Pulmonary Sporotrichosis Treated With Itraconazole*

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A 62-year-old woman had chronic cavitary pulmonary sporotrichosis refractory to medical management over an 8-year period. She was treated with oral itraconazole and had an apparent microbiologic and clinical response; however, the patient succumbed to progressive pulmonary hypertension. The early use of oral itraconazole for treatment of pulmonary sporotrichosis is advocated.

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Pulmonary sporotrichosis is a rare disease. Rippon[1] reported about 150 cases in the literature in 1988. We describe a case of chronic cavitary disease caused by pulmonary sporotrichosis that responded to itraconazole after being refractory to medical management for 8 years.

Case Report

A 62-year-old woman first sought medical attention in 1982 for a 2-year history of hemoptysis and dyspnea on walking up 4 flights of stairs. Her last reported chest x-ray film in 1975 was normal, but her initial chest radiograph showed bilateral apical cavitary disease. She had smoked 2 packs per day since the age of 14 years. Her father died of pulmonary tuberculosis. A first and second strength purified protein derivative of tuberculin test was negative in 1982, and three smears for acid-fast bacilli were also negative. Bronchoscopy was performed in October 1982, and pulmonary sporotrichosis was diagnosed. Between October and December, the patient received amphotericin B in a total dose of 1,981 mg, with sputum cultures remaining positive. She was placed on therapy with a saturated solution of potassium iodide (SSKI), 75 drops per day, from 1983 until 1986 and received ketoconazole concurrently with SSKI in 1985 and 1986. Cultures of sputum remained positive, and therapy with SSKI and ketoconazole was stopped, since the patient had become permanently hypothyroid.

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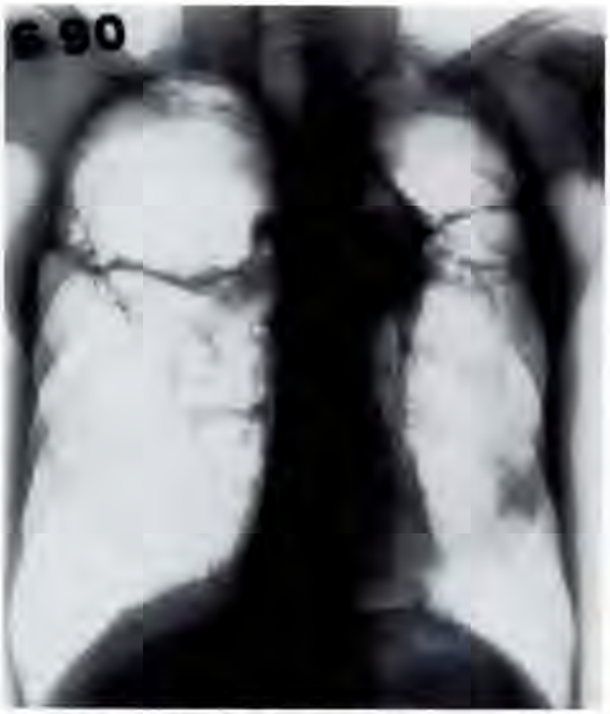

Figure 1. Chest radiograph of patient in 1990.

The patient referred herself to Brigham and Women's Hospital in 1990. At that time, she had lost 25 percent of her ideal body weight and had a chronic productive cough and low-grade fevers. Physical examination showed 4+ clubbing of the digits, a loud pulmonary component of the second heart sound, and amphoric breath sounds at both lung apexes. The chest radiograph revealed marked apical cavitation and a nodular infiltrate (Fig 1). Chest computed tomography confirmed the fibrosis and retraction of the remaining lung (Fig 2). A culture of sputum was positive for *Sporothrix schenckii*.

The patient was placed on therapy with itraconazole (Janssen), 200 mg *per os* twice daily; and after 1 month a serum level of 4.5 μg/ml was measured 2 hours after the dose. She was treated for 12

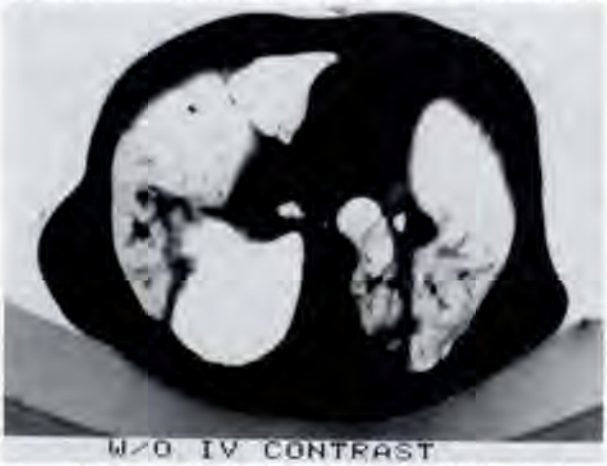

Figure 2. Computed tomogram of chest in 1990, showing large apical bullae and fibrotic scarring of remaining lung with nodular infiltrate.

months without toxic effects, and cultures of sputum became negative after the fourth month. The patient's functional status stabilized, and she regained most of her lost weight. Unfortunately, she died from progressive pulmonary hypertension in June 1991.

Discussion

Sporotrichosis is most often acquired as a primary infection from the inhalation of conidia. Two radiologic patterns are recognized: (1) involvement of the tracheobronchial lymph nodes; and (2) chronic cavitary disease. This patient represents an 8-year course of chronic cavitary disease with fever, cough, malaise, weight loss, and nodular apical masses associated with thin-walled cavities, fibrosis, and pleural thickening. Her smoking history is consistent with other reported cases and seems to confer susceptibility to infection. Although her history of exposure to tuberculosis was strong, she was repeatedly evaluated for tuberculosis over the 8-year period, and all cultures were negative.

Medical treatment of chronic cavitary pulmonary sporotrichosis has been unsatisfactory.[2] Unlike the cutaneous form of the disease, SSKI usually is ineffective. Amphotericin alone, even in doses greater than 2 g, has been associated with failure, especially if surgical resection cannot be performed. Most reviews emphasize that surgical removal of the infected tissue has proven to be the most effective therapy.[3]

The use of azole antifungal agents for sporotrichosis has met with partial success for cutaneous disease but not for pulmonary disease. Calhoun et al[4] reported that 8 of 11 patients with deep-seated sporotrichosis (no pulmonary cases) had a response to ketoconazole, 400 to 800 mg/day, when treated for more than 1 year. Dall and Salzman[5] reported failure of ketoconazole in chronic pulmonary forms of the disease.

Itraconazole is an investigational triazole antifungal agent with *in vitro* activity against sporotrichosis at achievable serum levels. Restrepo et al[6] treated 17 patients with lymphocutaneous disease with 100 mg/day for an average of 115 days. All had resolution of their disease. Lavalle et al[7] and Borelli[8] also reported success with itraconazole in cutaneous or deep subcutaneous disease. Baker et al[9] reported a case of fungemia with an amphotericin B-resistant isolate of *S schenckii* that responded to itraconazole. We believe that this is the first case of chronic cavitary disease caused by *S schenckii* to be treated with itraconazole, with apparent microbiologic response, as gauged by the sterilization of sputum cultures, and a clinical response, as gauged by the patient's subjective recovery and gain in weight; however, by the time she received this agent, irreversible lung damage had occurred, and end-stage pulmonary hypertension prevented subsequent attempts at cure by surgical resection. We advocate early use of itraconazole in the initial treatment of pulmonary sporotrichosis.

References

1 Rippon JW. Medical mycology: the pathogenic fungi and the pathogenic Actinomycetes. 3rd ed. Philadelphia: WB Saunders, 1988

2 Gerding DN. Treatment of pulmonary sporotrichosis. Semin Respir Infect 1986; 1:61-5

3 Pluss JL, Opal SM. Pulmonary sporotrichosis: review of treatment and outcome. Medicine (Baltimore) 1986; 65:143-53

4 Calhoun DL, Waskin H, White MP, Bonner JR, Mulholland JH, Rumans LW, et al. Treatment of systemic sporotrichosis with ketoconazole. Rev Infect Dis 1991; 13:47-51

5 Dall L, Salzman G. Treatment of pulmonary sporotrichosis with ketoconazole. Rev Infect Dis 1987; 9:795-98

6 Restrepo A, Robledo J, Gomez I, Tabares AM, Gutierrez R. Itraconazole therapy in lymphatic and cutaneous sporotrichosis. Arch Dermatol 1986; 122:413-17

7 Lavalle P, Suchil P, De Ovando F, Reynoso S. Itraconazole for deep mycoses: preliminary experience in Mexico. Rev Infect Dis 1987; 9(suppl 1):S64-S70

8 Borelli D. A clinical trial of itraconazole in the treatment of deep mycoses and leishmaniasis. Rev Infect Dis 1987; 9(suppl 1):S57-S63

9 Baker JH, Goodpasture HC, Kuhns HR, Rinaldi MG. Fungemia caused by an amphotericin B-resistant isolate of *Sporothrix schenckii*. Arch Pathol Lab Med 1989; 113:1279-81