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Postradiation gliosarcoma with osteosarcomatous components

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Abstract A 49-year-old man developed a gliosarcoma with prominent osteoid components 15 months after surgical resection and postoperative radiation and chemotherapy for a right frontal glioblastoma multiforme. The recurrent tumor was distinguished from the original lesion by the presence of dense ossification, visible on CT, at the original tumor site. The relevant literature is reviewed.

Keywords Gliosarcoma · Glioblastoma multiforme · Radiation injury

Introduction

The side effects of central nervous system irradiation, such as radiation necrosis, mineralizing microangiopathy, arteritis and progressive leukoencephalopathy, are well known. Several radiation-induced tumors have been described, including leukemias, lymphoma, thyroid cancer and peripheral fibrosarcoma. Radiation-induced intracranial lesions have also been reported, including neoplasms (the most common being meningioma [1]), cavernous angiomas and telangiectasia [2]. Gliosarcoma has primarily occurred following radiation therapy for pituitary adenomas and extracranial tumors such as lymphoma and leukemia [3, 4]. Predominance of osteoid-chondral elements within gliosarcomas is extremely rare, only three cases having been reported [5, 6, 7].

Case report

A 49-year-old man developed progressively worsening headaches, confusion, left-sided tonic/clonic seizures, and left leg weakness 15 months after treatment for a multicentric glioblastoma multiforme. At the time of the original diagnosis, he had presented with headaches, nausea, vomiting, and blurring of vision. CT and MRI had revealed two irregular ring-enhancing lesions in the right frontal lobe with surrounding edema (Fig. 1a, b). A stereotactic brain biopsy, followed by a right frontal craniotomy and resection disclosed glioblastoma multiforme. MRI and CT 2 days after the surgery showed no residual tumor. Postoperatively, the patient received external beam radiation therapy, 5900 cGy over 44 days, by a linear accelerator with bilateral parallel opposed fields on the frontal lobes, followed by chemotherapy with carmustine, procarbazine, and carboplatin over 3 months. He remained neurologically stable following treatment.

The patient underwent bimonthly CT, and approximately 2 months after the initial surgery, a new focus of nodular contrast enhancement in the genu of the corpus callosum was found, consistent with recurrent disease. By 13 months after completion of radiation therapy, new calcific densities were seen on CT within the right frontal lobe. Over the next 2 months, these were followed by CT and considered to be dystrophic, secondary to radiation therapy.

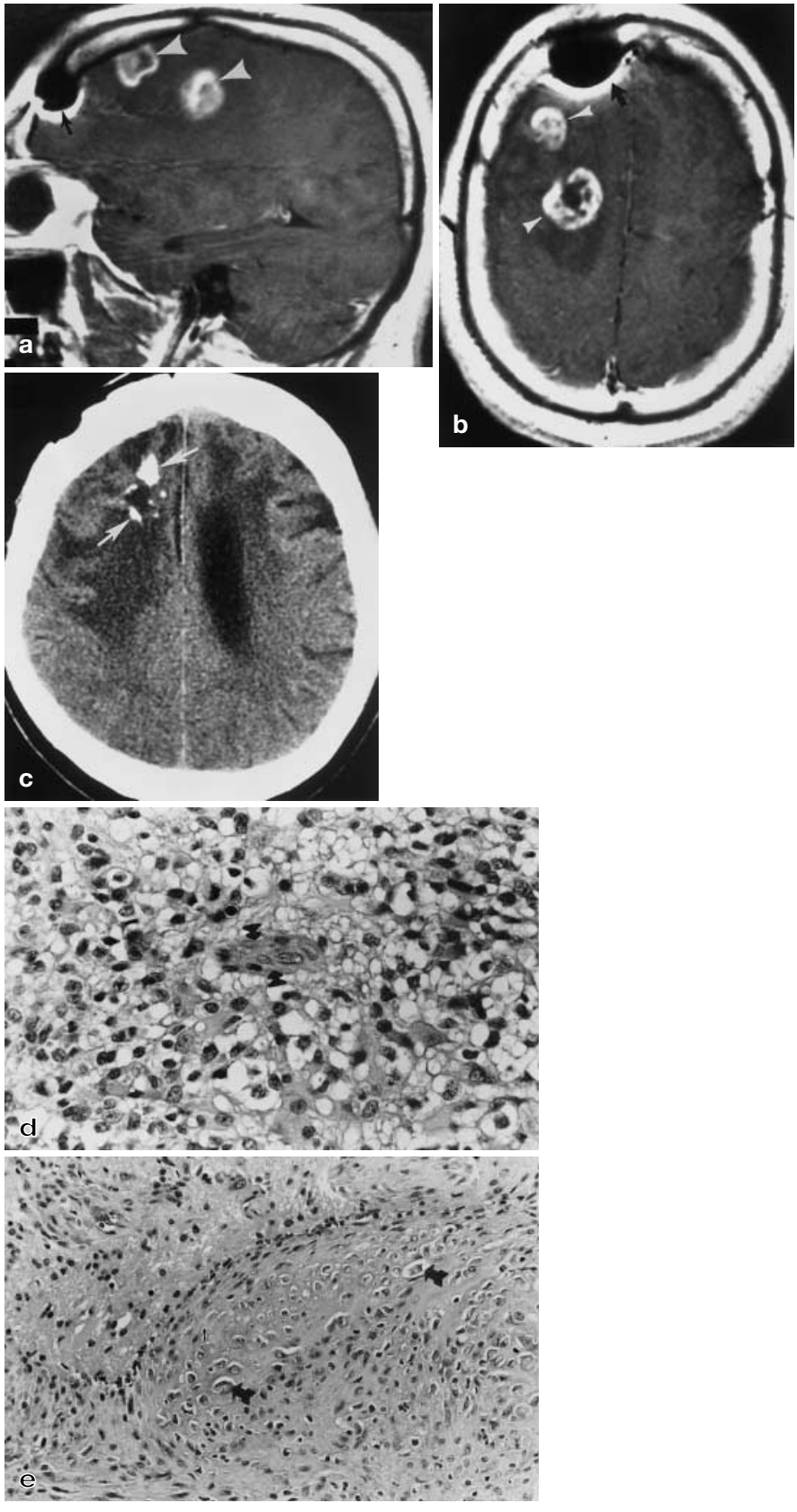

Fig. 1 a, b Contrast-enhanced sagittal and axial T1-weighted sagittal images at initial presentation demonstrate two right frontal ring-enhancing lesions (*arrowheads*). Ferromagnetic artifact (*black arrow*) is due to a tiny metallic foreign body in the scalp. **c** CT through the mid-frontal lobes at the time of recurrence demonstrating a cluster of calcific densities in the region of the previous surgical resection, above the right lateral ventricle (*white arrows*). **d** Photomicrograph of glioblastoma component showing pleomorphic astrocytes with fibrillar processes and vascular hyperplasia (*black arrows*) (hematoxylin and eosin, original magnification × 400). **e** Photomicrograph of osteosarcoma component showing highly atypical neoplastic cells (black arrows) within the lacunar spaces of an osseous matrix

At the time of a second admission 15 months after surgery, CT showed the calcific densities within the surgical bed to be increasing in size and number, with surrounding edema and mass effect (Fig. 1 c). The differential diagnosis included postradiation dystrophic calcification, tumor recurrence and a new primary neoplasm. The patient underwent a right frontoparietal craniotomy with frameless stereotactic guidance for resection of the lesion. Postoperatively, he developed a dense left hemiplegia; and was discharged to hospice care and succumbed to the tumor 24 months later.

Gross pathology of the second tumor resection revealed most of the tissue to be necrotic, with indistinct margins. Microscopy revealed a distinctly dimorphic tumor-cell population. The dominant morphology was that of a typical glioblastoma composed of diffusely infiltrating fibrillary cells with pleomorphic, hyperchromatic nuclei, numerous mitotic figures, vascular proliferation, and necrosis (Fig. d), similar to the original glioblastoma. The second component was sarcomatous, containing cells with spindle-shaped or irregular nuclei and scant eosinophilic cytoplasm in a prominent background of abundant osteoid and bone (Fig. 1 e). The neoplastic spindle cells were seen singly within lacunar spaces and in small aggregates within the osteoid matrix and invading the overlying meninges. Reticulin and trichrome staining highlighted these sarcomatous regions, that were absent throughout the glial component. These histological studies revealed a new tumor, a predominately osseous gliosarcoma. There was no evidence of sarcomatous regions, especially the osteoid components, in the first operative specimen.

Discussion

Gliosarcoma is an uncommon primary malignant brain tumor containing neuroectodermal and mesenchymal elements [8], first reported in 1895 by Strobe, as a glioblastoma with sarcomatous components [9]. In 1955, Feigin and Gross [10] presented a detailed review of its pathology. It is usually supratentorial, most commonly in the temporal lobes. There is a predilection toward a peripheral location with contact with the dura mater, falx cerebri or skull [11]. This tumor has an age distribution similar to that of glioblastoma multiforme, occurring primarily in adults, most often in the fifth through seventh decades. Like glioblastoma multiforme, it spreads by direct infiltration and has a poor prognosis [11]. Extracranial metastases are more common than with glioblastoma multiforme, occurring in 15–30 % of cases [11].

Gliosarcomas are malignant neoplasms of the central nervous system that contain gliomatous and sarcomatous components. Histologically, the neuroectodermal or glial component is identical to that of a typical glioblastoma. The mesenchymal or sarcomatous portion is usually comprised of spindle-shaped cells which are cytologically malignant, usually a fibrosarcoma [8]. There may also be prominent neoplastic smooth muscle elements, occasionally endothelial cells and rarely bone or cartilage components within the sarcomatous component [8].

CT findings are variable; the tumours can resemble meningiomas, being denser than brain, due to their high vascularity and cellularity [11]. Unlike meningiomas, gliosarcomas are usually not homogeneously dense, do not have a dural attachment and are almost always associated with edema. They show prominent homogeneous or irregular ring enhancement [11, 12]. The MRI appearances are also variable. On T1- and T2-weighted images, they have inhomogeneous signal due to necrosis and hemorrhage, but are usually isointense with brain parenchyma on T2-weighted images, with prominent irregular enhancement [13]. Angiography displays a prominent vascular stain with neovascularity and early cortical venous drainage; the blood supply is pial or pial and dural [14].

The etiology of gliosarcoma remains uncertain. It is recognized that gliomas can induce sarcomatous transformation in the supporting mesenchymal elements [15]. Feigin et al. [16] suggested that the sarcomatous portion may arise directly from neoplastic transformation of the vascular elements within a glioblastoma. It is well known that irradiation of the central nervous system may cause the development of malignant parenchymal and meningeal tumors, predominantly fibrosarcomas. The carcinogenic effect of radiation therapy in the etiology of gliosarcomas may occur by inducing neoplastic transformation of the vascular or astrocytic reactive component of the original tumor [4]. Several criteria have been established for showing a causal relationship between radiation therapy and the occurrence of a neoplasm [17]: a sufficiently long latent period between the irradiation and detection of the second tumor; the latter tumor must be in the irradiated field; the histology of the second tumor must be different from that of the initial one; and a family history of tumor diathesis, such as neurofibromatosis or tuberous sclerosis, must be excluded. A review of the literature on possibly radiation-induced gliomatous and/or sarcomatous brain tumors [4] revealed a latency period range for possible radiation induced gliosarcomas of 1–12 years and gliosarcomas occurring after doses ranging from 10 to 58 Gy. Another review on cerebral gliosarcomas [18] revealed a mean time from irradiation to diagnosis of gliosarcoma of 38 weeks. In our case, the patient underwent received 59 Gy over 44 days and the occurrence of the gliosarcoma was 52 weeks after the completion of the therapy. The gliosarcoma was in the radiation field. Pathological findings of this new gliosarcoma included anaplastic glial cells positive for glial fibrillary acidic protein and a sarcomatous area containing reticulin- and trichrome-staining regions along with vascular proliferation. The sarcomatous and osteoid components were not present in the original glioblastoma multiforme. Chondroid or osteoid components, as in this case, may arise by dedifferentation or from a multipotential precursor. As regards to the last criterion, our patient had no personal or family history of a tumor diathesis. In addition to meeting the established criteria,

the occurrence of such a histologically unusual tumor, a gliosarcoma with primarily osteoid components, supports the proposition of a radiation-induced neoplasm.

Despite its rarity, postirradiation gliosarcoma with osteosarcomatous elements should be considered in the differential diagnosis of new calcific densities within a prior tumor bed. Other considerations should include recurrent tumor or dystrophic calcification secondary to surgery, chemotherapy or radiation therapy. Mineralizing microangiopathy with secondary dystrophic calcification of the adjacent gray matter has been reported as a specific histopathologic sequel of radiation-induced damage to the cerebral microvasculature [19, 20]. Positron electron tomography with 18F-fluorodeoxyglucose has been reported to differentiate between postoperative and/or postradiation changes and recurrent tumor [21, 22]. Our case is unique in that the original neoplasm was a glioblastoma multiforme and the recurrence was a possibly radiation-induced gliosarcoma with as its primary component an osteoid matrix.

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