THE GROWTH OF GLIOBLASTOMA MULTIFORME
(ASTROCYTOMAS, GRADES 3 AND 4) IN NEUROSURGICAL PRACTICE

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In Bailey and Cushing's original series, the glioblastoma multiforme (astrocytomas, grades 3 and 4) made up about 40 per cent of their gliomas. In our series, this type of malignant glioma constitutes almost 60 per cent of the total number and more than 90 per cent of all gliomas in elderly patients.

Many pathologic investigations have been carried out regarding this type of tumor. The surgical treatment has not been solved. Attempts have been made by many neuropathologists to demonstrate the distribution of this highly malignant tumor in the brain, but their main interest has been its preferential sites and its microscopic differentiation in each location.

Ostertag described the location of the various types of gliomas, and recently Zülch published his own series of brain tumors and demonstrated preferential localization in each lobe. Ikuta suggested an embryologic reason for the location of certain gliomas in specific regions. However, few studies have been made concerning the gross aspect of growth and extension of this tumor on the laws governing structural development.

The earliest observations were made in this field by Stroebe in 1895. In 1934 Voris reported that 24 per cent of frontal-lobe gliomas have bilateral infiltration across the corpus callosum. In 1938 and 1940 Scherer worked on the forms of growth in gliomas and their practical significance. He obtained 120 gliomas at necropsy and studied the morphology of this type of tumor. At that time he said that “most investigators of the last twenty years have been fascinated by cytological and histogenetic problems to such a degree that they pay little attention to most of the other aspects of the morphology of glioma.” This curious state of things still seems to be true.

Astrocytomas, grades 3 and 4, have infiltrative characteristics of growth which make successful radical extirpation difficult. In the literature many workers frequently emphasized the fact that in a glioma “no capsule is formed.” In many cases that we have noted, astrocytomas, grades 3 and 4, have spread diffusely throughout much of the brain. Scherer said that primarily diffuse gliomas without formation of a definite mass and without pronounced destruction of the pre-existing tissue are encountered in about 25 per cent of gliomas in general.

Scherer also reported that in many glioblastomas, in medulloblastomas, in most of the oligodendrogliomas and cerebellar astrocytomas, and in the so-called polar spongiosblastomas, a narrow zone of infiltration is encountered. He thought that several factors such as an arresting of its spread at given pre-existing structures, especially in white matter at its junction with the cortex or deeper gray matter, would limit the growth of gliomas. He and others mentioned various types of growth in the glioma group and emphasized that the form of the glioma depends on the pre-existing brain tissue in which it is growing or on primary architectural properties of the brain. Recent studies...
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of growth and extension of gliomas have led to almost similar opinions by Russell and Rubinstein. Our investigation was designed to study the microscopic and gross morphology of glioblastoma multiforme (astrocytomas, grades 3 and 4) from the point of view of the feasibility of surgical excision of these neoplasms. Recent advance in neurosurgery makes it possible to locate a tumor in an early stage and to remove it widely with surrounding brain tissue. The feasibility of extensive hemispheral removal has been investigated in primates in our laboratories. The limitations of surgical excision of brain structures have been expanded to include the lenticular, caudate, amygdaloid nuclei and thalamus unilaterally. In recent years we have performed wide excision of these tumors, including removal of a portion of the basal ganglia and thalamus. One of us (C.S.M.) has mentioned that in most instances when a glioma had produced complete hemiplegia, the lesion had involved the internal capsule and the basal ganglia and had extended beyond the limits of operation. This concept might now be revised.

MATERIALS AND METHODS

In 100 consecutive cases of supratentorial astrocytomas, grades 3 and 4 (glioblastoma multiforme), tumors were obtained at necropsy for careful study. These tumors were from 57 males and 43 females and were investigated in the following manner:

1. Macroscopic observations were made on each brain. The clinical history of each case and the description of the tumor at the time of necropsy and photographs taken at that time were reviewed prior to examination of the brain itself.

2. The brains had been cut mainly by frontal sections at the time of necropsy, but further sectioning was done to determine the extent of the tumor. It was difficult to determine the gross limitations of most tumors because of their indistinct boundaries.

3. The macroscopic demarcation of tumor infiltration was carefully traced in so far as possible, with attention particularly to the relationship to anatomical brain structures such as external capsule, basal nuclei, internal capsule, diencephalon, mesencephalon, and especially the corpus callosum. Numerous microscopic sections were made from the tissue at the margin of each tumor.

4. Specimens for microscopic examination also were obtained from the normal-appearing areas at the edge of the macroscopic demarcation, especially the corpus callosum, basal ganglia, diencephalon, and mesencephalon.

On gross observation it was found that the tumor had not spread to the opposite hemisphere in 66 of the 100 cases. Microscopic preparations, however, showed infiltration into the opposite hemisphere, mesencephalon, or metencephalon in 13 of the 66 cases. The tumors in these 13 cases therefore were considered anatomically inoperable.

Consequently in 53 cases the tumor was limited to a single hemisphere, but 2 cases were included in which the tumors involved the hypothalamus unilaterally. Thus there were 51 cases in which macroscopically and microscopically the tumor appeared to be confined to one hemisphere without involvement of the hypothalamus.

It is well known that brain tumors spread along fiber tracts such as the corpus callosum or internal capsule. Gross inspection of the astrocytomas revealed that infiltration by the tumors is found frequently in some particular direction and that the anatomical background of the brain has a great influence on the spread of the tumor. For example, an astrocytoma of either grade 3 or 4 of the frontal lobe often spreads through the genu corporis callosi to the opposite hemisphere. However, an astrocytoma, grade 3 or 4, in the parietal or temporal regions is found more commonly with wide anteroposterior extension. Furthermore, the growth of the tumor is not infrequently retained from lateral spread by an internal or external capsule.

The 53 tumors involving a single hemisphere are classified and described according