Seborrheic dermatitis flare in a Dutch male due to commensal *Malassezia furfur* overgrowth

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This is a case of seborrheic dermatitis (SD) barbae from which *Malassezia furfur* (*M. furfur*) was isolated. The patient was a 57-year-old Dutch male, who was hospitalized for fever and weakness of extremities. He presented with symmetrical erythema with an abundance of greasy chaffy scales on his beard area. No reasons were detected for his fever following a routine search. *M. furfur* was identified through mycological examination, including direct microscopic examination, culture, Tween test, esculine splitting test and DNA sequencing, of samples from the skin lesions. The patient was treated with oral itraconazole capsules (200 mg, b.i.d. for 8 days, then 200 mg o.d. for 13 days), washing his scalp and face with 2% ketoconazole shampoo (once a day) and topical application of a cream containing 1% naftifine hydrochloride and 0.25% ketoconazole (b.i.d.). After treatment the fever subsided and the SD lesion gradually healed. *M. furfur* was not isolated again from skin scrapings and 7 days later therapy was terminated and no recurrence was noted after one week follow-up since the cessation of treatment.

**Keywords** seborrheic dermatitis, *Malassezia furfur*, itraconazole, ketoconazole

**Introduction**

*M. furfur* is a lipophilic yeast which is frequently found as a member of the human cutaneous flora. *M. furfur*, along with the other *Malassezia* spp. are well known agents of pityriasis versicolor, a superficial fungal infection of the skin. Seborrheic dermatitis (SD) presents with chronic erythematous and ill-defined greasy patches on the scalp, face and upper trunk. The etiology of the disease is unclear but *Malassezia* yeasts have been recently implicated in the pathogenesis of the disease [1,2].

**Case report**

A 57-year-old male from the Netherlands, who had been traveling in Southern Asia and China for almost 5 years, was hospitalized for bilateral weakness of his extremities and irregular fever (spiking over 38°C for 5 days). These symptoms were suspected to be the result of a brain embolism. Brain CT and MRI showed multiple, low-density lacunae in bilateral basal nuclei, thalami and frontal lobes denoting a brain embolism. Chest X-ray, abdominal ultrasound check, blood cultures, and serum HIV antibody were negative. Neutrophil count was 6.0 × 10⁹/l [normal range: 4.0 ~ 10.0 × 10⁹/l] (granulocytes: 88%, band neutrophils: 5%; lymphocytes: 5%), Cerebrospinal fluid (CSF) examination included culture and smear for bacteria (Gram stain) and fungi (India ink examination) and *Mycobacterium tuberculosis* antibody. All tests were negative. Since the reasons for fever were not clear, the patient was not given any antibiotics. A dermatology consultant was requested since he presented with bilateral erythema and desquamation that was distributed on his cheeks and submaxilla area. Although the erythema was present for 10 years, the patient did not experience any discomfort and thus he had ignored it. However, the erythema had become more severe within recent weeks, extending to the post aurums, temples and the hair line with increased numbers of greasy scales. The skin lesions became
aggravated with topical application of mometasone furoate cream after the first week of hospitalization.

On initial physical examination by a dermatologist, the patient showed symmetrical erythema with many greasy chaffy scales (Fig. 1a) on the bearded region (cheeks, mandible, neck, facial triangles and nasolabial sulcus) and forehead, hair line, temples and post aurums. Scale samples from the skin lesions were collected. Part of the samples were examined microscopically in 10% KOH and numerous oval or elongated yeast cells with broad-based budding were seen especially when they were stained with Methylthioninium chloride (Fig. 2a). The remaining samples were inoculated on a medium containing rapeseed oil (1% peptone, 4% glucose, 0.01% yeast extract, 1% agar, 0.25% glycerol monostearate, 1% Tween 80 and 2% rapeseed oil), which had been modified based on the reported of Faergemann [3] and incubated at 32°C. After 7 days incubation, we observed cream-colored, yeast-like colonies (Fig. 2b). The isolate was positive with Tween 20, Tween 40, Tween 60 and Tween 80 (Fig. 2c) and slightly positive in the esculine splitting test [4,5]. These results indicated Malassezia furfur.

To confirm the identification of M. furfur, DNA sequencing was carried out. Genomic DNA was extracted using the Yeast DNA kit (Omega bio-tek, USA) and amplification of the Intergenic transcribed spacer (ITS) 1 and 2 regions flanking the 5.8S region of the rDNA was performed by PCR employing the ITS1 (5'-TCC GTA GGT GAA CCT GCG G) and ITS4 (5'-TCC TCC GCT TAT TGA TAT GC) primers [6] provided by Shanghai Invitrogen Biotech Co. Ltd. The total volume of PCR system was 50 µl including 25 µl PCR pfuMix (dATP, dCTP, dGTP, dTTP and pfuDNA Taq polymerase; Beijing Tiangen Biotech Co. Ltd), 2 µl of each primer, 17 µl ddH2O and 4 µl DNA sample. DNA samples were denaturalized at 94°C for 5 min, followed by 30 cycles of 94°C for 45 sec, 55°C for 45 sec, and 72°C for 1 min and final extension at 72°C for 7 min. The amplified DNA was electrophoresed in 2% agarose gel, checked by Goldview staining (Beijing SBS Genetech Co. Ltd) and then sent to Invitrogen Life Technologies for DNA purification and bidirectional sequencing. The sequences were aligned by using Clustal X software [7] and has been deposited in the GenBank with the accession number EU513202. A Blast search showed 97.74% homology (755/757) to M. furfur CBS7982 (AB105150.1), which is a strain isolated in Europe. Since a clinical and mycological diagnosis of seborrheic dermatitis was made, treatment with mometasone furoate cream was stopped. The condition was treated with itraconazole capsules (Sporanox, XIAN-JANSSEN Pharmaceutical Ltd) orally (200 mg, b.i.d. for 8 days, then 200 mg o.d. for 13 days). Moreover, the patient was instructed to wash his face with 2% ketoconazole shampoo (Triatop, XIAN-JANSSEN Pharmaceutical Ltd) (o.d.) and to topically apply a cream containing 1% naftifine hydrochloride and 0.25% ketoconazole (CHONGQING HUAPONT PHARM. CO., Ltd)(b.i.d.). His temperature almost immediately returned to normal within one day of treatment and the erythema was lighter with less scaling after 7 days. Direct microscopy and culture were performed once a week for 3 weeks during therapy and one week after discontinuation of systemic and topical therapy. All examinations were negative.

Fig. 1 (a) Before treatment, (b) after treatment.
and no side effects were noticed with a total of 5.8 gram of itraconazole (Fig. 1b).

**Discussion**

Seborrheic dermatitis is a chronic inflammatory skin disease with scaled erythema. It has been demonstrated that the population density of *Malassezia* spp. is the highest on anatomic sites with the most abundance of sebaceous glands [2]. It is accepted that there are three interrelated factors in SD: *Malassezia* overgrowth, sebaceous glands over secretion, and abnormal host response to *Malassezia* yeasts on the skin [1,2]. The yeasts, having lipase activity [8], split the triglycerides in the sebum, and release free fatty acids that cause an irritant stimulation of the immune system [9] with resulting hyperproliferation of the epidermis, production of immature corneocytes that are dislodged as large clumps. In our patient ample UV exposure [10] in addition to the underlying condition, i.e., the cerebral embolism and the topical use of steroid cream could have been aggravating factors associated with the flare of SD.

*Malassezia* species that have been shown to be most closely associated with SD are *M. globosa* and *M. restricta*. However, some authors have also linked *M. furfur*, *M. sympodialis*, *M. obtusa*, and *M. slooffiae* [1]. Our data on dandruff, a mild form of SD, have shown the species composition recovered from 153 Chinese samples was *M. sympodialis* (33.33%), *M. globosa* (25.05%), *M. restricta* (15.47%), *M. furfur* (13.73%) and *M. obtuse* (12.42%) [11]. It is very interesting that this patient was European and his isolate seems to be genetically closer to another European isolate *M. furfur* CBS7982. Considering the long incubation period of SD and the sequencing result of the isolate, it is possible that the strain was part of the patient’s inherent skin flora, rather than being acquired in China. However, further research on deposited sequences and comparisons with sequencing of strains from Europe and East Asia is needed.

Itraconazole has been used to treat SD effectively and safely [12]. The case described herein shows that *M. furfur* is involved in SD because this patient had a large number of yeast cells in the scales. Various tests, e.g., Tween test, esculine splitting test and DNA sequencing confirmed the isolate as *M. furfur*. Additionally, the patient was cured with a combination of antifungal agents. Direct microscopic examination and culture after antifungal treatment were negative, which further implicates *M. furfur* as the etiologic agent of SD in this case.

It is difficult to demonstrate a relationship between the flare of SD and the fever, but the patient’s fever was unexpectedly alleviated through the use of itraconazole, without receiving any other antibiotics. This may indicate an undetected *Malassezia* fungemia [13] as blood and CSF cultures were negative for bacteria and neutrophil count was within normal limits. Unfortunately, appropriate lipid containing medium was not used for blood cultures and the causal association of *M. furfur* overgrowth, SD flare and fever can only be suggested.

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