Glial Origin of Monstrocellular Tumor
Case Report of Prolonged Survival

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There have only been a few reports of intracranial tumors characterized by gigantic or monstrous cells although they probably are seen more frequently. Their origin and classification are controversial; they have usually been described as either sarcomas or glioblastomas. We have recently examined one such tumor which, in our opinion, was of glial origin.

Case Report

A 22-month-old girl developed uncomplicated varicella. Three months later she developed decreased activity, anorexia, irritability, lethargy, and daily vomiting. Evaluation at another hospital was normal except for a cerebrospinal-fluid protein of 104 mg%; the studies included a normal pneumoencephalogram.

Examination. At the age of 2½ years she was small, thin, alert, irritable, and mildly cachectic. Neurological examination was normal except for hypactive deep tendon reflexes and moderately hypotonic extremities. Laboratory findings were normal except for a cerebrospinal-fluid protein of 88 mg%. The spinal fluid pressure, skull films, and electroencephalogram were normal.

Course. During the next 2 months the vomiting, weakness, irritability, and cachexia increased. The hypotonia persisted and the only new neurological finding was a left Babinski sign. Lumbar puncture at the time of repeat pneumoencephalogram showed a pressure of 250 mm and a spinal fluid protein level of 117 mg%. The lateral ventricles were slightly enlarged and the third and fourth ventricles were in normal position. Soon after the air study, signs of hydrocephalus appeared rapidly and papilledema developed. The child had two episodes of transient decerebrate posturing. Right retrobrachial arteriography confirmed the impression of hydrocephalus but was otherwise normal.

Operation. A ventriculo-caval shunt was then performed. After the shunt was established, the child improved; anorexia and vomiting continued, however, and she failed to gain weight. She was started on large doses of steroids. At the age of 34 months she showed a slightly wide-based gait and bilateral extensor plantar responses. The cerebrospinal-fluid pressure was 110 mm and protein 370 mg%. Complete spinal myelography was normal. She was placed on dexamethasone 1 mg three times a day; her oral intake improved, and her irritability diminished.

At age 3 years and 4 months (1½ years after the onset of the illness), the child was still irritable and vomiting daily. She remained alert but cachectic, with signs of hypercorticism. The shunt was functioning well. Neurological examination was unchanged. Lumbar puncture revealed a pressure of 100 mm; the spinal fluid protein level was now 1,720 mg%. The fluid contained 4 monocytes and 4 red blood corpuscles. Brain scan revealed a large abnormal uptake in the left temporo-occipital region. Ventriculography now showed displacement of the fourth ventricle to the right. The left temporal horn was displaced upward and laterally (Fig. 1). Left carotid arteriography demonstrated a tentorial artery together with elevation and straightening of the left middle cerebral artery (Fig. 2). An electroencephalogram showed diffuse slowing.

Second Operation. A left temporal craniectomy was performed and a small biopsy of grossly abnormal cerebral tissue at the posterior fusiform gyrus was obtained. Postoperatively the child was decerebrate, with a fixed and dilated left pupil. She died 34 hours after surgery. At autopsy there were no abnormalities except those in the brain.

Gross Examination of the Brain. The meninges were focally thickened over both cerebral hemispheres. Be-
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Fig. 2. Left carotid arteriogram. A tentorial artery is noted (arrow). There is elevation and straightening of the middle cerebral artery.

tween the left temporal lobe and midbrain there was an irregularly-shaped and rather well-circumscribed, firm, grayish-yellow tumor measuring 4.0×3.0×3.0 cm. A coronal section demonstrated that the neoplasm originated within the left hippocampal gyrus and penetrated the arachnoid with invasion throughout the cisterna ambiens (Figs. 3 and 5). The superior cistern was filled, and the pineal body was enveloped but not invaded by

Fig. 3. Coronal section of the brain showing that the tumor originated in the left hippocampal gyrus (arrow) and invaded the cisterna ambiens. Note widespread cortical softening.

Fig. 4. The tumor extends along the midbrain. Massive compression of midbrain and diffuse spread along the meninges is seen.
tumor. The lower part of the tumor reached the upper border of the pons, with compression but no invasion of the midbrain (Fig. 4). Neoplasm covered the tentorial surface of the cerebellum and focally invaded the cerebellar folia. Extensive areas of the cerebral cortex were soft, discolored, with a blurred gray-white matter demarcation, indicative of recent infarct.

Microscopic Examination. The tumor showed gradual transition from a fibrous astrocytoma to glioblastomatous foci and gigantocellular form.

Within the hippocampal gyrus the tumor was moderately cellular and was composed of fibrous astrocytes with irregular nuclei containing coarse chromatin clumps (Fig. 6). The matrix was composed of fine glial fibrils which stained blue with phosphotungstic acid-hematoxylin stain. There were elongated bipolar cells arranged in a piloid fashion, and Rosenthal fibers were present (Fig. 7). Few foci of necrosis or pseudo-palisading and minimal endothelial proliferation were found (Fig. 8). Some gemistocytic astrocytes were scattered throughout.

As the tumor emerged from the cortex into the meninges, the basic cell characteristics did not significantly change but the cell density increased markedly. Here monstrous giant cells were encountered (Fig. 9): the majority of them were found in large islands, devoid of intercellular matrix, though occasionally they appeared singly. Their size varied from 60 to 160 µ. Most
Fig. 8. Necrosis, pseudopalisading, and moderate pleomorphism are evident. H. & E. X110.

Fig. 9. Island of bizarre, multinucleated giant cells. H. & E. X100.

contained nuclei of proportional size, however; several had as many as 14 small nuclei. The nuclei of these bizarre cells showed extreme variability in shape; many were vacuolated, vesicular, twisted, and contained invaginations of cytoplasm. A moderate increase in connective tissue and thick fibers was shown with a tri-chrome stain, and reticulum was demonstrated predominantly around the vessels (Fig. 10). There was a slight increase in vascular density and some larger arteries were sclerotic. Surrounding some of the smaller vessels were small lymphocyte-like cells. Few of the giant cells were found close to the small vessels but there was no discernible relationship between the vessel walls and the arrangement of the neoplasm.

Fig. 10. Reticulum appears limited to the perivascular areas. Wilder’s reticulum stain. X95.

Fig. 11. Finger-like spread of the tumor along the Virchow-Robin spaces. H. & E. X35.
The tumor had spread throughout the arachnoid and invaded the brain along the Virchow-Robin spaces in finger-like processes (Fig. 11). There was direct focal invasion of the cerebellar folia, and the tentorium was penetrated at one site. Sections from the cerebral cortex showed recent extensive infarcts underlying meningeal metastases.

**Discussion**

A brain tumor composed in part of bizarre giant cell groups was first described by Oskar Meyer* in 1913 and termed by him a giant-celled glioma (Riesenzellengliom). His description of three cases included an illustration of the typical monster cells; they were noted to have cell processes which he thought identified them as being of glial origin. The tumors otherwise were described as typical glioblastomas with necrosis, hemorrhage, and endothelial proliferation.

In 1914, Schmincke\(^{12}\) reported a tumor he called a gangliocytoma. He considered the bizarre giant cells to be ganglion cells. However, some of the giant cells demonstrated glial foot processes attached to blood vessels. Basically the tumor had all the characteristics of a glioblastoma.

Four further reports of “immature gangliogliomas” appeared,\(^{4,5,9,13}\) Foerster and Gagel\(^{6}\) noted glial fibrils and astrocytes in their case report and would have called the tumor a glioblastoma were it not for the “ganglion cells.” However, in 1936, Scherer\(^{14}\) clearly demonstrated in his report of two cases that the giant cells were of glial and not neuronal origin. Foot and Cohen\(^{6}\) first raised the possibility of sarcomatous origin in 1933. They described a temporalparietal lesion which they termed retotheliosarcoma because they did not find glial fibrils with PTAH stain.

Zülch,\(^{15}\) in 1940, postulated a sarcomatous origin and in 1953,\(^{16}\) named this tumor monstrocellular sarcoma. He\(^{16}\) described as characteristic of this tumor a sharp demarcation from surrounding brain tissue, a fleshy firm homogeneous appearance, and frequent cyst formation. Microscopically, three major cell types were present: lymphoid cells, spindle cells, and bizarre giant cells. The marginal zone was highly vascular and usually consisted of a dense collection of spindle cells. Frequently the tumor spread along small vessels in finger-like projections. The lymphoid cells appeared similar to those seen in oligodendrogliomas and other brain tumors. He described transitional forms between all three cell types. Zülch claimed that the fibrils coming from the giant cells, as observed with Weigert and Holzer stains, were too coarse to be glial fibrils. He noted that reticulum was rare and usually absent in the monstrocellular part of the tumor but abundant elsewhere. Bingas\(^{2}\) and Brucher\(^{3}\) agreed with Zülch’s classification and theory of the mesodermal origin of this tumor from blood vessels. Kernohan and Uhlein\(^{7}\) believed the tumor to be a variety of fibrosarcoma and termed it giant cell sarcoma on the basis of gross appearance and abundance of reticulin fibers.

Russell and Rubinstein\(^{18}\) still considered this neoplasm to be a sub-type of glioblastoma. In two of four cases, they noted transition to areas of unequivocal glioblastoma or to gemistocytic astrocytoma, and did not consider the predominant presence of reticulum around blood vessels as sufficient evidence for interpreting the tumor as a sarcoma.

The malignant tumor in this report was grossly homogeneous and firm without variegation. Microscopically it seemed to originate as a typical fibrous astrocytoma showing gradual transition into a glioblastomatous pattern, in addition to containing many foci of monster cells. This kind of transition has been noted previously by others.\(^{10}\) The bizarre monster cells appear singly, but more characteristically in large groups.

In 1931, Alpers\(^{1}\) presented a case of a glioblastoma with many giant cells. His case appeared to be a transition between a glioblastoma and a giant-celled tumor because the giant cells were more numerous and more bizarre than expected in the usual glioblastoma. He noted the characteristic perivascular location of the giant cells reminiscent of Zülch’s description. In contrast to Zülch’s observations, however, he showed glial processes originating from these cells.

The development of reticular fibrils in our case was not extensive and was chiefly perivascular. Russell and Rubinstein\(^{18}\) did not think the presence of reticular networks proved a sarcomatous origin, because of the areas showing transition to an astrocytic neoplasm.

The blood vessels in giant-celled glioblastomas are generally abundant, but the endothelial lining is often of the normal flattened type.\(^{19}\) Some endothelial proliferation was found in our case. There may be adventitial overgrowth which, according to Kernohan and Uhlein,\(^{7}\) favors a diagnosis of sarcoma. Although this case and certain others reported are clearly giant-celled glioblastomas, it seems probable that a sarcomatous tumor, producing bizarre giant cells, also occurs.

Our patient lived 18 months after the initial onset of symptoms. During the last 9 months of life, she received large doses of steroids. It is probable that the steroid administration and the ventriculo-caval shunt prolonged survival, allowing further progression of tumor growth. Perhaps other cases of brain tumor with prolonged survival as a result of steroid administration may, in the future, yield further information concerning
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the origin, growth pattern, development, and de-differentiation of central nervous system neoplasms.

Summary
We have reported a case of monstrocellular tumor of glial origin. The tumor demonstrated a gradual transition from a fibrous astrocytoma to glioblastomatous foci and bizarre giganto-cellular form. The related hydrocephalus and reactive brain swelling were controlled for 18 months by a venous shunt and corticosteroids.

References