

# Saccharomyces cerevisiae fungemia due to an unexpected source in the pediatric intensive care unit

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## ABSTRACT

**Background.** *Saccharomyces cerevisiae* is one of the microorganisms commonly used as a probiotic. Although it is primarily known as non-pathogenic, it may cause fungemia, particularly in immunocompromised patients or children with a history of long-term hospital stay.

**Case.** A 6-month-old boy with a history of ventriculostomy, ventriculoperitoneal shunt implantation, and external drainage due to an intracranial mass and hydrocephalus was admitted to the pediatric intensive care unit (PICU) on postoperative day 14 due to respiratory distress and intubated on admission. He was started on broad spectrum antibiotics on day 25 of the admission due to fever and clinical deterioration. Culture of the central venous catheter (CVC) yielded *S. cerevisiae*, the CVC was removed, and the patient was started on caspofungin. We noticed that a patient near this patient was on a probiotic preparation containing *S. boulardii* for diarrhea before PICU admission. His fever subsided on day 2 of caspofungin, and laboratory findings normalized on follow-up.

**Conclusions.** Probiotics should not be used in PICUs because of the high risk for CVC-related sepsis in critically ill children.

**Key words:** *Saccharomyces cerevisiae*, sepsis, pediatric intensive care, probiotic, fungemia.

*Saccharomyces cerevisiae* (Brewer's yeast) is a facultative anaerobic budding yeast used since antiquity for baking and producing fermented beverages, bread, wine, and beer. They are ubiquitous and can be a part of the intestinal, vaginal, pharynx, pulmonary tree, and skin floras, particularly in patients with chronic disorders.<sup>1,2</sup> *Saccharomyces boulardii* is a yeast that is genetically very close or nearly identical to *S. cerevisiae* and is one of the microorganisms commonly used as a probiotic.<sup>3</sup> It is used to treat *Clostridium difficile* associated diarrhea and the prevention of antibiotic-associated diarrhea in humans.<sup>3,4</sup> It is generally non-pathogenic; however, it may cause fungemia, particularly in immunocompromised patients or children with

a history of long-term hospitalization.<sup>1,3,4</sup> The incidence of *S. cerevisiae* fungemia is unknown.<sup>5</sup> *S. cerevisiae* fungemia is unusual in previously healthy children, and the leading risk factor is the use of a probiotic or their use by other patients admitted to the same unit in nearby beds.<sup>5</sup> Intravascular catheter and prosthetic valve-related infections were also reported.<sup>3,5,6</sup>

Even though probiotic strains are widely considered safe, there are some safety concerns, especially in severely immunocompromised patients, in whom they may cause sepsis.<sup>7</sup> Probiotics are not used to restore the intestinal flora in pediatric intensive care units (PICU) because of the potential to cause fungemia, especially in patients with central venous catheters (CVCs).<sup>5,6</sup> We hereby present the course and successful treatment of a 6-month-old male with *S. cerevisiae* fungemia due to an unexpected source in our PICU.

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Received 12th June 2020, revised 20th February 2021,  
14th April 2021, accepted 14th April 2021.

### Case Report

A 6-month-old boy with a history of ventriculoperitoneal shunt implantation and external drainage for intracranial mass and hydrocephalus was admitted to the PICU on postoperative day 14 due to respiratory distress. He was intubated on admission, after which he had an oxygen saturation of 96% on a FiO<sub>2</sub> of 0.6. His heart rate was 125 beats/minute, his blood pressure was 115/80 mmHg, and his body temperature was 37.3°C. His Glasgow Coma Score was 5. 30 mL of cerebrospinal fluid (CSF) was drained four times daily. He was ultimately diagnosed with an inoperable atypical rhabdoid/teratoid tumor, so he was started on doxorubicin, cyclophosphamide, and vincristine. His white blood cell count was 5.24×10<sup>3</sup>/μL, the total neutrophil count was 3.63×10<sup>3</sup>/μL, hemoglobin level was 9.6 g/dL, hematocrit was 28.4%, platelet count was 652×10<sup>3</sup>/μL, blood glucose level was 101 mg/dL, aspartate aminotransferase 17 IU/L, alanine aminotransferase 10 IU/L, urea 7 mg/dL, creatinine level was 0.03 mg/dL, sodium level was 138 mmol/L, potassium level was 5 mmol/L, chlorine level was 104 mmol/L, calcium level was 8.1 mg/dL, CRP level was 11.3 mg/dL. Blood gas analysis was normal (pH: 7.39, HCO<sub>3</sub>: 21.8 mmol/L, pCO<sub>2</sub>: 37 mmHg, laktat 1,6 mmol/L).

The patient had a fever of 39°C on day 20 day of admission. Meropenem, fluconazole, amikacin, vancomycin, and colistin were consequently initiated empirically due to persistent fever. Blood, catheter, CSF, urine, and tracheal aspirate cultures were obtained; peripheral blood, CVC, urine, and tracheal aspirate cultures were negative for bacteria and fungi. A computed tomography scan of the chest was obtained for workup of sepsis of unknown origin.

Repeat cultures were obtained on the following days due to persistent high fever. The culture of the catheter tip yielded *S. cerevisiae* on day 25 of PICU admission. Fluconazole was discontinued and caspofungin was started, and other antibiotics were stopped (Table I). We noticed that our patient had a fever spike the day after a

**Table I.** Timeline of treatments, fever status, cultures, radiological imaging, respiratory support applied to the patient following PICU admission.

	14th day	20th day	25th day	27th day	39th day	52nd day	70th day
Fever	-	+	+	-	-	-	-
Antibiotic and antifungal therapy		Meropenem, fluconazole, amikacin, vancomycin, and colistin were started	Caspofungin was started and other antibiotics were stopped.	Caspofungin	Caspofungin was stopped	-	-
Cultures			<i>S. cerevisiae</i> was yielded in the CVC tip culture				
Radiological imaging		Thorax computer tomography was normal					
Respiratory support	IMV	IMV	IMV	IMV	IMV	Extubated and oxygene mask	Oxygene mask
Outcome							Transferred to the pediatric oncology ward

CVC: central venous catheter, IMV: invasive mechanical ventilation, PICU: Pediatric Intensive Care Unit.

neighbouring patient with inherited metabolic disease and gastroenteritis was started on a probiotic containing *S. boulardii*.

His fever subsided on day 2 of caspofungin, and laboratory findings normalized. Caspofungin was given for 14 days, until day 39 of PICU admission. He was extubated on day 52 of admission, whereafter he remained clinically stable. He was transferred to the pediatric oncology ward on day 70 of PICU admission.

Written informed consent was obtained from the patient's family.

## Discussion

Probiotics are becoming progressively available as food supplements and are widely used in the medical industry.<sup>3</sup> Henri Boulard isolated *Saccharomyces boulardii* in 1920 during a cholera outbreak and it was used as a probiotic for the treatment of gastrointestinal diseases.<sup>3</sup>

*S. Boulardii* is a yeast used as a dietary supplement. It is used to treat various diseases such as enteral-nutrition-related diarrhea, traveler's diarrhea, antibiotic-related diarrhea, *Helicobacter pylori* disease, HIV-associated diarrhea, *Salmonella typhi*, and *Clostridium difficile*, Crohn's disease, and other inflammatory bowel conditions.<sup>3,8</sup> *Saccharomyces boulardii* is genetically nearly identical to *S. cerevisiae* and is one of the microorganisms commonly used as a probiotic.<sup>3</sup>

Invasive *Saccharomyces* infections remain rare among invasive fungal infections even though the incidence has significantly increased since the 1990s.<sup>9</sup> The incidence of *S. cerevisiae* fungemia is unknown.<sup>5</sup> *Saccharomyces* fungemia has been reported to cause endocarditis, liver abscess, and disseminated disease.<sup>5</sup> The main risk factor for *Saccharomyces cerevisiae* fungemia in previously healthy patients is the use of probiotics or probiotic use by other

individuals in the same unit in neighboring beds.<sup>5</sup> Infection of CVCs have also been reported.<sup>5</sup> Predisposing factors are the same as those pertaining to invasive candidiasis, which includes the presence of a CVC, total parenteral nutrition, ICU admission, antibiotic use, and immunosuppression.<sup>1</sup> In a review of 60 cases conducted by Munoz et al.<sup>4</sup>, %31 of the patients were immunosuppressed, and %46 were critically ill with invasive *S. cerevisiae*. In this study, 13 patients were  $\leq 16$  years of age, and 7 patients were  $\leq 1$  year of age.<sup>4</sup> Many case reports also describe invasive *S. cerevisiae* in hospitalized patients in beds near patients using probiotics.<sup>1,4</sup> The cause of the fungemia was thought to be either translocation through the digestive system or contamination of the CVC through the colonized hands of healthcare personnel after administering probiotics.<sup>3</sup> Our patient was receiving chemotherapy, had a CVC, and was situated near a patient who was on probiotics, so he had several risk factors for disseminated infection. We think it is likely that the probiotic strain was transmitted to our patient through colonized hands of PICU staff.

It has been shown that after a package of freeze-dried yeast is opened, viable cells can be retrieved up to two hours later from surfaces as much as one meter away from the opening site and can persist on the hands of personnel even after vigorous hand hygiene.<sup>8</sup> If the package containing the probiotic is opened in a patient's room, meticulous hand hygiene and the use of gloves may still decrease the risk of infection.<sup>8</sup> Yeasts isolated from blood cultures are considered pathogenic, but transient fungemia can occur in immunocompetent patients with no catheter, no valvulopathy, and no organic severe underlying disease.<sup>10</sup> Blood cultures should be repeated and yeast colonies should be identified correctly.<sup>10</sup> Since a patient close to our patient was on probiotics, fluconazole treatment was initiated after the first catheter culture, and the probiotic treatment of the neighboring patient

was discontinued. Recommended treatment for disseminated bloodstream infection related to probiotic use is the removal of the CVC, and amphotericin B (1 mg/kg.day) or fluconazole (10 mg/kg.day), even though reports of strains resistant to fluconazole and amphotericin B have been reported.<sup>5</sup> A literature review by Munoz et al.<sup>4</sup> reported that the most common drugs employed were fluconazole (16 patients) and amphotericin B (28 patients). The mortality rate was 28% (17 of 60 patients) and only one child died. The role of echinocandins was not discussed in this study. However, several case reports of successful treatment of *S. boulardii* with caspofungin can be found.<sup>1,3</sup> Our patient had his CVC removed and he received a 14-day course of caspofungin. Repeat cultures remained negative.

In conclusion, probiotic use is a risk factor for invasive infection and sepsis in critically ill patients. Transmission can occur by air or from patients on probiotics situated on a nearby bed. Therefore, probiotics should not be used in intensive care units due to the risk of central line-related sepsis in critically ill patients.

#### Author contribution

The authors confirm contribution to the paper as follows: study conception and design: TK, EG, DBÇ; data collection: EG, DBÇ, EB; analysis and interpretation of results: TK, H.Ö, EG; draft manuscript preparation: EG, DBÇ. All authors reviewed the results and approved the final version of the manuscript.

#### Conflict of interest

The authors declare that there is no conflict of interest.

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