Successful treatment of *Trichosporon mucoides* infection with lipid complex amphotericin B and 5-fluorocytosine

Tanil Kendirli,1 Ergin Ciftçi,2 Erdal Ince,2 Selim Öncel,2 Nazan Dalgiç,2 Haluk Güriz,3 Emel Unal4 and Ulker Dogru2

Divisions of 1Pediatric Intensive Care Unit, 2Pediatric Infectious Diseases, 3Pediatric Microbiology Laboratory and 4Pediatric Oncology, Department of Pediatrics, Ankara University School of Medicine, Ankara, Turkey

Summary

Infections in immunocompromised children can stem from bacteria, fungi, viruses, or protozoa, but most importantly, from the host’s endogenous bacterial flora. Disseminated infection caused by *Trichosporon* species is one of the emerging mycoses in neutropenic patients, particularly when they are treated for haematological malignancy with cytotoxic and immunosuppressive chemotherapy. We report a 15-year-old boy with acute lymphoblastic leukaemia, whose *Trichosporon mucoides* infection was successfully treated with lipid complex amphotericin B plus 5-fluorocytosine.

Key words: *Trichosporon mucoides*, sepsis, lipid complex amphotericin B, 5-fluorocytosine.

Introduction

The genus *Trichosporon* includes approximately 30 species, at least six of which (*T. asahii*, *T. mucoides*, *T. inkin*, *T. asteroides*, *T. cutaneum* and *T. ovoides*) are associated with infection (trichosporonosis).1 The first two species mentioned are responsible for deep infections and the last four are involved in superficial infections, including white piedra. *Trichosporon asahii*, which is responsible for >90% of deep-seated trichosporonoses, may cause a life-threatening illness.1–3

These fungi are also normal inhabitants of the soil and are occasionally found in the normal flora of the skin and the mouth. Most patients with deep-seated trichosporonosis have an underlying haematological malignancy or another neoplasm. Neutropenia as the result of cytotoxic chemotherapy is the most common apparent risk factor for this infection. In immunosuppressed individuals, *Trichosporon* infections may disseminate to multiple organs, such as liver, spleen, lungs and gastrointestinal tract, often resulting in death.1,3,4 We report a 15-year-old boy with acute lymphoblastic leukaemia (ALL), whose deep-seated infection because of fluconazole-resistant *T. mucoides* was successfully treated with lipid complex amphotericin B plus 5-fluorocytosine.

Case report

The patient was a 15-year-old boy with ALL. He had been given delayed intensification chemotherapy (L-asparaginase, vincristine, idarubicine, dexamethasone and cyclophosphamide) 2 weeks previously. While he was in a good condition, a large thrombus (25 × 15 mm in size) was detected at the end of his double-lumen catheter. Because the thrombus did not dissolve with thrombolytic therapy, he had surgery.

After the operation, he had a prolonged unconsciousness, which was possibly related to hypoxia because of the obstruction of his endotracheal tube owing to secretion, which has resolved within seconds with the change of the tube. Two days later, he was admitted to our paediatric intensive care unit (PICU) for recurrent seizures, unconsciousness, respiratory failure and fever. His pathological signs in the physical examination were a temperature of 39.2 °C, left hemiplegia, absence of deep tendon reflexes and bilateral Babinski’s sign.

Laboratory investigation revealed a haemoglobin of 10.5 g dl⁻¹, a white blood cell count of 3200 μl⁻¹ (88% polymorphonuclear leucocytes (total granulocyte count:
1100 μL⁻¹), 12% lymphocytes], a platelet count of 255 000 μL⁻¹, an erythrocyte sedimentation rate of 67 mm h⁻¹ and a C-reactive protein concentration of 9.7 mg dl⁻¹. Urinalysis, blood biochemistries, chest X-ray and echocardiography were normal.

Mechanical ventilation was started. His recurrent seizures were taken under control with diazepam, phenytoin and midazolam infusion therapy. Meropenem was initiated for suspected sepsis. After mechanical ventilation was discontinued on the second day of PICU admission, cranial magnetic resonance imaging revealed diffuse ischaemic areas.

The patient’s fever persisted. Cracking rales were detected on the third day of meropenem therapy. Chest X-ray revealed diffuse infiltration in the right lung (Fig. 1) and right pleural effusion was demonstrated with computed tomography (CT). Despite the addition of vancomycin, his pneumonia deteriorated and he had to be intubated again on the sixth day of his admission. Hypotension, oliguria and cardiac tamponade developed rapidly. Pericardial effusion showing transudate characteristics was drained by tube pericardiocentesis; however, Gram stain and cultures were unrevealing. Streptokinase was instilled three times into pericardial space for fibrinoid adhesions. The pericardial fluid persisted for a 10-day period, at the end of which the drainage tube was pulled out.

Because of the prolonged fever, fluconazole (10 mg kg⁻¹ day⁻¹) was initiated on the fifth day of hospitalisation. No microorganisms were detected in tracheal aspirate cultures. Two of three blood cultures were positive for T. mucoides. All isolates were identified by conventional methods including germ tube formation, morphology on cornmeal Tween-80 agar and Staib agar,

**Figure 1** The infiltration at right-low lobe lung on his chest X-ray.

**Figure 2** The cavitation on right-low lobe lung on thorax computed tomography.

urease test and biochemical profile using the API 20C AUX and ID 32C system (Bio Merieux, Lyon, France). We determined antifungal susceptibility to itraconazole, fluconazole, 5-fluorocytosine and amphotericin B by ATB FUNGUS 2 (Bio Merieux). Minimal inhibitory concentrations of 5-fluorocytosine and amphotericin B were 1 and 2 mg l⁻¹ respectively. However, this strain had a very high minimum inhibitory concentration (MIC) values for fluconazole (64 mg l⁻¹) and itraconazole (>4 mg l⁻¹). Fluconazole treatment was discontinued and lipid complex amphotericin B (5 mg kg⁻¹ day⁻¹) plus 5-fluorocytosine (100 mg kg⁻¹ day⁻¹) were initiated. The patient’s temperature returned to normal on the fifth day of the new antifungal drug regimen. Meropenem and vancomycin were discontinued on their 14th day. The pneumonia gradually resolved and the combination antifungal chemotherapy was continued for 8 weeks. The patient’s pulmonary findings gradually improved within 10 days. His fever was taken under control in 5 days and he was extubated at 11th day of his second intubation. Repeat thorax CT revealed a cavity in the previously infiltrated area (Fig. 2). The patient was discharged from the PICU on the 32nd day of his admission. In the follow-up visit 4 months later, his neurological examination was completely normal.

**Discussion**

Infections in immunocompromised children can result from bacteria, fungi, viruses, or protozoa; but most
significant infections are caused by the host’s endogenous bacterial flora. The most common fungal infections in children with cancer are caused by *Candida* species. The fungal pathogens of great concern in the patient with neutropenia include *Aspergillus*, *Fusarium*, *Mucor*, *Pseudallescheria* and *Trichosporon* species, as these organisms cause rapidly progressive, extensively destructive infections.\(^1\)\(^3\) Our patient had various features (haematological malignancy, chemotherapy, mild neutropenia and open heart operation) that predispose him to an opportunistic infection caused by a fungus, such as *T. mucoides*. His steroid treatment ended 1 month before the onset of *T. mucoides* infection, and also dexametason (8 mg day\(^{-1}\), for 3 weeks) was given to him. The duration and nadir of his neutropenia were 5 days and 1100 \(\mu\)L\(^{-1}\) respectively.

Disseminated infection caused by *Trichosporon* species is one of the emerging mycoses in neutropenic patients, particularly when they are treated for haematological malignancy with cytotoxic and immunosuppressive chemotherapy.\(^1\)\(^3\) Disseminated trichosporonosis can be diagnosed with mycological, histopathological or serodiagnostic tests. However, as *Trichosporon* species frequently colonise the oral cavity, digestive tract, urinary tract or the skin; the detection of *Trichosporon* species in sputum or faeces is unreliable. Nonetheless, when a *Trichosporon* species is detected in an abscess, in pleural effusion or in normally sterile body fluids such as blood and spinal fluid, this finding is clinically significant.\(^3\)–\(^5\) In conclusion, *T. mucoides* must be considered as an etiological agent for sepsis and pneumonia in immunocompromised children. Amphotericin B in combination with 5-fluorocytosine may be a suitable treatment for severe fungal infections; but antifungal susceptibility should be performed for optimal therapy.

**References**