Aspergillus aortitis in an immunocompetent patient presenting with acute endophthalmitis

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Abstract

*Aspergillus* is a common environmental mold most often recognized as an infectious agent in patients with severe immune compromise. We present a case of an immunocompetent patient presenting with endogenous endophthalmitis in the absence of other infectious symptoms. The search for a systemic source revealed an ascending aortic pseudoaneurysm. Surgical resection and pathology revealed angioinvasive *aspergillus* aortitis. Recent cardiac surgery has been noted to be a risk factor for angioinvasive aspergillosis. Diagnosis is difficult as symptoms are mild and laboratory studies are often normal. To our knowledge this is the first case of *aspergillus* aortitis presenting as endogenous endophthalmitis without systemic signs of inflammation. These patients have a high mortality rate therefore early recognition is essential. It is important to consider angioinvasive *aspergillus* infections in patients with prior cardiac surgery presenting with occult embolic phenomena. Only with early diagnosis and prompt treatment can we improve outcomes of this disease process.

Introduction

*Aspergillus* is a relatively common mold, widely distributed throughout most environments.1 Multiple species can cause disease and invasive infection occurs almost exclusively in the setting of immune compromise.1 However, post-operative aspergillosis occurs more commonly in immunocompetent patients. Post-cardiac surgery *aspergillus* aortitis was first described in 1960.2 This infectious complication often presents with minimal symptoms and carries an extraordinarily high mortality.3 We present a case of angioinvasive *aspergillus* aortitis in an otherwise healthy woman who presented with acute endogenous endophthalmitis. Her only notable risk factor for invasive aspergillosis was recent cardiac surgery three months prior. Increased awareness of this rare post-surgical complication is essential to improve diagnosis of this highly fatal infectious process.

Case Report

A 76-year old woman with a bioprosthetic aortic valve replacement three months prior and well-controlled diabetes was referred to the ED by her optometrist with one day of right eye pain and decreased visual acuity. She denied having fevers, night sweats, dyspnea or chest discomfort, and did not report a history of chemical exposure or trauma to the eye. On exam, she was afebrile, HR 60 and BP 120/59. Her right eye had diffuse conjunctival injection, corneal opacification and a dense vitreous with loss of red reflex. Visual acuity in the right eye was intact only to hand waving. Extraocular movements were full and there was no periorbital erythema or swelling. LeB eye exam was normal with clear conjunctiva and 20/20 visual acuity. Ophthalmology evaluated the patient emergently and vitreous aspiration was performed. Empiric intravitreal vancomycin and ceftazidime were administered for a diagnosis of acute endophthalmitis. The patient was admitted due to concern for a systemic source of infection. Her cardiac exam was benign, without murmurs or pathologic heart sounds. Lungs were clear. There were no stigmata of endocarditis. Initial labs showed no leukocytosis and normal kidney function. An EKG was unchanged from prior. Gram stain from the vitreous aspiration was negative and cultures had no immediate growth. Blood cultures were also negative. A TTE revealed thickening of the posterior aspect of the aortic root but was otherwise unremarkable.

Further evaluation with CT angiography (CTA) of the chest was performed and revealed a 3.4x2.25 cm pseudoaneurysm of the ascending aorta with extensive thrombus extending to the mid-descending thoracic aorta (Figures 1 and 2).

The patient was taken for emergent surgery, which revealed disruption of the aortotomy suture line with a large thrombus both outside and within the aorta. The aortic valve was unaffected and there was no evidence of suppurative infection, therefore a Dacron patch was used to close the opening. Three days post-op, pathology of the aorta demonstrated invasive mycoses on Grocott’s methenamine silver stain (Figure 3). Subsequent *in situ* hybridization confirmed the diagnosis of *Aspergillus fumigatus*. Serum galactomannan enzyme immunoassay (EIA) was positive with an index of 0.55 (positive index >0.5).

Systemic and intravitreal Amphotericin-B was administered, and intravenous therapy was continued with voriconazole 350mg twice a day (voriconazole trough level 3.40 mg/L). Two weeks later, repeat CT imaging was concerning for a new peri-aortic abscess, however the patient did not wish to pursue further surgical intervention. She was maintained on systemic oral voriconazole with plans for surveillance imaging. At three months post-op, a CTA of the chest revealed a recurrent aortic pseudoaneurysm and serum galactomannan EIA had increased from an index of 0.55 to 1.40. Additional surgery with full aortic root replacement was performed. The patient tolerated the procedure well, however, her post-operative course was then complicated by an acute myocardial infarction and ventilator-associated pneumonia. After a prolonged, complicated hospital course, her family chose to focus on her comfort and she died the next day.

Discussion

Angioinvasive aspergillosis is usually seen in transplant patients or those receiving chemotherapy. However, there have been several case reports of *aspergillus* aortitis in immunocompetent patients after cardiac surgery.1-4 The mechanism of this infection is unclear but it is hypothesized that the exposure likely occurs intra-operatively, potentially through contaminated
ventilation systems. One case series documented an outbreak of five cases of *Aspergillus* aortitis in post-cardiac surgery patients in 1987. Epidemiologic evaluation revealed high concentrations of *Aspergillus fumigatus* in the ventilation system and on the surgical suite floor. The source was presumed to be due to nearby construction on the intensive care unit which shared ventilatory systems with the operating room. In our case, the initial surgery was done at a private hospital not affiliated with our university, therefore the results of any follow-up epidemiological evaluation for a potential environmental source are not known.

Notably, due to increases in the number of cardiac surgeries, the prevalence of this complication is also increasing. The largest case series to date evaluated 188 cases of post-cardiac surgery aspergillosis and identified the highest proportion occurring after aortic valve surgery. In this review, the most common presentation was fever of unknown origin or late embolic events. The above case is unique as the presenting symptom was acute endophthalmitis from an aortic embolization in the absence of any systemic infectious symptoms. Review of literature identified one prior case study where endophthalmitis heralded an underlying *Aspergillus* aortitis, however this patient also had significant signs of systemic inflammation. The most common time to presentation was approximately three months post-surgery, similar to our case, however there are case reports of patients presenting up to five years post-cardiac surgery. *Aspergillus* aortitis is almost universally fatal, with a reported mortality rate ranging from 93-100%.

The indolent nature of this disease contributes to its under-recognition, and often delayed treatment. In the aforementioned studies, ante-mortem diagnosis was made less than 50% of the time. Laboratory findings are often normal and only 6% of blood cultures are positive. Clinicians must have a high index of suspicion in order to facilitate timely diagnosis and immediate treatment. Trans-esophageal echocardiography (TEE) is an important imaging modality in diagnosing the pseudoaneurysm and provides better visualization of the aortic root than trans-thoracic echocardiography. However, multiple case reports identified no pertinent findings on TEE. In our case, recognition of the pseudoaneurysm occurred only after CT angiography of the chest, highlighting why CT angiography is considered the gold standard for diagnosis.

The role of serum biomarkers, such as the galactomannan EIA, in the diagnosis of invasive aspergillosis has been extensively

**Figure 1. CTA chest demonstrating a pseudoaneurysm of the ascending aorta (arrow) with intravascular thrombus formation.**

**Figure 2. CTA Chest with 3-D reconstruction re-demonstrating a 3.4x2.25 cm pseudoaneurysm of the proximal ascending aorta.**
studied in immunosuppressed populations. The test sensitivity is known to vary based on patient characteristics such as the presence of disseminated disease or the use of anti-fungal prophylaxis. However, due to the low prevalence of angioinvasive aspergillosis in immunocompetent patients, the efficacy of galactomannan testing in this setting has yet to be well defined. It is interesting to note that our patient had a positive serum galactomannan EIA (index 0.55). Notably, testing was sent after the surgical pathology demonstrated invasive aspergillus. No prior case reports of aspergillus aortitis reported a serum galactomannan level and it is unclear if this could provide diagnostic utility. Prior studies have shown that serum galactomannan EIA has a decreased sensitivity in the setting of a low pre-test probability. However, the sensitivity may be increased in the setting of aspergillus aortitis due to direct infection of the aorta. This could increase direct shedding of galactomannan into systemic circulation, thereby increasing serum concentrations. Due to the paucity of diagnostic tests available for invasive aspergillosis, further evaluation of this serum test merits consideration. We suggest having a low threshold to check a serum galactomannan EIA in post-cardiac surgery patients presenting with embolic phenomena or occult signs of infection to aid in the initial evaluation of aspergillus aortitis. Early diagnosis is essential as a positive test result could dramatically alter both medical and surgical management. In our patient, had the diagnosis of aspergillus aortitis been considered prior to the initial surgery, it is likely that she would have undergone more extensive aortic root replacement rather than an initial pseudoaneurysm repair. Increased awareness of this infectious complication in post-cardiac surgery patients is essential to improve diagnosis and treatment outcomes.

Conclusions

This case highlights the challenges of diagnosing angioinvasive aspergillus infections. Aspergillus aortitis is a rare complication of cardiac surgery but its prevalence is increasing. Infectious symptoms and laboratory studies provide limited diagnostic value and a high index of suspicion is required for timely diagnosis. Further evaluation of serum biomarkers such as galactomannan, could prove to have clinical utility. Most importantly, when the diagnosis is suspected, collaboration between a multidisciplinary team of physicians including infectious disease and cardiothoracic surgery is essential to determine the ideal management with both systemic anti-fungal therapy and definitive surgical correction. Only with improved recognition, prompt treatment and long-term follow-up will we be able to improve outcomes of this rare but fatal disease process.

Figure 3. Grocott’s methenamine silver stain of the ascending aorta displaying the branching hyphae of Aspergillus fumigatus.

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