PRIMARY FIBROBLASTOMA OF THE BRAIN *

Report of a Case

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Cerebral neoplasms composed almost exclusively of fibroblastic elements are extremely uncommon. Although the exact origin of these tumors is unknown, it seems permissible to call them fibroblastomas because their structure differs strikingly from that of the much more common tumors of neuro-ectodermal origin, and because of their resemblance to fibroblastomas elsewhere. Up to the present time only 4 such tumors have been reported in the literature. In 1929 Bailey [1] reported 2 cases. His 1st case was one studied by Dr. F. B. Mallory. This was a semiopaque, somewhat cartilaginous mass found in the right temporal lobe of a 42 year old female. It was adherent to the dura. Histologically the tumor was a fairly typical fibrosarcoma and was composed of spindle shaped cells. Between these cells were numerous reticulin and collagen fibers. Mitotic figures were numerous. Bailey's 2nd case was an operative specimen removed from the inner wall of the right lateral ventricle of a 19 year old male. This tumor was reddish in appearance and was so soft that it was removed by suction. The tumor was composed of streams of spindle shaped cells running in various directions. The cells had a delicate cytoplasm and an oval or elongated nucleus containing dust-like chromatin material. Mitotic figures were numerous. The collagen was most abundant in the degenerated areas of the tumor, while delicate reticulin and fibroglia fibrils made up the bulk of the remaining intercellular substance. Vascular sinuses were quite numerous.

In 1930 Mallory [2] reported a case of a 33 year old male in whom a tumor nodule measuring 5 cm. in diameter was found at autopsy in the right frontal lobe. Grossly this newgrowth was of unusual firmness and whiteness. Histologically it was described as being well differentiated, rather slowly growing, and a typical fibrosarcoma. This patient had also two large adrenal tumors that were apparently not related to the cerebral lesion.

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Alpers, Yaskin and Grant [3] in 1932 reported the removal of a tumor the "size of a walnut" from the right frontotemporal region of a 52 year old male. It was encapsulated, firm, white and fibrous. Histologically the tumor cells were loosely packed and in some regions had a definite myxomatous appearance. There was a rich intercellular substance composed chiefly of fibrous tissue and fibrils that were apparently fibroglia. Blood vessels were numerous and areas of degeneration were present. Neuroglial cells were found only at the edge of the tumor, but not within it. The authors described numerous tumor cells closely related to the walls of the vessels. These cells were in a stage of proliferation and were assumed to be "centers of growth" of the tumor.

Because of the rarity of this type of cerebral neoplasm and because of the interesting problems in histogenesis involved, a report of a further case seems permissible.

Report of Case*

Clinical History: The patient, a white female aged 10 years, was first seen at the University of Minnesota Hospital on Feb. 17, 1936, at which time she complained of headache, vomiting, visual disturbances and weakness of the left side of the face, left arm and left leg.

The birth history was uneventful: head presentation, spontaneous delivery, and a birth weight of 8 pounds. Physical development was quite normal. She had had the usual childhood diseases but no diphtheria, poliomyelitis, meningitis or mumps. The family history was negative, her father and mother both being well. There was no history of nervous disorders in the family. Two brothers and 3 sisters are living and well. There was no history of tuberculosis or contact with the disease.

The present illness dated from the first week in December, 1935, at which time she fell from a chair, striking the right occipital region. She did not lose consciousness. On careful questioning the patient herself stated that she had had a few headaches a short time prior to the accident. The headaches became almost constant afterward. Vomiting began about Jan. 1, 1936, occurred every 3 to 5 days, the interval becoming shorter until it was a daily episode. The vomiting was projectile in character.

Three weeks before admission (about Jan. 28, 1936) she awoke at night, cried out, and had a severe attack of vomiting, following which she noticed weakness and numbness of the left arm and hand. The weakness of the left side of the face was present after that time.

These symptoms progressed until admission to the hospital, at which time the patient complained of constant severe headache, daily attacks of vomiting and great weakness of the left side of the body. It was almost impossible for her to walk.

Physical Examination: The patient presented a bright, intelligent and cooperative girl of 10 years, well developed but slightly undernourished. The

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muscles of the left side of the face were relaxed, the right eyelid closed tighter than the left and the facial muscles retracted toward the right on showing the teeth. The pupils reacted to light. The eyegrounds showed a high degree of choking, 5–6 diopters with engorgement of the veins, a few, small, flame shaped hemorrhages and a partially developed macular star, suggesting that the choke was of considerable duration.

The chest was symmetrical, the lung fields clear, the heart not enlarged to percussion and the sounds clear. There were no murmurs. Abdominal examination was negative. No lymphadenopathy was present.

The right eye could not be moved upward or laterally. Diplopia was present. The tongue protruded in the midline. There was marked weakness of the lower left facial musculature. The abdominal reflexes were decreased on the left. The Babinski reflex was positive on the left. The deep reflexes could not be obtained. The stereognostic sense and sensation were normal. There was partial motor weakness of the left arm and leg.

The impression on admission was that the patient had a neoplasm in the midbrain, in the area of the mesencephalon on the right, involving the third and fourth cranial nerves, with pyramidal tract involvement before crossing.

Laboratory Data: There were no significant routine laboratory findings.

X-ray examination of the skull revealed evidence of intracranial pressure with irregular erosion of the inner table of the skull visible as multiple finger prints. There was beginning separation of the sutures. The sella and clinoid processes were not involved.

Course of Illness: The patient was given 75 cc. of 30 per cent sucrose intravenously, and on Feb. 19, 1936, a subtemporal decompression was performed inferior and posterior to the motor area on the right side. The amount of bone removed measured about 4 by 4 cm. There was considerable increased pressure encountered and extremely large blood vessels were present on the surface of the brain after cutting the dura. An attempt to enter the anterior horn of the ventricle was unsuccessful, considerable resistance being met with in that area. The impression of the surgeon was that this portion of the ventricle was infiltrated with tumor.

Following operation the temperature rose to 100.5° F., the pulse averaged between 80 and 100, going up to 130 on one occasion; the respirations averaged 15 to 20 per minute; and the blood pressure averaged 115/80. On Feb. 20, 1936, 70 cc. of 15 per cent sucrose was given intravenously. The patient's course for the next 2 weeks was essentially uneventful. A course of deep X-ray was begun on February 26th. She was given six treatments extending over 12 days, consisting of 140 per cent skin erythema dose to each lateral skull field. On March 13, 1936, 24 days following operation, the temperature rose abruptly to 105° F., the pulse to 140 per minute. She was restless and complained of severe headache over both eyes. The brain gradually herniated from the wound, extending finally about 3 cm. above the skin margin. Signs of meningitis were evident. The temperature remained elevated, averaging 103° F., with pulse about 130 per minute. On March 22, 1936, the temperature rose to 106° F., the pulse to 180, and the respiration was 60. The patient died the same day.

Autopsy Report

The autopsy was limited to an examination of the head. The entire surface of the brain was covered with a yellowish purulent

exudate which tended to accumulate within the large cisternae. There was a slight herniation of the brain tissue in the region of the decompression in the right middle frontal gyrus.

In the posterior portion of the right middle and inferior frontal convolutions there was a brownish discolored area measuring 5 by 4 cm., covered by a thin layer of brain tissue that apparently separated this discolored mass from the surface. Palpation over this region revealed a definite firmness and resistance to pressure. Separation of the cerebral hemispheres revealed a slight displacement toward the left of the medial border of the right cerebral hemisphere above the corpus callosum.

Coronal sections through the posterior third of the right frontal lobe of the brain exposed a well circumscribed, sharply demarcated brain tumor measuring 5 by 5 by 5 cm. (Fig. 1). The tumor did not appear to be invasive but merely replaced, probably by compression, portions of the cortex and white substance. Its lateral surface extended almost to the surface of the brain, being separated from the leptomeninges only by a thin layer of brain tissue. The mass itself was extremely firm, well outlined, but not encapsulated (Fig. 1). The cut surface was white, semiopaque, and almost gritty in appearance. There were no areas of degeneration, softening or obvious gross hemorrhage, although a few irregular reddish streaks were scattered throughout, apparently representing blood vessels or small hemorrhages within the tumor tissue. The tumor mass was entirely intracerebral and was not connected at any point with the meninges.

Microscopic Examination

Histologically the tumor presents a fairly uniform appearance. It consists of numerous fine and coarse strands of intertwining collagenous fibers that extend in various directions and present a fairly irregular architecture (Figs. 2 and 3). A moderate number of cells are interspersed among these strands of collagen (Fig. 2). The fibrous tissue composes the bulk of the intercellular substance and stains readily with the azocarmine stain. In some areas these intercellular fibers fuse to form dense, homogeneous wavy bundles of tissue that contain only an occasional cell nucleus and assume quite frequently a hyaline-like appearance. A plaque-like thickening of the tissue occurs in certain parts of these heavy fibrous bands.

These plaques stain more deeply than the surrounding connective tissue, probably because of its greater density. Only an occasional typical fibroblast is detected within the well defined plaques. In some of the relatively acellular regions the strands of collagen remain thin but intertwine with one another to give the effect of a reticular structure. No necrotic areas are apparent.

The tumor cells are irregular in outline. Some are round or oval in shape, although the majority are somewhat elongated and are composed of a small amount of cytoplasm surrounding a fairly irregular nucleus. These nuclei are large, slightly elongated, and contain a heavy, well demarcated nuclear membrane. Their chromatin is finely granular and although it is usually scattered throughout the nucleus, it occasionally assumes a peripheral distribution, being limited to the inner surface of the nuclear membrane. Frequently these granules merge to form larger chromatin clumps that resemble nucleoli in many instances. The cell body when visible extends from each end of the nucleus as bipolar cytoplasmic processes that merge with the surrounding intercellular substance. The cell cytoplasm stains very lightly with eosin and contains many fine granules.

In some areas the cells assume a definite stellate contour with numerous fine processes radiating out from the cell body. The intercellular substance in these regions is extremely fine and loose, causing the entire field to resemble myxomatous tissue quite closely.

Scattered among the fibroblasts are a few small cells with deeply staining round nuclei. These cells are probably microglia. No mitotic figures and no cells of glial origin can be made out within the tumor mass. The majority of the tumor cells present a structure quite typical of connective tissue cells and must be classed as fibroblasts and not as glial cells. With special stains numerous reticulin fibers can be seen scattered among the intercellular framework of the tumor (Fig. 3).

Blood vessels are numerous in all the sections studied. These vessels vary from endothelial lined cavities filled with blood to vessels composed of the typical layers ordinarily seen in cerebral arteries. The former are by far the more numerous and vary greatly in size and number. In those areas in which the vessels are most numerous, cells are also numerous. In no case, however, do these cells proliferate from or accumulate about the vessel wall to form

anything similar to the "centers of growth" described by Alpers, Yaskin and Grant [3] in their tumor.

Many hemorrhages are present within the tumor. Some of these are fairly well localized, while others are large and diffuse. Many of the hemorrhages consist merely of a fine film of erythrocytes scattered between the intercellular fibers, while others are composed of dense accumulations of red cells that completely mask the underlying structures. Most of the extravasations are not perivascular and appear to have no relation to the vessels. In some sections, however, a few hemorrhages that are distinctly perivascular in appearance are observed forming the so-called "ring" hemorrhages around the involved vessels.

In spite of the complete absence of a capsule the tumor is well demarcated from the surrounding brain tissue. The brain tissue adjacent to the neoplasm shows extensive glial and microglial reaction. The astrocytes reveal numerous proliferative changes and can be seen as large cells from which radiate numerous branching processes of variable length and thickness. Many of the astrocytes have become swollen to form giant glial cells. These cells frequently contain a finely granular cytoplasm and a considerably enlarged, irregular and often polymorphous nucleus. Many of these glial cells fuse to form large multinucleated cells. Although quite numerous in the adjacent brain tissue, these proliferating glial cells do not extend into the fibrous stroma of the tumor. Some of the astrocytes in the region of the tumor reveal degenerative changes consisting of fragmentation of the cell processes and pyknosis of the nuclei.

The microglia also reveal extensive alterations. As one passes from normal brain tissue toward the tissue adjacent to the tumor, all transitions of the microglia into rod cells and finally into fat granule cells can be observed. The latter cells are the most numerous and appear as large, irregular globular cells without cytoplasmic processes. The extensive proliferation and accumulation of these cells on the margin of the tumor have resulted in the migration of many of them into the adjacent tumor tissue. Many of these phagocytes are filled with hemosiderin which has been taken up from the region of a hemorrhage.

Discussion

We have called this tumor a primary fibroblastoma, even though the exact origin of these neoplasms is by no means certain. Since the

number of recorded cases of such tumors is so small, it is impossible to derive many definite facts concerning them from a review of these reports. It appears that these tumors may occur at any age period, since the youngest case occurred in a child 10 years of age, and the oldest in a man of 52 years. The tumor grossly presents a fairly uniform appearance. It is fairly well circumscribed, firm and whitish. One of the cases reported by Bailey was soft and red. Histologically all of these neoplasms present a picture quite typical of a well differentiated fibroma or fibrosarcoma. Mitotic figures were numerous in Bailey's cases and suggested somewhat less differentiation and more activity of the tumor cells. It is striking that all of the tumors occurred on the right side and were situated in the frontal or temporal regions of the brain.

It must be assumed that the origin of these tumors is most likely from the pia, from the vascular adventitia, or from the pial sheaths that surround the cerebral blood vessels. Bailey believes that they arise from the leptomeninges or its derivatives. In his 1st case the tumor was adherent to the dura and could easily have had its origin from this structure. The remaining reported cases, including our own, disclosed no connection with the surface meninges. However, it is well known that the cerebral blood vessels are surrounded by a sheath of cells of leptomeningeal origin which have invaginated from the surface to form the perivascular spaces of Virchow-Robin. It is entirely possible that tumors may arise from these perivascular cells and thus originally have a leptomeningeal origin. Alpers, Yaskin and Grant[3] described definite proliferation and accumulation of tumor cells around the blood vessels, which they designated as "centers of growth." In these "centers of growth" the tumor cells were in direct contact with the walls of the venules, arterioles and capillaries, appearing as an integral part of the vessel wall. The authors believed they were able to trace the adult fibroblasts from the cells around the vessels. It appears to us, however, to be quite difficult to determine with certainty whether these perivascular tumor cells actually arise from the sheath of cells of leptomeningeal origin or from the fibroblasts that normally are found within the adventitia of the blood vessels. If these tumors are of leptomeningeal origin, the question may be raised as to whether one is justified in calling them fibroblastomas, in view of the controversial embryological derivation of the leptomeninges.

There remain other possibilities of origin of such fibrous tissue tumors. Typical fibroblastic tissue is often seen in degenerating tumors of neuroepithelial origin. This fibrous tissue often becomes abundant and may lead to an erroneous diagnosis of fibroblastoma if only a small amount of the tumor is removed at operation. However, the total absence of any glial elements within a tumor and the similar absence of any signs of degeneration seem sufficient to rule out such a possibility.

Occasionally the healing of a solitary brain abscess results in an invasion and deposition of fibrous tissue, often obliterating almost all signs of the previously existing inflammatory process. Mallory [2] believed his case to be of this origin. Usually, however, these healed abscesses reveal, on careful study, some signs of the original inflammatory condition.

Finally, the use of deep X-ray therapy in the treatment of gliomas often results in their replacement by fibrous tissue and in some cases has made a histological diagnosis of the tumor quite difficult. In such cases large doses of X-ray seem necessary, and sufficient time must elapse after the treatment in order to allow such a transformation of tissue structure to occur. In our case the X-ray therapy was much too recent to result in such an extensive and complete alteration of a glioma into a fibrous tissue mass.

Considering all the above possibilities, and also considering the typical arrangement of the tumor cells, their characteristic morphology, the presence of large amounts of collagen fibers within the intercellular framework of the tumor, and the total absence of glial elements within the newgrowth, we feel fairly certain that we are dealing in this case with a primary fibrous tumor which we have elected to call a fibroblastoma of the brain.

Summary

1. A case of cerebral neoplasm is reported occurring in a 10 year old white female.

2. Pathological studies of this tumor reveal it to be composed almost entirely of fibroblastic elements. We have called this tumor a primary fibroblastoma of the brain.

3. The literature dealing with this type of newgrowth is reviewed.

REFERENCES

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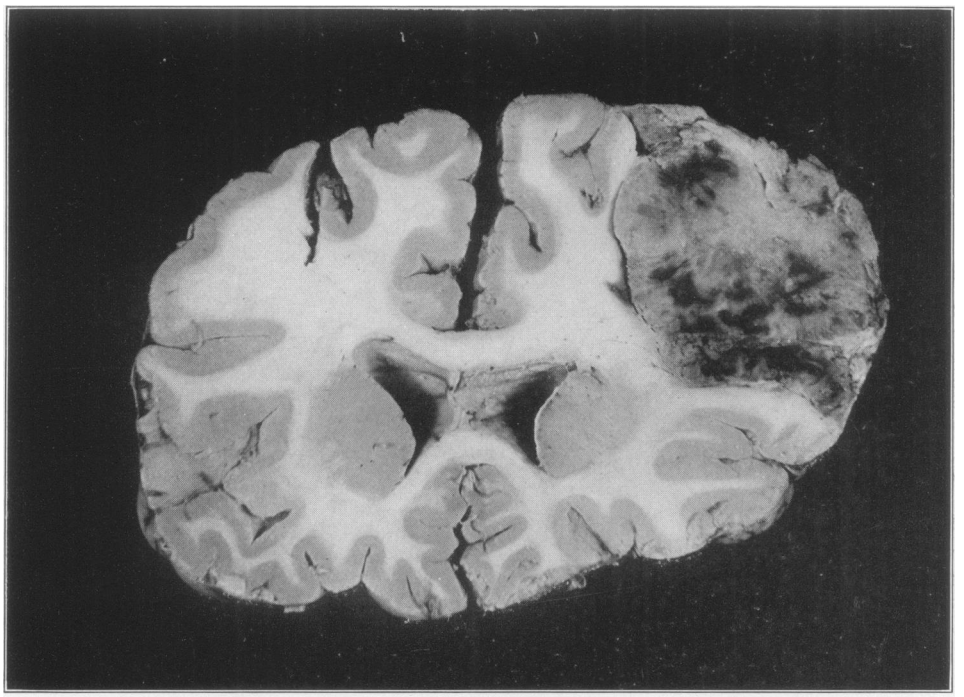
DESCRIPTION OF PLATE

PLATE 18

FIG. 1. Coronal section through the right frontal lobe of the brain. Note that the tumor is sharply demarcated from the surrounding brain tissue. The reddish streaks within the neoplasm are somewhat exaggerated in this photograph, and contrary to their appearance in the fresh specimen impress one as distinct areas of hemorrhage.

FIG. 2. Photomicrograph of a field from the interior of the tumor. Note its fibrous appearance and the paucity of cells. Azocarmine stain. × 120.

FIG. 3. Field from the center of the tumor showing the extensiveness of the reticulum and collagen fibers that make up the bulk of the intercellular substance. Perdrau's stain. × 120.



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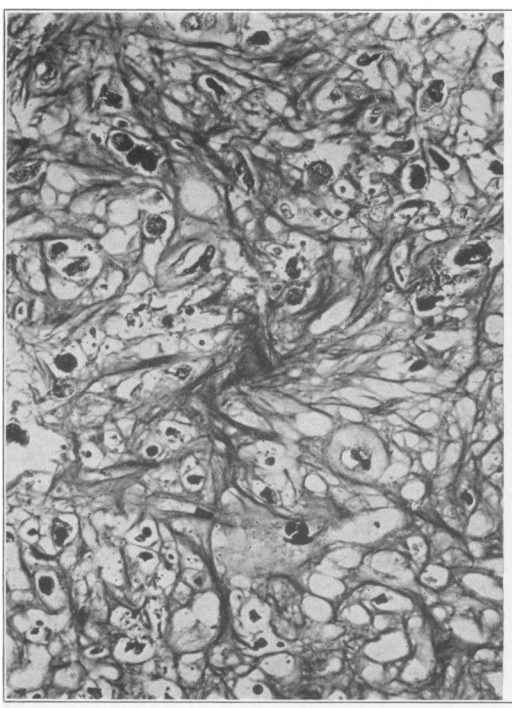

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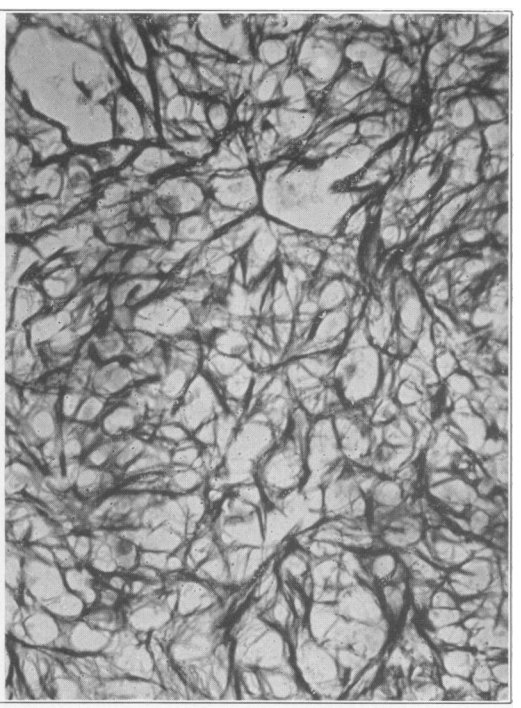

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Baker and Adams Primary Fibroblastoma of Brain