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Note

# *Rhodotorula dairenensis* fungemia in a patient with cancer

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ABSTRACT

*Background:* *Rhodotorula* species were traditionally considered non-virulent environmental microorganisms, but are nowadays considered important human pathogens, especially in immunocompromised individuals.
*Case report:* We present the case of a 73 year-old man with diarrhea, anorexia and fever. In the blood analyses, both aerobic blood culture bottles yielded the growth of *Rhodotorula dairenensis*. The MALDI-TOF MS score was inadequate to provide an identification, which was achieved by means of molecular techniques. Treatment with an echinocandin was started, but the patient died.
*Conclusions:* Basidiomycetous yeast genera such as *Rhodotorula* can cause invasive and severe infections, e.g., fungemia, especially in patients with central venous catheter or another indwelling device.


## Fungemia por *Rhodotorula dairenensis* en un paciente con cáncer

*Palabras clave:*
*Rhodotorula dairenensis*
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RESUMEN

*Antecedentes:* Las especies de *Rhodotorula* han sido tradicionalmente consideradas huéspedes ambientales no virulentos, pero hoy día han demostrado ser importantes patógenos humanos, sobre todo en individuos inmunocomprometidos.
*Caso clínico:* Se presenta el caso clínico de un varón de 73 años con diarrea, anorexia y fiebre. En los frascos de hemocultivos aerobios creció *Rhodotorula dairenensis*. El sistema MALDI-TOF MS no proporcionó un buen *score,* por lo que la identificación se realizó finalmente mediante técnicas moleculares. Se instauró tratamiento con una equinocandina, pero finalmente el paciente falleció.
*Conclusiones:* Las levaduras de géneros pertenecientes a los basidiomicetos, como *Rhodotorula,* pueden producir infecciones invasivas y graves como fungemia, especialmente en pacientes con catéteres venosos centrales u otros dispositivos invasivos.


*Rhodotorula* species are basidiomycetous yeasts that can be isolated from soil, water, fruit juices, and milk products, and they have traditionally been considered non-virulent environmental inhabitants. Among the eight species in this genus, *Rhodotorula mucilaginosa*, *Rhodotorula glutinis*, and *Rhodotorula minuta* are the most frequently isolated from blood cultures.[8] To our best knowledge, this is the first report of bacteremia due to *Rhodotorula dairenensis*.

## Case report

A 73 year-old man came to our Emergency Department on February 27th 2019 due to diarrhea, anorexia, and fever. He was under treatment with corticosteroids and chemotherapy (CPT-11 and cetuximab) for a colon adenocarcinoma. Blood analysis showed anemia, leukopenia, neutropenia, and high concentration (85.6 mg/l) of C-reactive protein (CRP), hemoglobin of 10.7 mg/dl, and white blood cell count of 2000/mm$^3$ (480 neutrophils/mm$^3$). He was admitted to the Department of Oncology, where an empirical therapy with intravenous ciprofloxacin (400 mg/12 h) and three doses of granulocyte colony stimulating factor (G-CSF) was started.

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On March 8th, 2019, multiple vomiting episodes led to employ peripheral parenteral nutrition; being the clinical presentation compatible with a small bowel obstruction secondary to peritoneal carcinomatosis, a CT scan was also ordered. A nasogastric tube was placed due to the persistence of the vomiting, but no central venous catheter was placed. On March 29th, 2019, the patient's temperature rose to 38.3 °C, and two sets of blood cultures (aerobic and anaerobic) were ordered. Both bottles yielded a positive result on day 5 of incubation. Samples were inoculated on two aerobic blood agar media: Columbia agar 5% sheep blood (Becton Dickinson, Franklin Lakes, NY), and Chocolate agar (Becton Dickinson); plates were incubated at 37 °C for 5 days. Gram staining of the culture growth on both plates showed yeast cells. The strain could not be identified using MALDI-TOF MS (Bruker Biotyper, Billerica, MA). Antifungal treatment with caspofungin was started and the isolate was sent to the National Center for Microbiology (Majadahonda, Madrid, Spain) for molecular study, amplifying the ITS1-5.8-ITS2 region of the ribosomal DNA and sequencing as previously reported.[2] The 587 bp fragment obtained was identical to the GenBank sequence for *R. dairenensis*.

E-test was used to determine the antifungal susceptibility of the strain, based on 2018 EUCAST criteria,[9] obtaining the following MIC values: amphotericin B 0.12 μg/ml, 5-fluorocytosine 0.5 μg/ml, fluconazole 32 μg/ml, itraconazole >8 μg/ml, voriconazole 0.25 μg/ml, posaconazole 2 μg/ml, isavuconazole 0.5 μg/ml, caspofungin >16 μg/ml, micafungin >2 μg/ml, and anidulafungin >4 μg/ml.

Since the intestinal subocclusion showed no improvement after medical treatment, intestinal resection and LL anastomosis were performed. At day six post-surgery, the patient suffered acute dyspnea and respiratory distress. Thoracic CT scan revealed a severe bilateral interstitial infiltrate, and pneumonia was suspected as the cause; however, no respiratory samples were obtained and the etiology remained unknown. The patient finally died on April 11th, 2019.

## Discussion

*Rhodotorula* species are common airborne microorganisms considered saprophytes or contaminants.[7] Over the past few years, some *Rhodotorula* species have emerged as opportunistic pathogens, particularly *R. mucilaginosa*.[7] *R. dairenensis* was first described by Gadanho and Sampaio in 2002 as a new species[5] but has not been found in human infections to date. To our best knowledge, this is the first report of a fungemia caused by this yeast.

Immunocompromised individuals are at high risk of infection with *Rhodotorula* species, especially if they carry a central venous catheter or other indwelling device. Risk factors for fungemia due to *Rhodotorula* are similar to those described for other opportunistic fungal bloodstream infections, including the presence of lymphoproliferative disease, solid cancer, diabetes, pulmonary disease, chronic renal failure, and/or HIV/AIDS infection.[1,10,11] Risk factors in the case under study were the presence of parenteral nutrition catheters, colon cancer and treatment with corticosteroids and cytotoxic drugs.

The diagnosis of *Rhodotorula* infections is based on the culture of an adequate sample, and the definitive diagnosis is obtained using phenotypic, proteomic, and/or molecular methods. However, the identification of *Rhodotorula* can be challenging and could not be achieved by MALDI-TOF MS in the present case, requiring a molecular study to identify the species. Nevertheless, diagnoses of this infection have been previously reported using MALDI-TOF MS, although no data about the scores obtained with this technique were provided by the authors.[4]

The lack of data on the susceptibility patterns of *R. dairenensis* prevents the drawing of conclusions on the best treatment option. To date, the genus *Rhodotorula* has not been considered a true pathogen, and some authors have reported survival without antifungal therapy and clinical improvements after intravenous catheter removal.[1,11] However, the current guidelines recommend treatment with amphotericin B (A-II evidence), with the option to combine with flucytosine when appropriate due to tissue penetration or infection severity. No MIC breakpoints have yet been established for *Rhodotorula* species, and MIC values can only be interpreted in an indicative manner. Interpretation is also hampered by the difficult growth of *Rhodotorula* in media for susceptibility testing. *Rhodotorula* species are considered intrinsically resistant to echinocandins and azoles but susceptible to amphotericin B and flucytosine.[3,6]

In conclusion, this is the first report of *R. dairenensis* as a cause of fungemia. Physicians and microbiologists should bear this infection in mind in immunocompromised patients. Improvements in MALDI-TOF MS platforms for the routine diagnosis of fungi are expected to increase the accuracy to identify opportunistic pathogens such as *Rhodotorula*.

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## Conflict of interest

Authors declare no conflict of interest.

## References

1. Alliot C, Desablens B, Garidi R, Tabuteau S. Opportunistic infection with *Rhodotorula* in cancer patients treated by chemotherapy: two case reports. Clin Oncol (R Coll Radiol). 2000;12:115–7.
2. Barnett JA. Yeasts: characteristics and identification. In: Kurtzman C, Fell JW, Boekhout T, editors. The yeasts: a taxonomy study. 5th ed. Elsevier Science; 2011.
3. Diekema DJ, Petroelje B, Messer SA, Hollis RJ, Pfaller MA. Activities of available and investigational antifungal agents against *Rhodotorula* species. J Clin Microbial. 2005;43:476–8.
4. Falces-Romero I, Cendejas-Bueno E, Romero-Gómez MP, García-Rodríguez J. Isolation of *Rhodotorula mucilaginosa* from blood cultures in a tertiary care hospital. Mycoses. 2018;61:35–9.
5. Gadanho M, Sampaio JP. Polyphasic taxonomy of the basidiomycetous yeast genus *Rhodotorula*: *Rh. glutinis* sensu stricto and *Rh. dairenensis* comb. nov. FEMS Yeast Res. 2002;2:47–58.
6. Gómez-López A, Mellado E, Rodríguez-Tudela JL, Cuenca-Estrella M. Susceptibility profile of 29 clinical isolates of *Rhodotorula* spp. and literature review. J Antimicrob Chemother. 2005;55:312–6.
7. Hazen KC. New emerging yeast pathogens. Clin Microbiol Rev. 1995;8:462–78.
8. Nunes JM, Bizerra FC, Ferreira RCE, Colombo AL. Molecular identification, antifungal susceptibility profile, and biofilm formation of clinical and environmental *Rhodotorula* species isolates. Antimicrob Agents Chemother. 2013;57:382–9.
9. Rodríguez-Tudela JL, Arendrup MC, Barchiesi F, Bille J, Chryssanthou E, Cuenca-Estrella M, et al. EUCAST definitive document EDef 7.1: method for the determination of broth dilution MICs on antifungal agents for fermentative yeasts. Clin Microbiol Infect. 2008;14:398–405.
10. Rusthoven JJ, Feld R, Tuffnell PG. Systemic infection by *Rhodotorula* spp. in the immunocompromised host. J Infect. 1984;8:241–6.
11. Samonis G, Anatoliotaki M, Apostolakou H, Maraki S, Mavroudis D, Georgoulias V. Transient fungemia due to *Rhodotorula rubra* in a cancer patient: case report and review of the literature. Infection. 2001;29:173–6.