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# Glioblastoma Multiforme Presenting as Osteoblastic Metastatic Disease: Case Report and Review of the Literature

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Glioblastoma multiforme is an extremely aggressive intracranial neoplasm that usually causes death prior to the occurrence of extraneural metastases. While extraneural metastases have occasionally been reported in association with this tumor after intervention (surgery), radiation, or chemotherapy, such cases are extremely rare. We present the case of an 11-year-old girl who initially presented with widespread osteoblastic metastases.

## Case Report

An 11-year-old girl presented with a 4-week history of nausea, vomiting, and diffuse bone and joint pain. This was preceded by a 6-month history of intermittent headaches. On physical examination, the patient was noted to have unequal pupils, papilledema, and hyperreflexia. Noncontrast and contrast-enhanced CT and MR imaging revealed masses in the suprasellar cistern and quadrigeminal plate/ambient cistern complex (Fig. 1A). A separate lesion was seen in the medial occipital lobe (Fig. 1A). An MR scan of the craniovertebral junction demonstrated an additional finding of a mass (Fig. 1B). A chest radiograph performed during the initial evaluation of the patient showed diffuse sclerosis of the ribs. Focal areas of sclerosis in the proximal humeri were also noted. One week after a CSF shunt placement, an anteroposterior radiograph of the abdomen revealed diffuse bony sclerosis (Fig. 2). A bone scan subsequently revealed multiple foci of increased activity corresponding to the sclerotic lesions noted on plain films. A complete (cervical, thoracic, and lumbar) myelogram demonstrated multiple intradural, extramedullary masses in the lumbar area. Biopsy of one of these lumbar masses prompted the diagnosis of glioblastoma multiforme (thought to represent a drop metastasis) (Fig. 3). To evaluate the bones and bone marrow for a biopsy site, an MR of the lower femurs was performed (Fig. 4). Biopsy of the distal left femur and bone marrow confirmed the presence of metastatic glioblastoma multiforme.

## Discussion

Before the first documented case of extraneural spread of a glioma was reported by Davis in 1928 [1], it was thought that cerebral tumors did not metastasize extracranially. Since

that time, there have been numerous case reports and studies of extraneural spread of primary intracranial neoplasms. Metastases have now been reported to nearly every organ and system. While there are a few reports of metastases prior to intervention [2–5], nearly all cases have been reported after surgery and/or radiation therapy. The lungs and pleura (43%), lymph nodes (30%), bone (14%), and liver (13%) are the most common sites of metastases [6–8].

In a review by Wisiol et al. [9], six (26%) of 23 cases of glioblastoma multiforme with extraneural spread exhibited bone involvement; Pasquier et al. [5] reported bone involvement with extraneural spread in 22 (30.5%) of 72 cases. The bone involvement seen with glioblastoma multiforme can be osteolytic [7–9] or osteoblastic [10, 11]. In most cases bone involvement is limited to one or a few sites, with diffuse metastases being quite uncommon. Schatzki et al. [10], Newman et al. [11], and Yung et al. [7] have recently reported cases of diffuse bone metastases, although these occurred after intervention. Our case represents a particularly rare situation in which the glioblastoma multiforme presented with extraneural spread prior to intervention and was manifested by diffuse osteoblastic involvement.

The reason for extraneural spread of glioblastoma multiforme prior to intervention is not well understood. A critical factor appears to be access to the extrameningeal tissues. Liwnicz and Rubinstein [6] stated that this access could possibly be gained directly from invasion of the vascular supply by glioblastoma multiforme, through surgical procedures (and possibly from radiation or chemotherapy), or from metastases to the CSF pathways. As previously noted, our patient had extensive metastases throughout the CSF pathways with deposits in the intracranial cisterns, the craniovertebral junction, and lumbar dural sac.

This case expands the current literature and documents the radiographic spectrum of glioblastoma multiforme. Extraneural metastases, though uncommon, do occur and may present even in the absence of prior surgical intervention or radiation therapy.

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Fig. 1.—Axial MR image (2000/80) of brain at level of quadrigeminal plate (QP) cistern (A) and midline sagittal image (1800/90) (B).

A, Areas of abnormally increased signal can be seen in the midline within QP cistern and extending laterally to left toward retropulvinar cistern. Cortex adjacent to trigone of left lateral ventricle is also involved (curved arrow). A separate area of abnormally increased signal can be seen in medial occipital lobe on left (open arrow).

B, Sagittal T2-weighted image shows abnormal signal within suprasellar cistern (curved arrow) as well as a focus posteriorly within craniovertebral junction (arrowhead).

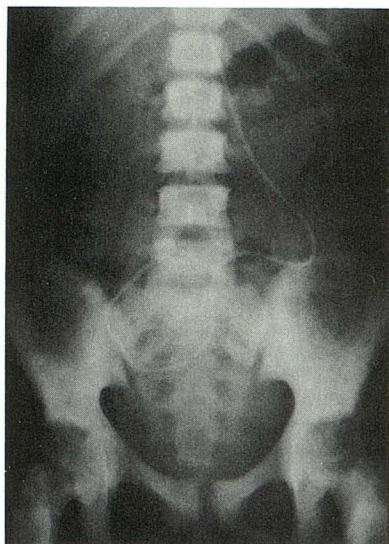
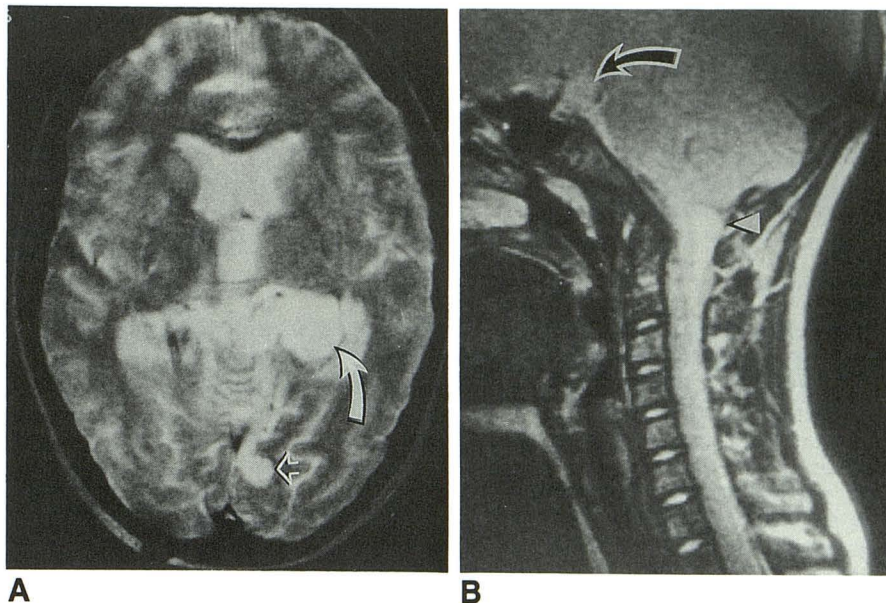


Fig. 2.—Plain radiograph, frontal view, of abdomen after placement of CSF shunt tube shows diffuse bony sclerosis involving vertebral bodies, pelvis, sacrum, and proximal femurs.

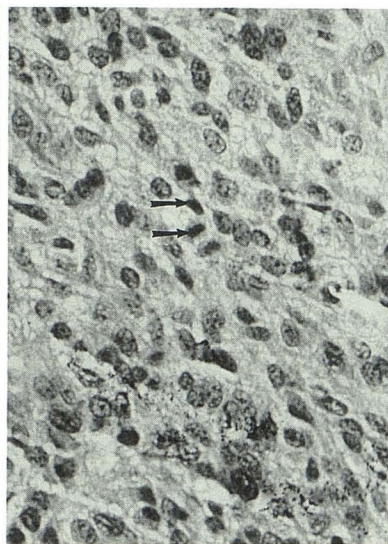


Fig. 3.—Photomicrograph of stained specimen from biopsy of a mass in lumbar area shows cellular pleomorphism and a high mitotic rate (two mitotic figures are shown, arrows). A glial fibrillary acidic protein (GFAP) stain of these biopsy specimens was positive. (H and E  $\times 40$ )

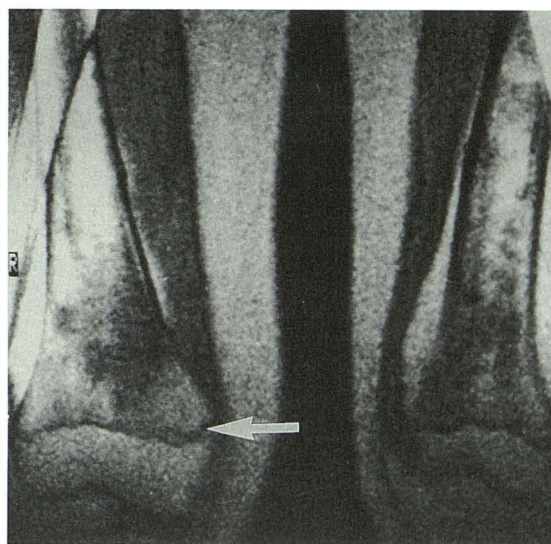


Fig. 4.—Coronal MR image (750/30) of distal femurs shows inhomogeneous signal from within cortex and marrow space. These changes are more prominent in the metaphysis. Note the limitation of the process by the physis (arrow), which spares the epiphysis.

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