Case Report

Multifocal spinal glioblastoma and leptomeningeal carcinomatosis in an elderly male with hydrocephalus and myelopathy

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ABSTRACT

Background: Primary spinal glioblastoma multiforme with multifocal leptomeningeal enhancement is rarely diagnosed or documented. We describe a rare case of multifocal spinal isocitrate dehydrogenase (IDH) wild type glioblastoma with leptomeningeal carcinomatosis in an elderly male presenting with a chronic subdural hematoma, progressive myelopathy, and communicating hydrocephalus.

Case Description: A 77-year-old male with a medical history of an acoustic schwannoma, anterior cranial fossa meningioma, and immune thrombocytopenic purpura presented with right-sided weakness after repeated falls. Magnetic resonance imaging of the brain and spine demonstrated a left-sided subdural hematoma, leptomeningeal enhancement of the brain and skull base, ventricles, and the cranial nerves, and along with florid enhancement of the leptomeninges from the cervicomedullary junction to the cauda equina. Most pertinent was focal thickening of the leptomeninges at T1 and T6 with mass effect on the spinal cord. A T6 laminectomy with excisional biopsy of the lesion was planned and completed. Findings were significant for glioblastoma the World Health Organization Grade IV IDH 1 wild type of the thoracic spinal cord. Subsequently, his mental status declined, and he developed progressive hydrocephalus which required cerebrospinal fluid diversion. Unfortunately, the patient had minimal improvement in his neurological exam and unfortunately died 2 months later.

Conclusion: In a review of the limited literature describing similar cases of primary spinal glioblastoma, the prognosis of this aggressive tumor remains unfavorable, despite aggressive treatment options. The purpose of this report is to increase awareness of this rare condition as a potential differential diagnosis in patients presenting with multifocal invasive spinal lesions.

Keywords: Glioblastoma, Leptomeningeal carcinomatosis, Thoracic myelopathy

INTRODUCTION

Glioblastoma multiforme (GBM) is a World Health Organization (WHO) Grade IV histological malignancy in the central nervous system. Cerebral GBM is the most common aggressive primary brain tumors in adults. However, primary spinal GBM are exceptionally rare, accounting for 1-5% of all GBM and about 1.5% of all spinal cord tumors. With multiple case reports and institutional case series published, multifocal glioblastoma is also a rare form
of spinal GBM and is associated with worse outcomes and shorter overall survival time compared with solitary spinal GBM.\[^{[1]}\] Leptomeningeal spread of glioblastoma is another rare entity that has been described in about 2% of patients with glioblastoma. Patients would more commonly present with long track signs secondary to this, and up to 40% of patients with leptomeningeal disease can develop communicating hydrocephalus.\[^{[3]}\]

We describe a rare case of multifocal spinal isocitrate dehydrogenase (IDH) wild type glioblastoma with leptomeningeal carcinomatosis in an elderly male presenting with a chronic subdural hematoma, progressive myelopathy, and communicating hydrocephalus.

**CASE REPORT**

A 77-year-old male with a medical history significant for acoustic schwannoma, anterior cranial fossa meningioma, and immune thrombocytopenic purpura presented with the right-sided weakness after repeated falls. Non-contrast head computed tomography (CT) scan demonstrated a left-sided subdural hematoma. On examination, he was found awake, but disoriented. He had weakness of the left arm and leg, along with long tract signs that included sustained clonus and hyperreflexia of the bilateral lower extremities. Magnetic resonance imaging (MRI) of the brain demonstrated leptomeningeal enhancement of the brain and skull base, ventricles, and the cranial nerves [Figure 1] MRI of the spine demonstrated florid enhancement of the leptomeninges from the cervicomedullary junction to the cauda equina. On examination, he was found awake, but disoriented. He had weakness of the left arm and leg, along with long tract signs that included sustained clonus and hyperreflexia of the bilateral lower extremities. Magnetic resonance imaging (MRI) of the brain demonstrated leptomeningeal enhancement of the brain and skull base, ventricles, and the cranial nerves [Figure 1] MRI of the spine demonstrated florid enhancement of the leptomeninges from the cervicomedullary junction to the cauda equina. Most pertinent was focal thickening of the leptomeninges at T1 and T6 with mass effect on the spinal cord [Figure 2]. Both lesions appeared to be intradural and infiltrative to the spinal cord, with an intramedullary component, with the T6 appearing larger and more infiltrative. An initial lumbar puncture demonstrated elevated immunoglobulin (Ig) G levels, but cytology and flow cytometry were nondiagnostic. For once having platelets within normal range a month prior, he developed thrombocytopenia with platelets of 40,000 uL. He was initially treated for this thrombocytopenia with intravenous Ig and platelet transfusion with minimal improvement. Once his thrombocytopenia was improved a biopsy was offered to the patient's family and they wished to proceed.

Subsequently, a T6 laminectomy was planned and completed. Intraoperatively, we noted a firm infiltrative lesion of the spinal cord. There was no clear plane separating the tumor and the spinal cord. A subtotal resection was achieved secondary to the infiltrative nature of the lesion. No intraoperative neuromonitoring changes were observed. The pathology report of the biopsied specimens demonstrated hypercellularity with atypical mitotic nuclei and astrocytic features. In addition, there were foci of microvascular proliferation [Figure 3a]. The histopathological staining of the biopsy sample demonstrated positivity for vimentin, glial fibrillary protein [Figure 3b], ATRX [Figure 3c] and negative for CAM 5.2, epithelial membrane antigen and IDH 1 [Figure 3d]. A p53 mutation was also seen. These findings were diagnostic for glioblastoma WHO grade IV IDH1-wildtype of the thoracic spinal cord.

Postoperatively, he was fully oriented and following commands in all extremities with more diminished strength and sensation on the right lower extremity compared to the left lower extremity. Over the course of a few days, he developed worsening encephalopathy. A lumbar puncture was completed as part of encephalopathy workup. Elevated opening pressures with an elevated protein level were observed. On placement of a lumbar drain, we identified a meaningful clinical improvement. A ventriculoperitoneal shunt was placed for cerebrospinal fluid diversion. Given the diagnosis with extensive leptomeningeal spread and overall poor neurological function, chemotherapy and radiotherapy

**Figure 1:** Magnetic resonance imaging T1 sequences with gadolinium contrast- parasagittal views. (a) Brain - Suprasellar enhancement, leptomeningeal enhancement seen along the ventral brainstem and pineal region. (b) Cervical spine - Diffuse leptomeningeal enhancement seen in the ventral/dorsal spinal cord. (c) Thoracic spine - Dorsally compressive thickened lesions at T1 (single asterick) and T6 (double asterick). (d) Lumbar spine - Diffuse enhancement of the conus medullaris and the cauda equina.
GBM had better survival outcomes compared to their cranial counterparts, however still dismal with median survival at ranging from 13 to 23 months.\textsuperscript{2,15,17} Spinal GBM with or without leptomeningeal spread has a poor prognosis with most therapeutic treatments demonstrating controversial results at best.\textsuperscript{12,15,18} In contrary, according to national registry data, older age was associated with worse prognosis. Other factors include tumor invasiveness, tumor size, and degree of resection.\textsuperscript{12,18} Cerebral and spinal glioblastomas are histomorphologically identical, with a comparable increase in the proliferation and accumulation of p53 protein seen on immunohistochemically studies.\textsuperscript{24,27} They share similar median survival times of 9–10 months as demonstrated in multiple single center and population based reports.\textsuperscript{2,14,16,18} The major cause of death with spinal GBM is noted to be, respiratory depression, seeding, and/or cerebral metastasis.\textsuperscript{23} Clinically, spinal GBM tend to behave differently from their cranial counterparts. Cranial GBM can manifest with a wide array of symptoms including headaches, confusion, aphasia, hemiplegia, and seizures.\textsuperscript{19} Whereas spinal GBM more commonly presents with signs and symptoms classified as limb weakness, unspecific back pain, radicular pain distribution, paraparesis, autonomic dysfunction, and resulting in bladder/bowel incontinence.\textsuperscript{13,21,22,25} It is not unusual to see motor, sensory, and autonomic pathways affected.\textsuperscript{26} In a systematic review of spinal GBM in 53 pediatric patients most common presenting symptom was limb weakness, followed by sensory disturbances, back pain, and bladder and bowel disturbances.\textsuperscript{13} While the first stage is marked by nonspecific symptoms, the second stage shows patterns of swift and dangerous neurological decline as the disease progresses, similar to the decline in functional status demonstrated by our patient.

Our patient demonstrated diffuse cranial and spinal leptomeningeal enhancement with at least one infiltrative tumor at T6. Features commonly associated with spinal GBM include hydrocephalus, increased intracranial pressure, early leptomeningeal infiltration, and malformation of the spinal cord.\textsuperscript{5,7,8} The diagnosis can be challenging with both nonspecific symptoms and radiological findings. An essential part of making a proper diagnosis is imaging the spinal cord including T1- and T2-weighted MRI with and without contrast.\textsuperscript{23} Symptoms from spinal GBM can progress from weeks or months, whereas low-grade astrocytomas progress over years.\textsuperscript{7,10,11} The diffuse enhancement seen for this patient on imaging was deemed leptomeningeal carcinomatosis. Leptomeningeal spread is a severe complication of GBM in which the disease spreads to the meninges surrounding the brain and spinal cord. Spinal GBM has a higher rate of leptomeningeal involvement than cranial GBM.\textsuperscript{27}

Historically, spinal GBM has been treated with a combination of radiation therapy and temozolomide.\textsuperscript{6,13,17} However, due to the rarity of this condition, very limited data are available to

**DISCUSSION AND LITERATURE REVIEW**

Primary spinal glioblastoma with leptomeningeal disease is a rare diagnosis.\textsuperscript{4-6} Table 1 depicts a few of the existing case reports of primary spinal GBM of which there were only two others seen that have demonstrated concurrent leptomeningeal spread. Our case of primary spinal GBM with leptomeningeal spread adds to this limited literature.

Spinal GBM most commonly presents in younger patients, as demonstrated by a systematic review where the median age of presentation was 35.5–41 years.\textsuperscript{13,14,16,17} A recent study has demonstrated that individuals diagnosed with spinal
support the treatment guidelines. The literature that is available remains controversial regarding optimal surgical management of spinal GBM. The surgical treatments currently described in the literature range from partial, subtotal, and total resection to a radical cordectomy.\cite{4,5} However, due to the inability to discriminate between infiltrative tumor and normal tissue, an aggressive total resection of the tumor was unachievable in our case. Even partial or subtotal resection may not always be possible due to the added challenges and risks of operating in certain areas, such as the cauda equina.\cite{4,23,26} At present, chemotherapy and radiotherapy are recommended despite uncertain therapeutic effect.\cite{23,26} In our patient’s case, the oncology and radiation oncology team did not believe that chemotherapy or palliative radiation would provide meaningful benefit to the patient. The patient opted for comfort care measures and died shortly after his initial diagnosis.

## CONCLUSION

While glioblastomas of the brain are the most common aggressive primary tumor in adults, primary GBM of the spine are exceptionally rare. Spinal glioblastomas are notorious for their nonspecific presentation, aggressive nature, and grim prognosis. Despite their rarity, primary spinal GBM should be considered in the differential diagnosis of scattered spinal lesions.

### Acknowledgments

Thank you to Annette Absellem and Harish Babu, MD for aiding in the completion of this manuscript and Timothy Richardson, MD for his pathology data.

### Declaration of patient consent

Patient’s consent not required as patients identity is not disclosed or compromised.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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Koutsouras, et al.: Multifocal spinal glioblastoma and leptomeningeal carcinomatosis in an elderly male with hydrocephalus and myelopathy

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How to cite this article: Koutsouras GW, Amsellem A, Richardson T, Babu H. Multifocal spinal glioblastoma and leptomeningeal carcinomatosis in an elderly male with hydrocephalus and myelopathy. Surg Neurol Int 2021;12:595.