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CLINICAL REPORT

Cutaneous *Scedosporium apiospermum* Infection in an Immunocompromised Patient and a Review of the Literature

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Scedosporium apiospermum* (also known as *Pseudallescheria boydii*) is a ubiquitous filamentous fungus. This fungus is known as a cause of mycetoma, which may occur in a normally immune host following trauma. However, in an immunocompromised host, *S. apiospermum* may cause a life-threatening infection. We describe a case of *S. apiospermum* infection of the right hand in a patient who was receiving long-term immunosuppressants for adult Still's disease. We also review the cases of *S. apiospermum* infection with cutaneous manifestations reported between 1998 and 2003.** ***Key words: **Scedosporium apiospermum; Pseudallescheria boydii;** ***cutaneous; immunocompromised host.***

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Scedosporium apiospermum (synonym: *Monosporium apiospermum*), also referred to as *Pseudallescheria boydii* (synonym: *Allescheria boydii*), is a ubiquitous fungus, which can be isolated from soil, polluted water and sewage (1–5). There is no difference in the virulence between the asexual stage of *S. apiospermum* and other stages (i.e. *P. boydii*, etc.) (2). The fungus causes not only mycetoma, but also pneumonitis, osteomyelitis, arthritis, meningitis, brain abscess, endocarditis, thyroid abscess and cutaneous and subcutaneous granuloma (5, 6).

Among *Scedosporium* spp., *S. inflatum* (synonym: *S. prolificans*) is another human pathogen. Various types of infections with *S. inflatum* have been reported, and invasive infections in immunocompromised patients have been described (7).

In recent years, an increasing number of cases of human disease with *S. apiospermum* has been reported, probably due to widespread use of corticosteroids, immunosuppressants, antineoplastics and broad-spectrum antibiotics (5, 6, 8). We describe here a case of cutaneous *S. apiospermum* infection in a man who was undergoing long-term therapy with corticosteroids. We also summarize cases of cutaneous manifestations of *S. apiospermum* infections.

CASE REPORT

A 65-year-old man presented with a 4-week history of a lesion on the right hand. He had adult Still's disease that had been treated with corticosteroids and other immunosuppressive agents for 13 years. At the time of presentation, his immunosuppression included oral betamethasone (1.5 mg daily) and methotrexate, (2.5 mg and 5 mg every other day). Physical examination revealed a fluctuating subcutaneous abscess with spontaneous purulent discharge. Grains could not be observed. Laboratory studies disclosed: WBC count 7980 cells/mm^3 (90.4% polymorphonuclear cells, 6.6% lymphocytes, 3.3% eosinophils and 1% monocytes); RBC count 3.84×10^6/mm^3; haemoglobin level 10.7 g/dl; haematocrit 34.6%; total protein level 5.9 g/dl; blood sugar 108 mg/dl; C-reactive protein (CRP) 1.56 mg/dl (normal <0.10 mg/dl). Direct microscopy of the pus and the scale was negative. Bacterial culture grew *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Cultures for acid-fast bacilli were negative. The patient was treated with oral minocycline 200 mg daily. However, 2 weeks later the lesion had spread and enlarged. There were new small satellite papules and pustules on the dorsal surface of the right hand. Although repeated direct microscopic examinations and the cultures of superficial scrapings were negative for fungus, treatment with oral itraconazole, 100 mg daily, was added. However, the lesion did not improve but spread. In addition, there was a new small nodule on the extensor side of the right middle finger (Fig. 1). Ultrasonographic examination revealed that the nodule was cystic with a diameter of 5.8 mm. At biopsy the nodule was well demarcated and contained pus but no grains. The wall of the cystic structure contained mixed inflammatory cells and branching hyphae. Periodic acid Schiff (PAS) staining revealed obvious, septate branching hyphae (Fig. 2). Cultures for fungus of both the biopsy specimen and the pus were performed and yielded white cottony colonies that later turned grey. Microscopic examination showed septate hyphae with conidia borne terminally, either singly or in small groups on elongated simple or branched conidiophores or laterally on hyphae. The conidia were ovoid, with the larger end toward the apex, and appeared to be cut off the base, with a distinct wall (Fig. 3). The fungus

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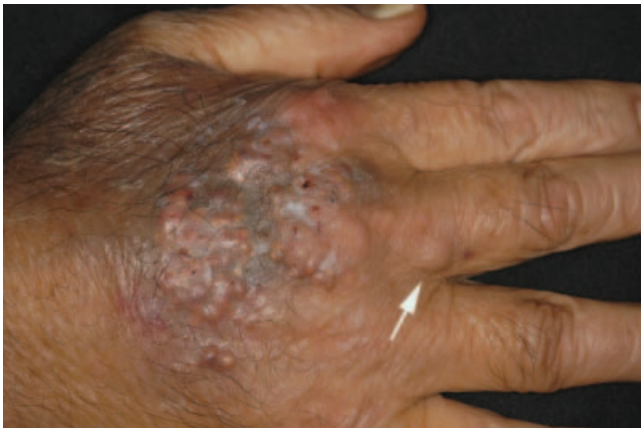

Fig. 1. Clinical appearance before the biopsy. The initial lesions were enlarged and a small nodule appeared (arrow) in the extensor of the right middle finger.

was identified as *S. apiospermum*. The patient was treated with oral itraconazole 200 mg daily and drainage. The number of nodules and pustules gradually decreased. However, 3 months later, the patient died of bacterial pneumonia.

LITERATURE REVIEW

We searched the literature on cutaneous manifestations of *S. apiospermumi* infection using PubMed (National Library of Medicine, USA). The key words were *P. boydii*/*S. apiospermum*/cutaneous/subcutaneous/lymphocutaneous.

Between January 1998 and November 2003, we encountered 19 cases of *S. apiospermum* and *P. boydii* infection that presented clinical manifestations of skin. Table I summarizes the demographics and clinical variables in 20 patients including our case [1–5, 8–20].

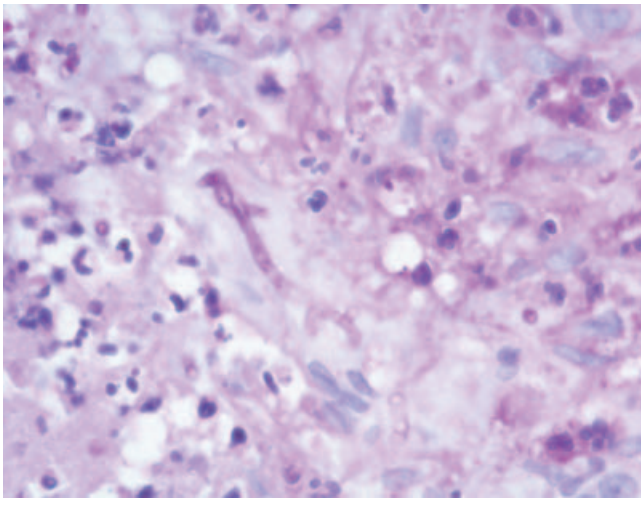

Fig. 2. Periodic acid Schiff staining of a cystic nodule revealed obvious septate and branching hyphae.

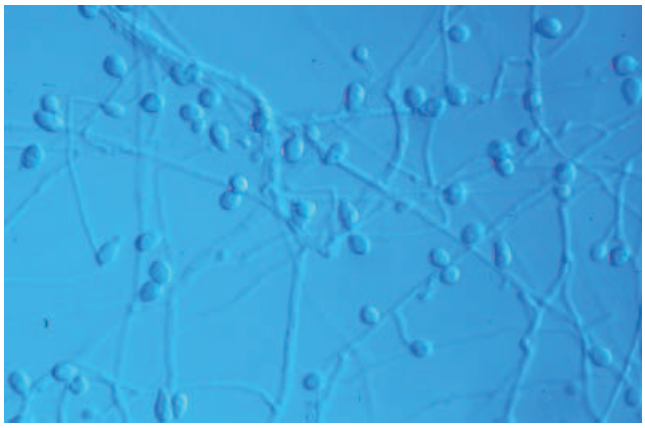

Fig. 3. Microscopic appearance of the slide culture at room temperature.

DISCUSSION

Miyamoto et al. (17) summarized 14 cases of cutaneous *S. apiospermum*/*P. boydii* infection between 1994 and 1997 (i.e. 2.3 cases annually). We summarize 19 cases reported between 1998 and November 2003 (i.e. 3.3 cases annually). The number of cases thus appears to be increasing in the literature. Recently, *S. apiospermum*/*P. boydii* has emerged as a cause of disease in immunocompromised patients, with potentially devastating consequences (3, 4, 6, 8). In our summary of 20 patients, 18 were immunocompromised – 16 were treated with immunosuppressive drugs and 2 had leukaemia. In the review by Miyamoto et al. (17), almost all patients were immunosuppressed. Cutaneous injury may be responsible for localized infections (3). In our summary, there were 16 cases with localized infection, but only 4 patients (25%) had an obvious history of injury. However, all localized lesions were on extremities, suggesting that minor injuries had triggered the infection.

Treatment is not well defined. The choice of antifungal drugs influences the prognosis because *S. apiospermum* is often resistant to amphotericin B and 5-flucytosine (4, 21). The fungus is most responsive to the imidazoles. Miconazole has shown high activity *in vitro* against clinical isolates of *S. apiospermum* (16) and is the treatment of choice. But in some countries, miconazole is no longer available (22). There are many reports of both successful and unsuccessful treatment of *S. apiospermu*m infection with itraconazole (22). Voriconazole is a new triazole agent exhibiting excellent *in vitro* effect on most clinical isolates of *S. apiospermum* (2, 16). In a report by Girmenia et al., voriconazole resulted in improvement even of cases with dissemination (11).

For the present, surgical debridement or drainage in addition to antifungal drugs is recommended (1, 23) and this coincides with our review of the literature.

Table I. *Summary of demographics and clinical variables in 20 patients*

Ref	Age/Sex	Underlying medical conditions	Immunosuppressive agents	History of trauma	Clinical features	Treatment	Outcome
1	65/M	Rheumatoid polyarthritis	Methylprednisolone	No	Local Right foot, skin and bone	Itraconazole	Cured
8	58/F	Rheumatoid polyarthritis	Corticosteroids Cyclosporine	No	Local Left forearm	Itraconazole	Cured
2	58/M	Kidney transplantation Chronic glomerulonephritis	Tacrolimus Prednisone	No	Local Left leg and foot	Itraconazole (not effective), voriconazole	Cured
9	65/M	Heart transplantation Dilating cardiomyopathy	Cyclosporine Prednisone Azathioprine	No	Local Left forearm	Itraconazole (not effective), miconazole and surgery	Cured
10	18/F	Hepatitis-associated severe anaemia, BMT, GVHD	Methotrexate Cyclosporine Methylprednisolone	No	Disseminated	Liposomal amphotericin	Death Systemic fungal infection
5	67/M	Heart transplantation Viral myocardia	Tacrolimus Prednisone	Yes, puncture while gardening	Disseminated	Itraconazole, voriconazole	Death Progressive multi-system failure
4	81/M	Lung fibrosis	Prednisone	Yes (gardening?)	Disseminated	Itraconazole	Recurrence
11	25/M	Acute myeloid leukaemia	No	No	Disseminated	Amphotericin B, voriconazole	Death Massive bleeding
12	83/M	Aplastic anaemia Diabetes mellitus	Prednisone	No	Local Dorsum of the hand and forearm	Itraconazole and hyperthermia	Death Bacterial pneumonia
13	35/M	Acute lymphoblastic leukaemia	No	Not described	Disseminated	Amphotericin B (not effective), voriconazole	Death Multiple brain abscesses and progressive fungal infection
14	79/M	Bronchospasm	Corticosteroids	No	Local Forearm	Itraconazole	Death
3	64/M	Systemic sarcoidosis	Prednisone	No (gardening?)	Local Right elbow	Ketoconazole (recurrence), itraconazole	Cured
15	45/F	Renal failure	Corticosteroids	No (injured 2 years before)	Local Left lower extremity	Not described	Not described
16	69/F	Rheumatoid arthritis, Sjögren's syndrome CRF, hepatitis C	Prednisone	Yes, catheter puncture site	Local Left upper extremity	Surgical debridement and itraconazole	Cured
17	69/M	Polymyositis	Prednisolone	No	Local Back of the right hand	Topical application of antifungal drug due to poor general condition	Death Liver failure, DIC
18	65/F	Degenerative change (knee and back pain)	Dexamethasone	No	Local Left forearm	Surgical drainage and itraconazole	Cured
18	48/M	No	No	Yes, pricked by thorns	Local Right hand	Surgical drainage and itraconazole	Cured
19	55/M	No	No	No	Local Left foot	Surgical excision and itraconazole	Cured
20	60/M	Renal transplantation Hypertension	Prednisone Tacrolimus	No (but walked barefoot)	Local Left foot	Itraconazole	Cured
This study	65/M	Adult Still's disease Diabetes mellitus	Betamethasone Methotrexate	No	Local Dorsum of the hand	Punctual drainage and itraconazole	Death Bacterial pneumonia

BMT, bone marrow transplantation; GVHD, graft versus host disease; CRF, chronic renal failure; DIC, disseminated intravascular coagulation.

The clinical outcome of cutaneous *S. apiospermum* infection in immunosuppressed patients is poor because they are susceptible to other fatal infectious diseases. In our review, four patients with localized skin lesions died because of complications, such as bacterial pneumonia. In addition, it should be kept in mind that there are several case reports that describe dissemination developing from localized cutaneous *S. apiospermum* infection, although this was not evident from our review of the literature after 1998.

Although *S. apiospermum* is an opportunistic fungus, an infection in the immunocompromised patient can be life-threatening and accurate diagnosis and prompt treatment are important (8).

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