Postoperative Fungal Arteritis Mimicking Vasospasm

—Case Report—

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Abstract

Intracranial arteritis due to fungal infection is an uncommon complication of neurosurgical operations. A 36-year-old female developed arteritis caused by *Aspergillus fumigatus* at the site of the temporary clip following the clipping of an initially uncomplicated intracranial aneurysm. The inflammatory, slowly progressing vascular occlusion mimicked the vasospasm common in subarachnoid hemorrhage.

Key words: aneurysm, *Aspergillus*, fungal infection, fungal arteritis, postoperative complication

Introduction

Intracranial *Aspergillus* infection causes not only meningitides, granulomas, and brain abscesses, but also infections of blood vessels.¹⁾ Such fungal arteritis^{3,7)} can lead to cerebral infarction due to vascular occlusion by a fungal embolus and to vessel rupture with resultant subarachnoid hemorrhage (SAH) or formation of an aneurysm.^{5,6)}

Cerebral infection with *Aspergillus* is usually secondary to a primary focus elsewhere in the body, but the infection may also be airborne, contaminating the tissues during a neurosurgical procedure.⁹⁾ Direct invasion of the arterial wall by extension of hyphae from an intraluminal embolus, or penetration of the adventitia by hyphae from an extraluminal, contiguous focus seems to be the initiating process in the development of a mycotic aneurysm or arteritis due to fungi.^{3,7)} In contrast, the development of mycotic aneurysms due to a bacterial embolus begins with embolic occlusion of the vasa vasorum, direct invasion of the arterial wall from within or from without the lumen, and finally leads to vascular injury *via* deposition of immune complexes.

We describe a patient who presented with an aneurysm causing SAH, who developed postoperative fungal arteritis mimicking vasospasm on trans-

cranial Doppler sonography (TCD).

Case Report

A 36-year-old female was admitted with the diagnosis of SAH of Hunt and Hess grade II. Two days prior to admission she had experienced sudden onset of severe headache, pain in the neck, and vomiting, which did not respond to treatment. A lumbar puncture performed in the referring hospital

Fig. 1 CT scan on admission, showing SAH in the basal cisterns and the interhemispheric fissure; clinically manifesting as Hunt and Hess grade II.

showed hemorrhagic cerebrospinal fluid but no signs of inflammation. Her past history was unremarkable.

Examination on admission found no neurological deficits. Computed tomography (CT) of the head demonstrated SAH with blood in the basal cisterns and interhemispheric fissure (Fig. 1). Selective cerebral angiography demonstrated an aneurysm of the anterior communicating artery (AComA) filling from the right side only (Fig. 2). Although TCD showed normal flow in the circle of Willis and absence of vasospasm, she received nimodipine 2 mg/hr.

As she had SAH grade II (Hunt and Hess), surgery was performed on the 3rd day after the onset. Immediately before the operation TCD was performed to check that no vasospasm was present. The aneurysm was approached *via* a right pterional route. Temporary clipping of the A_1 segments on each side was necessary because of marked arachnoid adhesions for 3 minutes to expose the aneurysm. This allowed application of the clip to the aneurysm properly. The operation lasted 130 minutes and no complication occurred. Perioperatively, treatment with a prophylactic broad-spectrum cephalosporin (cefuroxim 4.5 g/day) together with ranitidine 150 mg/day and dexamethason 16 mg/day was begun, while nimodipine 2 mg/hr treatment was continued.

After the operation she was conscious and neurologically unremarkable. On the 3rd postoperative day she became gradually somnolent. CT showed hypodense areas in the territories of the anterior cerebral arteries (ACAs) on both sides and

the middle cerebral artery (MCA) on the right, which due to the slight increase in brain volume on the right were regarded as ischemic lesions. TCD revealed an increase in blood flow velocities in the bilateral MCAs ($V_{\max}$ 129 cm/sec on the right, 89 cm/sec on the left) interpreted as vasospasm.

On the 6th postoperative day paresis of the left lower extremity and stupor developed. Serial CT showed complete infarction in the areas supplied by both ACAs. The increase in brain volume was considerable with consumed sulci and marked compression of the ventricles. In contrast to the previous TCD scan, the bilateral ACAs could not be demonstrated. The flow velocities in bilateral MCAs were still increased ($V_{\max}$ right 139 cm/sec, left 91 cm/sec). Because of the progressive course and the increase in brain volume, she was treated with moderate hyperventilation.

Her condition continued to deteriorate despite all initiated measures. On the 8th postoperative day her pupils became dilated, and body temperature fell to 35.2°C. TCD demonstrated no intracranial signal,

Fig. 2 Selective cerebral angiogram on the day of admission, showing an aneurysm of the AComA (arrow) filling from the right.

Fig. 3 *upper*: Photomicrograph of a section of the posterior communicating artery, showing the occluded lumen, and the thrombus and vessel wall infiltrated by hyphae. Grocott stain, $\times 40$. *lower*: An enlarged photomicrograph of upper figure, showing hyphae infiltrating the thrombus. Grocott stain, $\times 160$.

Fig. 4 Photomicrograph of a section of the right ACA, showing the vessel wall infiltrated by inflammatory cells, ruptured internal elastica interna lifted at the site of the temporary clipping (arrow), and the thrombosed lumen. Hematoxylin-eosin stain, $\times 40$.

while extracranially a to-and-fro movement was found in bilateral internal carotid arteries (ICAs), implying a severe disturbance of intracranial blood flow. After the 10th postoperative day electroencephalography detected no bioelectric activity, and she died of circulatory arrest on the 11th day.

Postmortem findings: Histological examination found thrombotic occlusion of the lumen in all basal cerebral arteries (both A_1 and A_2 segments of the ACAs, ICAs, M_1 parts of the MCAs, posterior cerebral arteries, posterior communicating arteries, and superior cerebellar arteries, all on both sides; the basilar artery) (Fig. 3) except the vertebral arteries, which were open on both sides. Both A_1 and A_2 segments had partially necrotic vessel walls heavily infiltrated with granulocytes and dense patches of fungal hyphae and, like the thrombi, presented a morphological appearance closely resembling *Aspergillus fumigatus*. In addition, ruptures of the elastica were present along both A_1 segments of the ACAs at the site of the temporary clipping (Fig. 4). The changes caused by fungal infection of the vessel wall were most marked in both A_1 and A_2 segments. Only slight infiltration by fungal hyphae could be found in the M_1 segments of bilateral MCAs and in bilateral ICAs. The other vessel walls of the basal arteries were free of fungal infection.

A typical saccular aneurysm was found at the AComA, which was occluded by a clip. The tear at the tip was covered by a thrombus. There was no histological evidence of the fungal origin of the aneurysm. Inflammatory infiltrates were found in several places surrounding the aneurysm.

In the infarcted territories supplied by the bilateral ACAs, massive fungal hyphae were found within the white and gray matter extending intravascularly. In addition, intravascular damage to the meningeal arteries and meningeal veins was found with local involvement of the leptomeninges.

No systemic fungal infection was found elsewhere in the body.

Discussion

Only a few of the about 300 species of the genus *Aspergillus*⁸⁾ are known to be pathogenic. The increasing use of antibiotics, corticosteroids, and immunosuppressive medications has increased the incidence of fungal infections, especially in patients with diminished resistance.⁹⁾ Intracranial fungal infections almost always occur as a result of a fungal infection of other organs.¹⁾ As the spores of the *Aspergillus fumigatus* can be found everywhere in the environment and as the possibility of a clinical nonmanifest infection or colonization of the patient (e.g. in the paranasal sinuses) with *Aspergillus fumigatus* cannot be excluded, it is also not possible to rule out an intraoperative infection with certainty in this case, although no predisposing factors were known.

The histological findings in this case suggest that the hyphae penetrated the vessel wall aggressively, which explains the rapidly developing arteritis. This impression of a fulminating necrotizing thromboarteritis is confirmed by other reports.^{10,11)} Asari *et al.*²⁾ and Komatsu *et al.*⁴⁾ showed that traumatized vessel walls following temporary occlusion are a predominant point of entry for hyphae. In our case the histological changes also point in this direction: ruptures of the elastic membrane were only seen at the site of the temporary clipping and the necrotic vessel changes were most marked there.

The vessel wall infiltration and the characteristic natural history of the fungal infection indicate an *intra vitam* genesis of the lesion, although thrombotic occlusions of basal arteries occur in brain death syndromes too. The fact that hyphae were found within the thrombi points to an *intra vitam* thrombosis. Thrombotic vessel occlusions in brain death syndromes do not contain hyphae. Whether the temporary vessel occlusion did lead to a disruption of the vessel wall in this case — making the penetration of hyphae easier — cannot be proven from the histological picture, but this seems likely.

The apparent vasospasm demonstrated by TCD may have been partly due to the changes occurring with SAH, but the histological findings of fungal

arteritis, with vessel wall infiltration and thrombotic changes, strongly suggest that this was the main cause of the TCD findings.

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