

Spine metastasis from glioblastoma multiforme: A case report

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Abstract

Primary brain and CNS tumor incidence is approximately seven per 100,000 individuals per year worldwide. Glioblastoma multiforme metastasis outside the CNS are extremely rare, occurring in <2% of patients, so therapeutic experience with these types of tumors is limited. Extracranial bone metastasis arising from glioblastoma multiforme are uncommon and mechanism of their diffusion is not well known. We report the case of a man affected by a glioblastoma who had a dorsal spine metastasis without any brain relapse after excision of cerebral glioblastoma multiforme and adjuvant radio-chemotherapy.

Keywords: glioblastoma; metastasis; CNS tumor

Introduction

Glioblastoma multiforme (GBM) accounts for about 50% of glial neoplasms and is the most common primary malignancy of the central nervous system (CNS) [1-2]. GBM is also the most aggressive brain tumor with poor prognosis and patients with GBM have a median survival time of about 14 months [3-4]. GBM metastasis outside the CNS are extremely rare, occurring in <2% of patients, so therapeutic experience with these types of tumors is limited [5-9]. Normally the brain is immunologically and anatomically separated from the body by the blood brain barrier. The spread from a GBM through the cerebrospinal fluid pathways follows the invasion of the ventricular cavity with consequent dissemination throughout the ventricular system and cerebrospinal leptomeninges as demonstrated in rare cases.

Herein, we report the case of a male affected by a GBM who had a dorsal spine metastasis without any brain relapse after excision of primary GBM and adjuvant radio-chemotherapy.

Case report

The patient is a 70-year-old male with no significant previous medical or surgical history, presented in June 2014 with a four month history of frontal headache and occasional vomiting. Neurological examination was entirely normal. A MRI of the brain was obtained, which showed an enhancing left fronto-temporal lesion (Figure 1). Ten days after diagnosis, a craniotomy was performed. After the bone flap was removed a tumor-infiltrated dura mater was exposed. A gross total resection was achieved. Post-operatively, no neurological deficits were detected.

Two days after surgery a new brain MRI was obtained (Figure 2), which demonstrated the total resection of the lesion. The final pathology report was GBM (WHO grade IV). The patient was discharged without any complications on the eighth post-operative day. He received adjuvant radiotherapy and chemotherapy treatment (60 Gy in 30 fraction and Temozolomide 75 mg/m² per Day) over six weeks period. A new MRI was performed one month after the end of Radiotherapy was negative for relapse. So patient was given six cycles of adjuvant Temozolomide at dose of 200 mg/m² for 5 days every 28. No relevant side effects were observed during this treatment.

One month after completing adjuvant chemotherapy the patient was referred to us with worsening pain at the dorsal spine and difficulty in walking for few weeks, so we performed a MRI of spine that highlighted an expansive lesion at the level of D11-D12, root canals, intradural and extramedullary right (Figure 3), there was no evidence of relapse of the central nervous system on brain CT

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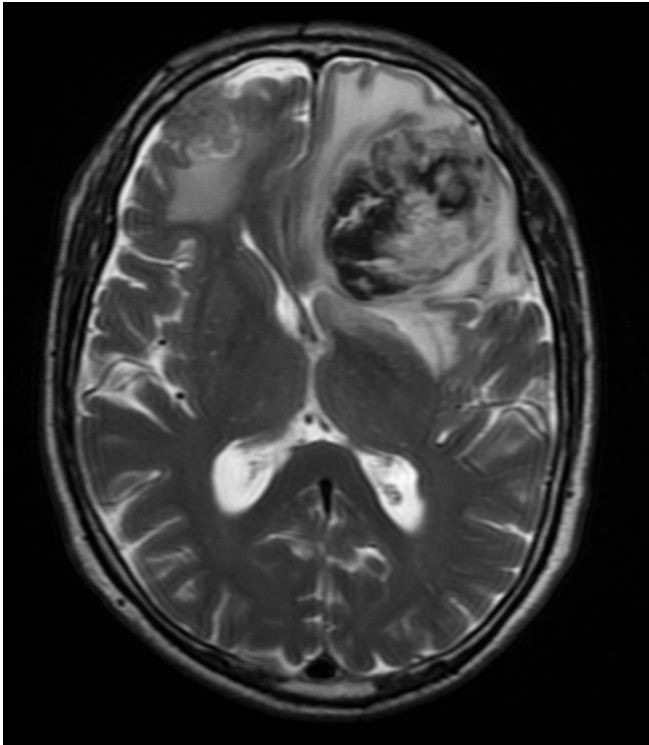


Figure 1 Axial contrast enhanced T2 brain MRI.

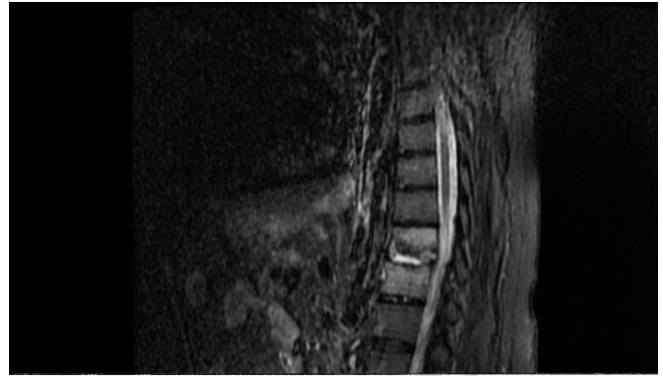


Figure 3 Sagittal stir MRI showing D11-12 lesion.

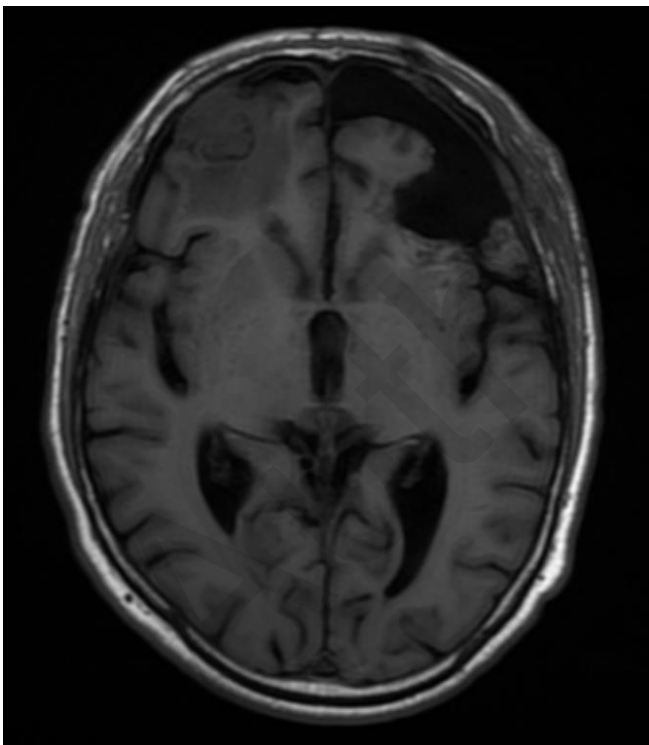


Figure 2 Post surgery T1 Flair brain MRI.

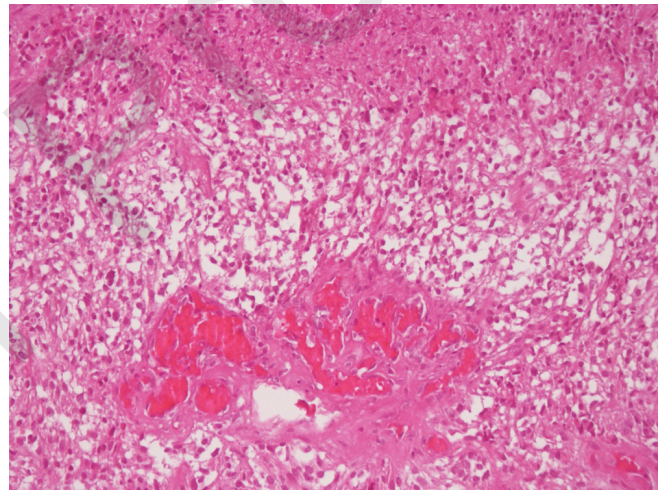


Figure 4a E/E 20x tumor with microvascular proliferation.

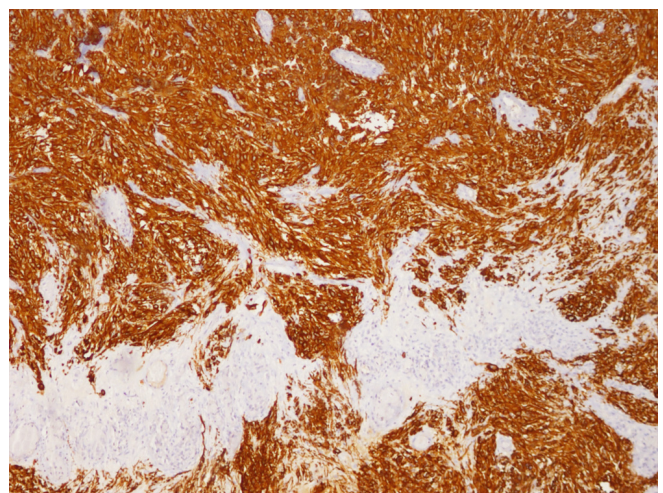


Figure 4b IIC10x = GFAP positive staining.

scan. No cytological examination of cerebrospinal fluid was done and on April 2015 the patient was subjected to surgery to remove the lesion and the subsequent histological examination showed a GBM (WHO grade IV) and immunohistochemistry of the lesion was positive for glial fibrillary acidic protein (GFAP) (Figure 4a, b). No post-surgery radiotherapy was performed and MRI examination performed during the follow up showed no evidence of brain or bone disease until now.

Discussion

Extracranial bone metastasis from GBM have been reported in the literature as single or multiple lesions [10-13]. When either extra-or intracranial metastasis occurs,

the median time from initial tumor diagnosis to recognition of metastasis is 8.5 months and the prognosis is bleak and nearly always leads to a fatal outcome and the mean survival time between diagnosis of dissemination and death is approximately 2 to 3 months [14]. The treatment is chiefly palliative. Radiotherapy is the most common treatment of choice, with a total dose of 25-40 Gy, which may provide pain relief and some improvements of neurological function, but no survival benefits. Chemotherapy has not found to be very useful to improve the overall survival. Surgery may be attempted if there is a symptomatic, large metastatic deposit causing cord compression [15-16]. In our case surgery was radical with excellent result.

Several theories on why GBM is rarely associated with extracranial metastasis have been proposed. According to one of those theories, due to the highly aggressive behaviour of GBMs, patients succumb to their intracranial disease before there is sufficient time for distant metastasis to develop. The majority of the patients succumb to GBM within 14 months, usually secondary to intracranial mass effect or invasion, sometimes with elevation of the intracranial pressure. Since metastasis is rare, systemic staging with body CT, MRI, or positron emission tomography imaging is not standard practice.

The blood brain barrier and the brain's lack of a lymphatic drainage system inhibit the spread of GBM cells but other potential pathways of GBM metastasis to extracranial sites exist. Besides the risk factors we listed, additional mechanisms of escape have been postulated, including vascular invasion, cranial nerve perineural spread, lymphatic spread, direct invasion, or iatrogenic spread into soft tissue.

Some authors reported that transfer of emboli could occur between the internal jugular vein, the thoracic duct and the right cervical lymphatic plexus, so that craniotomy seems to be the most accepted cause of metastasis of the primitive brain neoplasm [17-18].

Conclusion

Extracranial metastasis of glioblastoma remains a rare event. We must expect an increasing incidence, probably due to improvement in survival among these patients and better imaging techniques. Physicians must be aware of this complication and suspect spinal metastasis in all patients with a history of intracranial GBM who complain about symptoms or signs that cannot be explained by the primary lesion in spite of the rarity of this condition because the increase of survival in patients treated with a multimodality approach could lead to a higher incidence of extracerebral diffusion.

Conflicts of interest

The authors declare no conflicts of interest.

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