Journal de Mycologie Médicale (2016) **26**, 178—181

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CASE REPORT/CAS CLINIQUE

Rhodotorula fungemia: Report of two cases in Sfax (Tunisia)

Fongémie à Rhodotorula *: à propos de deux cas à Sfax (Tunisie)*

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Received 29 August 2015; received in revised form 17 February 2016; accepted 21 February 2016
Available online 16 April 2016

KEYWORDS
Rhodotorula;
Fungemia;
Susceptibility profile;
Tunisia;
Sfax

Summary *Rhodotorula* is emerging as an important cause of nosocomial and opportunistic infections. We present two cases of *Rhodotorula mucilaginosa* fungemia diagnosed at our hospital during the last decade. The first case was of a term neonate who presented congenital heart disease (interventricular communication) and body dysmorphic disorder. He was admitted for respiratory failure and sepsis. The second case involved in a 33-year-old woman that had Hodgkinien lymphoma associated to tuberculosis. Identification was performed using commercial systems and confirmed by PCR sequencing of internal transcribed spacer, ITS1 and ITS2 regions of rDNA. Antifungal susceptibility tested by sensititre yeast revealed susceptibility to amphotericin B and resistance to fluconazole for the two strains. These cases emphasize the emerging importance of *Rhodotorula* sp. as a pathogen and it must be considered a potential pathogen in patients with immunosupression and with central venous catheters. Correct identification is mandatory for appropriate management, as *Rhodotorula* spp. are resistant to antifungal agents, such as fluconazole.

MOTS CLÉS
Rhodotorula ;
Fongémie ;
Sensibilité aux antifongiques ;

Résumé Les levures du genre *Rhodotorula* sont des pathogènes émergents et opportunistes. Nous rapportons deux cas de fongémie à *Rhodotorula mucilaginosa* diagnostiqués dans notre hôpital durant la dernière décennie. Le premier cas était un nouveau-né à terme porteur d'une cardiopathie congénitale (communication inter-ventriculaire) et d'une dysmorphie. Il a été admis pour une insuffisance respiratoire et un sepsis. Le deuxième cas était une femme de 33 ans porteuse d'un lymphome de Hodgkin associé à une tuberculose. L'identification des souches a

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http://dx.doi.org/10.1016/j.mycmed.2016.02.020
1156-5233/

Sfax ;
Tunisie

été effectuée par les galeries commercialisées et a été confirmée par PCR séquençage des régions ITS1 et ITS2 de l'ADNr. L'étude de la sensibilité aux antifongiques, testée par la technique du Sensititre, a montré une sensibilité des deux souches à l'amphotéricine B et une résistance au fluconazole. Nos cas ont permis d'attirer l'attention sur l'émergence de ces levures opportunistes qui doivent être considérées comme des pathogènes potentiels chez les patients immunodéprimés et porteurs de cathéter. Une identification correcte de ces levures pour une prise en charge appropriée s'avère obligatoire puisque *Rhodotorula* est une levure résistance à certains antifongiques comme le fluconazole.

Introduction

Rhodotorula spp. is common environmental yeast that is found in air, soil, lakes, ocean water, milk, and fruit juice [25]. Previously considered non-pathogenic, *Rhodotorula* species have emerged as opportunistic pathogens with the ability to infect susceptible patients, especially those with malignancy or other immunosuppression. In the ARTEMIS surveillance project, *Rhodotorula* species were the fourth most common non *Candida* yeasts isolated from clinical specimens [13]. The incidence of fungemia caused by *Rhodotorula* ranged from 0.5% in USA to 2.3% in Europe [23]. *Rhodotorula* occurred most frequently in the Asia pacific region [13]. The most prevalent specie was *Rhodotorula mucilaginosa* [13] followed by *R. glutinis* and *R. minuta* [6,13,25]. We describe two cases of *Rhodotorula* fungemia in Tunisian patients diagnosed at our hospital during the last decade.

Case reports

The first case was a 3-month female child. She was born in term with a congenital heart disease (interventricular communication), body dysmorphic disorder and hypotrophy (−4 DS). She was admitted in pediatric department for respiratory disorder with fever. She was treated by broad-spectrum antibiotics (cefotaxim, gentamicin, amikacin and imipenem) but with resumption of the fever before stopping antibiotics. Peripheral blood cultures incubated in Bactec/Mycosis (BD diagnostic systems 9050, Oxford, UK) at 35 °C were negatives at this time. Few days after, she had high-grade fever with convulsion. She has not had central venous catheter. She has received fluconazole (FLZ) associated to antibiotics (imipenem and teicoplanin) immediately after explorations. Cerebrospinal fluid examinations were negative. Serological exploration of toxoplasmosis, CMV, rubella and HIV were all negatives. Blood culture was positive. The subculture on Sabouraud dextrose agar (SDA) yielded pink to salmon-red colored and mucoid colonies (Fig. 1). It was identified by ID32C (Biomérieux, France) as *Rhodotorula glutinis*. Microscopically, the cells were ovoid to spherical, occurring singly or in chains, with multilateral budding. No mycelium or pseudomycelium was seen (Fig. 2).

After 2 weeks of fluconazole and antibiotic therapy, the patient has improved and was discharged from the hospital.

The second case was a 33-year-old woman, having consulted for inflammatory pain of lumbar vertebra and thighs with fever, night sweats and graduate weight loss. Exploration showed many deep lymph nodes. Her cell blood count revealed high leucocytes level with predominance of neutrophils and her CRP was at 282 mg/mL. The biopsy of jugulocarotidien lymph node confirmed the diagnosis of hodgkinien lymphoma associated to tuberculosis. Peripheral blood culture was positive. No central venous catheter was used. The subculture on Sabouraud dextrose agar yielded the same side and identified by ID32C as *Rhodotorula mucilaginosa*. No antifungal therapy for *Rhodotorula* fungemia has been prescribed for this patient and the evolution was favorable.

The molecular identification of the cultured isolates was made by sequencing of internal transcribed spacer, ITS1-5.8-ITS2 regions of rDNA. The DNA was extracted from the cultured isolates using instruction supplied by the kit manufacturer (Qiagen, Hilden, Germany) and the ITS region was amplified with panfungal primers ITS1 (TCC GTA GGT GAA CCT GCG G) and ITS4 (TCC TCC GCT TAT TGA TAT GC) [24]. The ITS rDNA sequences were compared to those in the NCBI GenBank database by using BLASTIN algorithm for identification of species (http://www.ncbi.nml.nih.gov/Blast.cgi).

The nucleotide sequence of the ITS region of PCR amplicons (626 pb) obtained from cultures showed 99% similarity (e-value 0.0) with *Rhodotorula mucilaginosa* in both isolates.

Antifungal susceptibility was tested by SensititreYeastOne (Y08 TREK Diagnostic Systems, East Grimstead, UK). The first isolate of *R. mucilaginosa* show a low level of MIC to amphotericin B (AMB) (MICs = 0.125 μg/mL) and 5-flucytosin (MICs = 0.5 μg/mL), a high level to FLZ (MICs > 256 μg/mL), itraconazole (ITZ) (MICs = 1 μg/mL) and voriconazole (VRZ) (MICs > 16 μg/mL). For the second isolate, it shows also a low level of MICs to AMB (MICs = 0.5 μg/mL), VRZ (MICs = 1 μg/mL) and 5-flucytosin (MICs = 0.03 μg/mL), a higher level to ITZ (MICs = 0.5 μg/mL) and a very high level to FLZ (MICs > 256 μg/mL).

Discussion

The first report of fungemia caused by *Rhodotorula* was made by Louria et al. in 1960 [10]. Subsequently, an increasing number of cases have been mentioned, especially, in these last 2 decades. To our knowledge, more than 70 cases of *Rhodotorula* fungemia were reported in the world and the most of these cases date back to after 1994 [9,18,19,21,23,25].

The increase in cases number may be explained by the new recognition of this yeast as a pathogen and by the use of more aggressive treatment modalities, which includes intensive care units (ICU), use of central venous catheters,