Histogenesis of sarcomatous component of the gliosarcoma: an ultrastructural study

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Received May 4, 1990/Revised, accepted July 10, 1990

Summary. This report describes the ultrastructural findings of the sarcomatous component in five cases of gliosarcoma. The tumor contained a heterogeneous population of cells with collagen scattered in the interstitium. Three main cell types were found: histocyte-like cells, fibroblast-like cells and undifferentiated cells. The histocyte-like cells had oval nuclei, short and flat rough endoplasmic reticulum, prominent Golgi apparatus, lysosomes, phagocytic vacuoles, ruffled cytoplasmic membrane with filopodia, segmental basal lamina and occasional intercellular junctions. The fibroblast-like cells had elongated nuclei, prominent cisterns of rough endoplasmic reticulum and microfilaments. The undifferentiated cell cytoplasmic processes suggesting differentiation toward histiocyte-like cell. In addition, intermediate cells, myofibroblasts, multinucleated giant cells and xanthomatous cells were also present. Occasional glial processes were interposed between tumor cells. Some were enclosed by cytoplasmic processes of histocyte-like cells and others engulfed within the cytoplasm. Capillary showed surface infoldings, fenestrations of endothelial cells, thickened basal lamina, occasional pericytes and scattered collagen. Some capillaries were surrounded by aggregating histiocyte-like cells and undifferentiated cells. The present findings suggest that (a) the sarcomatous component in gliosarcoma is likely derived from undifferentiated cells with a broad differentiation into histiocytic, fibroblastic and other cell types, (b) endothelial cells and pericytes may not participate in sarcomatous development, (c) capillaries within the sarcomatous component are of non-gliomatous type, and (d) the histiocyte-like cells are capable of phagocytizing glial elements.

Key words: Gliosarcoma — Glioblastoma — Histiocyte-like cell — Fibroblast-like cell — Undifferentiated cell

Since the detailed histological description by Feigin and Gross [5] in 1955 and Rubinstein [33] in 1956, gliosarcoma (GS) has been accepted as a malignant mixed tumor of glial and sarcomatous components [19, 25, 27, 34, 35]. While the glial component is well recognized as glioblastoma, the histogenesis of the sarcomatous component remains unclear. Previous histological [6, 19, 27, 34], electron microscopic [1, 2, 4, 31, 44], immunohistochemical [21, 23, 39, 44] and tissue culture [12, 36, 44, 29] studies have resulted in varying interpretations of the origin of the sarcomatous component. Endothelial cells [6, 12, 31, 39, 44], pericytes [1, 16], myofibroblasts [4, 16], adventitial fibroblasts [19, 34] and differentiated gliomatous cells [23, 24] have been suggested as the origin of the sarcomatous component. Recent immunohistochemical studies have stressed that histiocytic cells may play an important role in its development [11, 17, 26]. This report describes the ultrastructural features of the sarcomatous component in five cases of GS. The aim of this study is to document the morphology of the principal cell types, their relation to the capillaries and correlates these findings with the published immunohistochemical characterizations of the sarcomatous component. The histogenesis of the sarcomatous component of GS is discussed.

Materials and methods

Twelve cases of GS were found in the pathology files of Henry Ford Hospital from 1966 to 1990. The histological and immunohistochemical criteria for the diagnosis of GS was discussed in the previous report [26]. In five cases, tissue blocks available for electron microscopic study contained a sarcomatous component (Table 1). Cases 2 and 4 were included in the previous report [26].

Brain biopsies were obtained on all five cases. A portion of the surgical specimen was minced into 1-mm slices and immersed in cold 3.5% glutaraldehyde. The specimens were then rinsed in buffer and postfixed in 1% osmic acid and dehydrated in graded alcohols. Two were embedded in Epon and three in araldite resin. Sections (2 μm) stained with toluidine blue were used to select areas from which thin sections were prepared and stained with uranyl acetate and lead citrate. Sections were examined in a Zeiss transmission electron microscope.
# Table 1. Clinicopathological data of gliosarcoma

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/sex</th>
<th>Location</th>
<th>Histology of sarcomatous components</th>
<th>Ultrastructural findings of sarcomatous components</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38/M</td>
<td>Lt. thalamus</td>
<td>MFH</td>
<td>HLC: +; FLC: +; UC: +; IC: -; MF: -; MNGC: +; XC: +; GT: +</td>
</tr>
<tr>
<td>2</td>
<td>45/M</td>
<td>Rt. temporal</td>
<td>Fibrosarcoma</td>
<td>HLC: +; FLC: +; UC: +; IC: +; MF: +; MNGC: -; XC: -; GT: -</td>
</tr>
<tr>
<td>3</td>
<td>60/M</td>
<td>Lt. temporal &amp; meninges</td>
<td>MFH</td>
<td>HLC: +; FLC: +; UC: +; IC: +; MF: +; MNGC: +; XC: +; GT: +</td>
</tr>
<tr>
<td>4</td>
<td>75/M</td>
<td>Rt. temporal</td>
<td>MFH with osteoid area</td>
<td>HLC: +; FLC: +; UC: +; IC: +; MF: +; MNGC: +; XC: +; GT: +</td>
</tr>
<tr>
<td>5</td>
<td>77/M</td>
<td>Rt. temporal</td>
<td>MFH with histiocytoid areas</td>
<td>HLC: +; FLC: +; UC: +; IC: +; MF: +; MNGC: +; XC: +; GT: +</td>
</tr>
</tbody>
</table>

Lt.: left; Rt.: right; MFH: malignant fibrous histiocytoma; HLC: histiocyte-like cell; FLC: fibroblast-like cell; UC: undifferentiated cell; IC: intermediate cell; MF: myofibroblast; MNGC: multinucleated giant cell; XC: xanthomatous cell; GT: glial tissue; +: present; -: absent

Case 3: Glioblastoma in 1988, followed by radiation therapy and chemotherapy, and GS in 1989

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**Results**

Because of histological and sampling variations, there were ultrastructural differences from one case to the next (Table 1). The sarcomatous component contained a heterogeneous population of cells. Three cell types were noted in greatest numbers: histiocyte-like cells, fibroblast-like cells and undifferentiated cells. In addition, intermediate cells, myofibroblasts, multinucleated giant cells and xanthomatous cells were also noted. Mononuclear cells recognized as lymphocytes, plasma cells and mast cells were occasionally identified.

**Fig. 1.** Typical histiocyte-like cell has abundant cytoplasmic organelles including short, flattened, rough endoplasmic reticulum, prominent Golgi apparatus, multivesicular bodies and dense bodies of various sizes, and characteristic cytoplasmic filopodia.

*Inset:* Intracellular junctions of macula adherens type between cytoplasmic processes of histiocyte-like cells. × 13,600, *inset* × 81,000

**Fig. 2.** Low magnification of typical field showing a fibroblast-like cell (*F*), histiocyte-like cell (*H*) and undifferentiated mesenchymal cell (*U*). The fibroblast-like cell contains dilated cisterns of rough endoplasmic reticulum. The histiocyte-like cell contains numerous lipid droplets suggesting xanthomatous transformation. A nuclear body (arrow) is present in the nucleus of the fibroblast-like cell. *Inset:* Higher magnification of a nuclear body. × 13,600, *inset* × 26,000

**Fig. 3.** An elongated fibroblast-like cell is entrapped in the fibrous stroma with mature collagen. The intracytoplasmic bundles of filaments show dense aggregates (arrows), suggestive of myofibroblastic differentiation. *Inset:* Higher magnification of dense aggregates of filaments. × 13,000, *inset* 27,200