Brain tumor of mixed mesenchymal and neuroepithelial origin

Case report

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A case is reported in which the intracerebral tumor was a mixed mesenchymal and neuroepithelial (glial) neoplasm. The mesenchymal part contained both lymphoma and dedifferentiated meningioma; the neuroepithelial portion was glioblastoma multiforme. The combined tumor had both gross and microscopic features of a “giant cell sarcoma” and “giant-celled glioblastoma.” The findings in this case and a review of the literature indicate the mixed mesenchymal and neuroepithelial origin of these tumors.

Key Words: brain tumor, meningioma, lymphoma, glioblastoma multiforme, giant cell sarcoma

Glioblastoma multiforme and meningiomas are common among intracranial neoplasms. Primary malignant lymphomas rarely occur in the neuraxis as judged by the paucity of cases reported under such diverse names as Hodgkin’s disease, microglioma, primary mesenchymal tumor, reticulum cell sarcoma, or malignant lymphoma. Combined meningiomas and glioblastomas are exceedingly rare, and we have been unable to find any description of a primary mixed meningioma, lymphoma, and glioblastoma multiforme of the brain as reported in our case.

Case Report

Six months before hospitalization, this 42-year-old white man lost consciousness for several seconds, but recovered spontaneously. He thereafter suffered progressively severe headaches. The history was otherwise insignificant, except for an episode of hematuria.

First Admission. The patient had difficulty remembering recent and remote events. The margins of the optic discs were indistinct, and the left disc was hyperemic. Other cranial nerves were intact. The tendon reflexes were equal and hyperactive bilaterally. General physical examination was normal. Chest and x-ray films and routine blood and urine analysis were normal. Skull films revealed shift of the pineal shadow of 8 mm to the right, and demineralization of the posterior clinoid processes. Brain scan and a left carotid angiogram demonstrated evidence of a mass in the rostral portion of the left temporal lobe.

Operation. At craniotomy, a firm, demarcated, cystic mass was largely embedded in the anterior half of the left temporal lobe and adherent to the adjacent dura. The tumor was removed with the anterior part of the temporal lobe.
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The patient was discharged 3 weeks after hospitalization, and received radiotherapy of 4500 R.

Histological Examination. The specimen consisted of multiple fragments of partly rubbery and partly soft tumor. The tissue was fixed in 10% formalin and embedded in paraffin. The following stains were used: hematoxylin and eosin (H & E), Mallory's phosphotungstic acid hematoxylin (PTAH), and Wilder's method for reticulin fibers. The mildly necrotic tumor contained multiple types of pleomorphic cells: there were elongated, pyramidal-shaped, monstrous, lymphocyte-like, and ghost cells. The elongated cells were arranged largely in streams or interlacing bundles (Fig. 1). One type of elongated cell had a few coarse blue processes extending from the distal ends in PTAH preparations, and was interpreted as a compressed astrocyte (spongioblast). Another type of elongated cell was largely spindle-shaped, lacked blue processes in PTAH preparations, and was considered to be a fibroblast. The pyramidal-shaped and monstrous cells mostly were scattered at random (Fig. 2). The lymphocyte-like cells occasionally were clustered around the blood vessels in concentric laminae separated by fine strands of reticulin fibers (Fig. 3), but mainly were distributed randomly (Figs. 1 and 2). Occasionally all types of neoplastic cells were closely approximated to the thick vascular adventitia. The pyramidal-shaped cells contained pale acidophilic cytoplasm in hematoxylin and eosin preparations. Their ovoid and vesicular nuclei often were eccentric. In PTAH stains, a few coarse blue processes occasionally extended from the angular margins; these cells were considered to be plump astrocytes.

The bizarre uni- and multi-nucleated giant cells (Fig. 2) contained glassy cytoplasm as did the astrocytes; several had intranuclear vacuoles and inclusion bodies. The appearance of the latter was similar to that of the cytoplasm. Mitotic figures, both normal and abnormal, abounded. The endothelium was mildly hyperplastic in some of the numerous blood vessels distributed throughout the tumor. Wilder's stain revealed abundant reticulin fibers (Fig. 4), especially around blood vessels or within the groups of lymphocyte-like cells; the fibers, however, were lacking in astrocytic areas. Sparse minute foci of necrosis surrounded by palisades of the neoplastic cells were disclosed in a few deep sections (Fig. 5). The anatomical diagnosis was mixed mesenchymal (dedifferentiated meningioma and malignant lymphoma) and neuroepithelial (glioblastoma multiforme) tumor.

Second Admission. Six months later, a small calculus was removed from his left ureter. Other physical findings, including the nervous system, were unremarkable at this time.

Third Admission. One year and 4 months after the craniotomy, the patient was readmitted because of progressive left-sided headaches and bilateral papilledema. Bilateral carotid angiograms demonstrated a widespread mass involving the left cerebral hemisphere, especially the temporal lobe. Parts of the recurrent tumor were removed from the left temporal lobe with uneventful recovery of the patient. The tumor was as previously described.

Fourth Admission. The patient returned 1.5 months later with right hemiparesis and signs of considerably increased intracranial pressure. He died the same day. Permission for necropsy was not obtained.

Comment. Although a necropsy to exclude metastatic tumor was not performed, we assume this neoplasm arose primarily in the brain as judged by the cerebral symptoms of 1.5 years and absence of evidence of systemic involvement. The hematuria was readily explained by the discovery of a ureteric calculus. Microscopic features of the tumor, furthermore, indicate that two of the three parts of the neoplasm were intracranial in origin.

Discussion

Original Problem

In 1913, Meyer reported an intracerebral neoplasm which he called "giant-celled glioma." Several workers subsequently described what appears to be the same type of tumor, but used diverse names: ganglioglioneuroma, ganglioglioma, ganglioglioma, spongioneuroblastoma multiforme ganglioides, retotheliosarcoma, spongioneuroblastoma, monstrocellular sarcoma, circumscribed sarcoma of the blood vessels, giant cell sarcoma, giant-cell fibrosarcoma, giant-celled glio-
Fig. 1. Numerous compressed astrocytes (spongioblasts) and fibroblasts are arranged in intertwined bundles. Many lymphocyte-like cells and a few plump astrocytes are disseminated at random. H & E, × 136.

Fig. 2. A uninucleated monstrous cell, several plump astrocytes and lymphocyte-like cells are mingled. The nucleus of the monstrous cell contains a large, homogeneous inclusion body. The astrocytes within the clusters (arrows) have processes extending from their margins. PTAH, × 265.

Fig. 3. Abundant lymphocyte-like cells are arranged in concentric laminae around a small blood vessel containing a few erythrocytes. H & E, × 104.

Fig. 4. Reticulin fibers are dispersed through the tumor, but are lacking in the areas of astrocytes; one of these areas is indicated by the arrow (top). Wilder's stain, × 110.
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blastoma,\textsuperscript{18} and monstrocellular astrocytoma.\textsuperscript{19} These multiple terms indicate that the nature of the tumors was thought to be either mesenchymal or neuroepithelial. Tönnis and Zülch\textsuperscript{25} once regarded the neoplasm as a neuroepithelial tumor. They called it "glioblastoma monstrocellulare ganglioides.” Zülch\textsuperscript{26} later classified it as a sarcoma. Characteristically, the tumor was described as well demarcated, often cystic, frequently infiltrating the meninges, and containing multiple types of bizarre cells, namely, monstrous, spindle-shaped or fusiform, plump or pyramidal, and having cytoplasmic processes and ghost cells.\textsuperscript{11,15,26,27}

The monstrous cells were considered as being “fantastic, not comparable to anything else in the human body;”\textsuperscript{27} they were uni- or multi-nucleated, and as large as 0.5 mm in diameter. Zülch\textsuperscript{26,27} considered these bizarre giant cells as the diagnostic hallmark of the tumor. The origin of this monstrous cell as well as the other types of tumor cells was thought to be either the vascular adventitia,\textsuperscript{11,26,27} or neuroglia.\textsuperscript{1,13} Numerous reticulin fibers in the tumor were described as uniformly distributed by Zülch\textsuperscript{26} but sparse in some areas by Kernohan and Uihlein.\textsuperscript{11} The vascular endothelial hyperplasia was noted by some authors,\textsuperscript{1} but was denied by others.\textsuperscript{18}

Based on the circumscribed outline of the tumor, the tendency to invade the meninges, and the presence of abundant reticulin fibers, some authors classified this tumor as a sarcoma.\textsuperscript{9,11,26,27} Russell and Rubinstein,\textsuperscript{18} however, argued that the amount of reticulin fibers was insufficient to interpret the tumor as a sarcoma; they placed it within the group of gliomas, and named it “giant-celled glioblastoma.”

Alternative Interpretation

The neoplasm in our case fulfills the criteria for a diagnosis of giant cell sarcoma because this demarcated and cystic tumor invaded the dura, contained monstrous, spindle-shaped, lymphocyte-like, and ghost cells as well as abundant reticulin fibers. Indeed, the tumor initially was diagnosed as giant cell sarcoma.

The presence of pleomorphic astrocytes, endothelial hyperplasia of blood vessels, and foci of necrosis surrounded by palisading neoplastic cells, however, indicates that a part of this giant cell sarcoma is glioblastoma multiforme.\textsuperscript{25} We do not agree with some workers who interpreted the mingled astrocytes in the tumor as reactive gliosis.\textsuperscript{16} Proliferation of the vascular endothelium is additional supportive evidence of the gliomatous nature of part of the mass. We are aware that endothelial hyperplasia may occur in other diseases,\textsuperscript{14,15} but its presence in various gliomas is well known. Furthermore, the mingled fibroblasts suggest a dedifferentiated meningiomatous portion of the tumor in our case. We use the term dedifferentiated meningioma as analogous to the terms fibrosarcoma of the meninges, meningeal sarcoma, malignant meningioma, or meningioma with sarcomatous component.\textsuperscript{20} The dedifferentiated meningioma may lack cellular whorls or psammoma bodies.\textsuperscript{20}

The presence of numerous lymphocyte-like cells raises the question whether they are neoplastic lymphocytes or merely an inflammatory process. In addition, are these small, round, dark cells lymphocytes? Undifferentiated neoplastic cells of small size, such as those found in lymphoma, medulloblastoma,ependymoma, neuroblastoma, and carcinoma, are not readily distinguished from

![Fig. 5. A small focus of necrosis is surrounded by palisading neoplastic cells, largely spongioblasts. H. & E., × 130.](image-url)
lymphocytes by the appearance of the individual cells in the light microscope. The small, round, dark cells in the tumor of our case, however, are arranged in concentric laminae separated by reticulin fibers, a characteristic feature of malignant lymphoma.

Russell and Rubinstein\(^\text{18}\) illustrated invasion of the leptomeninges by numerous small, round, dark cells (Fig. 186 of their textbook), and stated that these neoplastic cells are part of a cerebral glioblastoma infiltrating the leptomeninges. We are uncertain that these tumors are pure glioblastomas; they may be mixed lymphomas and glioblastomas.

From these various points of view, the tumor in our case might properly be diagnosed as a mixed mesenchymal and neuroglial tumor (combined dedifferentiated meningioma, malignant lymphoma, and glioblastoma multiforme). This diagnosis describes all neoplastic cellular components comprising the tumor, and resolves the dispute about the tissue of origin of "giant cell sarcoma" or "giant-celled glioblastoma." The inconsistencies among reported cases are thus readily explained. The mode of occurrence of these combined mesenchymal and neuroepithelial neoplasms, and the nature of the monstrous cells, have been discussed elsewhere.\(^\text{21}\)

References
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