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Clinical Study

Vertebral collapse with quadraparesis due to metastatic gliobla multiforme: case report and review of the literature

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Abstract

A case is reported of a patient rendered quadraparetic following collapse of a cervical vertebra due to neoplastic invasion by metastatic glioblastoma multiforme. The case is discussed in light of a review of the world literature regarding the clinical incidence and significance of metastasis of glial tumors. It is recommended that all patients with high grade glial tumors who complain of back pain be evaluated with plain radiographs and MRI of the spine or ^{99}Tc bone scan. The management of pathologic spine fractures from metastatic glial tumors with accompanying spinal instability or spinal cord compression due to intracanalicular bone should aim for immediate surgical decompression and stabilization followed by involved field irradiation.

In recent years, the adage that gliomas do not metastasize extraneurally has been shown to be incorrect. To date, such metastases have been rare and of little consequence, being either purely incidental or having only minimal relevance to the course of the patient. Here we present a case of a cervical vertebral metastasis which profoundly influenced the patients status and his medical treatment.

Case report

A 42 year old white male arose from bed and stumbled, falling onto a couch and then to the floor. He was unable to stand up and was transported to the Emergency Department where he was found to be quadraparetic with a C6 level.

His past medical history was remarkable for a right posterior temporal lobe glioblastoma multiforme which had been treated with subtotal resection 9 months previously, succeeded by limited field external beam irradiation (total dose of 60 Gy) in conjunction with the radiation chemosensitizer hydroxyurea, followed by sequential BCNU chemotherapy (total of 3 courses). There had been no interval progression of his glioma, either by neurological exam or CT scan of the brain. He also had suffered an injury to his cervical and lumbar spine 2 years previously which was without neurological deficit and unremarkable radiographically. Two months previously, he had complained of increased upper and lower back pain and had undergone MRI scanning of these regions which had revealed only degenerative disc disease. His back pain complaints stabilized as diffuse discomfort and stiffness. He had been seen in Neuro-Oncology clinic 4 days prior to admission, prior to initiating his fourth cycle of

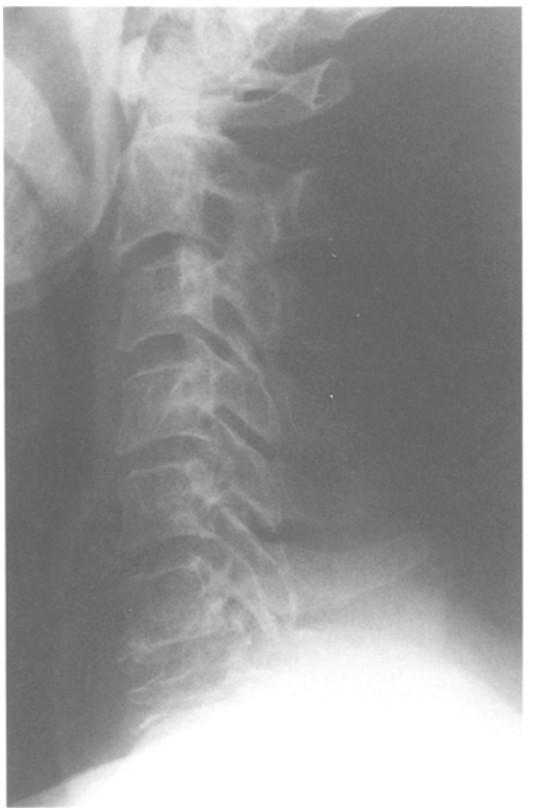

Fig. 1. Lateral cervical spine radiograph obtained upon admission, demonstrating collapse of C7 with anterior soft tissue swelling. The low bone density and irregular, inhomogeneous appearance of the fracture suggested its pathological origin.

chemotherapy, where his neurological exam and CT of the brain were stable.

Upon admission, physical examination demonstrated an awake, alert, fluent man with a flaccid quadriparesis and C6 sensory level. Normal laboratory studies included a chest radiograph, CBC with platelets, chemistry panel, PT, and PTT. A 99mTc MDP bone scan revealed increased uptake at the C7 lesion and in the region of the previous craniotomy. His plain cervical spine radiographs (Fig. 1) demonstrated a C7 burst fracture with unusual lucency at the involved level which, in light of the inconsistently mild mechanism of injury, was felt to be suspicious of a pathologic fracture. A CT scan confirmed lytic changes in the C7 vertebral body, pedicles, and transverse processes with retropulsion of bone. There was also evidence of a surrounding soft-tissue mass.

The patient underwent an anterior C7 vertebrectomy and, when it was recognized that the inferior border of C6 was also involved, a partial corpectomy was performed at this level. When intra-operative frozen section histology was felt consistent with metastatic glioblastoma multiforme, stabilization with methylmethacrylate was performed, using intramedullary threaded and recurved Steinmann pins to anchor the cement. This was followed by posterior interspinous wiring from C6 to T1 with methylmethacrylate fusion (Fig. 2). The patient tolerated the procedure well and was mobilized without external orthosis.

Histological examination of the permanent sections demonstrated a highly cellular spindle cell proliferation with a whorled pattern (Fig. 3A). There were occasional atypical or giant nuclei and mitotic figures and scattered areas of necrosis. By itself, the H&E preparations were consistent with a dedifferentiated tumor of uncertain origin. Immunohistochemistry for GFAP was strongly positive (Fig. 3B), however, confirming the tissue as glial in origin. Permanent sections from the prior craniotomy were reviewed and demonstrated glioblastoma multiforme with focal spindling of tumor cell nuclei in a manner similar to that seen in the metastatic tissue.

At the time of discharge, the patient had regained much proximal strength in his upper extremities but his hands, as well as both of his lower extremities, remained densely paretic. He complained of very little post-operative neck discomfort. He received 3000 cGy to the C5-T2 area with a local boost to 3600 cGy at C7.

The patient survived 14 months after discharge, eventually succumbing to his intracranial disease. During this period, he declined continued 'conventional' therapy for his intracranial disease, turning to 'holistic treatment'. He had very little neck discomfort and no clinical or radiographic evidence of cervical instability or metastatic disease at other spinal levels. He regained sufficient use of his legs to ambulate with difficulty using a walker but his hand function did not show significant recovery. There was no post-mortem examination.

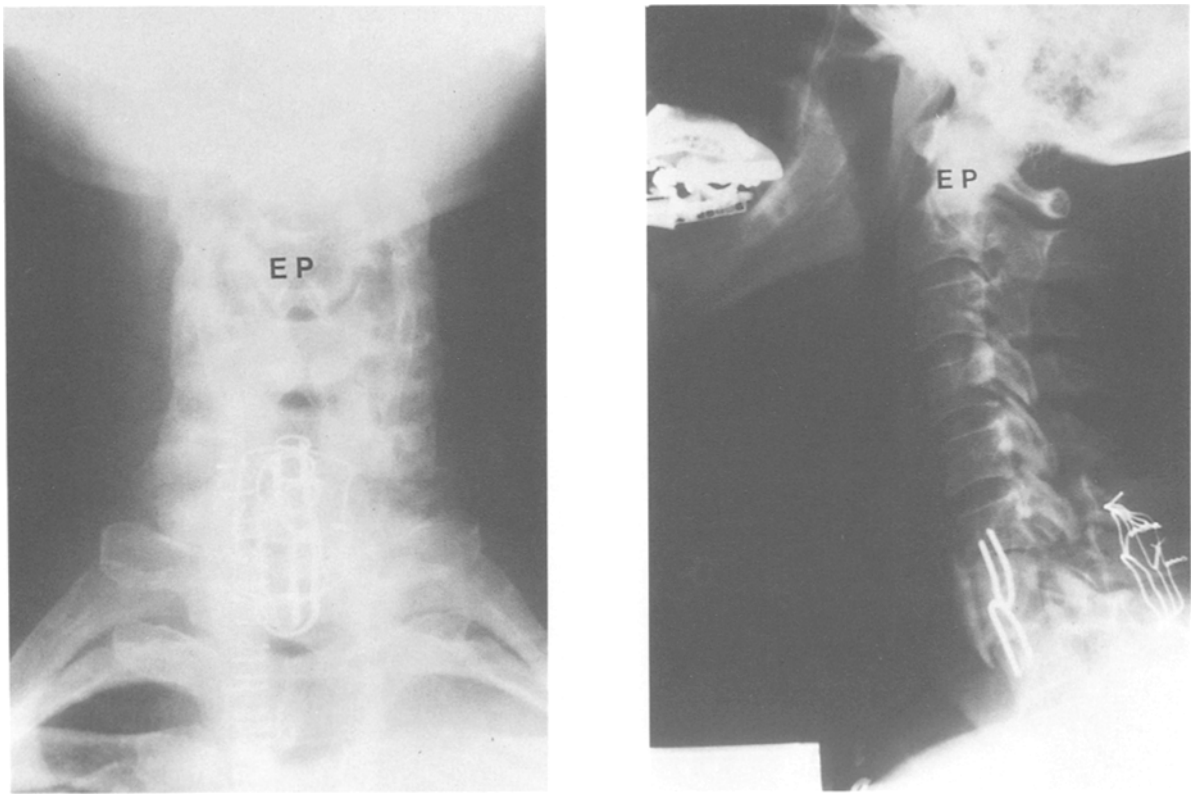

Fig. 2. AP and lateral post-fusion radiographs. Recurved, intramedullary Steinmann pins were placed into the bodies of C6 and T1 in order to anchor the methylmethacrylate used to replace the body of C7. Posterior interspinous wiring with methylmethacrylate fusion was then performed from behind. Postoperatively, the patient was managed without external orthosis.

Discussion

In their famous treatise, published in 1926, Bailey and Cushing stated that tumors of the central nervous system, with the exception of medulloblastomas, do not metastasize to extra-neural sites [2]. There are now, however, over 100 reports in the world's literature of cases wherein documented tumors of glial origin have been found outside of the central nervous system. Favorite sites for metastases appear to be lung and lymph nodes, each occurring in approximately 50% of patients with metastatic glioblastoma multiforme, and bone and liver, appearing in approximately 25% of these patients [20, 29]. Notably, vertebrae are involved in 72.7% of instances of bone metastases, making the spinal axis the most common site [20].

A review of the world's literature for reported cases of histologically proven metastases of glial tumors to the vertebrae documented 28 cases [1, 4, 5, 7–9, 11–17, 23–29, 32, 33]. In the vast majority of these metastases, the marrow of the vertebra was involved as a manifestation of metastatic spread to the hematopoietic system which appears to be the mechanism of vertebral involvement. Over half of these cases have been asymptomatic (17 of 28), being discovered during screening with plain radiographs (1 case) or bone scan (1 case) or when necropsy uncovered varying degrees of vertebral marrow replacement (15 cases). In 11 patients (39%), the patient complained of pain in the region of the axial skeleton involved by tumor. In 3 such cases, the pain and vertebral metastases were located at a point where there was also tumor within the spinal canal, generally with accompanying neurological deficit [4, 12, 28]. The precise relationship between

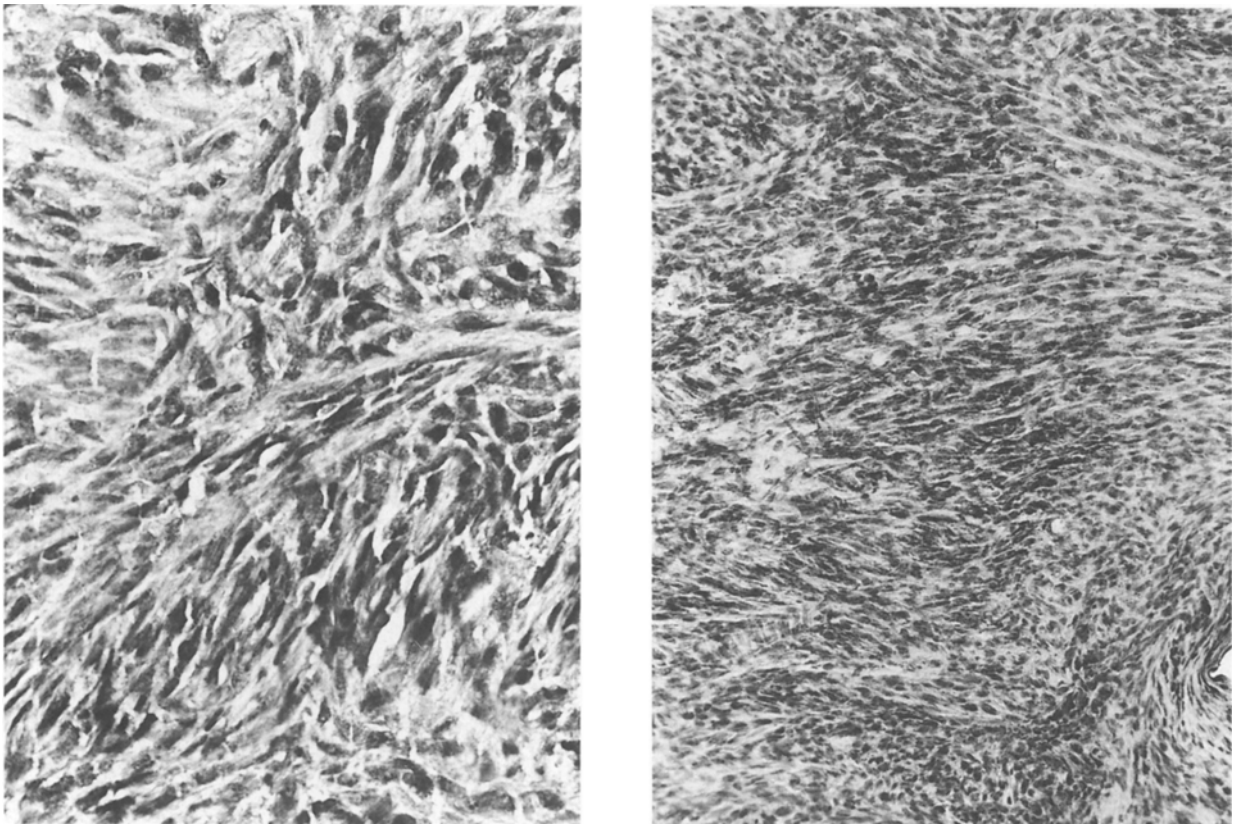

Fig. 3. A) H&E preparation of the permanent sections of tissue from C7 demonstrate a highly cellular spindle cell proliferation with a whorled pattern. Nuclear atypia is apparent and mitotic figures are seen. B) GFAP immunohistochemical staining of tissue from the same block. The tumor was intensely and diffusely positive throughout, represented here as dark granular staining in the cytosol, thereby confirming the glial origin of the tissue and the metastatic nature of the lesion.

the intracanalicular and the vertebral tissues is variable. Three reports have found vertebral tumors that have been directly associated with soft tissue masses [12, 28, 32], resulting in cord compression and neurological compromise in two cases [12, 28]. In other cases, however, intracanalicular tumors and vertebral tumors have been found in isolation, even in the same patient [17]. This suggests that metastatic involvement of the spinal neuraxis by high grade gliomas may arise from extraspinal metastases with intracanalicular extension via the neural foramen, by extradural metastases, by epidural extension of a vertebral metastasis, or by meningeal gliomatosis [10, 21].

Vertebral lesions may be discovered by bone scan, generally accompanied by other lesions in the long bones or pelvis and often in conjunction with evidence of diffuse marrow involvement. In several cases, the marrow involvement was so widespread as to result in diffusely increased uptake throughout the skeleton, resulting in a scan that lacked specific 'hot spots' and could easily have been interpreted as normal [15, 25]. Notably, however, bone scans were normal in 3 cases with vertebral metastases [5, 17]; in one instance in the presence of radiographically demonstrated tumor [17].

In the majority of patients, no radiographic abnormalities were reported. In those cases with bone metastases of any type, lesions could be either osteolytic, [5, 7, 11, 24, 32, 35] osteoblastic, [9, 15, 16, 25] or mixed [19]. For patients with vertebral metastases, the radiographic findings were either discovered pursuant to patient symptoms or lesions found on bone scans or incidentally. In the two cases

where CT findings were presented and discussed, there was internal destruction in the vertebral body, extending into the pedicle in one case, but no evidence of collapse or instability [17, 24]. In no cases were vertebral collapse, segmental instability, or neurological compromise reported. Our case appears to be the first instance of these factors arising in the situation of a high grade glioma metastatic to the spine.

Review of patients with vertebral metastases found that exitus occurred within 6 months of presentation of the vertebral lesion (range of 48 hr to 6 months; mean of 2.6 months) in the 10 cases wherein this information was available. It therefore appears that the surgical management of these patients is limited and is applicable only to patients with spinal instability or spinal cord compression due to intracanalicular bone. In these instances, patients may benefit from decompression and fusion in a manner offering immediate stability rather than reconstruction with a bone-graft construct which will require at least 12 weeks to become stable. Aggressive treatment in our patient reflected the limited extent of disease (solitary bone metastasis with stable primary tumor), patient age, and the lack of co-morbid medical conditions. Furthermore, outcome is improved in patients with metastatic epidural spinal cord disease treated with surgical decompression and involved field radiotherapy [22, 30, 31].

The characteristic nature of these tumors **not** to metastasize has been the subject of some debate. One of the major suggested barriers has been the inhospitable environment afforded by the extraneural tissue for the growth and reproduction of the metastatic glial cells. Nevertheless, glial tissue has demonstrated that it can survive outside of the central nervous system, via inadvertent implantation at the time of surgery, [3, 7] through various types of CSF shunting pathways, [4, 18, 33] and by extracranial explantation [3, 28, 34]. Of greater importance, however, has been the distinctly limited survival times for patients with glial tumors. This is the major contributing factor in the lack of manifestation *in vivo* of glial extraneural implants later found at necropsy by not allowing sufficient time for the metastatic tissue to grow to symptomatic proportions.

The true interest of this case lies in its chronology. Although the first extraneural metastasis of glial tumors was reported as early as 1928 [6], the number of cases has recently increased exponentially. Typically found at necropsy, an increasing number of cases have appeared documenting glial metastases which are diagnosed during life. This would appear to correspond with our slowly evolving ability to extend the post-diagnosis survival times for these patients. This is corroborated by Smith's report that the mean survival from time of first craniotomy in patients with metastases of any sort from glial tumors was 18 months [29]. As the present case is the first in which the metastatic tissue had proliferated to the extent that it resulted in vertebral collapse, it is suggested that this is the natural result of increased survival time and may represent a harbinger of increasing manifestations of glial metastases during life in this patient population.

We suggest that the possibility of extra-cranial metastatic disease in patients with high grade glial tumors be entertained when they present with evidence of a second site of proven or suspected neoplastic involvement. Patients complaining of bone pain should be particularly suspect and should undergo both plain radiography and MRI or bone scanning. As false negatives have been reported, repeating these studies at a later date should be considered if the patient's complaints are persistent. In questionable cases, or patients with concomitantly abnormal hematological profiles (not attributable to adjuvant chemotherapy), bone marrow biopsy may be helpful, as the hematopoietic system appears to be a favorite site for metastasis.

In the instance of metastases, attention should be directed at both the presumed metastatic site and the site of primary tumor. Treatment of extraneural metastatic disease required consideration of the roles of surgery and radiation therapy and, in the instance of vertebral lesions, the question of spinal stability and intracranalicular bone should be addressed. An extent of disease evaluation should be undertaken in addition to consideration of systemic chemotherapy in patients with evidence of extraneural glial metastases.

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