MENINGITIS CAUSED BY RHODOTORULA RUBRA IN AN HUMAN IMMUNODEFICIENCY VIRUS INFECTED PATIENT

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Abstract

Rhodotorula spp. are common saprophytes but may be responsible for systemic infections in immunocompromised patients. Meningitis caused by Rhodotorula spp. in human immunodeficiency virus (HIV) infected patients has been reported only rarely. We present a case of meningitis caused by Rhodotorula rubra in HIV infected patient. The presumptive diagnosis of cryptococcal meningitis was made on the basis of India ink preparation, Gram staining and latex agglutination test (LAT) for cryptococcal antigen. The final diagnosis was confirmed by isolation of Rhodotorula rubra from cerebrospinal fluid on culture. LAT was considered false positive. Amphotericin B and 5-fluorocytosine were administered but the patient succumbed to his illness.

Key words: Human immunodeficiency virus, meningitis, Rhodotorula

Invasive fungal disease continues to be a significant problem among immunocompromised patients. Most fungal infections are caused by commonly recognized opportunistic fungi such as Aspergillus spp., Candida spp., Cryptococcus neoformans and dimorphic fungi like Histoplasma capsulatum, Blastomyces dermatitidis and Coccidioides immitis. The fungi like Torulopsis glabrata, Trichosporon beigelii, Malassezia spp., Geotrichum candidum and Rhodotorula spp. are emerging pathogens of infections in immunocompromized patients. Rhodotorula spp. are common saprophytes in environment. Only rarely their etiological role in causation of infection has been described in immunocompetent and immunocompromized patients. Few reports include fungaemia, meningitis, ventriculitis, endocarditis and involvement of bone marrow.1-3 We report a case of meningitis caused by Rhodotorula rubra in an HIV infected patient.

Case Report

A 30-year-old-male was admitted with low-grade fever, easy fatigability and loss of appetite for one month. On physical examination, he had a temperature of 100°F, lymphadenopathy (cervical, axillary and inguinal) and white plaque on right buccal mucosa. Cardiovascular and respiratory systems were normal. There was mild hepatomegaly and no splenomegaly. Central nervous system (CNS) examination revealed altered sensorium, inconsistent response to verbal commands but no clear meningeal signs were observed. The examination of ocular fundus revealed bilateral papilloedema. Complete hemogram and blood chemistry revealed: Hb-12 gm%, ESR-10 mm in first hour, TLC-8600 per cmm, blood urea-37 mg%, blood sugar- 40 mg%, serum proteins-6 gm%, serum creatinine-0.9 mg%, serum Na+ 140 mg%, K 3.5 mg%, bilirubin-0.5 mg%, alkaline phosphatase-87 IU, SGOT- 66 IU and SGPT-51 IU. X-ray chest and cerebral CT scan were normal. The liver was enlarged on ultrasonography and the bile duct system was normal. Lumber puncture yielded clear cerebrospinal fluid (CSF). CSF was subjected to cell cytology examination, India ink preparation, Gram staining, Ziehl-Neelsen staining, bacteriological and fungal cultures by standard techniques.4 Cell cytology revealed -WBC count-198/cmm with lymphocyte- 55%, polymorphonuclear cells-45%, protein content -110 mg% and glucose concentration -20 mg%. India ink preparation of CSF showed encapsulated budding yeast cells. Gram stain of CSF showed inflammatory cells and round, narrow based budding yeast cells of size of 4-6 µm in diameter with wide clear halo around these cells (Figs. 1 and 2), Ziehl-Neelsen staining was negative for acid fast bacilli.

Figure 1: 10% nigrosin mount of CSF sample showing budding yeast cells with wide clear halo around cells (x400)

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Antigen detection for Cryptococcus neoformans was done by latex agglutination test (LAT) in a private laboratory. It was found to be positive with a titre of 32. Serologic test for HIV was performed after counselling. It was reactive for HIV-1 antibodies by ACON rapid card test (Acon lab inc, USA), ENZ AIDS HIV ELISA (Span diagnostics) and CAPILLUS HIV Test (Trinity biotech). CD4+T cell, CD8+T cell counts and CD4:CD8 ratio was 56/µL, 420/µL and 0.13 respectively. Serum for rheumatoid factor was negative. The CAPILLUS HIV Test (Trinity biotech), CD4+T cell, CD8+T cell, cycloheximide - 0.5 mg / L) and without antibiotics at 25oC dextrose agar with antibiotics (chloramphenicol - 0.05 mg / L; cycloheximide - 0.5 mg / L) and without antibiotics at 25°C and 37°C revealed growth of Rhodotorula rubra identified by its colony morphology i.e., coral red coloured, pasty and mucoid growth (Fig. 3), multiple lateral budding yeast cells on Gram staining and biochemical tests. Sporabolomyces spp., another red coloured yeast, was ruled out as there was no ballistospore formation. After CSF culture report, previous therapy was supplemented with 5-fluorocytosine (25 mg/kg) six-hourly and antiretroviral therapy. There was no improvement in patient’s condition and he succumbed to his illness after 23 days of hospital stay.

Discussion

The incidence of fungal infections of CNS has shown a steep rise, largely due to the advent of AIDS, wide spread use of broad-spectrum antibiotics, steroids and immunosuppressive drugs. However, Rhodotorula fungal infections of CNS continue to be uncommon. Rhodotorula belongs to family Cryptococcaceae, subfamily Rhodotorulodea and is a basidiomycetous encapsulated yeast. It produces mucoid yeast like soft, pasty colonies with red carotenoid pigment on SDA medium. Microscopically, the unicellular cells of this fungus are spherical in shape, size varying from 4.5 µm - 6 µm, surrounded by a capsule. No ascospores are present. Many species of genus Rhodotorula have been described. R. rubra and Rhodotorula glutinis are the most frequently isolated species from clinical specimens. Rhodotorula spp. and Cryptococcus spp. have many similar morphological and physiological properties and have been mistaken for each other. Rhodotorula spp. differs from Cryptococcus spp. by their inability to assimilate inositol and their carotenoid pigment. Rhodotorula spp. is a common saprophyte of skin, lungs, urine and faeces. But its isolation from blood and CSF is of greater significance when contamination has been ruled out. Rhodotorula spp. have been reported to cause septicaemia, sepsis and systemic infections like meningitis and endocarditis. Pore and Chen reported a case of R. rubra meningitis in an immunocompromized patient with acute lymphoblastic leukemia. He detected encapsulated budding yeast cells and confirmed it by culture. Without isolation on culture, this case could have been mistaken for Cryptococcus spp. Another case of meningitis caused by R. rubra in an HIV infected patient was reported by Gyaurgieva et al. Our case was also HIV-infected, initially diagnosed as a case of cryptococcal meningitis. But CSF culture on SDA medium grew Rhodotorula spp. The possibility of contamination has been ruled out as CSF is a sterile fluid and growth has been obtained twice on SDA medium containing antibiotics. Thus, it was considered to have pathogenic role in causing meningitis in the present case.

The LAT is quite sensitive and specific test when used with proper controls. Both false positive and false negative results occur. There are many causes of false positive LAT for cryptococcal antigen. These include presence of rheumatoid
factor, contamination during pipetting and use of hydroxyethyl starch for intravenous volume replacement. The infection with *Trichosporon* spp, capsulated bacteria like *Stomatococcus mucilaginosus, Klebsiella* spp, *Capnocytophaga canimorsus* also give false positive LAT. This is explained on the basis of presence of similar nature of capsule i.e., polysaccharide in these organisms and *C. neoformans*.\(^{5,9,10}\) The presence of *Acinetobacter* spp. in the blood may explain the false positive LAT in our case. Also, *Rhodotorula* spp. and *Cryptococcus* spp. cannot be readily differentiated in CSF or in tissue section.\(^8\) Therefore, fungal culture has been recommended for diagnostic confirmation of these encapsulated yeasts.

*Rhodotorula* spp. may be a cause of invasive fungal disease in immunocompromized and immunocompetent hosts but can be eradicated if treated aggressively.\(^{1,6,7}\) Amphotericin B, 5-fluorocytosine (5-FC) and azoles like itraconazole have been found to be effective drugs. Relapse of meningitis caused by *Rhodotorula* spp. has been reported by Gyaurgieva et al.\(^6\) They eradicated the infection with suppressive therapy and maintenance therapy of itraconazole. The antibiogram of this yeast ranges from sensitivity to all antifungal drugs and resistance to amphotericin B and newer azoles. Currently, it is essential to perform antifungal sensitivity testing of this yeast, once the pathogenic role of this fungus is proven.

**References**


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