Denton A. Cooley's 50th Anniversary in Medicine

Scopulariopsis Endocarditis Associated with Duran Ring Valvuloplasty

Layne O. Gentry, MD
Maher M. Nasser, MD
Marcia Kielhofner, MD

Fungal endocarditis is rare and is usually caused by Aspergillus *and* Candida *species. We present a patient with endocarditis caused by* Scopulariopsis brevicaulis. *The patient had a history of mitral valve disease and, 1 year earlier, had undergone valvuloplasty with the placement of a prosthetic Duran ring in the mitral valve position.* S. brevicaulis *was cultured from samples of a large vegetation on the mitral valve apparatus. The mitral valve was replaced with a St. Jude mechanical prosthesis. The patient was treated with amphotericin B but was later switched to oral itraconazole when antibiotic tests indicated susceptibility to that agent. We believe this is the 1st reported case of endocarditis caused by* Scopulariopsis. ***(Tex Heart Inst J 1995;22:81-5)***

We report a case of fungal endocarditis caused by *Scopulariopsis brevicaulis*, an organism usually considered a fungal contaminant. The fungus was cultured from a vegetative growth found on a prosthetic Duran ring that had been placed in the mitral valve position 1 year earlier for valve dysfunction secondary to recurrent rheumatic disease. We believe this is the 1st reported case of endocarditis caused by *Scopulariopsis*.

Case Report

A 36-year-old man presented at a regional hospital with abdominal pain and hematuria. Mildly elevated levels of amylase and lipase suggested pancreatitis. Ultrasonograms and roentgenograms, including a computed tomographic (CT) scan of the abdomen, excluded the presence of gallbladder disease or pancreatitis. On the CT scan, however, a large infarction of the kidney was noted (Fig. 1). The patient was initially started on a combination of ampicillin and sulbactam, but later was switched to cefoxitin and gentamicin. Because of the CT scan findings and the development of a new mitral regurgitation murmur, he was transferred to our institution on October 8, 1993, for anticoagulation therapy and transesophageal echocardiography.

The patient had a history of rheumatic valvulitis, and in October of 1992 he had undergone mitral valvuloplasty with a Duran prosthetic ring for mitral regurgitation. In addition, he had a family history of significant heart disease. He was taking lovastatin for hyperlipidemia.

At the time of admission to our institution, the patient's blood pressure was 125/70 mmHg, and his pulse rate was 102 beats/min. He was alert and appeared to be well. No adenopathy was noted, and mucous membranes were moist. No petechiae were noted in the subconjunctival area or on the mucous membranes of the mouth. However, 1 small petechial lesion was seen on the dorsum of the right foot and another one on the great toe of the right foot. Cardiovascular examination revealed attenuation of the 1st heart sound and a soft mitral regurgitation murmur. Mild tenderness of the abdomen was present, especially on the left side. He had active bowel sounds, and the rectal examination was normal.

Laboratory findings on admission were unremarkable. He had a white cell count of 7.0×10^9/L, with a slight left shift. Peripheral blood smear showed a slight eosinophilia. The patient's hemoglobin level was 11.6 g/dL, and his hematocrit was 33.6%. The prothrombin time and partial thromboplastin time were elevated because of anticoagulation therapy. Many red blood cells were seen on urinalysis. All other urinalysis findings were normal.

This series in recognition of Dr. Cooley's 50th anniversary in medicine is continued from the December 1994 issue.

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From: *Infectious Disease Section, St. Luke's Episcopal Hospital, Houston, Texas 77030*

Section editors:
Grady L. Hallman, MD
Robert D. Leachman, MD
John L. Ochsner, MD

Address for reprints:
Layne O. Gentry, MD, St. Luke's Episcopal Hospital, MC 2-233, P.O. Box 20345, Houston, TX 77225-0345

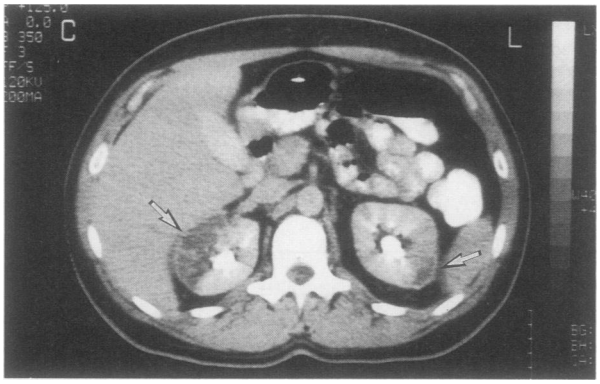

Fig. 1 *Computed tomographic scan of the kidney, illustrating bilateral renal infarctions.*

The patient underwent transesophageal echocardiography, which revealed a large mass on the mitral valve apparatus (Fig. 2). On October 14, 1993, the patient underwent surgery for exploration of his mitral valve. Recurrent thickening and fibrosis of the repaired valve leaflet were noted. A pannus-like vegetation was seen on the anterior leaflet of the mitral valve (Fig. 3). Samples were taken for histopathologic examination and microbiologic culture. His valve and Duran ring were replaced with a St. Jude's prosthesis. He was given vancomycin perioperatively for prophylaxis.

Histologic examination of the vegetative material taken from the mitral valve ring revealed mycotic endocarditis (Fig. 4). *S. brevicaulis* was cultured from the valve ring (Fig. 5). The patient received 335 mg of intravenous amphotericin B over the next 10 days. He was discharged with an intravenous catheter in place, and he received another 265 mg of amphotericin B over the next 8 weeks. The fungal culture was sent to Dr. Richard Graybill at the University of Texas Health Science Center in San Antonio, Texas, for antibiotic susceptibility testing. The organism was sensitive to itraconazole, with a minimum inhibitory concentration of 2 μg/mL at 48 hours and 4 μg/mL at 72 hours. The patient was switched to oral itraconazole, 1 dose (200 mg) per day.

Follow-up examinations were performed monthly for the next 3 months. The patient completed a 90-day course of itraconazole therapy. No further evidence of endocarditis has been noted, and his renal function has returned to normal. Hematuria has not been present. He had 1 episode of pain in his right calf, and Doppler echocardiography revealed an embolic occlusion in one of the arteries; however, the pain subsided and he has had no further episodes.

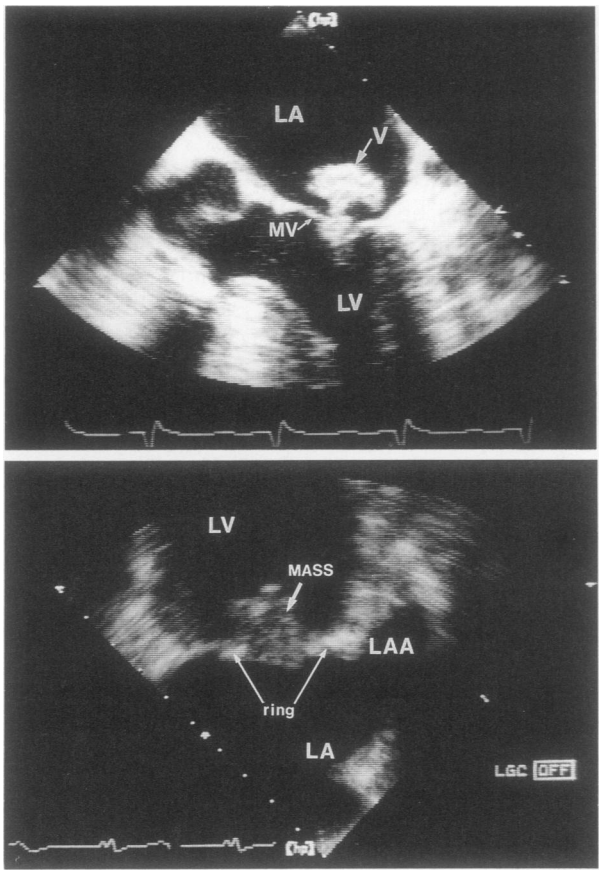

Fig. 2 ***A****) Transesophageal echocardiogram in the horizontal plane demonstrating a large, pedunculated vegetation on the anterior leaflet of the mitral valve.* ***B****) Transesophageal echocardiogram in the longitudinal plane demonstrating a large mass within the mitral annuloplasty ring.*

LA = left atrium; LAA = left atrial appendage; LV = left ventricle; MV = mitral valve; V = vegetation

Discussion

Scopulariopsis species are widely distributed in nature and are found on decaying vegetation and in

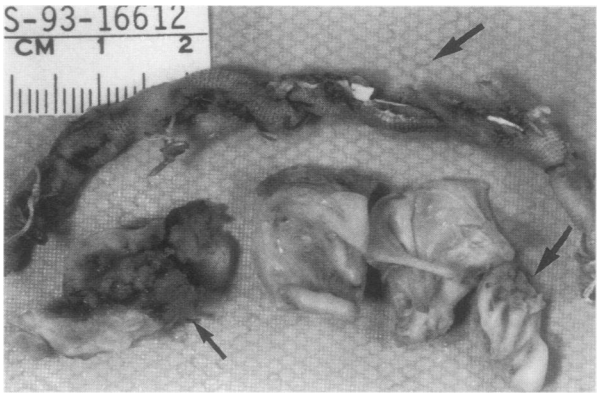

Fig. 3 *Gross pathologic specimen showing the Duran ring (top arrow) and vegetations (bottom arrows) on the mitral valve apparatus.*

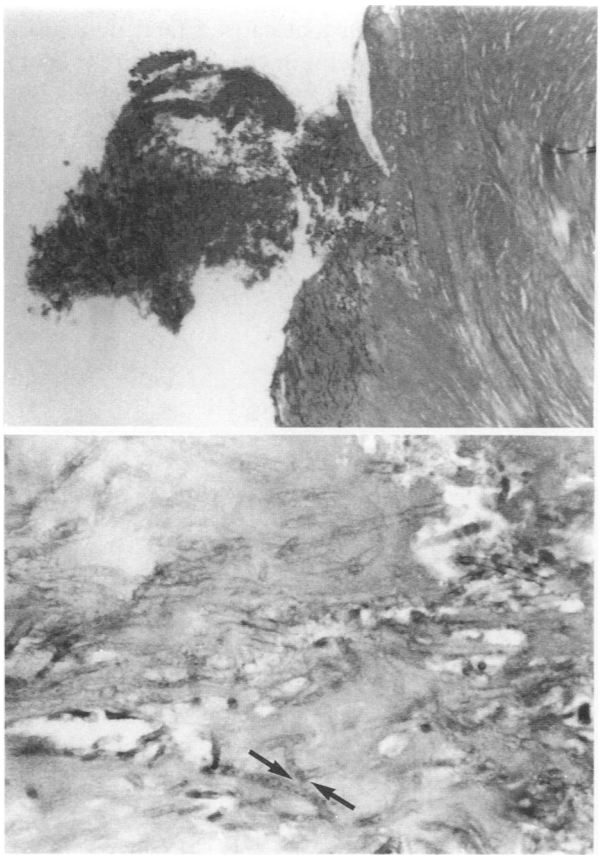

Fig. 4 ***A****) Photomicrograph showing the vegetative growth on the mitral valve. (H + E orig. ×40)* ***B****) Silver stain of vegetative material taken from the mitral valve. Arrows indicate branching hyphae. (orig. ×400)*

soil. Classified among the saprophytic hyaline hyphomycetes, these organisms grow readily at room temperature. The presence of abundant conidia causes the colonies to appear yellowish-brown, with a powdery surface.[1] The conidia, 6 to 9 μ long, have tuberculate or warty walls.[2] The large phialides are in a *Penicillium*-like arrangement.

Although they are common fungal contaminants, *Scopulariopsis* species are rarely considered pathogenic. The organism, however, may cause nail infections, resulting in discolored, hardened nails. In fact, *Scopulariopsis* species are among the most common nondermatophytic fungi that cause onychomycosis.[3] Furthermore, in a study of keratinophilic and saprophytic fungi in the nails of Egyptian students, *S. brevicaulis* was the 5th most common isolate.[4]

In 1932, Markley and colleagues[5] described the 1st deep-seated infection with *Scopulariopsis*. In their report, *S. brevicaulis* was isolated from persistent, ulcerogranulomatous lesions in the perineal, gluteal, and right inguinal regions of a previously healthy 21-year-old patient. The lesions, described as elevated, nodular, and dusky, resembled those seen in sporotrichosis, and were associated with necrotizing

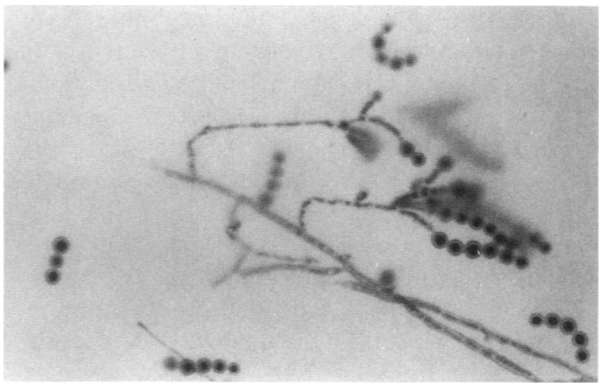

Fig. 5 *Photomicrograph of* Scopulariopsis brevicaulis *showing the* Penicillium*-like arrangement of the phialides. (orig. ×20)*

ulceration. Intravenous antimony potassium tartrate, combined with local radiation therapy, resulted in complete resolution of the lesions. Because no fungi were seen on histopathologic examination of the lesions, the authors could not conclusively cite *S. brevicaulis* as the definitive cause. However, in studies in guinea pigs and rats, the organism remained viable and caused similar lesions.

Sekhon and associates,[6] 4 decades later, reported another deep-seated infection with *Scopulariopsis* in a patient who initially had an ankle wound infected with *Enterobacter aerogenes*. After multiple débridement procedures and long-term antibiotic therapy, a secondary infection with *S. brevicaulis* was found. Histopathologic examination revealed a chronic, granulomatous infection involving subcutaneous tissue, tendon sheaths, and skeletal muscle.

Although it is rare, ocular disease secondary to infection with *Scopulariopsis* has been reported. Progressive keratitis and hypopyon developed in a 26-year-old man whose eye was injured by a nail embedded in a rotting wooden plank.[7] Despite systemic and topical therapy with amphotericin B and the addition of itraconazole, the patient required emergency keratoplasty. These authors cited several foreign cases of ocular *Scopulariopsis*.

Isolated pulmonary involvement with *Scopulariopsis* has been reported. *Scopulariopsis* has invaded pulmonary cavities caused by chronic infection with *Mycobacterium tuberculosis*.[8] Grieble and coworkers[9] reported pulmonary infection with *Scopulariopsis brumptii* in an intravenous drug user. This patient had multiple pulmonary nodules with interstitial pneumonia; tissue from an open lung biopsy revealed noncaseating granulomas with fungal elements. A pulmonary hypersensitivity reaction to the fungal spores was suggested.

Scopulariopsis, like *Aspergillus* and *Fusarium* species, may act as an opportunist, causing disease in immunocompromised hosts. Most cases of invasive

infection with *Scopulariopsis* have been in patients with hematologic malignancies or in recipients of allogeneic bone marrow transplants. Neglia and coauthors[10] described 2 immunosuppressed patients who had *Scopulariopsis* infection of the nasal septum and mastoid tissue that did not respond to aggressive surgical débridement and systemic antifungal therapy. At autopsy, both patients had residual disease, one with widespread involvement of the brain and lungs. Similar case reports in immunosuppressed hosts have documented *Scopulariopsis* infection of the lungs;[11] the sinonasal passages, with dissemination;[12] and the great toe, causing osteomyelitis.[13] Immunosuppressed patients have generally responded poorly to antifungal therapy. However, in a recent report of invasive sinonasal disease caused by *Scopulariopsis* in a child with Hodgkin's disease, a combination of surgery and therapy with amphotericin B and itraconazole eradicated the infection.[14]

Fungal endocarditis is relatively uncommon and is usually associated with intravenous drug abuse, previous cardiovascular surgery, or the prolonged use of antimicrobial agents and intravenous hydration.[15] In a review of patients with fungal endocarditis, McLeod's group[16] reported that 217 (68%) of 319 patients experienced embolization to major vessels. The mortality rate associated with fungal endocarditis may be as high as 80%.[14] The predominant species causing endocarditis on both native and prosthetic valves have been *Candida*, *Aspergillus*, and *Histoplasma*. However, endocarditis has been caused by opportunistic fungi, such as *Blastoschizomyces capitatus*,[17] *Conidiobolus*,[18] *Pseudallescheria boydii*,[19] *Penicillium*,[20] and *Cryptococcus*.[21] We believe that *Scopulariopsis* has not previously been cited as a cause of endocarditis.

In the patient described in this case report, the presence of a major arterial embolus was consistent with other cases of fungal endocarditis. Often, large bulky vegetations adhere to the valve surface in these patients. Although the source of infection in our patient was unclear, the patient did have onychomycosis and may have carried the organism underneath his nails. In an outbreak of endocarditis caused by *Aspergillus* in patients who had undergone cardiovascular surgery, the presence of *Aspergillus* species in pigeon droppings outside the operating suites and in air conditioning cooling coils suggested an environmental source of the outbreak.[22] Whether a similar source was present in our case is not known.

The optimal antimicrobial regimen for treating *Scopulariopsis* infection is unknown. Results from in vitro susceptibility tests vary widely, but the organism is often highly resistant to the usual array of agents used to treat systemic fungal infections. Two isolates of *S. brevicaulis* that caused fatal disseminated disease were resistant or only moderately susceptible to amphotericin B and 5FC.[10] In vitro studies suggested that the strains were susceptible to miconazole and ketoconazole, but resistant to itraconazole. However, the authors cautioned that in vitro susceptibility testing of imidazoles might not correlate with clinical outcome. Other studies have also suggested that *Scopulariopsis* may be resistant to amphotericin B.[6,7,11]

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