Brief Report

Pulmonary and Articular Sporotrichosis

Report of Two Cases

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• **Two rare forms of sporotrichosis were seen in one hospital within a two-year period. One, a case of primary sporotrichosis of the lung, represents the eighth case on record, to our knowledge. The other, a case of articular sporotrichosis, is not as rare, but is still an uncommon manifestation of the disease. The problems in management of these two patients are of interest because of the challenge to conventional concepts of therapy.**

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PRIMARY pulmonary sporotrichosis appears to be a rare disease. When we applied strict criteria (absence of lymphocutaneous lesions, repeated culture of the organism from sputum and bronchial washings or brushings, demonstration of delayed skin sensitivity, positive complement fixation or latex agglutination test, and culture of *Sporothrix schenckii* from animal inoculation of the material), we could authenticate only seven previous cases of human pulmonary sporotrichosis.[1-7] Primary pulmonary sporotrichosis presumably occurs by way of inhalation of the mycelial form of *S schenckii*, which grows on peat moss and a variety of other plants. A history of exposure to these materials is, however, not always obtainable. Several of the patients with primary pulmonary sporotrichosis were in a state of reduced immunologic competence, such as diabetes mellitus[6] and chronic alcoholism.[5,8] Others, including the patients in this report, had no sign of debility.

The occurrence of articular sporotrichosis, though less of a rarity, is far from common. We could find only 24 reports of lesions involving bone and joint in the English literature, the last two in 1972.[9,10]

Report of Cases

CASE 1.—A 36-year-old truck driver had been in good health throughout his life in Montana until a chest roentgenogram showed an infiltrate of the upper lobe of the right lung. The patient was admitted to Minneapolis Veterans Hospital for evaluation of the lesion. He could not recall agricultural or gardening activities, except for having occasionally picked roses at his sister's home. Physical examination did not reveal any pertinent abnormalities. A chest roentgenogram showed soft infiltrates in the right upper lobe with dense fibrotic strands extending to the right hilus (Fig 1).

Sputa were incubated at 25 C on Sabouraud dextrose agar, Mycosel agar, and brain heart infusion agar plates, as well as on brain heart infusion agar with added blood at 37 C. Tannish-yellow colonies could be observed within three to five days of incubation at 37 C. They consisted of budding cells and cells shaped like cigars, tadpoles, and exclamation points. Incubation at 25 C resulted in small creamy-looking colonies that slowly turned greyish-black, wrinkled, and membranous (Fig 2). They contained ovoid to spherical microconidia attached to the conidiophores in sleeve and bouquet sporulation patterns. Intraperitoneal inoculation of the sputum into mice resulted in necrotic lesions of liver, spleen, and brain that contained *S schenckii* in various stages of its tissue cycle. An intracutaneous skin test with *S schenckii* antigen was positive, as were serologic agglutination titers: by tube agglutination 1:256, by latex agglutination 1:64.

Since an anaerobic culture of the patient's sputum also disclosed *Actinomyces israelii*, he was treated for two months with penicillin G potassium, followed by intravenous administration of amphotericin B (Fungizone) to a total dose of 2.5 gm. The previously asymptomatic patient now complained of chest pain and a persistent, productive cough. He had remained afebrile. Chest roentgenograms now indicated cavitation of the pulmonary infiltrate, and, since cultures of sputa still indicated the presence of *S schenckii*, surgical removal of the lesion was indicated. After intravenous administration of an additional 35 mg of amphotericin B, the right upper lobe of the lung was resected. It contained a cavitating granulomatous lesion, from which *S schenckii* and *A israelii* were cultured with ease. There was no evidence of mycobacterial infection or neoplastic growth. Methenamine silver stains of sections of the resected pulmonary tissue also demonstrated the two organisms.

During the postoperative period of two months, the patient was given amphotericin B (50 mg on alternate days) and penicillin G potassium (10 million units/day intravenously). Sputa were now free of *S schenckii* and *A israelii*, and the patient recovered.

CASE 2.—A 77-year-old retired man had had a cystic lesion on the medial aspect of his right knee for two years prior to the hospitalization. A biopsy showed the histologic characteristics of chronic synovitis

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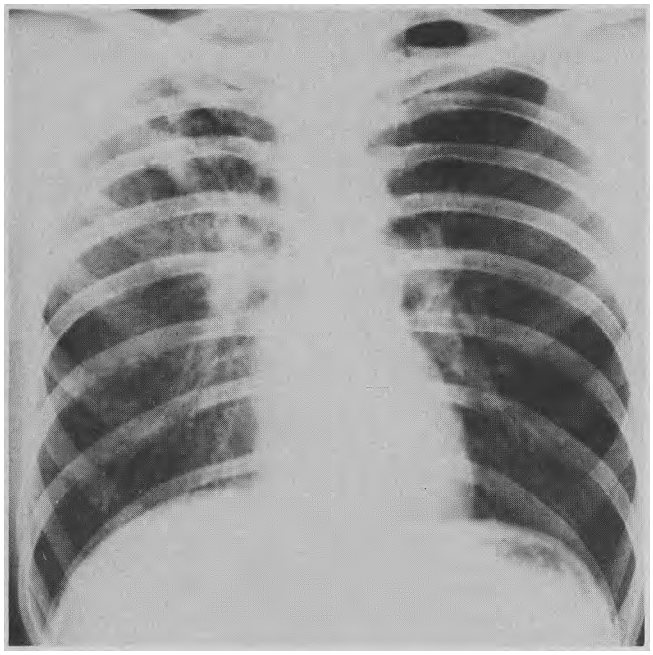

Fig 1.—Infiltrate in upper lobe of right lung, due to *S schenckii*.

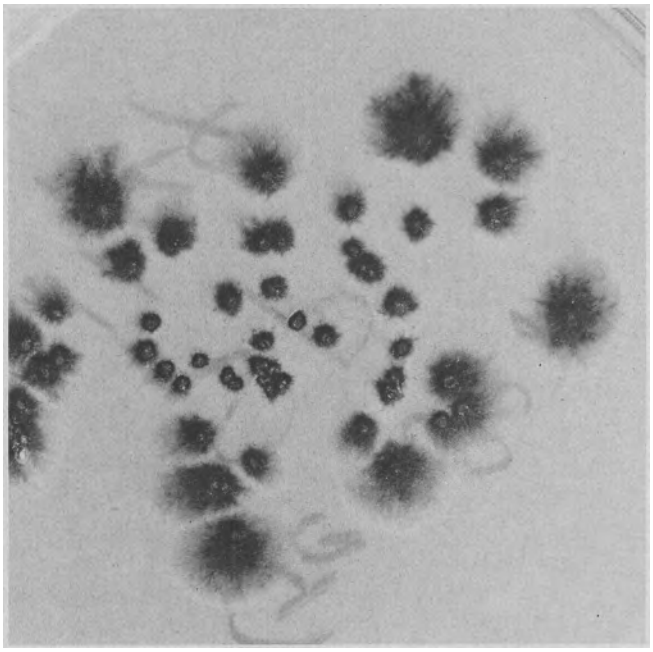

Fig 2.—Growth of *S schenckii* on Sabouraud dextrose agar plate at 25 C.

and was followed by a painful bloody effusion of the joint. On six occasions prior to the patient's referral to the Minneapolis Veterans Hospital, the joint had been aspirated and injected with hydrocortisone (Cortisol). The growing of roses had been his hobby of long-standing. He did not appear acutely ill. The right knee was grossly enlarged due to large synovial sacs at the posterior and medial aspects. The skin over these areas was purplish-red and tender. Passive motion was severely restricted, and attempts at active motion were quite painful.

Roentgenograms of the right knee showed marked narrowing of the joint space, degenerative changes of the knee joint, demineralization of the bones, and calcification of the popliteal artery (Fig 3). Results of laboratory studies included a hemoglobin level of 12.5 gm/100 ml, white blood cell count of 7,600/cu mm (76% polymorphonuclear leukocytes [PMN], 17% lymphocytes, 3% monocytes, and 4% eosinophils). The erythrocyte sedimentation rate was 63 mm in one hour (Westergren). Multiple biochemical determinations of blood and urine were within normal ranges. Cultures of aspirates of the brownish synovial fluid produced cream-colored colonies within five days on mycologic blood brain heart infusion agar plates at 37 C. After 20 days, these colonies became tan and assumed a "grape-nut" appearance. They contained oval, tadpole- and cigar-shaped bodies. Incubation at 25 C on Sabouraud dextrose agar produced the characteristically wrinkled light brown leathery colonies. They contained the typical conidiophores bearing elliptical conidiospores (Fig 4). Intraperitoneal inoculation of the joint fluid into six mice resulted in necrotic lesions of liver, spleen, and brain that contained *S schenckii* in various stages of its life cycle. Cigar bodies were the prominent forms in the peritoneal fluid of two mice killed after ten days (Fig 5). An intradermal skin test with *S schenckii* antigen was positive, and serum agglutination titers for *S schenckii* antigen were 1:32 by tube and 1:16 by latex agglutination method.

Amphotericin B was administered intravenously to a total dose of 1.95 gm. It was also injected directly into the affected knee joint, starting with 1 mg and gradually increasing to 7.5 mg/day, until a total of 198 mg had been administered locally. With this therapy, the function of the affected knee began to improve. After one month, the patient was able to stand and to walk with the help of a cane. The synovial fluid showed fungicidal activity against the autologous *S schenckii* at a dilution of 1:2 and growth inhibition at 1:4. The knee remained enlarged (by effusion), but less painful. When repeated aspirations of synovial fluid failed to grow *S schenckii*, the patient was released for further care in his home state, and has been lost to our efforts at follow-up studies.

Comment

A review of the literature concerned with the medical treatment of disseminated or visceral sporotrichosis is not encouraging. There are several reports of regression of pulmonary lesions with potassium iodide treatment,[4,5,11] but also of temporary regression of lesions without the benefit of such therapy.[8] Other reports have noted the ineffectiveness of potassium iodide treatment.[4,5,12]

The use of amphotericin B, stilbamidine isethionate, and griseofulvin (Grisactin) also has been ineffective without concomitant surgical removal of the lesion. At present, surgical excision appears to be the most reliable treatment of pulmonary sporotrichosis.

The therapeutic action of potassium iodide is not understood. Since the classic reports of De Beurmann and Gougerot,[13] it has held the undisputed position of an effective, even specific, drug, in spite of the report of Emmons et al[14] of *S schenckii* growing in media containing 10% potassium iodide. This in vitro discrepancy is negated by a long list of reported cures of lymphocutaneous sporotrichosis by the sole use of orally administered potassium iodide. Fortuitous coincidence is quite unlikely, since spontaneous clearing of cutaneous lesions has not been observed.

Levinsky[9] reports improvement with a therapeutic regimen of orally administered potassium iodide and intra-articular injections of ampho-

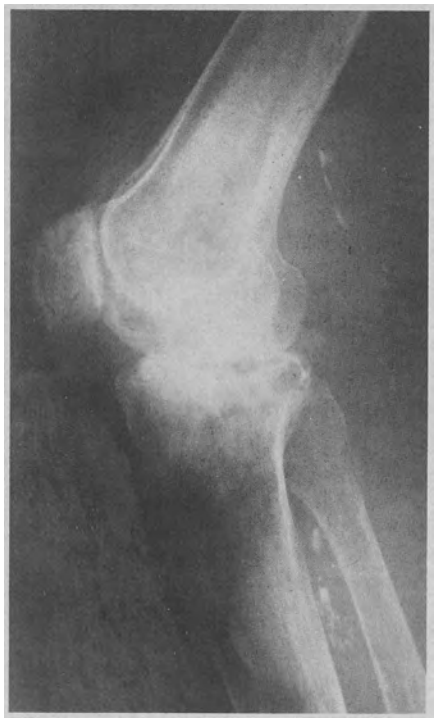

Fig 3.—Degenerative changes of right knee with narrowing of joint space, due to articular sporotrichosis.

Fig 4.—Typical conidiophores, bearing elliptical conidiospores from mycelial phase of *S schenckii*, grown on Sabouraud dextrose agar plates at 25 C. (Slightly reduced from ×450)

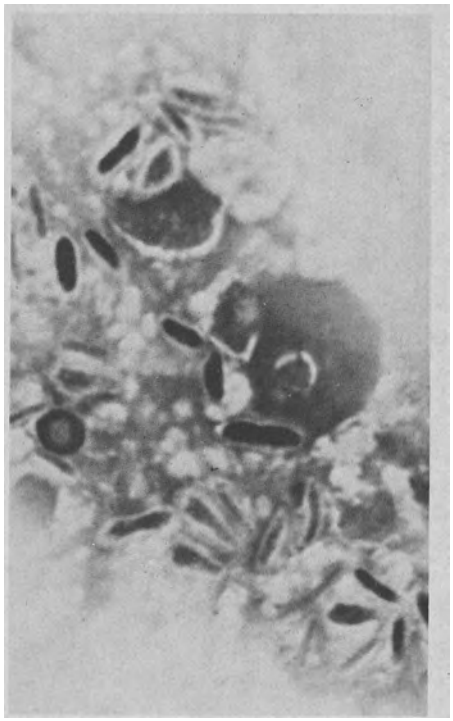

Fig 5.—"Cigar bodies" obtained from peritoneal fluid of mice, ten days after inoculation with *S schenckii*. (Slightly reduced from ×980)

tericin B. Intra-articular administration of amphotericin B resulted in definitive improvement in our patient with sporotrichosis of the knee joint. The residual joint effusion may have been due to chemical synovitis.

Cures have been reported, however, with nothing other than the use of temperatures known to be unfavorable to optimal growth of the fungus. Trejos and Ramirez[15] immersed a limb afflicted with lympho-cutaneous sporotrichosis into a water bath of 44 C four times daily for periods of 30 minutes. Clinical improvement could be observed after three days, and complete healing after one month. This type of result could be duplicated by others in experimentally infected animals as well as in humans.[16,17] The combination of locally applied heat with rubefacients, such as thurfyl nicotinate (Trafuril; available only in Britain), also was successful,[18] and microwave diathermy, together with additional locally applied heat, eliminated facial lesions on a pregnant woman.[19] The importance of temperature was also demonstrated by its enhancement of amphotericin B treatment of experimentally infected mice.[17] The results of this last experiment should encourage the combined use of amphotericin B and heat (diathermy or externally applied) in deeper seated lesions of sporotrichosis, such as in the arthritic involvement of our second patient.

Herbert F. Hasenclever, PhD, Mycology Section, National Institutes of Health, Bethesda, Md, helped in identifying the fungus and confirming our laboratory diagnosis of fungal disease in case 1.

Norman F. Conant, MD, Duke University, Durham, NC, provided the *S schenckii* antigen.

Leo Kaufman, MD, Immunology Department, Center for Disease Control, Atlanta, Ga, did the serum agglutination tests in both case 1 and case 2.

Nonproprietary Name and Trademark of Drug

Amphotericin B—*Fungizone.*

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