

Congenital Multiple Cavernous Angiomas Associated With Thrombosed Arteriovenous Malformation of the Brain

—Case Report—

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Abstract

A 16-year-old girl presented with multiple cerebral cavernous angiomas with calcifications due to repeated hemorrhages and a thrombosed cerebral arteriovenous malformation (AVM). Her 18-year-old elder sister also had multiple cerebral cavernous angiomas associated with calcifications, which suggested presence of repeated previous hemorrhages. Surgical removal via a right occipital craniotomy resulted in a good outcome. The histological diagnosis was thrombosed AVM. Evaluation of congenital vascular anomaly needs to take into consideration the combination of other congenital vascular anomalies and their familial occurrence.

Key words: multiple vascular malformations, cavernous angioma, thrombosed arteriovenous malformation, familial occurrence

Introduction

Congenital vascular malformations of the brain are usually classified into arteriovenous malformation (AVM), cavernous angioma, venous angioma, and teleangiectasia.²⁰⁾ The correct diagnosis can be made preoperatively based on magnetic resonance (MR) imaging.^{3,12,16,28)} Cavernous angioma typically appears as mixed intensity surrounded by a margin of hypointensity thought to represent hemosiderin. MR imaging can distinguish cavernous angioma from thrombosed AVM. The margins of AVMs are irregular whereas those of cavernous angiomas are smooth in all planes on T₂-weighted MR images.¹²⁾

Cavernous angioma may coexist with other types of cerebrovascular malformations, such as venous angioma, AVM, or capillary telangiectasia. Only three cases of cavernous angioma associated with AVM have been reported.⁶⁾ We report a case of multiple cavernous angiomas associated with thrombosed AVM of the brain in a young patient with a familial history of cavernous angioma.

Case Report

A 16-year-old girl had suffered from attacks of loss of consciousness every few months for 2 years. She was admitted to our hospital, complaining of increasing frequency of attacks with nausea and vomiting. Neurological and physical examination revealed no abnormalities, especially in the skin and mucosa, and she had no mental retardation. Her coagulation system was normal. Electroencephalography showed focal spike waves in the left temporal lobe.

Computed tomography demonstrated small, slightly high-density areas in the left frontal and right occipital lobes with calcifications and delayed enhancement (Fig. 1). T₂-weighted MR imaging revealed multiple cores of small mixed signal intensity areas with hypointense rims in the bilateral frontal, right occipital, and left temporal lobes (Fig. 2A-C), and a hyperintense mass with an irregular hypointense rim and no perifocal edema in right occipital lobe (Fig. 2B). T₁-weighted MR imaging showed the lesion as a heterointense area and the rim of the lesion contained several well-enhanced spots (Fig. 2D). These findings indicated multiple cavernous angiomas with internal clots and a thrombosed vascular malformation in the right occipital lobe. The hemorrhages appeared to have occurred a few

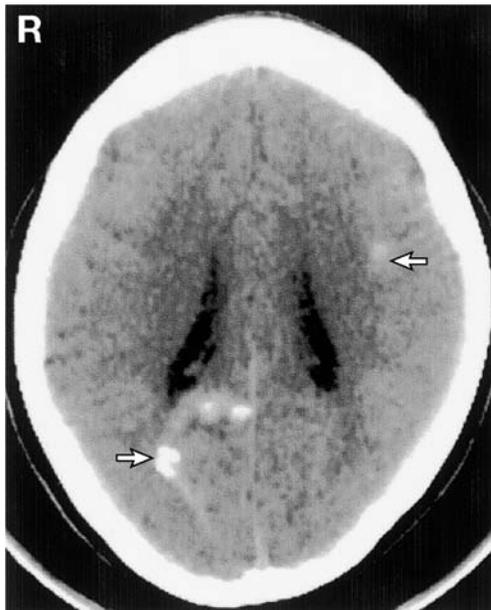


Fig. 1 Computed tomography scan showing calcifications in the left frontal lobe and right occipital lobe (arrows).

months ago. Right carotid and vertebral angiography showed no vascular anomaly except fenestration of the right vertebral artery (Fig. 3). The most likely diagnosis was multiple cavernous angiomas with a thrombosed AVM.

Family history revealed that her 18-year-old elder sister also had multiple vascular malformations, appearing on MR imaging as multiple small mixed signal intensity areas with hypointense rims, similar to the lesions in this patient, but no thrombosed AVM (Fig. 4). We considered that the diagnosis was multiple cavernous angiomas. Their female cousin died of intracranial hemorrhage when she was in high school. Cerebrovascular anomaly was suspected as the etiology of the intracranial hemorrhage, because she was so young. Their grandmother also suffered intracranial hemorrhage when she was 40 years old (Fig. 5).

Surgery was performed to prevent bleeding from the thrombosed AVM due to recanalization. The vascular malformation in the right occipital lobe was situated in contact with falx cerebri. The nidus and all small feeding arteries were almost thrombosed and a tortuous draining vein passed into the superior sagittal sinus via a cortical vein (Fig. 6). The lesion was totally resected en bloc without bleeding.

Histological examination revealed abnormal hyalinized arteries with numerous capillary-sized vascular channels and gliosis, hemosiderin deposi-

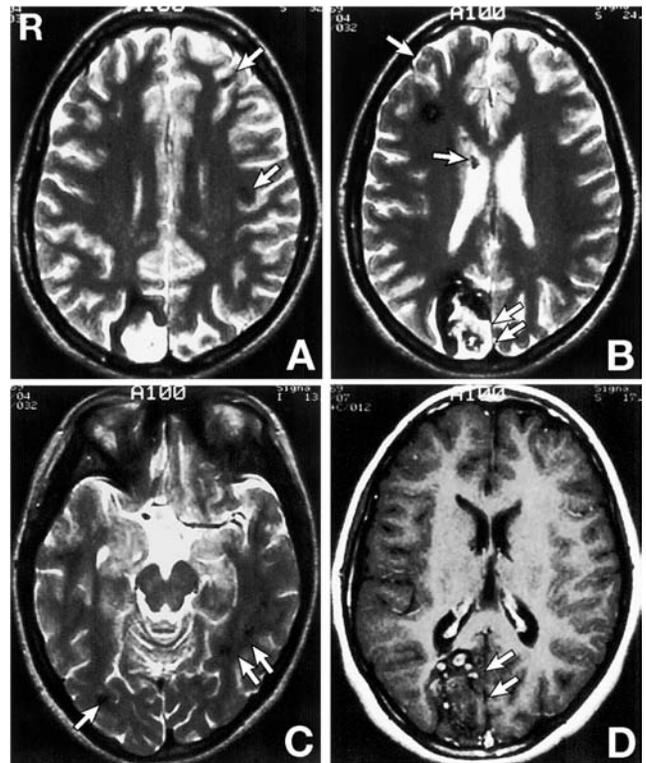


Fig. 2 A–C: Axial T₂-weighted magnetic resonance (MR) images revealing multiple small mixed signal intensity areas with hypointense rims (arrows) in the bilateral frontal, right occipital, and left temporal lobes. Axial T₂-weighted MR image also revealing a hyperintense lesion with a hypointense rim in the right occipital lobe (B, double arrows). D: Axial T₁-weighted MR image revealing a heterointense lesion with several well-enhanced spots in the right occipital lobe (double arrow).

tions, and calcifications in the intervening brain tissue. Most channels were thrombosed. The histological diagnosis was thrombosed AVM (Fig. 7A). The marginal zone of the thrombosed AVM was consistent with cavernous angioma (Fig. 7B).

She was discharged from the hospital on day 10 after the operation. Her postoperative visual field had no defect. MR imaging showed complete removal of the AVM and no changes in the multiple cavernous angiomas. The attacks of loss of consciousness were completely controlled by administration of anticonvulsant agent (300 mg carbamazepine). Two years later, she was doing well with no neurological deficits and no evidence of regrowth of vascular malformations.



Fig. 3 Right vertebral angiogram revealing no vascular malformation in the right occipital lobe except fenestration of the right vertebral artery.

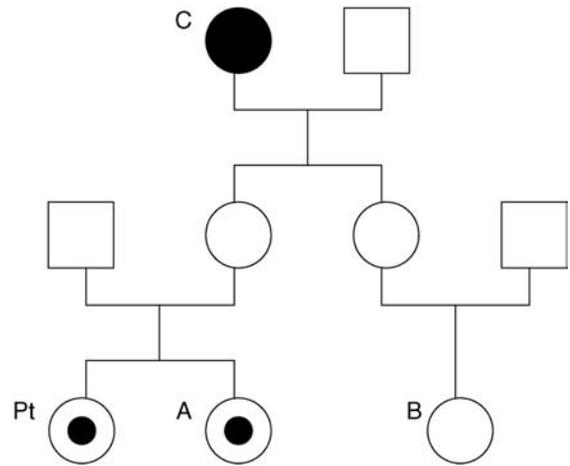


Fig. 5 Family tree of this patient (Pt). *Open square: healthy male, open circle: healthy female, solid circle: female with stroke, solid circle within an open circle: female with cerebrovascular anomaly. A: elder sister who had cerebral vascular anomalies, B: cousin who died of intracranial hemorrhage, C: grandmother who suffered from intracranial hemorrhage.*

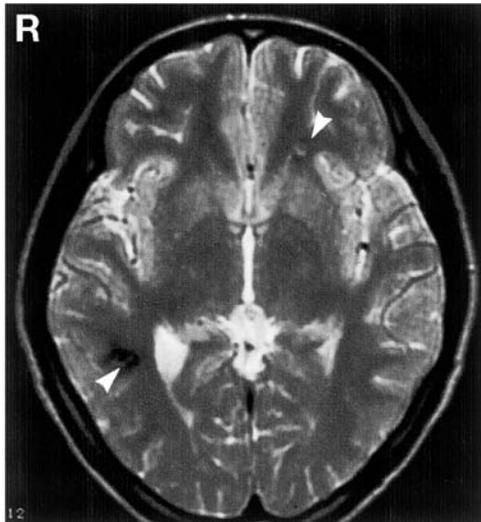


Fig. 4 Axial T₂-weighted magnetic resonance image of the elder sister of this patient revealing similar lesions in the left frontal lobe and right temporal lobe (arrowheads). They are suggested to be cavernous angiomas with calcifications.

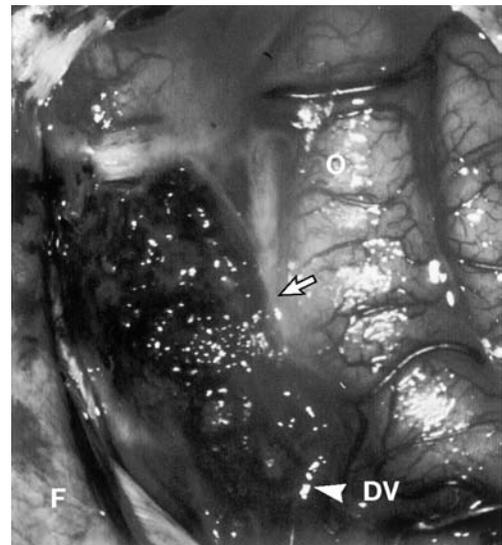
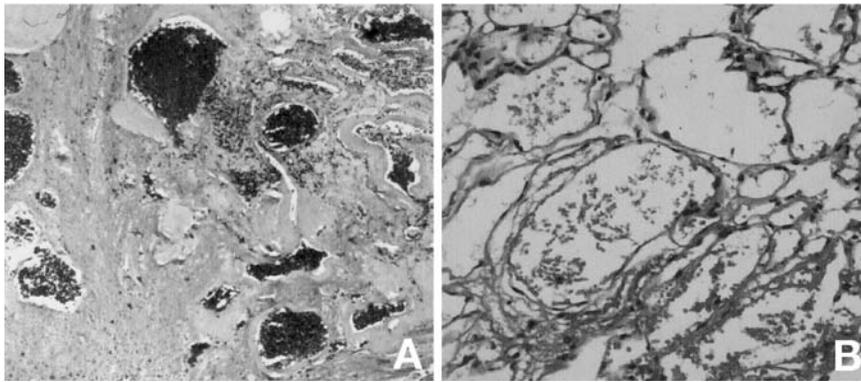


Fig. 6 Intraoperative photograph showing the vascular malformation (arrow) in the right occipital lobe (O) located in contact with the falx cerebri (F). The nidus and all small feeding arteries were almost thrombosed and a tortuous draining vein (DV; arrowhead) passed into the superior sagittal sinus.



←
Fig. 7 A: Photomicrograph of the specimen obtained during surgery showing numerous hyalinized capillary arteries and most channels are thrombosed. Gliosis, hemosiderin, and calcifications on the intervening brain parenchyma are also seen. The diagnosis was thrombosed arteriovenous malformation (AVM). B: Photomicrograph of the specimen of a marginal zone of the thrombosed AVM. The majority of the lesion consists of typical cavernous angioma. HE stains, $\times 150$.

Discussion

Multiple cavernous angiomas occur at a frequency of 16–33%.^{12,19)} Usually, the number of multiple lesions is four or five.³⁾ Familial occurrence of cavernous angiomas is rare. The frequency is unknown, but may be as high as 50% of clinical cases.^{13,14,17)} However, this frequency is probably overestimated due to the collection bias, particularly in Hispano-American families. The inheritance pattern is autosomal dominant with incomplete clinical penetrance as in the case of AVM, but the number of familial occurrence of cavernous angiomas or AVMs was too small to identify the genetic factors.^{4,15)} A gene associated with familial cavernous angiomas was mapped in a large Hispanic family to chromosome 7q11–q22.⁵⁾ Multiple cavernous angiomas can occur in all age groups,²⁸⁾ but young patients (under the age of 18 years) with multiple cavernous angiomas tend to have family histories of vascular malformations of central nervous system.²³⁾ In our patient, the grandmother and cousin also had cavernous angiomas, so the inheritance pattern might be autosomal dominant.

Most AVMs are easily identified based on the presence of angiographic arteriovenous shunts, but thrombosed AVMs are sometimes difficult to detect because these may lack such shunts. Thrombosed AVMs are not easy to differentiate from other vascular malformations. In our case, cerebral angiography demonstrated no arteriovenous shunts. T₂-weighted MR imaging revealed a mixed intensity area with an irregular hypointensity rim, which is a characteristic finding of thrombosed AVM.¹²⁾ Cavernous angiomas also appear as mixed intensity areas

on T₂-weighted MR imaging, but the margins are smooth, which is the most important point in the differential diagnosis from other vascular malformations.¹²⁾ The operative findings of our case included thrombosed nidus and feeders and a single draining vessel passing into the superior sagittal sinus. Histological examination found consistent findings of various sizes of abnormal vessels with thrombosis, intervening cerebral parenchyma, hemosiderin, gliosis, and calcification. Therefore, the final diagnosis of the lesion in the right occipital lobe was thrombosed AVM.

Thrombosed AVMs are the predominant type of angiographically occult vascular malformations.⁷⁾ Usually, thrombosed AVMs are less than 3 cm in size, so are not detected by angiography because of the small size, thrombosis, or obliteration by hemorrhage. Thrombosis may occur spontaneously due to several factors: compression of vessel walls due to hemorrhage, intravascular turbulence, or arteriosclerosis.^{6,25)} The natural history of thrombosed AVMs is unclear, but previous hemorrhages and varying degrees of thrombosis have been detected.^{2,24,26)} There is no doubt that hemorrhage occurs in some of these lesions. Recent reports indicate that late bleeding from AVM in asymptomatic patients occurs much more frequently than generally expected. Total excision should be the goal when the thrombosed AVM is present in accessible areas and is correlated with neurological symptoms.⁷⁾ Excision of the thrombosed AVM was performed in our case, because the lesion was located in the occipital lobe and presumably caused the attacks of loss of consciousness.

The clinical presentation in our patient was onset

of loss of consciousness, a kind of seizure, which was controlled by anticonvulsant agent. Electroencephalography showed the epilepsy originated from the cavernous angiomas in the left temporal lobe. Cavernous angiomas are generally silent, but seizures are the most common presenting events in symptomatic patients.^{3,8)} The estimated risk of seizures is about 1.5%/person-year.³⁾ The risk of developing seizures appears to be higher and the ages of onset earlier in patients with multiple lesions.³⁾

In our patient, the cavernous angioma component was contained in a part of the thrombosed AVM, in addition to the several separate cavernous angiomas. Cavernous malformations with mixed venous,^{18,22,27)} arteriovenous, or capillary components¹⁾ are most difficult to detect by imaging studies. These lesions may be more prevalent than previously thought.¹⁾ The mechanism of occurrence of AVMs associated with cavernous malformations is unclear. Abnormal vascular beds might result in microscopic arteriovenous shunting causing a predisposition to additional vascular recruitment and the genesis of discrete zones of arteriovenous shunting within the lesion.¹⁾ Hemodynamic stresses could then cause secondary thickening and hyalinization of the vascular walls. Another explanation involves neoproliferation of smooth muscle cells in the wall of budding caverns.^{9,11)} Pluripotential cells may be present in zones of active angiogenesis.^{10,21)} Our case was probably a mixed lesion of cavernous angiomas and thrombosed AVM. Both the cavernous angioma and thrombosed AVM were angiographically occult thrombosed vascular malformations, a unique association of these two vascular malformations.

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