

Disseminated *Geotrichum* Infection

K P Ng, Ph.D*

T S Soo-Hoo, Ph.D*

M T Koh, MRCP**

P W Kwan, MRCP**

* Department of Medical Microbiology,

** Department of Paediatrics,

Faculty of Medicine, University of Malaya, 59100 Kuala Lumpur

Summary

Intensive chemotherapy has prolonged survival in cancer patients. Unfortunately it has also predisposed them to unusual infections because of their immunocompromised state. We report a case of fungal septicaemia caused by *Geotrichum candidum*, an imperfect yeast of low virulence in a young girl with acute lymphoblastic leukaemia. It was successfully treated with amphotericin B. The morphological characteristics of this fungus leading to its identification are described.

Key Words: *Geotrichum candidum*, Acute lymphoblastic leukaemia, Fungal septicaemia, Amphotericin B.

Introduction

Geotrichum candidum is a yeast-like saprophytic fungus. It belongs to the Class Fungi Imperfecti. It is widely distributed in nature including soil and decaying vegetable matters. It is a normal flora of the human skin and has been isolated from the stool sample of healthy subjects without gastrointestinal illness. However, it has been associated with opportunistic localised invasive infections of the lungs in patients with chronic diseases such as tuberculosis, lung cancer and bronchiectasis¹. It has also been reported to cause renal abscesses in patients with leukaemia and terminal cancer². Disseminated geotrichosis is rare and only a few cases have been documented in the literature³. We report a case of *Geotrichum* septicaemia in a patient with acute lymphoblastic leukaemia (ALL).

Case History

A 4-year-old girl was referred to University Hospital, Kuala Lumpur in April 1991 with a six-week history of intermittent fever. This was associated with marked

pallor two days prior to her admission. Physical examination then was unremarkable except for pallor. Investigations showed the following: Hb 5.0 g/100ml, platelet $166 \times 10^9/L$, TWC $2.4 \times 10^9/L$. A peripheral blood film did not reveal any immature cells. However, a bone marrow examination showed the presence of more than 80% immature cells which on cytochemical staining confirmed a diagnosis of acute lymphoblastic leukaemia.

She was then commenced on chemotherapy using standard protocol and after six weeks of treatment she was in remission. In October 1991, she was started on reinduction chemotherapy as part of the treatment. It was during this time that she developed high fever and cellulitis over her right knee. Blood cultures were obtained and intravenous ceftazidime and amikacin were started. Her fever settled after 48 hours and the blood cultures grew *Klebsiella* species sensitive to the two antibiotics. One week into the treatment she again developed high, spiking temperatures although she remained clinically well. A second blood culture was

taken. No bacterial pathogen was isolated but it grew a fungus which was subsequently identified as *Geotrichum candidum*. She received intravenous amphotericin B at an initial dose of 0.25 mg/kg body weight, increasing to 1 mg/kg/day over a week. Two days after starting amphotericin B her fever settled. A repeat blood culture was carried out on the 12th day of treatment. *G. candidum* was again isolated although she remained afebrile and was clinically well. It was decided then to continue with the amphotericin B as she responded clinically to the treatment. After three weeks on amphotericin B, a third blood culture was obtained. This time it was sterile and the amphotericin B was stopped after a further one week of treatment.

Her chemotherapy was then continued and she did not encounter any further problems. Neither was there a recurrence of the fungal infection. She subsequently completed her treatment for the ALL and she remained in remission eight months after stopping chemotherapy.

Mycological Examination

Blood sample was inoculated into a biphasic fungal blood culture medium (Brain Heart infusion agar slope plus Brain Heart Infusion broth with 10% glucose) and incubated at 37°C for 48 hrs. After initial identification i.e. Gram's stain, the organism was presumptively identified as a yeastlike fungus, it was inoculated onto Sabouraud dextrose agar (SDA) and incubated at 37°C for 48 hours. On SDA, the colony was flat, finely wrinkled, initially white then cream coloured with short white mycelium expanding on the edges of the colonies. Microscopically *G. candidum* was identified by the presence of septate hyphae with irregular branching and the hyphae segmented to form thin walled rectangular arthrospores. Blastospores were absent.

On the day that the patient was suspected of having fungaemia, blood was tested for *Candida* antigen (Pastorex Candida, Diagnostic Pasteur) and *Aspergillus* antigen (Pastorex Aspergillus, Diagnostic Pasteur). Both *Candida* and *Aspergillus* antigen were found to be negative.

Carbohydrate assimilation was performed by using

carbon free base agar (KH₂PO₄ 1g, MgSO₄ 0.5g, (NH₄)₂SO₄ 5g, agar 25g in 1L of distilled water) with 16 carbohydrate (glucose, maltose, saccharose, galactose, lactose, raffinose, inositol, cellobiose, xylose, trehalose, arabinose, adonitol, 2-keto-gluconate, methyl 2-glucoside, melezitose, n-acetyl glucosamine) discs (Diagnostic Pasteur). The isolate assimilated glucose, galactose and xylose but not 13 other carbohydrates. Urea was not hydrolysed. These biochemical characteristics were consistent with *G. candidum*.

The antifungal sensitivity test was carried out by using Casitone medium (Diagnostic Pasteur) and semi-synthetic medium (Diagnostic Pasteur). Casitone medium was used for nystatin, amphotericin B, econazole, clotrimazole, miconazole, and ketoconazole (Diagnostic Pasteur). 5-fluorocytosine (Diagnostic Pasteur) was tested only on semi-synthetic medium. It was found that *G. candidum* was sensitive to amphotericin B (100 µg), nystatin (100 IU), ketoconazole (50 µg); intermediately sensitive to econazole (50 µg), miconazole (50 µg) and cotrimazole (50 µg). It was resistant to 5-fluorocytosine (10 µg).

Discussion

Disseminated geotrichosis is a rare infection in humans. We documented a case of disseminated *G. candidum* infection in a patient with acute lymphoblastic leukaemia. *G. candidum* is a fungus of low virulence. Repeated isolation of this fungus from the blood of this patient demonstrated that a low virulent fungus can cause infection in an immunocompromised host.

Geotrichum is an imperfect yeast. The difference between *Geotrichum* and the perfect yeast is based on vegetative criteria but this criterion is not always distinct. The laboratory diagnosis of fungal infection is based on the isolation of fungus from the blood. But routine blood culture is time consuming and the rate of isolation of the fungus is low unless the blood culture medium is specially prepared to enhance the growth of the fungus. Morphological identification of the fungus requires expertise; in the case of *G. candidum*, the hyphae of the young culture may be indistinguishable from other fungi including *Candida* spp, *Trichosporon* sp and *Aspergillus* sp. However, the presence of true hyphae and branching of some of the

CASE REPORT

hyphae element make the diagnosis of candidiasis unlikely. *Trichosporon* sp produces arthrospores and is morphologically similar to *Geotrichum*, but *Trichosporon* sp produces blastoconidia and is urease positive and it assimilates maltose, saccharose, methyl 2-gluconate and melezoitose. Identification of the *Aspergillus* sp is not a problem for an experienced mycologist due to its numerous conidiophores, terminating in a vesicle with sterigmata and chains of conidia.

Geotrichum has been documented as sensitive to amphotericin B, nystatin and imidazoles anti-fungal agents. In our patient, the isolate was also sensitive to amphotericin B, nystatin and imidazoles but was resistant to 5-fluorocytosine. The efficacy of amphotericin B in the treatment of *G. candidum* is dependent on the degree of invasion of the organism and the status of the patient. It has been suggested

that the outcome of geotrichosis is poor if there is renal invasion with multiple abscesses. As the arthrospores of the *G. candidum* in the blood is rapidly cleared by neutrophilic phagocytosis of the host's defence mechanism, geotrichosis is not a fatal disease in patients with intact defence mechanism. The favourable response of this patient to amphotericin B may be due to early diagnosis of the infection prior to tissue invasion.

Fungal infection rates are increasing as the result of an increased use of immunosuppressive agents in modern medical practices, either to sustain organ transplants or as side effects of anti-cancer therapy. This case illustrates the importance of considering rare opportunistic pathogens as a possible causative agent especially in febrile patients with impaired defence mechanism.

References

1. Fisback RS, White DT, Finegold S. Bronchopulmonary geotrichosis. *Am Rev Resp Dis* 1973;108 : 1388-92.
2. Jagirdar J, Geller SA, Bottone EJ. *Geotrichum candidum* as a tissue invasive human pathogen. *Hum Pathol* 1981;12 : 668-71.
3. Anaissie E, Bodey GP, Kautarjian H, *et al*. New spectrum of fungal infections in patients with cancer. *Rev Infect Dis* 1989; 11(3) : 369-78.