STRUCTURE, NATURE AND CLASSIFICATION OF THE CEREBELLAR ASTROCYTOMAS

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Astrocytomas of the cerebellum are unusual among the gliomas of the brain. They differ materially, not only in symptomatology, but in operability, clinical course, and prognosis from astrocytomas of the cerebrum. They occur predominantly though not exclusively in children. They are usually associated with large cysts filled with a xanthochromic fluid of high protein content. They often arise within and destroy the vermis, while producing a cyst which involves one hemisphere of the cerebellum, thus giving rise to predominantly unilateral clinical manifestations of cerebellar dysfunction. These cysts are almost always outside of the tumor itself, the latter occupying only a small portion of the wall—the so-called mural nodule, although it should be noted that the solid mass of tumor is usually much larger than the word "nodule" would indicate. The remainder of the cystic wall is formed by compressed, sclerotic, non-neoplastic cerebellar tissue. Entirely solid tumors, unassociated with any cyst, are not uncommon.

Whether solid or partially cystic, these tumors, in striking contrast with the majority of the astrocytomas of the cerebrum and neural axis, are relatively circumscribed, only moderately invasive, but not encapsulated. They are usually readily extirpated, apparently in toto, although in a considerable number of cases minute microscopic nodules of tumor must be left by the surgeon. Nevertheless, in every case, in our experience, where the surgeon has believed that a complete extirpation of the tumor has been made the patient has subsequently recovered and to date shown no evidence of recurrence (Bailey, Buchanan and Bucy, 5). Cushing (15) in an extensive experience with 76 cases over a period of many years had a similar result. Ford (18) has recently regarded these tumors much more pessimistically and expressed the opinion that all ultimately recur. It can only be concluded that in his cases incomplete extirpations were made. Recurrence is the usual experience after a known incomplete extirpation, as is borne out by Cushing's experience and
by ours. The period between the initial operation and the recurrence is variable but always a matter of years. In one of Cushing's cases (No. 5) eleven years elapsed between evacuation of the cyst in 1911 and the recurrence of symptoms necessitating aspiration in 1922, and two more before extirpation of the tumor in 1924. In one of our cases the cyst was evacuated in 1930 and, because of the precarious condition of the patient, no attempt to remove the solid tumor was made. This boy is still alive and well without any evidence of recurrence over eight years later. Hausman and Stevenson (19) reported a case (the only one in the literature to our knowledge, although we have seen a similar case in which the tumor was a teratoid cyst) in which the relatively acute symptoms led to the diagnosis of a cerebellar tumor by Allen Starr. No treatment was undertaken. The symptoms subsided and at a necropsy examination many years later the presence of a cerebellar tumor was confirmed. The tumor proved to be a cystic astrocytoma.

Recurrence in cases of astrocytoma of the cerebellum may result either from refilling of the cystic cavity or more commonly from increase in the size of the tumor itself to the point where it fills and replaces the cyst cavity. Such growth of the tumor unquestionably occurred in 10 of Cushing's cases (Nos. 3, 4, 7, 14, 22, 25, 26, 41, 43, and 51), and we have noted it in several of ours.

Impressed by these differences between the cerebellar astrocytomas and astrocytomas elsewhere in the brain, we have re-examined the pathological material from our 25 cases of cerebellar astrocytoma to obtain a complete picture of these tumors and to evaluate the observations and conclusions recently recorded by others (Bergstrand, 9 and 10; Elvidge, Penfield and Cone, 17; Alpers and Rowe, 1). The sections were stained with hematoxylin and eosin or phosphotungstic acid-hematoxylin and impregnated by Perdrau's or Laidlaw's method for reticulin and collagen and Cajal's gold-sublimate method in every instance. In addition Weil's method for myelin sheaths, and Cajal's, Freeman's or Bodian's methods for nerve fibers were used in many cases. Furthermore, whenever possible sections were impregnated by Rydberg's silver diamino-carbonate method as advocated by Bergstrand. Although this method occasionally gave some beautiful impregnations it was non-specific in the extreme. It will impregnate almost anything which presents a surface to which the silver can adhere. Thus astrocytic processes, glial fibrillae, connective tissue, nerve fibers, cellular and even nuclear membranes are at times clearly outlined.

**Age Incidence and Location**

In our group of 25 cases the age varied from twenty-one months to twenty-two years, with an average age of 8.9 years. In Cushing's (15) 76 cases the ages varied from twenty-two months to forty-one years, with an average age of thirteen years. Of Bergstrand's 56 patients (10) none was over fifty years of age and forty-four (78.6 per cent) were under twenty-six years.

Elvidge, Penfield and Cone (17) in a recent study of the gliomas reported 14 cerebellar astrocytomas. Of these, 7 are said to have occupied the midline and 7 the cerebellar hemisphere. All of the former appeared between the ages of six and thirteen years, the average age being 9.5 years. All of the tumors of the hemisphere were in patients from seventeen to fifty-eight years of age.
FIG. 1. A. SOLID PROTOPLASMIC ASTROCYTOMA OF THE RIGHT CEREBELLAR HEMISPHERE OF A FIFTEEN-MONTHS-OLD GIRL

Liquefaction is occurring in the interior. The neoplasm is quite sharply circumscribed and readily distinguishable from the cerebellar tissue.

B. POSTOPERATIVE SPECIMEN

A tumor of the fourth ventricle has been removed. The origin of the tumor from the floor of the ventricle is clearly shown. Thionin. × 10.
age and the average age was 34.2 years. Although it is not clear just what criteria were chosen in distinguishing midline from hemispheric tumors, no such age differentiation is present in our slightly larger series of 25 cases. Five of our cases could be classified as strictly of the midline, 4 arising from the walls or floor of the fourth ventricle and lying within it (Fig. 1b), and one being a solid tumor of the vermis without any major lateral extension. The ages of these patients varied from three to fourteen years, with an average of 8.6 years. In 6 of the cases the solid portion of the tumor lay in or near the midline with a large extra-neoplastic cyst involving one hemisphere of the cerebellum. Although from a pathological point of view these tumors may be regarded as of the midline, such a description is clinically misleading, as the cystic involvement of the hemisphere gives rise to predominantly unilateral manifestations of cerebellar dysfunction. These patients ranged from three to ten and a half years of age with an average of 7.25 years. In two cases huge cysts involved the cerebellum bilaterally. In one, in an infant twenty-one months of age, the solid mural tumor lay in the inferior part of the left cerebellar hemisphere; in the other, in a man twenty-one years old, the location of the solid tumor is not clear from the records. In a third patient, a girl two and a half years old, a solid tumor involved the entire cerebellum. In 11 cases the lesion whether solid or cystic seemed confined to one cerebellar hemisphere. These patients varied in age from four to twenty-two years, average ten years.

**GROSS APPEARANCE**

As noted above, cerebellar astrocytomas may be cystic or solid, and the solid tumor whether associated with a cyst or not may be in any part of the cerebellum. The solid portion varies greatly in size. Usually it is rather
FIG. 3. 

A. **Fibrillary Astrocytoma**: Glial Fibrillae Arranged in Parallel

B. **Fibrillary Astrocytoma**: Fibrillae without Orderly Arrangement

C. **Protoplasmic Astrocytoma**: Fibrillary Processes Absent, in Contrast with the Fibrillary Astrocytoma

A, B, and C. Phosphotungstic acid-hematoxylin. × 290. Protoplasmic processes (Fig. 4c) are not well shown by this method.

D. **Protoplasmic Astrocytoma Showing Degenerative Changes**. Phosphotungstic Acid-Hematoxylin. × 130
large and may invade and destroy one entire cerebellar hemisphere, as in Case 1 reported here or as shown in Fig. 1A, a specimen from a fifteen-months-old child (not included in our 25 cases). Even when associated with cysts the tumors usually attain considerable size, although very occasionally a small mural nodule may constitute the only neoplasm present. Such an instance is illustrated by Fig. 2. This specimen is from a twenty-one-year-old woman, a victim of the erroneous advice, all too frequently repeated, that a carefully performed lumbar puncture can be made without any danger in cases of brain tumor. Following such a "carefully" performed lumbar puncture, in another institution, this patient became very ill and died two hours later of respiratory failure. Herniation of the cerebellar tonsils through the foramen magnum was demonstrated at necropsy.

The solid portion of the cerebellar astrocytoma varies in appearance from soft gelatinous white tissue which can be more or less readily removed with a suction apparatus to a grayish or brownish, firm, tough tissue which cannot be so removed. It is common to find small cysts containing a yellow fluid within these tumors. The tumors are rather sharply circumscribed and readily separable from the surrounding cerebellar tissue. They are relatively avascular and bleed little at operation.

Usually these tumors arise from the cerebellar substance, whether from cortical tissue or white matter can seldom be determined, though they rarely are visible on the exposed surface of the cerebellum. Those tumors which lie within the fourth ventricle arise from its walls and, as in the case illustrated in Fig. 1B, from the floor of that cavity.

**Microscopic Structure**

*Cytology:* Cerebellar astrocytomas present a more uniform microscopic appearance than most other gliomas. They are relatively acellular as compared with the others, but even they vary considerably in cellular density from case to case. The great majority of the cells are typical stellate astrocytes (Fig. 4c and d), and though they vary considerably in size from one tumor to another, they exhibit a striking constancy of size in the same tumor, aside from degenerative changes. The cells in the typical protoplasmic astrocytoma tend to have a larger cell body with more cytoplasm and fewer and shorter protoplasmic processes than those in a fibrillary astrocytoma, where the cell body is small due to the limited amount of cytoplasm and the processes are more numerous, longer, and of smaller diameter. In the protoplasmic astrocytoma the loose, rather coarse, lace-like matrix of the tumor is formed almost exclusively by these cytoplasmic processes (Fig. 3c and d). In the fibrillary astrocytoma, on the other hand, the dense, fine fibrillary matrix is formed in large measure by the fine fibrillae, which greatly outnumber the cellular processes (Fig. 3a and b). Unlike the astrocytes in healthy or sclerotic but non-neoplastic brain tissue, processes with vascular terminations are uncommon in either type of tumor. Hortega (20) found such vascular feet as do exist to be somewhat more numerous in the protoplasmic astrocytomas.

In addition to the astrocytes, various other glial cells of the spongioblastic series (spongioblasts, astroblasts, and oligodendroglia) are often demonstrable
Fig. 4. A. Area in a Fibrillary Astrocytoma resembling an Oligodendrogloma; Deposits of calcium present in lower part of field. Hematoxylin and eosin. × 160

B. Area from a Mixed Astrocytoma and Astroblastoma containing many astroblasts. Cajal's gold sublimate. × 300

C. Protoplasmic Astrocytoma. Cajal's gold sublimate. × 325

D. Fibrillary Astrocytoma (from same case as Fig. 8a). Cajal's reduced silver method for nerve fibers. × 250
but, except for those tumors, rare in the cerebellum, which represent a transition between, or an admixture of, astrocytoma and spongioblastoma, astroblastoma or oligodendroglioma, such cells form a distinct minority of those present, certainly far less than 1 per cent. In one astrocytoma of the fourth ventricle which contained numerous deposits of calcium there was in one region particularly rich in calcium a small field which presented the typical appearance of an oligodendroglioma (Fig. 4A). As no other similar areas were found, it was not possible to impregnate these cells by the various methods for oligodendroglia. One cerebellar tumor contained areas typical of a protoplasmic astrocytoma and others typical of an astroblastoma (Fig. 4B). As the latter predominated the tumor was classified as an astroblastoma. Still another cerebellar tumor represented an admixture of astrocytoma and spongioblastoma polare and, for the same reason, was classified as a spongioblastoma.

Investigators have been aware of this tendency for all gliomas to contain the various cellular elements, both embryonic and adult, of the spongioblastic series (Bailey and Cushing, 8; Bailey, 2; Bailey and Bucy, 6; Elvidge, Penfield and Cone, 17; Loisel, 24; Hortega, 20, and others), and Bailey (2, 3, 8) has repeatedly pointed out that the classification of any tumor should depend upon the predominant cell-type present, with the possible exception of a cerebral astrocytoma undergoing malignant transformation toward a glioblastoma, in which case the tumor should be classified as a glioblastoma or its potentially malignant nature indicated.

Of all the intracranial gliomas the cerebellar astrocytomas present the typical cell, the astrocyte, in the "purest culture" and contain the fewest "contaminations" by embryonic cells and other adult glial cells. It is accordingly not a little surprising to find that Bergstrand has been so impressed by the presence of occasional spongioblasts and astroblasts in these cerebellar tumors as to have objected that the term astrocytoma is inappropriate and on one occasion (9) to have advanced the term *gliocytoma embryonale* and on another (10) to have insisted that these tumors are not neoplasms at all but congenital malformations. With the question of malformations we shall deal more fully later. But if we are to apply the term *gliocytoma embryonale* to these tumors then we must apply it as well to all other gliomas, as none is absolutely pure as to cell-type; all contain other cells of the spongioblastic series and frequently they are of embryonic type. Of all the gliomas, a less appropriate one for the term *gliocytoma embryonale* than the astrocytoma could hardly have been chosen.

The nuclei of the astrocytes usually are small, round or oval, moderately well supplied with chromatin granules, devoid of a definite nucleolus, and somewhat eccentrically placed in the cytoplasm. Occasionally, however, particularly in tumors with large or giant cells, the nuclei are much larger, usually round, vesicular, with less chromatin and one or two distinct nucleoli. These nuclei are readily confused with those of neuroblasts or neurocytes, though more thorough examination will reveal no other characteristics of such cells. Fortunately such confusing and atypical nuclei are rarely found in the cerebellar astrocytomas, although they are not infrequent in such tumors in the cerebrum and basal ganglia. Mitotic figures are never found in a typical cerebellar astrocytoma. Although it would not be surprising to find mitoses
Fig. 5. A. Mixed protoplasmic and fibrillary astrocytoma with small areas of cystic degeneration. Phosphotungstic acid-hematoxylin. × 110

B. Protoplasmic astrocytoma: neighboring areas of healthy (right side) and degenerated (left side) tumor tissue. Hematoxylin and eosin. × 60
in a tumor transitional between an astrocytoma and a more embryonic form, such as an astroblastoma, they have not been present in the few cerebellar tumors of this type which we have examined. It has been stated that amitotic cellular division occurs in the astrocytomas (Bailey and Cushing, 8), but examples even of this type of cellular proliferation are difficult to find.

In the cerebellar astrocytomas glial fibrillae are almost always demonstrable but they vary greatly in number. In the typical compact fibrillary astrocytoma myriads of glial fibrillae are present in a dense network (Figs. 3A and B). Often they are arranged in an interlacing feltwork (Fig. 3B); at other times they are parallel to one another (Fig. 3A). In the typical protoplasmic astrocytoma, with its loose reticulated matrix composed of protoplasmic cellular processes, no fibrillae are found. Such tumors, completely devoid of glial fibrillae, are rare in the cerebellum and a few fibrillae can usually be found. There are, however, many astrocytomas composed predominantly of protoplasmic astrocytes which do not form fibrillae (Fig. 3c and d). In the majority of cerebellar astrocytomas both fibrillary and protoplasmic astrocytes are present but these vary in proportion from case to case (Fig. 5A).

Degenerative Changes: Degenerative changes are common in the cerebellar astrocytomas (Fig. 5B). In the degenerated areas the cellularity is greatly reduced; in fact, the cells may disappear entirely, leaving behind a ghost-like non-staining reticular framework except for a few glial fibrillae here and there which still retain their tinctorial characteristics (Fig. 6B). This, however, is not a common development. Usually a fair number of cells persist in a variable state of health, many of them showing degenerative changes. Their protoplasmic processes become swollen and tortuous, and break off from the cell-body forming spheroid, club-shaped, and irregular band-like structures. These will be dealt with later. The cytoplasmic body becomes swollen, granular, and eosinophilic, and the nucleus is displaced to one side or may disappear. This is the typical process of clasmatodendrosis common to degenerating astrocytes everywhere. Not infrequently large multinucleated cells appear (Fig. 6c), although seldom in the number or with the frequency common to the glioblastoma. The intercellular tissue becomes vacuolated (Fig. 3d and 5B), and at times liquefaction of the tissues gives rise to microscopic cysts of various size, filled with a fluid of high protein content (Fig. 5A). At times (Fig. 3d) the astrocytes about the blood-vessels are better preserved than those in the intervascular tissue. The glial processes and fibrillae disintegrate or liquefy, as Elvidge, Penfield and Cone illustrated. It is not common to find much fat in the degenerated areas but occasionally numerous globules of fat engulfed by phagocytes are present (Fig. 6E).

Above we have referred to the hyalinized spheroid, club-shaped, band-like and thread-like bodies which arise from degeneration of the cytoplasmic astrocytic processes (Fig. 6d). These bodies have been observed by numerous investigators in various gliomas; they are not peculiar to cerebellar astrocytomas. Verhoeff (29), seeing them in gliomas of the optic nerves and chiasm, referred to them as "cytoid bodies." They have been encountered in various sclerotic processes in the central nervous system, about syringomyelic cavities, etc., where they have been called "Rosenthal fibers" (22, 23). They stain by almost every method, indicating their degenerated nature. They are eosino-
FIG. 6.  

B. FEW REMAINING GLIAL FIBRILAE IN AN OTHERWISE COMPLETELY DEGENERATED AREA IN AN ASTROCYTOMA. PHOSPHOTUNGSTIC ACID-HEMATOXYLIN. × 230

C. MULTINUCLEATED GIANT CELLS IN AN ASTROCYTOMA. HEMATOXYLIN AND EOSIN. × 300

D. SWOLLEN DEGENERATING GLIAL PROCESSES KNOWN AS CYTOID BODIES OR ROSENTHAL FIBERS

Several fine, normal glial fibers can be seen, particularly in the upper left-hand quadrant of the field. Various stages in the transformation of these fibers can also be seen. Weil’s method for myelin sheaths. × 160.

E. FATTY DEGENERATION IN A PROTOPLASMIC ASTROCYTOMA. HERXHEIMER’S SCHARLACH R. × 150

Philic in hematoxylin and eosin preparations; blue, usually, in phosphotungstic acid-hematoxylin sections; dark blue in tissues stained for myelin sheaths, etc. They are finely granular or homogeneous, are of course devoid of nuclei, and are most prevalent in areas of moderate degenerative change. Bergstrand considered them to be obviously malformed myelinated nerve fibers ("offenbar missgebildete markhaltige Nervenfasern"). It seems to us that this contention is erroneous. Degenerating myelin sheaths are not uncommon in the periphery of any cerebellar astrocytoma (Fig. 8B), but they never assume the 

1 There is no Fig. 6A.
characteristics of these structures. In fact, in the degenerating areas where these bodies are seen myelin sheaths and nerve fibers are not encountered. Furthermore, where in the degenerating or malformed nervous system can similar structures indubitably related to the myelin sheaths be found? Certainly that they stain with hematoxylin in the various methods for myelin sheaths is no proof of such a relationship, since too many other structures obviously of no kinship to myelin stain by the same methods. We have endeavored to show in Fig. 6D the transformation of the glial processes into these degenerated spheroid and club-like forms. Some of the spheroid bodies may represent the degenerated cytoplasmic body of an astrocyte which has lost its nucleus.

It is obvious from Bergstrand's first two illustrations (10: Abb. 1 and 2, p. 726) that the marked variation in the cerebellar astrocytomas which he has stressed is due to the degenerative changes described above. His first figure is a typical example of degeneration in an astrocytoma. The tissue is relatively acellular. Several of the cells have swollen granular cytoplasm with eccentric nuclei (lower right-hand corner). There is a large multinucleated cell in the upper right-hand corner. There are also several variously shaped anuclear "cytoid bodies." The single blood vessel, though markedly shrunken and torn away from the surrounding tumor tissue by too rapid dehydration, was obviously distended and thin-walled in the intact tumor. Cushing (15) has fallen into the same error of placing too much emphasis on degenerative changes.

Blood Vessels and Connective-tissue Stroma: In healthy tumor tissue the blood vessels are few and small (Fig. 7A). Their thin walls are often composed of little more than the endothelial lining and a supporting connective-tissue adventitial coat. There is rarely any connective tissue present aside from the vessel walls. In the degenerated areas the blood vessels are grossly altered. They become distended, probably because of the removal of the usual support of a healthy fibrillary tissue from their walls. Sprouting and proliferation of new blood vessels occurs giving rise to a telangiectatic appearance (Fig. 7B). Frequently these vessels have abnormally thin walls, often composed of little more than endothelium. Many of the vessels show changes of a different character. Proliferation of the endothelium and adventitia has occurred, the lumen is greatly reduced or obliterated, and often the wall has undergone hyalinization (Fig. 7C). It is not to be assumed that these vascular changes are peculiar to the cerebellar astrocytomas. The same changes are even more prevalent in the glioblastomas (Elvidge, Penfield and Cone, 17), in which degenerative changes of all kinds are also much more common. Such changes may also be observed in other, non-neoplastic pathological areas. Proliferation of the endothelium with reduction of the lumen and hyalinization of the walls is also commonplace in the oligodendrogloma (Bailey and Bucy, 6). The proliferation of the adventitia is usually more or less compact and concentrically arranged (Fig. 7C) and as a rule does not have the lacy character seen in the astroblastoma (Bailey and Bucy, 7). Occasionally in degenerated areas there will develop intervascular bands of connective tissue in addition to that confined to the vessel walls.
FIG. 7. VASCULAR CHANGES IN FIBRILLARY ASTROCYTOMA

In A are seen the few small thin-walled blood-vessels in a healthy portion of the tumor (Perdrau's method. × 75). B shows proliferation of vessels giving rise to a telangiectatic area in the same tumor (Perdrau's method. × 130). C shows the marked thickening of the vascular wall, causing obliteration of some of the lumina, also in the same tumor (Perdrau's method. × 75).

D shows another fibrillary astrocytoma. The wall of the smaller vessel contains two plaques of calcium. In the lower right-hand corner is a larger plaque of calcium free in the tissue (hematoxylin and eosin. × 325).
Calcification may occur but is not frequent in these tumors as it is in the oligodendroglomiomas (Környey, 21; Bailey and Bucy, 6); even when it is present there is little evidence that the calcium is deposited in the vessel walls as Bergstrand (10) contends. The mere fact that it is deposited in concentric rings forming typical calcospheres (see Bergstrand's Abb. 4) is meager proof that it has been laid down within the wall of a blood vessel. Usually the deposits are scattered throughout the neoplastic tissue with no relation to the vessels. Only rarely have we observed calcification in a vessel wall and in those cases the calcium deposit usually consisted of a small sphere (Fig. 7). 

*Nerve Cells and Nerve Fibers in the Tumor:* That the intracerebellar tumor contains nerve fibers, abnormal (degenerating) myelinated fibers, and embryonic glial cells is certainly true, but not in the sense of primary heterotopic constituents as Bergstrand states. Nerve fibers, both those still retaining their myelin sheaths—which are few—and those from which these envelopes have disappeared, are present only at the periphery of the tumor, just within its invasive edge where tumor cells are infiltrating among the normal constituents of the cerebellum (Fig. 8a). The myelin sheaths withstand this invasion poorly; they soon disappear, are never found in great numbers, and when they are present lie only a short distance within the invading margin (Fig. 8b). The axis cylinders are somewhat more resistant and are found in greater numbers. At the margin of the tumor they can be seen passing from the more normal cerebellum into the tumor tissue (Fig. 8a). Toward the interior of the tumor they rapidly diminish in number and are rarely found more than a few millimeters from the invading edge. (Diffuse astrocytomatos hypertrophy of the brain stem presents a different appearance and in a recent case of this type involving the thalami we have found more or less intact nerve fibers and ganglion cells throughout the tumor.) Just within the margin of a cerebellar astrocytoma there may occasionally be found a degenerating ganglion cell which has been surrounded by the invading tumor and temporarily survives in an impaired state of health. Such a finding, however, is rare, as would be anticipated, because the ganglion cells are the first to disintegrate in the compressed cerebellum before the advancing margin of the tumor. Neuroblasts either at the margin of the tumor or within its interior we have never seen.

*Neighborhood Changes:* That there is no sharp boundary between cerebellar tissue and tumor, and no encapsulation is, of course, true of this and all other encephalic gliomas. That the overlying cerebellum is abnormal and the pia-arachnoid membrane often likewise, is true, and to be expected, but we believe that these abnormalities are for the most part simple of explanation, the result of compression, distortion and invasion by the tumor and not in the nature of a heterotopism as Bergstrand contends.

*A priori,* what would we expect to find in the cerebellar tissue overlying an astrocytoma, compressed and distorted by it? That the tissue would be compressed, thinned, vacuolated, and degenerated, that the ganglion cells would be disintegrating or have disappeared, that the glia would have undergone hypertrophy and proliferation (gliosis), unless the process were so severe as to have destroyed it, and that the folia would be widened and flattened just as are the cerebral gyri overlying any subcortical tumor. These are the changes which
A. Fibrillary astrocytoma: On the left is the cerebellar tissue containing many intact nerve fibers; on the right the tumor tissue containing disintegrating fragmented nerve fibers. Between them is the zone of invasion of cerebellar tissue by the neoplasm. Same case as Fig. 4d. Cajal's reduced silver method for nerve fibers. × 300.

B. Fibrillary astrocytoma: Similar in orientation to A above but the myelin sheaths are stained rather than the nerve fibers. A and B are from different tumors. Weil's method. × 300.
are found and part of the ones which Bergstrand has cited as heterotopic. Certainly the alteration in the contour of the cerebellar folia is of obvious origin and need detain us no further. The microscopic changes in the cerebellar tissue are of interest, even though largely the result of compression and the resultant ischemia.

In the cerebellar tissue overlying the tumor the Purkinje cells lying at the junction of the molecular and granular layers are usually either destroyed or degenerating. The granular layer seems to be equally susceptible to compression (Fig. 9B). The cells are usually either greatly reduced in number or occasionally are all destroyed. The tissue is vacuolated and the astrocytes within it hypertrophied and increased in number. The underlying white matter is more or less demyelinated and the axis cylinders may show evidence of degeneration and reduction in numbers, although in general they withstand compression much better than their enveloping myelin sheaths. Gliosis, with the production of gigantic astrocytes, is most marked in the white matter, and the glial fibrillae have a parallel arrangement (Fig. 9A), apparently determined by the nerve fibers, giving rise to a columnar gliosis typical of glial sclerosis in any bundle of nerve fibers.

The molecular layer is thinned, its cellularity is reduced, and gliosis is not a prominent feature. Bergstrand states that in the outer part of the molecular layer he finds an unusual layer of neurofibrils and glia which are connected with the “heterotopic tumor network” in the pia mater by numerous bridges. We have been able to demonstrate and examine the structures he describes and illustrates but are unable to concur in his conclusions.

The glial structure of the molecular layer of the cerebellum, as Cajal (13) has shown, is composed, apart from the “epithelial” cells of Golgi whose cell bodies lie in the Purkinje-cell layer, of long cytoplasmic glial processes which pass across this layer perpendicular to the surface. The cell bodies from which these processes arise consist of protoplasmic astrocytes in the granular layer and fibrillary astrocytes in the underlying white matter. The processes pass upward toward the surface parallel to each other. On reaching the outer surface of the molecular layer they turn at right angles to form a layer of glial processes just beneath the pia mater (Cajal, 13). It is undoubtedly these glial processes which Bergstrand has impregnated with Cajal’s reduced silver method (see his Abb. 16) and interpreted as neurofibrils. This error is the result of too much confidence in the reduced silver method of Cajal for nerve fibers. Although the method does usually stain such fibers well, it usually impregnates connective-tissue fibers equally well and can be made to impregnate glial processes also (Fig. 4D) (Bucy and Muncie, 11). That the method was not specific in the illustration cited (Abb. 16) is obvious—the reticulin and collagen of the pia-arachnoid membrane are densely impregnated.

The bridges connecting the molecular layer and the overlying abnormal pia-arachnoid membrane we have also seen (Fig. 10A), not only in connection with cerebellar astrocytomas but with glioblastomas of the cerebral hemispheres as well, and Oberling (25) has described them in connection with a glioma of the mesencephalon. The glial processes traversing the molecular layer from the granular layer and white matter may pass outward through these bridges into the pia-arachnoid membrane, as Bergstrand illustrates.
FIG. 9. DEGENERATION IN NEIGHBORING CEREBELLM

A. Columnar gliosis in the white matter. Phosphotungstic acid-hematoxylin. \( \times 70 \).

B. In the upper part of the illustration is the white matter with many hypertrophied fibrillary astrocytes. Beneath it is the vacuolated degenerated granular layer and at the bottom the relatively normal molecular layer. There are no Purkinje cells. Cajal's gold sublimate. \( \times 80 \).
(Abb. 10), but more frequently the glial processes forming these bridges arise from the superficial tangential layer just described, turn at a right angle and pass outward. This is in agreement with Oberling's illustrations. In spite of repeated effort, we have been unable to demonstrate any nerve fibers in these bridges and find them purely glial. In the pia-arachnoid membrane these processes are always readily distinguishable from the connective-tissue fibers. We have been unable to draw any definite conclusions as to whether these glial bridges are congenital malformations, as Bergstrand and Oberling contend, or are the result of compression and distortion of the tissues by the tumor. We have not seen them except in areas where the pia-arachnoid membrane has been invaded by tumor (Fig. 10A).

The pia-arachnoid membrane covering the folia overlying a tumor or its cyst are frequently abnormal, though we have by no means been able always to find such change as Bergstrand reports. The alteration may take one of two forms. Not infrequently it consists of a simple connective-tissue hyperplasia, and is not dissimilar to that found overlying other gliomas. The cause of this hyperplasia is not clear. It is not peculiar to cerebellar astroblastomas, and we see no reason to conclude that it constitutes a congenital malformation. More interesting are the not uncommon areas in which tumor tissue has actually invaded the subarachnoid space (Fig. 10B). Unlike the primary intracerebellar tumor, this has an alveolar structure due to its growth among the hyperplastic connective-tissue bands (Fig. 10C). This alteration in microscopic appearance is comparable to that of all other gliomas, e.g., medulloblastoma, glioblastoma, etc., which invade the subarachnoid space, but we have never seen metastasis from the astrocytomas to the subarachnoid space as occurs with the medulloblastomas and such as Cairns and Russell (12) describe. We have carefully investigated this tissue. There is no evidence that it is composed of other than the neoplastic glial cells of which the primary tumor is composed. It is sharply separated from the cerebellar tissue by the pia mater, as Bergstrand clearly shows in his Abb. 11. We have never observed it invading the cerebellar cortex along the perivascular sheaths, although it is conceivable that it might rarely do so. Restrained between the connective-tissue bands of the pia-arachnoid membrane, the tumor cells and fibrillae tend to have a more parallel arrangement than is usual in the primary tumor. This, however, is a relative matter and cannot be stressed. In this subarachnoid tumor, contrary to the statement of Bergstrand, we have never been able to demonstrate a single nerve fiber or a single cell remotely resembling a neurocyte or neuroblast. Certainly Bergstrand's contention that neuroblasts are the chief cellular constituent of the tumor within the pia-arachnoid membrane ("Neuroblasten bilden das Hauptbestandteil des heterotopen Tumorgewebes in der Pia") is clearly erroneous. Those cells shown by him as neuroblasts in his Abb. 17 are not convincing. The fact that they were impregnated by Cajal's reduced silver method is inconclusive evidence, for that method, as we have previously noted, is far from being exclusively specific for cells and fibers of the neuroblastic series (see Fig. 4D). That the tumor constitutes invasion of the subarachnoid space from the primary intracerebellar tumor and is not a malformation developing originally in the pia-arachnoid membrane seems clear from the fact that actual invasion from the tumor can be seen (Fig. 10A).
FIG. 10. INVASION OF PIA-ARACHNOID MEMBRANE

A. In the upper half of the illustration is the tumor, which has broken through the pia mater and invaded the subarachnoid space. In the lower half is the neighboring cerebellar cortex connected with the pia-arachnoid membrane by several glial bridges. Hematoxylin and eosin. × 60.

B. The invaded pia-arachnoid membrane filled with astrocytes and glial processes. Phosphotungstic acid-hematoxylin. × 80.

C. From the same area as B, in a neighboring serial section, showing the connective tissue of the leptomeninx between the bundles of which the tumor lies. Perdrau's method. × 80.
NEOPLASM OR CONGENITAL MALFORMATION

Bergstrand repeatedly and clearly states that he believes these astrocytomas to be malformations—not tumors. Here one must be careful to distinguish between congenital tumors and malformations. If any one were to assert that astrocytomas, as well as many other intracranial gliomas, such as medulloblastomas, are neoplasms present at birth or arising from a developmental fault, we could have no quarrel with such a view. We might contend that the thesis is unproved, but that it is imperfectly and indirectly supported by many facts no one could deny. This, however, is apparently not Bergstrand’s view. What then is the difference between a congenital malformation and a congenital tumor? Each may consist of a mass of tissue abnormally present. We are even willing to admit that either might be associated with a cyst. The important difference appears to be growth—a malformation does not grow or at least does not grow disproportionately to the rest of the body. It represents an error in development in the tissues. It may lie quiescent or it may give rise to symptoms, but never as a result of the proliferation of abnormal cells. If its cells do proliferate, then it becomes a tumor. Thus one may find rests of stratified squamous epithelium in the hypophysis (Carmichael, 14). So long as they remain quiescent they constitute a malformation. If, however, they grow, as some contend (3), and produce a craniopharyngioma, this is regarded by all as a neoplasm. Similarly there occur in the midline of the back small epithelial sinuses—the congenital dermal sinuses of Walker and Bucy (30)—which lead downward from the skin to the spinal cord and its coverings. These sinuses frequently convey infection inward and thus give rise to symptoms. But no one would regard them otherwise than as congenital malformations. Occasionally, however, the tissues at the bottom of the sinus proliferate, forming a dermoid or epidermoid tumor (27), which is no longer a malformation but a neoplasm.

With this contention Bergstrand would seem to agree, for he appears to believe that the cerebellar astrocytomas do not grow but that they produce symptoms either by the production of cystic fluid or by the fact that they occupy required space and that pressure symptoms develop from the normal growth of the surrounding cerebellum ("Cystische Erweichung und ein Missverhältnis zwischen Wachstum von Missbildungen und Kleinhirn erklärt die Symptome"). He is not, however, perfectly satisfied with this view, for he states that growth of the tumor is possible but not certain, and then again says that, even so, such growth is not out of proportion to the growth of the normal structures, thus implying that such proportionate growth is probably to be expected in a malformation. He appears, however, to be slightly disconcerted by one of Cushing’s (15) cases in which at a second operation the tumor mass was so voluminous that growth must have occurred between the two operations. As a matter of fact there were 10 of Cushing’s cases (Nos. 3, 4, 7, 14, 22, 25, 26, 41, 43, and 51) in which growth of the tumor undoubtedly occurred between the first and second operations, and several others in which such growth probably took place. To quote Cushing himself, he has found “that symptomatic recurrence may be expected after mere cyst evacuation; that the cysts contain a mural tumor which may be expected to increase in size ulti-
mately to fill and largely replace the cavity." Our experience has been similar and we recite in detail one case in which growth of the tumor indubitably occurred.

CASE 1: I. H., a schoolgirl, was perfectly well until the age of seven and one-half years, when she began to suffer from headaches and to vomit. Her gait soon became unsteady, and her head began to enlarge. She was admitted to the hospital on Feb. 22, 1934, one and one-half years after the onset of symptoms. She was completely blind, was confined to bed, and had a huge hydrocephalic head.

First Operation: Operation on March 1, 1934, disclosed a solid astrocytoma which occupied almost the entire right hemisphere of the cerebellum, lying only 5 mm. beneath the surface of the cortex. An estimated two-thirds or three-fourths of this tumor was removed,
not be delivered through the suboccipital craniectomy in one piece. It was therefore removed piecemeal (Fig. 11). The extirpated tumor weighed 111 gm. After its removal no cerebellar tissue could be seen in the right side of the cerebellar fossa.

The patient made a rapid recovery from the operation, was discharged from the hospital after twenty-two days, and has since been in excellent health except for the blindness.

There can be no question but that marked growth of this solid tumor occurred during the almost three years which elapsed between the two operations. No question of refilling of a cystic cavity was involved.

This case and those reported by Cushing would seem to leave no doubt that these tumors grow. That the cysts are a potent force in the production of symptoms no one would deny. But that they are essential is refuted by the occurrence of solid tumors without cysts (Fig. 1A), and in any case their presence, common to many types of gliomas everywhere as well as to other tumors, is no argument against a neoplastic nature. Cellular proliferation and growth of these tumors having been established, Bergstrand's contention would seem insupportable. We have already discussed the other points which he has marshalled in support of his hypothesis. We are, therefore, forced to conclude that cerebellar astrocytomas are true neoplasms, composed almost exclusively of mature astrocytes, although, like every other glioma, they may contain a variable number of other adult or embryonic cells of the spongioblastic series. They present no definite evidence of a congenital origin. It is true they often appear early in childhood and this makes attractive such an unproved thesis. But a similar one applies to the medulloblastoma, the other common cerebellar tumor of childhood, with considerably greater weight of evidence (Bailey, 3; Ostertag, 26). The glial bridges which pass from the molecular layer of the neighboring cerebellar tissue to the pia-arachnoid membrane which has been invaded by tumor may conceivably be of congenital origin, although this is certainly not an established fact. Nevertheless, even though this and other facts may, in some small measure, point toward a congenital origin of these tumors, or to their genesis from a developmental fault, they do not give any support to the idea that cerebellar astrocytomas are congenital malformations rather than neoplasms or that they are composed of cells of embryonic type.

**Cyst Formation**

As Penfield and his associates (17) have pointed out, and as many have long realized, there are two types of associated cysts and tumors, *i.e.*, cysts within the tumor (Figs. 1A and 5A) and tumors within the cyst (Fig. 2). We agree with Elvidge, Penfield and Cone (17) that the intraneoplastic cysts, particularly the small ones, arise as a result of liquefaction of the tumor tissue. However, that the cysts outside the tumor are, as they apparently believe, similarly formed by liquefaction of the tumor we cannot accept. In our opinion such cysts, and possibly the large intraneoplastic cysts as well, are formed by transudation from the tumor's surface and for the following simple reason: If, as the following case fully illustrates, a cyst be evacuated by aspiration it soon refills and considerable intracystic pressure develops. In view of the known slow growth of these tumors, it is inconceivable that they could grow, refill the cavity, and again liquefy in the short time required for re-accumulation of the cystic fluid.
Case 2: J. M., a young man born on Oct. 6, 1904, began at the age of twelve and a half years to suffer from headaches and vomiting, staggering gait, and failing vision.  

First Operation: Six months after the onset of symptoms, October 1926, the patient was operated upon elsewhere. A cerebellar cyst was evacuated but the solid mural nodule of tumor was not removed. Relief was obtained until two years and two months later, when, in December 1928, his symptoms returned.  

First Aspiration: The patient was admitted to the University of Chicago Clinics and on May 11, 1929, a needle was inserted through the cerebellar decompression and 25 c.c. of xanthochromic cystic fluid removed. He was subsequently quite well until a short time before his readmission to the Clinics six months later, Nov. 14, 1929.  

Second Aspiration: The cyst was again punctured and 15 c.c. of xanthochromic fluid, which soon coagulated, was removed. Immediate improvement was the result. Headaches disappeared and uncertainty of gait was definitely improved. This improvement was short-lived, however, and on Dec. 6 the patient was readmitted.  

Second Operation: On Dec. 7, 1929, the cerebellum was exposed. A large cystic astrocytoma extending upward toward the mid-brain was disclosed and removed. The patient survived for five days in a state of unconsciousness and then died. Necropsy disclosed neoplastic invasion of the pons, part of which had been removed in extirpating the tumor.  

This case, showing unmistakable evidence of refilling of the cystic cavity within six months after the aspiration of 25 c.c. of its contents, leaves little doubt but that cystic fluid lying outside of the tumor does not develop from degeneration of neoplastic tissue.  

**Classification**  

In their original studies Bailey and Cushing (8) classified astrocytomas as fibrillary and protoplasmic, in accordance with the two types of astrocytes normally found within the brain. Since both are present in the normal cerebellum (Cajal), it was not surprising that both types of tumor were found in that structure. Since this original and classical study, many workers have tried to improve the classification (Roussy and Oberling, 28). That the majority of these attempts are without merit is clearly shown by the fact that, in contrast to the classification of Bailey, they have not been adopted by others. In a recent paper on modern conceptions of the structure and classification of glial tumors Bailey (4) has discussed many of these abortive schemes, so that it is not necessary to mention them further here.  

Classifications serve a useful purpose only when properly conceived and regarded. Obviously when the various rubrics within a classification are based upon criteria of entirely different qualities the result is needless confusion. Thus in a recent classification (1) we find the astrocytomas divided as follows: (1) fibrillary, (a) solid and (b) cystic, based on the finer structure of the cell and the gross characteristics of the tumor; (2) giant-cell, based on the grosser microscopic characteristics of the cell; (3) cellular, based on the general microscopic appearance of the tumor. Such a classification leaves any reader confused. If some are fibrillary, where are the a fibrillary ones? It would be only natural to conclude that the tumors of the other two classes are devoid of fibers, but such is not the case, for the authors state that the giant-cell type “is usually quite fibrillar” and the cellular type is “probably” the same as Bailey’s protoplasmic astrocytoma. Thus this illogical classification with three divisions, each based on a different type of criterion, is found on careful inspection to return to the original two types of tumor. But to con-
found already existing confusion it would appear from their Figs. 1 and 4 that
the authors have classified undoubtedly protoplasmic astrocytomas as fibrillary.
Furthermore, our study does not confirm their experience that in the cystic
group "the solid portion of the tumor is always . . . a fibrillary type of
astrocytoma."

Classifications must be regarded as providing merely arbitrary pockets into
which we can place tumors of similar character in order that they may be more
easily considered. But to alter an existing classification, or its terminology,
unless on further examination it proves to be erroneous (which this has not),
is only to bring confusion to a field already none too simple. No two gliomas
are identical. Placing two or more of them together is defensible only if their
general characteristics are sufficiently similar to make such grouping of value
to those, pathologist and clinician, who have to deal with them. The patholo-
gist, because of the variegated picture which he sees through his microscope,
will always seek to spread the classification wider and wider until the ultimate
and natural point is reached at which each tumor, differing as it does from
every other, occupies a little class all its own. The clinician on the other hand,
seeing only the grosser aspects of the problem, will persistently tend to narrow
the classification down until he is left with only two, "hard and soft," "cystic
and solid," "vascular and avascular," depending on his point of view, but usu-
ally "benign and malignant." But in so simplifying the problem he has lost
all the usefulness of classification. Not only have all the finer qualities dis-
appeared, but with this simplification the ability to distinguish benignity and
malignancy has gone too.

What single characteristic, or what group of characteristics, can we accept
as constantly indicative of malignancy? Cellularity is notoriously mislead-
ing—oligodendrogliomas and many meningiomas are as cellular as medullo-
blastomas, yet are benign. As a generalization the presence and number of
mitotic figures are highly significant, but many meningiomas containing mitotic
figures have been removed without recurrence over a long period of years
(Cushing and Eisenhardt, 16). A complete knowledge of the histologic char-
acteristics of the tumors is essential to a thorough understanding of their
biological characteristics, and an accurate, well-conceived classification is of
importance to such a knowledge.

Penfield and his co-workers (17) have divided the astrocytes into three
groups: pilocytic, gemistocytic, and diffuse. It is apparent that their pilocytic
type is identical with Bailey's fibrillary type. Obviously their term is apt, but
it is no improvement upon the one applied by Bailey years earlier, while
Bailey's has the added advantage that it is derived from the terminology of
the long recognized cell type occurring in the normal brain. It was our origi-
nal impression that the term pilocytic was reserved by Penfield and his associ-
ates for those fibrillary astrocytomas having a parallel arrangement of cells
and fibrils. It is obvious from their present description (17) that if such
qualifications were ever applied they have now been discarded. These au-
thors found only pilocytic (fibrillary) astrocytomas in the cerebellum.

Their gemistocytic type seems also to be a fibrillary astrocytoma, but one
with plump cells and "neuroglia fibrils of large caliber." It seems to us very
questionable if this type of tumor should be regarded as a distinct entity, and
similar considerations seem to have perturbed the authors, for they stated that these plump astrocytes "may occur as occasional forms in any astrocytoma [or glioblastoma, as they have also noted] so that it is difficult to be sure whether the cells are merely astrocytes [presumably from the normal invaded brain tissue] reacting in this way to the abnormal conditions provided by the neoplasm." Our doubts are somewhat different. We do not question that these cells are truly neoplastic, as Penfield and his associates finally concluded, but we do doubt that they represent the healthy neoplastic type cell of the tumor. The plump astrocyte or "gemästete Zell" is never a constituent of a normal brain. It is always the result of degenerative changes. Likewise in tumors containing astrocytes it is commonly associated with areas of degeneration. It is our opinion that these cells are usually representative of degenerative change, that they may be either protoplasmic or fibrillary astrocytes—and here apparently Alpers and Rowe (1) would agree—and that they can no more be regarded as a basis for classifying the tumor in which they are found than any other degenerative change.

The nature of the so-called "astrocytoma diffusum" is far from clear. It is not stated whether it contains glial fibrillae. If we may assume that this omission is indicative of the absence of such structures, and further, in view of the fact that the classification includes no protoplasmic astrocytoma as such, perhaps it may be safely concluded that this type is synonymous with Bailey's protoplasmic type. In further support of this supposition is the fact that Penfield et al. have found embryonic types of cells, spongioblasts and astroblasts, more prevalent than in the fibrillary varieties. In this laboratory we have found embryonic cells and malignant transformation far more common in the protoplasmic type. In our experience, however, astrocytomas which we would classify as "diffuse" have often been composed of fibrillary astrocytes. In these tumors, which have never been observed in the cerebellum but one of which has been seen to invade both thalami, the astrocytes grow among the ganglion cells and nerve fibers and an hypertrophy of the invaded structure with little distortion results.

Again, then, we return to Bailey's original classification and can see no reason why pilocytic is preferable to fibrillary or why diffuse (a term unfortunately of entirely different genre from pilocytic) is better than protoplasmic.

Restudy of our astrocytomas of the cerebellum leaves us convinced that fibrillary and protoplasmic are correct and useful terms. Hortega (20) agrees that these two fundamental types exist. These terms are, however, relative when applied not to individual cells but to entire tumors. Tumors in the cerebellum composed exclusively of either type are rare, if indeed they exist. Cerebellar astrocytomas are, in other words, more or less fibrillary, or predominantly fibrillary or protoplasmic, as the case may be and as one prefers (see Figs. 3 and 5). We have only rarely seen tumors wholly devoid of glial fibrillae and in those instances have been unable to avoid the suspicion that, if some other area had been examined, fibrillae would have been found. Fortunately all cerebellar astrocytomas are benign, slowly growing neoplasms, which are fairly well circumscribed, and complete gross enucleation apparently provides a cure in every case. Accordingly, from the clinical standpoint, the division of these tumors into fibrillary and protoplasmic types is unimportant.
and it is necessary only that the pathologist realize that a variation in the number of glial fibrillae exists in order that he may be fully conversant with the microscopic picture presented by these neoplasms.

Summary

Cerebellar astrocytomas occur for the most part in children, are solid or cystic, well circumscribed gliomas which can usually be readily and successfully enucleated. They are composed predominantly of fibrillary and protoplasmic astrocytes in variable proportion, in association with a very small percentage of other adult and embryonic cells of the spongioblastic series. They contain no ganglion cells or nerve fibers other than those engulfed as a result of the invasion of the cerebellum by the tumor, and no neuroblasts. They not infrequently invade the subarachnoid space and in such areas glial bridges connecting the molecular layer of the cerebellum and the subarachnoid space may be found. Degenerative changes involving the cells, their processes and fibrillae and the blood vessels are common and are not infrequently misinterpreted by the unwary. The surrounding cerebellum shows the effects of compression and ischemia.

Although it is possible that many cerebellar astrocytomas are congenital tumors or arise from a developmental fault, such a hypothesis is unproved. There is no evidence to support the contention that these are congenital malformations rather than neoplasms.

The small intraneoplastic cysts which develop in these tumors are the result of liquefaction of tumor tissue, but the extra-neoplastic cysts, and perhaps the large intra-neoplastic ones as well, appear to be formed by transudation.

The original classification of these tumors into fibrillary and protoplasmic astrocytomas is accurate and valuable. More recent efforts at alteration of the classification or its terminology are illogical, of little value and confusing.

References