Cerebral hemangioma with glial neoplasia (angioglioma?)

Report of two cases

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Two patients are reported who had intracerebral mass lesions composed of hemangioma and glial neoplasm. After excision, one recurred as an oligodendroglioma, and the remnant of the other remained static over a 5-year period. These lesions may represent a subgroup of cerebral hemangiomas that have the biological potential for future glial neoplastic growth. Reference is made to experimental work with polyoma virus which can induce cavernous hemangiomas in the central nervous system in mice, and which is a papovavirus. Other papovaviruses can induce ependymomas in hamsters.

KEY WORDS cerebral hemangioma, cavernous hemangioma, glioma, brain tumor, polyoma virus

We are reporting the cases of two patients with intracerebral lesions composed of hemangioma and glial neoplasm. One of these tumors recurred as an oligodendroglioma 5 years after excision. These cases suggest that among the lesions classified as cerebral hemangiomas or cavernous hemangiomas there may be a group that are low-grade tumors rather than developmental abnormalities. The evidence that cerebral cavernous hemangiomas can be induced in mice by polyoma virus places further doubt on their completely developmental origin in humans. In addition, there have been reports of combined hemangioma and neurilemmoma, both intracranially and in the peripheral nervous system, and arteriovenous malformations have been found combined with astrocytoma and oligodendroglioma.

Case Reports

Case 1

This 11-year-old boy experienced focal motor seizures of the right arm for 1 month, and two grand mal seizures associated with transient dysphasia. Examination. His neurological examination was normal. An area of calcification was seen on plain skull films in the posterior medial portion of the left frontal lobe. Computerized tomography (CT) did not show any additional mass effect or area of enhancement after the administration of contrast material, and a carotid arteriogram was normal. A technetium-99 sodium pertechnetate brain scan was positive in this region, and an electroencephalogram showed slowing on the left side, with numerous bursts of 1 to 5 Hz paroxysmal polyspike and slow waves.

First Operation. A greenish-brown-colored mass was found beneath the cortex, well demarcated from the surrounding brain. After gross total removal, abnormal electrical activity persisted in the adjacent frontal cortex, where additional resection was limited because it was considered to be unsafe. During the subsequent 5 years, the patient continued to have seizures at monthly intervals, the spells consisting of both grand mal and lesser attacks. The latter were manifested by the patient emitting an expletive-like noise or grunt followed by a minute or so of inability to speak. In a second kind of attack, he was propelled to the ground while conscious, and he had suffered injury as a result of several of these events. Because of poor seizure control, he underwent further electrocorticography and cortical resection under local anesthesia.
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**Second Operation.** Preoperatively, his CT scan showed no change in the defect in the left frontal cortex and no evidence of enhancement after the administration of contrast material. The second cortical resection was adjacent to the site of previous surgery. The tissue removed seemed slightly tougher than normal brain, but several parts had a gelatinous appearance. In the 6 months since the operation, his seizures have been controlled with medication.

**Pathological Examination.** The tissue obtained at the first operation consisted of anastomosing islands of glial tissue closely intermingled with clusters of thick-walled hyalinized vascular spaces of variable size (Fig. 1 left). In some areas, the lesion was made up of a large number of small astrocytes and oligodendroglial cells, while in other parts it had been heavily mineralized (Fig. 1 center). Tightly packed large blood vessels occupied a substantial portion of the mass (Fig. 1 right). The tissue removed 5 years later consisted of large masses of uniform oligodendroglial cells with small nuclei surrounded by empty-appearing cytoplasm. The lesion was regularly intersected by thin-walled branching vessels and clusters of fibrillary astrocytes. Occasionally, groups of cells were separated by mucoid material (Fig. 2).

**Case 2**

This 19-year-old woman presented with back pain. She had had headaches for several months and complaints of abnormal visual phenomena on the left. She had chronic papilledema and a partial left homony-
mous hemianopsia. Roentgenograms of the skull demonstrated a large calcified mass in the right temporal occipital region, and a CT scan demonstrated hydrocephalus in addition. The administration of contrast material did not reveal any other abnormality. A right carotid arteriogram showed stretching of vessels in the region of the mass, but no pathological vessels, early-filling veins, or tumor blush.

Operation. The lesion consisted of areas of rock-hard calcification in a matrix of softer tissue. There were many adhesions between the mass and the dura, and a multiloculated brown-walled cyst was present, suggesting earlier hemorrhage. All but a small portion of the mass was removed. Postoperatively, a ventriculoperitoneal shunt was required. The patient's neurological examination has remained unchanged, and in the 5 years since her operation CT scans have shown no increase in the small residual mass.

Pathological Examination. There were three major components to the lesion. The first consisted of many large vascular spaces with thick collagenous walls that were devoid of elastica and lamina muscularis. They were either packed together and embedded in vast masses of collagen (Fig. 3 upper left) or widely separated by glial tissue. The second component was made up of extensive mineral deposits, which often enclosed spaces that appeared to be vascular (Fig. 3 upper right). The third component consisted of large fields of glial tissue appearing much more neoplastic than in the first patient. There were cells with highly pleomorphic, plump, and often bizarre nuclei and scanty cytoplasm (Fig. 3 lower), and occasional multinucleated cells. Hyaline droplets and Rosenthal fibers were also encountered.

Discussion

The tumors in these two patients appear to represent examples of cerebral cavernous or capillary hemangioma combined with glial neoplasm. One neoplasm subsequently grew as an oligodendroglioma, and the remnant of the other was shown by CT scan to have remained stable over 5 years. In both cases, the neoplastic cells occupied large areas, replaced normal parenchyma, and were independent of the vascular spaces, old hemorrhage, or calcification. We believe that these tumors are probably not a chance combination of cavernous hemangioma and glioma, but a distinct form of hemangioma, portions of which contain neoplastic glial tissue that may have biological potential for future growth. "Angioglioma" may be an appropriate designation for these lesions, a term entertained by Russell and Rubinstein but rejected because they thought that most of the cases were either hypervascularized gliomas or vascular malformations with undue glial reaction.

The combination of cavernous hemangioma and glioma may have existed in other patients reported in the literature. Falconer and Pond described two heavily calcified angiomatous lesions in the temporal lobe containing "tumour-like proliferation of astrocytes and oligodendrocytes." Averback reported another possible example consisting of a heavily mineralized lesion in the temporal lobe with a haphazard arrangement of numerous capillaries, dense nests of oligodendroglia, many astrocytes, and occasional single or paired neurons. White, et al., reported a patient in whom a cavernous hemangioma was present in the temporal lobe, liver, and lung; their patient died following surgery for a glioma of the septum pellucidum. They did not state whether there was any juxtaposition of tumor and hemangioma.

Cerebral telangiectases and cavernous hemangiomas are generally considered to be congenital malformations. Their most prominent clinical features are seizures and fatal hemorrhage. Transitional forms exist containing elements of both telangiectases and cavernous hemangiomas, and a variety of names have been employed to describe related nonarteriovenous vascular lesions of the brain that vary in the size of the vascular spaces and in the degree of mineralization or calcification. These lesions are frequently found in the distribution of the middle cerebral artery, especially in the anterior temporal lobes. Their occurrence may be multiple throughout the brain and spinal cord, or may be associated with cavernous hemangiomas in other organs, and may be familial. Russell and Rubinstein cited earlier authors who thought that cavernous hemangiomas might be neoplastic lesions rather than malformations, and the observations in our patient may be compatible with such a view. Additional support for the possible neoplastic nature of these lesions may be found in the experimental production of cavernous hemangiomas by viruses in mice.

The polyoma virus induces cavernous hemangiomas throughout the nervous system when inoculated into mice of less than 1 week old. This virus, which is a pathogen only for mice, belongs to the papovavirus family, another member of which is the virus associated with progressive multifocal leukoencephalopathy, JC virus. Glial tumors are not induced by polyoma virus, although SV 40 virus, another papovavirus, causes ependymomas when inoculated intracerebrally in newborn hamsters. The type of lesion produced by polyoma virus depends on the dose injected. The highest doses result in multiple capillary, cystic, or cavernous hemangiomas in brain and spinal cord, causing death from hemorrhage at 14 to 29 days of age. Intermediate doses result in multiple tumors such as renal sarcomas, mesenchymomas, osteogenic sarcomas, exostoses, subcutaneous fibromatoses, and in some animals a "diffuse hemangiomatosis." Low doses result in a single tumor, usually renal sarcoma. Tumor induction by polyoma virus is greatly reduced after 7 days of age; however, induction of cavernous hemangiomas can be greatly enhanced by suppression of immune

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FIG. 3. Case 2. Photomicrographs of the excised mass. H & E. Upper Left: Large vascular spaces with hyalinized walls merge imperceptibly into surrounding collagen. × 14. Upper Right: There is extensive mineralization of the vessel walls and intervening parenchyma. × 140. Lower Left: Moderately cellular neoplastic tissue is seen with highly pleomorphic nuclei, thin-walled vessels, and some hyaline droplets. × 56. Lower Right: Glial cells are shown with large bizarre nuclei and scanty cytoplasm. × 225.

mechanisms, even though the suppression does not increase the recoverability of virus from various organs of the animal. In addition, administration of antilymphocyte globulin results in the induction of cerebral hemangiomas when the virus is injected as late as 4 weeks of age.

The observation that viruses can induce in mice lesions resembling the cerebral cavernous hemangiomas seen in man highlights the difficulties that have existed in classifying cerebral telangiectases and cavernous hemangiomas purely as developmental abnormalities. Because of the role viruses play in both animal and human oncogenesis, it is at least conceivable that a single stimulus could produce a human brain tumor composed of elements of both cavernous hemangioma and glioma.

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