Rhodotorula fungemia: two cases and a brief review

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Rhodotorula is emerging as an important cause of nosocomial and opportunistic infections. We present two cases of Rhodotorula mucilaginosa fungemia diagnosed over a period of 3 months at our hospital. The first case was of a pre-term neonate in the neonatal ICU who presented with respiratory failure and sepsis. The second involved an adult female who had been injured in a road traffic accident requiring an operation for a hematoma and was later shifted to the medical ICU. For a new hospital like ours, finding two cases of Rhodotorula fungemia within a span of 3 months prompted us to describe them in this report. These cases emphasize the emerging importance of Rhodotorula mucilaginosa as a pathogen and the importance of identification and MIC testing for all fungal isolates recovered from the blood stream.

Keywords Rhodotorula mucilaginosa, fungemia, central line, voriconazole

Introduction

Rhodotorula is a pigmented yeast, a normal environmental inhabitant but it can cause opportunistic infections such as those of the blood stream, endocarditis, meningitis, peritonitis, and endophthalmitis. While it was previously considered non-pathogenic, it has emerged as an opportunistic etiologic agent, particularly in immuno-compromised patients.

We present two cases of Rhodotorula mucilaginosa fungemia, not epidemiologically linked to each other. The first involved a pre-term neonate in the neonatal ICU from whom the yeast was isolated twice in blood cultures. The second involved an adult female in the medical ICU from whom it was isolated in blood culture after a neurosurgical procedure.

Case 1

A preterm baby (30 weeks) was transferred to our hospital at day 9 after a twin delivery. The neonate had respiratory distress and sepsis with very high C-reactive Protein (CRP) value of unknown etiology and negative blood cultures. The other twin showed no features of septicemia.

In view of sepsis, CRP studies and blood cultures were repeated and empiric treatment was started with vancomycin, meropenem and fluconazole. A central venous catheter had been inserted in the previous hospital and continued at our facility for a total of 7 days.

The baby was initially ventilated but weaned after 2 days. On day 3 (65 h of incubation in BACTEC9120), growth of a yeastlike organism was seen in the blood culture bottle, which was later identified as Rhodotorula mucilaginosa. Antifungal therapy was changed from fluconazole to amphotericin B, 0.5 mg/kg, increased to 1 mg/kg body weight after one day. The patient showed signs of improvement, accepted oral feeding, and CRP and total leucocyte count (TLC) became normal.

Colonies of Rhodotorula spp. were presumptively identified on the basis of their colony characters and positive urease test. They were rapid growing, smooth, glistening, soft and mucoid, and orange-pink in colour (Fig. 1). Its identification as Rhodotorula mucilaginosa was made through the use of assimilation tests performed with the API 20C yeast identification system. Using an E-test [1], we found this isolate after 48 h to have an in vitro MIC of 1.5 mcg/ml for amphotericin B (Amp B), 0.38 mcg/ml for voriconazole and >16 mcg/ml, i.e., resistant, to caspofungin and to fluconazole (MIC > 256 mcg/ml). While other Rhodotorula isolates had MIC50s of 1 mcg/ml [2], we decided not to alter the patient’s therapeutic protocol since the neonate had started to positively respond clinically to the antifungal. For Amp B, the MIC end points were defined as the
lowest drug concentration exhibiting reduction in growth of 90% or more when compared with that of the control growth. For azole drugs, the MIC end point was defined as 50% of inhibition [3].

Blood culture after 10 days was sterile but the patient started deteriorating 2 weeks later, presenting again with septicemia and rapidly falling platelet counts. He had increased frequency of apnea and also developed abdominal distension. X-ray showed distended gaseous bowel loops and pneumatosis intestinalis. Repeat blood culture grew Rhodotorula mucilaginosa along with Klebsiella pneumoniae. At this point of time, CRP was raised to 105.20 mg/l and platelet count was 6000/μl of blood (Fig. 2). Treatment was again modified in view of renal impairment and Amp B was replaced with voriconazole at 10 mg/kg BD for a period of 3 weeks. Antifungal susceptibility testing (AFST) results after 48 h showed the isolate to have a raised Amp B MIC of 3 mcg/ml but the MIC results obtained with voriconazole remained unchanged. The patient responded very well to voriconazole, the platelet counts started rising and the patient was discharged in a stable condition. Close follow up for 6 months did not reveal any evidence of recurrent infection with Rhodotorula.

**Case 2**

A 50-year-old female, known hypertensive, presented to the emergency room after a fall that resulted in trauma and unconsciousness. Right fronto-temporo-parietal craniotomy and removal of acute subdural haematoma was done and subsequently she was shifted to the intensive care unit under empirical antibacterial therapy. A central venous line was inserted and tracheostomy was done. Post surgery she was having periodic episodes of fever, with procalcitonin values between 0.5 and 2.0 indicating systemic infection, with moderate risk for progression to severe infection. Blood culture in BACTEC 9120, after 80 h yielded Rhodotorula mucilaginosa. Antifungal susceptibility studies (E-test) revealed the isolate to have an in vitro amphotericin B MIC of 0.5 mcg/ml and a voriconazole MIC of >32 mcg/ml. The presence of the fungus was attributed to the use of a central venous catheter and consequently it was removed, treatment with amphotericin B was recommended. Cultures of the catheter tip were not carried out. Meanwhile on two occasions, cultures of urine specimens yielded Trichosporon spp. but never Rhodotorula. The patient responded to treatment, subsequent blood cultures after 14 days of therapy were sterile and she was discharged in a stable condition.

**Discussion**

Invasive fungal infection (IFI) has been defined as those caused by Candida species and other yeasts isolated from blood samples of patients with temporally related clinical signs and symptoms compatible with relevant organisms [4]. IFI constitutes a significant burden in patients with impaired immunity. The spectrum of fungal pathogens is growing, with limited treatment options [5]. Rhodotorula is a basidiomycetous yeast genus which produces mucoid colonies with a characteristic carotenoid pigment ranging from yellowish to red [6]. It is widely distributed in the environment, and also is a constituent of the normal human respiratory, gastrointestinal, genital flora and moist skin [7]. Among isolates of non-Candida, non-Cryptococcus yeasts reported in the ARTEMIS Surveillance project, Rhodotorula was most prominent in Asia-Pacific regions [6]. Rhodotorula causes disseminated infections similar to Candida spp. and has been related to emerging infections in immunocompromised patients [8]. Rhodotorula fungemia has been associated with crude mortality of up to 20% and has been reported with patients with indwelling vascular catheters,
granulocytopenia, damage to the normal anatomic barriers (skin, mucosa, especially gastrointestinal), cellular immune dysfunction and parenteral nutrition [6]. It is the etiological agent in 0.5–2.3% of all cases of fungemia described in some epidemiologic studies [9]. In a systemic review of 128 cases of Rhodotorula infections, 79% were fungemia (Rhodotorula mucilaginosa being the most common etiologic species), 7% eye infections and 5% peritonitis associated with continuous ambulatory peritoneal dialysis. Eighty-seven percent of Rhodotorula infections are associated with underlying immunosuppression or cancer. The most common isolated risk factor associated with Rhodotorula infection was the use of a central venous catheter, which was found in 83.4% cases of fungemia [10]. Based on our literature search, we found a single case report on Rhodotorula sepsis and encephalitis [11] and three reported cases of Rhodotorula meningitis from India [12–14].

Rhodotorula is a skin and environmental saprobe with low virulence [15]. It was previously considered non-pathogenic but during the last few decades, it has emerged as an opportunistic etiologic agent and fulfils the criteria of an emerging pathogen especially in cases of fungemia associated with catheters, endocarditis, peritonitis, meningitis, and endophthalmitis [16].

In our first case this fungus was repeatedly isolated from the patient’s blood samples. The risk factors were immunosuppression related to pre-maturity and central venous line, whereas the second patient had a neurosurgical procedure and was hospitalized for about 4 weeks. However, both these cases had a favourable outcome following treatment with antifungals. AFST was performed using the E-test strips and interpreted by the CLSI (Clinical and Laboratory Standard Institute’s) protocol [3]. The first case was successfully treated with voriconazole and the second with amphotericin B. The treatment of Rhodotorula infection involves removal of the catheter or amphotericin B (with or without fluconazole) or both [10,16].

In a study by Zaas et al. [17] using NCCLS (now the CLSI) M27-A method reported that the isolates of R. mucilaginosa from 8 cases had MICs of amphotericin B of 0.25–1 μg/ml, fluconazole 32 – >64 μg/ml and voriconazole 1– >8 μg/ml. They also found poor in vitro activity of caspofungin and micafungin, highlighting the lack of effectiveness of the echinocandins in the treatment of infections caused by heterobasidiomycetous yeasts.

The resistance mechanism of Rhodotorula for fluconazole is not known but the repeated pattern of high MICs suggests the presence of intrinsic resistance in some isolates. Recent antifungal agents, such as second-generation triazoles and echinocandins, provide the potential to improve therapeutic options against invasive fungal infections. However, this has been hampered by both intrinsic and acquired resistance of Rhodotorula to antifungal agents including echinocandins and fluconazole [2,18]. Echinocandins should therefore not be considered appropriate therapy for Rhodotorula species but voriconazole as an antifungal agent must be considered, if susceptible, in a setting of amphotericin B resistance and in renal compromised states. Finally, prompt identification of isolates causing deep mycosis is important in selecting the most appropriate antifungal therapy.

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References

11 Pamidimukkala U, Challa S, Lakshmi V, et al. Sepsis and meningoencephalitis due to Rhodotorula glutinis in a patient with systemic


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