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Case Report

Diffuse vertebral metastases from glioblastoma with vertebroepidural diffusion: A case report and review of the literature

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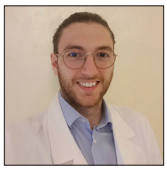

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ABSTRACT

Background: The occurrence of extraneural metastasis in patients diagnosed with glioblastoma (GBM) is rare with an estimated incidence ranging from 0.4% to 2.0%. Short clinical history is believed to be a possible explanation of the paucity of such cases. Furthermore, to date, only few papers describe cases of vertebral metastases from GBM without evidence of synchronous visceral involvement.

Case Description: The authors report on the case of a 46-year-old woman presenting with a history of surgically treated GBM who developed multiple metastases located in the posterior laminae and vertebral bodies with a single dural metastasis at D6-D8 level 5 years after the initial diagnosis. Total-body computed tomography did not show signs of either intracranial recurrence or visceral involvement. Postoperative pathological examination confirmed the diagnosis of the World Health Organization-2016 Grade IV GBM metastases.

Conclusion: From a clinical point of view, the awareness of the possibility of spinal and vertebral metastasis from intracranial GBM is crucial. The present case demonstrates that distant dissemination from the primary tumor is possible despite the absence of intracranial recurrence.

Keywords: Case report, Dural metastasis, Glioblastoma metastasis, Neurosurgery, Vertebral glioblastoma

INTRODUCTION

Glioblastoma (GBM), or 2016 World Health Organization (WHO) diffuse astrocytic and oligodendroglial tumor,[14] is the most common and most malignant astrocytoma of the central nervous system (CNS) representing 45% of primary brain tumors.[9] Recent epidemiological estimates show global incidence of 2–3 cases in 100,000 people with most patients being diagnosed in their 5th decade.[17] Despite decades of research progress, modern brain imaging, and innovative surgical techniques, median survival does not exceed 15 months after initial diagnosis.[21]

Until recently, extracranial GBM dissemination was not believed to occur because of the presence of CNS safeguard mechanisms as the blood–brain barrier and the overall short median survival of these patients. However, advancements in early detection and therapy protocols allowed the exponential growth of such condition which is now reported to occur between 0.4% and

2.0% of intracranial GBM cases.[10] Most common sites of extracranial involvement from GBM include the lung (60%), lymph nodes (51%), bones (31%), and liver (22%)[6] with vertebral body and posterior laminae metastasis representing a rare event displaying a significant male preponderance, and usually associated with poorer outcomes.[6,10]

Hereby, the authors present a case of multiple vertebral bone metastases with further localization in the subdural space in a patient who received the diagnosis of GBM 5 years before.

CASE REPORT

A 46-year-old woman presented in 2016 with a brief history of worsening headaches without any significant medical history. Physical examination was unremarkable and did not indicate any evidence of neurological deficits. Magnetic resonance of the brain demonstrated a right frontoparietal lesion surrounded by vasogenic edema showing avid contrast enhancement. In the suspect of a GBM, a right parietal craniectomy followed by gross-total resection of the tumor was performed and the patient recovered without neurological deficits. Histologic examination confirmed the diagnosis of primary GBM, isocitrate dehydrogenase wild type; World Health Organization 2016 Grade IV, O[6]-methylguanine-DNA methyltransferase methylated, and alpha-thalassemia/mental retardation, X-linked retained. The patient did not experience any postoperative complications and the headache disappeared, therefore was discharged 6 days after surgery. Adjuvant chemotherapy plus concomitant radiotherapy was administered according to the Stupp protocol.[22]

However, 5 years after the initial diagnosis, the patient experienced low back pain irradiating to the legs which was unresponsive to symptomatic pharmacotherapy. Subsequently, she developed numbness and loss of sensitivity in the lower extremities and, in January 2021, was readmitted to our department. Neurological examination revealed a right leg hyposthenia (MRC 3/5) with absent deep tendon reflexes (DTR) and bilateral hypoesthesia at the D5-D6 level. Three days after admission, a sudden worsening of the neurological condition with onset of paraplegia (ASIA A) was noticed. Therefore, an emergency magnetic resonance imaging (MRI) scan of the brain was performed which revealed no evidence of primary site GBM recurrence [Figure 1]. However, spinal MRI demonstrated what appeared as a vertebroepidural metastasis at the D6-D8 level causing posterior compression of the spinal cord. Furthermore, diffuse alterations of the vertebral bodies exhibiting hyperintense signal on T1- and T2-weighted images were noticed [Figure 2].

In the hypothesis of epidural metastasis from GBM, the patient was treated with D6-D8 laminectomy followed by partial tumor resection. On intraoperative inspection, the neoplastic tissue presented as ovoidal, white colored, capsulated, and roughly 0.5–1.3 cm in diameter. Microscopic examination demonstrated glial components with marked desmoplasia, deponing for a WHO-2016 Grade IV GBM.[14] Immunohistochemical staining with glial fibrillary acidic protein confirmed the tumor's glial origin. Cerebrospinal fluid (CSF) analysis did not demonstrate the presence of malignant cells.

Postoperatively, sensory and motor deficits persisted; the patient exhibited slight improvement in muscle strength (MRC 4/5) in the lower extremities and reduced but present DTRs. Neurological examination revealed a persistent hypoesthesia of the D5-D6 dermatome. Total-body computed tomography (CT) showed no further localizations of the tumor, therefore, the patient was transferred to a physical rehabilitation center and evaluated for adjuvant radiotherapy. After 6 months, the patient was able to walk although the gait was insecure and slow; she had regained sensation in the lower thoracic dermatomes and brisk reflexes were evoked.

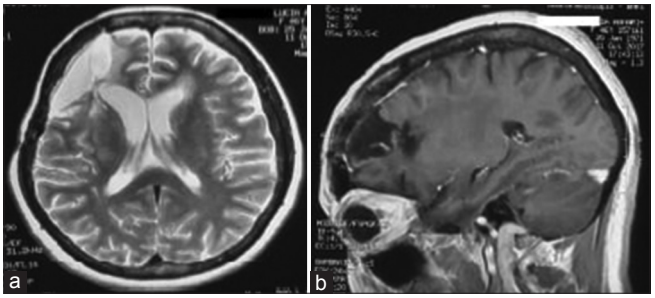

Figure 1: (a) Axial and (b) sagittal magnetic resonance imaging (MRI) scan demonstrating the absence of primary site tumor recurrence and the evidence of previous surgical resection.

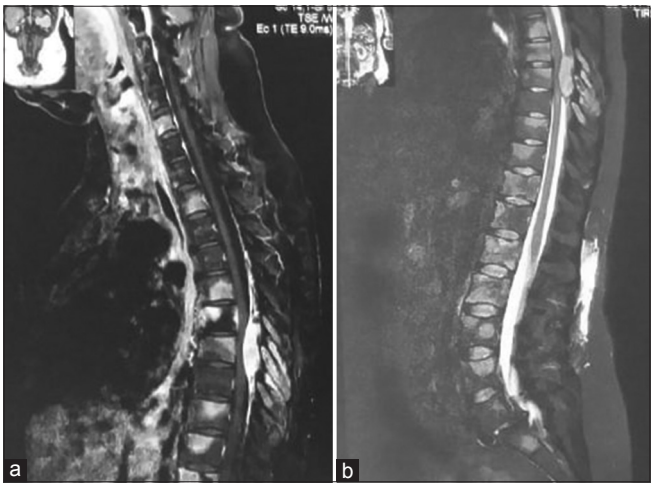

Figure 2: (a) Sagittal T1WI magnetic resonance imaging (MRI) scans showing diffuse involvement of the vertebral bodies and posterior laminae exhibiting heterogeneous hyperintensity. (b) Sagittal T2WI MRI scan: evidence of D6-D8 laminectomy with partial lesion resection.

Table 1: Summary of previous cases of patients with vertebral metastases from GBM.

Authors	Sex	Age	Time from initial diagnosis (months)	Localization	Clinical manifestation	Survival after vertebral involvement (months)
Beauchesne *et al.*	M	54	7	D5, D8, D10, D11	Diffuse drug-resistant low back pain	9
Chestnut *et al.*	M	42	9	C6	Quadriplegia due to vertebral collapse	14
Fabi *et al.*	M	43	39	L1, L3	Low back pain	-
Sadik *et al.*	M	48	18	L4	Low back pain	-
Li *et al.*	M	51	18	C4	Neck pain	21

DISCUSSION

Extraneural metastases from GBM represent a rare entity occurring late in the course of the disease, after a median of 2 years and in only 0.2–4% of all patients diagnosed with this highly malignant tumor.[6,10] In general, visceral GBM dissemination is primarily found, of frequency, in the pleura and/or lung (60%), lymph nodes (51%), bone (31%), and liver (22).[6] In their review, Longee *et al.*[13] found the vertebral body as the most common bone site for GBM metastases (73%), followed by ribs, pelvis, and appendicular skeleton. In a review of the 28 published cases of histologically diagnosed vertebral GBM metastases, Goodwin *et al.*[10] reported a mean overall survival of approximately 26 months after initial diagnosis with an average time from vertebral involvement to death of 10 months. Leptomeningeal spread is described to be the single most common route of dissemination for extracranial metastases,[1] occurring in 15–25% of supratentorial GBMs.[2] In more than half of the cases, vertebral body involvement is clinically silent.[20] When present, symptoms can be either acute or insidious, with low back pain unresponsive to pharmacological treatment as the most frequently encountered manifestation.[10] Vertebral metastases are reported to be either osteolytic or osteoblastic on plain radiograms and computed tomography imaging.[16] Both MRI with gadolinium and Tc-99m single-photon emission computed tomography scans show high sensitivity in detecting vertebral involvement,[3] with MRI frequently demonstrating hypointensity on T1WI and heterogeneous hyperintense lesions on T2WI.

Notwithstanding recent advancements, pathophysiological pathways of extraneural seeding of tumor cells need to be clarified. Detection of high levels of proteases within neoplastic tissue including urokinase-type plasminogen activator along with lower levels of their inhibitors is believed to be a possible explanation of GBM extradural diffusion.[4] Proximity to the ventricles has been speculated as a putative cause of malignant cell dissemination increasing the likelihood of metastatization through the CSF. In a case series of 34 patients, Dardis *et al.*[7] reported that primary GBMs were located adjacent to the lateral ventricles in half of the cases of leptomeningeal dissemination. Nonetheless, the recent finding of intracranial lymphatic vessels[15] and the growing evidence demonstrating the importance of the glymphatic system in the CNS pathology,[18] should bolster further research in this field.

Typically, following spinal dissemination, the neurological condition rapidly deteriorates, and management is primarily palliative with most patients undergoing decompressive laminectomy when spinal cord compression is observed.[3,10]

In the present report, a case of multiple and diffuse extraneural vertebral metastases from intracranial GBM is described. Although it cannot be excluded, this was a primary spinal localization of the tumor, the author speculates of a possible distant site dissemination in the absence of intracranial recurrence, as was previously described by other groups.[8,12] The patient was previously diagnosed with frontotemporal GBM treated with craniectomy followed by gross-total surgical resection. After 5 years, the onset of rapidly progressive low back pain unresponsive to pharmacological treatment prompted a further investigation which demonstrated extraneural vertebral dissemination from the primary tumor. Although vertebral metastases in the absence of primary site recurrence and other synchronous localizations were previously reported,[3,5,8,12,19] survival time did not exceed 39 months after initial diagnosis [Table 1]. Exceptional survival time length from primary diagnosis could be speculated to be a potential explanation for the development of extraspinal vertebral metastases from this tumor.[11] Postoperative microscopical examination of the vertebral lesions showed glial cells positive for glial fibrillary acidic protein, confirming the diagnosis of GBM WHO 2016 metastases. Surgical decompression and palliative resection of symptomatic lesions of the vertebral body and laminae significantly improved the patient's quality of life.

CONCLUSION

A rare case of extraneural diffuse vertebral bone metastases in a patient previously treated for intracranial GBM is presented. The exceptional survival time length highlights the importance of suspecting distant dissemination of the tumor when progressive changes in the patient's general condition occur albeit no evidence of primary site recurrence

is confirmed on head MRI. As previously reported, rapid deterioration of the neurological picture and sudden onset of paraplegia due to spinal cord compression was seen in this case, and urgent palliative treatment was performed.

Declaration of patient consent

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

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Alatakis S, Malham GM, Thien C. Spinal leptomeningeal metastasis from cerebral glioblastoma multiforme presenting with radicular pain: Case report and literature review. Surg Neurol 2001;56:33-7; discussion 37-8.
2. Arita N, Taneda M, Hayakawa T. Leptomeningeal dissemination of malignant gliomas. Incidence, diagnosis and outcome. Acta Neurochir (Wien) 1994;126:84-92.
3. Beauchesne P, Soler C, Mosnier JF. Diffuse vertebral body metastasis from a glioblastoma multiforme: A technetium-99m Sestamibi single-photon emission computerized tomography study. J Neurosurg 2000;93:887-90.
4. Bindal AK, Hammoud M, Shi WM, Wu SZ, Sawaya R, Rao JS. Prognostic significance of proteolytic enzymes in human brain tumors. J Neurooncol 1994;22:101-10.
5. Chesnut RM, Abitbol JJ, Chamberlain M, Marshall LF. Vertebral collapse with quadraparesis due to metastatic glioblastoma multiforme: Case report and review of the literature. J Neurooncol 1993;16:135-40.
6. Cunha ML, Maldaun MV. Metastasis from glioblastoma multiforme: A meta-analysis. Rev Assoc Med Bras (1992) 2019;65:424-33.
7. Dardis C, Milton K, Ashby L, Shapiro W. Leptomeningeal metastases in high-grade adult glioma: Development, diagnosis, management, and outcomes in a series of 34 patients. Front Neurol 2014;5:220.
8. Fabi A, Vidiri A, Carapella C, Pace A, Occhipinti E, Caroli F, *et al*. Bone metastasis from glioblastoma multiforme without central nervous system relapse: A case report. Anticancer Res 2004;24:2563-5.
9. Gilard V, Tebani A, Dabaj I, Laquerrière A, Fontanilles M, Derrey S, *et al*. Diagnosis and management of glioblastoma: A comprehensive perspective. J Pers Med 2021;11:258.
10. Goodwin CR, Liang L, Abu-Bonsrah N, Hdeib A, Elder BD, Kosztowski T, *et al*. Extraneural glioblastoma multiforme vertebral metastasis. World Neurosurg 2016;89:578-82.e3.
11. Hansen S, Rasmussen BK, Laursen RJ, Kosteljanetz M, Schultz H, Nørgård BM, *et al*. Treatment and survival of glioblastoma patients in Denmark: The Danish neuro-oncology registry 2009-2014. J Neurooncol 2018;139:479-89.
12. Li ZG, Zheng MY, Zhao Q, Liu K, Du JX, Zhang SW. Solitary vertebral metastatic glioblastoma in the absence of primary brain tumor relapse: A case report and literature review. BMC Med Imaging 2020;20:89.
13. Longee DC, Friedman HS, Phillips PC, Burger PC, Oakes WJ, Heffez D, *et al*. Osteoblastic metastases from astrocytomas: A report of two cases. Med Pediatr Oncol 1991;19:318-24.
14. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, *et al*. The 2016 World Health Organization classification of tumors of the central nervous system: A summary. Acta Neuropathol 2016;131:803-20.
15. Louveau A, Smirnov I, Keyes TJ, Eccles JD, Rouhani SJ, Peske JD, *et al*. Structural and functional features of central nervous system lymphatic vessels. Nature 2015;523:337-41.
16. Myers T, Egelhoff J, Myers M. Glioblastoma multiforme presenting as osteoblastic metastatic disease: Case report and review of the literature. AJNR Am J Neuroradiol 1990;11:802-3.
17. Pietschmann S, von Bueren AO, Kerber MJ, Baumert BG, Kortmann RD, Müller K. An individual patient data meta-analysis on characteristics, treatments and outcomes of glioblastoma/gliosarcoma patients with metastases outside of the central nervous system. PLoS One 2015;10:e0121592.
18. Plog BA, Nedergaard M. The glymphatic system in central nervous system health and disease: Past, present, and future. Annu Rev Pathol 2018;13:379-94.
19. Sadik AR, Port R, Garfinkel B, Bravo J. Extracranial metastasis of cerebral glioblastoma multiforme: Case report. Neurosurgery 1984;15:549-51.
20. Smith DR, Hardman JM, Earle KM. Metastasizing neuroectodermal tumors of the central nervous system. J Neurosurg 1969;31:50-8.
21. Thakkar JP, Dolecek TA, Horbinski C, Ostrom QT, Lightner DD, Barnholtz-Sloan JS, *et al*. Epidemiologic and molecular prognostic review of glioblastoma. Cancer Epidemiol Biomarkers Prev 2014;23:1985-96.
22. Weller M, van den Bent M, Hopkins K, Tonn JC, Stupp R, Falini A, *et al*. EANO guideline for the diagnosis and treatment of anaplastic gliomas and glioblastoma. Lancet Oncol 2014;15:e395-403.

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