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Case Report

An unusual case of *Candida ciferrii* fungemia in an immunocompromised patient with Crohn's and *Mycobacterium bovis* disease

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Abstract

We present a case report of a fungal bloodstream infection due to an unusual pathogen. This is a 30 years-old female patient diagnosed with Crohn's disease and a disseminated *Mycobacterium bovis* infection subsequently complicated by fungemia due to the emergent yeast pathogen *Candida ciferrii*, who was unresponsive to fluconazole and made a full recovery after treatment with posaconazole. To our knowledge, this is the first report of *Candida ciferrii* isolation from blood in an adult associated to a central venous catheter and which was successfully treated with posaconazole.

Key words: Candidemia; *Candida ciferrii*; immunosuppression; posaconazole.

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Introduction

Fungal bloodstream infections are severe diseases that lengthen hospital stay, have elevated morbidity and mortality, and increase medical care costs. The incidence of these infections has increased in the last decades, most likely due to an increase in susceptible hosts. Several surveillance programs worldwide have documented this increase [1,2]. Non-*albicans Candida* spp. have been increasingly found as causative agents in human infections with important therapeutic implications [3]. In this way, the unusual yeast species *Candida ciferrii*, which was first discovered in 1965 [4] and is the anamorph of *Stephanoascus ciferrii*, has been described as a pathogen in superficial mycoses and very rarely as a systemic disease [5,6]. We report a case of a successfully treated patient with invasive disease due to this fungal pathogen.

Case Report

A 30 year-old Mexican female patient with history of Crohn's disease and use of immunosuppressives (prednisone, azathioprine) was admitted to the hospital, presenting with diffuse abdominal pain and vomiting. Blood analysis showed a C-Reactive protein of 155 mg/dL and after thorough examination, imaging studies and laparoscopy procedure, she was diagnosed with intestinal pseudo-obstruction as a complication of inflammatory bowel disease. She was treated with intravenous (IV) methylprednisolone 1 g/day for 3 days and several days later after a full recovery she was discharged and prescribed on augmented dose of immunosupressors (prednisone 2 mg/kg for a total 100 mg/day). A month later she came back to the hospital and was admitted to the Intensive Care Unit for a strong headache, fever and disorientation. Cranial tomography (CT) and magnetic resonance images of the brain were inconclusive; blood chemistry showed bicytopenia (Hb 8.9 g/dL and WBC 1.45 k/µl) and lumbar puncture was performed. Cerebrospinal fluid (CSF) was acellular with normal proteins and normal glucose ratio; cryptococcal antigen and coccidioidomycosis serologic tests were negative; blood cultures were negative and tuberculin skin test was reactive (10 x 10 mm), but QuantiFERON Tb Gold was negative. GeneXpert MTb/RIF of CSF was carried out and *Mycobacterium tuberculosis* complex DNA was detected. The patient started with rifampicin, isoniazid, pyrazinamide and ethambutol. The mental status of the patient improved. However, she continued with fever and later on it was accompanied by abdominal pain. An abdominal CT

showed the presence of multiple abscesses and paracentesis was performed, evidencing the presence of *M. tuberculosis* complex by GeneXpert MTb/RIF; later on *Mycobacterium bovis* was isolated and identified from the CSF original sample, and fever was resolved.

The patient evolution after one month was torpid and even though through treatment with multiple antibiotics, she presented a new onset of fever, so new tests, images and cultures were taken. Yeast colonies identified by Gram stain were isolated from central venous catheter (CVC) and three different peripheral blood cultures. This clinical isolate was submitted to the Department of Microbiology, School of Medicine UANL, for its identification and antifungal susceptibility testing. Fluconazole IV was given to the patient and CVC was removed, but fever persisted and chills accompanied the symptoms. Fluconazole was discontinued and posaconazole was given orally with a total patient recovery.

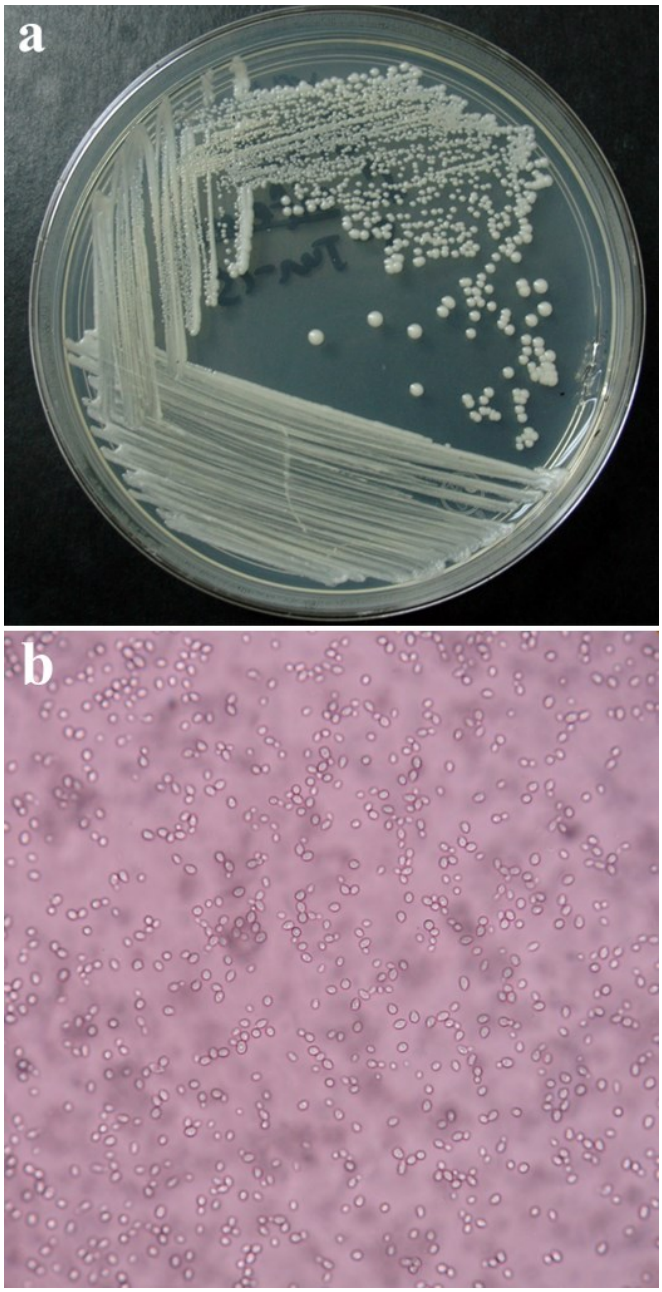
The isolated yeast was sub-cultured on potato dextrose agar (PDA) and incubated at 37°C. After 24 hours of incubation, white, creamy yeast-like colonies grew (Figure 1a). Microscopically budding oval blastoconidia of approximately 3 × 6 µm were observed (Figure 1b). Carbohydrate assimilation was performed using Vitek 2 automated system (bioMérieux, Marcy L'Etoile, France) and the strain was identified as *Candida ciferrii*. The antifungal susceptibility of the strain was evaluated according to the CLSI broth microdilution method (M27-A3 document) [7], obtaining the following results: amphotericin B = 0.125 µg/ml, itraconazole = 0.25 µg/ml, fluconazole = 32 µg/ml, caspofungin = 0.125 µg/ml, and posaconazole = 1 µg/ml.

Discussion

C. ciferrii is an infrequent pathogen, which has been reported on several occasions as a causative agent of human infection and almost always in risk populations [6,8,9]. In the literature it has not been reported that an isolation of this agent from blood in an adult and neither associated to a CVC, but Agin *et al.* reported a fatal case of a child in which they isolated a multi-resistant strain of *C. ciferri* from a blood culture [4]. Several species of non-*albicans Candida* spp. (NAC) are inherently resistant to the most common azole drugs [10], which are used commonly as empirical treatment in the suspicion of fungal disease. The abuse of fluconazole as empirical treatment in systemic mycoses has caused a shift in the emergence of NACs, and also predisposes antifungal resistance of the strains [11]. Measures have been taken to avoid this problem and some propose the use of high dose fluconazole in suspected invasive candidiasis, while international guidelines suggest the use of broad-spectrum antifungals as initial empirical therapy, especially in populations at risk [12,13].

This opens the debate of taking into account the non-*albicans Candida* spp. as an important cause of hospital bloodstream infections. This situation was considered in recent changes of candidiasis therapeutic guidelines, supporting the decision of using a broad spectrum antifungal agent as initial empirical therapy

Figure 1. Clinical isolate of *Candida ciferrii* grew in a potato-dextrose agar plate after 24 h at 37°C (a) and microscopically observed in a wet preparation (b).



[10], but it is still very important to identify and to test antifungal susceptibilities in relevant clinical isolates as exemplify in this case, in which the susceptibility of the strain to fluconazole was MIC = 32 μg/ml and the patient did not respond clinically, while others reports of this species have shown different susceptibilities [6]. Finally, it was necessary to use posaconazole, a broad-spectrum drug, to treat this patient.

In conclusion, it is of utmost importance to consider neglected pathogens as a cause of infection, especially in immunocompromised, previously treated, or long hospital stay patients as it is becoming an everyday occurrence and current algorithms of diagnosis and treatment should change to take this into account for finding better treatment and the best outcome for the patients.

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