SPONGIOBLASTOMA MULTIFORME OF THE BRAIN

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Virchow [1] was perhaps the first to identify a large group of intracranial tumors which have their origin from the glial tissue of the brain. He described such neoplasms as slow-growing, infiltrating, vascular masses which are prone to contain hemorrhages, cysts and large areas of degeneration. He

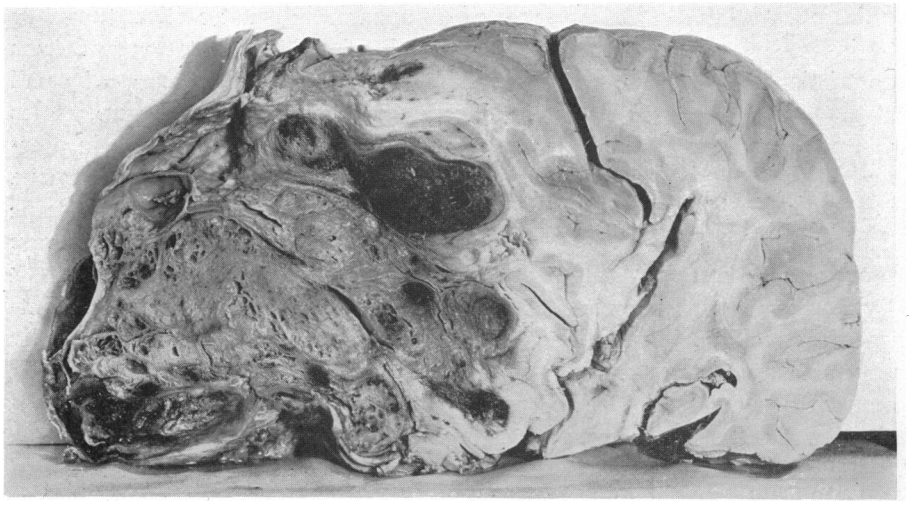

Fig. 1.—Coronal section of brain showing extensive cystic and hemorrhagic degeneration in the tumor which practically replaced the cortical tissue.

gave the name *glioma* to these new growths. At present such tumors are considered to be of ectodermal origin and to consist of glial cells and extracellular fibres. They are said to be found only in the central nervous system and its outgrowths, such as the retina.

Until recently, the rather inclusive and ill-defined term *glioma* has been given to all intracranial tumors to which Virchow's description applied. It may be realized how large a group of neoplasms came under this heading when it is remembered that gliomas constitute about forty per cent. of all intracranial new growths. That many of these tumors exhibit a gross pathological appearance and a clinical course which are entirely different from those of other growths in the same category had been recognized by many neurologic surgeons. It has remained for Cushing and Bailey,[2] however, to furnish a microscopical differentiation which may be correlated with the clinical course of the lesion. This has been done by the application of many of the gold and silver staining methods developed by Cajal and his school.

Such a study has furnished a means of reclassifying and subdividing the large number of gliomas into smaller groups, each with its characteristic gross pathological, microscopical and clinical picture. That such a reidentification should have for its basic principle the normal histogenesis of the brain seems only logical and natural. It has allowed these authors to identify in Cushing's series of intracranial tumors practically every cellular type found in the development of the central nervous system. Their work has afforded a definite and invaluable step forward in the surgical treatment of this large group of tumors of glial origin.

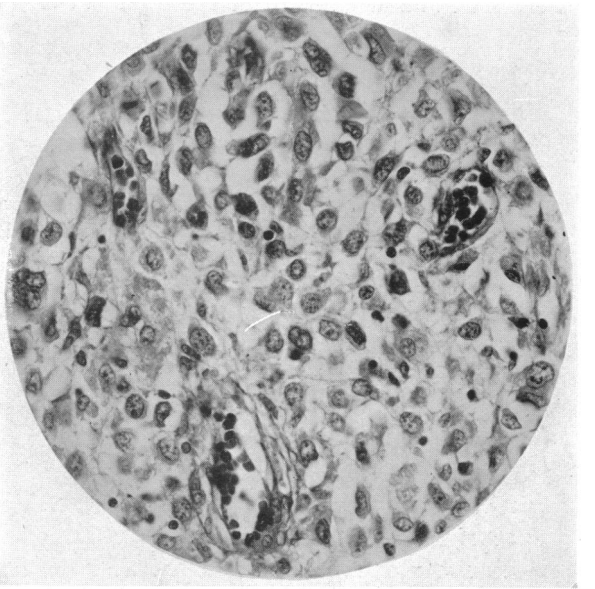

FIG. 2.—Section of tumor mass removed from brain. Blood-vessels show proliferation of endothelium and tumor cells appear to invade lumen. Alzheimer stain x 380.

It will be remembered that the medullary plate, from which the central nervous system develops, consists primarily of one layer of columnar epithelial cells known as the medullary epithelium. From this layer three types of cells may develop: (1) primitive spongioblasts, (2) medulloblasts or indifferent cells and (3) neuroblasts. The *primitive spongioblast,* in the course of its normal development, passes through a bipolar and unipolar stage to the astroblast which is the immediate forerunner of the adult fibrillary and protoplasmic astrocyte. The *medulloblast* or indifferent cell, as its name implies, has no prescribed line of development but may become either a glia or a nerve cell. The *neuroblast* passes through a series of stages like the spongioblast and eventually forms the adult nerve cell. As stated before, Cushing and Bailey have identified tumors arising from these cells in practically every stage of their development.

Globus and Strauss [3] and later Ribbert [4] proposed the name *spongioblastoma* for a large group of tumors whose cells are of neuroglial origin, and the qualifying adjective *multiforme* because their striking feature is their multiform appearance. Many of the cells are multinucleated and represent true giant cells. The amount of cytoplasm varies greatly while the nuclei are of various sizes and shapes and contain a variable amount of chromatin. In Cushing's large series of intracranial neoplasms the spongioblastoma multiforme was found most often.

It is known that some of these neuroglial tumors may be accompanied by multiple primary growth centres situated at some distance from one another within the brain. It is recognized also that the medulloblastoma may become disseminated through the subarachnoid spaces where, upon implantation, it loses its original characteristics. It is questionable, however, whether either of these processes constitute what is recognized as metastatic growth. That carcinoma of many viscera commonly metastasize to the central nervous system is well known, but a metastatic growth formed from a primary focus in the brain and situated at a distance and within fundamentally different tissue is a pathological entity which assumes clinical importance because of its rarity.

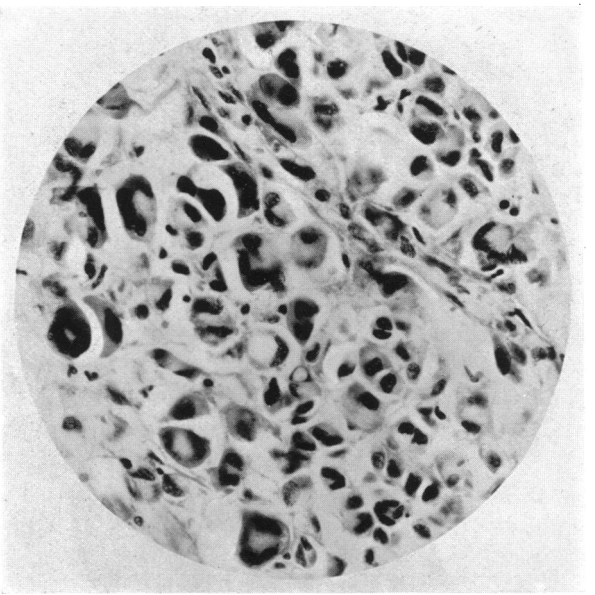

FIG. 3.—Section of tumor mass from brain showing multinucleated cells and division of cells. Mallory phosphotungstic acid-hematoxylin stain x 380.

Such an instance was met during the clinical course of the patient whose history is given in abstract:

Rapid onset of intracranial symptoms. Operation and removal of an apparently enucleable tumor from the left temporal lobe. Improvement in the symptoms. X-ray therapy. Progression of the symptoms. Second operation with removal of eighty grams of tumor tissue. Death three months later. Necropsy. Spongioblastoma multiforme with metastases in the right arm, left lung and the soft tissues over the right scapula and the left costal margin.

History.—K. K., aged thirty-one years, was referred by Dr. H. A. Richter, of Evanston, Illinois, and entered Wesley Memorial Hospital on January 10, 1926.

The patient was a concert pianist and felt quite well until October, 1925. She then noticed that she was playing the piano poorly because she could not take in a large sweep of notes at one glance. This made her playing uneven, irregular and choppy. In order to read ahead, it became necessary for her to turn her head in short movements to the right. After a time, which was very indefinite in her mind, she noted that she had diplopia. The false image alternately faded away and came back into her field of vision. Soon she developed a frontal headache which was very marked and was accompanied by vomiting.

These events occurred between October and December 25, 1925. She then was fitted for glasses, but three changes of lenses failed to give relief. About January 1, 1926, she first noted difficulty in saying words and in completely verbalizing her train of thought.

Examination.—There was a high degree of papilloedema in both fundi, and both blind spots were greatly enlarged. A right homonymous hemianopsia was quite evident. This was complete to the median line. There were never any hallucinations of light or

form in either the hemianopic or normal field. There was weakness of the left external rectus muscle and a ptosis of the left upper eyelid. There was no weakness of the right arm or leg and no sensory changes over the body. The patient had an incomplete verbal, nominal and semantic aphasia.

Course.—On January 14, 1926, an osteoplastic flap was made to expose the left temporal and parietal lobes and the posterior portion of the frontal lobe. A circumscribed tumor mass was found to occupy the posterior portion of the superior and middle temporal convolutions and the inferior portion of the parietal lobe. This was two centimetres beneath the surface of the cortex. The mass was separated from the surrounding cortical tissue by moist cotton pledget dissection. The portion of the tumor delivered was about the size of a large hen's egg. At its base the line of demarcation became indistinct and this edge of the mass removed was irregular. The remaining cavity was treated with Zenker's solution. A decompression opening was left in the flap which was replaced.

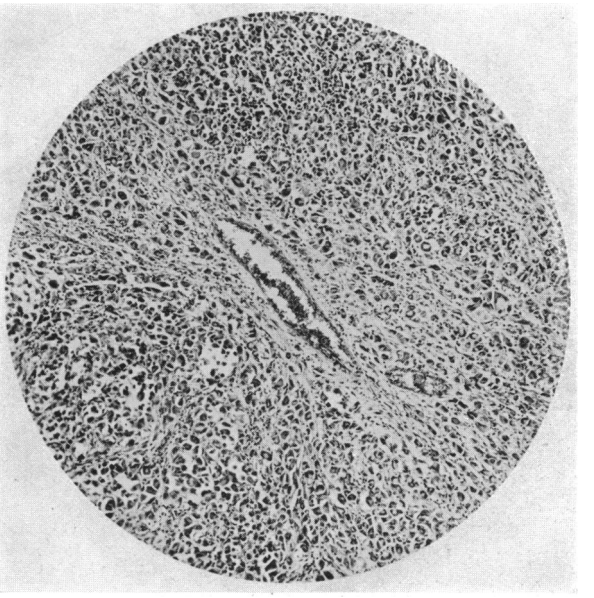

FIG. 4.—Tumor mass removed from soft tissue of right arm. Hematoxylin-eosin stain x 80.

The patient did well although her aphasia increased and her hemianopsia remained as complete. She went home on February 9, 1926. On February 15, she complained of stiffness in her right arm and leg, and her aphasia was increasing. She returned to the hospital on March 11, and upon five successive days received deep X-ray therapy over the area of the decompression and osteoplastic flap.

Following this, the decompression area began to herniate and by March 19 had assumed enormous proportions. I then reëlevated the bone flap and found that the tumor mass occupied the entire field. I removed about eighty grams of tumor tissue and replaced the flap without the bone. The patient's speech then became better and she became able to walk, although with a marked hemiplegic gait. She returned home on March 31, 1926. Her subsequent course from this time until May 17 was irregular, but on the whole she was comfortable and her condition did not become worse. On May 17 she suddenly developed a tremendous and acute increase in intracranial pressure and was returned to the hospital. The intravenous administration of hypertonic glucose solution gave immediate relief. Examination at this time revealed a tumor mass about the size of an English walnut over the posterior aspect of the right arm. This was firm, circumscribed and not painful. The aphasia and hemiplegia were unchanged. The herniation through the decompression area was quite large and was evidently a tumor mass. The patient again returned home on May 23.

On June 2, she returned to the hospital. She was then obviously failing rapidly. Hypertonic solutions were without effect. The mass over her right arm had grown to the size of a small orange, but was still circumscribed. The skin over it was not movable and was quite red. A small marble-sized tumor was found in the left axilla. On

June 15, a small mass exactly similar to those described was found over the eleventh rib anteriorly. It seemed to lie just beneath the skin. On June 18, a nodule was found in the substance of the right pectoral muscle. Exitus occurred July 20, 1926.

Necropsy.—There was a firm, movable, dark purplish mass in the soft tissues of the posterior surface of the right arm which measured 7 cm. in diameter. Another small firm nodular mass 1 cm. in diameter was present over the right scapula, and another 1.5 cm. in diameter at the left lower costal margin.

On the lateral surface of the lower lobe of the left lung were two small firm nodules measuring from 2 to 5 mm. in diameter. Another nodule 1.5 cm. in diameter was present in the centre of the upper lobe of the left lung. On section these nodules were flesh-like and slightly gray. No masses were found in the right lung.

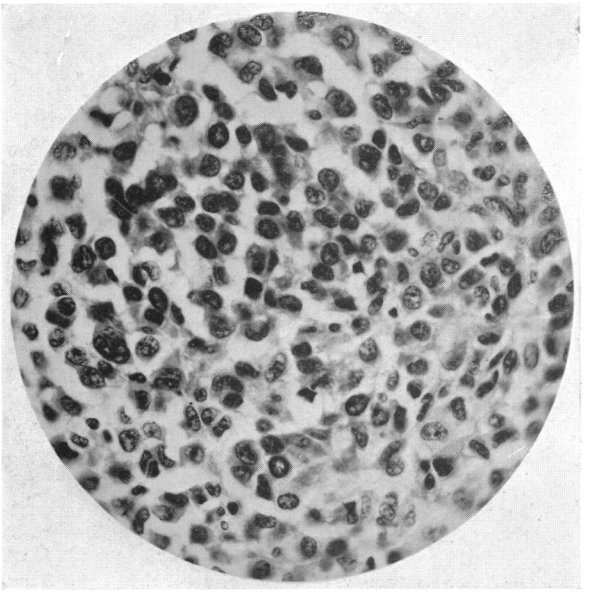

FIG. 5.—Section of tumor mass taken from soft tissues of right arm shows multinucleated cells similar to those found in the neoplasm of the brain. Hematoxylin-eosin stain x 380.

Upon fixation and removal, the brain showed a tumor mass which projected from the lateral surface of the left cerebral hemisphere. This was spheroidal and measured 15 cm. in diameter. It was composed of lobulated masses with numerous cystic and degenerated areas (Fig. 1). The opposite hemisphere was symmetrically shaped and showed no tumor masses.

Microscopic Anatomy.—A microscopic section of the neoplasm in the brain is made up chiefly of large glial cells which resemble the pyriform cells described by Globus and Strauss in cases of spongioblastoma multiforme. Many giant cells are present. The nuclei have bizarre shapes and seem to be dividing directly. No mitotic figures are present, although the unusual shapes of the nuclei give the appearance of mitosis. The cytoplasm is voluminous and stains opaquely. The lumen of many of the blood-vessels in the tumor tissue is closed by a proliferation of endothelial cells. The neoplasm appears to invade these hypertrophied vessels, but tumor cells are not found within the lumen of the vessels. There is a tendency for the cells to form a pseudo-palisade about the vessels. No nerve cells are found, and there is no tendency for the cells to develop into astrocytes.

The cells of the growths in the lung and in the soft tissues of the arm and back are similar in all respects to those found in the cerebral neoplasm. In these instances, however, the cells infiltrate fibrous connective tissue. Moreover there is no endothelial proliferation in the vessels such as is seen in the brain tumor. The similarity of the microscopic picture leaves little doubt that these tumors are metastases from the spongioblastoma multiforme of the brain (Figs. 2, 3, 4, 5, 6).

Dr. Wilder Penfield, of New York City, was kind enough to examine sections of the brain tumor and the metastases. His diagnosis was spongioblastoma multiforme. He adds, " There is one thing which is absent in this tumor which is found in most spongioblastomas, that is, the numerous small nuclei in cells with a scanty cytoplasm which I

have always considered to represent the spongioblast. In one or two areas of this tumor there are collections of these smaller cells but they are nearly altogether absent. Multiplication has taken place along the pyriform and giant cells."

Comment.—The tumors classified as spongioblastoma multiforme are the most common of the cerebral neoplasms. The unusual point of clinical interest in this instance is the occurrence of metastases at a distance in tissues embryologically distinct from the nervous system. Such metastases are so uncommon as to make them a rarity. The opposite process of metastasis from other viscera to the brain is not infrequent and has been well described by Grant,[5] Hassin [6] and many others.

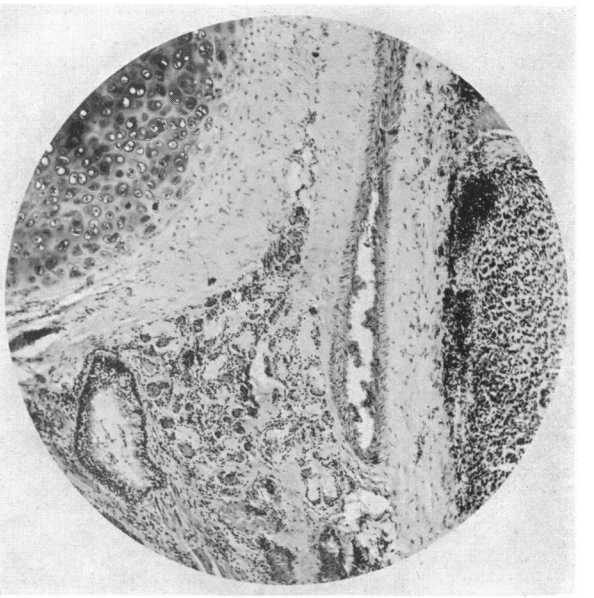

FIG. 6.—Section of tumor mass found in the lung which shows characteristic cells of spongioblastoma multiforme. Hematoxylin-eosin x 60.

In their excellent article upon the spongioblastoma multiforme, Globus and Strauss record no instance of metastases and attribute this fact to the limited migratory tendency of the spongioblast due to its special morphology. Spongioblastomas invade the surrounding cerebral tissue diffusely and produce degenerative changes in the neighboring normal brain cells. It is this constant process of destruction and repair which, in the opinion of Cushing and Bailey, produces the multiformity of their structure.

In Cushing's large series of verified intracranial tumors the spongioblastomas represented about one-third of all the classified gliomas. Because of their tendency to recur, even after the most extensive attempts at surgical removal, they have no doubt been the cause of the discouraging impression prevalent with regard to gliomas as a group. The clinical course of the case here reported furnished a typical example of their outstanding characteristics. At the first operation it was thought that an apparently enucleable mass had been removed. The photograph of the autopsy section shows how extensive and wholly undemarcated from normal brain tissue the tumor was at that time. The rapid growth and extension in spite of intensive deep X-ray therapy adds another discouraging chapter to the story. At present, at least, it appears that surgical treatment of these tumors can serve only to prolong life, save vision and alleviate pain. It should not be forgotten that the

spongioblastomas of the brain do not stand alone in this respect among malignant tumors.

BIBLIOGRAPHY

[1] Virchow, R.: Krankhafte Geschwülste. Vorlesungen, vol. ii, p. 129, 1864.

[2] Cushing, H., and Bailey, P.: Tumors of the Glioma Group. J. B. Lippincott Company, Philadelphia, 1926.

[3] Globus, J. H., and Strauss, I.: Spongioblastoma Multiforme. A Primary Malignant Form of Brain Neoplasm: Its Clinical and Anatomic Features. Arch. Neur. and Psych., 1925, vol. xiv, p. 139.

[4] Ribbert, H.: Ueber das Spongioblastom und das Gliom. Virchow's Archiv., 1918, vol. ccxxv, p. 195.

[5] Grant, F. C.: Intracranial Malignant Metastases. ANNALS OF SURGERY, 1926, vol. lxxxiv, p. 635.

[6] Hassin, G. B., and Singer, H. D.: Histopathology of Cerebral Carcinoma. Arch. Neur. and Psych., 1922, vol. viii, p. 155.