

RHODOTORULA RUBRA FUNGEMIA IN AN IMMUNOCOMPROMISED PATIENT

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Medical advances during the past decade have improved preventive, diagnostic and therapeutic capabilities for a variety of diseases. However, certain therapies that involve the use of invasive surgical procedures and immunosuppression predispose the host to an expanding group of opportunistic pathogens. Most fungal infections are caused by commonly recognized opportunistic fungi such as *Candida* species, *Aspergillus* species, *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Coccidioides immitis*, and *Cryptococcus neoformans*. Of late, fungi such as *Candida glabrata*, *Trichosporon beigeli*, *Malassezia* species, *Hansenula* species, *Rhodotorula* species and *Geotrichum candidum*, are emerging as significant causes of infection in immunocompromised patients. In this report, we describe a case of *Rhodotorula rubra* sepsis in an immunocompromised patient, and discuss the clinical aspect and management of the condition, with a review of the relevant literature.

Case Report

A 65-year-old female was admitted at King Fahd General Hospital in Jeddah, Saudi Arabia, in February 1999, with intestinal obstruction, septicemia and fecal fistula. She was treated with cephradine 500 mg iv/6 hr, metronidazole 500 mg iv/8 hr, and cefoxitin 1 mg iv/8 hr for seven days. An emergency laparotomy was done one week later. Her bowel was fragile, with multiple adhesions and multiple perforations during dissection. Hemicolectomy and jejunoileal anastomosis were performed, and about 100 cm of small bowel and jejunum were removed. The patient was put on metronidazole 500 mg iv/8hr, amikacin 500 mg iv/12hr, and cefuroxime 750 mg iv/8hr.

Postoperatively, the patient developed a recurrence of fecal fistula through the operation site, and was put on total parenteral nutrition. The histopathology report confirmed



FIGURE 1. Gram-stained smear of *Rhodotorula rubra* isolated from blood culture.

metastatic mucoid epidermoid carcinoma. One week later, she had pyrexia of 39°C, and one set of blood was withdrawn from the peripheral line and sent for culture, using Bactec 9240 (Beckton Dickinson Company, USA). The blood culture was positive two days later, and the gram-stained smear showed blastoconidia with a budding (no lyphae) faint capsule (Figure 1). Culture of the blood on Sabouraud agar grew pink, mucoid colonies (Figure 2) that were identified with the use of Candifast (International Microbio., France) and Vitek (Bio Merieux, France) as *Rhodotorula rubra*. The antifungal susceptibility test using Candifast showed the organism to be sensitive to fluconazole and miconazole, but resistant to amphotericin B, flucytosine, econazole and ketoconazole. The patient was treated with miconazole 200 mg iv/8hr for 10 days. Her total and differential white blood cells before the fungemia were within normal limits.

Ten days after the fungal therapy, the patient's temperature rose sharply, her condition deteriorated and she was transferred to the intensive care unit. Blood sent for culture was positive for *Pseudomonas aeruginosa*, but negative for *Rhodotorula rubra*. She was treated with piperacillin 4 g iv/8hr and aztreonam 1 mg iv/12hr. Although the patient responded to antibiotic therapy, she died two weeks later. Her past history showed that she had been admitted a year earlier to King Fahd General Hospital, and had had a total hysterectomy and radiation therapy

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FIGURE 2. Culture of *Rhodotorula rubra* on Sabouraud agar.

because of adenocarcinoma. A month before that admission, she had been admitted to a private hospital with acute abdominal pains, where an emergency laparotomy had been performed and unhealthy bowel resected.

Discussion

Rhodotorula species are normal inhabitants of moist skin, and can be found in such environmental sources as shower curtains, bathtub grout and in toothbrushes.¹ In rare instances, *Rhodotorula* species have been reported to cause septicemia,² meningitis,³ systemic infection,⁴ and sepsis related to complications from indwelling central venous catheters.⁵ *Rhodotorula* species have a rapid growth rate on culture and mature in four days. The colony is usually pink to coral, but can also be orange-red to yellow. Colony on Sabouraud agar is yeast-like, soft and smooth. On cornmeal Tween 80 agar at 25°C for 72 hours, the microscopic morphology shows oval or round budding cells and occasionally, a few rudimentary pseudohyphae. No ascospores are present.⁶ A faint capsule is sometimes formed. *Rhodotorula* species and *Cryptococcus* species have many similar physiologic and morphologic properties. Both are round to oval multilateral budding yeast with capsules, produce urease enzyme, and fail to ferment carbohydrates. *Rhodotorula* species differ from *Cryptococci* by their inability to assimilate inositol and their obvious carotenoid pigment.¹ *Rhodotorula* is commonly known as a contaminant, and its presence in the terminal stages of debilitating diseases such as leukemia and carcinoma may indicate an ability to colonize particularly susceptible individuals.

Our patient had an adenocarcinoma of the uterus, which was removed by total hysterectomy about one year ago. She developed *Rhodotorula rubra* septicemia after two major abdominal operations, and was treated with two courses of broad spectrum antibiotics, central venous catheter insertion and total parenteral nutrition, all of which are known risk factors for fungemia. The digestive tract

could have been the source of *R. rubra* fungemia in this patient, and this may have been facilitated by the previously mentioned risk factors.

In 1984, Rusthoven et al.⁴ reported a case of systemic *Rhodotorula* infection in a patient with acute myeloid leukemia. *Rhodotorula* was isolated from the bone marrow on two separate occasions, despite initial treatment with amphotericin B and from liver biopsy. The patient survived after aggressive antifungal and antileukemia treatment. In 1994, Marinova et al. reported a case of *Rhodotorula* fungemia in a 13-year-old boy after neurosurgery. The case was successfully treated with miconazole and 5-flucytosine.⁷ In 1992, Kiehn et al.⁵ reported 23 patients who had catheter-related *Rhodotorula* sepsis within five years at Sloan Kettering Cancer Center (New York). All 23 patients had indwelling central venous catheters that had been in place from one to 22 months (average 9.3 months). They all survived the fungemic episode and experienced no recurrence of the infection after treatment with antifungal therapy and by either removal or non-removal of the catheters, or by catheter removal without antifungal therapy. Infections with unusual fungal pathogens including *Rhodotorula rubra* have been reported by Anaissie et al.⁸ They studied 44 cancer patients who had serious infections with these fungal pathogens. Twenty-four patients had disseminated infection, 12 had involvement of a single organ, and eight had only fungemia. Features that correlated with poor prognosis were persistent neutropenia and disseminated visceral infection, but not fungemia alone.

Rhodotorula rubra has been reported to cause meningitis. In 1976, Pore and Chen³ reported a case of *Rhodotorula rubra* meningitis in a 21-year-old male compromised with acute lymphoblastic leukemia. Recently, a case of meningitis caused by *Rhodotorula rubra* in an HIV patient was reported by Gyaurgieva et al.⁹ Although initial treatment with 5-flucytosine for 15 days was successful in eliminating the yeast from the CSF, eight months later, the meningitis relapsed and *Rhodotorula rubra* was recovered from the CSF. Suppressive therapy with itraconazole (400 mg daily for three months) followed by maintenance therapy 200 mg daily eradicated the infection.

Unusual fungi that are commonly found in the skin and in the digestive tract of healthy people may be responsible for deep infections, as well as for cutaneous mucosal diseases. Such deep infections are facilitated by immunosuppression, or by factors that enable the opportunistic organisms to proliferate in the gut, skin or mucosa, and to penetrate deep tissues. Intravascular catheter insertion, broad spectrum antimicrobials, surgery and immunosuppression are predisposing factors for opportunistic fungemia. Unusual fungi have now emerged as significant pathogens in the cancer patient population, newborns and in the elderly. A high level of suspicion should be maintained when any of the unusual fungi are

cultured from clinical specimens from immuno-compromised patients. The antibiogram of the unusual yeasts range from resistant to the most recent azole and amphotericin B to those which are highly susceptible to all antifungal agents.

It was not possible in this report to use the micro- or macrobroth dilution method which has been standardized to the National Committee for Clinical Laboratory Standards (NCCLS). Therefore, the antifungal susceptibility test was done using Candifast, a reasonable alternative with an indicative value on the interaction of the antifungal yeast pair during *in vivo* treatment.¹⁰ Considerable advances in the standardization of techniques for antifungal susceptibility tests have been made over the past five years through the NCCLS subcommittee on antifungal susceptibility testing.¹¹ Excellent performance within established quality control limits has been consistently found for *Candida parapsilosis* (ATCC 22019) and *Candida krusei* (ATCC 6258), when tested by broth dilution against amphotericin B, flucytosine and fluconazole.¹¹ The techniques have now been standardized, and the *in vitro* antifungal susceptibility test results of the drug tested can be used to predict *in vivo* clinical response. The recognition of unusual yeasts as agents of sometimes life-threatening infections and their unpredictable antifungal susceptibilities increases the burden on the clinical microbiology laboratory to complete species identification and determine minimal inhibitory concentration (MIC).¹²

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