“Angioglioma” and the arteriovenous malformation-glioma association

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The term “angioglioma” denotes a highly vascular glioma, most of which are low-grade lesions associated with a favorable prognosis. The authors encountered an example of this pathology, a cystic oligodendroglioma associated with prominent vasculature which both clinically and histologically mimicked an occult arteriovenous malformation (AVM). This case and reports of the association of AVM and glioma prompted a histological review of 1034 surgically resected AVM’s, both angiographically occult and visible, among which no oligodendrogial or astrocytic forms of “angioglioma” were found. Eight cases were observed, however, wherein oligodendrogial cells were increased in number within or about the malformation. Two basic histological patterns of oligodendrogial cell excess were seen; one appeared to be malformative in nature with abnormal disposition of oligodendrogial cells being an integral part of the AVM, whereas in the other an apparent increase in cellularity seemed the result of chronic ischemia with condensation of white matter. It appeared that the areas of increased oligodendrocyte content seen in association with AVM are non-neoplastic lesions that exhibit two rather distinct histological patterns of differing origin.

In an attempt to determine the frequency of “angioglioma,” the authors examined Tissue Registry data for several glioma groups in which highly vascular examples are prone to occur. Tumors selected for study included 104 cerebellar-type (pilocytic) astrocytomas, 82 oligodendrogliomas, and 51 supratentorial pilocytic astrocytomas. Histological hypervascularity mimicking a vascular malformation (that is, an “angioglioma”) was encountered in 5%, 4%, and 12% of the cases, respectively. Based upon clinical, radiological, and pathological reviews of these cases, as well as a careful review of the literature, it was concluded that 1) “angiogliomas” are neither rare nor represent a distinct clinicopathological entity; 2) in histological but not necessarily angiographic surgical terms, they represent simply highly vascular gliomas, usually of low grade; and 3) the clinicopathological and angiographic features as well as the prognosis of such lesions do not differ from those of similar gliomas without angioma-like vasculature. Finally, “angiogliomas” must not be confused with gliomas of high-grade malignancy which, due to neovascularity, may be highly vascular at angiography and at surgery.

KEY WORDS: angio-glioma • arteriovenous malformation • glioma • brain neoplasm

Cases of a primary intracranial tumor associated with a true arteriovenous malformation (AVM) are rare. The spectrum of neoplasms is broad and includes: gliomas, most often astrocytomas, ganglieneurinomas, meningiomas, hemangioblastomas, neurilemomas, and craniopharyngiomas. Our review of “angiogliomas” and the AVM-glioma association was prompted by our treatment of a patient with a cystic oligodendroglioma which possessed sufficiently prominent vasculature to mimic an angiographically occult AVM with hemorrhage and cyst formation.

The final pathological diagnosis in this case was that of a neoplasm (that is, an “angioglioma”). Although the designation “angioglioma” originally was a descriptive term applied to what is now recognized as a hemangioblastoma, it quickly became linked with glial neoplasms of astrocytic or oligodendrogial type possessing angioma-like vasculature.

Nazeck, et al., in reviewing the literature and reporting three cases of an oligodendroglial “prolifera-tive” abnormality associated with true AVM, expressed doubt regarding the neoplastic nature of the oligodendrocytes found in this setting. Their article, as well as
Case Report

This 17-year-old right-handed boy experienced the relatively acute onset of left cerebral symptoms consisting of right-sided incoordination and weakness, slurring of speech, and headache 6 months prior to admission. After a 1-month period of stabilization, his deficits became progressive.

Examination. A right hemiparesis and reduction in pain and temperature sensation were detected on neurological examination. A cystic hemorrhagic lesion in the left thalamus was demonstrated on computerized tomography and magnetic resonance (MR) imaging of the head (Fig. 1). The angiogram showed some in-
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<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Clinical Profile</th>
<th>Angiography</th>
<th>Angiography</th>
<th>Computerized Tomography</th>
<th>Tumor Grade</th>
<th>Follow-Up Period &amp; Findings</th>
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<td>oligodendroglioma</td>
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<tr>
<td>1</td>
<td>17, M</td>
<td></td>
<td>headache, hemiparesis; prior hemorrhage</td>
<td>avascular mass</td>
<td>thalamic cyst, hemorrhagic cyst</td>
<td>1 decreased cyst size</td>
<td>1 yr: mild aphasia</td>
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<td>calcified occipital mass</td>
<td>2 no recurrence</td>
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<td>syncopal spells, drowsiness</td>
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<td>frontal cyst</td>
<td>2 recurrence</td>
<td>8 yrs: tumor-related death</td>
<td></td>
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<td>cerebellar-type (pilocytic) astrocytoma</td>
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<td>5</td>
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<td>headache, ataxia</td>
<td>not done</td>
<td>cerebellar cyst</td>
<td>1 no recurrence</td>
<td>5 yrs: NED</td>
<td></td>
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<td>headache, ataxia</td>
<td>not done</td>
<td>pneuromencephalogram: posterior fossa mass</td>
<td>1 no recurrence</td>
<td>2 yrs: NED</td>
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<td>supratentorial pilocytic astrocytoma</td>
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<td>headache, ataxia</td>
<td>with papilledema</td>
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<td>9 yrs: mild residual ataxia</td>
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<td>21, M</td>
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<td>headache</td>
<td>avascular mass</td>
<td>cerebellar cyst</td>
<td>1 no recurrence</td>
<td>11 yrs: unknown</td>
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<td>9</td>
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<td>respiratory depression, ataxia</td>
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<td>cerebellar cyst</td>
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<td>14 yrs: brain-stem deficits</td>
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<td>headache, papilledema</td>
<td>vascular mass without AV shunt</td>
<td>occipitoparietal mass</td>
<td>1 recurrence</td>
<td>10 yrs: mild ataxia</td>
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<td>2, F</td>
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<td>headache, ataxia</td>
<td>not done</td>
<td>temporal mass</td>
<td>1 no recurrence</td>
<td>20 yrs: hemianopia</td>
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<td>12</td>
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<td>visual defects</td>
<td>not done</td>
<td>supratentorial mass</td>
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<td>15 yrs: panhypopituitarism</td>
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<td>8, F</td>
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<td>not done</td>
<td>thalamic mass</td>
<td>1 recurrence</td>
<td>11 yrs: hemianopsia</td>
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<tr>
<td>14</td>
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<td></td>
<td>seizures</td>
<td>not done</td>
<td>temporal mass</td>
<td>1 no recurrence</td>
<td>6 yrs: NED</td>
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<td>15</td>
<td>19, M</td>
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<td>seizures</td>
<td>not done</td>
<td>parietal mass</td>
<td>1 no recurrence</td>
<td>28 yrs: NED</td>
<td></td>
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</table>

* Tumor grading according to the World Health Organization classification.24 NED = no evidence of disease; AV = arteriovenous.
† Operative and microscopic evidence of remote hemorrhage.

increased vascularity in the left thalamic area only at the capillary phase. Some mass effect was attributed to the presence of the cyst.

Operation. Exposure of the lesion was by way of a left frontoparietal craniotomy and transcapsular intraventricular approach. The cyst containing clear xanthochromic fluid was evacuated and the underlying lesion, which was considered to be grossly consistent with either an occult AVM with associated hemorrhage or a hemorrhagic glioma, was excised. It was soft, grossly vascular, and, on microscopic examination, was found to be oligodendrocyte-rich tissue overshadowed by prominent vasculature (Fig. 2). The lesion was diagnosed as a highly vascular oligodendroglioma (that is, "angioglioma").

Postoperative Course. Postoperatively, the patient exhibited a mild aphasia, persistence of a right hemiparesis, and transient right-sided focal motor seizures. At his 1-year follow-up consultation, neurological examination revealed improvement of the aphasia, apraxia, and hemiparesis. Seizure control was achieved by anticonvulsant therapy. No evidence of recurrent neoplasm or hemorrhage was seen on MR imaging.

Clinical Material and Methods

The files of the Mayo Clinic Tissue Registry were systematically searched for cases of AVM (1950–1989), pure oligodendrogliomas (1960–1982), cerebellar-type (pilocytic) astrocytomas (1960–1984), and supratentorial pilocytic astrocytomas (1963–1984). In total, 1034, 82, 104, and 51 cases were found, respectively.

All AVM cases were reviewed histologically in a search for examples in which oligodendrogliarial or astrocytic elements were conspicuous. Although lesions in which astrocytes were prominent showed typical features of chronic astrogliosis, we encountered eight AVM cases (0.1%) that showed an apparent increase in the oligodendrogliocyte content. Paraffin blocks were recut and stained by the hematoxylin and eosin, elastic-van Gieson, Mallory's trichrome, Prussian blue, Luxol fast blue/periodic acid-Schiff, and the Bielschowsky methods. In addition, immunostains for glial fibrillary acidic protein were performed (dilution 1:300).* In the series of 82 oligodendrogliomas and 177 cerebellar and supratentorial pilocytic astrocytomas studied, only original microsections were examined.

In all cases, including AVM's with oligodendrogial prominence and "angiogliomas," neuroradiological operative and follow-up data were compiled.

Results

The clinical, radiological and follow-up data on our 15 "angiogliomas," including the index case, are summarized in Table 1. Similar data regarding the eight

* Immunostains obtained from DAKO, Carpinteria, California.
TABLE 2
Lesions encountered in review of 1034 arteriovenous malformations (AVMs)*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Clinical Presentation</th>
<th>Angiography</th>
<th>Computerized Tomography</th>
<th>Follow-Up Findings</th>
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<td></td>
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<td>Radiological</td>
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<td>AVM &amp; oligodendrogial prominence</td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>16</td>
<td>37, M</td>
<td>seizures, headache, tinnitus, drowsiness</td>
<td>AV shunt</td>
<td>not done</td>
<td>not done</td>
</tr>
<tr>
<td>17</td>
<td>14, F</td>
<td>headache, seizures, hemiparesis</td>
<td>slow-flow AV shunt</td>
<td>rt hemispheric AVM</td>
<td>CT: rt hemispheric cyst</td>
</tr>
<tr>
<td>18</td>
<td>42, F</td>
<td>hemorrhage, headache, hemiparesis</td>
<td>AV shunt</td>
<td>intraventricular hemorrhage</td>
<td>not done</td>
</tr>
<tr>
<td>19</td>
<td>23, F</td>
<td>hemorrhage, headache, gait, blurred vision</td>
<td>AV shunt</td>
<td>parietal AVM</td>
<td>CT: parietal cyst</td>
</tr>
<tr>
<td>20</td>
<td>16, F</td>
<td>headache, seizures, hemianopsia, weakness of rt side</td>
<td>AV shunt</td>
<td>parietal AVM</td>
<td>CT: normal</td>
</tr>
<tr>
<td>21</td>
<td>27, M</td>
<td>hemorrhage; seizures, dizzy spells</td>
<td>slow-flow AV shunt</td>
<td>zone of hypervascularity adjacent to low-attenuation frontal lesion</td>
<td>MRI: normal</td>
</tr>
<tr>
<td>22</td>
<td>17, M</td>
<td>seizures</td>
<td>AV shunt</td>
<td>not done</td>
<td>MRI: normal</td>
</tr>
<tr>
<td>23</td>
<td>24, M</td>
<td>headache, seizures, aphasia</td>
<td>AV shunt</td>
<td>frontal calcified lesion with minimal enhancement</td>
<td>CT: normal</td>
</tr>
<tr>
<td>separate AVM &amp; glioma</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>65, F</td>
<td>seizures</td>
<td>tempo-occipital dural AVM with AV shunt</td>
<td>frontoparietal mass (glioma)</td>
<td>CT: recurrent tumor</td>
</tr>
</tbody>
</table>

*AV = arteriovenous; CT = computerized tomography; MRI = magnetic resonance imaging.

patients with AVM found from the records to be associated with oligodendrogial prominence are presented in Table 2.

"Angiogliomas"

The increased vasculature observed in the "angioglioma" group, which consisted of four oligodendrogliomas (including our index case), five cerebellar-type (pilocytic) astrocytomas, and six supratentorial pilocytic astrocytomas, was substantial and superficially resembled that of an AVM. Nonetheless, it was typically focal, being present in only a portion of the tumor (Fig. 3). In most cases, it consisted of hyalinized ectatic vascular channels rather than well-formed veins or arteries. Several cases showed evidence of prior thrombosis with recanalization or luminal obliteration (Fig. 4). The gliomatous nature of the intervening tissue was readily apparent in all but our index case, in which the oligodendroglioma was overshadowed by the vasculature. Perivascular hemosiderin deposits, gliosis, or vascular calcification (a noticeable feature, particularly in oligodendrogliomas) tended to further obscure architectural features. The follow-up findings are summarized in Table 1.

Arteriovenous Malformation with Oligodendrocyte Prominence

Among the 1034 cases of AVM that we reviewed, no "angiogliomas" were noted; however, eight cases were encountered in which the AVM was accompanied by oligodendrogial prominence. The abnormal vasculature was typical of an AVM, consisting of large-caliber
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FIG. 4. Photomicrographs of the “angioglioma” in Case 5. A: The abnormal vasculature in this cerebellar-type astrocytoma is not only zonal but hyalinized. H & E, × 56. B: Less vascular portions of the lesion show the typical histology of this childhood tumor. H & E, × 142.

vessels of arterial, venous, or indeterminant type. Mural hyalinization, often prominent and extensive, obscured the nature of many vessels. The tunica muscularis of veins and arteries varied in thickness and was occasionally attenuated or incomplete; the same was true of arterial elastica. Prior hemorrhage, evidenced by the presence of numerous hemosiderin-laden macrophages and a dense Prussian blue reaction, was present in one instance. Scattered histiocytes were noted in all cases, their numbers being proportionate to the degree of myelin pallor and axon loss. Astrogliosis was generally moderate to marked. No mitotic activity was evident, but in two cases mild anisonucleosis and hyperchromasias were noted in the oligodendroglial cells. Calcification, primarily of the vasculature, was mild in three cases and moderate in one.

Two distinct but not exclusive histological patterns were observed relative to the distribution of the numerically increased oligodendrocytes. One, dubbed the “collapse pattern,” predominated in five cases; its histological features suggested that the apparent increase in oligodendrocytes was due simply to condensation of tissue (Fig. 5). To some extent, the uniform appearance of scattered histiocyte nuclei and reactive astrocytes

FIG. 5. Photomicrographs of the arteriovenous malformation with “collapse” pattern of oligodendroglial prominence in surrounding white matter in Case 16. A: There is an apparent increase in cellularity attributable to condensation of white matter with associated reactive changes. H & E, × 35. B: Crowding of resident oligodendroglia is associated with astrogliosis. H & E, × 220.
contributed to its overall appearance of cellularity (Fig. 5). A second pattern of oligodendrocyte prominence, the "malformation pattern," was noted in three cases and appeared to be the result not of degenerative change but of a developmental disturbance related to the genesis of the vascular malformation. It consisted of islands of somewhat oligodendrocyte-rich tissue entrapped by aberrant vasculature (Fig. 6).

Discussion

The term "angioglioma" was coined by Councilman who used it to describe a highly vascular cerebellar neoplasm with features of what is now recognized as the cellular variant of hemangioblastoma. Subsequently, the term was used in like manner by Roussy and Oberling. Over the years and by convention, the designation has been applied indiscriminantly to gliomas of various kinds, most of low grade, with prominent vasculature. Although Russell and Rubinstein recognized this use of the term, they attributed no clinical significance to the presence of AVM-like vasculature in gliomas. Instead, in a more recent publication with coauthors, Rubinstein suggested restriction of the term "angioglioma" to denote a tumor with combined features of capillary hemangioblastoma and astrocytoma. If intended to indicate an admixture of an inherently vascular lesion with glioma, this definition is premature, in that the vascular nature of hemangioblastoma is unproven. Indeed, the cytogenesis of its principal or "stromal" cells remains entirely unsettled.

This study was prompted by our index case of oligodendroglioma with prominent vasculature (Case 1, Table 1) which, both histologically and clinically, mimicked an occult AVM with hemorrhage. Similar cases have been reported previously (Table 3). To determine the frequency with which oligodendroglioma is associated with AVM, we reviewed 1034 AVM's operated on at the Mayo Clinic and found no examples. There were, however, eight cases in which oligodendroglial cells were increased in number within the malformation. Each was studied in detail by histochemical and immunocytochemical methods. Two basic patterns were observed; one appearing malformative, the other presumably the result of chronic ischemia with condensation of white matter and gliosis. These lesions are similar to the cases described by Nazek, et al., in which the oligodendrogial "proliferation" was not considered truly neoplastic. In contrast to AVM's, the majority of which were angiographically evident and...
showed arteriovenous shunting, oligodendrogliomas with AVM-like vasculature appear to be angiographically occult.

The term “angioglioma” has been loosely applied to glial neoplasms, either astrocytic or oligodendroglial, in which a vascularity is prominent. Although not stated in so many words, the designation has been used in such a way as to imply a particularly favorable prognosis. In an effort to determine the frequency of angiogliomas and whether they are in any way unique, we examined a number of oligodendrogliomas of all grades, cerebellar-type (pilocytic) astrocytomas, and supratentorial pilocytic astrocytomas—all tumors prone to hypervascularity. Fourteen (6%) of these were sufficiently vascular to be considered “angiogliomas.” The clinical, neuroradiological, and follow-up data for these as well as our index case (Case 1) are summarized in Table 1. Based upon our institutional experience, the biological behavior of these tumors differed in no way from that of similar grade gliomas unassociated with excess vasculature. The 5-year and 10-year survival rates of 38 cases of low-grade (World Health Organization grade I to II) oligodendroglioma (76% and 43%, respectively; EG Shaw, et al., unpublished data), 51 supratentorial pilocytic astrocytomas (86% and 82%, respectively; D Forsythe, et al., unpublished data), and 104 cerebellar pilocytic astrocytomas (94% and 91%, respectively; CJ Hayostek, et al., unpublished data) were entirely comparable to those of the corresponding angiogliomas included in our study group (Table 1).

It should be noted that true AVM's may, on rare occasions, be associated with glioma, the elements either abutting one another in the manner of a “collision tumor” or being spatially separated, either in different lobes or opposite hemispheres. In the course of this study, we encountered one of the latter (Case 9, Table 2). The clinicopathological and angiographic features of other reported cases of “collision” and independent lesions are summarized in Table 3.

Although topographically combined AVM's and gliomas are usually found simultaneously, several instances have been reported in which they seem to be sequential lesions, the angioma preceding the glioma. Such cases are too few to draw conclusions regarding the etiological relationship, if any, between the components. Goodkin, et al., reviewed the literature on this issue and summarized current theories.

From the neuroradiological point of view, true AVM's as well as AVM-associated neoplasms are usually angiographically apparent, whereas “angiogliomas” are either avascular or show only a tumor blush without evidence of shunting. It appears, therefore, that the angiographic pattern assists in their distinction. Based upon our experience and that summarized in the literature, the term “angioglioma” seems to be of no diagnostic or prognostic importance since patient survival is unrelated to the presence of a vascular component but depends rather upon the histological type and grade of the associated glioma.

Although a quite different definition of angioioma has been suggested by Bonnin, et al. (hemangioblastoma accompanied by astrocytoma), we are reluctant to adopt this usage in that no evidence exists to indicate that hemangioblastoma is fundamentally a vascular neoplasm. We have, however, observed three lesions of the type described by Bonnin, et al., in our review of 98 hemangioblastomas and 125 cerebellar astrocytomas; these cases will be the basis of separate publication.
Conclusions

From our study of AVM’s, as well as so-called “angiogliomas,” we conclude the following:

1. A small proportion of oligodendroglialomas (4%), cerebellar-type (pilocytic or microcystic) astrocytomas (5%), and supratentorial pilocytic astrocytomas (12%) are highly vascular. Unlike true AVM’s, these tumors are angiographically occult. In that they do not differ in clinical or prognostic terms from gliomas of similar type and grade unassociated with hypervascularity, we suggest abandonment of the term “angioglioma.”

2. Arteriovenous malformations associated with gliomas, either separate or as “collusion tumors,” are rare and represent fortuitous associations rather than true mixed tumors. In such cases, the vascular lesion is angiographically detectable, whereas the glioma may be an unexpected finding.

3. Patterns of oligodendrogial prominence seen in association with AVM’s appear to be the result of either tissue condensation (presumably due to chronic ischemia and gliosis) or of aberrant vascular development. Patients affected by such lesions do not seem to develop glial neoplasia. Their neurological outcome in terms of postoperative recovery and seizure control does not differ from that of patients with ordinary AVM’s.

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References


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