Glioblastoma Multiforme: A Rare Case of Spinal Drop Metastasis

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Key words
- Glioblastoma multiforme
- Leptomeningeal disease
- Spinal drop metastasis
- Tumour dissemination

Abbreviations and Acronyms
CSF: Cerebrospinal fluid
GBM: Glioblastoma multiforme
MRI: Magnetic resonance imaging

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BACKGROUND: **The occurrence of spinal drop metastasis in patients diagnosed with glioblastoma multiforme (GBM) is rare. In previous reports, this diagnosis occurred after surgical resection of GBM, which was believed to increase the likelihood of tumor seeding. Diagnosis of spinal drop metastasis prior to surgery remains rare.**

CASE DESCRIPTION: **We report a 57-year-old woman with a brief history of confusion, altered behavior, and agitation without any other significant past medical history. Computed tomography and magnetic resonance imaging (MRI) of the head demonstrated an intra-axial lesion of the right temporal lobe as well as evidence of leptomeningeal disease around the medulla. A spine MRI scan revealed spinal drop metastases at the level of C1 and T6/T7. Subsequent biopsy confirmed WHO-2016 grade IV GBM.**

CONCLUSIONS: **The awareness of the possibility of spinal drop metastasis prior to surgical resection of GBM is important. The use of routine MRI of the whole neuroaxis in patients diagnosed with GBM can aid in prognosis and management options.**

INTRODUCTION

Glioblastoma multiforme (GBM), or World Health Organization grade IV tumor, is the most common type of malignant primary brain tumor, accounting for 12% to 15% of intracranial neoplasms.[1] It has a reported global incidence of 2–3 in 100,000 people.[2] Despite advancements in diagnosis and therapeutic approaches, GBM continues to have a poor prognosis of approximately 15 months survival after diagnosis.[3]

Historically, it was believed that GBM metastasis does not occur, primarily due to a number of physiological factors that safeguard the central nervous system.[1,4] However, advancements in early detection and therapeutic approaches have resulted in increased patient median survival, and consequently in increased detection of extracranial metastases of GBM.[4] The majority of GBM metastases occur within the central nervous system through leptomeningeal or intramedullary spread to the spinal cord as spinal drop metastases. Drop metastases refer to intradural extramedullary spinal metastases that originate from intracranial lesions.[5] This remains a rare and unique event, presenting in only 1% to 2% of patients with GBM.[1] The specific mode of spread remains unclear, although a number of hypotheses have been proposed. The primary mechanism is believed to be tumor extravasation directly through the cerebrospinal fluid (CSF), with surgical debulking increasing the likelihood of tumor seeding.[6]

There is typically an average lag time of 8.5 months after GBM diagnosis prior to detection of spinal drop metastasis.[4] In our case, however, spinal metastasis was detected simultaneously at the time of GBM diagnosis. Reported cases of GBM metastasis in the absence of surgical intervention remain rare, and existing accounts have been retrospective post mortem reports. To date, there has been no reported case of diagnosis of GBM spinal drop metastasis prior to surgery or biopsy. We hereby present a case report on a 57-year-old woman who presented with spinal drop metastases prior to surgical intervention.

CASE DESCRIPTION

A 57-year-old woman was referred to our neurosurgery center from a local hospital with a brief history of altered behavior, confusion, and agitation. She did not have any significant past medical history. On examination, her Glasgow Coma Scale score was 14 of 15 (E4, V4, M6). She had no focal neurological deficits, and mobilized independently. Patient had a computed tomography scan and subsequently magnetic resonance imaging (MRI) of the head, which showed intra-axial lesion of the right temporal lobe. The lesion measured approximately 4.5 x 4.3 x 4.3 cm, and showed areas of necrosis, cystic degeneration, and micro-hemorrhages (Figure 1). Leptomeningeal disease was also noted around the medulla. In view of this finding, a whole-spine MRI scan was performed. This showed intraspinal lesions at the level of C1 and T6/T7 (Figures 2–4). The

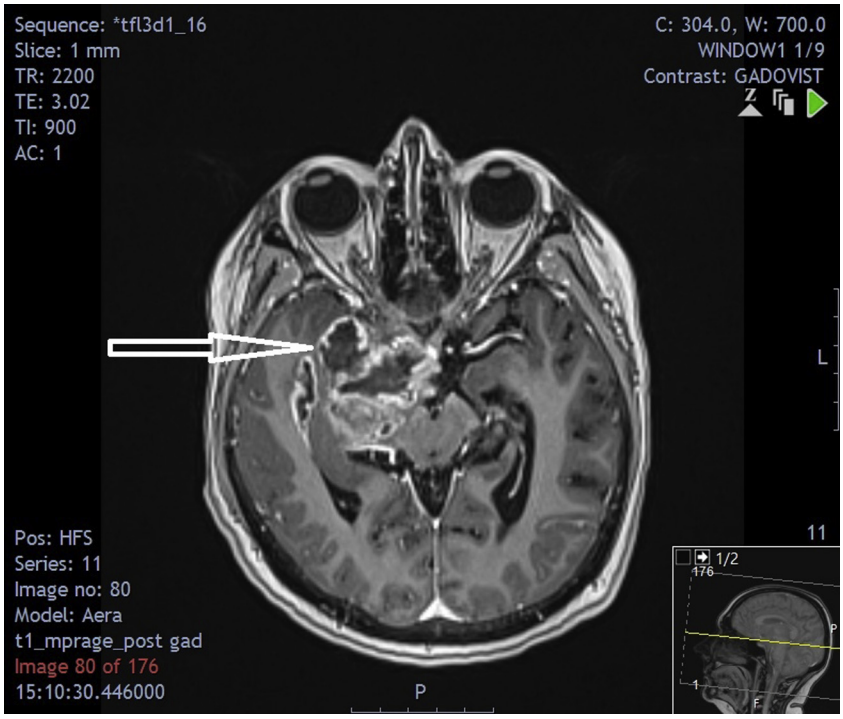

Figure 1. Axial post contrast MRI scan of the head showing right temporal tumor.

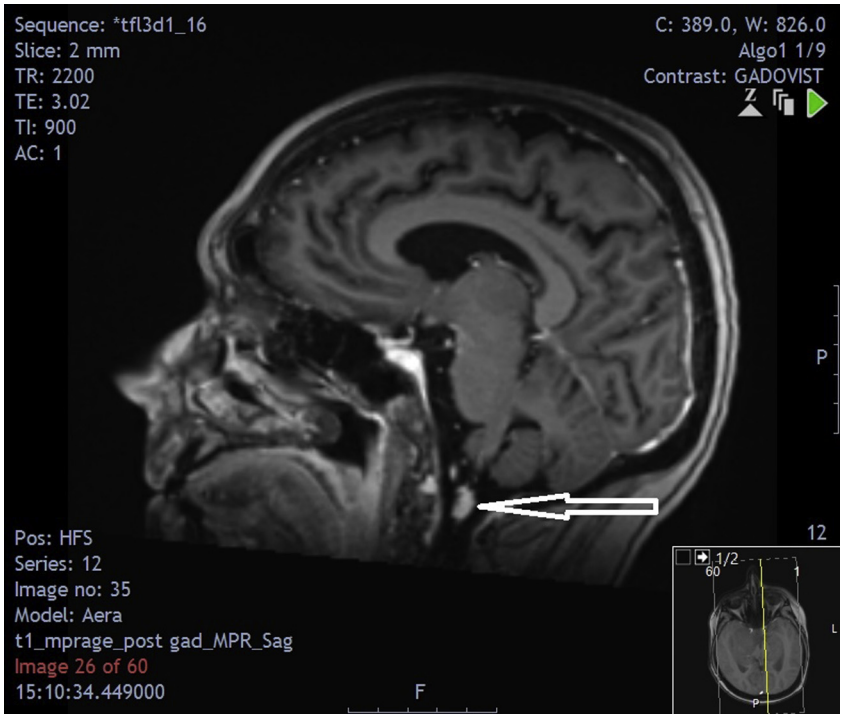

Figure 2. Sagittal post contrast MRI scan of the head showing leptomeningeal lesion at the level of the Medulla.

patient did not have any signs of spinal cord compression, nor did she complain of any related symptoms. Given the appearance of the lesion on spine MRI, there remains a possibility of an alternative diagnosis, although in the context of intracranial GBM, a diagnosis of metastatic GBM to the spine was concluded. The patient was commenced on dexamethasone, and the consensus opinion of the neuro-oncology multidisciplinary team was to proceed with neuronavigation-guided biopsy of the intracranial lesion. Histology confirmed glioblastoma, IDH-(isocitrate dehydrogenase) wild type; World Health Organization 2016 grade IV, MGMT (O[6]-methylguanine-DNA methyltransferase) unmethylated, ATRX (alpha-thalassemia/mental retardation, X-linked) retained, antigen Ki67 index of 15%. Given unexpectedly rapid disease progression, no further biopsies or investigations of additional lesions were performed. Furthermore, due to raised intracranial pressure, lumbar puncture was not feasible. Patient deteriorated quite rapidly and unfortunately deceased within 3 weeks of diagnosis. In the absence of further investigations, the specific cause of death remains inconclusive.

DISCUSSION

In this case report, we describe a patient who presented with spinal drop metastasis prior to surgical intervention for a right temporal GBM. This is particularly unique as although prior literature has elucidated extracranial metastases in the absence of craniotomies, these have all been retrospective post mortem case reports.[7-10] Therefore, the detection of GBM spinal drop metastasis prior to surgery is vital as it provides additional context regarding mechanisms of GBM spinal metastasis.

It was previously believed that extracranial GBM is uncommon because of the presence of physical barriers, such as the thickened basement membrane, the dura mater, and the blood–brain barrier.[I] However, it has since been recognized that in approximately 2% of patients undergoing surgical resections of GBMs, they later present with spinal drop metastasis. This has been suggested to be due to surgical breaching of the blood–brain barrier.[I,II] The case of our patient is exceptional as no surgery was

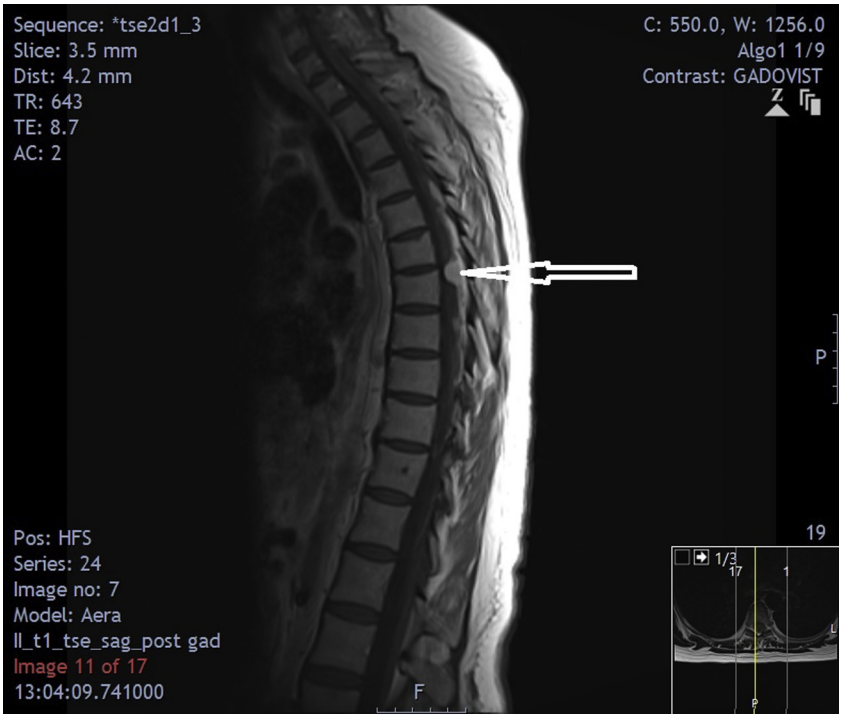

Figure 3. Sagital post contrast MRI of the spine showing leptomeningeal lesion at the level of T6/7.

undertaken prior to the diagnosis of spinal drop metastasis.

The primary mode of spinal GBM metastasis is understood to be via intramedullary or leptomeningeal spinal cord dissemination. Additionally, a hematogenous mode of metastasis has also been implicated. This could be further supported by the extensive vascularity of a typical GBM tumor, with tumor cells monopolizing existing cerebral vasculature, allowing for extracranial metastasis to the spine.[4,12]

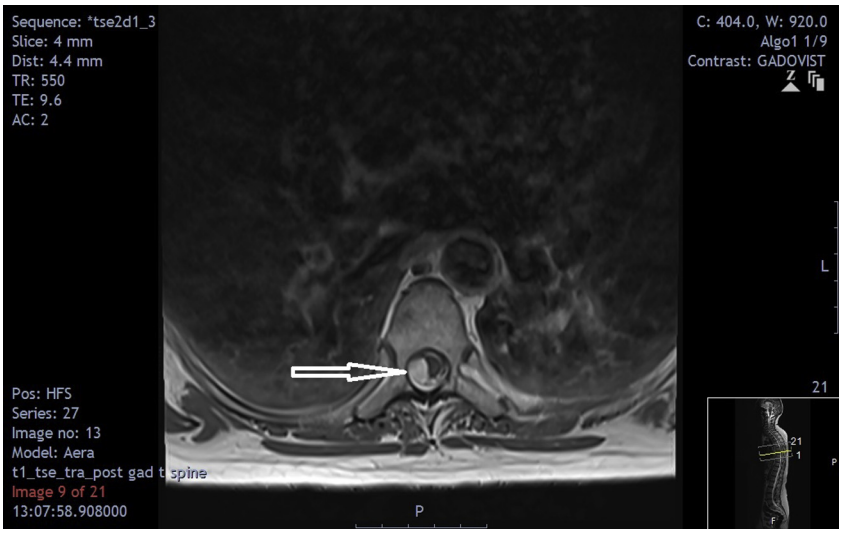

Figure 4. Axial post contrast MRI of the spine showing the same lesion at T6/7.

In the case of our patient, the GBM was located in the right temporal region, adjacent to the temporal horn of the lateral ventricle. This location could facilitate seeding of the tumor into the CSF and subsequent development of spinal drop metastasis. Some uncertainty remains regarding the association between tumor proximity to ventricles and the likelihood of metastasis through CSF. A review undertaken by Elliott et al. between 1987 to 1991 concluded that there is no significant effect of proximity of the tumor to the ventricular system in CSF tumor dissemination.[13] However, multiple other reports have documented the involvement of the third and fourth ventricles in spinal drop metastasis of GBM, with increased metastasis from tumors that are located proximal to these ventricles.[6,14-16] Additionally, in a case series of 34 patients, Dardis et al. found that in 50% of their patients presenting with leptomeningeal metastasis, the primary GBM was located adjacent to the lateral ventricle, as seen in our case.[7] This is in accordance with the hypothesis that CSF seeding is a principal mechanism of spread.

The simultaneous diagnosis of GBM and spinal drop metastasis in the case of our patient, highlights the importance of considering routine MRI of the whole neuroaxis. This could aid in determining whether the presence of spinal metastasis represents a negative prognostic factor or if such a finding should lead to a change in treatment management in selected patients. Typically, MRI spine is only indicated in patients with symptoms that are suggestive of spinal metastasis such as back pain. Given that spinal drop metastasis secondary to GBM is considered to be a highly unlikely occurrence, even in cases when patients present with radicular pain, this is typically not investigated or adequately managed.[17] In addition to radicular pain, typical presenting features of leptomeningeal metastasis are interscapular and neck pain, followed by increasing paresis with disease progression.[17] Leptomeningeal disease of the brainstem is likely to solely present with altered mentation and confusion.[17] Awareness of this may be of significance

as in some patients this may be the solitary indicator of spinal drop metastasis, as seen in leptomeningeal disease observed in the medulla of our patient.

In the majority of cases, patients with spinal drop metastasis remain asymptomatic, with pain radiation apparent in only 25% to 33% of cases.[18] This highlights the importance of considering the possibility of spinal drop metastasis in asymptomatic GBM patients and emphasizing the value of MRI spine even in such patients.

Typically, after spinal dissemination of GBM, patients rapidly deteriorate and management is primarily palliative. In some cases, radiochemotherapy regimens have been demonstrated to aid in symptom management.[19] Given the rapid deterioration of the patient, a biopsy of the spinal lesion could not be performed, leaving the possibility of an alternative diagnosis to GBM metastasis. Thus a prospective study to determine the incidence of metastatic GBM prior to surgery could be considered. The earlier detection of spinal drop metastasis as a delayed complication of GBM is important as it aids in decision-making regarding commencement of palliative care in preference to more aggressive treatments that would not necessarily improve patient outcomes.

CONCLUSIONS

A rare case of preoperative diagnosis of spinal drop metastasis in a patient harboring a GBM is presented. This case highlights the importance of recognizing the possibility of spinal drop metastasis in patients diagnosed with GBM prior to undergoing surgery. Therefore, routine MRI of the whole neuroaxis could be an important consideration in such patients as detection of spinal drop metastasis may function as a prognostic factor or provide guidance in treatment options.

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