Candida kefyr as an Emerging Pathogen Causing Nosocomial Bloodstream Infections in Neutropenic Leukemia Patients

Sir—Nosocomial candidemia occurs predominately in patients who have hematological malignancies and/or have undergone stem cell transplantation and is associated with a high mortality rate [1]. Although Candida albicans fungemia is most common, non-albicans species of Candida, which are often resistant to antifungal agents, are increasingly observed as pathogens (Candida parapsilosis, 20%–40% of cases; Candida tropicalis, 10%–30% of cases; Candida krusei, 10%–35% of cases; Candida glabrata, 5%–40% of cases; Candida lusitaniae, 2%–8% of cases; Candida guilliermondii, 1%–5% of cases; followed by Candida rugosa, Candida stellatoidea, Candida norvegensis, and Candida famata, <1% of cases) [1, 2].

Here we describe Candida kefyr bloodstream infections in 3 neutropenic leukemia patients after chemotherapy and/or stem cell transplantation. The infections were diagnosed using the Bactec 9240 system (Becton Dickinson) and the ID32C yeast identification system (bioMérieux) and on the basis of Gram-staining of culture isolates.

Patients 1 and 2 (a 41-year-old woman and a 54-year-old man) developed fever during neutropenia and after receipt of mitoxantrone, topotecan, and cytarabine salvage chemotherapy for relapsed acute myeloid leukemia 10 months and 9 months after autologous peripheral blood stem cell transplantation, respectively. C. kefyr was detected in 3 blood cultures (2 aerobic and 1 anaerobic), on a central venous catheter, and in mouth washings from patient 1; C. kefyr was found in 2 blood cultures (1 aerobic and 1 anaerobic) from patient 2. Patient 1 had several pulmonary infiltrates, and patient 2 had several hepatic lesions, but no other organs were involved. Blood culture results were negative after therapy with amphotericin B (patient 1) or caspofungin (patient 2).

The patient 3 (a 63-year-old woman) developed fever during neutropenia after undergoing human leukocyte antigen-matched unrelated allogeneic peripheral blood stem cell transplantation for relapsed Philadelphia chromosome–positive acute lymphoblastic leukemia. Over 19 days, C. kefyr was detected in blood cultures (9 aerobic and 3 anaerobic), 2 mouth washings, 3 stool specimens, and on a central venous catheter, reflecting colonization. Unspecific arthritis of the talocalcanean joints was observed, suggesting Candida arthritis, but no other organs were involved. Therapy with fluconazole and amphotericin B was immediately started and granulopoiesis was stimulated.

Despite hematopoietic regeneration, can-

Figure 1. Response of Candida kefyr bloodstream infection in patient 3 to combination antifungal therapy that included caspofungin. Staphylococcus epidermidis was also detected in 2 blood cultures but disappeared after antibiotic treatment, according to the antibiogram. Day 0 was the day of allogeneic peripheral blood stem cell transplantation (PBSCT). a, Graph depicting recovery of the leukocyte and the granulocyte counts. b, Serum levels of C-reactive protein (CRP). +, Blood cultures positive for C. kefyr. *Blood cultures positive for S. epidermidis. c, Graph showing the highest daily body temperature. d, Schematic representation of the antifungal therapy given after PBSCT. Dosages were as follows: nystatin, 1.5 million IU/day orally; caspofungin, 50 mg/day intravenously; fluconazole, 600 mg/day intravenously; amphotericin B, 3 mg/kg/day intravenously.
didemium persisted for 9 days and disappeared only after therapy with fluconazole, liposomal amphotericin B, caspofungin, and nystatin (figure 1). All 3 patients fully recovered after resolution of leukopenia.

Resistance to amphotericin B but not to fluconazole has been reported among some C. kefyr isolates [2, 3]. Antifungal susceptibility testing revealed MICs for fluconazole of 0.19 μg/mL for the isolate from patient 2 and 0.25 μg/mL for the isolate from patient 3, indicating microbiologic susceptibility. Caspofungin is at least as effective as amphotericin B for the treatment of candidemia [4, 5]. Our results indicate that caspofungin is also effective against C. kefyr fungemia.

The unusual occurrence of C. kefyr bloodstream infections in patients with neutropenia may be linked to dietary habits, because patients 2 and 3 had a history of ingesting dairy products containing live C. kefyr. This organism has been isolated from multiple milk products (e.g., bovine milk contains 16 different species of yeast, including C. kefyr) [6–8]. Because prophylactic fluconazole treatment (100–200 mg/day, orally) in stem cell transplant recipients has been associated with emergence of infection due to fluconazole-resistant non–albicans species of Candida, our patients did not initially receive fluconazole prophylaxis [9]. However, recently, higher doses of fluconazole (400 mg/day) given for 75 days after stem cell transplantation have been reported to provide clinically important protection against invasive yeast infection [10]. The occurrence of C. kefyr fungemia reflects the growing diversity of Candida species responsible for disseminated infections in neutropenic patients.

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References


Anti–BK Virus Activity of Ciprofloxacin and Related Antibiotics

SIR—I read with interest the recent article by Leung et al. [1] on the use of ciprofloxacin to decrease the polyoma BK virus load. The authors determined the inhibitory concentrations for the virus using an assay that inhibits the cytopathic effects of the polyoma BK virus. This is a slow and laborious assay that requires an incubation period of 28–35 days. I have used the Gardner strain of the polyoma BK virus to determine the 50% virus inhibitory concentrations of ciprofloxacin and related antibiotics using a faster assay, which employs PCR to measure virus replication directly over a period of 7 days. At the same time, this assay measures the drug concentration that causes a 50% reduction in host cell replication as a measure of drug toxicity. Technical details of this assay have been published [2]. The antiviral activities of different antibiotics measured by this assay are presented in table 1.

These data show that, although the 50% virus inhibitory concentrations of different antibiotics vary from 79.7 to 266.6 μg/mL, the toxicity profile as measured by the 50% reduction in host cell replication also changes proportionately, so that the selectivity index (defined as the ratio of the 50% reduction in host cell replication value to the 50% virus inhibitory concentration value) never exceeds 3.6. To put this in perspective, the pharmaceutical industry generally does not pursue clinical development of antimicrobial drugs that have a selectivity index of <10.0. Thus, these data show that ciprofloxacin and related antibiotics have only a modest anti–polyoma BK virus effect. There is no evidence that any of these compounds are...