PUBLICAÇÃO OFICIAL DO NÚCLEO HOSPITALAR DE EPIDEMIOLOGIA DO HOSPITAL SANTA CRUZ E PROGRAMA DE PÓS GRADUAÇÃO EM PROMOÇÃO DA SAÚDE - DEPARTAMENTO DE BIOLOGIA E FARMÁCIA DA UNISC

Revista de Epidemiologia e Controle de Infecção

Hospital Santa Cruz

EXPERIENCE REPORT

Rhodotorula fungemia in a patient with acute lymphoblastic leukemia

Fungemia de Rhodotorula em paciente com leucemia linfoblástica aguda

Fungemia por Rhodotorula en un paciente con leucemia linfoblástica aguda

https://doi.org/10.17058/reci.v12i1.16325

Received: *04/14/2021*
Accepted: *06/15/2021*
Available online: *05/24/2022*

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ABSTRACT

Objectives: *Rhodotorula* is an environmental yeast that belongs to *Basidiomycota* Phylum. *Rhodotorula* species are ubiquitous in nature, can be found in soil and freshwater. Immunocompromised patients can develop Rhodotorulosis due to wide-ranging exposure to *Rhodotorula* in the hospital environment. **Case Discussion:** The patient was a 3-year-old male with a diagnosis of Pro B-Acute Lymphoblastic Leukemia (ALL). He was admitted to the hospital with complaints of malaise, fatigue, weight loss, and diarrhea between courses of chemotherapy. *Rhodotorula* was isolated from the patient's blood culture obtained during the elevation of temperature. After 14 days of amphotericin B treatment, clinical situation of the patient was improved and he was discharged. **Conclusion:** *Rhodotorula* spp. as a rare yet emerging pathogen, often presents as fever of unknown etiology resistant to antibacterial treatment and can be associated with fungemia and other severe complications.

Keywords*: Rhodotorula. Amphotericin B. Precursor Cell Acute Lymphoblastic Leukemia-Lymphoma.*

RESUMO

Objetivos: *Rhodotorula* é uma levedura ambiental que pertence ao filo *Basidiomycota*. As espécies de *Rhodotorula* são onipresentes na natureza, podem ser encontradas no solo e na água doce. Pacientes imunocomprometidos podem desenvolver rodotorulose devido à ampla exposição a *Rhodotorula* no ambiente hospitalar. **Descrição do caso:** O paciente era uma criança de 3 anos de idade com diagnóstico de Leucemia Linfoblástica Aguda Pro B (LLA). O paciente deu entrada no hospital com queixas de mal-estar, cansaço, perda de peso e diarreia entre os ciclos de quimioterapia. A *Rhodotorula* foi isolada da hemocultura do paciente obtida durante a elevação da temperatura. Após 14 dias de tratamento com anfotericina B, a situação clínica do paciente melhorou e o paciente recebeu alta. **Conclusão:** *Rhodotorula* spp. como um patógeno raro, porém emergente, frequentemente se apresenta como febre de etiologia desconhecida resistente ao tratamento antibacteriano e pode estar associada a fungemia e outras complicações graves.

Palavras-chave: *Rhodotorula, Anfotericina B. Leucemia-Linfoma Linfoblástico de Células Precursoras*

RESUMEN

Objetivos: *Rhodotorula* es una levadura ambiental que pertenece al filo *Basidiomycota*. Las especies de *Rhodotorula* son ubicuas en la naturaleza, se pueden encontrar en el suelo y en agua dulce. Los pacientes inmunodeprimidos pueden desarrollar Rhodotorulosis debido a una amplia exposición a *Rhodotorula* en el entorno hospitalario. **Descripción del caso:** El paciente era un niño de 3 años con diagnóstico de leucemia linfoblástica aguda Pro B (LLA). El paciente ingresó en el hospital con quejas de malestar, fatiga, pérdida de peso y diarrea entre ciclos de quimioterapia. Se aisló *Rhodotorula* del hemocultivo del paciente que se obtuvo durante la elevación de la temperatura. Después de 14 días de tratamiento con anfotericina B, la situación clínica del paciente mejoró y fue dado de alta. **Conclusión:** *Rhodotorula* spp. como patógeno poco común pero emergente, a menudo se presenta como fiebre de etiología desconocida resistente al tratamiento antibacteriano y puede asociarse con fungemia y otras complicaciones graves.

Palabras clave: *Rhodotorula. Anfotericina B. Leucemia-Linfoma Linfoblástica de Células Precursoras.*

INTRODUCTION

Rhodotorula is an environmental yeast that belongs to *Basidiomycota* Phylum. *Rhodotorula* species produce carotenoid pigments usually causing pink or coral mucoid colonies, multilateral budding cells, undistinguished pseudohyphae and infrequently, an indistinct capsule [1]. *Rhodotorula* species are ubiquitous in nature, can be found in soil and freshwater.[1] *Rhodotorula* isolation from food such as fruit juice and milk, several medical equipments, such as dialysis equipment, fiber-optic bronchoscopes, and other environmental sources, such as shower curtains, bathtubs, and toothbrushes due to strong affinity with plastic, was also reported.[2]

In the last three decades, *Rhodotorula* species have become an increasing challenge, especially in immunocompromised patients as an opportunistic yeast.[3] Extensive use of central venous catheters (CVC) and intensive treatments may be the potential explanation for the greater number of *Rhodotorula* infection cases after the first reports in late 1980s.[4]

Immunocompromised patients can develop Rhodotorulosis that is usually associated with endocarditis, peritonitis, meningitis, and endophthalmitis due to a wide-ranging exposure to *Rhodotorula* in the hospital environment.[4]

CASE DESCRIPTION

The patient was a 3-year-old male with a diagnosis of Pro B-Acute Lymphoblastic Leukemia (ALL). He was admitted to hospital with complaints of malaise, fatigue, weight loss, and diarrhea between courses of chemotherapy. At hospital admission, the cardiac examination was normal, lymphadenopathy, hepatomegaly, and splenomegaly were not found. At admission, c-reactive protein (CRP) was found 35.44 mg/L (normal range: 0-5 mg/L), white blood cell count was 4.02 10^3/µL (normal range : 3.8-8.76 10^3/µL) and hemoglobin was 8.4 g/dL. Rapid immunochromatographic test from stool sample for Rotavirus, *Giardia intestinalis*, *Entamoeba histolityca*, and Adenovirus antigens and *Clostridium difficile* Toxin A was negative. Direct microscopic examination of stool and stool sample culture were also negative. Teicoplanin and amikacin therapy were prescribed as empiric antibiotics. Although antibacterial therapy was administered, the patient had fever episodes. Tuberculosis was excluded with acid-fast stain and PCR tests. Fungal infection was suspected but anti-mannan antibody and galactomannan antigen tests were negative.

After eight days of hospital stay, *Rhodotorula* was isolated from the patient's blood culture obtained during the elevation of temperature. Standard procedure for blood cultures was followed. When the patient had a fever, two sets of blood cultures were collected from different peripheral veins. Blood culture sample from the CVC was also collected simultaneously in order to find differential time to positivity. Blood samples were inoculated into aerobic blood culture bottles and administered to the BACTEC FX-400 system (Becton Dickinson, USA). Bottles with the positive signal in BACTEC FX-400 system were inoculated onto Columbia Agar (with 5% Sheep Blood) and Eosin Methylene Blue Agar (BD, USA). The inoculated plates were incubated at 36°C in 5% CO2. After 24h incubation, colonies were identified with BD Phoenix automated system (BD, USA). After the first isolation of *Rhodotorula*, eight subsequent blood cultures were *Rhodotorula* positive in ten-day periods, but CVC culture was negative. After the isolation of *Rhodotorula* spp, amphotericin B was added to the prescription of the patient. After 14 days of amphotericin B treatment, the clinical situation of the patient was improved and he was discharged. The c-reactive protein remained high for a very long time and was high even at patient's discharge.

DISCUSSION

Rhodotorula species are an increasing health problem with their ability to colonise and infect patients with depressed immunity, and account for 0.5%-2.3% of fungemia in the USA.[5] Approximately 90% of patients with *Rhodotorula* infections have immunodepressant clinical conditions such as AIDS, solid or hematologic malignancy, organ/bone marrow transplant, or immunosuppression due to corticosteroid use, neutropenia, or malnutrition.[6] *Rhodotorula* infections in patients with hematologic

Please cite this article as: *Erinmez, M., Zer, Y, & Büyüktaş Manay, A. (2022). Fungemia de Rhodotorula em paciente com leucemia linfoblástica aguda. Revista De Epidemiologia E Controle De Infecção, 12(1). https://doi.org/10.17058/reci.v12i1.16325*

malignancies are usually associated with CVC and result in fungemia, whereas *Rhodotorula* infections in patients with AIDS usually result in central nervous system infections.[7] In our case, having the negative culture of CVC indicates the difficulty of finding a source for contamination. Therefore, detailed environmental surveillance may be necessary especially in case of outbreaks.

Intestinal colonization is found in up to 5% of healthy children and in up to 12% of young adults.[8] Although one of the patient's complaint at admittance was diarrhea, to our knowledge there is no report for *Rhodotorula* species causing diarrhea. However, it may be responsible for unsettling gut flora in immunocompromised patients. Furthermore, they often colonise hands of medical staff.[9] Control interventions, including training to reemphasize hand washing for reducing nosocomial transmission risk, were applied in our hospital for the prevention of an outbreak infection.

The isolation of *Rhodotorula* species from sterile site samples, such as blood, peritoneal fluid or cephalo spinal fluid, is generally suggestive of the infection, especially in patients without indicative symptoms of infection. Morphological and biochemical confirmation of the diagnosis is usually necessary, as yeast cells can usually be seen on microscopic examination.[6] Overall, mortality from *Rhodotorula* fungemia is 17.3%.[7] Expected mortality may be higher in immunocompromised pediatric patients.

Rhodotorula species are susceptible to amphotericin B and flucytosine *in vitro*, resistant to fluconazole and caspofungin, and have varying susceptibility to voriconazole.[7] Amphotericin B is the first choice drug for *Rhodotorula* infections.[10] In our case, Amphotericin B was effective as a treatment.

In conclusion, *Rhodotorula* spp. as a rare yet emerging pathogen, often presents as fever of unknown etiology resistant to antibacterial treatment and can be associated with fungemia and other severe complications, especially in immunocompromised patients.

ACKNOWLEDGEMENT

We thank pediatric-hematology staff for their cooperation.

FUNDING

No fund was granted for this study.

CONFLICT OF INTEREST

The authors have no conflict of interest.

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Yasemin Zer contributed to the conception, article design, review and final approval of the article;

Mehmet Erinmez contributed to the planning, analysis and article writing;

Ayşe Büyüktaş Manay contributed and article design.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.