International Journal of Infectious Diseases (2009) 13, e27—e29

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CASE REPORT

Rhodotorula mucilaginosa lymphadenitis in an HIV-infected patient

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Received 31 March 2008; accepted 23 April 2008
Corresponding Editor: Andy I.M. Hoepelman, Utrecht, The Netherlands

KEYWORDS
Rhodotorula mucilaginosa;
Lymphadenitis;
HIV infection

Summary We report a case of lymphadenitis due to *Rhodotorula mucilaginosa* in a man with well-controlled HIV infection. The diagnosis was established microbiologically by positive lymph tissue cultures, and clinically by responses of lymphadenitis to antifungal therapy. The patient was asymptomatic and was treated with itraconazole 200 mg orally once daily as an outpatient. Clinical response was evident within three weeks with improvement of lymphadenopathy on serial computed tomography scans. Lymphadenopathy resolved completely after 8 months of itraconazole therapy and had not recurred 9 months after treatment was stopped.
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Introduction

Rhodotorula is a basidiomycetous yeast belonging to the family Cryptococcaceae.[1] It is characterized by the production of carotenoid torularhodin, a pigment that gives their colonies the typical salmon-pink to coral-red appearance (hence the common name, 'red yeast').[2] *Rhodotorula* species are ubiquitous and have been recovered from human skin, nails, conjunctiva, the respiratory, gastrointestinal and urinary tracts, as well as various environmental sources such as soil and water. They are generally considered to be non-pathogenic commensals or contaminants. Their pathogenic potential has only been recognized during the past decade.[3]

Infections due to *Rhodotorula spp* are uncommon with less than a hundred cases reported in the English literature over the past 40 years.[2,4] The majority of cases were fungemias in patients with central venous catheters, but other infections such as meningitis, ventriculitis, endocarditis, peritonitis, dacryocystitis, keratitis, and endophthalmitis have been reported.[2,5] Among the *Rhodotorula spp* that have been described as human pathogens, *Rhodotorula glutinis* and *Rhodotorula mucilaginosa* (formerly known as *Rhodotorula rubra* or *Rhodotorula pilimanae*) are the most common species.[1,4,6,7] Immunosuppression and the use of an indwelling catheter are the major risk factors for Rhodotorula infections.[2,4,6,8]

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1201-9712/$36.00. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.
doi:10.1016/j.ijid.2008.04.006

Case report

We describe a case of *R. mucilaginosa* lymphadenitis in a patient with HIV infection. The patient was a 46-year-old African-American man with a past medical history significant for anemia, chronic renal insufficiency, shingles, toxoplasmic encephalitis, and HIV infection. He had no known drug allergies. The patient had been diagnosed two years previously with Toxoplasma encephalitis and AIDS with a nadir CD4 cell count of 40 cells/mm^3, and had been on effective antiretroviral therapy ever since. His past antiretroviral regimens, in chronological order, included zidovudine/lamivudine/indinavir (8 months), stavudine/lamivudine/indinavir (3 months), stavudine/lamivudine/abacavir (1 month), and zidovudine/lamivudine/abacavir (8 months). Changes in his antiretroviral regimen were prompted by adverse drug reactions including anemia, nephrolithiasis, and peripheral neuropathy rather than poor viral control. He tolerated his current regimen (abacavir 300 mg twice daily, lamivudine 150 mg twice daily, and efavirenz 600 mg once daily) well without any adverse effects. For one year before presentation, his HIV disease was well controlled by this regimen with viral loads ranging from $<$50 copies/mL to 1781 copies/mL and CD4 cell% ranging from 23% to 27%. His CD4 cell counts had been consistently $>$200 cells/mm^3 for more than two years.

The patient presented to the infectious diseases clinic for a routine follow-up visit. Upon presentation, he was afebrile and had a respiratory rate of 16 breaths/minute, a heart rate of 92 beats/minute, and a blood pressure of 140/80 mmHg. The patient felt well in general and had had a 30-lb (13.6-kg) weight gain over the past 6 months. Physical examinations revealed a firm, non-tender swelling of 3—4 cm in diameter in the right neck below the thyroid gland. A computed tomography (CT) scan of the neck was ordered and subsequently showed a 5 $\times$ 4 $\times$ 6 cm lobulated lesion consistent with lymphadenopathy in the medial right supraclavicular region, effacing the right thyroid gland and displacing the trachea to the left. An incisional biopsy of the neck mass was performed and two lymph nodes were sent for evaluation: one to the pathology laboratory for histocytology studies and one to the microbiology laboratory for Gram-stained smear, KOH fungal prep, and acid-fast bacillus (AFB) smear, as well as bacterial, fungal, viral, and AFB cultures. While no yeasts were seen with special stains on histocytology studies of one lymph node, direct plating of the other lymph node on Sabouraud-dextrose agar grew many colonies of *R. mucilaginosa* in 5 days (Figure 1). Identity of the isolate was confirmed by Vitek automated system for identification and API manual biochemical tests (BioMerieux Diagnostics). Examinations of the Gram-stained smear, KOH fungal prep, and AFB smear of the specimen were unremarkable. All other cultures were negative. The patient was diagnosed with *R. mucilaginosa* lymphadenitis, and itraconazole 200 mg orally once daily was immediately initiated. Three weeks into treatment, a follow-up CT scan of the neck revealed mild improvement of the right supraclavicular lymphadenopathy that measured 5 $\times$ 4 $\times$ 5 cm (previously 5 $\times$ 4 $\times$ 6 cm). Therapy with itraconazole was continued for a total of 8 months during which time the neck swelling resolved. The patient tolerated itraconazole treatment well without adverse effects. His liver enzymes remained normal throughout treatment. There was no evidence of clinical relapse 2 months after the discontinuation of itraconazole. His HIV disease remained well controlled on abacavir/lamivudine/efavirenz with low-grade viremias ($<$1000 copies/mL) and CD4 cell counts $>$800 cells/mm^3.

Figure 1 Salmon-pink colonies of *Rhodotorula mucilaginosa* from biopsied lymph nodes on Sabouraud-dextrose agar.

Discussion

For a long time, Rhodotorula was considered to be a nonpathogenic, ubiquitous contaminant. Its pathogenic potential has only been recognized during the past decade.[9] Infections due to *Rhodotorula spp* are usually opportunistic, occurring predominantly in immunocompromised patients with a central venous catheter.[1,9] In a case series of 43 patients with Rhodotorula fungemias reported in the literature between 1960 and 2000, 42 patients had a central venous catheter and 33 patients had either an underlying malignancy or a diagnosis of AIDS.[4] Broad-spectrum antibiotics, corticosteroids, hyperalimentation, surgery, chronic renal failure, diabetes mellitus, granulocytopenia, and damage to skin and mucosa have also been suggested as predisposing factors for Rhodotorula infections.[2,4,8] Our patient was HIV-infected and his infection was apparently well controlled with low grade viremia ($<$1000 copies/mL) and CD4 cell counts persistently greater than 200 cells/mm^3 before presentation. He also had mild chronic renal insufficiency with serum creatinine values ranging from 115 μmol/L to 203 μmol/L for the past year. HIV infection and possibly chronic renal insufficiency could have predisposed our patient to Rhodotorula infections.

Rhodotorula appears to be less virulent than other pathogenic yeasts, but there is a 15% mortality rate for systemic infections.[2] In addition to fungemias, Rhodotorula has been reported to be the causative agent for a wide variety of infections including meningitis, ventriculitis, endocarditis, peritonitis, dacryocystitis, keratitis, and endophthalmitis.[2,5] We report a suspected case of lymphadenitis caused by *R.*

mucilaginosa. Although the diagnosis could not be confirmed without observing *R. mucilaginosa* on histocytology studies, it was established microbiologically by positive cultures from the lymph node, and clinically by responses of lymphadenitis to antifungal therapy. Unlike other Rhodotorula infections that usually present with fevers,[2] our patient was asymptomatic. The absence of symptoms in our patient was probably due to the sequestration of *R. mucilaginosa* in the lymph node tissues.

Susceptibility data on *Rhodotorula spp* are scarce, but they appear to be generally more susceptible to amphotericin B and flucytosine than to the azole and echinocandin antifungal agents.[6] Zaas et al.[6] and Espinel-Ingroff[10] studied the susceptibility of a total of 13 strains of *R. mucilaginosa* and two strains of *R. glutinis*. The tested strains were susceptible to amphotericin B (minimum inhibitory concentration (MIC) range 0.25—1.0 μg/mL) and flucytosine (MIC range 0.125—0.25 μg/mL), intermediate to itraconazole (MIC range 0.25—4.0 μg/mL) and voriconazole (MIC range 0.25—8.0 μg/mL), and resistant to fluconazole (MIC range 32—>64 μg/mL) and caspofungin (MIC range 16—>16 μg/mL). However, it must be noted that methods for antifungal susceptibility testing are currently not standardized, and results of in vitro testing do not necessarily correlate with clinical outcomes. Susceptibility testing for fungi is not performed at our institution. Our patient was minimally symptomatic following incisional biopsy and therefore was treated with oral itraconazole as an outpatient. Clinical response was evident within three weeks and verified by improvement of lymphadenopathy on serial CT scans.

The appropriate duration of treatment for Rhodotorula infections has not been determined. Depending on the nature of the infections, treatment durations of two weeks to several months have been proposed.[11] Our patient was treated with itraconazole for 8 months until the swelling (lymphadenopathy) was clearly resolved. Lymphadenopathy was no longer noticeable on physical examinations 2 months after and had not recurred 9 months after treatment was stopped.

To our knowledge, this could be the first case report of lymphadenitis due to *R. mucilaginosa*. The patient had no other predisposing history such as an indwelling intravenous catheter or hospitalization receiving intravenous therapies for at least one year prior to this event. The only predisposing risk factor was his immunologic status due to HIV infection, which was well controlled. Although *R. mucilaginosa* lymphadenitis in our patient was successfully treated with 8 months of itraconazole, the optimal antifungal agent and duration of treatment for this infection in an outpatient setting has not been established. Infections due to *Rhodotorula spp* are rare, yet clinicians should maintain a high index of suspicion for such opportunistic yeast infections in immunocompromised patients.

Conflict of interest: No conflict of interest to declare.

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