CASE REPORT

Scopulariopsis Brevicaulis Infection in a Patient with Acute Myeloid Leukemia

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Summary

Scopulariopsis brevicaulis is a soil fungus normally associated with onychomycosis. It causes subcutaneous infection in immunocompromised patients and is rarely isolated from blood. A case of systemic *Scopulariopsis brevicaulis* infection was reported in a patient with acute myeloid leukemia. The patient developed persistent fever that did not respond to wide spectrum antibiotics and amphotericin B. *Scopulariopsis brevicaulis* was the only pathogen isolated from blood cultures. The fever subsided with itraconazole and there was no recurrence of fungal infection with prolonged maintenance of oral itraconazole.

Key Words: Acute myeloid leukemia, *Scopulariopsis brevicaulis*, Opportunistic fungal infections

Introduction

Fungi are emerging as important hospital-acquired pathogens in tertiary care hospitals such as the University of Malaya Medical Centre (UMMC). The incidence of AIDS-defining opportunistic fungal infections appears to be leveling off since 1996. The reduction of fungemias in HIV-infected patients coincides with the introduction of highly active antiretroviral therapy (HAART) [1]. The common opportunistic fungi isolated from immunosuppressed patients include *Candida* species, *Cryptococcus* species, *Aspergillus* species, *Chrysosporium* species and Penicillium species. With the exception of *Candida* species which is a yeast-like organism and endogenous in origin, the great majority of the opportunistic fungi are molds and are mainly environmental contaminants of soil origin. However, opportunistic fungal infections remain associated with high rates of morbidity and mortality in hemato-oncology patients. Opportunistic fungal infections are likely to increase in this group of patients due to prolonged neutropenia, prolonged hospital stay with broad spectrum antibacterial therapy and the increasing use of central venous access devices. In recent years, there has been increasing number of disseminated mycoses in immunosuppressed patients caused by fungi with low inherent virulence, Gan et al [2] reported the isolation of non-sporulating *Chrysosporium* in a neutropenic patient.

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Case Report

A 33-year-old single man was admitted to UMMC in April, 2002 with a 3-week history of unremitting fever and headache. On physical examination, he was febrile with a temperature of 42°C. There was no neck stiffness and no papilloedema. Cardiovascular and respiratory systems were normal and there was no hepatosplenomegaly or lymphadenopathy. Full blood investigations revealed a pancytopenia with Hb of 10.6 g/dl, white blood cells count of 19.7x10^9 /L with blast cells seen and platelet counts of 17,000 x 10^6/L. A diagnosis of acute myeloid leukemia, subtype M0 was made on the findings of flow cytometry and morphology after a bone marrow examination. HIV screening was negative. Blood cultures (Fungal biphasic medium and BacTec plus Aerobic / Anaerobic, Becton Dickinson) were taken on admission and empirical broad-spectrum antibiotics consisting of intravenous piperacillin and gentamicin were instituted. Two days later, patient appeared drowsy with high spiking fever and the antibiotics were changed to a carbapenam group. A brachial vein peripherally inserted central catheter (PICC) was inserted under ultrasound guidance for chemotherapy administration. Induction chemotherapy comprising idarubicin and cytosine arabinoside was started 4 days after admission despite the high fever. The blood counts did not improve and he remained leucopenic (WCC ranges from 0.2-1.1) for the next 3 weeks. Intravenous amphotericin B was started at a dose of 1mg/kg/day and intravenous vancomycin was added a week later when there was no sign of the fever subsiding. The PICC was then removed. Repeat blood cultures over the next 4 weeks did not yield any positive growth of fungi or bacteria. Repeat CXR showed progressive changes with bilateral lower zone infiltrates. CT scan of thorax revealed bilateral lower lobes alveolitis. A bronchoscopy was performed and the bronchoalveolar lavage culture did not grow any organism. Screening for tuberculosis and *Pneumocystis carinii* was negative. A transthoracic 2D echocardiogram did not show any vegetation. Widal Weil Felix (WWF) and stool cultures were also negative. Four weeks after chemotherapy, the blood counts finally showed signs of improvement with platelet counts raised above 200,000 x 10 ^{6}/L and total white blood cells count of 1.3 x 10 ^{9} /L. General condition of the patient improved although the fever was still present. It was then decided to discontinue vancomycin and amphotericin B. A repeat set of blood culture including biphasic medium for fungus was taken 5 weeks after admission. The antifungal therapy was changed to syrup itraconazole at a dose of 400mg daily. Two days later, the patient's clinical condition improved and he became afebrile. He was discharged with oral itraconazole 38 days post-chemotherapy. On discharge, the total white blood cell count was 3.2 x 10^9/L (ANC > 1000/mm) and platelet counts 331,000 x 10^6/L. The blood fungal culture, which was taken on the day when the antifungal therapy was changed, grew *Scopulariopsis brevicaulis*. A repeat bone marrow aspiration 7 weeks after induction chemotherapy showed that the leukemia was in remission. He did well for his consolidation chemotherapy without any significant prolonged fever. Throughout the second admission, he was on syrup itraconazole. He was afebrile, repeat blood cultures for fungus were negative and no clinical recurrence of fungal infection.

Mycological investigation

The fungus isolated from the fungal biphasic medium was subcultured on SDA plate on day 3. The SDA plate was incubated at 30°C. After 48 hours of incubation, a white, waxy and wrinkled colony appeared. The fungus matured rapidly in about 5 days. The colony became velvety and then powdery light brown centrally with a white periphery (Fig.1a). The reverse was tan with brownish center. The colony was avellaneous but not green. Microscopically, the hyphae were septated and synnemata absent. The conidiophores were short and branching occasionally. The conidia-producing cells were annellides, cylindrical in shape but became slightly elongated before the production of each new

conidium (Fig. 1b). The conidia were large and arranged in chains that break apart easily. The conidia were round to lemon-shaped with truncated base or forming a short neck at the basal edge where they are released from the annellide. The mature conidia were usually thick walled, rough and spiny.

Scopulariopsis brevicaulis resembles *Penicillium* species in many aspects. In *Penicillium* species, the colony may be green, the conidiophores are longer and have secondary branches called metulae. The flask-shaped phialides that bear chains of smooth, round conidia are arranged in whorls on the metulae. However, the conidia-bearing cells in *Scopulariopsis brevicaulis* are more cylindrical with an elongated tip. The conidia of *Scopulariopsis brevicaulis* are larger (5-9 μm in diameter) with rough and spiny surface as compared to smaller (3-5 μm in diameter) and smooth conidia in *Penicillium* species.

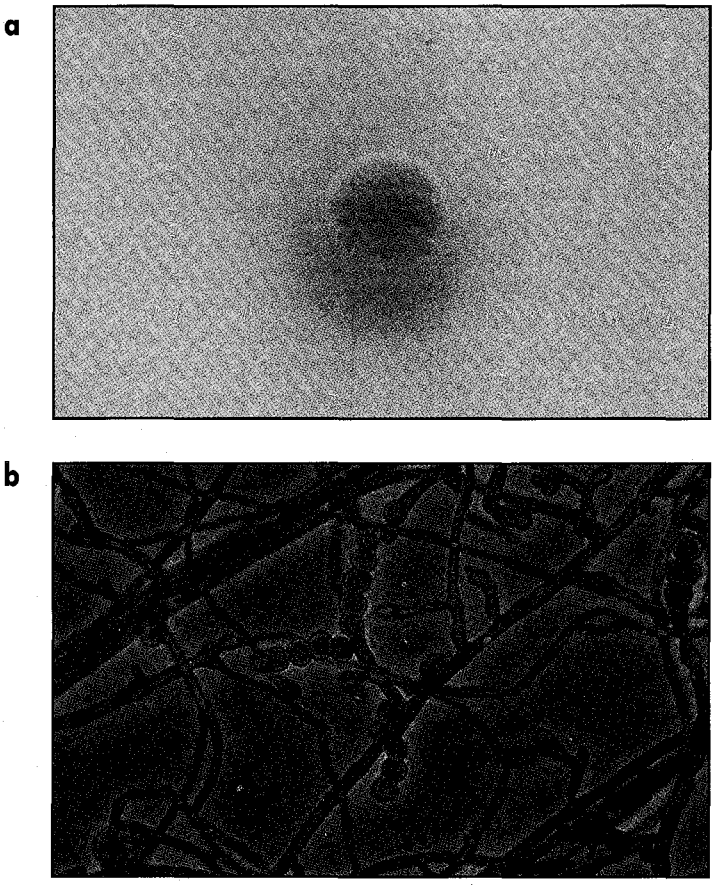

Fig 1: Macroscopic and microscopic structure of *Scopulariopsis brevicaulis* on SDA (a) and slide culture (b)

Discussion

The genus *Scopulariopsis* is a large group of fungi comprising 8 species. The members of the genus are mainly soil species and are frequently isolated from paper, food and material contaminated with soil. *Scopulariopsis* species is considered by many mycologists as a common laboratory contaminant, but the isolation of this species from clinical specimens at present time implies a pathogenic role. Members of the genus *Scopulariopsis* are frequently involved in onychomycoses. *Scopulariopsis brumptii* and *Scopulariopsis acremonium* have been associated in lung infection and sinusitis in patients with impaired cellular immunity. *Scopulariopsis brevicaulis* is the most frequently reported opportunistic fungus associated with infection in humans. In normal subjects, *Scopulariopsis brevicaulis* is most frequently associated with onychomycoses. In patient with immunosuppression, *Scopulariopsis brevicaulis* has been associated with endocarditis and endophthalmitis. This fungus is also frequently associated with subcutaneous infection in patients with cellular immunity suppression [3]. However, *Scopulariopsis brevicaulis* is rarely involved in systemic infections and it is rarely isolated from blood of patients with chronic diseases including human immunodeficiency virus infection. We reported the isolation of *Scopulariopsis brevicaulis* in a patient with acute myeloid leukemia. This patient developed prolonged fever despite initial broad-spectrum antibacterial therapy and later amphotericin B infusion. The patient had no other clinical manifestation, nor any dermatosis or organomegaly.

Scopulariopsis brevicaulis is a soil fungus. The source of infection is likely via inhalation of fungal spores in the hospital environment or in the community. Hospital environment harbors large numbers of fungi. In a recent hospital airborne mycological survey in UMMC, 91.6% of fungi isolated from the hospital air were molds including known opportunistic fungal pathogens such as *Chrysosporium* species, *Aspergillus* species and *Penicillium marneffei*. *Scopulariopsis brevicaulis* was also isolated from hospital air; it made up 0.74% of the fungal isolates, suggesting that hospital environment could be a source of opportunistic fungal infection. The risk of nosocomial fungal infection in patients with impaired cellular immunity increased with prolonged hospitalization, presence of indwelling extravascular catheter and prolonged immunosuppressive therapy. The isolation of *Scopulariopsis brevicaulis* from blood was a significant finding because multiple blood cultures were negative for other bloodstream pathogens.

The in-vitro anti-fungal sensitivity of *Scopulariopsis brevicaulis* isolated was not determined. Itraconazole and terbinazine are the anti-fungal used in immunocompromised patient with subcutaneous infection or onychomycoses in normal individual caused by *Scopulariopsis brevicaulis*. The anti-fungal therapy, however, required long term oral maintenance to prevent relapse. The patient documented in the report had persistent fever despite amphotericin B therapy, suggesting that amphotericin B is not a drug of choice in treating the patient with infection associated with *Scopulariopsis brevicaulis*.

Recent advances in medical technology and the development of new treatment approaches have increased the life expectancy of critically ill patients. The introduction of HAART in patients with human immunodeficinecy virus infection has resulted in increased number of severely ill immunocompromised patients in the hospital. The numbers of opportunistic fungal infections are likely to increase and the fungi of low virulence or environmental fungi may be potential opportunistic pathogens in patients with impairment of cellular immunity. The isolation of *Scopulariopsis brevicaulis* from blood in this patient demonstrated one of the many possible fungal opportunistic pathogens that can be isolated in patients with prolonged neutropenia.

References

1. Garbino J, Kolarova L, Lew D, Hirschel B & Rohner P. Fungemia in HIV-infected patients: a 12-year study in a tertiary care hospital. AIDS Patient Care STD 2000; 15(8): 407-10.
2. Gan GG, Kamarulzaman A, Goh KY, et al Non-sporulating *Chrysosporium*: An opportunistic fungal infection in a neutropenic patient. Med J Malaysia 2002; 57(1): 118-22.
3. Sellier P, Monsuez JJ, Lacroix C, et al. Recurrent subcutaneous infection due to *Scopulariopsis brevicaulis* in a liver transplant recipient. Clin Infect Dis 2000; 30(5): 820-23.