in adults than in children. The optimal treatment of these lesions has been controversial in both populations. In particular, debate centers about the nature and extent of

surgery and the relative roles of surgery and radiation therapy in the treatment of these lesions ^(13, 15).

1. SURGERY:

The advent of modern microsurgical techniques had yielded a significant change in the approach to IMSCTs. The pioneering work of Epstein and colleagues ^(16,21, 23) and the legacy of detailed neurosurgical studies over the last 24 years have dramatically improved the outcome for the pediatric population harboring these tumors.

In the adult population 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 radiation therapy) ^(24,25). Recently, some recongnized authorities in the field have recommended that complete removal of the lesion should be the first goal of IMT surgery and should be performed whenever possible, i.e., when it is possible to visualize a clear cleavage plane between the tumor and healthy spinal cord⁽²¹⁾. We absolutely agree with the previous phrase when it is applied in the appropriate context like when one speaks of ependymomas.

Ependymomas are completely resectable since they displace rather than infiltrate the spinal cord ⁽⁹⁾. But if no such plane is found, which is usually the case in astorcytomas that are known to be infiltrating by nature, an attempt at complete tumor removal is impossible, hazardous, and pointless.

The authors believe that astrocytomas are deceiving lesions as they may show a nice cleavage plane in some areas, but in other parts infiltrate surrounding tissue diffusely. This was a common finding that had been encountered by each one of the different operators when attempting to resect spinal astrocytoma. Therefore, the identification of cleavage planes carries considerable risks and may even be outright impossible and regardless of the dissection technique, the danger of creating and artificial cleavage plane that does not exist is real. Case 9 (Table 8.) was a striking evindence of this situation which ended up with unfavorable functional outcome. Surprisingly case 5 (Table 8.) did absolutely well on biopsy sampling and radiotherapy.

Constantini, et al., advocate a radical surgical approach for intramedullary low grade spinal cord astrocytomas in children⁽¹⁷⁾. We can understand the impetus behind this comes from two things. First, their institute is equipped with

the most advanced microsurgical technology such as the ultrasonic aspirator, laser, intraoperative ultrasound, and intraoperative neurophysiological monitoring that permit a safer aggressive surgical resection. Constantini have stated that intraoperative monitoring with somatosensory evoked potentials and motor evoked potentials (MEPs) has become a key factor in making the critical decision about when to stop a surgery.”If, during surgery, the MEPs are maintained at more than 50% of their original amplitude, tumor removal can be safely continued. If a substantial change in MEPs occurs, further spinal cord manipulation should be stopped”, he said ^(17,27).One need not say that this technical innovation along with the experienced technological support personnel are not available in every centre.

The second issue related to the radical approach adopted by Constantine , et al, in their study is that most of these children received an early diagnosis which means they were in good functional grade before surgery which gives good postoperative outcome since it is well known that the risk of surgery-related morbidity to the patient increases in proportion to preoperative neurological dysfunction⁽¹⁸⁾. The circumstances involving treatment of adult IMSCTs are complex in our community. The patient's reluctance to seek medical attention for progressive symytons and the physicians' reluctance to initiate an aggressive evaluation lead to longer prodrome-to-treatment duration with profound preoperative neurological deficits.

Moreover, Constantini and others adopt a conservative approach when they address lesion within the conus medullaris and malignant astorcytomas.

2. RADIOTHERAPY:

Some authorities believe that radiation therapy should have the major role in the management of intramedullary tumors of glial origin. Kopelson, et al., believed that the operation should consist of the minimum surgical procedure necessary to establish a diagnosis, and that radiotherapy was the most effective treatment modality ⁽⁵⁾. Wood, et al., advocated subtotal surgical resection, and noted that the average longevity of their patients treated with surgery followed by radiation therapy was better than surgery alone ⁽⁸⁾. However, others have remarked that the efficacy of radiation therapy has not been proven. ⁽⁹⁾

We adopted the policy of postoperative radiotherapy in all our cases without deferment irrespective of extent of resection.

The efficacy of radiotherapy cannot be dissociated from the concept of dosimetry. It has been known for long time that the effective dose, i.e. 40 Gy or more is hazardous to the spinal cord. In children, myelopathy has been reported to occur with doses of 30 Gy. The deleterious effects of radiotherapy on the vertebral column growth are well known to orthopedic specialists. In adult patients, doses exceeding 40 Gy cause subclinical functional abnormalities in the spinal cord, manifested by alterations in the motor and somatosensory evoked responses. In spite of this, some authors have continued to use these high doses. However, in 1991, Whitaker et al. recommended fractionated radiotherapy up to a total 50 Gy for both children and adults, irrespective of the tumor localization, extent of removal (complete or not), and histological grade, benign or malignant⁽¹⁴⁾. The optimal radiation dose has been assumed to be the maximum tolerance, that is, approximately 5000 cGY given in daily fractions of 180 to 200 cGY, in keeping with the principles of radiation treatment for childhood intracranial astrocytomas^(12,20). While there is general agreement on this treatment, it is clear that the dose-response curve has a shallow slope, because researchers have been unable to show superior improvement for doses in excess of 4500 cGY.

All the patients in our series received postoperative radiotherapy to a median dose of 45 Gy in 25 fractions over 5 weeks. The authors observed no spinal cord damage related to radiotherapy.

The volume to be irradiated should be local that is, the involved segment of the spinal cord plus a margin of two vertebral bodies. It may be that a margin of only a single vertebral body is adequate for well-defined tumors on magnetic resonance imaging. Seven patients received treatment to the involved segment of the cord. Three patients had craniospinal treatment (one patient had GM, and two had anaplastic astrocytoma) as sort of prophylactic treatment against distant spread in these malignant. This decision of this elective treatment was the responsibility of our fellow colleagues in the department of radiotherapy. We understand the possibility of metastasizing in malignant spinal astrocytomas. This possibility is rare and we think that the low rate of distant spread does not justify the risk of morbidity associated with elective craniospinal irradiation, especially when, treatment of relapse maybe possible.

MORBIDITY, RELAPSE, AND OUTCOME:

We observed permanent surgical morbidity in two cases (

case 6&9, Table 8.). Severe postoperative motor deterioration occurred immediately after surgery. A follow-up MRI scan was obtained to rule out hematoma. Nothing was found and the tumor beds were clean and it was obvious that the surgical manipulation and the aggressive attempts to debulk and resect the lesions resulted in severe postoperative neurological deficits. The rest of aforementioned complications in Table 7. were transient. Three patients had increased sensory dysesthesias which improved by time. We believe this maybe due to edema from surgical manipulation or an alteration of blood flow. One case of CSF leak required wound revision and spinal drainage. Two case of wound infection responded quickly to antibiotics.

We witnessed an improvement in functional grade during the long-term follow-up period. Overall, the improvement was one functional grade. Surprisingly, Case 7 (Table 8.) improved two grades. One grade improvement happened postoperatively which maybe due to the decompressive effect of laminectomy and durotomy and postoperative corticosteroid. This was followed by one more grade improvement six months postradiotherapy. Another striking feature was in case 3 (Table 8.), an anaplastic astrocytoma that showed improvement in the long term follow-up and this 44 yr- old woman is doing well up to the time of typing down this research.. According to many authorities and numerous studies, it is well known that the survival rate for malignant IMT is less than five years, despite all efforts. In our work, the results of the other two malignant tumors (case 6 &8, Table 8.) were nothing but frustrating as they died within 24 months of surgery regardless of the amount of resection and adjuvant radiotherapy.

Local relapse is the chief obstacle o success in the management of adult spinal cord astrocytomas. Relapse is defined as progression, primary tumor recurrence, or distant spread. There was no any relapse in seven cases (biopsy sampling or tumor resection) including case 3 of malignant astrocytoma with among (Table 8.). Postoperative radiation treatment was clearly effective in achieving local control and improving survival in these patients.

O'Sullivan, et al., reported that the extent of resection did not significantly affect the local relapse rate, which was 77% for 20 patients who underwent resection and 75% for eight patients who underwent biopsy only⁽²²⁾. The extent of tumor resection did not have an impact on patient survival in our study. Indeed, there was a trend toward poorer survival in

patients who underwent more aggressive resection compared to those who underwent biopsy alone (case 6 & 10, Table 8.).

CONCLUSION

Intramedullary spinal cord astrocytomas are of infiltrating nature resulting in lack of a good plane of cleavage during their removal, and the risk of neurological deterioration after major resection. Studies demonstrate that there is no significant effect of the extent of resection on local relapse. We believe that the traditional management paradigm of conservative surgery and radiotherapy provides a balanced strategy in the treatment of adult spinal astrocytoma to maintain neurological outcome and prevent tumor recurrence. We hope that modern treatment planning and imaging allow more accurate target definition and respect for related normal tissue tolerances.^(28, 29)

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