Aspergillus Endocarditis: Cure Without Surgical Valve Replacement

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ALTHOUGH RARE, cardiac fungal infections are usually fatal, with a reported survival rate of less than 20% despite aggressive medical and surgical treatment.1 Approximately two thirds of cases of fungal prosthetic valve endocarditis are caused by Candida; Aspergillus is the next most common cause, accounting for approximately 12% of cases.2,3 Only two survivors have been reported after documented Aspergillus infections of a prosthetic valve,4,5 and there has been only one reported survivor of Aspergillus endocarditis on a native heart valve.6 All three survivors required surgical replacement of the infected valve and prompt antifungal therapy. In this report, we describe a patient with Aspergillus endocarditis who was treated with amphotericin B, and recovered from the infection without surgical removal of the affected valve.

CASE REPORT

A 72-year-old man was hospitalized on Feb 28, 1985 with a 24-hour history of chills, left leg pain, and fever (103°F [39.4°C]). He had a past history of intermittent claudication of both lower extremities. In November 1984 he had had aortic valve replacement with a porcine valve, and subsequently had a sternal wound infection and osteomyelitis with Pseudomonas aeruginosa, for which a sternectomy was done in December 1984, followed by intravenous antibiotic therapy for seven weeks. He was discharged home with a large granulating sternal wound, which required continued wound care at home.

On admission, rectal temperature was 103.5°F (39.7°C), pulse rate 125/min, and blood pressure 120/70 mm Hg. There were bilateral conjunctival petechiae, a small retinal hemorrhage, and palatine petechiae. A harsh systolic murmur was heard from the prosthetic valve. Both lower extremities were cool and without palpable pulses below the knees, as in previous examinations.

The patient had leukocytosis (WBC of 46,000/cu mm), with a left shift. An echocardiogram showed normal function of the aortic porcine valve without evidence of vegetation. No vegetations were seen on the mitral valve, but small ones could not be ruled out because the leaflets were thickened with heavy annular calcifications. A chest x-ray film was normal, and the electrocardiogram showed sinus tachycardia with infralateral ischemia. Blood cultures were drawn, and treatment was started with mezlocillin and tobramycin for a presumptive diagnosis of bacterial prosthetic valve endocarditis. Under conservative management, the patient's condition improved within the next 24 hours, but low-grade fever and leukocytosis persisted. On March 5, 1985, severe pain suddenly developed in the left forearm, and an arteriogram showed the left brachial artery to be totally occluded. Embolectomy was done, and smears of the recovered embolus showed fungi with multiple septate right angle branching hyphae, characteristic of Aspergillus sp. Postoperatively, circulation to the left arm was restored, and treatment was started with amphotericin B, 1 mg/kg/day intravenously.

Valve replacement surgery was not considered possible because of the actively infected gaping sternectomy wound and the suspicion that the aortic valve ring was infected. Medical therapy with amphotericin B was therefore continued. On the 29th day of amphotericin B therapy, the dosing frequency was reduced to every other day, and later (April 8, 1985) was further reduced to once every two weeks. The every-other-week regimen was based upon the elimination half-life of amphotericin B of 15 ± 2 days7 and a previous report indicating that serum may remain fungistatic to Aspergillus fumigatus for 14 days after a 60 mg dose.8

On May 9, embolic obstruction to the left brachial artery developed. The embolus recovered at embolectomy again showed the septate branching hyphae of Aspergillus. An echocardiogram this time showed a definite mass in the anterior mitral valve leaflet consistent with a vegetation. He recovered and was discharged home on June 21, 1985. He continued to receive amphotericin B infusions every two weeks until February 1987. The decision to stop therapy after two years was arbitrary. Since the last follow-up in May 1988, he has continued to do well without antifungal therapy for 15 months.

DISCUSSION

We do not suggest that Aspergillus or any fungal endocarditis be treated with medical therapy alone. In fact, we believe that surgical intervention is needed in all cases, primarily to reduce the danger of repeated embolization, which occurred in our patient as well as in 83% of reported cases of Aspergillus endocarditis.9 This case, however, illustrates that in some patients with correctable predisposing factors (in this case, prolonged broad spectrum antibiotic therapy), it is possible to achieve a cure with aggressive and prolonged medical therapy alone. Contributing to the success in this case might be the involvement of the native mitral valve rather than the prosthetic aortic valve (since we have no evidence of prosthetic valve involvement), and the early embolization that led to a relatively early diagnosis. It is also possible that dislodgment of large vegetations by embolization unwittingly helped our patient by removal of a large portion of infected material that might have taken a longer time to resolve.

SUMMARY

We have reported a case of fungal native valve endocarditis due to Aspergillus sp in which cure was effected by medical therapy alone. An infected sternectomy wound from a previous aortic valve replacement was considered a contraindication to surgery.

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**Torulopsis glabrata** Fungemia in a Diabetic Patient

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**TORULOPSIS GLABRATA**, a yeast of the family Cryptococcaceae, is closely related to *Candida albicans*, and is normally considered saprophytic. Like *Candida*, it can often be isolated from multiple sources in healthy individuals without associated clinical disease. 1,2 *T. glabrata* is an occasional cause of localized infection in compromised hosts and has been reported to cause systemic infection even less frequently. We describe a case of a stable diabetic outpatient with *T. glabrata* fungemia responsive to antifungal therapy.

**CASE REPORT**

A 61-year-old woman had a one-day history of sharp, left-sided abdominal pain associated with nausea and diarrhea but without apparent fever or dysuria. She was admitted with the diagnosis of possible diverticulitis. She had a ten-year history of type II diabetes, hypertension, hyperlipidemia, ischemic heart disease, and hypothyroidism. She had had recurrent urinary tract infections, all easily treated, but no history of pyelonephritis or urolithiasis. She had had no recent operation or urinary tract infection.

Admission physical examination was unremarkable except for diffuse abdominal tenderness, most prominent in the left lower quadrant, without peritoneal signs. Laboratory studies showed hyperglycemia and normal blood counts except for 28% band neutrophils. Urinalysis disclosed mild pyuria and hematuria as well as budding yeast.

Several hours after admission, the patient's temperature was 104°F (40°C); multiple cultures were obtained, and triple antibiotic therapy was begun (mezlocillin, gentamicin, and clindamycin). Despite therapy, sepsis developed, as well as acute oliguric renal failure, which improved with diuresis and short-term hemodialysis. Two urine cultures and nine blood cultures, including several cultures obtained before the initiation of antibiotic therapy, were positive for *T. glabrata*. She was treated with amphotericin B for a total of 1.5 gm. Further cultures were negative, and fever and sepsis resolved.

A search for the source of infection was undertaken. Abdominal ultrasonography and CT scan were normal except for an apparent nonobstructing stone in the left renal pelvis. A retrograde ureteropyelogram showed a stone in the distal portion of the left ureter, without evidence of hydronephrosis. A ureteral stent was placed, and recovered sediment revealed urate crystals, but cultures were negative. Barium studies of the GI tract were normal. The ureteral stent was subsequently removed without incident, and blood and urine cultures after completion of amphotericin B therapy were negative. The patient continues to do well three years later.

**COMMENT**

In recent years, fungi such as *Torulopsis* have increasingly been implicated as pathogens in a wide variety of human infections. 3-7 These infections have most often been opportunistic, and the predisposing conditions have included diabetes, alcoholism, malignancy, deep intravenous lines, underlying infections or surgery, and antibiotic, steroid, or cytotoxic therapy. 8,9 *T. glabrata* has been isolated from the urine of diabetic patients (especially women) more commonly than from any other source, 1 but reported cases of significant fungal infection in diabetics have consistently been associated with other pathogenic factors including chronic pyelonephritis, neurogenic bladder, or obstructing renal calculus. 1,2,3-5,9 None of these factors was present in our patient, though a non-obstructing renal calculus was present.

Reports of fungemia with *T. glabrata* in patients without multiple immunocompromising conditions are extremely rare. One recent report identified the organism as the cause of acute cholecystitis (without fungemia) in an otherwise healthy individual. 6 Ahearn et al described a diabetic patient who had urinary tract symptoms for several weeks, and eventually was found to have *Torulopsis* fungemia. Other immunocompromising factors in that patient were not discussed.

Valdivieso et al commented on *Torulopsis* fungemia in six patients, all of whom had cancer and had been given antibiotic therapy before fungemia was proved (unlike our case, in which cultures were positive before antibiotics were given). In addition, most had received chemotherapy or steroids and had