Case Reports

Brain Tumors of Diverse Germinal Origin
Arising in Juxtaposition
Report of Three Cases

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Patients with multiple brain tumors have always been a topic of interest. Several categories of cases have been described. These include; tumors of single cell type such as multiple meningiomas in the same patient; mixed gliomas which seem to embody subdivisions of different histological structures, such as astrocytoma and oligodendroglioma, forming parts of the same tumor; less common are the multiple tumors of different germinal origins such as meningiomas and astrocytomas. The latter may occur independently of each other in the same host and several instances of this phenomenon have been reported.

When these tumors occur in juxtaposition, the question of etiological relationship must be raised; and when both tumors are malignant, the situation is still more provocative. Several cases of this type have previously been reported. The usual interpretation has been that a secondary malignant gliomatous reaction was set up by the primary sarcoma. Our report concerns 3 cases of juxtaposed malignant tumors of different germinal origins; at least 1 case demonstrates that a glioblastoma was the primary tumor.

Case Reports

Case 1. T.T. First Admission. A 50-year-old man was admitted to the Hartford Hospital in October 1958, with incapacitating headaches behind the right eye, a roaring sound in both ears and the impression of wave-like structures which interfered with his vision from time to time.

Examination. The patient had slight weakness on the left side including the face, with increased deep tendon reflexes on the left. There was also tenderness in the right supraorbital region. An electroencephalogram revealed a large amount of slow activity through the anterior regions with very slow delta pattern of maximal voltage in the right frontal area. An arteriogram of the right carotid arteries showed displacement of the arteries to the left of the midline and downward displacement of the middle cerebral artery with tumor stain in the right frontal lobe. A ventriculogram confirmed the localization of the tumor to the right frontal lobe.

First Operation. A large cystic glioblastoma was re-

moved. The immediate postoperative course was gratifying, and the patient returned to work asymptomatic.

Second Admission. He was readmitted in 3½ months with recurrence of his symptoms and signs. The pineal was seen to be displaced 5 mm. to the left, and a repeat ventriculogram revealed a massive lesion in the right frontal area.

Second Operation. At reoperation there was a firm friable mass that extended through the dura and was adherent to the overlying bone. This was removed along with the underlying glioma, and a right frontal lobectomy was performed.

Immediate postoperative results were good with return to work. He received cobalt therapy but succumbed to the tumor 8 months later.

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Fig. 1. Glioblastoma showing pleomorphic glial cells, many of protoplasmic type. H. & E., X100.
Biopsy Findings. The original tumor was composed of glial tissue and presented a variable picture. In some zones the cells were of protoplasmic type (Fig. 1). In other regions an increased pleomorphism and mitotic activity was present. Endothelial proliferation was prominent in these areas. Palisading of glial cells at the margin of necrosis was also seen. The findings were typical of a glioblastoma multiforme.

The recurrent tumor showed typical glioblastoma but intermingled with and bordering the glioma was a tumor composed of masses of atypical fibrous tissue in which there were numerous mitoses (Figs. 2 and 3). Silver stains showed abundant reticulum, and Masson stains demonstrated the presence of collagen (Fig. 4). The appearance was that of glioblastoma multiforme with an adjacent fibrosarcoma.

Autopsy Findings. Examination of the brain at necropsy showed extensive neoplastic invasion of the right frontal lobe, and the anterior portion of the right temporal lobe. The tumor also crossed the midline through the corpus callosum to involve the medial aspect of the left frontal lobe. Separate tumor nodules were present in subcutaneous tissues overlying the operative site.

Microscopically the neoplasm was composed of both gliala and sarcoma. The two elements were mixed, with the sarcomatous element being dominant. The sarcoma was composed of spindle-shaped cells which had layed down reticulum and which stained green in Masson's Trichrome stain. The subcutaneous tumor was entirely sarcomatous.

Case 2. A.G. This patient was admitted to the Hartford Hospital in May, 1961, with complaints of intense left periorbital pain of several months' duration, emotional depression, mental sluggishness and memory changes. During the past month, he had noted diminished vision and excessive drowsiness.

Examination. There was proptosis of the left eye, drowsiness, aphasia and definite fullness in the left temporal area. The left pupil was smaller than the right with ptosis of the left lid. There was a drift of the right arm with clumsiness in its use. X-rays of the skull showed a marked loss of the squamous portion of the temporal bone and a pineal shift to the right. Arteriogram revealed a space-occupying lesion in the left fronto-temporal area.

Operation. A large extradural tumor was found attached to dura and destroying and replacing the temporal bone, sphenoid wing and even invading the temporals muscle. A second large, soft glial tumor occupied a large part of the left temporal lobe. This had the gross characteristics of a glioblastoma. The tumor was grossly removed with a partial temporal lobectomy. The tumors were in juxtaposition at the dura, but the glial tumor was not adherent to the dura. The patient gradually improved and was started on cobalt therapy. His symptoms and neurological signs cleared although he
tired easily. He succumbed 9 months later from recurrent disease.

Microscopic examination of the temporal lobe tumor showed a cellular glioma. The glial cells varied in size and shape and numerous mitoses were present. In areas of necrosis there was a palisading of glial cells at the margins of the necrotic areas (Fig. 5). Endothelial proliferation was striking. The histologic pattern was typical of a glioblastoma multiforme.

Sections of the thickened dura overlying the glioma showed a different and separate tumor composed of interlacing spindle-shaped cells which took the Masson stains for collagen. There were moderate numbers of mitoses. The tumor invaded the overlying bone. The pattern was compatible with a fibrosarcoma of meningeal origin (Fig. 6).

Case 3. E. R. was a 51-year-old man with 6 weeks' history of headaches, anorexia, occasional vomiting, vertigo and poor equilibrium. Examination showed slight emotional left facial weakness and blurred optic discs, the right more than the left. X-ray of the skull showed definite pineal shift to the left. An electroencephalogram was characterized by diffuse slow waves over the right cerebral hemisphere, localized slightly more laterally and posteriorly. A brain
scan demonstrated a large right mid-temporal focus, extending to the base and close to the surface of the skull.

**Operation.** A firm mass was found attached to the dura in the floor of the middle fossa from which it received a rich blood supply. This tumor was surrounded in the temporal lobe by a second soft yellow gelatinous tumor having the gross appearance of glioblastoma. Gross total removal of the firm tumor and partial removal of the glioma were effected.

**Biopsy Findings.** Part of the tumor tissue was made up of whirls and thick bands of fibrous tissue in which were large spindle-shaped bizarre cells showing active mitosis typical of fibrosarcoma (Fig. 7). Other areas showed masses of closely packed large cells with large irregular nuclei. Many cells were in mitosis. In some areas palisading of tumor cells surrounding areas of necrotic tumor was present (Fig. 8). A prominent feature was the extensive endothelial proliferation of blood vessels throughout the tumor. The pattern was that of a mixed glioblastoma multiforme and fibrosarcoma.

**Discussion**

The production of experimental malignant tumors in animals with the use of carcinogens such as Methylcholanthrene or Dibenzanthracene commonly excites mixed tumors of diverse cell origin and even tumors whose cells are of different germinal origin as demonstrated by Zimmerman and Arnold. This feature is, in fact, often an annoyance to the investigator. When this occurs clinically it suggests the presence of some common etiological agent in the host. In published reports of this phenomenon in the past, it has been suggested that a primary sarcoma may incite a glial reaction of neoplastic quality although there is some question as to which incites which. In 1910, Merzbacher and Uyeda described a case of a right frontal sarcoma that arose from the leptomeninges and appeared to be largely encompassed by an extensive glioma. They felt the sarcoma had generated frank gliomatous formations. Although the tumors appeared to be sharply demarcated to the naked eye, microscopically there was a merging of both types of tissue. This feature characterized some of our cases.

Gullotta in 1933,9 Bailey and Ley in 1934,3 French in 19497 and Courville and Edmonson in 19539 described fibrosarcomas in various parts of the brain in direct contact with subjacent glioblastoma multiforme. These authors suggested the sarcoma had stimulated the development of a malignant glioma in the underlying brain. Gass and van Wagenen described a meningioma which was felt to arise from a much larger oligodendro-glioma which was considered to be the older lesion.9 Feigen and Gross in 1955 reported 3 cases of cerebral tumor, each of which contained glioblastomatous and fibrosarcomatous elements.8 In 1956, Rubinstein reported 5 cases and raised the question of the mode of development of such neoplasms in the central nervous system.12 He felt...
that his cases showed true neoplastic changes in the glial tissue excited by the fibrosarcomas.

In our 3 cases the first patient had a definite glioblastoma with the sarcomatous changes revealed only at the 2nd operation. The microscopic studies suggest that this was more typical of a true sarcoma than of mesodermal hyperplasia. In the other 2 cases, there were 2 highly malignant tumors lying in direct contact but not adherent to each other. We may conjecture: Did these tumors arise from a common carcinogenic or carcinogenic focus? Does sarcoma under certain conditions act as a carcinogen or inciting focus to the glial tissue to produce a glioblastoma, or vice versa as in case 1? Or can the agent which produced one tumor incite malignant changes in the other? One may even theorize that juxtaposed elements of mesodermal and glial origin may undergo simultaneous and independent neoplasia forming a so-called composite tumor.

Summary

We have reported cases of juxtaposed malignant tumors with different germinial origins (fibrosarcomas and glioblastomas). In one instance, the glioblastoma definitely existed first. In the others, it is impossible to tell which arose first or if the tumors arose from a common carcinogenic site.

References