Familial occurrence of arteriovenous malformation of the brain

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Brain arteriovenous malformations are considered to originate from a congenital maldevelopment of the brain vessels. Although there have been occasional reports suggesting a familial incidence of these lesions, data for only 10 families have been accumulated in the literature. Recently, we encountered six patients with AVM in three families. These are reported here and the literature is reviewed.

Case Reports

Case 1

This 50-year-old man presented for evaluation of a seizure in December, 1974. His history was noncontributory. Diagnostic angiography revealed the presence of an AVM (Fig. 1), which was totally removed in July, 1975, without neurological complication.

Case 2

This 16-year-old boy was the son of the patient described in Case 1 (Fig. 2). He presented with a chief complaint of convulsions, his first seizure having occurred when he was 8 years old. In May, 1978, he had a seizure, which resulted in unconsciousness. While he was being evaluated for this condition, a right parietal AVM was revealed by right carotid angiography (Fig. 3). The lesion was totally removed; the only complication was a transient postoperative hemiparesis.

Case 3

This 11-year-old boy suddenly had a severe headache and became unconscious. On admission, he was co-
matose and had no spontaneous respirations or brainstem responses. A lumbar puncture revealed bloody cerebrospinal fluid; a right carotid angiogram was not diagnostic. The vertebrobasilar system was not depicted by a left retrograde brachial angiogram. He was treated conservatively and died shortly after admission. Autopsy revealed a large cerebellar hematoma and a cast-like intraventricular hematoma. Enlarged tortuous vessels, hardly identifiable as arteries or veins, were seen at the margins of the cerebellar hematoma on histological examination (Fig. 4); the lesion was diagnosed as a cerebellar AVM.

Case 4
This 24-year-old woman was a cousin of the patient described in Case 3 (Fig. 5). She suffered a severe headache and became unconscious. A computerized tomography (CT) scan demonstrated a left temporal hematoma and an intraventricular hemorrhage. Left carotid angiography revealed an AVM in the left temporal lobe (Fig. 6). The AVM was totally removed at surgery, but a right homonymous hemianopsia persisted 3 months after the operation.

Case 5
This 21-year-old woman presented with the chief complaints of a headache and left hemiparesis. A lumbar puncture disclosed bloody cerebrospinal fluid and right carotid angiography revealed an AVM in the right temporal lobe (Fig. 7). The artery feeding the AVM was clipped. Postoperatively, the patient suffered frequent seizures, so two more operations were performed on the AVM. Ultimately, the lesion was totally removed. Although a left hemiparesis remained postoperatively, the patient could walk without help at the time of her discharge.

Case 6
This 18-year-old man was the son of the patient described in Case 5 (Fig. 8), and had a history of headaches. He suffered a seizure and became unconscious. A CT scan demonstrated a left parietal hypodense area, which was partially enhanced after administration of contrast medium. A left carotid angiogram revealed a small AVM in the left parietal region (Fig. 9 left). The AVM was totally removed without neurological complication; histological examination revealed dilated tortuous vessels (Fig. 9 right).

Discussion
It is thought that AVM's are formed as congenital developmental anomalies of the blood vessels; however, their genetic origin has not yet been clarified. Arteriovenous malformations have been recognized as one group of complicating lesions in such familial brain diseases as Sturge-Weber-Dimitri disease, von Hippel-Lindau disease, and Osler-Weber-Rendu disease. To
Familial occurrence of arteriovenous malformation

our knowledge, familial occurrences of brain AVM's unassociated with these diseases have been reported in only 10 families.\textsuperscript{2,4,8,11,14} The previously published familial cases and the six cases reported here (a total of 29 cases in 13 families) are summarized in Table 1. Analyses of these cases were performed as follows:

**Age and Sex Distribution**

Excluding two patients whose age was not recorded, the age range was 10 to 19 years in 12 patients, 20 to 29 years in five, 30 to 39 years in six, and 40 to 49 years in two; one was aged 50 years and one aged 66 years. The average age was 27 years. The nationwide Japanese survey on cerebrospinal vascular anomalies indicated that brain AVM's become manifest most frequently in the 20- to 39-year age group;\textsuperscript{9} thus, it appears that familial AVM cases exhibit symptoms at a somewhat younger age than do overall AVM cases. The same survey indicated that the male:female ratio of AVM cases is about 2:1.\textsuperscript{9} The familial cases summarized in Table 1 consisted of 18 males and 11 females, indicating

![Fig. 6.](image1.png)  
**Fig. 6.** Left carotid angiogram in Case 4 showing an arteriovenous malformation seated deeply in the temporal lobe, fed by the anterior choroidal artery and draining into the lateral atrial vein (arrow).

![Fig. 7.](image2.png)  
**Fig. 7.** Right carotid angiogram in Case 5 showing an arteriovenous malformation in the right temporal region, fed by the lenticulostriate, precentral, central, and posterior cerebral arteries and draining into the internal cerebral vein, Trolard's vein, and the cavernous sinus.

![Fig. 8.](image3.png)  
**Fig. 8.** Family tree of Case 5 (5) and Case 6 (6). Squares = males alive; circles = females alive.

![Fig. 9.](image4.png)  
**Fig. 9.** Case 6. Left: Left carotid angiogram showing an arteriovenous malformation (arrow) in the left parietal region, fed by the angular artery and draining into the rolandic vein. Right: Photomicrograph of the lesion showing dilated tortuous vessels. H & E, × 10.
that familial AVM's have a tendency to occur more frequently in females than do AVM's in general.

**Familial Incidence**

Familial AVM's were observed in parent-child combinations in six families, in siblings in five families, and in cousins in two families. Among the parent-child combinations, there were two mothers and daughters, one mother and son, two fathers and sons, and one father and daughter. In the sibling combinations, there were one sister-sister, three brother-brother, one sister-brother, and one brother-brother (with stepfathers) combination. Thus, we cannot find a specific familial relationship that is particularly prone to AVM manifestation, although there is some tendency for the same sex to be affected by familial AVM.

**Location of AVM**

In 27 cases in which the AVM locations were described, 20 (74%) were supratentorial, five (19%) were deep-seated, and two (7%) were infratentorial. This finding is in accordance with the results of the nationwide Japanese survey. There was no observed tendency for similar AVM locations within the same family.

The number of reported familial AVM cases is too small to draw conclusions regarding the possibility of genetic factors controlling the occurrence of AVM's. However, in the fairly isolated Hida district of Japan, which has a population of about 150,000, we have personally encountered 24 patients with AVM's in the last 10 years; among these were the six cases in three families reported here. This fact is suggestive of the possibility that genetic factors may be involved in the occurrence of AVM's.

**References**

Familial occurrence of arteriovenous malformation


Manuscript received October 10, 1989. Accepted in final form December 20, 1990.
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