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Case Reports & Case Series

Multiple vertebral metastases from brain glioblastoma: An insidious complication

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ABSTRACT

Glioblastoma (GBM) is the most malignant and the most frequent of primary astrocytomas, typically involving the Central Nervous System (CNS) alone. Extra-CNS localizations (ECM) are exceptional, and vertebral dissemination is extremely uncommon.

We present the case of a patient with vertebral dissemination from an intracranial GBM without intra-dural space invasion. The patient underwent a gross total tumor removal followed by radiation therapy (RT) with concomitant temozolomide chemotherapy (STUPP protocol).

Following the appearance of back pain, patient underwent whole body computed tomography (CT) and spinal magnetic resonance imaging (MRI) scan.

Spinal-MRI highlighted multiple vertebral lesions not infiltrating dura mater being confined to vertebral bodies. CT scan demonstrated the absence of other repetitive lesions in both thorax and abdomen. Histological examination from a percutaneous CT-guided vertebral biopsy confirmed the suspicious of secondary localization from intracranial GBM.

To the best of our knowledge this is the second reported case of vertebral metastases from GBM in absence of other ECM. This case raises the need for clinical suspicious of vertebral dissemination in case of GBM patient presenting with radicular, myelopathic symptoms or less specifically, back pain.

1. Introduction

Glioblastoma (GBM) is the most frequent and malignant lesion among primary brain malignancies, accounting for more than 60% of brain tumours and 50% of glioma subtype [1].

GBM typically involves the Central Nervous System (CNS) alone because of its rapid growth and the specific architecture of CNS which lacks lymphatic ducts and is surrounded by dura mater and blood brain-barrier (BBB) [2].

Extra-CNS localizations (ECM) are rare with a reported incidence of 0.2%. Metastases to vertebral bodies, lungs, pleura and cervical lymph nodes are rare, with only 28 described cases of vertebral metastases (VM) from intracranial GBM [2–4]. In all cases except one VM were accompanied by other localizations.

We present the second case of multiple VM from a GBM without brain-recurrence or other localizations also reviewing existing literature.

2. Case report

A 21-year-old woman was admitted to our department with a 3-week history of worsening headache, diplopia and visual disturbances.

A brain magnetic resonance imaging (MRI) showed a rim-enhancing cystic lesion in the left parieto-occipital lobe with a significant edema (Fig. 1). She underwent gross total tumor removal, post-operative period was uneventful and she was discharged four days after surgery.

Histological examination demonstrated a GBM (IDH1–2-wt, Ki67 40%, unmethylated MGMT promoter). Post-operative treatments included radiation therapy (RT) (60Gy/30 fractions) plus concomitant temozolomide (TMZ) (75 mg/m^2/day) (STUPP protocol) and three additional cycles of TMZ. Four months later she presented with progressive back pain without focal neurological deficits.

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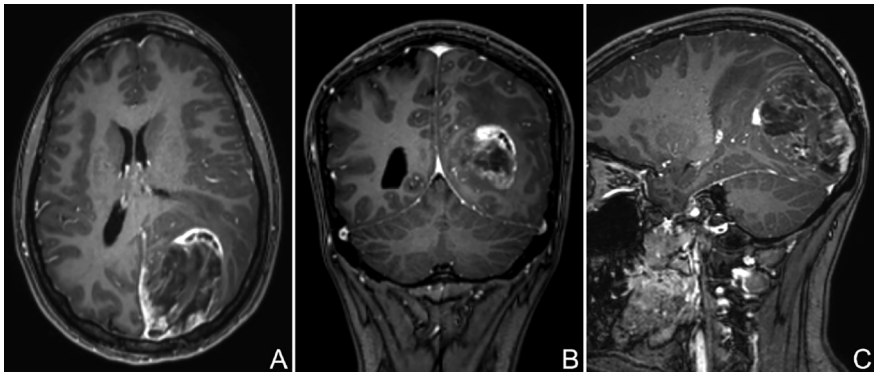

Fig. 1. Axial (a), sagittal (b) and coronal (c) contrast-enhanced T1-weighted MRI demonstrating a heterogeneously enhancing left occipital mass lesion.

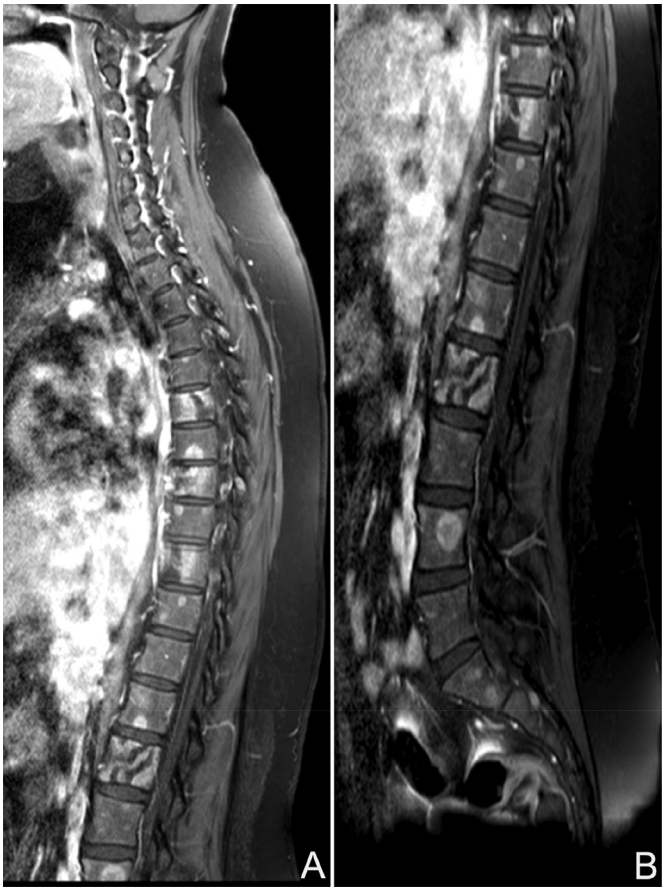

Fig. 2. Sagittal contrast-enhanced T1-weighted MRI of the cervical, thoracic (a) and lumbar spine (b), demonstrating multiple vertebral body metastases (especially at T10, T11 and L2 level) without intra-dural space invasion.

A brain-MRI demonstrated no recurrence of the primary lesion while spinal-MRI showed multiple vertebral body contrast enhancing masses from T6 to L2 without epidural involvement, spinal cord compression or fractures (Fig. 2). Whole-body-CT scan demonstrated the absence of repetitive lesions in both thorax and abdomen.

A percutaneous CT-guided-biopsy performed at L2 confirmed the suspect of GBM metastases with superimposable histological-molecular features.

Patient underwent RT to thoracic-lumbar vertebras (20Gy/5fractions) with a mild improvement in symptoms.

Six months later brain-MRI showed diffuse recurrence in supra and infratentorial spaces. Few months later she died.

3. Discussion

ECM have been described in only 28 cases involving lung and/or pleura (60%), cervical lymph nodes (51%), bones (31%) and liver (22%) [2–4]. Vertebral dissemination alone is extremely uncommon [3]. Most frequently involved are thoracic, lumbar, followed by cervical and sacral vertebrae [3].

Mechanism explaining ECM remains unclear [2]. Direct access through dural vessels, possibly initiated by surgical intervention, is considered the most liable path [3]. This is supported by pulmonary and lymphatic seeding and by the chance to find circulating tumor cells in blood stream in 20–30% of operated GBM patients [3]. In this hypothesis, tumor cells overcome BBB after surgery, also aided by RT and constitutive GBM BBB disruption and surviving in the bloodstream thanks to immune system depression [3,5,6].

An alternative explanation could be direct invasion of dura mater, bone and neighbor tissues in presence of genetic and molecular features facilitating GBM invasion [3,7,8].

Elevated expression and activation of enzymes such as gelatinase-A and gelatinase-B may predispose to ECM inducing degradation of extracellular matrix in CNS, leptomeninges and BBB [8]. Dissemination has been associated with PTEN mutation as well as a higer MIB-1 labelling index [9]. However, further studies are needed to understand the molecular mechanisms predicting ECM.

Currently there is no effective treatment for vertebral dissemination indeed decompressive surgery, steroids, RT and systemic chemotherapy (TMZ, carboplatin, bevacizumab) have no clear influence on overall survival [3,10].

Surgical decompression should be limited to patients with potentially reversible spinal cord compression causing neurologic deficits [3].

4. Conclusion

ECM are uncommon, while VM without other intra-cranial or ECM are exceptionally rare [11]. The exact mechanism is still unclear [12], though it is probably related to vascular seeding of tumor cells.

Our case highlights the importance of investigating vertebral district in the diagnostic work-up of patients with GBM presenting with radicular myelopathic symptoms or back pain.

No specific treatments for VM have demonstrated a survival advantage but, in these cases, palliative therapies could improve symptoms and preserve an acceptable quality of life [9].

Disclosures

Nothing to disclose.

Consent

Next of kin has consented to the submission of the case report for

submission to the journal.

Declaration of Competing Interest

The authors declare that there are no conflicts of interest.

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