Juvenile Pilocytic Astrocytoma in Association with Arteriovenous Malformation

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Summary

Pilocytic astrocytomas are highly vascular, relatively common primary brain tumors in the pediatric population, but their association with a true arteriovenous malformation (AVM) is extremely rare. We describe an eight-year-old girl with a right supratentorial juvenile pilocytic astrocytoma (WHO grade I) with an angiographically documented AVM entangled in the tumor mass who presented with intracranial hemorrhage due to a ruptured anterior choroidal artery pseudoaneurysm encased in the lesion. The AVM nidus as well as the hemorrhage site was embolized with Onyx. A literature review revealed only one previous report of a true intermixture of these two lesions. We hypothesize whether the association of vascular malformations and primary brain tumors are merely coincidental or if they point to the existence of a distinct entity and/or a common etiologic factor.

Introduction

Pilocytic astrocytomas are generally well-circumscribed, slow growing masses that may at any point stabilize or even regress. These tumors commonly occur in children and young adults¹. Although pilocytic astrocytomas are highly vascular, and regressive changes in some of them can be seen as hyalinized, ectatic vessels with features of a cavernous angioma, association of these primary intracranial tumors

with a true arteriovenous malformation (AVM) are rare. We describe an eight-year-old girl with right supratentorial pilocytic astrocytoma associated with an angiographically documented AVM within the tumor mass. She presented with intracranial hemorrhage due to a ruptured anterior choroidal artery pseudoaneurysm encased in the lesion. The AVM nidus as well as the hemorrhage site was embolized with ethylene vinyl alcohol (Onyx, ev3).

Case Report

An eight-year-old girl with a medical history of intermittent headaches for approximately two months, presented to the Emergency Department (ED) with loss of consciousness. Prior to her presentation, she had experienced sudden onset of severe right temporal headache, ataxia, and slurred speech followed by two episodes of emesis and unresponsiveness. Physical examination revealed hypertension and bradycardia. Neurologic examination showed a Glasgow Coma Scale of 7 with a nonreactive, dilated right pupil and a sluggish, 3mm left pupil. The patient withdrew her left upper extremity and both lower extremities in response to pain. She spontaneously moved her right upper extremity. A CT scan of the brain demonstrated a large (4.5-5 cm), hyperdense, acute intraparenchymal hemorrhage in the right basal ganglia and thalamus in addition to hemorrhagic extension into the ventricles. A 1.1 cm midline

Figure 1 Initial NECT obtained immediately after presentation demonstrates a large hematoma (A) with mixed attenuation centered in the right basal ganglia with extension of hemorrhage into the ventricular system (B) and midline shift.

Figure 2 Axial (A-C) and coronal (D-F) images from a CT angiogram obtained on admission. A,D) The arrows point to the pseudoaneurysm of the A Cho artery most compatible with the site of hemorrhage. B,C) The arrows point to the nidus of the AV shunt. E,F) Arrows point to the draining vein.

shift and secondary obstructive hydrocephalus were noted (Figure 1). CT angiograms revealed a pseudoaneurysm arising from the anterior choroidal artery along with AV shunting and

the draining vein (Figure 2). MR brain imaging confirmed the aforementioned findings and demonstrated minimal patchy enhancements within the hematoma (Figure 3). In an attempt

Figure 5 A,B) AP and lateral views of microcatheter injection in the right A Cho artery demonstrating the pre-nidal pseudoaneurysm (arrow) and the shunting nidus (dashed arrow). C) Roadmap image showing the microcatheter placed just proximal to the nidus to initiate the embolization process. D) Onyx injection into the pseudoaneurysm with extravasations of Onyx through the rupture site (arrow). E,F) AP and lateral views of microcatheter angiography at the level of the shunting nidus (arrow). G) Final Onyx cast. Extension of Onyx through the rupture point of the pseudoaneurysm into the surrounding hematoma (dashed arrow) as well as the catheter tip (arrow) is visible.

← **Figure 3** (in the upper left page) Initial MR brain. A,B) T2 axial images demonstrating the hemorrhagic lesion centered in the right BG with IVH. C) GRE T2 image demonstrating the blooming artifact associated with products of hemorrhage. D,E) Pre-contrast T1W axial images. F) Axial SPGR T1W post-contrast image showing minimal patchy enhancement of the lesion (arrow). G) Coronal T1W image demonstrating patchy enhancement of the medial portion of the hemorrhagic lesion (arrow).

← **Figure 4** (in the lower left page) Initial angiogram: A,B) AP views of RICA injection demonstrating the AV shunt supplied by the right A Cho artery and the draining vein (arrow). C,D) Lateral views of RICA injection showing the A Cho artery and the associated pseudoaneurysm/rupture site (arrow) in addition to the main draining vein (dashed arrow).

to find a unifying diagnosis, this finding was attributed to possible hemorrhage of different ages with enhancement associated with an earlier subacute bleed.

A left frontal external ventricular drain (EVD) was placed and she underwent a conventional brain angiogram (Figure 4). This demonstrated an arteriovenous malformation nidus supplied by the right anterior choroidal artery and shunting to a draining vein but without evidence of a tumor blush. Two intra-nidal aneurysms as well as a pre-nidal pseudoaneu-

rysm of the anterior choroidal artery were identified. The pre-nidal pseudoaneurysm was centered within the hematoma and therefore considered the most likely site of rupture.

Two days later the patient underwent Onyx embolization of the anterior choroidal artery and the AVM nidus. The rupture site was identified as a small trickle of Onyx extending from the base of the pseudoaneurysm into the extravascular space (Figure 5). Control angiogram of the right internal carotid artery following embolization confirmed obliteration of the pseudoaneurysm and AVM nidus. The patient continued to suffer left spastic hemiplegia and homonymous hemianopsia as a sequelae of the presenting basal ganglia hemorrhage.

Follow-up MR brain imaging revealed a right-sided heterogeneous mass involving the thalamus and basal ganglia ($4.3 \times 4.9 \times 3.8$ cm). The mass had increased in size and appeared to be contrast enhancing at the tumor hemorrhagic site (Figure 6). At this time, the co-existence of a neoplasm with the AVM was suspected.

The patient underwent surgical resection of a 3-3.5 cm heterogeneous mass. The lateral inferior aspect of the mass traversed the anterior choroidal artery and AVM, which contained the Onyx embolic agent. Figure 7 demonstrates follow-up MR brain images five months after tumor resection. Histopathological examination of the mass demonstrated a biphasic glial neoplasm with compact and loose areas, eosinophilic granular bodies, Rosenthal fibers, and numerous small and medium sized vessels, consistent with a pilocytic astrocytoma -WHO grade I. Intermingled with the tumor were large, dilated thick and thin walled vessels containing embolization material with foreign body giant cell reaction, consistent with an AVM. Vascular endothelial growth factor (VEGF) staining of the tissue yielded a negative result (Figure 8). Clinically, the patient continued to suffer from left hemiplegia and left homonymous hemianopsia, but she recovered ambulation and partial muscle strength (left upper and lower extremity strength = 3/5; right extremity strength = 5/5).

Discussion

Gliomas are well known to have disorganized vascular anatomy due to an extensive proliferation of small intra-lesional vessels. The

formation of convoluted, glomerular-like channels due to endothelial proliferation is the most common angiogenic pattern and is more often described in grade IV glioblastomas². It has been hypothesized that VEGFs secreted from these tumor cells may contribute to the abnormal angioarchitecture observed in such cases^{3,4}. These vascular abnormalities should be distinguished from true AVMs. Conversely, patterns of oligodendroglial prominence seen in association with AVMs may be the result of either tissue condensation (presumably due to chronic ischemia and gliosis) or of aberrant vascular development⁵. In a study by Lombardi et al.⁵, a histological review of 1034 surgically resected AVMs, both angiographically occult and visible, revealed no cases of oligodendrogliomas associated with AVMs. There were, however, eight cases in which oligodendroglial cells were increased in number within the AVMs. Lombardi et al. conclude that in contrast to AVMs, the majority of which were angiographically evident and showed arteriovenous shunting, oligodendrogliomas with AVM-like vasculature appear to be angiographically occult. Therefore, histologic and angiographic criteria must clearly be rigorous to definitively distinguish the coexistence of a true AVM and vascular neoplasm rather than the above entities.

In this unique case, the presence of two separate components was clear: an angiographically evident AVM with arteriovenous shunting, and a histopathologically proven juvenile pilocytic astrocytoma (WHO Grade I) without VEGF staining. Such cases are extremely rare.

In 1990, Goodkin et al.⁶ reviewed the literature and found 14 cases of coexisting vascular malformation and primary intracerebral tumors including their own case. However, in 11 of these cases the two lesions were in separate locations, were sequential findings, or the tumors were associated with vascular malformations other than AVMs (e.g. hemangiomas, non-specific increase in vasculature). They listed two cases^{2,7} of simultaneous but separate existence of AVMs and primary brain tumors: Heffner et al.² described a 17-year-old male with right frontal benign astrocytoma (WHO grade II) and an angiographically documented AVM in the meninges overlying the tumor. Martinez-Lage et al.⁷ described a right intraventricular oligodendroglioma co-occurring with a right parietal cortical AVM in a 43-year-old male who presented with SAH. The hem-

Figure 6 Follow-up MRI. A,B) Axial T2W cross-sections. C,D) Axial pre-contrast T1W images. D,E) Axial T1W post-contrast cross-sections. The images demonstrate an enhancing mass (arrows) medial to the hematoma cavity.

orrhage was believed to have been caused by the tumor rather than the AVM.

Goodkin et al. found three cases⁸⁻¹⁰ with simultaneous and combined occurrence of AVMs and primary brain tumors. However, these differed from our case as follows: Raynor and Kingman described an AVM associated with a hemangioblastoma in a 19-year-old male⁸, Crowell et al. described an angiographically evident AVM in the right temporal lobe of a 17-year-old male but this was not supported by the histopathological examination of the resected mass⁹, and Zuccarello et al. described the simultaneous occurrence of malignant astrocytoma (without WHO grade) and an angiographically evident AVM in the left temporal lobe of a 50-year-old male (10). The remaining cases were either associated with vascular malformations other than AVMs or were sequential findings.

Harris et al.⁴ described a case of AVM inter-

mingled with an anaplastic astrocytoma. Due to the diffusely positive VEGF staining of the lesion, the authors postulated that the tumor created a hyperangiogenic environment that fostered growth of the aberrant vasculature. Immunostaining with VEGF did not yield diffusely positive results in the present case (Figure 8).

In 2003, Kupnicka et al. described an unusual cerebral tumor composed of three components (pilocytic astrocytoma, AVM, and a neoplastic ganglion component) in a 46-year-old man with recurrent seizures¹¹. These three components were intimately entangled and created the tumor mass. Thus, the authors proposed the term angioanglioglioma for this entity.

In 2008, McKinley et al.¹² described the *de novo* occurrence of an arteriovenous lesion within an anaplastic oligodendroglioma in a 55-year-old female with previously unremark-

Figure 7 Final MRI brain following lesion resection. A,B) Axial T2W images. C,D) Axial pre-contrast T1W cross-sections. E,F) Post-contrast axial T1W images. The images demonstrate the resection cavity as well as residual hematoma.

able MR brain imaging. Diagnostic imaging at presentation revealed a mass lesion with large arteriovenous shunts and a vascular nidus compatible with an AVM. Due to the absence of the AVM on imaging acquired 27 months prior to the patient's presentation, the authors postulated that the neoplasm induced the formation of the large AVM. VEGF staining of the lesion was not provided. We found no technical differences between the embolization of this lesion and non-neoplastic AVMs. Endovascular embolization has been used successfully in the adjunctive treatment of other vascular intracranial neoplasms without associated AVMs. Despite technically routine embolization, resection of such lesions appears hazardous, and significant blood loss may be expected given the lack of a glial plane usually associated with AVMs^{4,12}. However, we did not experience excessive bleeding or difficult hemostasis during the surgical resection of the lesion.

Conclusion

Although there have been reports of astrocytomas in association with vascular malformations in the literature, their intermixture has only been reported once previously¹¹. Multiple etiologies for the association of vascular malformations and tumors within the same patient have been proposed. These include: fortuitous association⁵, a distinct entity¹¹, a secondary or reactive neoplastic glial change to a previously existing vascular malformation¹⁰, and a vascular malformation induced by the tumor environment^{4,12}. However, the exact association, if any, between AVMs and gliomas still remains unclear. Although the presence of a true AVM entangled in a pilocytic astrocytoma in the present case may be a coincidence; a growing number of such reports would point to the existence of a distinct entity and/or a relationship between the two lesions.

Figure 8 A) JPA and AVM. H & E $\times 40$. Large vessel with embolization material and adjacent pilocytic astrocytoma with areas of alternating densely packed and loosely packed cells. B) Higher-power photomicrographs of the JPA. H&E $\times 400$. Predominance of oligodendroglia-like cells with uniform round nuclei and scant to moderate amount of clear cytoplasm in loose myxoid areas with an eosinophilic granular body (arrow). C) Pilocytic astrocytoma adjacent to embolization material. H&E $\times 200$. Compact area of the tumor with astrocytic cells having elongated hyperchromatic nuclei and eosinophilic, fibrillary cytoplasm and Rosenthal fibers (arrow). Adjacent vessel with multinucleated foreign body giant cells engulfing embolization material. D) VEGF stain ($2\times$) with positivity around the embolization material in the AVM and a non-specific background blush in the adjacent tumor. E) VEGF stain ($40\times$): VEGF positivity in the multinucleated giant cells in the vessels and macrophages in-between the tumor cells. The tumor cells themselves show a faint blush and the endothelial cells (arrow) are negative.

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