Successful Treatment of Post-Mitral Valve Annuloplasty Aspergillus flavus Endocarditis

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Aspergillus flavus endocarditis is associated with a very high mortality. Of approximately 67 cases reported in the English language literature, there have been only two known survivors. This report describes a patient with Aspergillus flavus endocarditis after mitral valve annuloplasty who recovered with combined surgical and antifungal therapy. This is the first successfully treated case due to A. flavus and the first involving an annuloplasty ring.

Untreated fungal endocarditis is fatal, and even with surgery and antifungal treatment, the mortality is high [1-3]. In a large review of postoperative fungal endocarditis from 1976, 43 of a total of 170 cases reported were due to Aspergillus species [2]. Of these 43 cases, there were only two survivors. One of the survivors was treated with valve replacement alone and had a follow-up of approximately one year. The other patient was treated with surgery, amphotericin B, and flucytosine [4,5]. This patient did well for approximately three years after treatment, but died of congestive heart failure due to valve dysfunction. No vegetations were described at the time of autopsy.

We describe a patient successfully treated for post-mitral valve annuloplasty Aspergillus flavus endocarditis. This patient is doing well more than one year after treatment.

CASE REPORT

The patient was a 54-year-old white woman with a 20-year history of an asymptomatic heart murmur who was in her usual state of health until the summer of 1982. At that time, symptoms of progressive left ventricular failure developed, characterized by shortness of breath, orthopnea, decreased exercise tolerance, and a nonproductive cough. She was hospitalized in August 1982 for her complaints. Results of physical examination at that time were significant for a systolic murmur of mitral insufficiency. Left ventricular function was evaluated noninvasively during that hospitalization with multiple gated acquisition and disclosed normal left ventricular wall motion with a resting left ventricular ejection fraction of 87 percent, increasing to 70 percent following exercise. Cardiac catheterization demonstrated severe mitral valve prolapse and mitral regurgitation. Pulmonary capillary wedge pressure was normal. Results of coronary angiography were also normal.

The patient was discharged in stable physical condition, and was readmitted in September 1982 for repair of her mitral valve prolapse. Her past medical history was unremarkable; there was no history of rheumatic fever. On September 23, 1982, she underwent mitral valve repair. At the time of surgery, the mitral valve was redundant and thickened, with hooding and annular dilatation typifying the myxomatous valve. A large cord to the center of the posterior leaflet was completely ruptured, causing the middle third of the posterior leaflet to be completely flail. No calcifications were palpated, and no vegetations were seen. The segment of posterior leaflet...
was resected and the leaflet repaired primarily. The repair was completed by insertion of a 32 mm Carpentier-Edwards annuloplasty ring. On the seventh postoperative day, cardiac catheterization was performed, demonstrating no angiographic or hemodynamic evidence of mitral regurgitation or mitral valve prolapse. She remained asymptomatic until approximately the fifth postoperative week.

At that time, low-grade fevers developed followed by acute low back pain, paresthesias, and weakness in both lower extremities. She was rehospitalized, and physical examination revealed cool lower extremities with absent peripheral pulses. Emergent angiography was performed, documenting occlusion of both common iliac arteries. The patient underwent embolectomy without complication. The removed clot revealed heavy infiltration with mycotic elements consistent with Aspergillus (Figure 1). Results of the patient's cardiac examination were unremarkable at this time. Additionally, echocardiography failed to demonstrate any thrombus formation or valvular abnormalities. Blood cultures for aerobes, anaerobes, and fungi showed no growth. Urgent surgical exploration of the mitral valve for presumed Aspergillus endocarditis was performed. The native valve was grossly involved with vegetations (Figure 2), and on subsequent culture, grew A. flavus. The Carpentier-Edwards ring and remaining native mitral valve were excised and replaced with a 31 mm St. Jude mitral valve prosthesis.

The native valve annulus, the St. Jude prosthesis, and all sutures used were soaked in amphotericin B. Her postoperative hemodynamic values were excellent. Amphotericin B (20 to 30 mg per day) and flucytosine (initially 8.0 g per day in four divided doses) were initiated preoperatively and continued after surgery. Her postoperative course was complicated by rupture of a mycotic aneurysm of the right hypogastric artery on November 13, 1982, manifested clinically by an acute condition within the abdomen, shock (systolic blood pressure of 45 mm Hg), and a precipitous drop in hematocrit. Exploratory laparotomy was performed, and ligation of the ruptured hypogastric artery was achieved. Culture material from the operative site subsequently grew A. flavus. The remainder of this patient's hospital course was complicated by a respiratory arrest and aspiration pneumonia necessitating prolonged mechanical ventilatory support, development of idiopathic transudative ascites, progressive renal failure requiring temporary peritoneal dialysis, recurrent urinary tract infections, and per-
sistent leukocytosis (40,000 to 50,000/mm³) and fevers. Right hydronephrosis developed secondary to ureteral stenosis, and she eventually underwent right nephrectomy.

The renal failure was believed to be multifactorial (nephrotoxic medications, i.e., amphotericin B, aminoglycosides; acute tubular necrosis secondary to hypotension, sepsis, and hypoxemia). On February 5, 1983, after she received 2.5 g, amphotericin B was discontinued. The patient was discharged home in stable physical condition on April 1, 1983. She has done well since discharge and had no evidence of recurrence at a follow-up visit in March 1984.

COMMENTS

Fungal endocarditis, once thought uncommon, has been increasingly recognized as a complication of open heart surgery [1,2,6-14]. It is estimated that 13 to 20 percent of all cases of endocarditis following open heart surgery are due to fungi, and of these cases, 75 percent are due to Candida species and 20 percent are due to Aspergillus species [15]. Newman and Cordell [16] described the first case of post-cardiac surgery fungal endocarditis due to Aspergillus species in 1964.

In a review of cases of fungal endocarditis from 1975 [1], of 82 patients with Aspergillus or Candida endocarditis following cardiovascular surgery, Aspergillus species were responsible for 33 cases. The diagnosis was difficult especially in patients with Aspergillus endocarditis, as blood cultures almost always showed no growth. The most characteristic clinical feature was embolization to a major vessel, and antemortem diagnosis was usually made by embolectomy or exploratory cardiotomy. Of the 33 patients with Aspergillus endocarditis, eight were treated and only two survived. These are the same two patients described in the introduction of this case report.

In a more recent article, mycotic embolization to peripheral vessels was reviewed [17]. Of 44 cases analyzed, 20 were due to Aspergillus and only one survivor was reported. This patient is the second patient just described.

Our patient was typical in that she presented with major arterial emboli (both common iliac arteries). Even though she had unremarkable results of cardiac examination, the patient was taken promptly to surgery where the mitral valve was found to be grossly involved with vegetations. The valve was replaced, and amphotericin B and flucytosine, which had been initiated preoperatively, were continued postoperatively. The St. Jude valve was chosen because of its very low incidence of thrombotic complications. We were concerned that the patient would manifest further problems secondary to systemic mycotic emboli (i.e., cerebral abscess or mycotic aneurysm) that would require cessation of anticoagulation. Indeed, she did experience rupture of a mycotic aneurysm and had a prolonged complicated hospital course. During the hospitalization (five months), her prothrombin time was maintained at near-normal values without evidence of valve "dysfunction" or valve-related thromboembolism. She endured prolonged ventilatory support and progressive renal failure, and was able to complete a total dose of 2.5 g of amphotericin in combination with flucytosine. The patient has been seen in follow-up more than one year after therapy. She enjoys a normal active lifestyle and is free from signs of valvular dysfunction.

Optimal therapy for fungal endocarditis involves both a surgical approach (embolectomy and valve replacement) and antifungal chemotherapy. Chemotherapy alone is not recommended because of resistance of many Aspergillus species [8], and poor penetration into tissues, fungal vegetations, and artificial blood clots [18]. Furthermore, no survivors have been reported with chemotherapy alone.

There is only one reported case of survival after valve replacement alone [2]. This patient was fortunate in that her infection was discovered prior to dissemination (embolization), and apparently all of the Aspergillus was removed at surgery. Usually, dissemination has occurred at the time of diagnosis, so concomitant chemotherapy is necessary.

Since the review by McLeod and Remington [2], many post-open heart surgery cases of Aspergillus endocarditis have appeared in the English language literature. Of 24 additional cases [10, 12-14, 19-28], there are no reported survivors. To our knowledge, this is only the second successfully treated case of disseminated post-open heart surgery Aspergillus endocarditis: the first successfully treated case involving A. flavus, and the first case involving a mitral valve annuloplasty ring. Because of the life-threatening nature of this disease, we recommend an aggressive approach, including embolectomy, early valve replacement, combination antifungal chemotherapy, and close surveillance for signs of systemic mycotic emboli.

REFERENCES


