Familial intracranial aneurysms

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Six cases of intracranial aneurysms are described in three families: two sisters, identical twins, and a mother and daughter. The cases suggest a hereditary basis for some intracranial aneurysms.

KEY WORDS intracranial aneurysm familial aneurysm

Several factors suggest a hereditary basis for some intracranial aneurysms. The occurrence of familial aggregates of intracranial aneurysms is rare but well documented. The inherited condition of polycystic kidneys is associated with an increased incidence of intracranial aneurysms. The familial occurrence of intracranial aneurysms has been described in association with hereditary connective tissue disorders (Ehlers-Danlos syndrome and pseudo-xanthoma elasticum).

The following six cases of intracranial aneurysm in three families are unique for several reasons. Cases 1 and 2 are siblings with several other congenital stigmata and a strong family history of Friedreich's ataxia and retinal degeneration; Cases 3 and 4 are identical twins; and Cases 5 and 6 are a mother and daughter with multiple intracranial aneurysms. The family tree of each case is presented.

Case 1

A 23-year-old white woman was examined at the Church Home Hospital, Baltimore, Maryland, in 1960 when she had moderate horizontal nystagmus, several small yellowish-white spots about both maculae, electrocardiographic evidence of incomplete right bundle branch block, and a history of leg cramps. Her blood pressure was normal. In December, 1966, she had a subarachnoid hemorrhage. Bilateral carotid arteriograms showed aneurysms of the left internal carotid-posterior communicating artery, left internal carotid bifurcation, and right supraclinoid internal carotid artery. Five days later the aneurysm of the left internal carotid-posterior communicating artery was clipped intracranially. Six months later except for severe impairment of both recent and remote memory, she was functioning fairly well at home.

Case 2

The 22-year-old sister of the patient in Case 1 was examined at the Johns Hopkins Hospital in 1960. She had normal blood pressure, mild horizontal nystagmus, electrocardiographic evidence of incomplete right bundle-branch block, intermittent numbness of the hands, and leg cramps. Several years later she developed night blindness and was noted to have high arched feet. In April, 1967, she had a subarachnoid hemorrhage. Right retrograde brachial and left carotid angiograms demonstrated a left middle cerebral artery aneurysm near the trifurcation. Four days after the initial hemorrhage a left frontotemporal craniotomy was performed and the aneurysm was clipped.
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clipped. Subsequent arteriography showed that the aneurysm had been obliterated. When last seen in June, 1967, the patient's neurological examination was normal except for mild horizontal nystagmus.

Comment. Cases 1 and 2 have a carefully documented family history of Friedreich's ataxia, retinal degeneration, and abnormal cardiac and musculoskeletal findings (Fig. 1).13,14 The sisters' mother has crippling Friedreich's ataxia. One maternal aunt has Friedreich's ataxia, and two maternal aunts have retinal degeneration. Three other siblings died in infancy. A 32-year-old half-sister (maternal) has had headaches during the past 15 years which became much more severe during the past year; left carotid and right retrograde brachial arteriograms were normal.

Case 3

A 35-year-old white woman had a subarachnoid hemorrhage in 1963. When the patient was examined at the Neurological Institute, New York, bilateral carotid and left brachial arteriography failed to show the site of bleeding. The patient recovered and remained asymptomatic. In 1967 her identical twin sister (Case 4) died from a ruptured aneurysm. The patient's mother had died at the age of 62 years of a subarachnoid hemorrhage. An aneurysm was not found at autopsy. Two other members of the family had died from cerebrovascular accidents (Fig. 2). The patient requested to be re-studied. A left common carotid arteriogram (February, 1968) demonstrated a lobulated

\[ \text{Friedreich's Ataxia} \]
\[ \text{Retinal Degeneration} \]

\[ \text{Intracranial Aneurysm} \]

\[ \text{Died in Infancy} \]

Fig. 1. Pedigree of Cases 1 and 2.

Fig. 2. Pedigree of Cases 3 and 4.
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left middle cerebral artery aneurysm at the trifurcation. A right brachial arteriogram showed a small aneurysm of the right middle cerebral artery just distal to its bifurcation into two main branches. On March 1, 1968, the left middle cerebral artery aneurysm was clipped intracranially. Twelve days later the right middle cerebral artery aneurysm was clipped; at surgery it was 1 cm in its greatest diameter. The patient tolerated both procedures well and now has minimal neurological deficits.

Case 4

The identical twin sister of the patient in Case 3, a 35-year-old normotensive white woman, died in a sudden attack of left hemiparesis and coma in 1968. Autopsy at the Neurological Institute, New York, showed a ruptured aneurysm of the right internal carotid artery at the junction of the middle and anterior cerebral arteries.

Case 5

A 36-year-old hypertensive Negro woman (Fig. 3) had mild subarachnoid hemorrhages in 1958, 1962, and 1966. At the Neurological Institute, New York, a left carotid arteriogram in 1958 showed an aneurysm at the bifurcation of the left internal carotid artery and at the bifurcation of the anterior cerebral artery into the supramarginal and pericallosal arteries. A right carotid arteriogram showed two aneurysms of the right internal carotid artery proximal to the bifurcation. The patient was considered a poor surgical risk and was treated conservatively with antihypertensive medication and rest. It is now 12 years since her initial subarachnoid hemorrhage and she is doing well, with minimal neurological deficits.

Case 6

The daughter of the patient in Case 5, a 25-year-old normotensive Negro woman (Fig. 3), had a subarachnoid hemorrhage in 1965. When the patient was examined at the Philadelphia General Hospital, bilateral carotid and right brachial arteriography demonstrated aneurysms of the left internal carotid artery (intracavernous, supraclinoid, and bifurcation), anterior communicating artery, and right supraclinoid internal carotid artery. A Selverstone clamp was applied to the left common carotid artery. The patient had minimal neurological deficits at the time of the last follow-up in 1968.

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Fig. 3. Pedigree of Cases 5 and 6.
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Discussion

Review of the literature reveals 25 other families in which more than one member had an intracranial aneurysm documented by arteriography or autopsy. Including the present cases, the aneurysm was on the same artery in both family members in 16 of the 28 families. Aneurysms were on the same side in 17 of the 28 families.

Some studies have suggested a relatively high incidence of familial intracranial aneurysms. In a series of 541 cases of proven intracranial aneurysms, 10 had a familial incidence. Five more cases of patients with documented aneurysms had relatives who died of subarachnoid hemorrhage but had no arteriography or autopsy. Jansen reviewed 147 patients with subarachnoid hemorrhage and 688 members of their families. Fifteen relatives of 11 patients had subarachnoid hemorrages. Only one of the 15 had been studied and shown by arteriography to have an intracranial aneurysm.

The occurrence of intracranial aneurysms in the general population is not infrequent. An autopsy incidence of 2.1% has been reported. A clinically derived incidence of ruptured intracranial aneurysms was 6 per 100,000 in 1 year. It has not been clearly established that a relative of a patient with an intracranial aneurysm carries a greater than average risk of developing a subarachnoid hemorrhage.

Neither of the two sisters reported here (Cases 1 and 2) has clinical Friedrich's ataxia or detectable retinal degeneration. Both, however, have had nystagmus, electrocardiographic abnormalities, and a history of leg cramps. One has high arched feet and complaints of night blindness. These are a few of the stigmata tending to occur within this pedigree which reflect a hereditary predisposition to certain degenerative disease. Insufficient arteriographic and autopsy data may explain the absence of other reports of intracranial aneurysms in this particular family.

Blood vessel abnormalities have been noted occasionally in association with Friedrich's ataxia. In 1887, Pitt described one case with "absence of one radial pulse, endarteritis of one vessel, and a replacement of one vessel by fibrous cord." Nadas, et al. studied a 6-year-old boy with Friedrich's ataxia whose coronary arteries showed marked medial hypertrophy, intimal proliferation, and varying degrees of obstruction. Widespread involvement of small arteries of the myocardium and lungs has been demonstrated by James and Fisch. He found intimal hyperplasia, amorphous endothelial deposits which were usually Schiff-positive, and degeneration of the tunica media (with or without small cyst formation).

Degeneration or hypoplasia of the muscle in the tunica media and elastic fibers have been cited as an important factor in the formation of intracranial aneurysms. In the two sisters with intracranial aneurysms and stigmata of Friedrich's ataxia reported here, the weakness in the intracranial blood vessel wall may reflect a hereditary tendency for degeneration of cardiac muscle and/or blood vessels associated with Friedrich's ataxia. Of 160 members of this family who had been studied for cardiac disease previously, only 13 were found who met the criteria for cardiac disease of Friedrich's ataxia. Both sisters with intracranial aneurysms had incomplete right bundle-branch block and were therefore included in this group. Their intracranial aneurysms were asymptomatic at that time. James and Fisch suggest that disease of small coronary arteries may explain the cardiopathy of Friedrich's ataxia. If this is true, then the supposed genetic defect responsible for the transmission of cardiac disease in Friedrich's ataxia may be one that causes blood vessel pathology.

The occurrence of intracranial aneurysms in identical twins has been suggested in a previous report. In Case 3 an awareness of the familial occurrence of some intracranial aneurysms led to the proper diagnosis and treatment in an asymptomatic identical twin.

Multiple intracranial aneurysms in more than one member of the same family were reported by Kak, et al. Cases 5 and 6 represented another family with multiple intracranial aneurysms. Multiple aneurysms occur in approximately 20% of all aneurysm patients. The infrequent occurrence of multiple aneurysms in the reported cases of familial aneurysm may reflect the omission of four-vessel arteriography in many of these cases.

The familial aggregation of intracranial aneurysms suggests a hereditary basis for...
some intracranial aneurysms. Awareness of this association may help in the early diagnosis and treatment of a suspected patient who has a relative with a proven aneurysm.

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References

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