Fungemia Due to *Saccharomyces* Species in a Patient Treated with Enteral *Saccharomyces boulardii*

As a pharmaceutical biotherapeutic agent, *Saccharomyces boulardii* has been used for years outside of the United States to treat diarrhea [1] and is considered to be safe. Nevertheless, serious side effects can occur. A 78-year-old immunocompetent woman was admitted to the intensive care unit because of an acute exacerbation of chronic obstructive pulmonary disease. Current treatment consisted of antibiotics (amoxicillin/clavulanic acid), mechanical ventilation, and enteral feeding via a gastric tube. On hospital day 12, diarrhea appeared. Investigation for stool pathogens was negative; loperamide and *S. boulardii* (Ultra-Levure, 1.5 g/day [Biocodex, Montrouge, France]) were administered via the gastric tube (day 13) for 15 days. On day 18, antibiotic therapy was changed to that with cefazidime and ciprofloxacin because of a nosocomial pulmonary infection. On day 34, the temperature was elevated to 39°C and the WBC count was 8,600/mm³. From day 34 to day 37, seven cultures of blood were positive for *Saccharomyces* species; the organism was initially identified as *Saccharomyces cerevisiae* and later as *S. boulardii*. Cultures of arterial and venous catheters removed on day 35 were negative. A colonoscopy was normal and no parasites were found in the stool. Complete recovery was observed after fluconazole therapy for 15 days.

Routine identification of *Saccharomyces* species often fails to distinguish *S. boulardii* from *S. cerevisiae* [1, 2]. Fungemia due to *Saccharomyces* species has already been reported in patients receiving high enteral dosages of Ultra-Levure. Transfer of *Saccharomyces* species from an affected bowel (e.g., ischemic or inflammatory) appears to be the primary origin of these fungemias [3–7], especially when antibiotics effective against anaerobes are given [5–9]; in other cases, infected catheters have been implicated as the source of infection [6]. Patients who develop fungemia due to *Saccharomyces* species are generally immunocompromised (e.g., patients with AIDS and patients receiving corticosteroid therapy) [3–8]. In all reported cases, therapy has consisted of supportive care, anti-fungal drugs, and the cessation of Ultra-Levure. To our knowledge, we have described the first case of *S. boulardii* fungemia in a non-immunocompromised patient without bowel disease who was receiving high doses of enteral Ultra-Levure. As is true for the other reported cases, the primary identification of the *Saccharomyces* species was incorrect, with the usual confusion between *S. boulardii* and *S. cerevisiae* [1, 2, 5].

Given that *S. boulardii* may be initially misidentified as *S. cerevisiae*, it is likely that *S. boulardii* is responsible for saccharomyces fungemia in patients receiving enteral Ultra-Levure. High doses of Ultra-Levure associated with antibiotics effective against anaerobes, bowel diseases, and/or immunodeficiency seem to be risk factors for such fungemia; our observation suggests that fungemia due to *Saccharomyces* species can also occur in immunocompetent hosts without bowel disease. Enteral *S. boulardii* is widely used in the prevention or treatment of diarrhea; therefore, physicians must be aware of the possibility of potentially serious side effects. The reported occurrence of such side effects is infrequent at present, and no current guidelines exist for their treatment.

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References
Foscarnet Activity on Human Immunodeficiency Virus Type 1 in the Central Nervous System

Foscarnet, a reverse transcriptase inhibitor, has been shown to decrease HIV-1 replication in vitro [1, 2]. Recently, reports of two studies about the effects of this antiviral agent on HIV replication in vivo were published [3, 4]. Both investigators observed significant reductions of HIV plasma viral loads in patients who were treated with foscarnet. Herein, we report an observation that foscarnet is also active in the CNS when used to treat HIV encephalopathy-related symptoms.

A 55-year-old HIV-1-infected man with a Burkitt’s lymphoma was treated with indinavir (800 mg t.i.d.) and saquinavir (400 mg b.i.d.). Therapy with this combination of two protease inhibitors was started during multidrug chemotherapy for his lymphoma to avoid myelotoxicity induced by nucleoside analogs. Since the platelet count remained low (30,000/mm³) and plasma HIV viral load was undetectable, antiretroviral therapy was not modified after completion of the antineoplastic treatment, which led to complete remission. The CD4+ cell count was 150/mm³.

The patient works as a translator. Six months after beginning therapy with protease inhibitors, he experienced a first episode of somnolence, lack of concentration, and inability to work. Brain CT scan and MRI showed no abnormalities. A CSF specimen contained 3 lymphocytes/mm³ and protein levels were normal. Microscopic examination and cultures of CSF were negative for bacteria, parasites, and fungi. A search for neoplastic cells and cryptococcal antigen was negative. A PCR assay of CSF was negative for herpes simplex virus types 1 and 2, cytomegalovirus (CMV), JC virus, and Toxoplasma gondii. The CSF HIV viral load was 4.23 log₁₀ HIV RNA copies/mL, whereas the plasma viral load was still undetectable. Zidovudine at low doses (100 mg t.i.d.) was added to the treatment. After 2 weeks, the patient regained his fluency in six languages, and CSF HIV viral load levels decreased to 2.77 log₁₀ HIV RNA copies/mL.

Three months later, a lumbar puncture was performed because of recurrent drowsiness. An HIV RNA viral load of 4.36 log₁₀ copies/mL was detected in an otherwise normal CSF specimen. A PCR assay of CSF for CMV was negative. Tests for CMV antigen remained negative. Lamivudine (150 mg b.i.d.) was added to the therapeutic regimen, but no clinical improvement was noted after 10 days. Stavudine was not proposed, as the patient previously had a severe peripheral neuropathy induced by this antiretroviral agent. Therapy with intravenous foscarnet (100 mg/kg b.i.d.) was started, leading to complete linguistic recovery and disappearance of detectable CSF HIV RNA after 2 weeks. Foscarnet was then continued for 3 months at maintenance doses (100 mg/[kg⋅d]). CSF and plasma viral loads remained undetectable.

To improve the quality of life for our patient, we decided to interrupt foscarnet administration without modifying the rest of the treatment. A lumbar puncture performed 2 weeks later showed a detectable HIV RNA viral load at 3 log₁₀ copies/mL. A third episode of mental dysfunction, associated with an important rise in CSF viral load (5.1 log₁₀ RNA HIV copies/mL), occurred 6 weeks after stopping foscarnet. Therapy was switched to that with new drugs available at this time, abacavir, nevirapine, and nelfinavir, with successful clinical and virological response.

Foscarnet has been shown to penetrate the blood-brain barrier [5]. In our patient, foscarnet was highly effective in reducing the CSF HIV viral load and neurological symptoms, and this effect was sustained throughout the 3 months of therapy. The CSF HIV RNA load rebounded 2 weeks after cessation of therapy, and clinical symptoms reappeared a few weeks later.

The CNS is a protected compartment, known to be difficult to reach, since antiretroviral drugs like protease inhibitors do not cross the blood-brain barrier efficiently. This phenomenon is illustrated in the case we described, given the occurrence of neurological symptoms associated with a high CSF viral load despite undetectable HIV RNA in plasma. In our patient, clinical evolution paralleled changes in CSF HIV RNA, indicating that high CSF viral loads can be a marker of HIV encephalopathy. Our observation suggests that foscarnet might be helpful for the treatment of HIV-associated mental deterioration in cases of resistance or intolerance to all antiretroviral drugs known to be active in the CNS.

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