Sporotrichosis-An Occupational Mycosis

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Padhye, A.A. 1995. Sporotrichosis-An Occupational Mycosis. In: Landis, T. D.; Cregg, B., tech. coords. National proceedings, Forest and Conservation Nursery Associations. Gen. Tech. Rep. PNW-GTR-365. Portland, OR: U.S. Department of Agriculture, Forest Service, Pacific Northwest Research Station: 1-7. Available at: http://www.fcnanet.org/proceedings/1995/padhye.pdf

Sporotrichosis is a chronic infection usually limited to cutaneous and subcutaneous tissues. It involves all layers of skin and the subcutaneous lymphatic. The disease is caused by a dimorphic fungus *Sporothrix schenckii*. The fungus, present in nature in a variety of plants and soil, invades through a skin injury. Many times, the injury to the skin is so minor that it goes unrecognized and neglected. The fungus produces an indolent lesion which appears as a small erythernatous nodule which may remain localized or spread centrally though the local lymphatics, establishing a chain of granulomatous, ulcerating nodules. Sporotrichosis generally affects the exposed parts of the body, namely, the hands, arms and legs. Pulmonary sporotrichosis presumably results from inhalation of the fungal spores and occurs only rarely in humans with a variety of underlying conditions such as sarcoidosis, malignant neoplasms, diabetes mellitus, and chronic alcoholism. The infection may disseminate beyond lungs to become a generalized infection involving bones, joints, and the central nervous system (Goodman, 1983; Kaplan et. al., 1982; Kwon-Chung and Bennett, 1982; Rippon, 1988; Scott et. al., 1987). Extracutaneous sporotrichosis shows a marked male predominance (6: 1) in widely scattered geographic areas. Even though the cutaneous disease affects men and women of all ages, majority of cases observed are among males between 25-40 years of age.

The disease occurs in those who are exposed to material contaminated with *S. schenckii*. Occupations that predispose persons to infection include gardening, farming, masonry, floral work, outdoor labor, nursery workers, horticulturists, forestry workers, tree planters, orchid growers, and people involved in activities and exposure to contaminated soil, and vegetation such as sphagnum moss, salt marsh hay, prairie hay, or roses (Adam et. al., 1982; Brown et. al., 1947; D'Alessio et. a]. 1965; Goodman, 1983; McDonough et. al., 1970; Padhye and Ajello, 1990; Skilling, 1983). There are more than I I cases of laboratory acquired sporotrichosis (Kwon-Chung and Bennett, 1992). Sporothrix schenckii enters the body generally through traumatic implantation or rarely from inhalation spores. In nature, *S. schenckii* has been isolated from dried edible mushrooms, *Auricularia polytricha* and *Letimus edodes* imported from Asia, and from insects that are in direct contact with the fungus. The most common form of trauma to the skin involves punctures from thorns, splinters, cuts from sedge barbs, or handling of reeds, sphagnum moss, or grasses. Other types of trauma reported include: bites from rodents, parrots, cats, dogs, and horses; pecks from hens and other birds and insect stings. In Uruguay, close to half of the recognized human sporotrichosis cases are associated with the hunting of armadillos. Infection follows scratches from armadillos and injuries from the tools used to dislodge the animals from their nests and burrows. Nine-banded armadillos, (*Dasypus nevemeinctus*) often used as laboratory animals in leprosy

studies, were found to be infected with systemic sporotrichosis (Kaplan et. al., 1982).

Several reports have described large scale epidemic outbreaks of sporotrichosis. In 1927, Pijper and Pullinger (Pijper and Pullinger, 1927) reported a sporotrichosis outbreak involving 14 gold mine workers in Witwatersrand, a town near Johannesburg, South Africa. Between 1941 and 1944 in the mines of the same area, nearly 3000 workers were infected with *S. schenckii* (Brown et. al., 1947; Kwon-Chung and Bennett, 1992). The source of the remarkable epidemic in South African gold mines was traced to contaminated mine timbers over grown with S. scherickii. High humidity and high temperatures inside the mines provided ideal conditions for S. scherickii to grow on those timbers. Outbreaks of cutaneous sporotrichosis have occurred in Mississippi, Florida, Ohio, Wisconsin, Illinois, Pennsylvania, New York, Vermont, and other eastern and midwestern states of the United States (Adam et. a]., 1982; D'Alessio et. al., 1965; Dixon et. al., 1991; El-Gholl, 1986; Goodman, 1983; Grotte and Younger, 1981; McDonough, 1970; Skilling, 1983). In 1988, the largest North American epidemic of sporotrichosis occurred in 15 states involving 84 cases, with the majority of cases having associated with handling pine seedlings packed in sphagnum moss (Dixon et. al., 1991). The sphagnum moss used for packing the seedlings by a nursery in Pennsylvania proved to be the source of *S. schenckii*.

The latest outbreak of lymphocutaneous sporotrichosis was at the Disney World in Florida during March to May 1994, where 9 of the 65 workers at Nursery A involved in production of sphagnum moss topiaries developed lymphocutaneous sporotrichosis (Hajjeh, 1995). Fungal cultures of some sphagnum moss samples used in topiaries at Nursery A since January 1, 1994, and collected at different stages of topiary production grew S. schenckii.

NATURAL HABITAT OF S. SCHENCKII

Sporothrix scherickii has been isolated from soil, humus, fertilizer, the stems of beech trees, vegetable debris, moist wood, and refrigerated meat. It has also been isolated from many types of plants, such as: horsetails, rose bushes, cacti, salt meadow hay, residual packing straw, carnations, wood splinters, and most commonly sphagnum moss (Adam et. al., 1982; D'Alessio et. al., 1965; Grotte and Younger, 198 1; Padhye and Ajello, 1990; Skilling, 1983). The fungus is worldwide in distribution, occurring in all temperate and tropical climates. Its wide distribution is illustrated by its isolation from soil and plant material from all parts of the world.

CLINICAL FORMS OF SPOROTRICHOSIS

Cutaneous Lymphatic (Lymphocutaneous) Sporotrichosis:

Infection is usually acquired by traumatic implantation with injury to the skin caused by the prick of a thorn, splinter or similar object that is contaminated with *S. schenckii*. Following such a penetrating wound, a papule may develop at the site within two to three weeks. The papule slowly enlarges and ulcerates (Figure 1). Without treatment, secondary lesions develop along the lymphatic channels, draining the initial site of infection. The lesions form nodules, which ulcerate and drain (Figure 2). Without treatment, lesions persist for years.

Figure 1. An early ulcerating lesion on a finger caused by Sporothrix schenckii

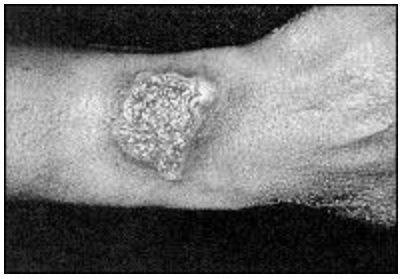

Figure 2. An ulcerating, chronic lesion on a wrist caused by schenckii

Cutaneous Nonlymphatic Sporotrichosis:

In some cases, the lesion remains localized and does not involve the lymphatic system. Such a solitary lesion usually becomes chronic. These "Plaques" and "fixed" type of lesions, as they are often referred to, can persist for years, the longest being known to persist for 26 years (Villaca-Neto et. al., 1988). Although the lesion may temporarily wane, it regresses eventually, and spontaneous resolution is not common. These chronic, single lesions commonly occur on face, neck, trunk, arm or hand and can vary in appearance. They are usually erythematous papules or plaques that tend to become ulcerated or verrucous (Figure 3). In some cases, skin lesions may result from hematogenous dissemination. There are several lesions scattered over the body, not on the same extremity, or even at the site of trauma.

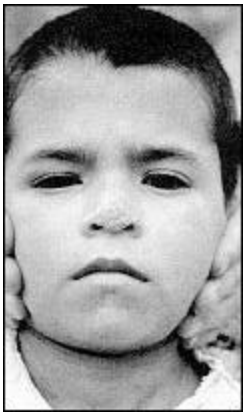

Figure 3. A solitary, granulomatous, fixed type lesion on nose caused by *S. schenckii*

Extracutaneous Sporotrichosis:

This includes the following types:

1) Pulmonary, with the associated symptoms of cough, low-grade fever, loss of weight and sputum production. In some cases, hemoptysis occurs, and can be massive, even fatal. The infection results in cavitation in the lungs. The disease is more commonly seen in males (6:1 male to female ratio) than in females. The natural course of the lung lesion is gradual progression to death, although spontaneous remission of noncavitory pneumonia has been reported.

2) Osteoarticular which involves the bones, joints, and bursa. The majority of patients in this category present with the indolent onset of stiffness and pain in a large joint. Radiologic evidence of osteomyelitis develops slowly with diffuse osteolysis. Almost all cases of arthritis involve knee, elbow, ankle or wrist. Although fever may be present early in the illness, most patients are afebrile. Fluid accumulation in the olecranon or prepatellar bursa may occur as may Baker's cysts. In untreated patients, additional joints become involved and skin over the joint becomes erythematous and may eventually develop a draining sinus.

3) Ocular which is caused by trauma to the eye by material contaminated with *S. schenckii* or occurs as a result of dissemination of the disease;

4) Central nervous system sporotrichosis: a rare disease with symptoms of headaches, back pain and mental confusion, and

5) Multifocal form: patients may present with multiple skin lesions resulting from hematogenous spread, with or without lung or bone lesions. Although patients who are apparently immunologically intact may develop hematogenously disseminated, fatal infection only rarely, however, in immunosuppressed patients, the probability of hematogenous dissemination to the skin and bones increases. Patients with acquired immunodeficiency syndrome (AIDS), or other severely depressed states of immunosuppression are at greater risk of dissemination of infection.

Diagnosis:

A positive diagnosis of sporotrichosis is made by:

1) Direct examination: Although yeast form cells may be seen occasionally in a Gram-stained smear, a wet mount of pus, or a biopsy specimen, direct examination is often not helpful because of the paucity of fungal cells. By examining multiple slides of biopsy tissue stained with PAS or GMS, one can demonstrate the presence of *S. schenckii* yeast cells. These fungal yeast cells may be spherical and surrounded by a PAS-positive capsule, or have uncharacteristic elongated "cigar-shaped" cells (Figure 4). The fluorescin-labeled *S. schenckii* antiglobulins brightly stain yeast cells of *S. schenckii*, even when they are few in number and provide a rapid and reliable diagnostic test to diagnose sporotrichosis (Kaplan, 1982; Kaufman, 1976).

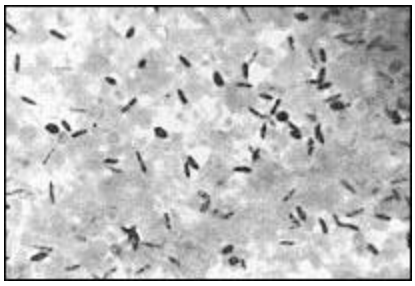

Figure 4. Cigar-shaped yeast-like cells of *S. schenckii* in spleen tissue, Gomori methanamine silver + hematoxylin and eosin X160.

2) Isolation of *S. schenckii* from clinical material: The causal agent s. *schenckii is* a causal fungus, that is, it grows as a mycelial fungus at room temperature and in nature. It grows on mycologic media producing moist, glabrous, white colonies, which soon become gray to black and develop radial striations (Figure 5). Microscopically, hyphae are hyaline, branched, septate bearing lateral and terminal conidiophores. The conidiophores produce ovoid, spherical, pyriform conidia, 2 - 4 x 4 - 6 microns in size, home singly on denticles in a rosette-shaped manner, or in a form of a bouquet.

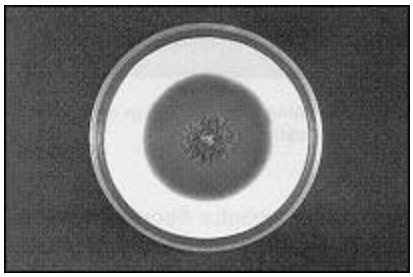

Figure 5. Two-week-old dark dematiaceous colony of *S. schenckii* on Sabouraud dextrose agar at 250C

The conidia are also produced directly on the sides of vegetative hyphae, and are borne on small denticles (Figure 6). As colony ages, the dark color of the colony is due to dark-walled pigment produced by the conidia. In animal and human tissue, S. *schenckii* reproduces by budding like a yeast. The yeast form can be produced in vitro by culturing mycelia or conidia on rich media such as brain heart infusion (BHI) agar, or Pine's medium, or BCG agar at 370°C. The yeast form colony appears dull white, with a dry wrinkled surface. The blastospores produced in vitro are oval, subglobose, or cigar-shaped. The conversion of the mycelial form to a yeastlike form at 370°C confirms the dimorphic nature of the fungus and serves as a confirmatory test for the conclusive identification *of S. schenckii.*

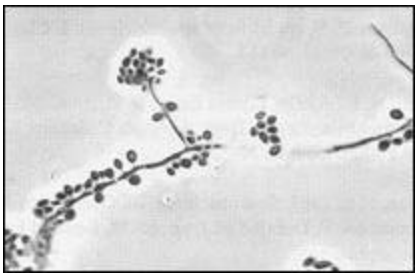

Figure 6. Lateral conidiophore bearing ovoid conidia in a rosette manner and single conidia produced laterally on vegetative hyphae X 160.

Serology:
Serological tests for sporotrichosis may be applied to sera from patients with skin lesions, subcutaneous nodules, bone lesions, lymphoadenopathy, or pulmonary disease. Because of its sensitivity (94%), high specificity, and ability to provide results in 5 minutes, the LA (latex agglutination) test is used routinely in the clinical laboratory. The TA (tube agglutination) test has comparable sensitivity, but sera being tested for sporotrichosis may show false-positive reactions with 1: 8 and 1: 16 dilutions of sera from patients with leishmaniasis. Slide latex agglutination titers *of* 1:4 or greater are considered presumptive evidence *of* sporotrichosis. Sera from patients with localized, subcutaneous, disseminated subcutaneous, or systemic sporotrichosis may show titers ranging from 1:4 to 1: 128. The test has limited prognostic value, since antibody levels may show little change during and after convalescence (Kaufman, 1976; Scott *et. al,* 1987).

PROTECTIVE MEASURES AND CONTROL

a) Workers handling sphagnum moss or those likely to be traumatized by objects such as thorns, splinters or sticks should wear gloves and long-sleeved shirts to protect their hands and arms. Heavy clothing or an apron should also be worn while working to prevent trauma to the body, as well as thick shoes to protect feet.

b) After handling potentially contaminated material, individuals should thoroughly wash their arms and other exposed parts *of* the bodies with soap and water to reduce chances of infection.

c) If any injury by a thorn or splinter, etc. is noticed, a disinfectant such as tincture of iodine should be applied immediately (El-Gholl *et. al,* 1986).

d) Supplies of sphagnum moss should be stored indoors under **dry conditions.** Sphagnum moss with a high moisture content stored in a warm environment supports the proliferation of S. *schenckii.* When disturbed, the airborne conidia *of S. schenckii* may be inhaled by workers and induce pulmonary infection (El-Gholl *et. al,* 1986; Goodman, 1983).

e) In areas likely to contain dust or aerosols from the handling of sphagnum moss, proper exhaust fans with biologic filters should be installed. In such areas, a protective mask should be used to avoid inhalation of the infectious conidia of S. *schenckii*.

f) All storage and packing areas should be decontaminated monthly with a disinfectant.

g) Stored sphagnum moss should be regularly cultured for the presence of S. *schenckii* (El Gholl *et. al.,* 1986)

Unfortunately there are no established methods for decontaminating sphagnum. moss infected with *S. schenckii*. Chemical decontamination with formaldehyde or methyl bromide has been suggested, but has never been used on a regular basis (Padhye and Ajello, 1990). Burning of infested moss is an effective control method.

Treatment of Sporotrichosis:

Cutaneous lesions respond well to treatment with orally administered potassium iodide. A variety of side effects and the slow response to treatment require perseverance. The bitter taste of KI and the development of nausea, rumbling stomach, excessive salivation, and anorexia are better tolerated if the dose is begun small and gradually increased. A common initial dose is 10 drops of saturated KI solution given three times daily. The bitter taste is lessened if the patient drinks water or juice immediately after taking the medicine. The dose is increased once a week by about five drops per dose up to 25 to 40 drops three times daily for children under 10 years, and up to 40 to 50 drops three times daily for adults. This dose is continued till all lesions become flat and soft, a period of 6 to 12 weeks being usual. Immersing lesions in hot water for 20 to 30 minutes three times daily also helps. Heating pads or pocket warmers have been used with some success. Occasionally cutaneous sporotrichosis responds well to ketoconazole 10 mg/kg once daily, but success has been noted only in a small number of cases. Oral itraconazole 100 to 200 mg, given daily for several months has been successful in a small number of patients (Kwon-Chung and Bennett, 1992).

For pulmonary sporotrichosis involving only one lobe without any contraindication to surgery and no lesions anywhere else, the best treatment is by surgery. Although use of amphotericin B in doses totaling over 2 grams for adults has cured some patients with pulmonary sporotrichosis,

therapeutic failures are common. The combination of flucytosine with intravenous amphotericin B may be useful in refractory cases. Local injections of amphotericin B into the knee, olecranon bursa, or Baker's cyst may also be useful in refractory cases. Ketoconazole (400 to 800 mg daily) or itraconazole (400 mg daily) has improved up to half the cases of osteoarticular sporotrichosis, but the treatment may extend months or years to be effective. These drugs are less effective in cavitory pulmonary sporotrichosis (Kwon-Chung and Bennett, 1992).

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