

Foot bleb infection due to *Rhodotorula mucilaginosa* in a diabetic patient: Case report and review of the literature.

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Abstract

***Rhodotorula* spp. are capsulated, pigmented, ubiquitous basidiomycetous yeasts causing different superficial and deep-seated opportunistic infections in the debilitated and immunocompromised patient. Earlier considered as saprophytes, fungi belonging to this genus are now considered as emerging pathogens. This is a report of foot bleb infection due to *Rhodotorula mucilaginosa* in a diabetic patient.**

Keywords: *Rhodotorula* spp., basidiomycetous, Diabetes mellitus.

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Introduction

Rhodotorula spp. are capsulated, basidiomycetous, round to oval, multilateral budding yeasts belonging to the family Cryptococcaceae, subfamily Rhodotoruloideae. They were previously considered as saprophytes and laboratory contaminants and have been recovered from environmental sources like soil, shower curtains, bathtub grout, and toothbrushes⁽¹⁾. They are also found as commensal yeasts in skin, nails and mucous membranes⁽²⁾. However according to current scientific literature, they are considered important in the causation of sepsis and disseminated infection in the immunocompromised and debilitated host. *Rhodotorula* spp. have been implicated in the causation of meningitis, endocarditis, ventriculitis, peritonitis, fungemia, central venous catheter infection and keratitis in debilitated and immunocompromised patients. *Rhodotorula* spp. are usually resistant to triazoles and caspofungin and sensitive to amphotericin B. The genus *Rhodotorula* comprises several species, of which *R. mucilaginosa* has not yet been reported as a causative agent of sepsis in Diabetes mellitus.

Case Report

S, a 55 year-old female patient residing in Chandigarh, north India was admitted in the Emergency Ward of the Institute, on 13.08.2009 with the chief complaints of generalized swelling of the body since 15 days, shortness of breath since 7 days and cough since 5 days. She was a known hypertensive since 6 years and diabetic for the past 12 years, for which she was taking oral hypoglycemic agent. Clinical diagnosis of pneumonia and diabetic

triopathy (nephropathy, neuropathy and retinopathy) with diabetic foot was made. The patient had also developed blebs in both feet. Initial laboratory investigations revealed a serum creatinine value of 4.8 mg/dl, total serum bilirubin of 0.6 mg/dl, hemoglobin of 8.9 gm% and total Leucocyte Count of 4200 cells/ μ l. Her Random Blood sugar value was 319 mg/dl preterminally. The patient was put on Injection Cloxacillin, Clindamycin, Piperacillin-Tazobactam and Insulin. She was not administered any antifungal agent. She died of cardiac asystole resulting from septic shock. Blood sample was sent before death for bacterial culture in Tryptone Soya Broth (TSB) and Bile broth, which showed no growth of any microorganisms after 5 days of incubation at 37°C aerobically. Bleb fluid from the foot lesions was aspirated and sent to the mycology laboratory. Microscopic examination of a 10% KOH Mount of the same showed polymorphonuclear leucocytes and oval budding yeasts of 4-5 μ m size. The fluid was subjected to bacterial and fungal culture. Culture was done on 2 sets of Saboraud's Dextrose Agar (SDA) at 37°C and 22°C respectively, and Brain Heart Infusion Agar (BHIA). Pink mucoid yeasts grew on all the tubes. Lactophenol Cotton Blue Mount showed oval budding yeasts. The yeast isolate was Urease positive, capsulated on India Ink staining, did not assimilate inositol (using Yeast Nitrogen Base) and did not form pseudohyphae on Corn Meal Agar at 22°C after 48 hours of incubation. Nitrate assimilation test using Yeast Carbon Base was negative. Based on these biochemical tests, it was identified as *Rhodotorula* spp. For species identification DNA was extracted by the method described⁽³⁾. DNA sequencing of D₁ and D₂ regions of rDNA by Sanger's method revealed it to be *Rhodotorula mucilaginosa*. MIC values of Am-

photericin B, Fluconazole, Voriconazole and Caspofungin against the isolate were 0.25 µg/ml, 16 µg/ml, 1 µg/ml and 2 µg/ml respectively by broth microdilution method. Thus the isolate was sensitive to Amphotericin B and Voriconazole but resistant to Fluconazole and Caspofungin.

Discussion

Rhodotorula spp. are ubiquitous yeasts and normal inhabitants of moist skin as well as the conjunctiva and respiratory, gastrointestinal and urinary tracts of humans [4]. *Rhodotorula* spp. have been recovered from faeces and cloacae of pigeons (*Columbia livia*) along with *Cryptococcus* spp., which highlights its widespread distribution⁽⁵⁾. Their physiologic and morphologic properties are similar to *Cryptococcus* spp except for red to pink carotenoid pigment production (Torulene, β-Carotene and Torularhodin)⁽⁶⁾, inability to assimilate inositol and a smaller capsule⁽¹⁾. *Rhodotorula* species, previously thought to be saprophytic yeasts and environmental contaminants, are being increasingly recognized as an emerging pathogen in the immunocompromised and debilitated host since the past decade, along with *Trichosporon* spp, and *Geotrichum* spp.⁽⁷⁾. The first case of *Rhodotorula* infection, a patient with endocarditis, was reported in 1960 by Louria and coworkers⁽⁸⁾. An increase in the number of *Rhodotorula* infections has been reported, mainly in the last two decades. However, this increase could be a publication bias after the recognition of *Rhodotorula* as a pathogen. Other explanations are dramatic expansion in new modalities of treatment related to critical care medicine and transplantation, short and long term Central Venous Catheter usage with or without parenteral nutrition, broad spectrum antibiotics, hematologic neoplasms leading to neutropenia and chemotherapy with resultant immunosuppression⁽⁹⁾. *Rhodotorula* spp. have been implicated in the causation of meningitis, endocarditis, ventriculitis, peritonitis, fungaemia, central venous catheter infection and keratitis in debilitated and immunocompromised patients⁽¹⁰⁾. In general, they seem to have lower virulence in comparison to other yeasts, with about 15% mortality overall⁽¹¹⁾. However, infection can occasionally be life threatening, particularly in immunocompromised individuals. Resistance to azoles can favour its colonization on human skin when the growth of other fungi is inhibited or restricted⁽¹²⁾. Several virulence factors have been studied in the yeast, like extracellular phospholipases, but factors like reduced growth at 37°C and absence of dimorphism probably contribute to its reduced pathogenic potential⁽¹³⁾. The genus *Rhodotorula* comprises about 34 species⁽¹⁴⁾ which include *R. glutinis*, *R. mucilaginosa* (formerly known as *R. rubra* or *R. pili-manee*)⁽⁴⁾, *R. minuta*, *R. himalayensis*, *R. gracilis*, *R. slooffiae* and others. This was a case of foot bleb infection due to *Rhodotorula mucilaginosa* since blebs were pre-

sent on both feet that yielded the pigmented yeast isolate on routine mycological media which did not assimilate inositol and nitrate. Many other cases of *Rhodotorula* infection are reported in the literature, mostly in HIV-infected patients. Though it is a saprophytic yeast, its isolation from blood cultures and other sterile body fluids such as Cerebrospinal Fluid (CSF) is of greater significance when contamination has been ruled out⁽¹⁵⁾. Among *Rhodotorula* species, *R. mucilaginosa* is the most frequently isolated one⁽¹⁶⁾. This species can be differentiated from other *Rhodotorula* species by positive assimilation of glucose, raffinose, sucrose, D-arabinose, trehalose and D-xylose and inability to assimilate galactose, maltose and Nitrate⁽¹⁷⁾. Sepsis due to *Rhodotorula* spp. has been reported in patients with malignancy. In diabetic patients, skin and superficial tissue infection by *Rhodotorula* spp. has been noted^(18, 19). *Rhodotorula mucilaginosa* has been reported to be the causative agent of lymphadenitis in HIV-infected patients⁽⁴⁾. Chincholikar and Pal have reported *R. mucilaginosa* (*R. rubra*) in the causation of about 03.64 % cases of fungal diabetic foot infection⁽²⁰⁾. There is one reference of bloodstream infection due to *R. mucilaginosa* in neonatal Intensive Care Unit related to the use of indwelling vascular catheter⁽²¹⁾. Garcia-Suarez and coworkers have reported one case of catheter-related fungemia due to the same in a patient suffering from multiple myeloma⁽²²⁾. This species has also been associated with femoral prosthesis infection⁽²³⁾. All these reports can be attributed to the affinity of *Rhodotorula* spp. for synthetic biomaterials in general⁽²²⁾. This isolate was sensitive to Voriconazole and Amphotericin B and resistant to Fluconazole and Caspofungin. Diekema *et al* have studied the antifungal susceptibility pattern of 64 isolates of *Rhodotorula* spp., 24 of which were *R. mucilaginosa*, against Fluconazole, Echinocandins, Flucytosine and Amphotericin B [24]. They found that the most active agents were 5-flucytosine and Amphotericin B. All the isolates in their study were resistant to echinocandins and fluconazole, with ravuconazole showing some antifungal activity among the new azoles. These findings are concordant with other studies which report universal resistance of *Rhodotorula* spp. to azoles [25]. As far as our knowledge goes, this is the first report of isolation from foot bleb fluid of *Rhodotorula mucilaginosa* in a diabetic patient.

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