March 2014

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Recommended Citation

Khan, M. B., Riaz, M., Bari, M. E. (2014). Is surgical spinal decompression for supratentorial GBM symptomatic drop down metastasis warranted? A case report and review of literature. Surgical Neurology International, 5(1), 1-5.

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Is surgical spinal decompression for supratentorial GBM symptomatic drop down metastasis warranted? A case report and review of literature

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Received: 12 November 13  Accepted: 17 February 14  Published: 27 March 14

Abstract

Background: Symptomatic spinal metastasis from an intracranial primary glioblastoma multiforme (GBM) is very rare. Our literature search identified a total of 42 such patients of which 11 were treated with surgical decompression for spinal metastasis with only one such report from the pediatric age group. Previous studies have reported variable outcomes after surgical management.

Case Description: We report the case of a 16-year-old boy who underwent surgical spinal decompression for spinal metastasis after intracranial GBM. The patient regained motor and autonomic function following surgery and reported improvement in pain. We also present findings from a literature review using the PubMed database from 1985 to June 2013 on this subject and compare radiation therapy with surgical decompression as palliative modalities in such patients.

Conclusion: There are no evidence-based guidelines available on the subject and no treatment regimen has yet demonstrated survival benefit in these patients. Surgical decompression may be a better option for patients with focal resectable lesions and who are medically stable to tolerate the procedure.

Key Words: Decompression, glioblastoma multiforme, laminectomy, metastasis, palliation, spinal cord compression, surgery

INTRODUCTION

Glioblastoma multiforme (GBM) is the most common primary malignant brain tumor.\(^\text{[1,2]}\) It arises mostly from astrocytes but may also derive from oligodendrocytes.\(^\text{[1]}\) The peak incidence is at 54 years of age and increases thereafter.\(^\text{[11]}\) The incidence among 18- to 24-year-olds is about 1 per million and it is even lesser in younger children.\(^\text{[11]}\) The reported incidence of extra cranial metastasis in these tumors is between 0.4% and 0.5%.\(^\text{[15]}\) Leptomeningeal and spinal metastasis are even rarer with a relatively poor prognosis.\(^\text{[12,21,24]}\) Our literature search identified a total of 42 reported cases of spinal drop down metastasis following GBM and only 11 of these patients underwent a surgical spinal decompression. There has only been one such case reported from the pediatric age group.\(^\text{[11]}\) We report the case of a 16-year-old boy who was initially diagnosed and treated for a left parietooccipital GBM and then developed spinal metastasis for which he underwent surgical spinal decompression. We also review the literature on the efficacy of spinal surgical decompression on clinical outcomes in these patients and...
report and compare outcomes in patients who received surgical decompression with those who did not.

CASE REPORT

This 16-year-old male child presented with spontaneous onset of headache, nausea, and slight drowsiness since 2 weeks. The neurological examination revealed intact higher mental functions and no cerebellar signs. However, there was a bitemporal heteronymous hemianopia confirmed by perimetry. Power in right upper and lower limb was 4/5 according to Medical Research Council (MRC) scale with positive pronator drift.\(^{[17]}\) The gait was otherwise normal. Magnetic resonance imaging (MRI) showed a left parietooccipital lesion with intraventricular extension [Figure 1]. Both solid and cystic components were present with calcifications marked on the medial aspect. The patient underwent a craniotomy with neuronavigation-guided biopsy of the mass and gross total excision. Intraoperatively, a soft-firm mildly vascular lesion was identified, which was clearly demarcated in most dimensions. A frozen section confirmed the diagnosis of World Health Organization (WHO) grade IV GBM and this was consistent with the final histopathology report. The tumor was Glial fibrillary acidic protein (GFAP) and s-100 positive and 40% of the cells showed nuclear positivity with MIB-1 antibody to the Ki-67 antigen (MIB-1). Postoperatively, the patient developed a subtle sensory aphasia. The rest of the hospital course was unremarkable and the patient was discharged in stable condition. The patient received postoperative local radiotherapy with a total dose of 54 grays (Gy).

Eight months later the patient presented with acute onset bilateral lower limb paraplegia. There was a complete loss of sensation in dermatome thoracic 7 (T-7) and T-8. Abdominal and cremasteric reflexes were absent. The power was 0/5 with increased spasticity and 3+ reflexes and normal bulk in both the lower limbs.\(^{[17,25]}\) The Babinski’s sign was positive bilaterally and the patient had lost bladder control. An MRI showed recurrence of GBM with multifocal cranial deposits [Figure 2] and spinal MRI showed an intradural extramedullary mass measuring 1.1 × 5.0 cm in anterioposterior (AP) and craniocaudal dimensions at T-5 to T-7 level with significant cord compression [Figure 3].

The patient underwent a T5-7 laminectomy and excision of metastatic mass. Intraoperatively, a fragile highly vascular intradural extramedullary mass was noticed and sent for histopathology analysis. The histopathological examination of the mass revealed multiple fragments of a cellular tumor with hemangiopericytomatous vasculature. The cells revealed hyperchromatic round to oval nuclei with scant cytoplasm [Figure 4]. Increased mitotic figures and glycogen were also seen. On immunohistochemical staining, the mass was focally positive for GFAP, epithelial membrane antigen (EMA), cluster of differentiation 99 (CD 99) and Vimentin [Figure 5]. The MIB-1 was raised and a diagnosis of metastatic GBM was made. Postoperatively, the patient showed recovery of autonomic function and the power was 3/5 in both the lower limbs, which gradually improved to 5/5 over the next one month. The patient was given postoperative radiotherapy with a total dose of 28 Gy.

Three months later, the patient presented to the emergency room (ER) with fever of 39°C and seizures since 3 days. He also complained of urinary and fecal incontinence. We evaluated him for these complaints with urine culture, which grew *Escherichia coli* and *Psuedomonas* and the patient was given appropriate

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**Figure 1:** (a) CT scan head; (b-d) T1-contrast enhanced MRI showing a left parietooccipital lesion with intraventricular extension. Both solid and cystic components can be appreciated with calcifications on the medial aspect

**Figure 2:** (a-c) T1-contrast enhanced MRI head performed 6 months postoperatively suggestive of recurrent disease
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supportive care and antibiotics and discharged from the hospital once in stable condition.

Three weeks later, the patient presented with severe pain in right arm and loss of sensation, which now involved both the upper arms. The family signed a do not resuscitate (DNR) form and the patient passed away 2 days later following cardiopulmonary arrest after significant brain stem herniation and extension of GBM.

DISCUSSION

The incidence of symptomatic spinal metastasis from a primary intracranial metastasis has been reported between 1% and 2.7%. The exact number maybe even higher as GBM is a rapidly progressive disease in which many patients probably die before spinal metastasis become symptomatic. Technological advances have slightly improved the life expectancy of patients with GBM and increased use of MRI may lead to a higher incidence being reported in the future.

The exact mechanism for intramedullary spread remains unclear. A probable pathway of dissemination includes invasion of the basement membrane and choroid plexus. This theory is supported by reports in literature where increased incidence is associated with tumor presence proximal to ventricular structures and craniotomies. However, dissemination has been known to occur even without a craniotomy and many studies have found that tumor proximity to ventricular system is not an independent risk factor for spinal metastasis. The immunocompromised status from adjuvant radiation and chemotherapy may render these patients more prone to metastatic disease. The spread of GBM has also been reported along white matter tracts. Mutations in the tumor suppressor gene PTEN, higher MIB-1 labeling index and GFAP expression have been associated with a higher risk for intramedullary metastasis. Neurological symptoms such as back pain, gait disorders, sensory and motor deficits are common in patients with drop metastasis and depend on the segment of the cord affected and the long tracts, which are compromised. The most common neurological deficit is paraparesis. Spinal metastasis is reported to occur 5-13 months after the diagnosis of primary intracerebral glioma. The median time from diagnosis of GBM to death is less than 2 years. The median time from diagnosis of spinal metastasis to death was one month, with only one patient surviving for 5 months. Our patient passed away within a year of diagnosis of GBM and about 4 months after symptomatic spinal metastasis, which is consistent with reports in literature.

The overall survival after a diagnosis of GBM has only marginally improved over the decades. The addition of temozolomide has improved the 5 year survival rate to about 10% as opposed to 1.9% with radiation alone. Despite temozolomide, 70% of the patients die within 2 years of diagnosis. Our patient did not receive adjuvant chemotherapy with temozolomide despite recommendation because of financial constraints. This raises questions as to the extent of palliative measures that should be adopted in resource-deprived developing countries and severely hampers our ability to care for these very sick patients.

Consensus exists that younger age and good neurological status at presentation confer better outcomes. Adjuvant chemotherapy, radiotherapy, and total tumor resection have been shown to increase life expectancy in patients with GBM. The molecular genetics of GBM may be the most important determinant of patient outcomes. Patients with O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation have a 2-year survival of 48.9% and 5-year survival of 13.8%, as compared with 14.8% and 8.3%, respectively, among those with unmethylated MGMT.

Many authors have recommended the use of steroids. We also administered steroids to our patient. The outcomes following steroid administration are variable and mostly depend on the outcomes of adjuvant radiotherapy and treatment with temozolomide.
However, it seems reasonable to use steroids in acute settings till appropriate guidelines become available.

At present no evidence-based radiation schedule exists for spinal metastasis of GBM. Authors have previously described using radiation doses of 20, 21, 30, and 39 Gy. This has generally been of limited advantage in terms of regaining lost function or survival benefit. However, some authors have reported good palliative outcomes in terms of pain relief.

Surgical spinal decompression with laminectomy has only been described in some case reports [4,5,9,11,23,24] [Table 1].

Out of the 11 cases that we found during our literature search, there were 5 male and 5 female patients (gender of 1 patient was not mentioned). The median age at the time of surgery was 34 years (inter-quartile range; IQR = 43.5). Three patients received chemotherapy for their spinal metastasis, while eight patients received radiation therapy. Overall, good palliative outcomes were described in six (54.5%) patients, three (27.3%) patients did not have improvement in symptoms, while the outcomes could not be determined for two (18.2%) patients. At the same time, we identified 31 patients who received radiation therapy or concomitant chemoradiotherapy (CCRT) for their spinal metastasis. Out of these 31 patients, pain relief was significant in only 6 patients (19.4%), no improvement was noticed in 16 patients (51.6%), while outcomes could not be determined for 9 patients (29%). In comparison, less than 20% of the patients who underwent radiation therapy alone reported improvement in symptoms. Our patient also reported significant improvement in symptoms following a surgical spinal decompression. However, this sample size is too small for any meaningful statistical analysis. Moreover, the reports are compiled over more than 25 years and the efficacy of radiation and chemotherapy has changed over time. Also there may be a selection bias favoring those patients for surgical decompression who have focal resectable lesions and are in a relatively better medical condition. In our opinion, treatment should be individualized for every case till uniform evidence-based guideline becomes available on the subject.

**Table 1: Previous reports of spinal metastasis with GBM and outcomes**

| Author (year)       | Age (sex) | Spinal segment affected | Symptoms                                                                 | Chemotherapy | Radiotherapy | Improvement in symptoms |
|---------------------|-----------|-------------------------|--------------------------------------------------------------------------|--------------|--------------|-------------------------|
| Khan et al. (current report) | 16, M     | Thoracic                | Paraplegia, loss of sensation in T7-T8                                   | No           | Yes          | Yes                     |
| Amitendu et al., 2012 | 63, F     | Lumbar                  | Bilateral sciatica, lower limb weakness, lower limb weakness             | No           | No           | Yes                     |
| Tincho et al., 2012  | 27, M     | Sacral                  | Right sided sciatica                                                     | No           | No           | Yes                     |
| Arzbaecher et al., 2007 | 63, F     | Thoracic                | Paraplegia, autonomic dysfunction and sensory level                      | Yes          | Yes          | Yes                     |
| Jahraus et al., 2003  | 6, F      | Cervical, Thoracic and Lumbar | Bilateral lower extremity paraparesis                           | Yes          | Yes          | No                      |
| Hubner et al., 2001   | 36, F     | Cervical, Lumbar and Sacral | Paraparesis, Bladder incontinence                                       | No           | No           | Unknown                 |
| Hamilton et al., 1993 | 70, M     | Thoracic                | Urinary incontinence, paresthesia and lower limb weakness, sensory level at T10 | No           | Yes          | Yes                     |
| Vertosick et al., 1990 | 21, F     | Thoracic                | Paraparesis                                                              | No           | Yes          | No                      |
| Onda et al., 1986     | 42, M     | Cervical                | Weakness of lower extremities, flaccid paraplegia, sensory impairment below T9, dysuria | No           | Yes          | Unknown                 |
| Bukeo et al., 1985    | 32, M     | Thoracic                | Paraplegia, urinary incontinence                                         | No           | Yes          | Unknown                 |

GBM: Glioblastoma multiforme
CONCLUSION

No evidence-based guidelines have yet been developed due to the rare incidence of spinal metastasis from a GBM and no treatment regimen has yet demonstrated survival benefit. Treatment modalities need to be individualized to the needs and resources of the patients and hospitals. Surgical decompression may be a better option for patients with resectable focal lesions who are medically stable to tolerate the procedure.

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