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Clinical Study

Spinal cord glioblastoma: 25 years of experience from a single institution

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ABSTRACT

Accounting for less than 0.2% of all glioblastomas, high grade gliomas of the spinal cord are very rare. Here, we discuss our approach to managing patients with high grade spinal cord glioma and review the literature on the subject. Six patients with high grade spinal cord gliomas who presented to our institution between 1990 and 2015 were reviewed. Each patient underwent subtotal surgical resection, with a subset receiving adjuvant chemotherapy and radiation. Our primary outcomes of interest were pre-operative and post-operative functional status. One year survival rate was 100%. All patients had stable or improved American Spine Injury Association score immediately after surgery, which was maintained at 3 months in 83.3% of patients. Karnofsky Performance Status (KPS) was stable at 3 month follow up in 50% of patients, but all had decreased KPS 1 year after surgery. A subset of patients received post-operative radiation and chemotherapy with 0% tumor recurrence rate at 3 months. We assessed the molecular profiles of tumors from two patients in our series and found that each had mutations in TP53, but had wildtype BRAF, IDH-1, and MGMT. Taken together, our data show that patients with high grade spinal cord gliomas have an excellent survival at 1 year, but with some decline in functional status within this period. Further studies are needed to elucidate the natural history of the disease and to explore the role of adjuvant targeted molecular therapies.

1. Introduction

High grade glioma of the spinal cord is an uncommon pathology. A survey of all patients (173 males and 294 females) registered with primary intraspinal neoplasms in the Norwegian Cancer Registry from 1955 through 1986 found that spinal glioblastomas (GBM) accounted for 0.2% of all GBM, and 1.4% of spinal gliomas [1]. A number of individual case reports [2–16] and a few small studies involving 3–15 patients [17–21] have been reported in the literature, totaling fewer than 200 cases [9,11]. Given the paucity of cases, conclusive evidence-based management of spinal high grade gliomas has yet to be defined. Herein, we discuss our experience with intrinsic spinal cord high grade gliomas over the past 25 years and review current treatment paradigms.

2. Methods

2.1. Patient selection

Following Institutional Review Board approval, we retrospectively analyzed data gathered from patients undergoing laminectomy for resection of high grade intramedullary glioma between 1990 and 2015. Various faculty neurosurgeons performed the operations with the assistance of resident physicians at a tertiary care level, university affiliated teaching hospital. Patient and operative characteristics were recorded for all patients meeting study criteria, including age, sex, presenting symptoms, type of operation performed, and pre-operative and post-operative functional status.

2.2. Treatment characteristics

Surgery was performed for all patients via a posterior approach with laminectomy overlying the involved spinal cord segments, primary dural opening, resection of the tumor in a subtotal fashion, and closure of the dural defect utilizing a dural graft.

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Table 1
Characteristics of six patients with spinal cord glioblastoma meeting study criteria

Patient characteristic	Metric
Age mean [range], years	40 [30–72]
Sex, male/female	2/4
Spinal level	
Cervical	3
Thoracic	3
Pre-operative ASIA score	
A	2
B	1
C	2
D	1
E	0

ASIA = American Spine Injury Association.

2.3. Outcomes

Our primary outcomes of interest were pre-operative and post-operative functional status. Overall follow-up and survival were also assessed where possible. Neurological examination was assessed in the immediate post-operative period, at 3 month follow-up, and at 1 year follow-up. It was categorized according to the American Spine Injury Association (ASIA) grading system. Overall functional status was assessed at these same time points using the Karnofsky Performance Status (KPS) scale. Post-operative treatment details, including chemotherapy and radiation therapy, were also investigated in all cases. Tumor pathology underwent careful review. This included tumor genomics and mutational status where available. All complications were rigorously recorded including pulmonary embolism, urinary retention (requiring placement of temporary indwelling urinary catheter), durotomy (full thickness dural tear requiring primary suture closure), cerebrospinal fluid leak (post-operative transcutaneous cerebrospinal fluid drainage), surgical site infection, neurological deficit, pneumonia, urinary tract infection, and myocardial infarction.

2.4. Search strategy

The review of recent literature was performed by employing the following search terms and appropriate combinations thereof: "spinal glioblastoma" and "spinal glioblastoma multiforme." The primary literature database queried was PubMed. All 28 studies published during the past 5 years (2010–2014) were reviewed. A subset of 22 studies (involving a total of 33 patients) had outcome data pertinent to our focus and were included in the analysis.

3. Results

3.1. Patient characteristics

In this retrospective study, six patients were identified who met the inclusion criteria of spinal cord high grade glioma over the study period of 25 years at our institution. The mean patient age was 40 years, with a median age of 33 years. The age range was 30 to 72 years. Of the six patients, two were men and four were women. Three patients had cervical tumors and three patients had thoracic tumors. Two patients presented with an ASIA A examination below the involved cord level, one patient with an ASIA B examination, two patients with an ASIA C examination, and the remaining patient with an ASIA D examination. All patients underwent laminectomy with subtotal resection and duraplasty as described in the Methods section. The patient characteristics are summarized in Table 1.

3.2. Patient outcomes

All patients, at a minimum, were followed-up for 1 year. The 1 year survival rate was 100%. Unfortunately, two patients were lost to follow-up thereafter. The maximum follow-up period was 3 years. This was experienced by one patient. The mean follow-up period was 1.5 years. With regard to neurological status, all patients had a stable or improved ASIA score post-operatively. Five of these patients maintained a stable examination at 3 month follow-up. However, four of these patients had a decrement of at least one ASIA grade by their 1 year follow-up appointment. The KPS was used to assess functional status as described in the Methods. Three patients had a stable KPS at 3 month follow-up. However, all six patients had a decrement in their functional status by the time 1 year had passed. These outcomes are summarized in Table 2.

Three patients, all of whom received surgery after 2003, received post-operative radiation and chemotherapy. These patients began fractionated radiation therapy with a total dose of 54 Gy in 30 fractions to the involved spinal cord 6 weeks after surgery and after a thorough wound assessment. They also started concurrent temozolomide (75 mg/m^2) and bevacizumab (10 mg/kg). These patients had follow-up imaging every 3 months, and all patients demonstrated no evidence of tumor recurrence.

3.3. Pathology

Two of these patients had molecular pathology information available. Of these patients, TP53, BRAF, IDH-1, and MGMT methylation status were assessed. All patients had mutations in TP53 and demonstrated wildtype BRAF, IDH-1, and MGMT. These findings are summarized in Table 3.

3.4. Complications

As described in the Methods section, all complications were rigorously assessed including pulmonary embolism, urinary retention (requiring placement of an indwelling urinary catheter), unintended durotomy (full thickness dural tear requiring primary suture closure), cerebrospinal fluid leak (post-operative transcutaneous cerebrospinal fluid drainage), surgical site infection, neurological deficit, pneumonia, urinary tract infection, and myocardial infarction. One patient had a pulmonary embolism within 3 months (at 2.5 months). Four patients required the placement of an indwelling urinary catheter post-operatively, and all of these patients required subsequent scheduled straight catheterization. No patients had an unintended durotomy or cerebrospinal fluid leak. No patients had surgical site infections or other complications. These findings are summarized in Table 4.

Table 2
Outcomes for six patients with spinal cord glioblastoma

Patient outcomes	Metric
Follow-up mean [range], years	1.5 [1–3]
Neurological status (stable or improved ASIA score)	
Immediate post-operative	6
3 months	5
1 year	1
Functional status (stable or improved KPS)	
Immediate post-operative	5
3 months	3
1 year	0
Post-operative radiation	3
Post-operative chemotherapy	3
1 year survival	100% (6/6)

ASIA = American Spine Injury Association, KPS = Karnofsky Performance Status.