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Supratentorial glioblastoma multiforme with spinal metastases

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Abstract

Glioblastoma multiforme is the most common malignant brain tumor in adults. Metastasis of intracranial glioblastoma via the cerebrospinal fluid to the spine is a rare occurrence. We present two cases of glioblastoma multiforme with spinal leptomeningeal spread who presented with back pain and paraparesis.

Keywords: Glioblastoma multiforme, leptomeningeal metastasis, spine

INTRODUCTION

Glioblastoma multiforme (GBM) accounts for about 50% of glial neoplasms and is the most common primary malignancy of the central nervous system (CNS). Metastasis of intracranial GBM to the spinal cord has been described with increasing frequency in recent years. Autopsy series suggest that approximately 25% of patients with intracranial glioblastoma have evidence of spinal subarachnoid seeding, although the exact incidence is not known because postmortem examination of the spine is not routinely performed.[1,2] Symptomatic spinal metastasis from primary glioblastoma are rarely reported. We report two cases of symptomatic leptomeningeal metastasis from primary intracerebral glioblastoma.

CASE REPORTS

Case 1

A 51-year-old right handed male presented with headache, behavioral changes, and forgetfulness. A neurological examination revealed the patient to be disoriented to place and person with impairment of recent memory. He was unable to name objects and also had mild slurring of speech. Magnetic Resonance Imaging (MRI) revealed a solid and cystic lesion in the left temporal lobe with heterogenous contrast enhancement [Figure 1a]. The patient underwent a left temporal craniotomy with excision of the temporal tumor. Histopathology revealed GBM. Immunohistochemistry showed the tumor to have a MIB – 1 (Ki-67) proliferation index of 22–25%. The patient was subjected to radiotherapy dose of 60 Gray in 30 fractions over 6 weeks. He was also treated with adjuvant temozolamide. One and a half months later, the patient came back with severe backpain, paraparesis, and bladder-bowel incontinence. On neurological examination power in both lower limbs was grade 1-2 with a sensory level at T 10. A repeat MRI of the brain did not show any evidence of the tumor at the primary site [Figure 1b]. A post-contrast MRI of the spine showed leptomeningeal enhancement with nodularity [Figure 1c]. A diagnosis of leptomeningeal metastasis was made and the patient was subjected to palliative spinal radiotherapy. The patient succumbed within a month of radiotherapy due to complications of spinal metastases.

Case 2

A 22-year-old male presented with the complaints of headache and vomiting since 8–10 days. Neurological

examination revealed bilateral papilledema. Computed Tomography (CT) scan of the brain showed a partly cystic and partly solid lesion in the right posterior frontal region with enhancement on contrast. MRI scan showed a solid and cystic lesion with peripheral enhancement in the right posterior frontal region [Figure 2a]. A total excision of the right posterior frontal glioma was achieved by a right frontal parasagittal craniotomy. Histopathology revealed a glioblastoma multiforme. Postoperative CT scan confirmed a total excision of the tumor [Figure 2b]. The patient was subjected to radiotherapy and administered concurrent temozolamide. Three months after completion of radiotherapy the patient presented with fever, neck pain, and severe backache. Examination revealed neck stiffness with no neurological deficits. A CSF cerebrospinal fluid analysis did not reveal any abnormality. MRI of the spine showed diffuse nodular leptomeningeal deposits suggestive of spinal metastases [Figure 2c]. The patient developed a rapidly progressive quadriparesis with respiratory difficulty and succumbed to the illness within a week.

DISCUSSION

The prognosis of patients with leptomeningeal metastasis in cases of glioblastoma multiforme is bleak and nearly always leads to a fatal outcome with 75% of the patients dying almost within 18 months of the diagnosis.[3]

The ability of supratentorial GBM to metastasize along CSF pathways to the spinal cord was first described in 1931.[4] CSF dissemination occurs in 15 to 25% of cases of supratentorial GBM[1,5] but with a higher incidence of up to 60% for infratentorial GBM.[6] The rate of leptomeningeal metastasis in cases of GBM has been reported variably. In a study involving 600 patients with intracranial GBM, only 2% had symptomatic CSF tumor dissemination.[7] A review of literature by Erlich *et al.* in 1978 revealed only 14 well documented cases of spinal subarachnoid seeding.[1] Intramedullary spinal metastases are still rarer with only six cases reported till 2008.[8] However, in recent years the number of cases of spinal metastasis from primary intracranial GBM seems to be increasing. This might be due to improved diagnostic tools like CT and MRI,[9] prolonged survival time due to improved therapy,[9] or due to changes in the biological properties of tumors as a result of surgery, radiotherapy, and chemotherapy.[10]

The most common sites for spinal GBM metastases are the lower thoracic, upper lumbar, and lumbosacral regions.[11,12] The common sites of spinal metastasis are the nerve roots of the cauda equina, the root sleeves and the fundus of the thecal sac². Reports of intramedullary metastasis are quite rare in the literature.[12]

The most common clinical features of leptomeningeal metastasis are radicular pain in the upper and lower limbs, lower back, interscapular area, and neck.[4,13] This is frequently followed by paraparesis or, infrequently quadraparesis.[7] It has been suggested that the variability and lack of signs of leptomeningeal metastasis are because of the tumor cells infiltrating between nerve fibers rather than destroying them.[6,14] Once destruction has occurred, symptoms and signs are permanent.[7] Both of our patients initially presented with severe backpain and later progressed to paraparesis and quadriparesis.

Ventricular entry at operation, multiple resections and male sex were all associated with a statistically significant increased incidence of CSF dissemination in a study of supratentorial gliomas in children by Grabb *et al.*[15] Ependymal invasion, fissuring of the ependyma due to hydrocephalus, and fragmentation of the tumor in contact with CSF are also risk factors for CSF dissemination.[4] Repeated tumor resection is associated with an even greater risk of CSF dissemination, because of repeated tumor manipulation, more aggressive tumor cell types, and depressed immune function after radiotherapy and chemotherapy.[15] In both the patients the tumors were in close proximity to the ventricles and there was ependymal enhancement in the first patient. During surgery the ventricles were inadvertently opened in both the patients. This could explain the rapid dissemination in both the patients.

Previously, CT myelography was used in the diagnosis of leptomeningeal metastasis but spinal MRI with gadolinium enhancement is now the investigation of choice. Lumbar CSF cytology is not routinely used for diagnosis of spinal metastasis due to the high number of false negative results.[16] CSF analysis was done in case 2 as he had initially presented with fever, headache, and backache, but it did not reveal anything significant.

Treatment options for leptomeningeal metastasis are not very satisfactory. Surgery may be attempted if there is a

large metastatic deposit, but usually leptomeningeal metastases are not amenable to surgery due to the diffuse nature of the disease. In both of our patients there was diffuse involvement of the spine, hence surgery was not possible. Intravenous or intrathecal chemotherapy has not found to be very useful. The treatment of leptomeningeal metastasis is mainly palliative. External beam radiotherapy is the most common modality of palliation used, but it only causes pain relief with no improvement in neurological deficit. Although case 1 was given radiotherapy, the patient succumbed within a month's time, whereas in case 2 the patient succumbed to the disease before he could be started on radiotherapy.

Atalakis *et al.* have suggested that treatment modalities to prevent cerebrospinal fluid (CSF) dissemination should be part of the management of high risk patients with GBM.[17] They have suggested stereotactic biopsy with cranial irradiation and delayed resection and also the use of intrathecal radiolabelled monoclonal antibody as options.

The prognosis in patients with spinal metastasis is very poor and nearly always leads to a fatal outcome. The median time from diagnosis of the primary intracranial GBM to diagnosis of CSF tumor dissemination ranges from 8 to 14 months, median survival ranges from 11 to 17 months, and the average time interval between diagnosis of leptomeningeal metastasis and death is 2 to 3 months.[7, 15] Diligent surveillance must be maintained in the postoperative management of patients with GBM. Although treatment may not affect survival in these patients, it may improve the quality of life.

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Figures and Tables

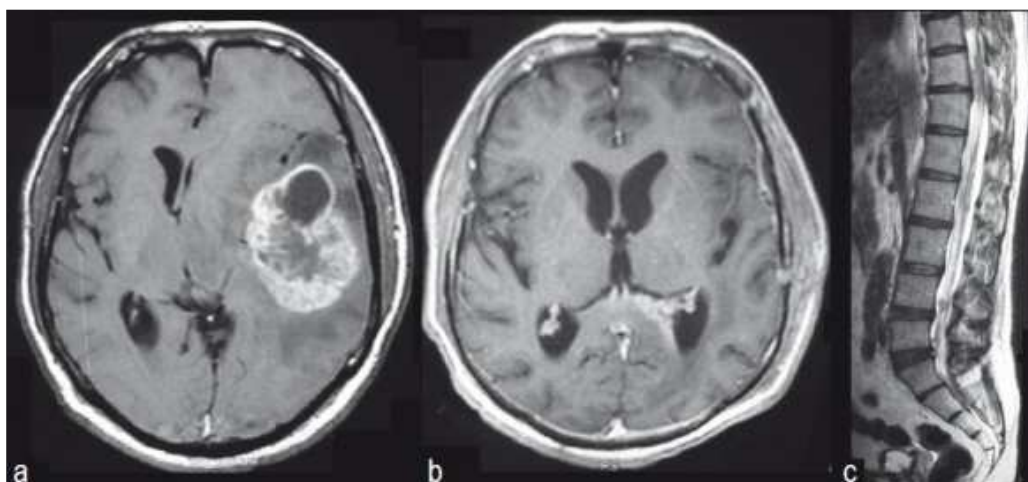


Figure 1

(a) Post-contrast axial magnetic resonance imaging (MRI) scan shows a heterogeneously enhancing left temporal tumor. Cerebral edema is noted around the lesion. There is early subfalcine herniation to the right and the ipsilateral ventricle is compressed. (b) Post-excision and adjuvant therapy post-contrast axial MRI scan demonstrates a complete excision of the left temporal tumor. Ependymal enhancement is noted within the left atrium and occipital horn. (c) Multiple nodules are noted in the lower dorsal and lumbar spine suggestive of spinal metastases

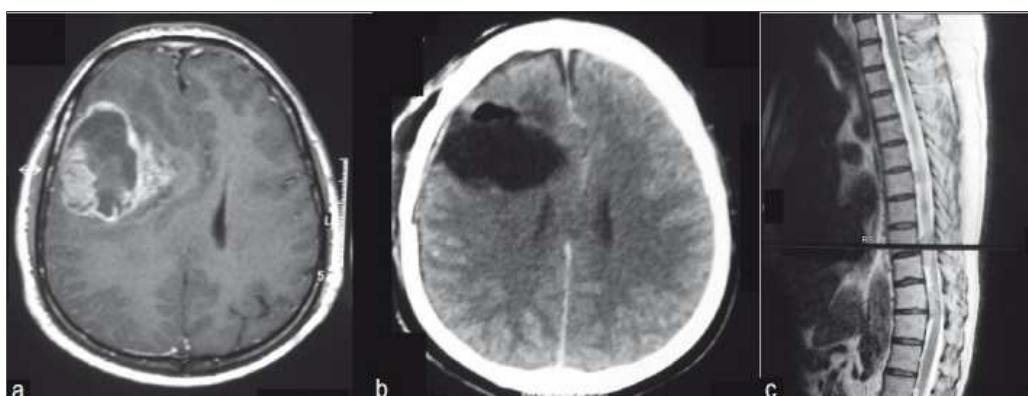


Figure 2

(a) Post-contrast axial MR scan demonstrates a malignant right frontal tumor with mass effect. (b) Post-contrast computed tomography scan shows a complete excision of the right frontal mass. (c) T2-weighted sagittal scan shows multiple nodules in the dorsal and dorsolumbar anterior subarachnoid space