Trichosporon beigelii Fungemia with Cutaneous Dissemination. A Case Report and Literature Review

Sir,

Trichosporon beigelii (*T. beigelii*) is a fungus found in soil, stagnant and fresh water, animal excreta and, occasionally, in human skin (1, 2). It is of low pathogenicity and is known to be the causative agent of the superficial hair infection white piedra. Disseminated fatal infection by *T. beigelii* was first described by Watson et al. in 1970 (3). Since then, sporadic case reports and a case series of this invasive infection in immunocompromised patients have appeared. Most of these patients had had acute leukemia and were neutropenic when they developed the infection. Response to therapy is usually disappointing, and the overall mortality rate is high (1). Here a case of *T. beigelii* fungemia with cutaneous dissemination is described.

CASE REPORT

The patient was a 39-year-old man with acute myelomonocytic leukemia. Complete hematologic remission was achieved after induction chemotherapy with adriamycin and low dose cytosine arabinoside. Bone marrow transplantation was planned, and three courses of consolidation chemotherapy with combinations of adriamycin, cytosine arabinoside and mitoxantrone were given. During the myelosuppression periods after chemotherapy, severe neutropenia with fever, sepsis and even frank septic shock were noted. Antibiotics, including ceftazidime, amikacin, metronindazole and piperacillin, were used to control the infections. Seven months later, he had a relapse of leukemia and received a combination of mitoxantrone and high dose cytosine arabinoside. Because of severe neutropenia and fever, the possibility of bacterial sepsis was strongly considered. The patient was treated with vancomycin, ciprofloxacin and amikacin, without clinical improvement. *Klebsiella pneumoniae* and *T. beigelii* were recovered from blood and urine, respectively. Antifungal therapy was not considered because of a clinically insignificant colony count of less than 1000/ml. Two weeks later, many purpuric macules and papules developed all over the body (Fig. 1). A series of cultures were done, and a skin biopsy specimen was obtained. The patient was then started on amphotericin B, daily. Five days later, staphylococcus epidermidis, coagulase(-) staphylococcus and *T. beigelii* were identified from previous blood cultures. *T. beigelii* was also recovered from the tip of a port-A catheter. The carbohydrate assimilation patterns and positive urease test were compatible with *T. beigelii*. When results of the skin biopsy were available, histologically, many fungal elements composed of hyphae, arthrospores and blastospores were noted scattered between dermal collagen bundles and in the lumen of blood vessels both in the papillary and reticular dermis (Fig. 2). Fever, up to 40°C with a spiking pattern, persisted despite aggressive antibiotic therapy and increasing dosages of amphotericin B, up to 50 mg per day. Yet another blood culture was positive for the same fungus. The patient developed heart failure and hemodynamic instability. His blood pressure continued to fall, cardiopulmonary arrest followed and he died.

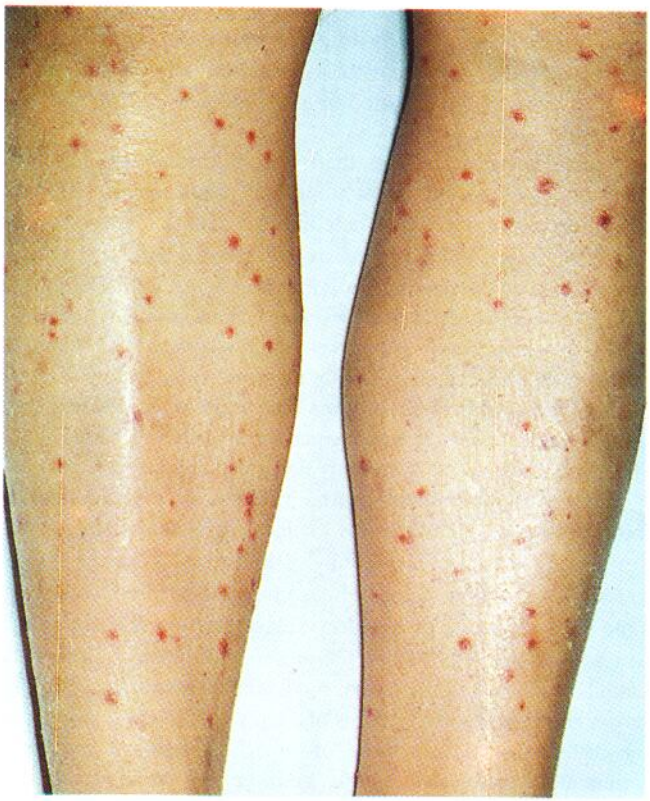

Fig. 1. Many rice grain to pea-sized, purpuric papules and macules are noted on both lower legs.

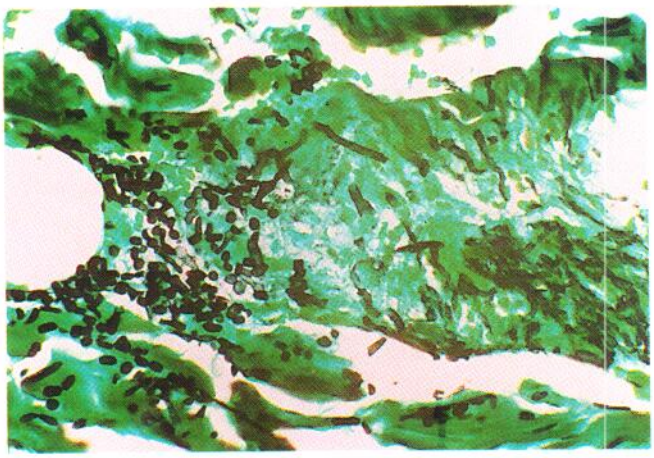

Fig. 2. Hyphae and arthrospores are noted scattered along blood vessels and between collagen bundles of reticular dermis (Grocott's methenamine silver stain).

DISCUSSION

Invasive fungal infections are important causes of morbidity and mortality in immunocompromised hosts and have increased in frequency over the past three decades, coincident with the use of immunosuppressive and cytotoxic drugs. The major fungal pathogens in immunosuppressed hosts are species of *Candida, Aspergillus, Mucoraceae* and *Cryptococcus*. However, other organisms previously considered to be contaminants or saprophytes have increasingly become pathogens in such patients. *T. beigelii* has been recognized as another opportunistic pathogen. Various conditions, such as hematologic malignancy with or without chemotherapy, intravenous drug use, organ transplantation, cataract extraction, valve prosthesis operation and chronic active hepatitis, have been reported in association with *T. beigelii* infection (1, 2).

Severe neutropenia (less than 100 neutrophils/μL for more than one week) is the most important predisposing factor for infection and predictor of outcome for such patients (4). The mode of presentation of invasive *T. beigelii* infection is also determined by the patients' polymorphonuclear (PMN) count. It has been seen as manifested diversely, from relatively localized soft tissue infection in patients with an adequate PMN count to full-blown dissemination involving skin and multiple internal organs in patients with profound neutropenia (5). Cutaneous involvement occurs in approximately 30% of all patients (2). The skin lesions most frequently described are purpuric papules, nodules with or without central necrosis or ulceration. Skin biopsy usually reveals dermal invasion by fungal elements and /or septic vasculitis. The colony of invasive *T. beigelii* is variously described as being white, cream-colored to yellowish, smooth to wrinkled or powdery-velvety to rugose. Microscopically, it is characterized by the presence of blastoconidia, rectangular or oval arthroconidia, hyphae and pseudo-hyphae. The gross and microscopic features of deeply invasive *T. beigelii* can be differentiated from those of superficial clinical and environmental isolates and can thus be of help in the in recognition of the cultured strains as systemic pathogens versus skin contaminants (6). In this patient, the diagnosis of Trichosporonosis was based on the identification of deeply invasive *T. beigelii* from blood and characteristic morphologic criteria in tissue.

Therapy for disseminated *T. beigelii* infection is not well established. *T.beigelii* is known to be sensitive to amphotericin B and 5-fluorocytosine (5-FC), and most reported cases were treated with them. However, a rapid fatal course was common for patients with profound neutropenia. In in vitro susceptibility studies by Walsh et al., *T. beigelii* was inhibited, but not killed, by amphotericin B at achievable serum level (5). This reaction of resistant *T. beigelii* to amphotericin B may be inadequate as a therapy for severe neutropenic patients, in whom there are not enough granulocytes to facilitate host clearance of the organisms. This might explain why most of the surviving patients in the literature have had hematologic remission. In short, a resolution of the immunocompromised state may play an important role in the recovery from infection. Combination antifungal therapy with amphotericin B and 5-FC or rifampin, or derivatives of azoles and norfloxacin have been tried with variable success rates (4, 5). If repeated blood cultures continue to yield *T. beigelii* while a patient is receiving amphotericin B, modifications of antifungal therapy are warranted. In addition, the use of fluconazole as a prophylactic agent for patients at risk of *T. beigelii* infection was believed to be able to reduce, or even eliminate, infection by this organism (4).

The exact cause of death in the presented patient, in whom polymicrobial infections existed, was difficult to assess. However, as reported previously, *T. beigelii* alone can cause significant morbidity and mortality (1). Trichosporonosis remains a rare infection, but it seems to become more frequent in immunocompromised patients. Awareness of the microorganism and early recognition of this serious infection with appropriate treatment might, hopefully, improve survival rates.

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