Chapter 213

Report of six cases of fungemia related to health care by Saccharomyces cerevisiae (SC) in a hospital in São Paulo-SP

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ABSTRACT
Objective: To report six cases of fungemia by Saccharomyces cerevisiae, in patients hospitalized in the Intensive Care Unit of General Hospital of São Paulo/SP/Brazil and the relationship with the use of probiotics. Method: a retrospective survey of data from hospital records. Discussion: Analyzing the 6 cases, we found a mean age of 65.8 years, male predominance (4/6), association with heart disease and lung disease (5/6), use of parenteral diet (3/6), use of venous access (6/6), admission to the Intensive Care Unit (6/6) and use of probiotics (5/6). The correlation between the use of probiotics and the occurrence of fungemia by Saccharomyces cerevisiae seems to be related to factors involved in the probiotic preparation process at the time of its administration to patients. Contamination of surfaces in the hospitalization environment and contamination of central venous accesses by the hands of professionals who handle probiotics during their administration may be the main predisposing factor to these infections.

Keywords: Probiotics, Fungemia, Emerging germs, Saccharomyces cerevisiae.

1 INTRODUCTION

The genus Saccharomyces constitutes a group of yeasts whose main representative is Saccharomyces cerevisiae, used in the production of bread, beer, wine, and ethanol (1). Saccharomyces boulardii, a strain of Saccharomyces cerevisiae (6) is used as a probiotic in the treatment of gastrointestinal tract disorders (7).

Probiotics are live microorganisms that, if administered in adequate doses, can confer benefits to the patient, such as the prevention and treatment of diarrhea due to the use of antibiotics, and improvement of inflammatory bowel disease by immunomodulation, among others (9,10).

It has long been known that yeasts of the Saccharomyces genus can colonize the gastrointestinal, respiratory, and urinary tracts in patients with underlying diseases(2-4) and infections have recently been detected in our midst(2,5). Although rare, Saccharomyces cerevisiae is recognized as an emerging germ that can cause fungemia, with an incidence that can reach 4% of fungal isolates in blood cultures(2). Person-to-person contact and exposure to associated commercial strains in food may contribute to human host colonization and infection. Clinical conditions and risk factors are the same as for systemic candidemia, including central venous catheter, neutropenia, broad-spectrum antibiotic therapy, and gastrointestinal tract surgery (11,12,13).

2 CASUISTIC

Table 1: Description of the studied cases.

ID	DATE OF HOSPITALIZATION	GENDER	AGE	COMBITIES	PARENTERAL NUTRITION	CVC	ICU	REASON FOR ADMISSION	USE OF PROBIOTICS	PLACE OF HOSPITALIZATION	ANTIFUNGAL TREATMENT	DEATH
1	3/22/17	MALE	61 ANOS	COPD/IC	YES	YES	YES	SEPSIS	YES	ICU	FLUCO/ MICA/ VORICONAZOL	NO
2	5/10/18	FEMALE	88 ANOS	SAH/ARRHYTHMIA	NO	YES	NO	BCP	NO	ENF	ANFO B	NO
3	3/14/19	MALE	38 ANOS	CEREBRAL PALSY	YES	YES	YES	BCP ASP	YES	ICU	None	NO
4	7/7/19	MALE	62 ANOS	SAH/ARRHYTHMIA /DM	YES	YES	YES	SEPSIS	YES	ICU	FLUCO	NO
5	3/22/17	MALE	59 ANOS	COPD	NO	YES	YES	BCP	YES	ICU	VORICONAZOL	YES
6	5/10/18	FEMALE	87 ANOS	COPD, SAH, HYPOTHYROIDISM, ARRHYTHMIA	NO	YES	YES	SEPSIS	YES	ICU	ANFO B	NO

In our sample, we identified six patients with Saccharomyces cerevisiae growth in blood cultures between March 2017 and July 2019, which are described in Table 1.

A fungi gram was not possible for any of the isolated cases. The methodology used was automated continuous monitoring for yeast, filamentous and dimorphic fungi, with manual identification or mass spectrometry (MALDI-TOF). The incubation time of up to 30 days.

The distribution of the cases described according to gender showed four males (66%) and two females (33%), with a mean age of 65.8 years.

The associated comorbidities were heart disease and lung disease, being present in 83% (5/6) of the patients, 50% (3/6) of the cases used a parenteral diet and 100% (6/6) used a central venous catheter. All patients were admitted to the Intensive Care Unit (6/6) and 83% (5/6) used probiotics.

Antifungals were used for treatment in 83% (5/6) of cases. A single patient who did not receive antifungal medication was discharged from the hospital and was asymptomatic 4 days after the arrival of the result of the blood culture showing the growth of Saccharomyces cerevisiae.

Lethality was 16% (1/6) below that described in the literature and all patients had other infections by multidrug-resistant bacteria having used broad-spectrum antimicrobials.

3 DISCUSSION

Our casuistry consisted mainly of male patients, over 65 years of age, with underlying heart and lung diseases, hospitalized for serious health problems, who required intensive care, use of broad-spectrum antimicrobials, central venous access, and most received probiotics.

The incidence of fungemia due to Saccharomyces cerevisiae is unknown and, in most reports, it occurs in isolation, although some cases of endocarditis, liver abscess, and disseminated disease have already been described. There are few descriptions of fungemia by Saccharomyces cerevisiae in previously healthy patients, the main risk factor being the use of probiotics by the patient himself or by other individuals hospitalized in the same unit, in nearby places(6). In addition, infection associated with the presence of a central venous catheter is reported (15).

Based on this, despite the benefits, the use of probiotics must be individually evaluated, especially when dealing with immunosuppressed patients.

S. cerevisiae should be considered a well-established cause of nosocomially acquired disease. Prophylaxis or treatment with probiotics (S. boulardii), should be considered a risk factor for nosocomial bloodstream infection in patients with predisposing conditions (15).

Infection can occur in two ways: intestinal translocation and contamination of the venous catheter, either by the hands of health professionals handling the medication or by airborne dispersion of the strains after opening the capsules. There are reports of infection not only in individuals who received treatment with probiotics but also in patients who shared a room with the person undergoing treatment(6). Some studies have shown that viable strains could be detected up to one meter away from the handling site and

persisted on surfaces after two hours, thus making it more prudent to handle them away from patients (15). In addition, strains of Saccharomyces cerevisiae persist in the hands of professionals who handled it without gloves, even after proper cleaning(16).

Therefore, we consider that a great risk of contamination arises from opening the sachet in the environment where the patients are located, regardless of the use of probiotics.

The treatment of bloodstream infection by Saccharomyces cerevisiae consists of removing the venous catheter and using antifungals such as amphotericin B (1mg/Kg/day) and fluconazole (10mg/Kg/day), although there are descriptions of strains resistant to both and especially to fluconazole(15).

In hospital practice, probiotics are handled and prepared in medication trolleys at the bedside or at nursing stations in the inpatient unit itself, which may have contributed to environmental contamination and that of the reported patients.

Another important fact is that the identification of Saccharomyces cerevisiae can be confused with other pathogens such as Candida haemolunii and Candida auris, the latter an emerging fungus identified for the first time as a cause of disease in humans in 2009 in Japan and which represents a serious threat to global health since some strains of Candida auris are resistant to all three main classes of antifungal drugs and their identification requires specific laboratory methods (14) a fact that may overestimate the lethality of infections by Saccharomyces cerevisiae.

We conclude that the preparation and handling of probiotics should take place in environments other than inpatient units and be associated with the implementation of well-defined protocols for indication, handling, and administration. We believe that the preparation of probiotic should be done outside the patient's room and using disposable gloves, thus avoiding the contamination of surfaces around the patient, and reducing the possibility of contamination of the central venous access by the professional's hands during the manipulation of this access.

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