ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Clinical Professor of Neurological Surgery, School of Medicine, State U. of NY at Stony Brook.

SNI: Neuro-oncology

Editor
Mitsutoshi Nakada, MD
Kanazawa University, Ishikawa, Japan

SNI
Open Access

Case Report

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

George W. Koutsouras[1], Annelle Amsellem[2], Timothy Richardson[3], Harish Babu[1]

[1]Department of Neurosurgery, Upstate University Hospital, Syracuse, [2]Department of Internal Medicine, New York Institute of Technology College of Osteopathic Medicine, Glen Head, [3]Department of Pathology, Upstate University Hospital, Syracuse, New York, United States.

E-mail: *George W. Koutsouras - koutsoug@upstate.edu; Annelle Amsellem - aamselle@nyit.edu; Timothy Richardson - richatim@upstate.edu; Harish Babu - babuh@upstate.edu

***Corresponding author:**
George W. Koutsouras,
Department of Neurosurgery,
Upstate University Hospital,
Syracuse, New York,
United States.

koutsoug@upstate.edu

Received : 29 September 2021
Accepted : 16 November 2021
Published : 08 December 2021

DOI
10.25259/SNI_985_2021

Quick Response Code:

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.[26] 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.[9,20,27] 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. 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

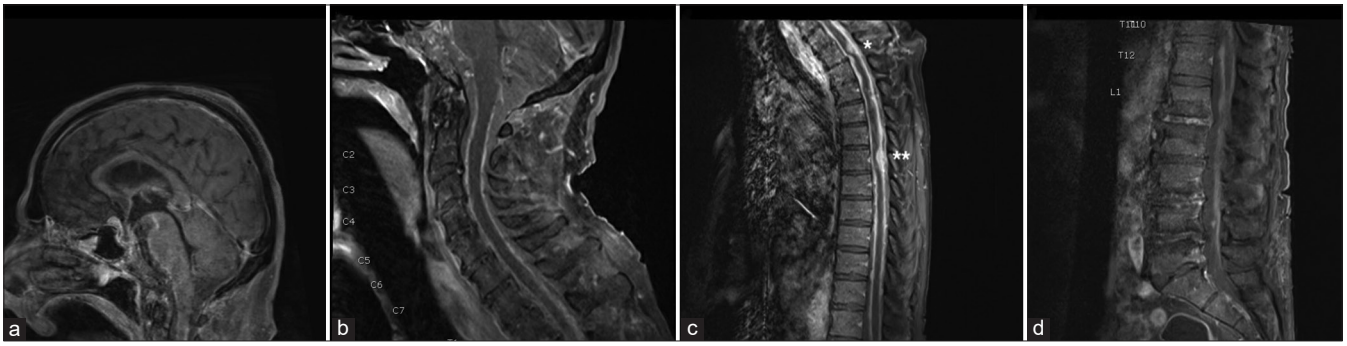

Figure 1: Magnetic resonance imaging T1 sequences with gadolinium contrast- parasagittal views. (a) Brain - Suprasellar enhancement, leptomeningeal enhancement seen along the ventral brainstem and pineal region. (b) Cervical spine- Diffuse leptomeningeal enhancement seen in the ventral/dorsal spinal 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.

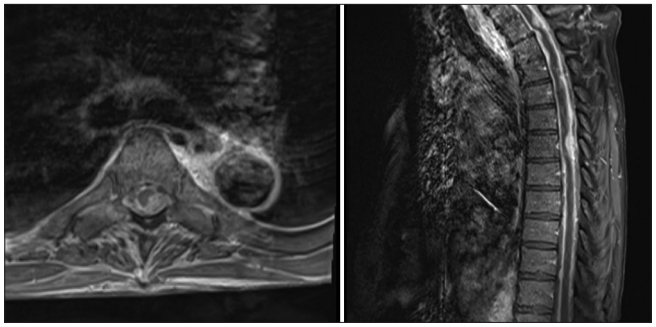

Figure 2: Magnetic resonance imaging thoracic spine T1 sequence with gadolinium contrast, axial (left) and sagittal (right) images at the T6 level. There is an enhancing lesion that appears to be intradural and intramedullary.

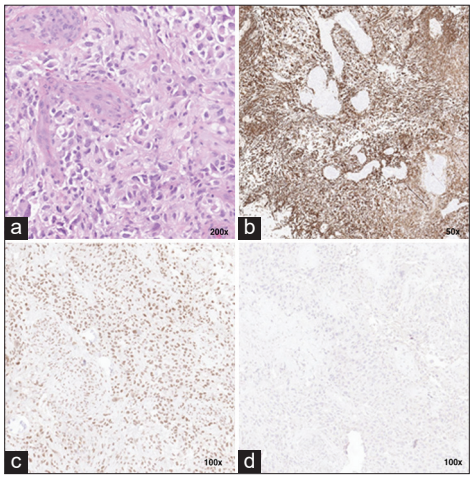

Figure 3: Histopathological stains of T6 lesion. (a) Tumor cells with hypercellularity, atypical mitotic nuclei and astrocytic features. There are foci of microvascular proliferation. Hematoxylin and eosin ×200 (b) Positive stain for Glial Fibrillary acidic protein ×50. (c) Positive for ATRX gene ×100. (d) Tumor cell negative for mutant IDH1 ×100.

were deferred by the oncologists and the family. The patient continued to decline and subsequently passed away 2 months after his surgical diagnosis.

DISCUSSION AND LITERATURE REVIEW

Primary spinal glioblastoma with leptomeningeal disease is a rare diagnosis.[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.[13,14,16,17] A recent study has demonstrated that individuals diagnosed with spinal GBM had better survival outcomes compared to their cranial counterparts, however still dismal with median survival at ranging from 13 to 23 months.[2,15,17] Spinal GBM with or without leptomeningeal spread has a poor prognosis with most therapeutic treatments demonstrating controversial results at best.[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.[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.[24,27] They share similar median survival times of 9–10 months as demonstrated in multiple single center and population based reports.[2,14,16,18] The major cause of death with spinal GBM is noted to be, respiratory depression, seeding, and/or cerebral metastasis.[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.[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.[13,21,22,25] It is not unusual to see motor, sensory, and autonomic pathways affected.[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.[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.[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.[23] Symptoms from spinal GBM can progress from weeks or months, whereas low-grade astrocytomas progress over years.[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.[27]

Historically, spinal GBM has been treated with a combination of radiation therapy and temozolomide.[6,15,17] However, due to the rarity of this condition, very limited data are available to

Table 1: Existent case literature of spinal glioblastoma.

Author	Year	Location	#Case	Metastatic spread	Age	Symptom	Treatment	Survival
Caro-Osorio *et al.*[5]	2018	Cervical	1	None	48	Paresthesias	Surgery/ Chemotherapy	8 months
Scarrow *et al.*[16]	2000	Conus	1	None	62	Right lower extremity radiculopathy	Surgery/XRT/ Chemotherapy	LTFU
Delgado *et al.*[6]	2019	Thoracolumbar	1	None	21	Paraplegia/ Neurogenic bowel/ bladder	Surgery	N/A
Purkayastha *et al.*[17]	2018	Cervicomedullary to Conus	1	Yes, intracranial focal lesion	23	Paraplegia/ Neurogenic bowel/ bladder	Surgery/XRT/ Chemotherapy	8 months
Kataria *et al.*[18]	2011	Thoracolumbar	1	Yes, intracranial focal lesion 3 months later	15	Paraplegia/ Neurogenic bowel/ bladder	Surgery/XRT/ Chemotherapy	3 months
Jeong *et al.*[19]	2010	Thoracic	1	Yes, intracranial focal lesion 4 months later	22	Paraplegia	Surgery/XRT/ Chemotherapy	Death, Not stated
Strik *et al.*[8]	2000	Lower thoracic	1	Yes, Leptomeningeal and Intracranial lesions	31	Paraplegia	Surgery/XRT	13 months
Yeung *et al.*[2]	2006	Cervical	1	Yes, Leptomeningeal spread at T10-T12	35	Neck pain, BUE and BLE parasthesias, Neurogenic Bladder	Chemotherapy	Not stated
Shastin *et al.*[9]	2017	Cervical	1	None	75	Deceased mobility, memory loss, confusion, left sided weakness and increased tone	Steroids	3 weeks

XRT: Radiation therapy, BLE: Bilateral lower extremity, LTFU: Loss to follow up, BUE: Bilateral upper extremity

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.[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.[4,23,26] At present, chemotherapy and radiotherapy are recommended despite uncertain therapeutic effect.[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.

REFERENCES

1. Abou-El-Ardat K, Seifert M, Becker K, Eisenreich S, Lehmann M, Hackmann K, *et al.* Comprehensive molecular

characterization of multifocal glioblastoma proves its monoclonal origin and reveals novel insights into clonal evolution and heterogeneity of glioblastomas. Neuro Oncol 2017;19:546-57.
2. Adams H, Avendano J, Raza SM, Gokaslan ZL, Jallo GI, Quinones-Hinojosa A. Prognostic factors and survival in primary malignant astrocytomas of the spinal cord: A population-based analysis from 1973 to 2007. Spine (Phila Pa 1976) 2012;37:E727-35.
3. Birzu C, Tran S, Bielle F, Touat M, Mokhtari K, Younan N, *et al*. Leptomeningeal spread in glioblastoma: Diagnostic and therapeutic challenges. Oncologist 2020;25:e1763-76.
4. Caro-Osorio E, Herrera-Castro JC, Barbosa-Quintana A, Benvenutti-Regato M. Primary spinal cord small-cell glioblastoma: Case report and literature review. World Neurosurg 2018;118:69-70.
5. Ciappetta P, Salvati M, Capoccia G, Artico M, Raco A, Fortuna A. Spinal glioblastomas: Report of seven cases and review of the literature. Neurosurgery 1991;28:302-6.
6. Delgado BJ, Moosavi L, Rangel E, Stull W, Polineni RD, Chen J, *et al*. An unusual presentation of spinal giant cell glioblastoma in a 21-year-old female. J Investig Med High Impact Case Rep 2019;7.
7. Henson JW. Spinal cord gliomas. Curr Opin Neurol 2001;14:679-82.
8. Hernandez-Duran S, Bregy A, Shah AH, Hanft S, Komotar RJ, Manzano GR. Primary spinal cord glioblastoma multiforme treated with temozolomide. J Clin Neurosci 2015;22:1877-82.
9. Hsu S, Quattrone M, Ostrom Q, Ryken TC, Sloan AE, Barnholtz-Sloan JS. Incidence patterns for primary malignant spinal cord gliomas: A surveillance, epidemiology, and end results study. J Neurosurg Spine 2011;14:742-7.
10. Jeong SM, Chung YG, Lee JB, Shin IY. Intracranial dissemination from spinal cord anaplastic astrocytoma. J Korean Neurosurg Soc 2010;47:68-70.
11. Kataria R, Bhasme V, Chopra S, Sinha VD, Singhvi S. Intracranial metastasis of spinal intramedullary anaplastic astrocytoma. Asian J Neurosurg 2011;6:116-8.
12. Khalid S, Kelly R, Carlton A, Wu R, Peta A, Melville P, *et al*. Adult intradural intramedullary astrocytomas: A multicenter analysis. J Spine Surg 2019;5:19-30.
13. Konar SK, Bir SC, Maiti TK, Nanda A. A systematic review of overall survival in pediatric primary glioblastoma multiforme of the spinal cord. J Neurosurg Pediatr 2017;19:239-48.
14. Lam S, Lin Y, Melkonian S. Analysis of risk factors and survival in pediatric high-grade spinal cord astrocytoma: A population-based study. Pediatr Neurosurg 2012;48:299-305.
15. Liu J, Zheng M, Yang W, Lo SL, Huang J. Impact of surgery and radiation therapy on spinal high-grade gliomas: A population-based study. J Neurooncol 2018;139:609-16.
16. Luksik AS, Garzon-Muvdi T, Yang W, Huang J, Jallo GI. Pediatric spinal cord astrocytomas: A retrospective study of 348 patients from the SEER database. J Neurosurg Pediatr 2017;19:711-9.
17. Moinuddin FM, Alvi MA, Kerezoudis P, Wahood W, Meyer J, Lachance DH, *et al*. Variation in management of spinal gliobastoma multiforme: Results from a national cancer registry. J Neurooncol 2019;141:441-7.
18. Nunna RS, Khalid S, Ryoo JS, Mehta AI. Adult primary high-grade spinal glioma: A nationwide analysis of current trends in treatment and outcomes. J Neurooncol 2020;147:633-41.
19. Philippon J. Brain tumors in the elderly. Psychol Neuropsychiatr Vieil 2004;2:29-33.
20. Purkayastha A, Sharma N, Sridhar MS, Abhishek D. Intramedullary glioblastoma multiforme of spine with intracranial supratentorial metastasis: Progressive disease with a multifocal picture. Asian J Neurosurg 2018;13:1209-12.
21. Sabatino G, Della Pepa GM, Esposito G, Brodbelt A. Glioblastoma multiforme intraxial metastasis to the conus medullaris with primary disease under control: A rare unexpected finding. Br J Neurosurg 2013;27:388-9.
22. Scarrow AM, Rajendran P, Welch WC. Glioblastoma multiforme of the conus medullaris. Clin Neurol Neurosurg 2000;102:166-7.
23. Shastin D, Mathew RK, Ismail A, Towns G. Cervical spinal glioblastoma multiforme in the elderly. BMJ Case Rep 2017;2017.
24. Strik HM, Effenberger O, Schafer O, Risch U, Wickboldt J, Meyermann R. A case of spinal glioblastoma multiforme: Immunohistochemical study and review of the literature. J Neurooncol 2000;50:239-43.
25. Tinchon A, Oberndorfer S, Marosi C, Ruda R, Sax C, Calabek B, *et al*. Malignant spinal cord compression in cerebral glioblastoma multiforme: A multicenter case series and review of the literature. J Neurooncol 2012;110:221-6.
26. Urbanska K, Sokolowska J, Szmidt M, Sysa P. Glioblastoma multiforme-an overview. Contemp Oncol (Pozn) 2014;18:307-12.
27. Yeung YF, Wong GK, Zhu XL, Ma BB, Hk NG, Poon WS. Radiation-induced spinal glioblastoma multiforme. Acta Oncol 2006;45:87-90.

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.