Gliosarcoma With Liposarcomatous Differentiation
The New Member of the Lipid-Containing Brain Tumors Family

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Gliosarcoma is a rare, biphasic brain tumor composed of glioblastoma multiforme and sarcomatous components. Various types of sarcomatous differentiation are described in this tumor: fibrosarcomatous, malignant fibrous histiocytoma-like, chondrosarcomatous and osteosarcomatous types. We report an extremely unusual variant of liposarcomatous differentiation in gliosarcoma in 72-year-old woman. Fat cells were presented by atypical multivacuolar and monovacuolar lipoblasts, stained positive for S100. p53 that was positive in both glial and mesenchymal cells of the tumor were negative in the lipoblasts. To the best of our knowledge, this is the first report in the literature of liposarcomatous differentiation in gliosarcoma.

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Materials and Methods
Paraffin sections of the tumor were stained with hematoxylin and eosin and for reticulin. Immunohistochemical stains included S100 (1:2000), glial fibrillary acidic protein (GFAP) (1:1800), smooth muscle actin (1:1200), CD31 (1:60), CD34 (1:50) (all from DakoCytomation, Glostrup, Denmark), and p53 (1:600) (Zymed Laboratories, San Francisco, Calif).

Pathologic Findings
Pathologic examination of the tumor revealed 2 components: 1 typical glioblastoma multiforme (Figure 2, a)
with extreme cellular polymorphism, numerous mitotic figures, necrosis, and endothelial vascular proliferation; the other component was associated topographically with the vascular proliferation areas, showing a pattern of spindle cell sarcoma (Figure 2, b). The cells of this portion of the tumor were negative for CD31 and CD34 staining, excluding their endothelial origin; few of the cells were positive for smooth muscle actin. The biphasic nature of the tumor was clearly emphasized by GFAP, S100, and reticulin staining (Figure 2, c and d). Within the areas of sarcomatous differentiation, clusters of and individual fat cells were present in the form of monovacuolated and multivacuolated lipoblasts, a typical finding for liposarcoma (Figure 3, a and b). The lipoblasts were positive for S100 protein (which is usually positive in fat cells), contrary to the negative-staining background sarcomatous areas (Figure 3, c). The GFAP was negative in the lipoblasts, as well as in the entire sarcomatous component of the tumor. The cells of glioblastoma and the sarcomatous components of the tumor showed diffuse strong positivity for p53 in their nuclei. The lipoblasts were negative for p53 (Figure 3, d).

**COMMENT**

Gliosarcoma is a rare tumor, presenting in 0.48% of all intracranial tumors and 2% to 4.9% of glioblastoma cases.1 The presence of nonglial sarcomatous portions in these tumors was explained by malignant transformation of the hyperplastic vascular elements.2 The studies of Boerman et al,7 Horiguchi et al,8 and others demonstrate that both glial and nonglial compartments of gliosarcoma bear the same genetic abnormalities, thus showing evidence of their common origin, probably from pluripotential stem cells. The usual structure of the sarcomatous portion of the tumor resembles fibrosarcoma or malignant fibrous histiocytoma,1 but various other lines of mesenchymal differentiation have been described in gliosarcoma.

We report an extremely unusual variant of liposarcomatous differentiation in gliosarcoma displaying clusters of and isolated lipoblasts in the sarcomatous portion of the tumor. The lipoblasts demonstrated multivacuolar or monovacuolar pattern and atypical nuclei, and were S100 positive, as are “usual” fat cells. The GFAP staining was negative in the lipoblasts and in the entire sarcomatous component of the tumor.
Fat-containing tumors of the brain are very rare and may be divided into 2 groups: lipid-rich tumors without lipocytes and tumors with lipocytes or lipocyte-like cells. The first group includes tumors with intracytoplasmic accumulation of lipids and xanthomatous appearance of cells, as in pleomorphic xanthoastrocytoma and the extremely rare, heavily lipidized glioblastoma multiforme.\(^9\) The second group includes lipomas\(^{10,11}\) and lipomatous hamartomas,\(^12\) neuroectodermal and glial tumors with an admixture of fat cells: lipomatous medulloblastoma,\(^{13,14}\) neurocytoma and lipomatous primitive neuroectodermal tumors with a glioblastoma component, and lipoastrocytoma.\(^15\) The latter tumor has been described in pediatric patients and presents as low-grade astrocytoma with pronounced transformation of tumor cells.

Generally, all tumors with a lipomatous component that have been reported in the literature contain mature fat cells. In our patient, the lipocytes were highly atypical multivacuolar and monovacuolar lipoblasts, typical of liposarcoma. They were negative for GFAP (contrary to the lipocytes in cases of lipoastrocytoma) and were S100 positive, as is usually typical of lipocytes. According to recent molecular studies, all cellular components of gliosarcoma are derivatives of pluripotential progenitor cells. The interesting finding in our case is the absence of p53 staining in the lipoblasts, contrary to diffuse and strong staining in both glioblastoma and sarcoma components of the tumor. It could be that the lipomatous differentiation occurs in the population of tumor cells devoid of the p53 mutation.

In conclusion, the tumor in our case presents a variant of gliosarcoma with liposarcomatous divergent differentiation. This unique type of differentiation has not been described previously and expands the spectrum of possible divergent mesenchymal differentiations in this rare brain tumor.

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References