Unusual Massive Spinal Metastases from a Recurrent Intracranial Glioblastoma Multiforme

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Received: 10 October 2012 / Accepted: 19 March 2013 / Published online: 2 April 2013
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Introduction

Glioblastoma multiforme (GBM) is a highly malignant primary brain tumor and is the most common primary malignancy of the central nervous system (CNS). It is also locally aggressive, invasive, and resistant to therapy. Extracranial seeding of GBM is very rare, but cerebrospinal fluid (CSF) seeding is observed in approximately 15–25 % of supratentorial GBM cases [1–3]. Spinal seeding of GBM metastasis is frequently observed in autopsy series, whilst symptomatic spinal metastases from primary GBM are rarely reported [3–5]. Here, we report the clinical features, radiographic findings, and management of a unique supratentorial GBM case presented with paraplegia secondary to massive spinal metastases.

Case Report

A 23-year-old female patient was admitted to our outpatient clinic with the chief complaints of headache and vomiting lasting for nearly 7 days. Furthermore, she has realized that she could not move her legs and has some urinary and bowel problems starting just on the morning of the outpatient clinic. The patient has a history of craniotomy surgery for frontal GBM followed by adjuvant radiotherapy and chemotherapy nearly 18 months

ago. Neurological examination revealed some confusion and recent memory deficits. She was paraplegic and had some sensory deficits under T1 dermatome. Cranial and whole spinal magnetic resonance imaging (MRI) examinations were performed. Cranial MRI showed a left frontal recurrent mass lesion (Fig. 1). Spinal MRI demonstrated multiple nodular mass lesions with intradural-extramedullary localization at the levels of C6-7 (24×10 mm), T4 (19×10 mm), T5-6 (36×12 mm), T7 (26×10 mm), and T10 (23×13 mm). The lesions were isointense on T1-weighted sequences, applying significant pressure to the spinal cord, and were hyperintense on T2-weighted sequences. The thoracic spinal cord thickness was increased and changes consistent with edema were exactly seen. Furthermore, hyperintense seeding was observed inside the cord on T2-weighted sequences at the level of T5-6 measuring 3×1 cm. Edema in the spinal cord between the levels of C3-4 and C6-7, and an extra-axial lesion of approximately 10 mm in diameter at the bulbous level were observed (Figs. 2 and 3). Therefore, the patient was treated with radiation therapy to the spinal axis and chemotherapy for this spinal metastasis. She was also included to a rehabilitation program. The patient developed a rapidly progressive respiratory difficulty and died within months.

Discussion

GBM is the most common and most malignant primary brain tumor that occurs in adults [6–8]. Spinal and extra-spinal metastases are rarely observed with this entity while intracranial relapses are very common. The reported spinal metastases rate of GBM is different in clinical reports and in autopsy series, but symptomatic cases like the one reported here are very rare in the literature [8–10].

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Fig. 1 **a** Histological examination of a tumor reveals it to be a glioblastoma multiforme. A specimen of GBM showing pleomorphism, moderate hypercellularity and necrosis (hematoxylin-eosin stain, $\times 100$). **b-c** Sagittal and coronal T2W images reveal postoperative

bone alterations in the left frontal lobe, and a heterogeneous solid mass lesion can be seen inside the parenchyma of the front left corpus callosum, showing signs of pressure/invasion, consistent with relapsed GBM

It is well known that tumors localized into the ventricles or very close to the cerebrospinal fluid (CSF), such as the medulloblastoma, ependymoma, germinoma, and brainstem glioma, can spread via the CSF [5, 9, 11]. However, GBM recurs in the previous region as a result of local invasion, but it rarely spreads via the CSF [1, 7, 11]. Sometimes ventriculoperitoneal and ventriculoatrial shunts are suspected for this type of metastases [7, 10, 11]. In addition, it has been reported that subtotally excised tumors contribute to metastasis [1–3].

Extracranial metastasis of GBM is extremely rare, with a reported frequency of only 0.5–2 % [3, 7]. The most common site is the lumbosacral spine, followed by thoracic and cervical regions. This phenomenon might reflect the effects of gravity and the natural flow of cerebrospinal fluid (CSF). Of note, some studies have reported that GBM can extraneurally metastasize to the lymph nodes, lungs, bones, liver, and other organs of the body [5, 7, 10].

In 1931, Cairns and Russell showed spinal metastasis in 8 of the 22 cerebral GBM patients they autopsied

Fig. 2 In sagittal T2W images of the cervical and thoracic spinal canal, metastatic masses with intradural, extramedullary spreading can be seen at the level of the cervicomedullary junction, at the C7 vertebrae alignment, between T4 and T7 (multiple lesions), and at the level of

T10 (metastasis of GBM through the subarachnoid space). A T2 signal increase is observed owing to pressure in the lower cervical and thoracic spinal cord and edema in the cord

Fig. 3 In T2W axial sections obtained from different levels of the thoracic spinal canal, intradural, and extramedullary metastatic masses are more clearly observed applying pressure to the cord and causing local edema

[6]. Furthermore, Onda et al. observed spreading of GBM via the CSF at autopsy in 14 of 51 patients that died after a diagnosis of GBM [11]. Yung and colleagues detected spinal subarachnoid spreading in 9 of 53 cerebral GBM patients, and Stark and colleagues reported spinal metastasis in 3 of 267 GBM patients [8, 10]. While the autopsy series ratio of metastasis from supratentorial gliomas to the spinal canal has been reported to be 20–40 %, few reports of symptomatic spinal metastasis are associated with decreased survival in patients [2, 5, 9]. Another possible explanation for the rarity of metastasis is that the meninges function as a barrier to infiltration of tumor cells through the CSF [1, 4, 5].

Hübner and colleagues reported a total of 36 cases of symptomatic spinal metastasis that derived from intracerebral high-grade tumors, in the literature [2]. However, factors that increase local parenchymal invasion or spreading via the CSF could not be clearly explained. The spread of glial tumors is dependent not only on the malignant properties of the tumor cell but also on the tumor cell's capacity to pass the pia mater and spread into the leptomeningeal space, its antigenic and metabolic factors, and its proximity to the subarachnoid space [1, 3, 9].

In their 14-case autopsy series, Onda and colleagues concluded that tumors that immunohistochemically stain negative for glial fibrillary acidic protein (GFAP) have a tendency to spread via the CSF, whilst tumors that stain positive for GFAP have a tendency to invade locally [11]. In our case, the result of GFAP staining for the histopathological evaluation of the tumor was negative.

Schwanger and colleagues observed predominantly paraparesis in 23 patients where spinal spreading was detected by clinical symptoms [5]. Paraplegia was also present in our patient. It has been reported that spinal spreading of GBM is more frequently observed in young patients [2, 3, 7]. Furthermore, some studies have reported that patients with spinal metastasis live for 1 year on average, but they die within 2–3 months after the onset of spinal

canal symptoms [1–3]. Similarly in our case, the patient died approximately 4 months after symptoms began.

For detecting the spinal seeding of primary CNS tumors such as GBM, computed tomography (CT), myelography, and cytological analysis of CSF can be used, but the best method for diagnosis is MRI [1, 2, 10]. Therefore, we used MRI for our patient's diagnosis and follow-up. Schwanger and colleagues performed lumbar punctures on 23 patients and found elevated protein levels in 6 patients, malignant cells in 3, both increased protein levels and malignant cells in 3, and normal results in just 1 patient; reliable information could not be obtained for 10 patients [5]. In cases where a diagnosis of spinal seeding is possible, MRI, which is a noninvasive method, should be supported by cytological analysis of CSF via lumbar puncture. The diagnosis should not be disregarded even though cytological analysis of CSF alone can occasionally yield a false-positive result [3–5].

The most commonly observed locations for spinal metastases arising from GBM are the lower thoracic, upper lumbar, and lumbosacral regions [2, 3, 9]. Symptoms of spinal leptomeningeal metastasis may include focal back pain, radicular pain, numbness, paraparesis, tetraparesis, sphincter dysfunction, and other symptoms referable to the intracranial tumors such as headache, seizures and nausea. In our case, metastases were located between the upper cervical and thoracic regions. For the treatment of patients in whom spinal seeding is detected, surgery and RT can be used [1, 5, 11]. In GBM, the average life expectancy after surgery and RT is 1 year. However, owing to new chemotherapeutic agents and surgery techniques such as neuronavigation, 5–25 % of patients can live for more than 1.5 years [2, 4, 5]. In patients with leptomeningeal spreading, death occurs 2–3 months after metastasis is diagnosed [3, 5, 9]. The patient in this case presented with spinal symptoms and findings only 1.5 years after diagnosis. In MRIs performed in the cervical, thoracic, and lumbar regions, leptomeningeal spreading in the spinal canal and metastatic lesions in the cervicothoracic junction were seen.

The occurrence of symptomatic spinal metastasis is more probable in young GBM patients, such as the one reported in this case. In GBM patients with spinal complaints, such

as lower back and neck pain, radicular pain, or the loss of strength, the possibility of spinal leptomeningeal spreading or metastasis should be kept in mind.

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