Abstract. The extraneural diffusion of malignant gliomas is not frequent and some authors have reported single or multiple bone metastases from glioblastoma contemporary to the time of primary cerebral tumor or accompanying relapse on the brain. We report the case of a man affected by a glioblastoma who had a lumbar spine metastases without any brain relapse after excision of cerebral glioblastoma multiforme and brain radiotherapy.

Extracranial bone metastases arising from glioblastoma multiforme are uncommon and the mechanism of their diffusion is not well known. Metastatic diffusion has been documented in association with the presence of primary tumor or with the relapse of the central nervous system also after treatment (surgery, radiation and chemotherapy). The spread from a glioblastoma through the cerebrospinal fluid pathways follows the invasion of the ventricular cavity with consequent dissemination throughout the ventricular system and cerebrospinal leptomingeas as demonstrated in rare cases. Some authors have reported extraneural diffusion at the time of primary cerebral tumor or accompanying relapse on the brain (1-3).

We report the case of a male long-survivor affected by a glioblastoma who had a lumbar spine metastases without any brain relapse after excision of cerebral glioblastoma multiforme and brain radiotherapy.

Case Report

In March 1997, a 43-year-old white man with a two-month history of persistent cefalea underwent a Magnetic Resonance (MR) of the brain that showed a mass in the right temporal area; after a negative total body CT scan, in April 1997 the patient was submitted to right temporal craniotomy and a glioblastoma multiforme was radically excised. Postoperative radiation therapy (Linear Accelerator 10MV – total cGY 6000) was performed. In January 1998, the patient entered an Italian multi-istitutional trial including association therapy of melatonina, bromocriptine, retinoid acid and somatostatine (4).

In June 2000, the patient had a sudden lumbar spine pain; a bone scan (Tc-99m) demonstrated a focal abnormal uptake of the first lumbar vertebral body. The MR showed a diffuse hypointensity and a dishomogeneous hyperintensity signal of the body of the first lumbar vertebra in T1 and in T2, respectively (Figure 1). There was no evidence of relapse of the central nervous system on brain CT scan.

In October 2000, the patient was submitted to somatectomy of the first lumbar vertebra; the histology documented metastasis by glioblastoma multiforme and the immuno-histochemistry of the lesion (immunoperoxidase preparation) was positive for glial fibrillary acidic protein (GFAP). The patient received radiotherapy on the first lumbar vertebra (total cGy 3800).

The MR examinations performed during the follow-up showed no evidence of brain or bone disease until September 2002, when a brain MR demonstrated the presence of two extrassial lesions showing homogeneous enhancement after Gadolinium-injection (Figure 2); a MR of lumbar spine documented a bone metastases on the left peduncle of the thirld lumbar vertebra (Figure 3). The brain lesions were excised and resulted as atypical meningiomas. After the surgery, the patient had radiotherapy on the fourth lumbar vertebra (total cGy 3800).
Discussion

Extracranial bone metastases from glioblastoma multiforme have been reported in the literature as single or multiple lesions (1-3, 5). This is an interesting case because it is the first one that has reported distant metastases without cerebral tumor relapse from a removed glioblastoma multiforme. Despite the theory of the "blood-brain" barrier that sets apart the central nervous system from the body (6), extracranial metastasis can be found in the lung (60%), nodes (51%), bone (30%) and liver (22%) (7-8). After craniotomy the direct permeation of the
meningeal venous system by the tumor could be possible. The anatomic distribution of the vertebral venous system, that connects with the abdominal and portal system, could facilitate metastasis in the mediastinal and abdominal lymph node.

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 metastases of the primitive brain neoplasm (9, 10).

In Pasquier’s cohort of patients (9), eight were not submitted to craniotomy and Myers et al. (3) reported a metastatic glioblastoma case without surgery on the brain; thus, the diffusion of the disease could be explained by vascular invasion caused by locoregional radiation therapy.

Secondary tumors are a well known, long-term complication, induced by radiotherapy, that is very unusual in malignant glioma patients due to their poor prognosis. We observed, in this long-survivor patient, two atypical meningiomas in the radiation field.

Conclusion

Our case of spine metastasis, from previously excised glioblastoma multiforme with no recurrence to date, could be due to cellular diffusion through the meningeal venous system occurring after surgery, even if this case is very uncommon due to the length of disease-free time and survival or widespread disease without any brain relapse.

Systemic disease of malignant glioma is not frequent, but the increase of survival in patients treated with a multimodality approach could lead to a higher incidence of extracerebral diffusion.

References


Received March 15, 2004
Accepted June 7, 2004