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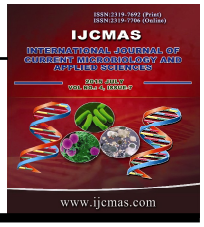

Original Research Article

Rhodutorella muciliganes Sole cause of Sacral Abscess in a Neutropenic Child (ALL) after Lumber Puncture - A Case of Hospital Acquired Infection

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Keywords

ALL,
PUO,
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A B S T R A C T

Rhodutorella is a rare infection, which has the potential to cause severe disease in patients with underlying immunosuppression. Rhodotorula is emerging as an important cause of nosocomial and opportunistic infections. We present case of *Rhodotorula mucilaginosa* which is isolated from sacral aspirate of a neutropenic (ALL) child associated with post lumber puncture sepsis and presented as pyrexia and sepsis, not responding to antibiotics, prompted us to describe them in this report. This case 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 immunosuppressed patients.

Introduction

*Rhodotorula*s species are pigmented basidiomycetous yeasts in the family Sporidiobolaceae (Arendrup *et al.*, 2014). The genus contains 37 species, of which only three, including *R. mucilaginosa* (formerly *R. rubra*), *R. minuta*, and *R. glutinis*, have been reported as causes of infection in humans (Biswas *et al.*, 2001). Three novel species, which are non-pathogenic to humans, have recently been described: *R. rosulata*, *R. silvestris* and *R. straminea* (Capoor *et al.*, 2014). Most *Rhodotorula* species produce colonies that are pink to coral in color but can also be orange to red on Sabouraud agar due to the presence of carotenoid pigments (Figure 1). Colony morphology has been described as soft, smooth, moist, and sometimes mucoid. *Rhodotorula* species are nutritionally non-fastidious, grow easily on most media, and are characterized by a rapid growth rate.

They appear as round or oval budding cells under microscopy, and pseudohyphae are rarely present. A faint capsule is sometimes formed. *Rhodotorula* species produce the enzyme urease and do not ferment carbohydrates. They can be differentiated from *Cryptococcus* species by their inability to assimilate inositol and from *Candida* species byproductionof pigmented colonies and the lack of pseudohyphae (Capoor *et al.*, 2014). *Rhodotorula* is a genus of unicellular pigmented yeasts, part of the division Basidiomycota. It is readily identifiable by distinctive orange/red colonies when grown on SDA (Sabouraud's Dextrose Agar). This distinctive color is the result of pigments

that the yeast creates to block out certain wavelengths of light that would otherwise be damaging to the cell. Pathology–Only *Rhodotorula mucilaginosa*, *R. glutinis*, and *R. minuta* have been known to cause disease in humans. There were no reported cases of *Rhodotorula* infections before 1985. There were however forty-three reported cases of *Rhodotorula* bloodstream infections (BSIs) between 1960 and 2000 (Chitasombat *et al.*, 2012). *Rhodotorula* is most commonly found in patients who are immunosuppressed and/or are using foreign-body technology such as central venous catheters. *Rhodotorula* is commonly treated by removing the catheter and the use of anti-fungals. *Rhodotorula* is susceptible to amphotericin B and Flucytosine *Rhodotorula* can also cause infections in animals (Chitasombat *et al.*, 2012). There have been reports of skin infections in chickens and sea animals and lung infections and otitis in sheep and cattle (Forés *et al.*, 2012).

Case Report: 3 years, male child presented with complaints of intermittent fever 3 months and sacral swelling since last 1 month. Patient had decrease in body weight and generalized weakness. Sacral swelling was increasing in size and cystic in consistency (Fig. 6). On further detailed examination patient admitted that for same complaints he was taking treatment and was hospitalized 2–3 times in different tertiary level hospitals. In his previous hospitalization in tertiary level hospital where he was admitted as PUO patient only his Lumber Puncture was done and CSF was collected along with other routine investigations. In that center bone marrow aspiration and trephine biopsy was also done and patient was diagnosed as acute lymphatic leukemia from fluid was aspirated from and sent for culture by Bactac system. In other investigation patient had Hb -4.5, Pletelet - 42 thousand, WBC - 3.25 10^3 Bone marrow aspirate showed –Morphologically acute lymphoblastic leukemia, significant clinical history pancytopenia under investigation received one unit blood transfusion, total platelet were 31,000/cumm, DLC - Blast 02%. Neutrophil - 00%, Lymphocyte - 90%, Monocyte - 08%. On Microscopic examination showed hypercellular, mild interstitial infiltrates, errythroid were adequate with normal maturation, myeloides were decreased, megakaryocytes were decreased and hypolobated, reticuline were moderately increased bone trabeculae were normal. Hypercellular marrow with mild interstitial infiltrates of immature cells. RFT, LFT Normal.

Serum LDH was 783. Patient was given inj. Linazolid, Inj. Azetranam,Inj, Ceftazedine, Tab. Acyclovir along with blood transfusion. There was no improvement in clinical condition of patient and fever persists despite of all. Sacral fluid was aspirated from sacral abscess and sent for culture by Bactac system. In direct Microscopy, KOH examination budding yeasts were seen, sample was processed for culture and pigmented fungus grew on SDA & CHROM AGAR medium, antimycotic sensitivity test was done and it was sensitive to Amphotericin-B, Fluconazole, Ketconazole. Patient was put on Fluconazole and responded very well as repeat culture after 7 days was negative for fungal growth (no fungus grew on SDA from swab taken from sacral aspirate or in BACTAC blood culture). Confirmation of yeast as *Rhodutorella* was done as there was salmon red color colony on SDA & Chromagar plate, mucoid in consistency, it was urease positive (Figures 2,3,4,5,6) Germ tube test was negative, no capsule was demonstrated in Indian Ink stain, sugar fermentation was negative & assimilation of Maltose, sucrose, trehalose, galactose, cellobiose, xylose, rafinose was positive and assimilation was

negative with lactose, dulcitole, melibiose, Nitrate reduction was negative, urease test was positive. In antimycotic sensitivity was positive with ampho-B, fluconazole, voriconazole and nystatin.

Rhodotorula mucilaginosa have been isolated from sputum, urine and blood, either in terminal stages of a debilitating disease such as carcinoma, or at autopsy from heart blood and from various organs. Species of *Rhodotorulla, Torulopsis* and many other yeasts have been isolated from bovine mastitis. Recovery of this organism from clinical sample is generally of academic interest only because rare infections caused by this yeast have been reported. There have been reports of skin infections in chickens and sea animals and lung infections and otitis in sheep and cattle. *Rhodotorula* infections occur among patients with immunosuppression and/or central venous catheters. *Rhodotorula* species have emerged as human pathogens due to immunosuppression and foreign-body technology.

Forty-three cases of *Rhodotorula* bloodstream infections (BSIs) were reported between 1960 and 2000. Risk factors include central venous catheters (CVCs) and malignancies Lack of standardization for susceptibility testing and a paucity of cases hamper treatment recommendations. A standardized method for antifungal susceptibility testing of yeasts (*Candida* and *Cryptococcus* species) has been defined by the NCCLS (NCCLS, 1997; Espinel-Ingroff, 1998; Barry *et al.,* 2000). *Rhodotorula* species, like *Cryptococcus* species, are hetero basidiomycetes and thus might be reliably tested by this protocol. Treatment of *Rhodotorula* infection involved the removal of CVCs and, generally, 14 days of amphotericin B or fluconazole therapy. But successful treatment with an antifungal agent demonstrating an elevated MIC could be attributed to catheter removal alone or to decreased hardiness of the temperature-sensitive phenotype. One non immunocompromised patient had clinical failure with fluconazole but cleared fungemia with amphotericin B and catheter removal. One patient cleared fungemia with two doses of amphotericin B alone. Clinical data include previous reports of successful therapies for *Rhodotorula* BSIs, including recovery of neutropenia catheter removal amphotericin B or combinations thereof. The largest reported series of *Rhodotorula* fungemia demonstrated favorable outcomes in all patients with either catheter removal or amphotericin B treatment. *Rhodotorula* species have emerged as human pathogens due to immunosuppression and foreign-body technology.

The pathogenesis of infection due to *Rhodotorula* species has not been studied. As mentioned previously, in almost all cases there is underlying immunosuppression and/or the presence of a foreign body. The low pathogenicity of *Rhodotorula* spp. is probably related to its reduced ability to grow at 37°C.

Immunocompromised individuals form few epithelioid cells or multinucleated giant cells thereby promoting yeast growth (Espinel-Ingroff, 1998). It has been demonstrated that *Rhodotorula* species are able to form biofilms which could play a role in the pathogenesis of infections caused by these species (Barry *et al.,* 2000).

According to one study, *R.minuta* and *R. mucilaginosa* are able to produce more biofilm than *R. glutinis*. It can be speculated that invasive infections are associated with nosocomial association in an immunocompromised host. In present case diagnosis of PUO was not confirmed and patient took consultation from 3 to 4 centers, when all routine investigations were

negative lumber puncture was done and CSF tape was done but with no conclusion. Ultimately bone marrow aspiration and trephine biopsy was done and patient was diagnosed as acute lymphatic leukemia. Patient was discharged and again after 15 days patient developed sacral swelling with pyrexia.

Patient was rehospitalised along with all routine investigation, digital X ray of spine was done keeping osteomyelitis in differential diagnosis. Sacral aspirate was cultured from which *R. muciliganes* was isolated and patient responded to antifungal fluconazole treatment.

As patient was neutropenic at time of lumber puncture, with Hb-4.5 gms % only with pancytopenia and most probably R. muciliganes opportunistic infection took place might be by absence of aseptic precaution either through skin or from lumber puncture needle as nosocomial infection.

Before culture report various antibiotics were administered to patient (Inj. Linazolid, Inj.Azetranam, Inj.Ceftazedine & Tab. Acyclovir) but there was no improvement in clinical condition of patient. Patient become afebrile after instituting antifungal treatment and now patient is on chemotherapy for ALL.

Prophylaxis

General prophylaxis

As with other opportunistic infections, an important aspect of prevention of *Rhodotorula* species infections is to minimize associated risk factors. CVCs should be used judiciously and should be removed as soon as they are no longer needed. Great care should be taken to maintain sterility when inserting intravascular and intraperitoneal catheters, and sterility should be maintained during the long term maintenance of these and other devices (Braun and Kaufmann, 1999).

Antifungal prophylaxis

There are no studies to date evaluating antifungal prophylaxis for prevention of *Rhodotorula* species infections. Given the rarity of these infections, specific prophylaxis is not recommended. There are no data to suggest that antifungal agents used for prophylaxis in other situations (e.g., after bone marrow transplantation) are effective in the prevention of *Rhodotorula* species infection. Breakthrough infections have been reported in patients receiving azoles or echinocandin prophylaxis

Infection control

Patients infected with *Rhodotorula* species do not require any specific infection control precautions. The organisms are common in the environment and are likely acquired through colonization with environmental strains. There is no evidence of human to human transmission of *Rhodotorula* species. However, health care workers' hands (as well as any rings) can be contaminated with *Rhodotorula* spp (Braun and Kaufmann, 1999). In the absence of specific data, standard infection controlprecautions, including hand washing and proper skin cleansing and preparation prior to invasive procedures should be emphasized.

Infections from *Rhodotorula* species are uncommon but are observed in hosts with CVCs and/or immunosuppressant. Antifungal preparations, in addition to catheter removal, are acceptable therapies for *Rhodotorula* infection, with excellent in vitro activity and reports of successful use.

Flucytosine possesses excellent activity in vitro. Based on our in vitro data, narrow spectrum azoles are not appropriate therapy. Further studies are needed to determine the role of extended-spectrum azoles, given the wide spectrum of activity against *Rhodotorula* species. Echinocandins should not be considered appropriate therapy for *Rhodotorula* species.

Fig.1 10% KOH – direct examination of aspirate showing bodding yeast

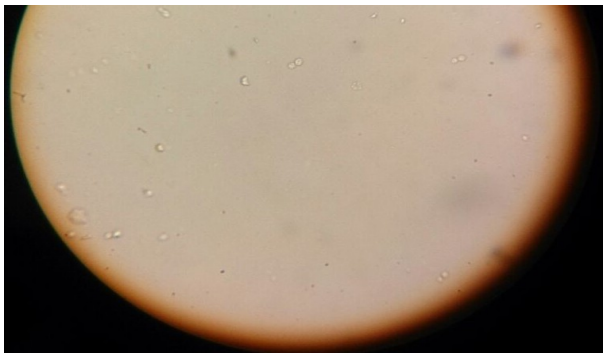


Fig.2 Antimycotic sensitivity testing

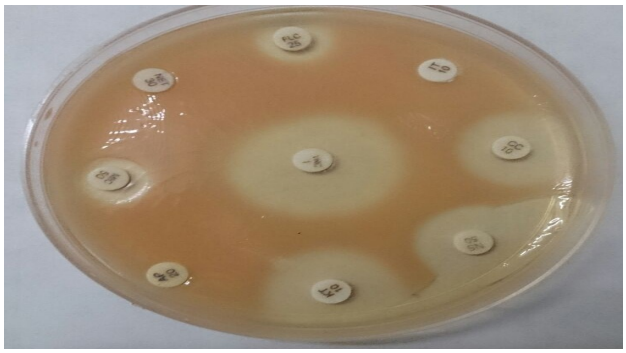


Fig.3 Gram's Staining-100X

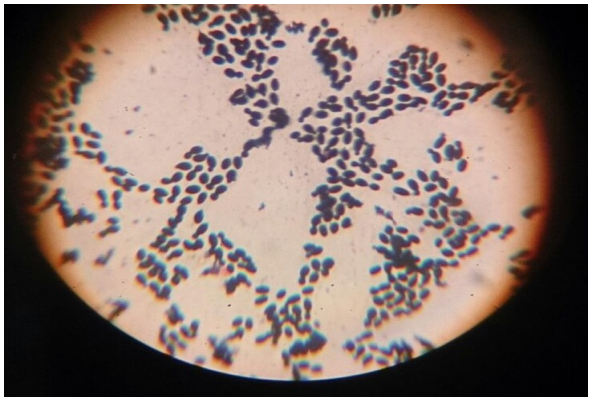


Fig.4 10% KOH – direct examination of aspirate showing bodding yeast

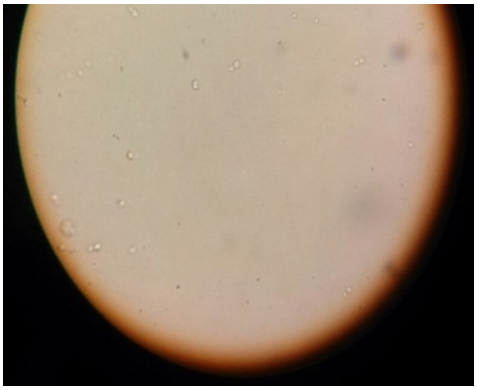


Fig.5 (a) Urease test positive; **(b)** salmon colored pigmented colonies on SDA & Chromagar

(a) Urease test positive

(b) Salmon colored pigmented colonies on SDA

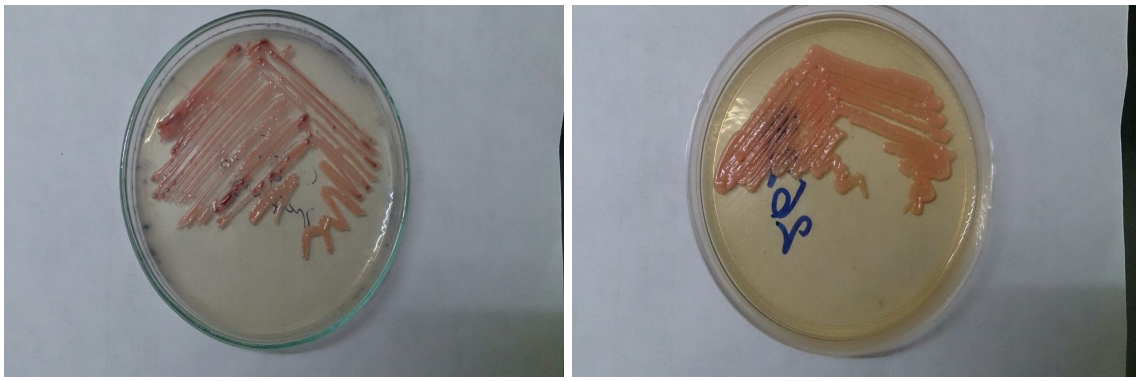
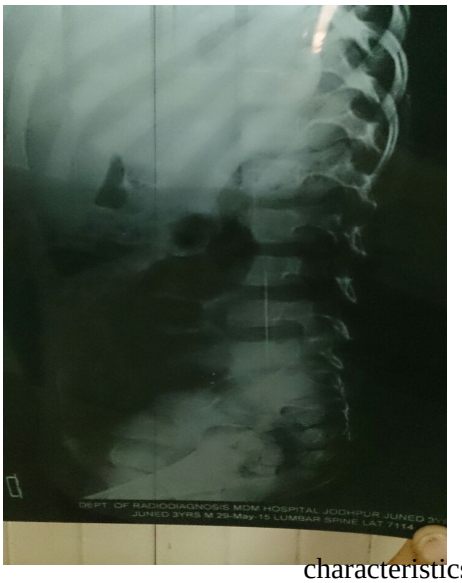


Fig.6 Sacral swelling



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