References


First Report of Chronic Meningitis Caused by Trichosporon beigelii

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Trichosporon beigelii (Trichosporon cutaneum) was identified as the causative agent of chronic meningitis in a 15-year-old boy with acute lymphocytic leukaemia. After a neutropenic episode following cytostatic treatment and itraconazole therapy as prophylaxis, cerebrospinal fluid (CSF) samples yielded growth of Trichosporon beigelii. Treatment with amphotericin B, flucytosine and high doses of fluconazole was followed by clinical improvement, although CSF pleocytosis remained. The cross-reactivity between Cryptococcus neoformans and Trichosporon beigelii in a cryptococcal antigen latex test was used as a means of diagnosis in CSF and serum samples.

Trichosporon beigelii (Trichosporon cutaneum), a fungus belonging to the family Cryptococcaceae, is the causative agent of white piedra, an

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innocuous hair shaft infection encountered mostly in tropical and temperate countries. The fungus is widely distributed in the environment and has been recovered from normal skin and mouth flora.

Invasive infection in immunocompromised hosts has been reported since the early 1970s (1–6). Most cases occurred in patients suffering from leukaemia and other malignancies, or in artificial heart or prosthetic valve recipients (4, 7, 8). Clinical manifestations include episodes of fungaemia, pneumonia, endocarditis, and papular or nodular purpuric skin lesions (4). Prognosis in terms of mortality seems to be related to polymorphonuclear leukocyte count rather than to fungistatic treatment.

To our knowledge no case of meningitis due to *Trichosporon beigelii* has been reported previously. We describe a case in a leukaemic patient with special emphasis on clinical signs, diagnostic tools, cerebrospinal fluid (CSF) findings and difficulties encountered in treatment with one of the recently developed imidazoles.

Case Report. A 15-year-old boy suffering from acute lymphocytic leukaemia received successful remission induction therapy consisting of one dose of cyclophosphamide (1.2 g/m²), four doses of vincristine (2 mg), three doses of daunorubicin (45 mg/m²), six doses of L-asparaginase (10,000 U/m²), and methylprednisolone (48 mg/day) for 22 days. As part of consolidation therapy he received one dose of methotrexate (1 g/m²) and a four-day course of arabinosyl cytosine (3 g/m²) from 2 January to 6 January 1988. Since his history included an episode of fungaemia during the preceding year with isolation of *Trichosporon beigelii, Torulopsis glabrata* and *Torulopsis candida* from blood cultures, he was discharged on itraconazole therapy 100 mg b.i.d. per os.

From 22 February to 26 February he received a second four-day course of high-dose arabinosyl cytosine (3 g/m²). He was discharged on itraconazole 100 mg b.i.d. and norfloxacin 400 mg t.i.d. per os in order to obtain selective bowel decontamination during the period of neutropenia. Eight to 15 days after cystostatic treatment was stopped, his leukocyte count dropped to numbers varying between 0.2 × 10⁹/l and 0.5 × 10⁹/l.

On 10 March he developed fever, nausea and occipital headache. He was admitted on 11 March and from this date until 6 April, 12 blood cultures and four CSF samples were taken: all remained sterile for bacteria, mycobacteria and fungi. CSF pleocytosis varied between 100 and 600 cells/mm³, with 55–75 % neutrophils. Protein content varied between 70 and 80 mg/dl; CSF glucose levels were within normal limits. Despite broad-spectrum antibiotic treatment including amoxicillin, ceftazidime, vancomycin, erythromycin and chloramphenicol, CSF pleocytosis remained. On 25 March fluconazole in a dose of 100 mg/day per os was substituted for itraconazole. Meanwhile, the patient developed lower limb neuropathy and neck stiffness.

Further CSF samples taken on 12 April and 4 May yielded growth of *Trichosporon beigelii* on Sabouraud's dextrose agar after ten to 14 days of incubation at room temperature. Identification was based on the following criteria: typical morphology with presence of blastospores and arthrospores, production of urease and a compatible biochemical profile on API 20 C AUX strip (2145737: *Trichosporon beigelii* identification percentage 99.1). Identification was confirmed by the Laboratory for Medical and Veterinary Mycology, Institute for Tropical Medicine, Antwerp, Belgium (Prof. De Vroey). Since cross-reactivity between *Cryptococcus neoformans* and *Trichosporon beigelii* has been reported in latex agglutination tests for cryptococcal antigen detection, CSF and serum samples were tested (Latex Crypto Antigen System; Immuno-Mycologics, USA). CSF samples produced a weakly positive reaction (titer 1:4); serum samples were negative.

Treatment was started on 23 April with amphotericin B (50 mg i.v. 3 times weekly) and flucytosine (37.5 mg/kg per os q.i.d.), and was extended to include fluconazole 400 mg/day per os. Fever dropped and successive CSF samples remained sterile after culture on Sabouraud's dextrose medium; the cryptococcal antigen detection test was negative as well. On 2 August amphotericin B and flucytosine were discontinued, but treatment with fluconazole was continued. Clinical and laboratory findings, and antifungal therapy are summarized in Table 1.

At that time no information could be obtained on the sensitivity of *Trichosporon beigelii* to fluconazole, a drug with documented good penetration into the CSF. Despite clinical improvement, CSF pleocytosis remained, varying between 20 and 800 cells/mm³. Subsequent stool cultures grew *Trichosporon beigelii* three months after extended fungistatic treatment, while CSF samples remained sterile with the patient still under fluconazole therapy. The susceptibility of the strain isolated from the first positive CSF sample was tested using both a broth method in buffered medium (high resolution antifungal assay medium Oxoid CM 845; Oxoid, UK) and an agar plate dilution method in the same medium solidified with agar