Fungal Aneurysms of Intracranial Vessels

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Intracranial fungal aneurysms arise from major cerebral arteries. Fungi directly invade vessel walls from the luminal surface (fungal emboli) or from the adventitia (fungal meningitis). The vasa vasorum are free of fungi. Aneurysmal rupture is common with extensive hemorrhagic necrosis of the surrounding brain. Aspergillus is the usual causative agent; its sources are nasal sinusitis or endocarditis.

(Arch Neurol 33:577-579, 1976)

The dilation of a blood vessel produced by an infectious agent is termed a mycotic aneurysm. Osier and Eppinger introduced this term and provided early clinical and pathologic descriptions. However, in 1852, Kirks had already noted the association of ruptured aneurysms with bacterial endocarditis. Throughout the next 100 years the association of intracranial mycotic aneurysms with bacteria was the rule. Although the designation "mycotic" encompassed not only bacteria but also fungi, no such fungal intracranial aneurysm was described until 1968.

Including the present case, four such intracranial aneurysms have now been documented. In size, shape, and angiographic presentation, these vascular aneurysms closely resemble the common berry aneurysm. With the remarkable increase in fungal infection among hospitalized patients over the past 15 years, one may anticipate a corresponding increase in true mycotic intracranial aneurysms.

REPORT OF A CASE

History

A 3-week-old girl was noted to have a harsh systolic murmur. When she was 3 years old, cardiac catheterization revealed a patent ductus arteriosus, a ventricular septal defect, aortic stenosis, and possible mitral stenosis. The patient ductus arteriosus was ligated. She had increasing dyspnea during the following 12 years, and at age 15 a subvalvular aortic fibrous band was excised. Dyspnea and fatigue persisted, and at age 17 open heart surgery was again performed with removal of subaortic scar. Recovery was uneventful.

One and a half months later, she complained of poorly localized headache. Two weeks later, she awoke with incoordination and right-sided numbness. She developed a severe generalized headache and then suffered a right-sided focal motor seizure, after which she was unresponsive.

Examination

Following hospital admission, the patient gradually awoke. There was a right hemiplegia with right central facial paresthesia. The cerebrospinal fluid was grossly bloody. Three days later, bilateral carotid arteriograms (Fig 1) showed an aneurysm 7 mm in diameter arising from a branch of the right middle cerebral artery within the Sylvian fissure. A second aneurysm, 3 mm in diameter, arose from a callosomarginal branch of the right anterior cerebral artery. The clinical impression was ruptured mycotic aneurysm, and antibiotic therapy was instituted. However, on the ninth hospital day the patient became unresponsive and died. A cerebrospinal fluid culture submitted two days ante-mortem subsequently yielded Aspergillus fumigatus.

Pathologic Findings

Firmly adherent to an endothelialized suture line in the anteromedial wall of the ascending aorta was a mass of friable nodules embedded in thrombus. The mass, measuring 1 cm in diameter and 6.5 cm in length extended proximally into the non-coronary cusp of the aortic valve and distally into the arch of the aorta. Portions of suture material were embedded within the nodular areas. Microscopically, these nodules consisted of radiating hyphae with dichotomous branching and true septations. Postmortem culture of the mass yielded A fumigatus. There were recent infarcts of the spleen and both kidneys. Microscopically, fungal emboli occluded splenic and renal interlobular arteries, with formation of a fungal aneurysm in one kidney.

Fig 1—Subtraction right carotid arteriogram. Large aneurysm (white arrow) arises from middle cerebral artery. Second aneurysm (black arrow) arises from anterior cerebral artery.

Accepted for publication April 5, 1976.

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The brain weighed 1,350 g. Extensive subarachnoid hemorrhage encased the inferior surface. There was bilateral tonsillar herniation and softening of the right temporal lobe. Dissection of the circle of Willis and its immediate branches revealed a ruptured saccular aneurysm, 6 mm in length, protruding from a proximal Sylvian branch of the right middle cerebral artery. Coronal brain sections demonstrated hemorrhagic necrosis of the right frontal lobe with right temporal intraventricular hemorrhage. The cerebral hemispheres elsewhere were congested but otherwise unremarkable except for central herniation. Direct hemorrhages were present in the brain stem. The cerebellum and pituitary gland were unremarkable.

The ruptured aneurysm was embedded in paraffin. Serial sections were sequentially stained with hematoxylin-eosin, PAS, Masson trichrome, and Gomori methenamine silver. At the point of rupture (Fig 2), the vessel wall was infiltrated by dichotomously branching hyphae with true septations (Fig 3) identical to the fungi present within the aortotomy incision. The remainder of the aneurysmal sac was composed of attenuated fibrous tissue. The vasa vasorum were free of fungi.

Proximal to the rupture, minute hyphae and many giant cells were adherent to the arterial wall and locally embedded within proliferating intima. Rare hyphae extended through the intima up to small clefts in the fibrillated elastica; on occasion, a hypha penetrated the elastica to protrude into the adventitia. Here also the vasa vasorum were free of hyphae.

COMMENT

Bacteria are the most common pathogenic agent of intracranial mycotic aneurysms, and it is from the study of these bacterial aneurysms that virtually all our present knowledge of mycotic aneurysms is derived. The intracranial bacterial aneurysm is usually small (1 to 2 mm in diameter) and is located within the peripheral branches of the middle cerebral artery. In Characteristically, there are many such aneurysms within a

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**Fig 2.** Ruptured fungal aneurysm of right middle cerebral artery with extruded mass of *Aspergillus* hyphae (solid arrow) seen adjacent to point of rupture (open arrows). Remainder of aneurysmal sac extends as attenuated fibrous tissue (star) to encompass laminated thrombus (asterisk) (methenamine silver, original magnification ×35).

**Fig 3.**—Detail of hyphae illustrated in Fig 2. Note septation and branching characteristic of *Aspergillus* (methenamine silver, original magnification ×480).

### Fungal Intracranial Aneurysms

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**Table:**

- **Source:** Various studies.
- **Case/Age, yr/Sex:** Age and sex of the patient.
- **Prior Illness:** Previous medical conditions.
- **Site of Aneurysm:** Location of the aneurysm.
- **Organism:** Type of fungi identified.
- **Source of Fungus:** Method of infection.
Intracranial Fungal Aneurysms—Horton et al

The Table, which summarizes these reports, emphasizes features of the intracranial fungal aneurysm that set it apart from the bacterial variety. The fungal aneurysm arises from major cerebral arteries and is large (5 to 10 mm); the bacterial aneurysm protrudes from arterial branches and is small (1 to 2 mm). Occasionally, large bacterial aneurysms are reported, but in general most are minute. The predominant organism of the intracranial fungal aneurysm is Aspergillus. Sources include adjacent sinusitis or surgical contamination of other meninges or endocardium with subsequent fungal emboli. The most common fungi of sinusitis are Mucor and Aspergillus, and the fungus isolated in 70% of fungal endocarditis is Candida.

Despite this prevalence of Mucor and Candida, there seems to be a peculiar predisposition of Aspergillus to cause intracranial aneurysms. Although there is as yet no experimental model to establish the pathogenesis of the fungal aneurysm, the primary mechanism seems to be direct invasion of the arterial wall from an intraluminal embolus that extends its hyphae outward, or from fungal meningitis (secondary to sinusitis) that penetrates into the adventitia. The vasa vasorum play little part in this process, which therefore contrasts with Molinari's model of bacterial aneurysms.

In the past 50 years, the percentage of intracranial aneurysms attributable to bacteria has decreased. In 1916, 80% of intracranial aneurysms at London Hospital were mycotic. By 1939, McDonald and Korbi found 6% among 1,123 intracranial aneurysms, and in 1965, Roach and Drake noted 2.6% among 191 cases. By contrast, the decline of these bacterial lesions has been paralleled by the rise of opportunistic fungal infections. It was in this clinical setting that the first report of a fungal intracranial aneurysm appeared in 1968. Including the present report, four cases have now been documented.