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Case Report

Onychomycosis caused by *Trichosporon mucoides*

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SUMMARY

A case of onychomycosis caused by *Trichosporon mucoides* in a man with diabetes is presented. The infection was characterized by a brown–black pigmentation of the nail plates and subungual hyperkeratosis of the first three toes of both feet. Onychogryphosis was also visible on the third left toe. Direct microscopic examinations revealed wide and septate hyphae and spores. Three cultures on Sabouraud–gentamicin–chloramphenicol 2 agar and chromID Candida agar produced white, creamy, and smooth colonies that were judged to be morphologically typical of *T. mucoides*. Microscopic examinations of the colonies showed arthroconidia and blastoconidia. The urease test was positive. A sugar assimilation test on yeast nitrogen base agar showed assimilation of galactitol, sorbitol, and arabinitol. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF) confirmed the diagnosis of *T. mucoides* infection. The patient was treated with topical urea and oral itraconazole. Three months later, a mild improvement was observed. The patient was subsequently lost to follow-up.

1. Introduction

Trichosporon spp are yeast-like fungi found in soil and water. Furthermore, they belong to the normal flora of the human skin and gastrointestinal tract.[1,2] The first case of onychomycosis caused by *Trichosporon mucoides* was published in 2011 by Sageerabanoo et al.[1] An additional case was published in 2015 by Capoor et al.[2] Both patients were Indian. To the authors' knowledge, no other cases have been reported. A case of onychomycosis caused by *T. mucoides* in a patient with diabetes is presented here.

2. Case report

A 76-year-old Caucasian man was admitted because of onychodystrophy of the toes. The patient stated that he was being treated with metformin for type II diabetes. He also declared that the onychodystrophy had appeared approximately 7 years earlier.

Dermatological examination revealed a brown–black pigmentation of the nail plates and subungual hyperkeratosis of the first three toes of both feet. Onychogryphosis was also visible on the third left toe (Figure 1).

A general physical examination did not reveal anything pathological. Laboratory tests showed hyperglycemia (136 mg/dl) and an increase in urea (56 mg/dl). Three direct microscopic examinations of nail clippings, previously prepared with 30% potassium hydroxide, revealed wide and septate hyphae and spores. Three cultures on Sabouraud–gentamicin–chloramphenicol 2 agar (SGC2) and chromID Candida agar (CAN2) produced white, creamy and smooth colonies within a few days, which were judged to be morphologically typical of *T. mucoides* (Figure 2). Microscopic examinations of the colonies showed arthroconidia and blastoconidia. All cultures were negative for dermatophytes. The urease test was positive. A sugar assimilation test on yeast nitrogen base agar showed assimilation of galactitol, sorbitol, and arabinitol. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) confirmed the diagnosis of *T. mucoides* infection (bionumber 6376777777377771). Three bacteriological examinations were negative. In accordance with the criteria of English[3] and Gupta et al.,[4] the final diagnosis was onychomycosis caused by *T. mucoides*.

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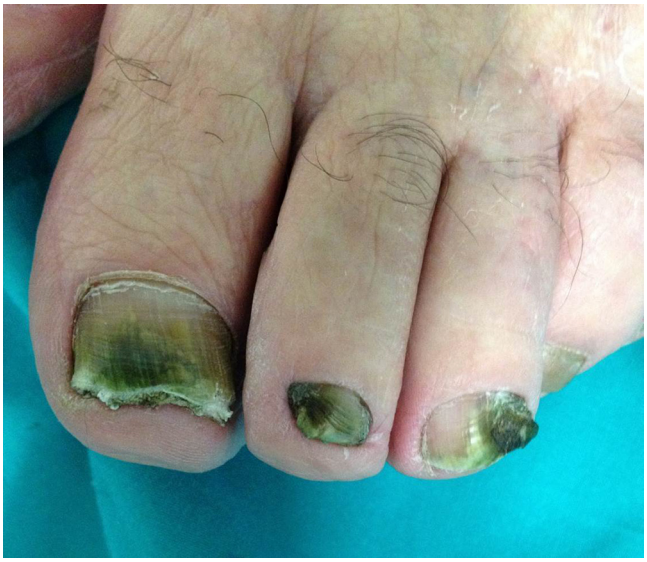

Figure 1. Brown–black pigmentation of the nail plates and subungual hyperkeratosis of the first three toes of the left foot.

The patient was treated with 40% urea cream and oral itraconazole. The latter was chosen because of his previous history of urticaria caused by terbinafine. Three months later, a mild improvement was observed. The patient was subsequently lost to follow-up.

3. Discussion

In the 1990s, it was observed that *T. mucoides* was sometimes responsible for white piedra.[5,6] Previously, white piedra was considered to be caused by Trichosporon beigelii. Subsequently, this species was divided into six distinct species: Trichosporon asahii, Trichosporon asteroides, Trichosporon cutaneum, Trichosporon inkin, *T. mucoides*, and Trichosporon ovoides.[5] *T. mucoides* is currently included in the clade of T. cutaneum. White piedra had not been described in tropical regions of Africa until a study carried out in Libreville (Gabon) showed that the incidence of this infection was rather high (18%) in a female population aged 15–60 years, with a predominance in young patients (15–44 years). Fifty-two Trichosporon strains were isolated from pubic hairs and inguinal folds. Three species were recognized: *T. mucoides* (25 strains), T. inkin (20 strains), and T. asahii (seven strains).[6,7] The identity of these strains was confirmed by means of an agglutination method performed with monospecific antisera. This method allowed the verification of the presence of antigens common to the genera Cryptococcus and *Trichosporon*.[8] One additional case of white piedra of the scalp caused by *T. mucoides* has been described in India.[9]

Figure 2. White creamy and smooth colonies of *Trichosporon mucoides*.

Trichosporon mucoides has also been responsible for severe cases of deep infections in premature newborns,[10,11] heart, kidney, and liver transplant recipients,[12,13] patients with acute lymphoblastic leukemia,[14] patients on peritoneal dialysis,[15] and patients with diabetes mellitus.[16] The main reported risk factors for *T. mucoides* invasive infections are antibiotic therapy, admission to an intensive care unit, and the presence of a central venous catheter.[11] According to Capoor et al.,[2] predisposing factors are genetic abnormalities, old age, low socioeconomic level, climatic conditions, hyperhydrosis, atherosclerosis, diabetes, immunodeficiency, and trauma.

No therapeutic guidelines exist for systemic *T. mucoides* infections. In a study published in 2004, all species were susceptible to amphotericin B.[11] Resistance to itraconazole and fluconazole was observed in 4% and 6% of cases, respectively.[11] The in vitro activity of amphotericin B, fluconazole, itraconazole, and voriconazole against 27 clinical isolates of Trichosporon spp (14 *T. mucoides* and 13 T. asahii), using the National Committee for Clinical Laboratory Standards (NCCLS) M27-A2 reference microdilution, Etest, and disk diffusion methods, was determined in a study published in 2005.[17] With the microdilution and Etest methods, Trichosporon sp demonstrated relatively high minimum inhibitory concentrations (MICs) for fluconazole (MIC_{90} 4 and 6 μg/ml, respectively) and relatively low MICs for voriconazole (MIC_{90} 0.125 and 0.125 μg/ml, respectively). MICs for amphotericin B determined on antibiotic medium 3 were lower (MIC_{90} 0.06 μg/ml) than those on Roswell Park Memorial Institute (RPMI) medium (MIC_{90} 1 μg/ml).[17]

In the same year, another study evaluated the in vitro activity of combinations of micafungin with amphotericin B or fluconazole, itraconazole, ravuconazole, and voriconazole against isolates of Trichosporon spp. Ten isolates of T. asahii and two of *T. mucoides* were tested. Drug interactions were assessed by the checkerboard technique using the NCCLS M27-A2 microdilution method. The fractional inhibitory concentration index (FICI) was used to classify drug interactions. Results were interpreted as follows: synergy, FICI $\leq$0.5; no interaction, FICI $>$0.5 and $\leq$4.0; or antagonism, FICI $>$4.0. Micafungin combined with amphotericin B showed the highest percentage of synergic interactions (78%), followed by micafungin/itraconazole and micafungin/ravuconazole (48% for each), and micafungin/fluconazole and micafungin/voriconazole (34% for each).[18]

The isolates from the patient reported by Capoor et al.[2] showed resistance to fluconazole (MIC 256 μg/ml), itraconazole (MIC 32 μg/ml), and voriconazole (MIC 32 μg/ml), and sensitivity to amphotericin B (MIC 0.32 μg/ml) and terbinafine (MIC 0.125 μg/ml) (the patient was treated with terbinafine). A heart and kidney transplant recipient was successfully treated with oral fluconazole;[12] a liver transplant recipient was successfully treated with posaconazole;[13] a boy with acute lymphoblastic leukemia was successfully treated with lipid complex amphotericin B and 5-fluorocytosine.[14]

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