Multiple intracranial aneurysms due to \textit{Coccidioides immitis} infection

Case report

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True mycotic (fungal) aneurysms are distinctly uncommon. The case of a young woman with multiple intracranial aneurysms of \textit{Coccidioides immitis} origin is presented. \textit{Coccidioides immitis} organisms are not uncommon central nervous system pathogens and usually cause basilar meningitis and hydrocephalus. There are no previous reports of a coccidioidal mycotic aneurysm. The management of intracranial coccidioidomycosis and fungal aneurysms is reviewed.

\textbf{KEY WORDS} • \textit{Coccidioides immitis} • mycotic aneurysm • fungal aneurysm • coccidioidomycosis

The dimorphic mycotic organism \textit{Coccidioides immitis} is endemic in the southwestern United States and Central and South America and is a common human pathogen in those regions.\textsuperscript{4} It is estimated that there are 100,000 infections due to this organism annually, most of which are mild and localized to the respiratory system. Approximately 1\% of patients with a \textit{C. immitis} infection will not develop lasting immunity to the organism and will develop systemic disease. One-third of these patients will become symptomatic from central nervous system (CNS) dissemination.\textsuperscript{3,5,8} This usually manifests as basilar meningitis, a common complication of which is obstructive hydrocephalus. Coccidioidomycosis of the CNS rarely results in abscess formation and even less frequently in cerebral vasculitis.\textsuperscript{1,4,17} In this report, the case of a young woman with severe basilar meningitis from coccidioidomycosis is reviewed. She presented with subarachnoid hemorrhage (SAH), and angiography revealed multiple intracranial aneurysms. This is the first known report of mycotic cerebral aneurysms of \textit{C. immitis} origin.

\textbf{Case Report}

This 20-year-old woman was evaluated in the emergency department after her parents found her unconscious. Over the previous 6 months, she had been treated sporadically with intravenous amphotericin B for \textit{Coccidioides immitis} meningitis. She had repeatedly rejected a recommendation for cisterna magna amphotericin B injections. Her medical history was significant for asthma since childhood with repeated bouts of pneumonia. She had moved to Arizona from North Dakota 4 years prior to admission.

\textbf{Examination.} The patient was intubated, breathing spontaneously, and had stable vital signs. She was unresponsive to all but painful stimuli and had a Glasgow Coma Scale score of 6. Pupils were equal and reactive; there were no cranial nerve deficits. She would not open her eyes in response to pain and demonstrated purposeful flexion of her right upper extremity; however, she exhibited extensor posturing of the other three extremities. A chest x-ray film revealed a spherical cavity lesion in the right apex, and a computerized tomography (CT) scan of the head demonstrated SAH and hydrocephalus.

A ventriculostomy was placed in the right lateral ventricle, and cerebral angiography was performed. These studies demonstrated two intracranial aneurysms, one arising from the left internal carotid artery (ICA) and the other from the distal basilar artery. Intravenous amphotericin B therapy was initiated on
the day of admission, and the next day the patient was taken to the operating room for clipping of the ruptured left ICA aneurysm.

Operation. The aneurysm was approached via a left pterional craniotomy. The arachnoid of the sylvian fissure was opened, the left frontal lobe elevated, and the ICA identified. The carotid artery was distinctly abnormal in appearance and was covered with a whitish granulomatous exudate. After meticulous dissection through this meningitic exudate, the proximal segments of the anterior and middle cerebral arteries were identified. The ruptured aneurysm was located at the posteriorinferior portion of the carotid artery bifurcation. A 7-mm curved Yasargil clip was placed across the neck of the aneurysm. Care was taken to preserve the anterior choroidal and posterior communicating arteries. There was no evidence of residual aneurysm and no other aneurysm was identified. A portion of the aneurysm wall was excised and submitted to the pathology department for analysis. Coccidioides immitis organisms were identified in the fibrous aneurysm dome. The craniotomy was closed in routine fashion and the patient was returned to the neurosurgical intensive care unit.

Postoperative Course. The patient's neurological examination was only modestly improved after surgery. She would flex both upper extremities in response to painful stimuli and did not exhibit spontaneous extensor posturing. Her intracranial pressure remained high and required continuous cerebrospinal fluid (CSF) drainage. A follow-up CT scan obtained 4 days postoperatively revealed the craniotomy site and aneurysm clip, but no new pathology. A xenon-133 CT blood flow study was performed and demonstrated reduced cerebral perfusion in the frontal lobes and temporoparietal regions bilaterally. Follow-up angiography 7 days following surgery revealed that the initial ICA aneurysm was excluded from the cerebral circulation. A second lobulated aneurysm of the left ICA was visualized, located posteroinferiorly with respect to the treated aneurysm. There was evidence of marked vasospasm. The basilar artery aneurysm was unchanged.

The patient gradually improved neurologically. Two weeks following surgery she would open her eyes in response to painful stimuli and localize with both upper extremities, the left more readily than the right. She required only intermittent CSF drainage and was treated with intravenous and intraventricular amphotericin B. On the 19th postoperative day she experienced a second, massive intracranial hemorrhage. A CT scan revealed severe intraventricular hemorrhage and marked ventricular dilatation. Neurologically, she was devastated; she had uncontrolled intracranial hypertension, the brain herniated, and she died 30 hours after the ictus.

Postmortem Examination. The lungs had multiple sites of coccidoidal granulomas with scarring. In the apex of the right lung there was a 3-cm cavity lesion containing hemorrhage and necrotic material which included numerous coccidoidal organisms. The thyroid gland and spleen were almost totally replaced by widespread coccidoidal granulomas. Foci of coccidoidal lesions were noted in the portal triads of the liver, both adrenal glands, and the mediastinal and periaortic lymph nodes.

The base of the brain, pons, and medulla were coated with a thick granulomatous basilar meningitis. Subarachnoid and intraventricular blood was evident and there was acute tonsillar and medial temporal lobe herniation. A distinct and separate aneurysm was found arising from the left ICA. The treated left ICA aneurysm was well clipped, and aneurysmal dilatation of the tip of the basilar artery was identified.

Histological sections of the ICA revealed invasion of the vessel wall by the Coccidioides immitis organisms. This was localized primarily to the vascular adventitia but was also present in the media at the neck of the aneurysm (Fig. 1 left), and was associated with fibrous replacement of the muscularis and disruption of the internal elastic membrane (Fig. 1 right). The sections through the aneurysms revealed them to be truly of mycotic origin. Microscopic aneurysms of the tiny vessels in the subarachnoid space were also encountered. Sections of the left temporal lobe revealed acute hemorrhage and infarction from aneurysm rupture. Multiple microscopic foci of coccidoidal cerebritis were discovered. Also noted was evidence of a coincident acute meningitis due to Candida albicans. This organism was present in fewer numbers than the Coccidioides immitis organism and, despite the presence of a few subarachnoidal microabscesses, was not found to be invading the blood vessel walls.

Discussion

Coccidioides immitis is a natural inhabitant in the soil of the semiarid regions of the United States and portions of Central and South America. It is endemic in California, Arizona, Nevada, Utah, New Mexico, and Texas.3,4,8,12,19 The organism is dimorphic but is contagious to humans in only the second of its two forms. The parasitic form is a spherule with a double refractile wall. Each spherule contains multiple endospores which may be liberated into the host tissue to form new spherules, advancing the disease process. The saprophytic form is free in the soil as an arthrospore and is highly infectious to man. The arthrospore is inhaled into the respiratory tree and results in a localized inflammation in the lung. In most patients lasting immunity to the organism results.3,10,12 Less than 1% of patients will develop systemic disseminated coccidoidal disease. Between one-half and one-third of these patients will develop CNS involvement.4,8,10,12,17 Bouza, et al.3 reviewed 114 cases of coccidoidal meningitis and described the common clinical manifestations, methods of diagnosis, treatment, and prognosis in infected patients.

It is distinctly uncommon for Coccidioides immitis
Multiple mycotic intracranial aneurysms

FIG. 1. Left: Photomicrograph showing coccidioidal organisms (spherules) in the media of the left internal carotid artery. The small black cells are lymphocytes. H & E, × 240. Right: Photomicrograph showing aneurysmal dilatation of the left internal carotid artery. Note the disruption of the internal elastic membrane (arrows) and marked fibrous replacement of the media. Elastica van Gieson, × 9.

to form a cerebral abscess. Moore demonstrated that the granulomatous arachnoiditis of coccidioidal meningitis can rarely penetrate adjacent brain parenchyma along vessels and produce focal abscesses. Vasculitis of the proximal cerebral vessels has been reported in conjunction with coccidioidal meningitis, and the typical patterns of arteritis with vessel irregularities, narrowing, and occlusion have been documented. Microscopic analysis of the vessel walls has revealed subintimal edema, lymphocytic and plasma-cytic infiltration, and periadventitial inflammation. Cerebral infarction has occasionally been an associated finding on CT scans or at autopsy. Vasculitis is probably present more frequently than is reported among patients with coccidioidal meningitis. Few patients with the diagnosis of basilar meningitis of coccidioid origin undergo angiography unless neurological deficits are present that are unexplained by meningitis and/or obstructive hydrocephalus. We know of no case of disseminated coccidioidomycosis reported in the literature that presented with SAH, nor has there been a prior report of a C. immitis mycotic aneurysm.

Kikuchi, et al., recently reviewed the literature and found 17 true mycotic (fungal) aneurysms. The most common causative agents identified were Aspergillus species followed by Phycomycetes species and Candida albicans. The associated acute candidal meningitis in the present case raised the suspicion that the aneurysms identified may not have been of coccidioid origin but due to C. albicans; however, histological analysis of the vessel and aneurysm walls confirmed invasion exclusively by Coccidioides immitis organisms. Fungal aneurysms occur more proximally on the intracranial vessels than bacterial aneurysms and more frequently involve the large arteries at the base of the brain. Eleven (61%) of the 18 cases of mycotic aneurysms reported thus far (including the present case) involved the ICA or the basilar artery. In contrast, only 29% of bacterial aneurysms reported by Bohmfalk, et al., involved the proximal intracranial vessels (including a cavernous sinus location). The majority of aneurysms of bacterial origin involve the more peripheral cerebral vasculature, notably the middle cerebral artery beyond its bifurcation.

Mycotic aneurysms are known to occur in immunocompromised patients, particularly in those with prolonged steroid use and in patients with diabetic ketoacidosis. However, most patients who develop disseminated cocci are healthy prior to the infection and are apparently normal hosts. Hart, et al., estimated that only 2% of patients with disseminated coccidioidomycosis have significant underlying disease. Other authors have suggested that the reduction of immunocompetence in patients with disseminated cocci is somewhat higher. All investigators agree that immunocompromised patients who develop coccidioidomycosis have a more rapid, progressive course and a worse overall prognosis. The patient described in this report had normal delayed hypersensitivity responses to cocci and normal lymphocyte numbers and function based on several mitogen studies (phytohemagglutinin P, pokeweed mitogen, and concanavalin A). The severity of her basilar meningitis and vasculitis was probably due to the prolonged course with inconsistent intravenous treatment and the lack of appropriate intracisternal antifungal therapy.

The treatment of true mycotic aneurysms is both medical and surgical. Appropriate antifungal agents (for Coccidioides immitis: amphotericin B) must be administered intravenously and into the basilar cisterns at the base of the brain. Cisterna magna injections are most efficacious, and the use of external or Ommaya reservoirs attached to a catheter to the cisterna magna has proven beneficial. Amphotericin B injected into
the lateral ventricles is minimally beneficial. Coccidioidomycosis rarely causes ventriculitis; the severe basilar meningitis often obstructs the fourth ventricular outflow tracts, precluding CSF flow into the basilar cisterns. Discrete intracranial mycotic aneurysms warrant surgical treatment if they have bled, if they represent a significant mass, or if they become larger or remain the same size on serial angiographic studies in the stable patient receiving optimal medical therapy.

In summary, vascular disease involving the proximal intracranial blood vessels is probably more common than is reported among patients with disseminated coccidioidomycosis and basilar meningitis. Severe arteritis can occur in these vessels and may lead to mycotic aneurysms of coccidioidal origin. Optimal treatment of these patients includes early diagnosis and intravenous and intracisternal amphotericin B administration. Microvascular surgery can be used to effectively treat the mycotic aneurysms.

References


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