Scedosporium prolificans fungemia

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Fungemia due to *Scedosporium prolificans* is described in a young woman with a relapse of acute lymphoblastic leukemia. Several days after starting reinduction chemotherapy, the patient presented with fever, neutropenia and blood cultures showing fungi on Gram stain. The patient died despite therapy with antifungal agents, including fluconazole and amphotericin B. Fungi grew from blood cultures, and was subsequently identified as *Scedosporium prolificans*.

Key Words: Acute lymphoblastic leukemia, Fungemia, Leukemia, *Scedosporium prolificans*

Septicémie fongique à *Scedosporium prolificans*

RÉSUMÉ : Une septicémie causée par *Scedosporium prolificans* est décrite chez une jeune femme accusant une rechute de leucémie lymphoblastique aiguë. Plusieurs jours après l'instauration d'une chimiothérapie de réinduction, la patiente s'est présentée avec de la fièvre, une neutropénie et des hémocultures révélant des champignons à la coloration de Gram. La patiente est décédée malgré l'administration d'un traitement antifongique comprenant du fluconazole et de l'amphotéricine B. La pousse des champignons à partir des hémocultures a par la suite permis d'identifier *Scedosporium prolificans*.

This report describes a case of fatal disseminated *Scedosporium prolificans* infection in a patient with acute lymphoblastic leukemia (ALL). To our knowledge, this represents the first case of *S. prolificans* infection reported in Canada.

CASE PRESENTATION

A 28 year-old woman with CALLA-positive ALL was initially induced with adriamycin, vincristine, prednisone and L-asparaginase, followed by maintenance chemotherapy for two years. She remained in complete remission for 18 months until the development of an asymptomatic thrombocytopenia was noted. A bone marrow aspirate confirmed relapsed ALL, and she was admitted to hospital for reinduction chemotherapy with mitoxantrone and cytosine arabinoside (day 0). On day 7, she developed a fever (38.5°C) and was found to be neu-

tropenic (absolute neutrophil count less than $0.1 \times 10^9/L$). Blood cultures were obtained, and she was placed on tobramycin and piperacillin as empirical therapy. Initial blood cultures grew *Escherichia coli*. Vancomycin was subsequently added on day 12 due to the presence of a low colony count (less than 10^4 colony forming units/mL) staphylococcal bacteriuria. The patient's fever persisted despite empirical antibiotic therapy. She required frequent platelet and red cell transfusions during the postinduction period. When she complained of a sore throat (day 13), acyclovir was added following herpes simplex virus type 1 isolation from a pharyngeal culture. Repeat blood cultures were also obtained on days 13 and 14, both of which showed (on days 14 and 15, respectively) yeast and short hyphae-like elements on Gram stain of aerobic bottles (Bactec 9240 System, Becton Dickinson, Maryland); oral fluconazole

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therapy (200 mg once daily), which was initiated empirically on day 11, was subsequently switched to intravenous fluconazole (200 mg once daily) after Gram stain results were available (day 14). On day 15, she became mildly confused, and complained of a headache; later that day, her confusion and agitation progressed. She was still febrile, and was found to have a stiff neck and brisk reflexes but no focal neurological signs. Computed tomography scan of the head showed no intraparenchymal lesions. A lumbar puncture was performed, but there were no cerebrospinal fluid abnormalities, and no organisms were seen or cultured. On day 17, she developed acute respiratory distress and required admission to the intensive care unit. Fluconazole was discontinued, and amphotericin B 25 mg was administered intravenously. Later, she became hypoxic and hypotensive, and had a cardiac arrest. Resuscitative attempts were unsuccessful.

An autopsy was not performed. After the patient's death, growth of a flat, olive-gray to black mold on Sabouraud dextrose agar was observed from blood cultures obtained on days 13 and 14; a wet mount preparation revealed septate vegetative hyphae with flask-shaped, basally swollen conidiophores bearing conidiogenous cells at their apices. Such an isolate was unique to the authors' laboratory, and it was sent, for identification, to a reference laboratory (Public Health Laboratory, Toronto, Ontario) where it was subsequently identified as *S. prolificans*.

DISCUSSION

S. prolificans (formerly called *Scedosporium inflatum*) has recently been recognized as an important opportunistic pathogen in both immunocompetent and immunocompromised patients (1). This mold, thought to be a soil saprophyte (2-4), was first described in 1984 after its isolation from a bone biopsy specimen in a six-year-old boy with osteomyelitis (5). Since then several cases of infection with *S. prolificans* have been reported in the literature (6,7). The majority of cases have involved localized infection, particularly of the soft tissues, bones and joints, and were often associated with antecedent penetrating trauma (6,7). Disseminated infection with *S. prolificans* has been reported mainly in immunosuppressed patients with hematological abnormalities and neutropenia (8); most of these cases have occurred in Australia and Spain (8). Although the organism has been isolated from the soil of

potted plants in an urban Canadian hospital (4), no cases of infection with this organism have been described in Canada. More is known about the closely related mold *Scedosporium apiospermum* (the asexual form of *Pseudallescheria boydii*) whose spectrum of infection appears to be similar (2,7). Infections caused by this organism have occurred in Canada and elsewhere (2-4,9). This organism, found commonly in soil, manure and polluted water (2-4,9), usually causes localized infection after traumatic inoculation and has been reported to cause focally invasive and disseminated infection (2,3,9).

Several reports of fatal disseminated *S. prolificans* infection have demonstrated, at autopsy, evidence of dissemination to various organs, including lung, liver, myocardium, kidney, thyroid, spleen, lymph nodes, bone, vitreous fluid and brain (8). Even though an autopsy was not conducted in this case, it is likely that the infection was disseminated due to isolation of the organism from the patient's blood. Disseminated *S. prolificans* infections in neutropenic patients are usually fatal despite antifungal therapy (8). *S. prolificans* shows in vitro resistance to most antifungal agents, including amphotericin B, although rare cases of success with azole antifungals have been reported (6,8).

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