Case Report

Cases of glioblastoma multiforme metastaosizing to spinal cord

Metehan Karaca, Meltem Nalca Andrieu, Ayse Hicsonmez, Yildiz Guney, Cengiz Kurtman

Department of Radiation Oncology, Ankara University Faculty of Medicine, Cebeci Hospital, Dikimevi Ankara, Turkey

Cases of glioblastoma multiforme (GBM) metastasizing to the leptomeninges or the intramedullary spine are quite rare and prognoses are relatively poor. We present three cases of GBM with spinal metastasis, one of which also had leptomeningeal dissemination. Three patients with GBM were admitted to our clinic for postoperative radiotherapy after surgery. Leptomeningeal metastasis and dissemination were diagnosed with magnetic resonance imaging. Radiotherapy provided only temporary relief from pain with small improvement in neurological deficit but no survival advantage.

Key words: Glioblastoma multiforme, intramedullary metastasis, leptomeningeal dissemination, radiotherapy

Introduction

Glioblastoma multiforme (GBM) is the most common primary malignancy of the central nervous system (CNS). Cerebrospinal fluid (CSF) seeding is observed in approximately 15-25% of cases of supratentorial GBM,[1-3] while a higher incidence is seen in patients with infratentorial GBM.[3] However, the exact incidence of CSF seeding is still uncertain because autopsy is not performed routinely. In addition, CSF cytology is not useful due to the high number of false negative results.[4]

Case Reports

Case 1

In February 2004, a 67-year-old man presented with a history of headache and disarthria of two months duration. Brain MRI demonstrated a contrast-enhancing lesion with edema measuring 7.5 x 5.5 x 5 cm in the left temporal lobe. Gross total resection was performed. Histopathological findings showed GBM (WHO Grade 4). After surgery, cranial radiotherapy (RT) was delivered with a total dose of 60 Gy in 2-Gy fractions. The patient complained of left leg weakness and back pain in the second week of RT. After a complete neurological examination and radiological evaluation, tumor recurrence in the operation field and a new lesion in the prepontine interpeduncular system were found [Figure 1]. Also, thoraco-lumbar spinal MRI revealed an expansive intramedullary lesion at the T11-L1 junction measuring 3.5 x 2 x 1 cm in diameter [Figure 2]. After palliative external radiotherapy to T10-L2 with a total dose of 21 Gy in 3-Gy fractions, neurological findings were diminished. Additionally, two cycles of CCNU adjuvant chemotherapy were given. One month after the end of RT, control MRI demonstrated no progression of the lesion.

Figure 1: The leptomeningeal implant in prepontine interpeduncular system (from first case)

Figure 2: An expansive intramedullar lesion at T11-L1 junction (from first case)

Yildiz Guney
Department of Radiation Oncology, Cebeci Hospital, Dikimevi Ankara, Turkey. E-mail: yildiz_guney@yahoo.com
Although good local control and palliation of symptoms were achieved with RT, the patient survived only about four months after diagnosis of metastases.

**Case 2**

In November 2003, a 20-year-old woman was admitted to the emergency unit with a history of headache and diplopia. After radiological evaluation, a lesion measuring 3.5 x 3.5 x 2.2 cm from the left lateral ventricle to the frontal lobe was found. Gross total resection was performed. Histopathological findings showed GBM. Postoperative cranial RT was delivered with a total dose of 60Gy in 2-Gy fractions. There was no complaint for one year after RT. However, at the last visit, the patient complained of left foot pain. After a thorough neurological examination and radiological evaluation, tumor recurrence in the operation field was found in December 2004. Also, lumbar MRI showed multiple lesions at the lowest thoracic and upper lumbar vertebral region and between fibers of cauda equina, but concurrent CSF study was negative [Figure 3]. Palliative RT to T12-L2 with a total dose of 30Gy in 3-Gy fractions was delivered in January 2005. Good palliation was achieved with RT, but the patient died in June 2005.

**Case 3**

In January 2003, a 28-year-old woman was admitted to the emergency unit with a history of headache and sudden weakness of the right side. After radiological evaluation, brain MRI demonstrated a contrast-enhancing lesion measuring 7 x 3.5 x 4.5 cm in the left frontal and parietal lobe. Gross total resection was performed. Histopathological studies showed GBM (WHO Grade 4). Postoperative cranial RT was delivered with a total dose of 60Gy in 2-Gy fractions. She received temozolamid as concurrent chemotherapy. After surgery and RT, there was no symptom or complaint for 17 months. Although a small residual lesion was found in all control MRIs, it was stable. At the last control in June 2005, the patient complained of lower limb weakness and intradural-extramedullar lesions at T6 (5-6 mm), T8 (10-12 mm), T9 (7 mm) and T12-L1 (3 x 1.5 x 1 cm) were found by MRI. In consideration of the high performance status of the patient and no change in the diameter of the primary lesion during the 17-months period of postoperative cranial RT, spinal RT was to be delivered to the limit dose of the cord. Palliation of symptoms was achieved with RT, but the patient died in September 2005.

**Discussion**

The most common clinical features of leptomeningeal metastases are radicular pain in the upper and lower limbs, lower back, interscapular area and neck. This is frequently followed by paraparesis or, infrequently, quadraparesis.[5] Accordingly, our patients presented with pain during leptomeningeal dissemination.

The most common sites for spinal GBM metastases are the lower thoracic, upper lumbar and lumbosacral regions.[6] Reports of intramedullar metastases are quite rare in the literature.[3] Since patients with GBM usually do not live long enough for small tumor implants to grow to the symptomatic size, it is difficult to clinically evaluate symptomatic metastasis. The rate of spinal leptomeningeal seeding after diagnosis of GBM has been variably reported. A review of the literature by Erlich and Davis in 1978 revealed only 14 well-documented cases of spinal subarachnoid seeding from primary intracranial GBM since 1931.[5] In a study of 600 patients with GBM, only 2% had symptomatic CSF seeding.[6] This result suggests that the symptomatic involvement occurs relatively late in the course of GBM. In our cases, metastases were diagnosed in the 2nd, 12th and 17th months after RT, respectively. Stark et al[8] reported three patients (1.1%) of 267 adult cases of GBM who developed spinal drop metastases 5, 8 or 11 months after craniotomy. The incidence of symptomatic metastasis is certainly lower than the incidence observed postmortem. Most of the large series describe patients with meningeal and spinal spread discovered at autopsy. Metastases, which were associated with pain and/or neurological deficit, were usually verified by radiological studies. We suspected CSF spreading because of back pain and neurological deficit during RT. Magnetic resonance imaging findings demonstrated the dissemination of disease in Case 1.

Until recently, myelography with CT follow-up was the most accurate diagnostic test for leptomeningeal metastasis,[9] but CT myelography has now been replaced with MRI. Spinal MRI with gadolinium enhancement is the current investigation of choice for leptomeningeal metastasis.

Although there is still no satisfactory treatment for leptomeningeal metastasis, RT is the most commonly used treatment modality, with a total dose of 25 to 40Gy. Because of the diffuse nature of the disease, leptomeningeal metastasis is often unsuitable for surgical decompression. The advantage of intravenous or intrathecal chemotherapy has not been proven for intramedullary metastasis. Because curative treatment is not applicable, the treatment modality for these patients is solely palliative. Our patients were treated with a total dose of 21 Gy,
39 Gy or 46 Gy and good palliation of symptoms was achieved. Leptomeningeal metastasis with CSF tumor dissemination almost always results in 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 two to three months. As mentioned by Fakhrai et al.,[10] survival periods are shorter in patients who have GBM with spinal seeding and these patients should be given adequate palliative care. One of our patients survived about four months after the diagnosis of metastasis, but the time between the initial diagnosis of GBM and leptomeningeal dissemination was only about two months. To our knowledge, Case 1 is only the second case reported in the literature with simultaneous leptomeningeal and intramedullary metastases. In conclusion, cases of GBM with recent extremity and back pain and/or associated spinal root nerve signs should cause clinicians to consider leptomeningeal and/or spinal dissemination of GBM.

References


Accepted on 23-05-2006
Source of Support: Nil, Conflict of Interest: None declared.