Intracranial Mycotic Aneurysm Caused by Aspergillus

—Case Report—

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Abstract

A 75-year-old female with chronic renal failure diagnosed as Wegener's granulomatosis was receiving steroids and immunosuppressive agents when subarachnoid hemorrhage developed. Cerebral angiography showed a fusiform aneurysm arising from an angular branch of the left middle cerebral artery. Hemorrhage occurred and the aneurysm was excised by emergency surgery. Microscopic examination of the aneurysm revealed dense infiltration of hyphae identified as Aspergillus. She died of subsequent hemorrhage. Autopsy showed numerous Aspergillus hyphae in the lung. Fungal mycotic aneurysm should be considered in the differential diagnosis of an immunocompromised patient with subarachnoid hemorrhage.

Key words: fungal aneurysm, mycotic aneurysm, Aspergillus infection, subarachnoid hemorrhage

Introduction

Any aneurysm caused by an infectious agent is termed a mycotic aneurysm.13) Most cerebral mycotic aneurysms are bacterial and secondary to endocarditis.3) Fungal aneurysms are very rare, with only about 30 reported cases. Antibiotic therapy has reduced the incidence of bacterial cerebral aneurysm. By contrast, opportunistic fungal infections have become more common with the widespread use of immunosuppressive agents and steroids. We report a case of fungal aneurysm caused by Aspergillus and review reports of intracranial fungal aneurysms.

Case Report

A 75-year-old female was admitted with high fever, pyuria, and azotemia on October 17, 1989. The clinical features and a renal biopsy suggested renal failure due to Wegener's granulomatosis. She received oral prednisolone (60 mg/day) and cyclophosphamide (50 mg/day) and dialysis therapy beginning on November 23, 1989. Thereafter, her general condition improved.

On December 22, 1989, she complained of a severe headache shortly after the dialysis procedure, and became unresponsive. On admission to the Department of Neurosurgery, she was semicomatose with equal and reactive pupils and right hemiparesis. Hematological and biochemical studies were normal except for azotemia (serum blood urea nitrogen 51.1 mg/dl, creatinine 2.9 mg/dl). There was no hemorrhagic tendency.

Computed tomographic (CT) scans revealed subarachnoid hemorrhage predominantly within the left Sylvian fissure (Fig. 1). Cerebral angiograms showed a fusiform aneurysm arising from an angular branch of the left middle cerebral artery, accompanied by extravasation of contrast medium. The Sylvian triangle was markedly elevated (Fig. 2). Unfortunately, rebleeding occurred during angiography.
Emergency craniotomy exposed a large intracranial hematoma and an aneurysm with a yellowish dome protruding from the left Sylvian fissure. The aneurysm adhered to the thickened dura, which was covered with purulent exudation. The aneurysm and dura were excised, and the feeding vessel clipped. The intracranial hematoma was removed.

Postoperatively, she remained stuporous. On December 28, 1989, 6 days after surgery, she suddenly became comatose during dialysis. Her pupils were dilated and fixed. CT scans showed massive hemorrhage in the left temporal lobe. Hemorrhagic tendency or hemorrhagic cerebral infarction was suspected. She died on December 29, 1989, 7 days after the operation.

At autopsy, the brain appeared edematous with extensive subarachnoid hemorrhage around the left Sylvian fissure. Tonsillar herniation and hemorrhagic infarction of the left temporal lobe were present. Microscopic examination of the aneurysm revealed extensive destruction of the arterial wall with dense infiltration of neutrophils throughout the aneurysm wall, forming a micro-abscess. Many branching fungal hyphae had penetrated the elastica into the adventitia. The hyphae were approximately 4 µm in diameter, septate, and exhibited acute-angle branching with spore formation. The hyphae were stained with HE and periodic acid-Schiff agents (Fig. 3). These features are characteristic of Aspergillus. No fungal culture was obtained. Sections through other arteries found neither inflammatory infiltration nor thrombi. The leptomeninges surrounding the aneurysm showed severe inflammatory reaction and fungal infiltration.

The lungs demonstrated focally cavitating bronchopneumonia containing numerous hyphae identified as Aspergillus. Other findings included rapidly progressive glomerulonephritis and pyelonephritis. The endocardium and valves were entirely normal. There was no evidence of Wegener's granulomatosis.

Discussion

Most cerebral mycotic aneurysms are secondary to bacterial endocarditis. Antibiotics have reduced the proportion of bacterial aneurysms from 30% of all intracranial aneurysms in 1916 to 2.6% in 1965. The steady increase in opportunistic fungal infections is attributed to the use of immunosuppressive agents, steroids, and broad-spectrum antibiotics. Ap-
Approximately 30 cases of fungal intracranial aneurysm have been reported.\textsuperscript{1,4-11,14,16,17} Table 1 shows the difference between bacterial and fungal aneurysms.

Intracranial bacterial aneurysms are usually small (1-2 mm in diameter) and located within the peripheral branches of the middle cerebral artery, and develop following endocarditis. Characteristically, there are multiple aneurysms within a single arterial distribution. The adjacent cerebral cortex is usually free of infarct or hemorrhagic necrosis.\textsuperscript{6,15} The most common agents are Streptococcus viridans and Staphylococcus aureus.\textsuperscript{3,6} Several pathogenetic mechanisms have been proposed for bacterial aneurysms: embolic occlusion of the vasa vasorum, direct invasion of the arterial wall from the lumen (emboli) or externally (meningitis), and vascular injury caused by deposition of immune complexes.\textsuperscript{6°12}

Fungal aneurysms are large (5-15 mm in diameter), usually single, and arise from major cerebral arteries. Aneurysmal rupture is common. The prognosis is extremely poor.\textsuperscript{5,9,11} This condition is characterized by fungal invasion of blood vessels, associated with contiguous, widespread vascular thrombosis, resulting in ischemic necrosis of various organs and tissues.\textsuperscript{5,9,11} The most common agents are Aspergillus followed by Phycomycetes and Candida albicans.\textsuperscript{5,7,9} Sources include paranasal sinusitis, surgical contamination, and disseminated fungal infection.\textsuperscript{4,9} The most common fungi associated with sinusitis are Phycomycetes and Candida. Seventy percent of endocarditis cases also involved Candida. However, Aspergillus has a peculiar predisposition for causing intracranial aneurysms.\textsuperscript{6,7} No experimental model has established the pathogenesis of fungal aneurysms. Possibly, the mechanism is direct vascular invasion, either from fungal emboli in the vessel lumen or through the adventitia from fungal meningitis, resulting in focal necrosis of the elastica.\textsuperscript{1,4,6,7}

The most common manifestation of cerebral aspergillosis is abscess.\textsuperscript{17} Meningeal infection, when present, is usually focal and adjacent to the primary lesion.\textsuperscript{17} Aspergillus definitely tends to invade blood vessels.\textsuperscript{5,16,17} Aspergillotic vasculitis commonly results in brain abscess or infarction, depending on the immune status of the host and virulence of the infection. Occasionally, immediate vessel rupture or aneurysm formation occurs.\textsuperscript{7,16}

Few early warning signs or symptoms indicate fungal aneurysm prior to hemorrhage.\textsuperscript{1,7} Meningitis may be present, but the exact cause of the aneurysm is difficult to identify from spinal fluid or blood culture.\textsuperscript{11} The diagnosis of fungal intracranial aneurysm is usually established by histological examination of surgical and autopsy specimens. In our case, her general condition was stable without signs of infection or neurological abnormalities prior to bleeding, so corticosteroid and immunosuppressive agents were administered. No primary focus of infection was found preoperatively. The absence of meningitis and the peripheral location of the aneurysm suggest that the aneurysm might be of bacterial origin. The emergency operation prevented speculation on the pathogenesis.

Recently, Komatsu et al.\textsuperscript{10} demonstrated two developmental processes of fungal aneurysms. Aneurysms secondary to fungal meningitis are usually large and located in the major arterial trunks, while aneurysms subsequent to fungal sepsis tend to be small and in peripheral branches. In this case, disseminated fungal infection and fungal emboli probably caused the aneurysm formation, as suggested by several fungal balls in the lung at autopsy.

Early fungal aneurysm diagnosis indicates antifungal agents administered intravenously or intrathecally and surgical intervention to prevent aneurysmal rupture. Surgery is indicated if the aneurysm has bled, or enlarged on serial angiograms.\textsuperscript{5,11,18} However, no case of ruptured fungal aneurysm, including our case, has been successfully treated.

Fungal aneurysms are rare, but the increasing frequency of opportunistic infections means that fungal mycotic aneurysm should be considered in the differential diagnosis of an immunocompromised patient with subarachnoid hemorrhage.

Table 1 Comparison of fungal and bacterial mycotic aneurysms

<table>
<thead>
<tr>
<th>Type</th>
<th>Organism</th>
<th>Predisposing disease</th>
<th>Location</th>
<th>Size</th>
<th>Number</th>
<th>Rupture</th>
<th>Associated thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fungal</td>
<td>Aspergillus, Phycomycetes, Candida albicans</td>
<td>immunocompromised host, steroid therapy, sinusitis, diabetes mellitus</td>
<td>major intracranial arteries</td>
<td>5-15 mm</td>
<td>single</td>
<td>common</td>
<td>common</td>
</tr>
<tr>
<td>Bacterial</td>
<td>Streptococcus viridans, Staphylococcus aureus</td>
<td>bacterial endocarditis</td>
<td>peripheral branches of MCA</td>
<td>1-2 mm</td>
<td>multiple</td>
<td>less common</td>
<td>less common</td>
</tr>
</tbody>
</table>

MCA: middle cerebral artery.
References


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