Disseminated Sporotrichosis and *Sporothrix schenckii* Fungemia as the Initial Presentation of Human Immunodeficiency Virus Infection

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Infection with *Sporothrix schenckii* causes a localized lymphocutaneous disease in the immunocompetent host, while it frequently results in disseminated disease in the immunocompromised patient. There are a growing number of reports of *S. schenckii* infection in the human immunodeficiency virus (HIV)-infected population, where the disease usually starts as a localized cutaneous lesion and subsequently disseminates. The optimal treatment of systemic sporotrichosis in HIV-positive patients is as yet unknown. This article presents a case report of disseminated sporotrichosis in an HIV-infected patient, a review of the literature, and discussion of treatment options for HIV-infected patients.

Sporotrichosis is caused by *Sporothrix schenckii*, a dimorphic fungus with a global distribution. It is found in soil [1] and plant material such as sphagnum moss [2]. Sporotrichosis commonly presents as limited lymphocutaneous lesions but in rare cases is disseminated [3]. The lymphocutaneous form results from cutaneous inoculation and subsequent lymphatic spread. Disseminated disease may be acquired through cutaneous inoculation, inhalation, or (rarely) ingestion [3, 4], and it usually results in diffuse cutaneous lesions with involvement of one or more additional organ systems.

Disseminated disease most frequently occurs in immunocompromised individuals such as alcoholics, diabetics [5], patients with chronic obstructive pulmonary disease [5] or a hematologic malignancy, solid organ or bone marrow transplant recipients, those receiving corticosteroid therapy, and those infected with HIV [5–7]. In this report we describe a case of disseminated sporotrichosis and *S. schenckii* fungemia occurring as the initial presentation of AIDS.

Case Report

A 47-year-old male presented to our facility for evaluation of skin lesions. Four months prior to presentation, he was evaluated at an outside clinic for a pruritic rash of 3 weeks’ duration. Physical examination revealed multiple scattered psoriasiform eruptions involving his neck, face, scalp, forearms, and chest. A presumptive diagnosis of pellagra was made, and the patient was treated with thiamine, riboflavin, and pyridoxine.

Two weeks later, the rash had progressed, and a punch biopsy of a chest wall lesion revealed spongiotic dermatitis with mixed superficial and perivascular inflammation compatible with an eczematous process. He responded to therapy with high-dose prednisone and cephalixin, but the lesions subsequently worsened.

Three months after presentation he was hospitalized with progressive disease involving an eschar on the distal thumb and prominent woody edema of the wrist. The patient underwent debridement of the right thumb, received ceftriaxone, and was referred to our institution for further evaluation.

On presentation a biopsy of a wrist lesion was performed, and high-dose prednisone therapy was given for presumed pyoderma gangrenosum. One week later, there was worsening of the skin lesions over the forearm (figure 1) and further ulceration and necrosis of the right thumb, with lymphatic streaking (figure 2). Periodic acid–Schiff staining and Grocott-Gomori methenamine–silver nitrate staining of the skin biopsy specimens revealed numerous cigar-shaped spores consistent with *S. schenckii*.

The patient was hospitalized and received amphotericin B (0.5 mg/[kg · d]) for disseminated sporotrichosis and ticarcillin/clavulanic acid for presumed secondary bacterial infection. He subsequently tested positive for HIV and had a CD4 cell count of 9/mm³. Skin and blood cultures yielded *S. schenckii*.

The fungus grew as small white colonies at 30°C and later became brownish-black with rosette-like clusters. The mycelia converted to yeastlike forms at 37°C, and microscopic examination also confirmed the presence of cigar-shaped bodies characteristic of *S. schenckii*. A bone scan revealed an increased uptake in the right thumb and right wrist, consistent with osteomyelitis.

Two weeks after initiation of therapy, amphotericin B was withdrawn temporarily because of renal toxicity, and daily administration of itraconazole (400 mg) was started. The serum creatinine level normalized, and the patient completed therapy with amphotericin B (total dose, 2.5 g).

During combination therapy with zidovudine and lamivudine, the viral load dropped from 114,858 copies/mL to <400 copies/mL. The patient continued receiving maintenance therapy with itraconazole (200 mg daily) and had no evidence of relapse in 9 months of follow-up.
Itraconazole is currently the drug of choice for osteoarticular, localized lymphocutaneous, and disseminated sporotrichosis in HIV-seronegative patients. Restrepo et al. reported a clinical and mycological response rate of 100% among 17 patients with lymphocutaneous diseases [20]. Sharkey-Mathis et al., reporting on their experience with the treatment of 27 patients with localized, osteoarticular, or systemic sporotrichosis [5], noted that 25 patients responded to a 6–18 month course of itraconazole (200–400 mg). However, seven patients relapsed within 7 months after completing therapy.

The optimal therapy for HIV-infected patients has yet to be determined. Amphotericin B was the initial therapy in eight of the 16 previously reported cases [1, 6–8, 11, 13, 18]. Five patients’ conditions improved after a total dose of 800–1,900 mg of amphotericin B [1, 6, 8, 11, 13], while in two patients there was no response [7, 11]. One patient underwent eye enucleation despite intravenous and intravitreal administration of amphotericin B for endophthalmitis [7]. Four patients had progressive disease and died with sporotrichosis [1, 10, 14, 18].

**Literature Review and Discussion**

*S. schenckii* infection, like *Histoplasma capsulatum* and *Cryptococcus neoformans* infections, is an opportunistic mycosis in the HIV-infected population. To date, disseminated sporotrichosis has been reported to occur in 16 HIV-infected patients (table 1). All patients presented with diffuse ulcerative skin lesions similar to those in the present case. Involvement of the CNS [2, 13, 14, 18], eye [7, 10], joints [1, 6, 9, 10], spleen [1], and bone marrow [10] have been previously reported. However, *S. schenckii* fungemia is rare, and the present case represents the second report concerning an HIV-infected patient. Fifteen of the 16 reported cases involved men (mean age, 38.8 years; range, 22–71 years). The mean CD4 cell count was 72.8/mm³ (median, 37.5/mm³; range, 9–345/mm³; n = 10) [2, 6, 10, 13–18]. Sporotrichosis was the initial event leading to a diagnosis of HIV infection in three of the 16 cases [6, 10, 11].

Therapeutic regimens for sporotrichosis in non-HIV-infected patients are well established. Treatment with saturated solution of potassium iodide (SSKI) for cutaneous sporotrichosis is almost always successful [3]. However, SSKI therapy requires meticulous dosage adjustment and poses a wide range of side effects [20, 21]. Moreover, iodide is ineffective for disseminated disease [21].

Amphotericin B has been the treatment of choice for osteoarticular and systemic sporotrichosis in HIV-negative patients; it has been associated with cure rates of 50%–80% in pulmonary sporotrichosis, especially if combined with surgical resection [20–22]. However, the response rate was 74% among patients with osteoarticular sporotrichosis, and there were frequent relapses [23].

Fluconazole therapy cured 10 (71%) of 14 and 5 (31%) of 16 patients with lymphocutaneous and visceral disease, respectively, and appears to be inferior to itraconazole therapy [24].

**Figure 1.** The left forearm of an HIV-infected man with presumed pyoderma gangrenogum; the superficial ulcerations worsened before *Sporothrix schenckii* was identified in skin biopsy specimens.

**Figure 2.** An erythematous punched-out ulcer on the right thumb of the patient in figure 1, before the pathogen was identified as *S. schenckii*. 
In summary, the optimal therapy for disseminated sporotrichosis in HIV-positive patients remains unclear, and the response to therapy is variable. On the basis of the favorable response in a selected number of cases, amphotericin B and itraconazole appear to be reasonable choices for initial therapy. Amphotericin B is frequently used in cases of disseminated disease [21], whereas itraconazole can be used for mildly to moderately ill patients or those with localized disease. Measuring the itraconazole serum concentration ensures adequate levels and might decrease the number of therapeutic failures [21].

Sporotrichosis probably poses a high risk of relapse in AIDS patients, similar to the risk in other fungal diseases. Itraconazole appears to be a reasonable choice for long-term suppressive therapy. It is easy to administer and has been shown to be effective in some patients. In addition, highly active antiretroviral therapy may restore the immune system and facilitate clinical response.

References


