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Histologic Evidence for Arteriovenous Malformation-Like Vasculature Occurring within an Intracerebral Schwannoma: A Case Report and Review of the Literature

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Abstract

Background—The phenomenon of intracerebral schwannoma is exceedingly rare, and its etiology still a matter of debate. No documented cases of intracerebral schwannoma containing vascular elements consistent with those of an arterio-venous malformation have been reported. We describe such a case here.

Case Description—A left temporal intraparenchymal lesion was discovered incidentally in a 34 year old male after suffering a mild trauma. The lesion was resected and found to be an intracerebral schwannoma with arteriovenous malformation (AVM) like vasculature upon histological examination. The patient made a full recovery after resection.

Conclusions—To our knowledge, this is the first case of an intracerebral schwannoma with AVM like characteristics to be reported in the literature. We hypothesize that the co-occurrence of this rare pathologic entity is due to an interrelated etiologic process, with the tumor microenvironment of the schwannoma inciting the development of the vascular malformation.

Keywords

Arteriovenous malformation; intracerebral; intraparenchymal schwannoma; schwannoma

Introduction

Intracranial schwannomas account for approximately 7% of all primary brain tumors in adults, and typically arise from the vestibular portion of the eighth cranial nerve^{15,14}. Comparatively, intracerebral schwannomas - specifically those arising within the brain parenchyma and not from the facial, trigeminal, or vestibular nerves - are exceedingly rare. A 2006 survey of the literature found just 65 reports of such cases⁷. Here we discuss the first

reported case of arteriovenous malformation (AVM) like vasculature occurring within an intracerebral schwannoma. Additionally, we review the literature regarding this unique finding, and propose an etiologic link between the two pathologies.

Case Report

History and Presentation

The patient is a 34-year-old previously healthy man, in whom an incidental left temporal lesion was discovered on head computed tomography (CT) as part of a workup for minor head trauma suffered during recreational activity. At the time the lesion was discovered, the patient was neurologically intact and denied any history of symptoms relating to the intracranial lesion.

Imaging

Non-contrast head CT demonstrated a 2.4cm intra-axial, iso-attenuating lesion within the anterior pole of the left temporal lobe, with an incomplete ring of calcification and mild surrounding edema (see **Figure 1**). Magnetic resonance imaging (MRI) demonstrated homogenous contrast enhancement of the lesion with evidence of increased blood flow to the center of the lesion on arterial spin labeling pulse sequence, and mild surrounding edema on FLAIR sequence (see **Figure 2**). Gradient echo sequences demonstrated areas of hemorrhage and a possible small intralesional traversing vessel (see **Figure 3**). Differential diagnosis included ganglioglioma, oligodendroglioma, or post-infectious sequelae. After a discussion with the patient surrounding the uncertain nature of the lesion and findings on MRI, the decision to undergo surgery was made for resection of the abnormality.

Surgical Procedure

A curvilinear incision and temporal craniotomy was performed. The dura was opened exposing the temporal lobe. With use of neuronavigation, a cortical entry point was planned, bipolarizing the superficial pia. The cortex was entered and immediately an abnormal yellow colored lesion was encountered. Dissection was carried out around the lesion, at which time prominent vasculature was seen feeding into the lesion. These abnormal appearing vessels were bipolarized along the surface interface of the lesion. Once the entire lesion was successfully resected it was sent for pathological evaluation.

Post-operative Course

Post-operatively the patient recovered well and was at his neurologic baseline without any deficits. He was discharged two days after surgery. Post-operative MRI demonstrated gross total resection of the lesion. Two and a half months later the patient suffered a tonic-clonic seizure during a stressful business trip, which spontaneously resolved. He was subsequently started on levetiracetam and has since been seizure-free without further complaints.

Pathological Findings

The resected specimen was a seemingly discreet non-infiltrative $2.2 \times 2.1 \times 1.9$ centimeter solid and cystic hemorrhagic mass with a heterogeneous yellow-tan and dark red-brown cut surface. Large blood vessels were obvious within the tumor.

Microscopic sections stained with hematoxylin and eosin (H&E) showed a neoplasm composed of variably well-aligned elongate cells with ovoid to spindle nuclei rarely forming ill-defined fascicles or swirling concentrically around vasculature. Degenerative nuclear atypia, hyperchromasia, and intranuclear pseudoinclusions were conspicuous. Abnormal vasculature was striking and often indistinguishable from an arteriovenous malformation or angioma (**Figure 4**). Some of the abnormal blood vessels were thick walled and positive for desmin and smooth muscle actin, confirming an arterial component in the abnormal vasculature, thus meeting histopathologic criteria for an arteriovenous malformation. Most areas had loosely textured cobweb-like meshworks of cells with multipolar processes (**Figure 5**), representing Antoni B architecture and fascicles of Antoni A composition were rare. Calcifications, many concentrically laminated, hence psammomatous, appeared within brain parenchyma at the pushing edge of the tumor (**Figure 6**) which showed a Rosenthal fiber-rich reactive piloid gliosis, implying chronicity.

Multiple foci of chronic inflammation with both lymphocytes and plasma cells were scattered through the neoplasm. Some fields were dominated by clusters of vacuolated cells representing either xanthic tumor cells or foamy macrophages, and one section included cholesterol crystal cleft spaces (**Figure 7**). Many fusiform and stellate tumor cells displayed S-100 nuclear and cytoplasmic positivity (**Figure 8**). CD34 was positive only in blood vessels. An epithelial membrane antigen (EMA) stain was mostly negative with focal weak positivity confined to regions with psammomatous calcifications, possibly representing reactive meningeal cells rather than neoplasm. A Ki-67 preparation showed low overall nuclear labeling except in foci of chronic inflammation, and many high-magnification fields were all together negative. Selected high-magnification fields displayed Ki-67 positive nuclei in, at most, 2-3% of tumor cells.

The neoplasm thus displayed both the gross appearance and microscopic and immunohistochemical features most consistent with an intracerebral schwannoma. While blood vessels are often conspicuous in schwannomas, they are usually thick-walled and hyalinized or thin-walled and ectatic^{21,20}, but in this tumor, the abnormal vessels were so conspicuous as to resemble a vascular malformation or angioma. Calcification is unusual in extraparenchymal schwannomas generally but has been reported in intracranial examples^{11,8}.

Discussion

Isolated intraparenchymal schwannomas are exceedingly rare occurrences, as the central nervous system is generally thought to be devoid of Schwann cells. As such, their etiology remains a matter of controversy. Broadly speaking, there are two general theories for this pathology, which Srinivas *et al*¹⁸ termed “developmental” and “non-developmental”.

The developmental theory suggests that ectopic Schwann cells arise in the brain parenchyma during embryogenesis, through one of a number of possible mechanisms. One such mechanism put forth by Ramamurthi *et al*⁶ is that ectopic Schwann cells may arise from disordered neural crest cell migration (i.e. into the central nervous system). Other authors have suggested that intraparenchymal Schwann cells arise via transformation of proliferating pial cells^{5,6}, an argument supported by the histologic similarity between ectodermal Schwann cells and mesenchymal pial cells⁶. Irrespective of mechanism, the developmental theory is further supported by the relatively young age of patient presentation for many of these rare tumors (often within the first three decades of life)^{3,4}.

The non-developmental theory, in contrast, suggests that intraparenchymal schwannomas may simply arise from neoplastic transformation of Schwann cells naturally occurring within the brain parenchyma. For instance, Schwann cells have been shown to exist both within the perivascular nerve plexi¹³, and within the adrenergic nerve fibers innervating certain cerebral arterioles, which helps explain the observed predilection for periventricular location of these tumors¹⁷.

Vascular malformations have traditionally been considered to be developmental anomalies² (i.e. congenital), which can evolve over the course of a person's lifetime¹². However, recent evidence has pointed towards an acquired etiologic component, in which vascular malformations may arise secondary to any number of “inciting event(s)” – ranging from traumatic insult to infection, irradiation, or even mechanical compression⁹.

In the case we present here, the co-occurrence of these two rare pathologies raises the question of etiologic mechanism, and specifically whether their coexistence resulted from two independent processes or an interrelated sequence of events. We hypothesize that in this case, an intracerebral schwannoma provided the inciting event necessary to trigger angiographic proliferation and subsequent development of vascular malformation features. We suggest this hypothesis based on the following evidence. Firstly, documented cases have described the co-occurrence of schwannoma and vascular malformations previously^{1,20}, although in each case the schwannoma was of extraparenchymal origin (in contrast to this case). While these reports of AVM's arising within extraparenchymal schwannomas do not definitively establish a temporal relationship between the two pathologies, their existence would at least suggest a link between the two.

Secondly, it is known that the tumor microenvironment for intracranial schwannomas expresses particularly high levels of vascular endothelial growth factor (VEGF) relative to other brain tumors¹⁹. Schwannoma expression of both VEGF and benign fibroblast growth factor (bFGF) – another potent mediator of neuroangiogenesis – has been shown to correlate positively with the tumor's microvessel density and growth index¹⁰.

Finally, examining our case from a purely statistical perspective, the odds of observing AVM-like vasculature occurring within an intraparenchymal schwannoma by chance alone would be an exceptionally unlikely event, making an interdependent process more probable.

This case represents the first report of AVM-like vasculature occurring within an intraparenchymal schwannoma. In reviewing the literature we hypothesize that these two

pathologies are interrelated, in that the tumor microenvironment within the schwannoma may have served as the inciting etiologic cause of vascular malformation.

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Abbreviations

AVM	arteriovenous malformation
bFGF	benign fibroblast growth factor
CT	computed tomography
EMA	epithelial membrane antigen
FLAIR	fluid-attenuated inversion recovery
H&E	hematoxylin and eosin
MRI	magnetic resonance imaging
VEGF	vascular endothelial growth factor

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Figure 1.

Axial (left pane) computed tomography image demonstrating the lesion in the left temporal pole (arrow). Coronal (right pane) computed tomography image revealing an isointense lesion with a rim of calcification (arrow heads).

Figure 2. Axial arterial spin labeling pulse sequence imaging (left pane) demonstrating increased blood flow to the center of the lesion (arrow), and FLAIR sequence imaging (right pane) demonstrating mild surrounding edema (arrowheads).

Figure 3. Axial gradient echo sequence imaging demonstrating areas of hemorrhage and what was thought to be a small vessel traversing the lesion (red arrows).

Figure 4.
H&E stained section (x10), showing striking angiomatoid vasculature.

Figure 5.
H&E stained section (x10), showing loosely textured proliferation of spindled cells between blood vessels.

Figure 6.
H&E stained section (x10), showing many psammomatous calcifications associated with a focus of spindled cells in a compact/fascicular arrangement.

Figure 7.
H&E stained section (x10) showing cholesterol clefts and xanthic cells corresponding with the focal yellow appearance grossly.

Figure 8. S-100 immunostain (x20) showing many fusiform and stellate tumor cells displaying S-100 nuclear and cytoplasmic positivity.