

Introduction

Cultured yogurts and probiotics are a \$28 billion worldwide industry¹ and are relatively cheap and readily available to consumers in supermarkets, pharmacies, and hospitals. They come in a variety of different forms, including commercial yogurts and capsules, and are well known in the baking and brewing industries. Many health care providers recommend cultured yogurts/probiotics for patients with altered bowel flora to restore the functional integrity of the bowel. There have been multiple adult randomized controlled trials²⁻⁷ of marginal quality that have shown the ability of these agents to prevent diarrhea associated with antibiotic usage and have been proposed to be used in conditions such as Crohn's disease and other inflammatory bowel conditions.⁸

Despite harboring live bacteria and/or fungi, cultured yogurts and probiotics are an uncommon cause of infection in humans⁹ and generally have been deemed effective and safe.² They are considered the "good bacteria" by many and, by definition, should be beneficial to the ingesting host. However, with an increase in the population at risk for chronic and debilitating diseases with exposure to significant risk factors, such as the use of immunosuppressive drugs and broad spectrum antibiotics, parenteral nutrition, and use of central venous

Use of Cultured Yogurt with Probiotics Causing Septic Shock and Intra-abdominal Abscesses

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catheters, the number of reported cases of infections due to these agents over the last century is clearly on the rise.¹⁰

Case Report

A 61-year-old male with a history of testicular germ cell cancer status post allogenic stem cell transplant and neutropenic immunosuppressive from therapy presented with abdominal pain and fever. Temperature was 100.1°F, blood pressure 128/68 mm Hg, pulse rate 85 beats per minute, and respiratory rate 18 times per minute. Initial blood count revealed a white blood cell count of 1.3 K/uL, platelet count of 20 K/uL, and an absolute neutrophil count of 0. A comprehensive metabolic panel (CMP) showed glucose of 110 mg/dL, creatinine of 1.58 mg/dL, sodium of 129 mEq/L, and albumin of 2.9 g/dL. Alpha fetal protein was 771 IU/mL. Urine culture showed no growth and Clostridium difficile toxin B by polymerase chain reaction was positive. Chest x-ray showed developing infiltrate and pulmonary edema (Figure 1).

The patient was started on metronidazole and improved over the course of the next few days, then suddenly deteriorated and was transferred to the medical intensive care unit with septic shock and respiratory failure requiring mechanical ventilation. Blood and sputum cultures showed *S*. cerevisiae. Subsequently, the patient's wife reported that she had been encouraged by the nursing staff and dietitians to feed her husband cultured yogurt sprinkled with probiotic powder to restore bowel flora. Aspiration (due to altered mental status), gastrointestinal tract translocation (due to altered mucosal integrity from clostridium difficile-associated diarrhea), and severe immunocompromised state (from chemocontributed therapy) likely to his deterioration. He recovered with voriconazole therapy which was based on sensitivities.

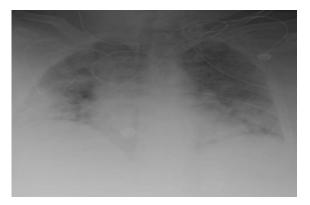


Figure 1. Chest x-ray showed developing infiltrate and pulmonary edema.

Further review of records revealed another case of invasive S. cerevisiae infection in the same hospital that occurred within months of the above case. The patient was a liver transplant recipient who had previous abdominal surgery and also presented with abdominal pain and severe sepsis. Initial temperature was 98.5°F, blood pressure 83/54 mm Hg, pulse rate 110 beats per minute, and respiratory rate 17 times per minute. Initial laboratory revealed a white blood count of 28.8 K/uL and a platelet count of 592 K/uL. A CMP showed glucose of 117 mg/dL, creatinine of 0.7 mg/dL, sodium of 135 mEq/L, and potassium of 4 mEq/L. Computed topography (CT) of the abdomen and pelvis showed 23 mm x 38 mm and 45 mm x 51 mm walled off areas suspicious for abscesses (Figures 2 and 3). CT-guided drainage and culture of the abscesses revealed *S. cerevisiae*.

This patient also was encouraged by the nurses and dietitians to eat cultured yogurt with probiotics to restore bowel flora. She was on an immunosuppressive transplant regimen and had previous bowel surgeries that likely contributed to the organism translocating through the gastrointestinal mucosa and contributed to abscess formation. This patient also improved with antifungal therapy.

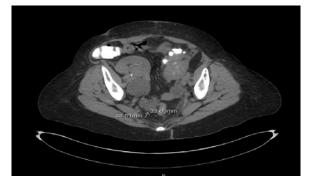


Figure 2. Walled-off abscess located near the right rectum.

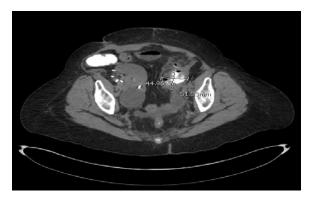


Figure 3. Large abscess in the left pelvis filled with contrast.

Discussion

Few cases of complications from *S*. *cerevisiae* have been reported. The number of documented infections from the ingestion of cultured yogurts and probiotics is increasing and considered an emerging type of infectious disease.⁹ Since the mid-1900s,

roughly 60-100 cases of *S. cerevisiae* fungemia from cultured yogurts/probiotics have been identified.^{9,11,12} Data released in the near future undoubtedly will show a higher number of cases of *S. cerevisiae* fungemia.

Probiotic-related fungemia may be asymptomatic or severe with unexplained fever, fungemia, endocarditis, pneumonia, liver abscess, peritonitis, and septic shock.¹³ Although the vast majority of reported cases occur in patients who are critically ill with significant comorbidities, S. cerevisiae should be considered a potentially dangerous micro-organism as there are cases causing fungemia in immunocompetent patients as well.⁹ Also, patients may not report they are ingesting cultured yogurt and probiotics as historically they have been viewed as benign, health promoting agents with no side effects. Patients should be asked about probiotic and cultured yogurt use when gathering historical data.

Enteral translocation of ingested microorganisms (as in the cases described above) is a potential portal of entry into the bloodstream.¹⁰ Approximately two-thirds of patients with *S. cerevisiae* fungemia had previous digestive tract disease.¹² Scant data, however, specifically document intraabdominal abscess caused by *S. cerevisiae*, which makes the second case above unique.

According to the Infectious Disease Society of America (IDSA),¹³ routine administration of available probiotics is not recommended to prevent primary *C. difficile* infection as there are limited data to support this approach and there is a potential risk of bloodstream infection. There is a potential benefit of using probiotics containing *S. cerevisiae* (subtype *boulardi*) with oral

References

¹ Transparency Market Research. Probiotics Market (Dietary Supplements, Animal Feed, Foods & Beverages) - Global

vancomycin to reduce the recurrence of C. difficile, however, the IDSA discourages routine usage of probiotics in critically ill patients and warns of potential fungemia if used in immunocompromised patients. national/international Other medical authorities (e.g., United Kingdom Health Protection Agency, American College of Physicians, World Gastroenterology Organization) have no definitive statements with regards to the overall safety of probiotic usage with antibiotic-associated diarrhea and C. diff-associated diarrhea.²

Conclusion

There is marginal randomized data on the effectiveness of probiotics to prevent antibiotic-associated and *C. difficile*associated diarrhea. The recent increase in incidence and severity of disease caused by hypervirulent strains of *C. difficile* has prompted some clinicians to increase their use of probiotics as drugs in combination with standard antimicrobial drug therapy. However, many organizations, such as the IDSA, do not recommend the routine usage of probiotics due to potential complications.

Clinicians should be aware that probiotic dietary supplements are not required by the US Food and Drug Administration to undergo rigorous premarketing evaluations for efficacy or safety.¹³ Furthermore, there multiple been reports about have complications such as fungemia from these agents. Saccharomyces cerevisiae should be considered as an emerging cause of nosocomially acquired yeast infection and the risks and benefits of probiotics should be carefully assessed, particularly in immunosuppressed or critically ill patients.⁹

Industry Size, Share, Trends, Analysis, Growth And Forecast 2012 – 2018. http://www.transparencymarketresearch.co m/probiotics-market.html.

- 2 Gao XW, Mubasher M, Fang CY, Reifer C, Miller LE. Dose-response efficacy of a proprietary probiotic formula of Lactobacillus acidophilus CL1285 and Lactobacillus casei LBC80R for antibiotic-associated diarrhea and Clostridium difficile-associated diarrhea prophylaxis in adult patients. Am J Gastroenterol 2010; 105(7):1636-1641. PMID: 20145608.
- ³ Safdar N, Barigala R, Said A, McKinley L. Feasibility and tolerability of probiotics for prevention of antibiotic-associated diarrhoea in hospitalized US military veterans. J Clin Pharm Ther 2008; 33(6):663-668. PMID: 19138244.
- ⁴ Wenus C, Goll R, Loken EB, Biong AS, Halvorsen DS, Florholmen J. Prevention of antibiotic-associated diarrhoea by a fermented probiotic milk drink. Eur J Clin Nutr 2008; 62(2):299-301. PMID: 17356555.
- ⁵ Beausoleil M, Fortier N, Guénette S, et al. Effect of a fermented milk combining Lactobacillus acidophilus Cl1285 and Lactobacillus casei in the prevention of antibiotic-associated diarrhea: a randomized, double-blind, placebocontrolled trial. Can J Gastroenterol 2007; 21(11): 732-736. PMID: 18026577.
- ⁶ Hickson M. Probiotics in the prevention of antibiotic-associated diarrhoea and Clostridium difficile infection. Therap Adv Gastroenterol 2011; 4(3):185-197.
 PMID: 21694803.
- ⁷ Guslandi M, Mezzi G, Sorghi M, Testoni PA. Saccharomyces boulardii in maintenance treatment of Crohn's disease. Dig Dis Sci 2000; 45(7):1462-1464. PMID: 10961730.

- ⁸ Muñoz P, Bouza E, Cuenca-Estrella M, et al. Saccharomyces cerevisiae fungemia: An emerging infectious disease. Clin Infect Dis 2005; 40(11):1625-1634. PMID: 15889360.
- ⁹ Cassone M, Serra P, Mondello F, et al. Outbreak of Saccharomyces cerevisiae Subtype boulardii fungemia in patients neighboring those treated with a probiotic preparation of the organism. J Clin Microbiol 2003; 41(11):5340-5343. PMID: 14605200.
- ¹⁰Herbrecht R, Nivoix Y. Saccharomyces cerevisiae fungemia: An adverse effect of Saccharomyces boulardii probiotic administration. Clin Infect Dis 2005; 40(11): 1635-1637. PMID: 15889361.
- ¹¹Enache-Angoulvant A, Hennequin C. Invasive Saccharomyces infection: A comprehensive review. Clin Infect Dis 2005; 41(11):1559-1568. PMID: 16267727.
- ¹² Riquelme AJ, Calvo MA, Guzmán AM, et al. Saccharomyces cerevisiae fungemia after saccharomyces boulardii treatment in immunocompromised patients. J Clin Gastroenterol 2003; 36(1):41-43. PMID: 12488707.
- ¹³Cohen SH, Gerding DN, Johnson S, et al. Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). Infect Control Hosp Epidemiol 2010; 31(5):431-455. PMID: 20307191.

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