Case Study

RARE CASE REPORT OF URINARY TRACT INFECTION CAUSED BY RHODOTORULA MUCILAGINOSA IN AN IMMUNOCOMPROMISED PATIENT

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ABSTRACT

Rhodotorula is a ubiquitous saprobic yeast that can colonize and infect susceptible patients especially those with malignancy or immunosuppression. We describe a rare case of fungal urinary tract infection due to Rhodotorula mucilaginosa in an immunocompromised human immunodeficiency virus (HIV) infected patient and the challenges faced in the diagnosis and management of this pathogen, which the patient may have acquired during his long hospital stay with several comorbid conditions. There is a paucity of literature as far as reports of Rhodotorula mucilaginosa associated Urinary Tract Infections (UTI) are concerned. To the best of our knowledge, there are no published case reports on hospital acquired urinary tract infection by Rhodotorula mucilaginosa in a patient infected with HIV.
INTRODUCTION:
The widespread use of broad spectrum antibiotics and immunosuppressive drugs have led to the increased incidence of fungal infections in humans. Over the last decade several emerging yeast and yeast like pathogens other than *Candida* spp. have been implicated in invasive diseases in immunocompromised patients. *Rhodotorula* is a ubiquitous saprobiotic yeast that can colonize and infect susceptible patients especially those with malignancy or immunosuppression.

Herein, we describe a rare case of fungal urinary tract infection due to *Rhodotorula mucilaginosa* in an immunocompromised human immunodeficiency virus (HIV) infected patient and the challenges faced in the diagnosis and management of this pathogen.

PRESENTATION OF CASE
A 9 year old male child, previously known as HIV positive presented to tertiary care hospital on 16th January 2016 with complaints of fever, altered sensorium (in the form of a staring look and not responding to his name) and yellowish discoloration of the eyes since two days. Prior to this episode, the child had complaints of high grade fever intermittently followed by dry and non-paroxysmal cough for 20-25 days. The child was taken to a private practitioner where he was nebulised and received oral antibiotics. No data was available regarding the antibiotics prescribed. He was then brought to the hospital on 4th January 2016 with respiratory distress. Respiratory examination revealed the presence of bronchial breath sounds and crepts. He was admitted in Intensive Care Unit for 10 days. Ultrasound chest revealed bilateral pleural effusion of 1.5cm. Pleural tap was performed and the fluid was sent for microbiological and pathological examination. Cytology showed polymorphonuclear cells, no RBCs and bacteriological culture was negative. He was put on ceftriaxone and vancomycin empirically for 10 days in view of empyema. Later the Gene Xpert for sputum and pleural tap came positive for tuberculosis (Rifampicin sensitive). Anti Tubercular Therapy (ATT) was started on 6th January 2016 and AntiRetroviral Therapy (ART) on 13th January 2016. Patient was discharged on oral antibiotics as general condition improved.

He developed jaundice at home on 14th January 2016 and was brought back to hospital. On general examination patient appeared sick. General examination showed plantar reflexes (positive Babinski sign) and also reduced muscle power. Glasgow coma scale was 9 (E4M4V1). Laboratory investigations revealed altered liver enzymes (ALT 1276 U/L, AST 1016 U/L, ALP 940 U/L) and raised serum bilirubin (15.4 mg/dl) levels. The patient was presumptively diagnosed as CLHA (Child living with HIV and AIDS) hepatitis with hepatic encephalopathy, with bilateral pleural effusion.

In suspicion of ATT induced hepatitis, the patient was put on modified ATT (Isoniazid and Ethambutol were removed). The jaundice resolved and there was improvement in sensorium.

However, the patient continued to have fever spikes with decreasing Total Leukocyte counts and thrombocytopenia. Patient complained of pericatheter burning sensation after around a month of admission for which blood and urine sample were sent for bacterial and fungal culture. Blood culture came as sterile whereas urine culture grew yeast like colonies producing red pigment. In order to confirm that the isolate was indeed a pathogen and not a contaminant, a repeat urine sample was obtained to verify funguria after 4 days. After isolation of yeast, the catheter was replaced with a new device and the second urine specimen was obtained from which same pathogen was again isolated in pure culture. The urine samples were cultured on two Sabouraud Dextrose Agars supplemented with 0.5 g/l chloramphenicol and Gentamicin in the Microbiology laboratory. At 48 h of incubation, a pure and profuse growth of small, salmon-pink, mucoid colonies were observed on
Sabouraud agar. The Gram staining of these colonies showed spherical to ellipsoidal budding yeast cells forming blastospores. The yeast was thought to be *Rhodotorula*, due to its orange-pink pigmented appearance. The urease test was performed which was positive. The isolate was presumptively identified as *Rhodotorula* spp. Sugar assimilation test using the HiCandida identification kit (bioMérieux) also gave results suggestive of *Rhodotorula* spp. The isolate was finally identified as *Rhodotorula mucilaginosa* according to the Vitek automated identifications system using Yeast Biochemical Card 2 (YCB).

Antifungal susceptibility was done by VITEK 2™ API system. The isolate was found to be sensitive to Voriconazole, Fluconazole, Amphotericin B and Flucytosine and resistant to Caspofungin and Micafungin (MIC>4). The patient was treated with fluconazole 400mg/day for 7 days following which he became afebrile. A repeat urine sample was collected after 7 days of treatment, which came as sterile. Patient was discharged on ATT and ART.

**DISCUSSION AND CONCLUSION**

*Rhodotorula* belongs to the family of Sporidiobolaceae of the phylum Basidiomycota. It forms spherical to ellipsoidal budding yeasts and may sometimes form rudimentary hyphae and small capsules. Microscopically, the unicellular cells are spherical in shape, their size varies from 4-6 µm and they are surrounded by capsules. Ascospores are absent in this fungus. Three species have been described as human pathogens; *Rhodotorula glutinis*, *Rhodotorula minuta*, and *Rhodotorula mucilaginosa* (formerly known as *Rhodotorula rubra*). *Rhodotorula mucilaginosa* is the most common species which is isolated from clinical samples, followed by *Rhodotorula glutinis*. The red colonies which are formed are due to the presence of the carotenoid pigment, torularhodin. The *Rhodotorula* species can be easily confused with Sporobolomyces, but presence of carotenoid pigment, absence of pseudohyph and ballistoconidia and other biochemical tests help in differentiating them. *Rhodotorula* species are shown to have low virulence and low mortality usually, however, fatal cases have been documented on autopsy. They are common saprophytes in the skin, urine and faeces, but they are rarely isolated from blood and CSF. *Rhodotorula* spp. were found to be the fourth most frequently observed species among non-Candida yeasts isolated from clinical specimens.

*Rhodotorula mucilaginosa* is an opportunistic pathogen that may cause localized and systemic infection in immunocompromised hosts. In this case the patient was on urinary catheter for prolong duration so he might have acquired the infection in the hospital settings during his long stay with several comorbid conditions. Urinary catheters inoculate organisms into the bladder and promote colonization by providing a surface for adhesion and causing mucosal irritation. The presence of a urinary catheter is an important risk factor for funguria. This is a rare case report of hospital acquired urinary tract infection by *Rhodotorula mucilaginosa* in an immunocompromised host. There is paucity of literature as far as reports of *Rhodotorula mucilaginosa* associated UTI is concerned. To the best of our knowledge, there are no published case reports on hospital acquired urinary tract infection by *Rhodotorula mucilaginosa* in a patient infected with HIV. There are few references which document its association with UTI as causative agent.

The genus *Rhodotorula* are very much prevalent in nature and are present in soils, lakes, milk, fruit juices, shower curtains, bath tubs, tooth brushes and even as the resident flora of moist skin in humans. *Rhodotorula* strains are usually commensals and they appear to be less virulent than more common yeasts (*Candida* and *Cryptococcus*). Members of the *Rhodotorula* genus, which were generally considered to be nonpathogenic, are nowadays being recovered from humans from the skin, pulmonary, conjunctiva, urine and CSF. Localised infections without fungemia including endophthalmitis, onychomycosis,
meningitis, prosthetic joint infections, and peritonitis (usually associated with continuous peritoneal dialysis) have been reported in immunocompromised and immunocompetent patients.\(^8\) Cases of *Rhodotorula* infections are being increasingly reported in patients on central venous catheter.\(^7,9\) In addition, several reports show that *Rhodotorula* species have emerged as opportunistic pathogens in immunocompromised patients, during the last three decades.\(^10\)

In a study by Seifi Z et al., most *Rhodotorula* strains were recovered from the cardiology, nephrology and urology wards. The patients with central venous catheters and urinary catheters usually stay for long durations in such wards and as a result, these patients are at risk of being getting infected by this organism.\(^11\) In our case, patient was catheterized for long duration and hence might have acquired the *Rhodotorula* infection from the hospital environment and his immunocompromised condition worsened the disease.

Treatment approaches against infections due to *Rhodotorula* are still controversial.\(^12\) In vitro susceptibility tests detected that amphotericin B, itraconazole, voriconazole, and 5-flucytosine are the most active antifungal agents, although voriconazole, particularly against *Rhodotorula mucilaginosa* isolates, did not exhibit adequate activity.\(^4\) On the other hand, resistance to fluconazole, caspofungin, and micafungin has been observed in certain studies.\(^13,14\) In the current case, according to the results of antifungal susceptibility tests, the MIC value for Caspofungin and Micafungin was \(>8\mu g/mL\). High MIC values for Caspofungin and Micafungin in the literature in patients with *Rhodotorula* infections (\(\geq 8\mu g/mL\)) were similar to the current results. MIC values determined for voriconazole (1\(\mu g/mL\)) and posaconazole (0.5\(\mu g/mL\)) were higher than those detected for itraconazole (0.125\(\mu g/mL\)). Higher MIC values for caspofungin determined were similar to articles in the literature.\(^15\)

In conclusion, *Rhodotorula* species are one of the emerging human pathogens particularly in the context of immunosuppression and instrumentation associated with solid organ transplantation, cancer and acquired immunodeficiency syndrome. The yeast is of low virulence and fatality rate. The removal of indwelling catheters is necessary to ensure an excellent outcome with or without administration of antifungal agents.

**REFERENCES**

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