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Femoral Prosthesis Infection by *Rhodotorula mucilaginosa*[▽]

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This case report is a case history of a femoral prosthesis infection caused by *Rhodotorula mucilaginosa* in a human immunodeficiency virus patient. Though the pathogenicity of this organism for bone tissue has been previously reported, this is the first reported case of an orthopedic prosthesis infection by this species of the genus *Rhodotorula*.

CASE REPORT

A 41-year-old female human immunodeficiency virus patient sustained a fracture of the left femoral epiphysis in a road traffic accident in 1996. Surgical internal fixation was done but was followed by an outbreak of chronic coxitis (confirmed by magnetic resonance) until a femoral prosthesis was finally inserted in 2006. During 2007, an acute infection of the implanted prosthesis was diagnosed, with the patient suffering from a fever (38.5°C), strong local pain, and tumefaction. Furthermore, a fistula developed from the internal site of the prosthetic infection as far as the skin of the femoral region, with continuous pus discharge from its external opening. No overt signs of septicemia were observed, and mild leukocytosis was documented, whereas CD4 and CD8 levels were found to be normal. After receiving a 10-day course of intramuscular piperacillin, empirically, followed by no clinical improvement, the patient was admitted to the hospital. Magnetic resonance and bone scintigraphy documented the prosthesis infection. Also, drainage from the fistula was cultured. Particularly, it was plated onto sheep blood agar, mannitol salt agar, MacConkey agar, and Sabouraud dextrose agar (plates were provided by bioMérieux, Marcy l'Etoile, France). Blood culture plates were incubated at 36°C in air, anaerobically, and under 5% CO_2-enriched atmosphere. Mannitol and MacConkey media were processed at 36°C under aerobic conditions. Finally, two Sabouraud plates were incubated at 36°C and 25°C, respectively, both in ambient air. After 24 h of incubation, neither bacterial nor fungal growth was observed, whereas Sabouraud cultures processed at 25°C yielded about 150 colonies of *Rhodotorula mucilaginosa*, as a single organism, after 48 h of incubation. Cultures from all of the other mentioned media remained negative, so that no aerobic, anaerobic, or microaerophilic organisms other than *Rhodotorula* were observed. Identifica-

tion of the isolate was suggested by the phenotype of colonies, which were typically pink-red and smooth, and by microscopic features (round-shaped yeast cells without hyphae) and confirmed by the Vitek2 system (YST card; bioMérieux) and by the mini API system (ID32C gallery; bioMérieux). Gram staining of the secretion was carried out and documented the presence of numerous images of phagocytosis by polymorphonuclear leukocytes against yeast-like cells (the yeast-like cells were mostly observed inside the cytoplasm of granulocytes), indicating acute infection caused by yeast-like organisms. Low MICs were observed for amphotericin B and flucytosine against the isolate studied (MICs, 0.25 µg/ml and ≤0.03 µg/ml, respectively), whereas higher values were documented for fluconazole (MIC, >256 µg/ml), itraconazole (MIC, >16 µg/ml), and voriconazole (MIC, 8 µg/ml). MICs were obtained by performing a Sensititre YeastOne test (Trek Diagnostic Systems Ltd., Imberhome Lane, East Grinstead, West Sussex, England). Particularly, the Sensititre plate was incubated for 48 h, at no more than 30°C. Liposomal amphotericin B treatment was started, thus leading to rapid resolution of fever, reduction of tumefaction and pain, and gradual disappearing of fistula drainage within 10 days. The fistula finally disappeared, too, within 2 weeks. Also, clinical improvement was documented by magnetic resonance and scintigraphy. The patient is currently waiting for surgical replacement of the femoral prosthesis.

Rhodotorula is a common airborne ubiquitous fungus (with a terrestrial and marine worldwide distribution), which has been known to cause fungemia, meningitis, ventriculitis, peritonitis, endocarditis, and infections of devices such as catheters and contact lenses (1, 2, 7, 10, 11). Furthermore, *Rhodotorula* has been collected as a saprophyte from skin, vaginal, and respiratory specimens, as well as a colonizing organism on hemodialysis machines and fiber-optic bronchoscopes, (6, 7). Most *Rhodotorula* isolates commonly show resistance to fluconazole, itraconazole, and voriconazole, while ravuconazole, amphotericin B, and flucytosine generally exert good in vitro activity (5, 8, 9, 12). Particularly, the

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Sensititre YeastOne technique (a colorimetric microdilution test) has shown its value for antifungal susceptibility testing of yeast-like fungi, given its correlation with reference procedures (4, 5), but 25°C to 30°C temperatures and at least 48-h incubations are needed (4, 6). The main species of the genus, *R. mucilaginosa* (formerly both *Rhodotorula rubra* and *Rhodotorula pilimanae*) and *Rhodotorula glutinis*, were previously labeled as nonpathogenic, contaminant yeasts but emerged as opportunistic agents of infections in the last two decades. While a prosthetic joint infection by *Rhodotorula minuta* (3) as well as an *R. mucilaginosa* osteomyelitis after traumatic bone fracture have been reported previously (7), the case we describe represents, to our knowledge, the first report of a prosthetic bone infection due to *R. mucilaginosa*. Given the ubiquitous distribution of this fungus, the contamination of cultures was also suspected. Anyway, this was unlikely, as drainage from fistula was obtained by means of sterile techniques and immediately subjected to culture. Furthermore, profuse pure growth of typical colonies was observed. In addition, Gram staining emphasized the role of the observed yeasts as pathogens, given the numerous images of phagocytosis observed. Finally, prompt response to antifungal treatment corroborated our findings.

In the case we described, the role of the underlying human immunodeficiency virus infection as a risk factor for acquiring such a fungal complication remained unclear, whereas we considered the femoral prosthesis as the major predisposing factor. Especially, this report first noted the affinity of *R. mucilaginosa* for orthopedic devices, besides further emphasizing the affinity of all members of the *Rhodotorula* genus for synthetic materials in general, such as intravenous catheters, contact lenses, plastic materials of fiber-optic bronchoscopes, and hemodialysis machines (3, 7). This is remarkable, as osteomyelitis by this fungus may represent a life-threatening disease if complicated by fungemia; in fact, fungemia would appear to be a difficult-to-treat infection, leaving few therapeutic alternatives and making the removal of the catheter a needed step for treatment, given the strong adherence of this yeast to the device surface. Finally, we would emphasize the widespread antifungal resistance among organisms of the *Rhodotorula* genus. This mainly appears to be an azole resistance, so that amphotericin B still remains a great weapon against serious infections by this yeast.

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