Felipe Henriques Alves da Silva[1], Fernando Ribeiro Paço[1], Eduardo Reis[1], Vinicius Amaral[1]

Saccharomyces cerevisiae infection – an unusual pathogen in the ICU

Infecção por Saccharomyces cerevisae – uma infecção atípica em UTI

1. Intensive Care Unit of Hospital Espanhol – Rio de Janeiro (RJ), Brazil.

ABSTRACT

A case of a mixed fungal yeast infection involving *Saccharomyces cerevisiae* - well known for its use in the bread and wine industries – and *Candida albicans,* is described in an intensive care unit patient. Mortality due to mixed fungal infections in the intensive care unit is high. An elderly smoker patient with chronic pulmonary obstructive disease and untreated bladder neoplasm was admitted to the hospital with diarrhea and progressed to septic shock. The above-mentioned yeasts were identified in blood cultures. This case with fatal outcome provides an opportunity to discuss one of the emergent germs found in the intensive care unit, in a case with an atypical presentation.

Keywords: *Saccharomyces cerevisiae*; Infection; Candidiasis; Fungemia; Sepsis; Yeasts; Case reports

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Corresponding author:
Felipe Henriques Alves da Silva
Rua Gurupi, 70 apto. 202 – Grajaú
Zip Code: 20561-100 - Rio de Janeiro (RJ), Brazil.
Phone: (21) 9809-6662
E-mail: felhenriques@uol.com.br

INTRODUCTION

The genus *Saccharomyces* comprises widely known yeasts, with *Saccharomyces cerevisiae* as the most famous representative, widely used in bread, ethanol and wines industries, and also used in the pharmaceutical industry to obtain lepuridin.[1] In the biomedical field, anti-*Saccharomyces cerevisiae* antibodies (ASCA) are relevant Crohn's disease diagnostic markers. Another species, *Saccharomyces boulardii*, is used to treat certain gastrointestinal diseases. In human beings, the genus *Saccharomyces* may colonize gastrointestinal, respiratory and urinary mucosas in patients with underlying diseases.[2-4] Although rare, 'uncommon' yeast infections are increasing,[2-5] with *Saccharomyces cerevisiae* acknowledged as an emergent germ, with an incidence of up to 4% among blood culture germs.[2] Its association with other yeasts (especially *Candida*) is also well described in the literature as determining high mortality rates. Early fungal therapy improves the prognosis.[6]

This article reports the case of an elderly male patient with chronic obstructive pulmonary disease (COPD) who experienced severe fungemia and discusses this rare condition's microbiological and epidemiological aspects.

CASE REPORT

A 73-year-old white, male, Argentinean patient, living in Rio de Janeiro, married and working as a musician, was admitted to the hospital with asthenia and diarrhea. He was a heavy smoker (30 packs-year) with urinary bladder cancer with local involvement and no signs of distant disease, diagnosed one month before by imaging tests. The patient's neoplasm therapy was scheduled

to be started within a week after his admission.

The symptoms started seven days before admission to the hospital, when he presented to his doctor with severe prostration, asthenia and changed sputum pattern. Levofloxacin therapy was performed without prostration or asthenia improvement for one week, when the patient started to experience fluid diarrhea, without mucus, pus or blood. He was admitted to the hospital with severe dehydration; upon admission, his physical examination showed an average general appearance, dehydration and normal vital signs; his admission chest radiograph showed signs of pulmonary hyperinflation, without apparent consolidations; white blood cell count (WBC) with important left-shifted leukocytosis; hyponatremia (130 mEq/L); increased creatinine (2.8) and increased C-reactive protein (CRP 26 mg/dL). Rehydration was started, the antibiotics were changed from levofloxacin to amoxicillin clavulanate plus ciprofloxacin after specimens for culture were obtained (including samples for stools culture). Additionally, *Saccharomyces boulardii* and loperamide were added.

During his stay in the internal medicine ward, while presenting improved WBC and cultures negative for germs, the patient experienced tachypnea and respiratory distress. New cultures were performed after the previous therapy schedule was suspended, and new antibiotics therapy was started with piperacillin/ tazobactam. The diarrhea ceased. The patient worsened within 24 hours and had high fever (39ºC), and was referred to the intensive care unit (ICU).

The patient was admitted to the ICU with signs of respiratory failure, tachycardia, and normal blood pressure. The respiratory system examination showed barrel chest, sparse pulmonary rhonchi and diffused crackling, and important accessory muscle deployment. Heart sounds showed no major changes. The abdomen was flaccid, with peristalsis. Legs had mild symmetric edema; calves were free. Urinary output was reduced/absent. No indwelling central venous catheter was installed before admission to the ICU. The patient was intubated and placed under mechanical ventilation, sedated with midazolam and fentanyl. New cultures were obtained; piperacillin/tazobactam was maintained, and clarithromycin was added to the schedule. Admission laboratory work-up showed left-shifted leukocytosis (12% rods); CRP and creatinine remained increased, and arterial gasometry showed compensated metabolic acidosis and severe hypoxemia.

The patient progressed with shock unresponsive to 30-mL/Kg volume replacement. Noradrenalin 0.3 μg/kg/min was started, with SvO_2 81%. The echocardiogram showed no dysfunction, with a 63% ejection fraction, vena cava without inspiratory fluctuation, PASP 59 mmHg, and no valve changes. The lower-limb venous Doppler showed no signs of deep-vein thrombosis. A chest X-ray revealed four-quadrants with diffuse reticular and nodular infiltration. The patient had moderate amounts of off-white sputum; PO_2/FiO_2, 200; 24-hour APACHE, 14. Hemodialysis for acute renal failure was requested and initiated 6 hours later.

Bronchoscopy revealed mildly swollen mucosa, with clear, moderate secretion. Specimens were obtained for culture and the identification of alcohol-acid-resistant bacilli (AARB). After these starting measures, the respiratory (PO_2/FiO_2 around 240) and metabolic features were improved, in spite of the fever and the need for vasoactive amines after 48 hours. The results of cultures obtained upon admission to the hospital revealed *Candida albicans* in two samples; *Saccharomyces cerevisiae* was identified in two additional blood cultures obtained upon admission to the ICU. Urine was culture positive for *Candida albicans*; anti-HIV was negative; and AARB was negative. Fluconazole was added to the antibiotic schedule. After treatment with fluconazole was started, clinical improvement was observed despite several daily peaks of fever. New cultures were obtained, and in accordance with the Hospital Infection Committee's recommendations, antifungal therapy was changed to amphotericin B after three days with fluconazole. The bronchoalveolar lavage (BAL) fluid culture revealed the presence of *Saccharomyces cerevisiae.*

Forty-eight hours after treatment with amphotericin B was started, the patient improved, with no fever, no further need for vasoactive amines, improved PO_2/FiO_2, balanced metabolic conditions, and positive laboratory progression. The patient was maintained on daily hemodialysis. Cultures for candidemia were obtained every 48 hours. Sedation was withheld in a respiratory weaning attempt; the patient failed the spontaneous breathing test and could not be weaned from the mechanical ventilation.

Seven days after treatment with amphotericin B was started, the patient developed septic shock and was therefore started on meropenem after new cultures were obtained, while maintaining antifungal therapy. The patient initially improved, but after two atrial fibrillation episodes occurring 48 hours from initiation of this new schedule, the patient experienced abdominal distension and the novel onset of refractory to high-dose amine shock. Mesenteric ischemia in association with the arrhythmia was suspected. A CT scan was not performed, due to the clinical conditions, which included high amine dose dependency and unsatisfactory gas exchange. The abdominal X-ray showed distended intestinal loops. Considering the patient's poor clinical and metabolic conditions, the

general surgeon contra-indicated an abdominal cavity exploration surgery. The patient eventually died 13 days after admission to the ICU, 24 hours after the initiation of the abdominal event. The tracheal secretion specimen obtained during the penultimate complication culture results revealed carbapenems-sensitive *Klebsiela oxytoca*. All blood cultures obtained until the day of death (at least one sample) were positive for *Candida albicans.*

DISCUSSION

Saccharomyces cerevisiae is a well-known microbe used intensively in industrial capacities.[1,2,7] Although widely distributed in nature and displaying low virulence against humans, invasive *Saccharomyces cerevisiae* infections have been increasingly common in recent decades, having been identified in about 4% of positive fungal blood cultures, including those from immunocompetent subjects.[2,5] It was first described as a pathogen in 1958 by Reihersol and Hoel in a bronchopneumonia patient's serial sputum sample.[4] Its epidemiology is not fully understood, having been recognized as a transient colonizer of the gastrointestinal mucosa (particularly after the contamination of food), the female genital tract and the respiratory tract.[2-4,7] Its access to the body is believed to be predominantly gastrointestinal, in spite of reports on catheter contamination due to contaminated hands. The presence of the microbe may therefore be considered a healthcare-related infection.[2,8] Its presence in otherwise sterile fluids indicates a broken barrier or a high fungal population.[2] The relevant risk factors are very similar to those for candidemia, such as indwelling catheters, parenteral nutrition, hemodialysis, broad-spectrum antibiotics, immunosuppression (human immunodeficiency virus [HIV] or neoplasm) and transplantation. In addition, in *Saccharomyces* fungemia, an isolated and exclusive risk factor is the previous use of *Saccharomyces boulardii* as a probiotic, which has been widely used for treatment of diarrheas, especially in antibiotics-associated cases.[2,3,5] This risk is due to the identification of strains of *S. boulardii* that are genetically identical to *S. cerevisiae* and that are currently considered taxonomically as *Saccharomyces cerevisiae* subtypes.[2,3] This deserves attention because, after the capsule is opened for enteral administration, the microbes may remain on surfaces within a one-meter range for up to two hours and are difficult to remove, even with hand-washing; this may constitute a possible focus for the dissemination to closed units.[3] According to the literature, fungemia is detected within approximately 10 days of probiotic use.[3]

The most important feature of *Saccharomyces* infection is fungemia, which can be clinically identical to *Candida* infection, including chorioretinitis and esophageal lesions.[2,3,5] *Saccharomyces* fungemia is described in immunocompromised patients. In addition to fungemia, other (rarer) features may include endocarditis, liver abscess, pneumonia, vaginitis and esophagitis.[2,3]

The identification of the fungus in cultures is simple and is based on its unique morphology, growth and biochemical aspects.[3] Differentiation from the *boulardii* subtype is not routine because no pathognomonic characteristics are available.[2]

There is no consensus on the therapy for this infection, with descriptions favoring fluconazole, voriconazole, flucytosine, amphotericin B or even the combination of amphotericin B plus fluconazole.[2-8] Other relevant measures include removing catheters and suspending the use of probiotic *Saccharomyces boulardii*.[3,7,8]

Mixed fungal infections, although more frequently described in relation to the improvement of diagnostic methods, is not frequently described in the literature and corresponds to 3-5% of all candidemias. Relative to monofungal infections, mixed fungal infections apparently do not increase mortality but also may have lower mortality rates (in some series, 20% versus 53%).[6] Therapy is not different from the conventional treatment for single-microbe fungemia. The sensitivity profiles of the microbes involved should also be considered.[7]

The reported case illustrates the diagnosis of disseminated candidemia in a patient with COPD who, although bearing this lung disease, had not previously used corticosteroids or had not been admitted to the hospital. The patient had incipient urinary bladder cancer, used no central venous catheter, underwent one outpatient cycle of antibiotics use, came from a community with few admission risk factors and developed a mixed fungal infection with *S. cerevisiae* and *Candida albicans.* The identification of *Saccharomyces* in cultures is likely to be associated with a broken intestinal barrier associated with the use of probiotic *Saccharomyces boulardii.* The use of the anti-diarrhetic loperamide probably accelerated the intestinal germ translocation, with the fungemia occurring more rapidly than described in the literature. This case highlights this microbe of increasing importance, associated with the clinically common use of probiotics, which were previously considered to be harmless. Antimicrobial therapy, first with fluconazole and then with amphotericin B, resulted in *Saccharomyces* being cleared from the blood culture, although no clear guidance is available with respect to therapy or a cure. Another interesting issue was the mixed fungal infection, a rare instance but reported increasingly in the intensive care literature.

RESUMO

Descreve-se aqui o caso de infecção fúngica mista por leveduras em paciente de UTI: por *Saccharomyces cerevisae* – levedura conhecida e de larga utilização na panificação e produção de vinhos – e Candida albicans. As infecções fúngicas mistas possuem alta mortalidade em terapia intensiva. Discutimos neste artigo o caso de paciente idoso portador de doença pulmonar obstrutiva crônica, portador de tumor não tratado de bexiga, tabagista, admitido no Hospital com quadro diarréico, evoluindo para choque séptico, com isolamento em hemoculturas das duas leveduras supracitadas. Quadro grave, de evolução letal, possibilitando a discussão de um dos germes emergentes em unidade de terapia intensiva e apresentação atípica em terapia intensiva.

Descritores: *Saccharomyces cerevisiae*; Infecção; Candidíase; Fungemia; Sepse; Leveduras; Relatos de casos

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