Case report

Disseminated sporotrichosis mimicking sarcoidosis

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A 40-year-old Caucasian man presented to the dermatology clinic at Baylor College of Medicine, Houston, Texas, in February 2003, for the evaluation of three nonhealing ulcers. The patient's past medical history was significant for hypothyroidism and pulmonary sarcoidosis, the diagnosis of which was made in June 2000. In March 2000, the patient had complained of cough and shortness of breath. A purified protein derivative (PPD) (Mantoux text) was negative. Computed tomography (CT) scans of the chest revealed diffuse hilar and mediastinal adenopathy and bilateral interstitial and alveolar infiltrates. Although consistent with sarcoidosis, these findings were insufficient to exclude other etiologies, including disseminated fungal infection. Cultures and stains of subsequent bronchoscopy specimens failed to reveal any organisms, and histopathologic evaluation of the specimens was nondiagnostic. Based on the imaging studies and the negative cultures, a diagnosis of sarcoidosis was made, and the patient was started on therapy with prednisone. Before coming to our clinic, the patient had been on several courses of prednisone.

In May 2002, the patient had presented to a private dermatologist with a 1-year history of a nonhealing 2.4 cm × 2.0 cm ulcer on the left medial forearm. Two biopsies were reported as nondiagnostic. The patient's presentation was interpreted as most consistent with Mycobacterium marinum infection, and so he was empirically treated with minocycline. This treatment was continued for almost 3 months without improvement in the ulcer. A few months after the minocycline had been discontinued, the patient was treated empirically for 2 months with ciprofloxacin. This treatment was also unsuccessful in ameliorating the ulcer. In between the two courses of antibiotics, specimens from the lesion were sent for bacterial and fungal cultures, which revealed normal skin flora.

In January 2003, the patient returned to his private dermatologist with three ulcerations. In addition to the nonhealing ulcer on his left forearm, which he had acquired several months earlier, he had also developed a 3.0 cm ulcer on his right arm and a 3.0 cm ulcer on his central back. The patient refused biopsies at this visit. Given the patient's previous diagnosis of pulmonary sarcoidosis, it was thought that the skin lesions might represent ulcerative cutaneous sarcoidosis. Pyoderma gangrenosum was also considered to be a likely diagnosis. Therefore, the patient was started on a course of oral prednisone, an effective therapy for both sarcoidosis and pyoderma gangrenosum.

Despite 1 month of treatment with 60 mg/day of prednisone, the ulcers increased, and the patient was subsequently referred to our clinic. Physical examination at the time of presentation revealed steroid acne on the trunk and upper extremities and three nontender ulcers with erythematous, undermined borders (Figs 1–3). On the left arm, there was an adjacent nodule which the patient attributed to a scar from a previously healed ulcer. Histologic examination of biopsy specimens from all three sites showed similar findings. The lesion contained diffuse, suppurative, granulomatous, inflammatory infiltrates with extensive central necrosis. The infiltrates were composed of histiocytes, multinucleated foreign-body-type giant cells, plasma cells, lymphocytes, neutrophils, and neutrophil fragments. No organisms were seen in the initial, routinely stained sections. However, periodic acid–Schiff (PAS) staining demonstrated small fungal spores (Fig. 4) morphologically consistent with sporotrichosis, within the cytoplasm of multinucleated histiocyte giant cells (Fig. 5). Additional stains for bacteria and acid-fast organisms were negative. Cultures of the biopsy specimens from all three sites grew Sporothrix schenckii. Further questioning of the patient failed to reveal an obvious source of the infection.
The patient denied any history of traumatic skin inoculation and did not engage in gardening or other outdoor activities that are classically associated with sporotrichosis. The patient did admit to blackberry picking on detailed retrospective questioning.

Once the diagnosis of sporotrichosis was made, the patient was given 200 mg/day of itraconazole. After 2 months, the patient’s ulcers were almost completely healed. The patient’s pulmonary complaints were also much improved.

Discussion

Sporotrichosis is a fungal infection caused by *Sporothrix schenckii*. This organism is widely distributed in nature and has been isolated from various plant sources throughout the world. The spores grow on plant debris, sphagnum moss, hay, and soil, and the disease is usually acquired by traumatic skin inoculation with spores on thorns, splinters, and woody fragments.

*Figure 1* Ulcer (3 cm) on the right arm

*Figure 2* Ulcer (3 cm) with adjacent erythematous nodule on the left arm

*Figure 3* Ulcer (3 cm) on the back

*Figure 4* Periodic acid–Schiff (PAS) staining demonstrating small fungal spores

*Sporothrix* infection has four manifestations: lymphocutaneous, fixed cutaneous, disseminated cutaneous, and extracutaneous. The lymphocutaneous variant is most common, comprising 80% of all sporotrichosis infections. In this type of infection, the primary lesion develops as a small nodule at the site of inoculation. This nodule enlarges and ulcerates, and the infection extends along the draining lymphatic channels. In contrast with lymphocutaneous disease, fixed cutaneous disease is an infection that remains at the site of...
inoculation without involvement of the lymphatic system. The morphology of fixed cutaneous sporotrichosis is variable, including acneiform, verrucous, nodular, ulcerated, or erythematous plaques. Disseminated cutaneous sporotrichosis is a rare manifestation, occurring in fewer than 2% of cases. This pattern of disease results from hematogenous dissemination from the primary lesion or may occur with multiple inoculation sites. Extracutaneous sporotrichosis results from the hematogenous spread from the primary inoculation site or from the inhalation of conidia. This form of sporotrichosis typically, but not exclusively, occurs in hosts with depressed cell-mediated immunity. The most common organs affected are the bones, joints, lungs, or meninges. Alternatively, a disseminated form may occur. Bone and joint sporotrichosis presents as an exuberant arthritis similar to rheumatoid arthritis. Pulmonary disease simulates tuberculosis and histoplasmosis with apical cavitary lesions. Meningeal sporotrichosis simulates tuberculosis and histoplasmosis with apical cavitary lesions. Meningeal sporotrichosis is often indolent and difficult to diagnose. Defective cell-mediated immunity, e.g. acquired immunodeficiency syndrome (AIDS), is often, but not always, present in disseminated disease.1,4

A definitive diagnosis of sporotrichosis is made by fungal culture.7 The yield of direct examination of periodic acid–Schiff (PAS)- or gomori methenamine silver (GMS)-stained biopsy specimens for the characteristic ovoid-to-cigar-shaped yeasts, asteroid bodies, or short hyphae is low because of the small number of organisms in the biopsy. Therefore, the diagnosis relies on cultures of purulent exudates or ground tissue.1

The treatment of choice for fixed cutaneous or lymphocutaneous sporotrichosis is itraconazole, 200 mg/day for 3–6 months.5 Open treatment trials have demonstrated a success rate of 90–100%.6,8 In addition, itraconazole is better tolerated and less hepatotoxic than other antifungal therapies such as ketoconazole. An oral saturated solution of potassium iodide (SSKI), the classic treatment for cutaneous sporotrichosis, is still commonly used because of its effectiveness, simplicity, and low cost.1 Although SSKI is clearly effective, the mechanism of action is unknown,1 and its use has not been subjected to specific treatment trials.

Because S. schenckii cannot grow at temperatures greater than 38.5 °C,13 heat therapy, such as warm compresses, hot baths, and bed warmers, can be an effective supplemental or alternative therapy. This form of therapy should be used when other therapies are contraindicated, as in pregnancy, or when other antifungals cannot be taken.9

Intravenous amphotericin B is effective in treating cutaneous sporotrichosis, but the potential for severe renal toxicity makes its use undesirable when safer agents (itraconazole or SSKI) are available; however, the treatment of extracutaneous sporotrichosis, especially in severe disease, e.g. meningitis, often requires amphotericin B.9 If the extracutaneous disease is not life-threatening, itraconazole therapy is a reasonable choice. There have been a few reports of the successful use of terbinafine in patients with cutaneous sporotrichosis;14–16 however, the available data are scarce, and further trials are needed to define the role of terbinafine in the treatment of sporotrichosis.

The differential diagnosis in our case included pyoderma gangrenosum and ulcerative sarcoidosis. Without lymphatic involvement and the classic history of gardening, cutaneous sporotrichosis can easily be mistaken for one of these other disease processes. The literature contains several reports of sporotrichosis mimicking pyoderma gangrenosum.17–19 Sporotrichosis is often mistaken for pyoderma gangrenosum when skin nodules are present without involvement of the lymphatic system. In our case, pyoderma gangrenosum was considered to be a possible diagnosis until fungal stains demonstrated S. schenckii. Pyoderma gangrenosum should be a diagnosis of exclusion after the appropriate laboratory tests have excluded diseases that can mimic this condition.

Our patient’s previous diagnosis of sarcoidosis, 1 year prior to the development of skin lesions, also complicated his clinical picture. Ulcerative sarcoidosis was a presumptive diagnosis of his skin lesions at one point during his evaluation. In addition, he had been treated with daily high-dose prednisone intermittently for 3 years prior to being diagnosed with disseminated sporotrichosis. This immunosuppression could explain the unusual presentation of multiple cutaneous lesions. Sporotrichosis with disseminated lesions has been reported in a patient on chronic steroid therapy.20

The patient is currently undergoing further evaluation to determine the true etiology of his pulmonary symptoms. He most likely has either pulmonary sarcoidosis with comorbid disseminated cutaneous sporotrichosis or primary pulmonary sporotrichosis with secondary disseminated cutaneous spread. The latter possibility is suggested by the improvement in pulmonary symptoms after therapy with itraconazole. The patient’s bronchial wash culture was negative for fungus, but...
repeated cultures are often required to make the diagnosis. Perhaps repeated fungal culture of bronchial washes would have demonstrated pulmonary sporotrichosis. Prior to the diagnosis of sporotrichosis, the differential diagnosis of the skin lesions had been narrowed to pyoderma gangrenosum and sarcoidosis, both of which are diagnoses of exclusion. At this point, although pulmonary sporotrichosis has not been proven definitively (and it may never be proven definitively if itraconazole clears the infection completely), the diagnosis of sarcoidosis is becoming harder to support.

References

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