

Systemic sporotrichosis

Pulmonary complications of a well-known cutaneous fungal disease

A case report

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Summary

Pulmonary involvement during *Sporotrichium schenkii* infection can present as either primary pulmonary or systemic disease. The clinical and radiological features in the primary form closely resemble those of adult-type tuberculosis. On clinical, radiological and histopathological grounds pulmonary involvement during systemic spread can be difficult to distinguish from sarcoidosis. The diagnostic and therapeutic problems encountered in a woman with systemic sporotrichosis infection with pulmonary involvement are described.

S Afr Med J 1982; 62: 451-453.

The fungus *Sporotrichium schenkii* exists as a saprophyte on organic material such as decaying vegetable matter, moss, bluegum wood and thorns. Labourers, farmers, florists and horticulturists are at risk of being infected,^{1,2} and the organism usually enters the body through abrasions or via skin penetration by infected material.³ It occurs world-wide, more than 3000 cases of cutaneous involvement having been documented,³⁻⁵ and South Africa is not excluded from this global distribution. This high prevalence calls for awareness of the clinical and radiological manifestations of primary pulmonary and systemic *S. schenkii* infection in developing countries.

Primary pulmonary sporotrichosis is rare, less than 50 cases having been reported in the world literature,⁶ and important because the clinical features of weight loss and haemoptysis and the radiological features of upper lobe cavitation and soft infiltrates are indistinguishable from those in adult-type tuberculosis.⁷ Patients with this clinical and radiological picture who are persistently sputum-negative for acid-fast bacilli should be investigated for *S. schenkii* infection. Two cases of systemic sporotrichosis with pulmonary disease (specifically, the combination of skin, bone and lung involvement) have been described.^{7,8} The present case provides additional information concerning this rare condition and emphasizes hitherto undescribed diagnostic, pathological and therapeutic features.

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Case report

This 56-year-old woman came from the Western Cape town of Moorreesburg. She gardened as a pastime but was not aware of having injured herself while so occupied or of having been exposed to any of the known forms of contaminated material. During September 1979 she noticed a tender red nodule on the dorsomedial aspect of her right foot. The lesion enlarged and ulcerated with exudation of a serous fluid. Three weeks later nodules and ulcers had spread over both legs, torso and skull. She was systematically ill with pyrexia, anorexia and weight loss. Respiratory symptoms were absent.

On clinical examination the patient appeared chronically ill, with a pulse rate of 100/min and a blood pressure of 110/70 mmHg. Oval to round ulcers up to 2 cm in diameter were noted on the right foot and right thigh, in the left popliteal fossa, on the scalp and over the right scapular region. The ulcers had indurated edges and secreted a serous fluid. Several nodules were present on the abdomen. The urine was normal. The haemoglobin concentration was 13,2 g/dl and the white cell count 8500/ μ l with 52% neutrophils, 38% lymphocytes, 8% monocytes, 1% eosinophils and 1% basophils. Blood sugar, electrolyte, urea and creatinine values, serum calcium and phosphate values and liver function were within normal limits. The alkaline phosphatase value of 125 IU/l was moderately raised (normal 30-85 IU/l).

Protein electrophoresis revealed a diffuse elevation of the gamma peak which was interpreted as a manifestation of a chronic inflammatory process. Bone marrow aspiration and trephine biopsy showed normal cellularity and precursor cell representation, with no signs of malignant disease. Radiographs of the chest and bones revealed a diffuse soft nodular infiltrate up to 1 cm in size in both lung fields, with no cavitation, hilar nodes or pleural fluid accumulation present. There was lytic destruction of the first metatarsal bone of the right foot, but the skull, ribs and pelvis were normal. Tests for systemic lupus erythematosus and syphilis were negative. Direct microscopy and culture of the pus, sputum, urine and alveolar washings for tubercle bacilli and other organisms were negative. Negative delayed hypersensitivity skin reactions to 10 U purified protein derivative, *Trichophyton*, *Candida* and streptokinase-streptodornase provided evidence of *in vivo* deficiency of T-cell-mediated immunity. This was borne out by a negative response to dinitrochlorobenzene sensitization. Differential determination of T cells and B cells was negative, figures of 46% and 21% respectively being obtained. Biopsy of a skin ulcer showed numerous micro-abscesses surrounded by epithelioid cells, Langhans cells and foreign-body-type giant cells. The bulk of the inflammatory reaction was situated in the mid- and deep dermis. In the centre of two of the micro-abscesses the asteroid body typical of *S. schenkii* was seen (Fig. 1). The fungus was cultured from the pus swabs obtained from the skin lesions. To exclude underlying malignant disease or sarcoidosis of the lung, alveolar lavage and transbronchial biopsy were performed. The differential count of the alveolar lavage fluid was normal and no

Date received: 23 December 1981.

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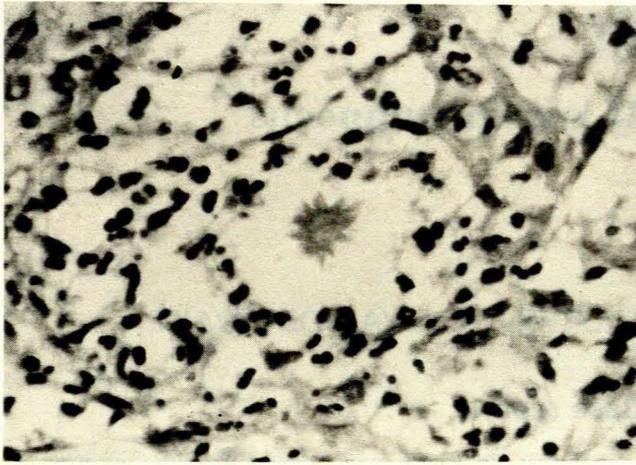


Fig. 1. Asteroid body of *S. schenckii* in centre of a micro-abscess (H and E).

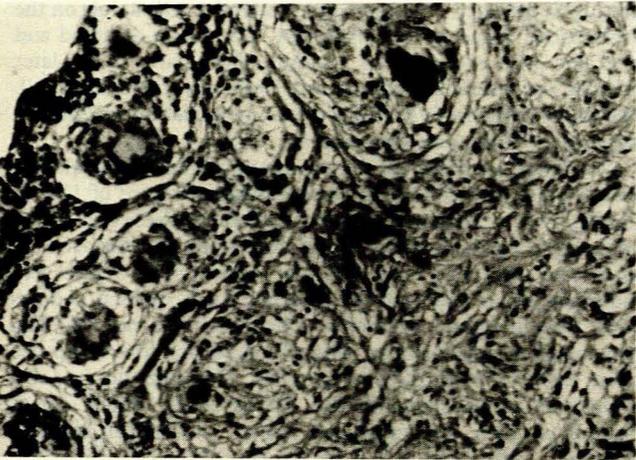


Fig. 2. Epithelioid cell granulomas with giant cells being replaced by fibrous tissue (H and E).

fungal growth was cultured from it. Transbronchial biopsy revealed three epithelioid granulomas of the non-necrotizing variety. No fungi could be demonstrated in the sections and the lung tissue between the granulomas appeared normal. There was uncertainty as to whether the transbronchial biopsy was representative, and an open lung biopsy was subsequently performed. This revealed groups of epithelioid cell granulomas with abundant Langhans cells and foreign-body-type giant cells. The granulomas appeared to have existed for some time because they were enclosed by fibrous connective tissue or in places partially replaced by hyalinizing fibrous connective tissue (Fig. 2). There was no evidence of necrosis, and fungal staining was negative.

Initial treatment consisted of potassium iodide drops 500 mg 4 times a day. During the 1st month of treatment the skin lesions healed. Intravenous amphotericin-B (Fungizone; Squibb) was then added as treatment for the systemic sporotrichosis. She received 40 mg/d for 5 days of the week. A total amount of 1.3 g was administered over a period of 2 months. Treatment had to be temporarily discontinued when the serum urea and creatinine levels rose to unacceptable levels. Dietary and intravenous potassium was given because of potassium loss caused by the amphotericin-B. The bone lesions healed and the lung infiltrates either became fibrotic or cleared. She was discharged after 6 months in hospital with no further treatment. One year later she was readmitted with complaints of appetite and weight loss, but with no respiratory complaints or recurrence of the skin lesions.

On clinical examination on this occasion the patient was afebrile with a pulse rate of 80/min and a blood pressure of 110/70 mmHg. The scars of the previous skin lesions were present but no new nodules or ulcers had formed. No respiratory or systemic abnormalities were detected.

The main reason for her second admission was that a chest radiograph showed extensive nodular and soft infiltrates with loss of lung volume (Fig. 3). Osteoporotic changes were noted in the bones of feet and ankles in the areas of previous involvement, but these changes were not associated with new bone disease. A haemoglobin concentration of 12.0 g/dl, a white blood cell count of 5800/ μ l and an ESR of 70 mm/1st h were recorded. A scintigram of the liver and spleen demonstrated no involvement of these organs. Bronchoscopy, alveolar lavage and transbronchial biopsy were repeated. Cultures of the alveolar lavage effluent and transbronchial biopsy specimens on the appropriate medium once again failed to produce a growth of *S. schenckii*. The features noted previously, i.e. nonspecific granulomas, were again found on histopathological evaluation of the lung tissue. Amphotericin-B to a total of 2100 mg was administered intravenously on weekdays during the ensuing months in hospital. Hydrocortisone 100 mg/d was added to the intravenous infusion to prevent chemically induced thrombophlebitis, and potassium supplementation was given daily. During the last 2 weeks of therapy the patient developed drug fever as manifested by a normal temperature during weekends with recurrence when treatment was reinstated during the week. While on treatment

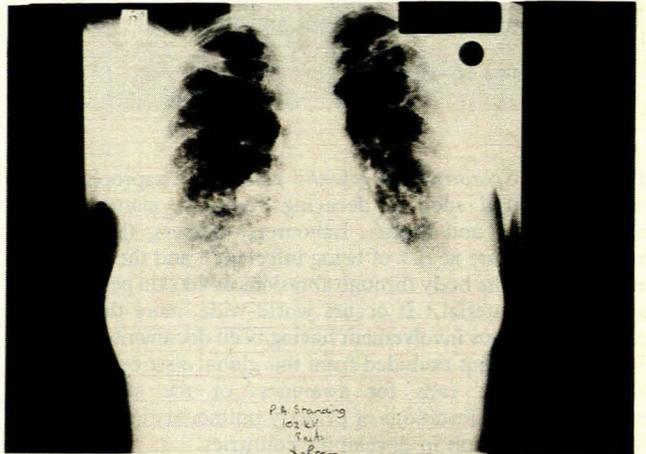


Fig. 3. A nonspecific diffuse reticulonodular pattern without pleural involvement. There is extensive pulmonary involvement with systemic sporotrichosis.

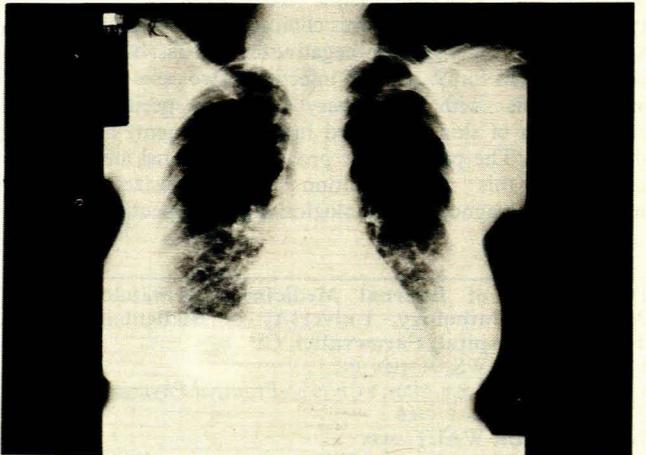


Fig. 4. Clearing of soft infiltrates with residual fibrotic changes after 3 months of treatment.

her body mass increased by 3,5 kg and clearing of the chest radiograph was evident during this period (Fig. 4). During a follow-up period of 6 months without treatment no new lung lesions appeared and she remained clinically well.

Discussion

Sporotrichosis may present clinically in one of the following ways: (i) primary cutaneous involvement; (ii) primary pulmonary disease; (iii) unifocal systemic involvement; and (iv) multifocal systemic involvement.

In the world literature 2 cases of systemic sporotrichosis with pulmonary involvement have been documented. Wilson *et al.*⁸ mention a patient with a solitary pulmonary lesion and generalized subcutaneous nodules, reported on in a Chinese medical journal. In a description of the other case, Comstock *et al.*⁷ emphasized the radiological differences between primary pulmonary and systemic sporotrichosis, the latter being characterized by a bilateral diffuse nodular appearance. A similar radiological pattern was present in our patient in whom skin and bone involvement had been found, a triad which resembles the description of the previous 2 cases.

Features of this form of pulmonary sporotrichosis are a lack of pulmonary signs and symptoms and radiological nonspecificity. In contrast to the ease with which *S. schenckii* organisms can be isolated from the sputum and lung tissue in the primary pulmonary disease, a noteworthy feature in this case was inability to culture the organism from alveolar lavage effluent and lung tissue specimens. Among the cases of cutaneous sporotrichosis reported from the RSA, Lurie found 1 patient with lung involvement.⁵ The inability to culture *S. schenckii* from lung tissue specimens, and the predominantly granulomatous histopathological changes, led to the conclusion that the patient suffered from pulmonary sarcoidosis with cutaneous and bone sporotrichosis. In retrospect this patient probably had systemic sporotrichosis with pulmonary involvement.

The histopathological features of the lung lesions in patients with systemic sporotrichosis has not previously been described. There are two possible explanations for the predominantly granulomatous changes found in biopsy specimens from the lung. They may relate to an underlying disease process such as sarcoidosis in which a generalized deficiency of T-cell-mediated activity may predispose to fungal infection. A second possibility is that a predominantly T-cell-mediated immune-inflammatory reaction adequately controls the local growth of the fungus and induces the clinical, radiological and histopathological lung

patterns found in the systemic form of the disease. Such an immunopathogenic mechanism may, however, be questioned in this patient, as a lack of T-cell-mediated activity was demonstrated by *in vivo* techniques. A possible explanation for this discrepancy may be that T-cell reactivity to the specific antigen was not tested.

The remarkable clinical, radiological and histopathological similarities between systemic sporotrichosis and sarcoidosis need to be considered when treatment for the latter condition with high doses of steroids becomes essential. This is particularly relevant in an African environment, where aggressive forms of sarcoidosis which involve bone, skin and lungs occur. In this case radiological clearing on antifungal therapy provided strong evidence that the histopathological changes were related to the established systemic sporotrichosis infection and that the granulomas detected histopathologically were not caused by an additional disease process.

Primary pulmonary sporotrichosis carries a bad prognosis, but nothing is known about the clinical course of the systemic disease. Clearing of the skin lesions was induced with potassium iodide, but prolonged courses of treatment with amphotericin-B had to be employed for the pulmonary involvement. The relapse of the pulmonary disease after 2 months of therapy provides evidence of the resistance of systemic sporotrichosis to treatment. Too short a period of follow-up has elapsed since the second course of amphotericin-B to determine whether the fungal infection has been completely eradicated.

Interstitial disease patterns in patients with few or no signs and symptoms are frequently found in communities where pneumoconiosis, sarcoidosis and even asymptomatic forms of tuberculosis occur. It is evident that if sporotrichosis is prevalent in the same population group it can pose a diagnostic and therapeutic problem.

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