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Microsporum audouinii tinea capitis in a Swiss school: assessment and management of patients and asymptomatic carriers

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We report three cases involving 7- to 8-year-old children from a Swiss school who had refractory tinea capitis due to an unusual strain of *Microsporum audouinii* which perforates hair *in vitro*. The patients showed no response to modern oral antifungal drugs like terbinafine and fluconazole. After switching to oral griseofulvin, two of the patients had a complete recovery, while the third was cured after the introduction of oral itraconazole. Given the high potential for contagion of this anthropophilic dermatophyte, all family members and three entire school classes were screened using the 'toothbrush technique'. Three family members and five class-mates were found to be asymptomatic carriers of *M. audouinii* and were consequently treated to avoid further transmission or reinfection of the treated patients. This is the first report of an outbreak of *M. audouinii* in Switzerland and underlines the importance of screening all contacts of patients with *M. audouinii* tinea capitis. Further, the effectiveness of griseofulvin in *Microsporum* tinea capitis has been corroborated, while newer antimycotic drugs like fluconazole or terbinafine failed.

Keywords *Microsporum audouinii*, tinea capitis, asymptomatic carriers, anthropophilic dermatophytes, griseofulvin

Introduction

Microsporum audouinii is an anthropophilic dermatophyte common in Africa. It typically causes tinea capitis and tinea corporis in children. While *Microsporum canis*, a zoophilic dermatophyte, is still the most common cause of tinea capitis in Europe, an increase in anthropophilic tinea capitis has been noted, mainly in urban areas [1]. The anthropophilic *Trichophyton tonsurans* is the most often reported etiologic agent in the UK, whereas *Trichophyton soudanense* and *M. audouinii* are most common in France. *M. audouinii* cases have also been reported in Italy [2], Spain [3] and Portugal [4]. These anthropophilic fungi are most prevalent in immigrant communities from Africa and Asia. They cause less inflammatory reactions and have an increased tendency to be associated with chronic disease as compared to infections due to *M. canis*. The latter may be the result of late detection due to the absence of subjective symptoms, even though kerion may occur.

Here we describe cases involving three children from the same after-school care facility who had tinea capitis due to an unusual strain of *M. audouinii*. Upon screening, eight asymptomatic carriers were found and members of this group and the patients were treated.

Case report

Patient 1

In May 2008, an 8-year-old boy of Afghan origin was referred to our clinic by his paediatrician because of a persistent (6 months) alopecic patch in the vertex area of the scalp with erythematous ground and fine scaling. He had been treated with oral terbinafine at 125 mg daily for 14 weeks in combination with topical ketoconazole, without clinical improvement. On the first visit to our clinic we

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collected samples for culture which yielded *M. audouinii*. We started a 12-week treatment with oral fluconazole at 35 mg (1.3 mg/kg) daily in combination with topical econazole. The patient failed to respond clinically and cultures inoculated with samples collected 7 and 11 weeks after initiation of treatment remained positive for *M. audouinii*. Fluconazole administration was then changed to pulse therapy with 200 mg (8 mg/kg) weekly for 8 weeks. Despite this treatment, further analyses conducted during and after therapy remained positive. In January 2009, treatment with oral griseofulvin was started (20 mg/kg once daily). This resulted in rapid clinical improvement and good tolerance, and was discontinued after 8 weeks as survey cultures were negative.

Patient 2

An 8-year-old Sri-Lankan boy was referred to us in March 2008 with the same clinical presentation as patient 1, except for a more pronounced scaling in the alopecic patch (Fig. 1). The lesion began in October 2007 and an oral (125 mg daily) and topical treatment with terbinafine were initiated in February 2008 by the paediatrician. Mycological cultures from patient samples yielded *M. audouinii* and led to a change of therapy from oral terbinafine to oral fluconazole (50 mg daily, i.e., 2.5 mg/kg), with topical terbinafine and salicylvaseline. After 10 weeks, fluconazole was discontinued because cultures for the fungus were negative and the patient had clinically improved, i.e., scaling and erythema had disappeared and hair regrowth had begun. Two months later, a clinical relapse was observed and testing again revealed the presence of *M. audouinii*. In September 2008, fluconazole was re-started using a higher dose of 120 mg daily (6 mg/kg), but no clinical or mycological improvements were observed over the subsequent 20 weeks of treatment. Oral griseofulvin (500 mg daily, i.e., 20 mg/kg) was started in February 2009 in combination with topical terbinafine and povidone iodine shampoo, which resulted in rapid clinical response and in negative mycological cultures after 8 weeks of treatment.

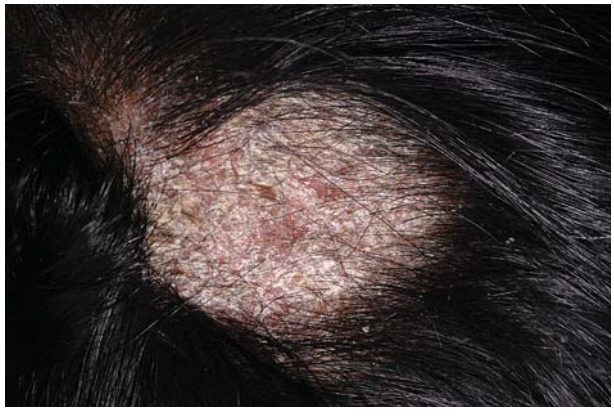

Fig. 1 Alopecic patch in the vertex area of the scalp with erythematous ground and pronounced scaling of an 8-year-old boy (patient 2).

Patient 3

A 7-year-old boy from an Israeli family presented with an isolated parietal alopecic area with very discrete, fine scaling which had begun in April 2008. Due to the failure of topical clotrimazole after 6 months of therapy, the patient was referred to our clinic. Culture of plucked hairs revealed the presence of *M. audouinii* and treatment with oral itraconazole was started (200 mg daily) in combination with a ciclopirox shampoo. The treatment was discontinued 12 weeks later after cultures were found to be negative.

Mycological analyses

Specimens included plucked hairs and skin scrapings from the affected area on the scalp. Direct microscopic examination was performed in a 5% SDS solution containing Congo red. Plucked hairs from patient 1 showed an ectothrix type of infection (Fig. 2) and hyphae were found in scales of patients 1 and 2. Hairs and scales were inoculated onto Sabouraud's dextrose agar with and without chloramphenicol and cycloheximide and incubated at room temperature. This resulted in the growth of flat, transparent, and spreading hyphomycete colonies that lacked pigmentation. Colonies subcultured to potato dextrose agar were grayish to skin colored. Upon microscopic examination pectinate hyphae and microconidia were observed after 7 days and macroconidia after 14 days. Macroconidia were long, slender and frequently constricted near the middle (Fig. 3). After 7 days, urease tests were weakly positive,

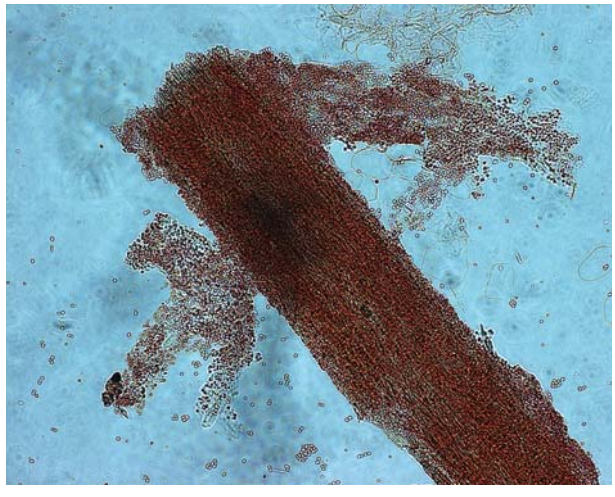

Fig. 2 Direct microscopic examination of hair from patient 1 in 5% SDS solution containing Congo red reveals masses of small spores around the hair shaft (Ectothrix).

whereas on bromcresol purple medium distinct clearing of casein was noted but no pH change was observed. Based on these findings, the isolates were presumptively identified as *M. audouinii*. For further confirmation, hair perforation tests with blonde pre-pubertal hairs and rice grain cultures were performed. Surprisingly, the strain was able to perforate hairs after 4 weeks and it grew and sporulated on rice grains. Therefore, the internal transcribed spacer (ITS) regions of the isolates of patient 1 and 2 were sequenced [5] and resulting sequences were compared to GenBank with a Blast search. The ITS sequences of the isolates were identical to each other and 99.9% identical (682/683 identities) to *M. audouinii* AJ000622 and 98.7% identical (678/687 identities) to *M. canis* GU291265, confirming the identification as *M. audouinii*. The sequence has been deposited in GenBank (accession number HM769946).

Epidemiological investigations

Due to the contagious potential of *M. audouinii*, family members of the first two index patients were carefully examined and screened for asymptomatic carriage. All three patients attended the same after-school care facility. The school's medical service performed a complete screening of all children attending the after-school care facility, as well as all the patients' class-mates. Screening was performed using the toothbrush method [6,7] by which different areas of the scalp including frontoparietal, temporoparietal, and occipital areas were vigorously brushed with a plastic toothbrush. The toothbrushes were streaked over Sabouraud's dextrose agar plates containing chloramphenicol and cycloheximide. The cultures were then incubated at room temperature for a maximum of 4 weeks. Upon clinical examination, family members of the patients were asymptomatic. However, samples from the father, mother and sister of patient 1 all yielded *M. audouinii* in culture, i.e., they were asymptomatic carriers. They were treated with the same regimen, i.e., oral griseofulvin for 8 weeks. Of a total of 95 class mates and children of the after-school care facility who were screened, five were found to be asymptomatic carriers. Of these five children; (i) all were boys, (ii) three children belonged to immigrant families from Africa, one to a Tamil family and one was a Swiss boy, (iii) four were class-mates of patient 2 (one of which was also in the same after-school care facility) and one was a class-mate of patient 3. Asymptomatic class mates were treated with topical ketoconazole (shampoo) once daily for 4 weeks. At this time, no further cases of *M. audouinii* tinea capitis have been reported from this school.

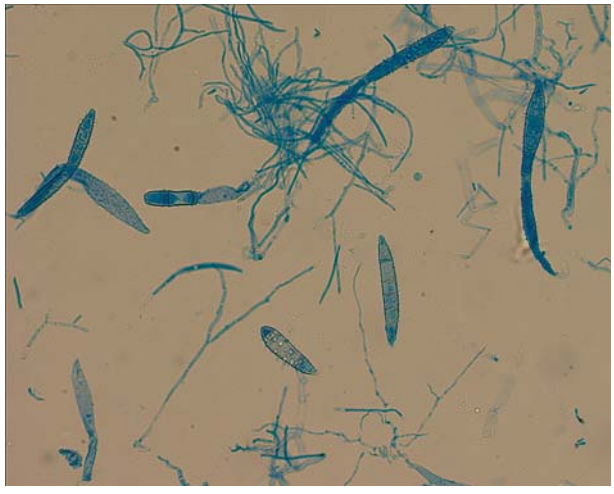

Fig. 3 Microscopic examination of a 14-day-old culture showing macroconidia which were long, slender and frequently constricted near the middle.

Discussion

The macroscopic, microscopic and physiological features of the strain we describe are compatible with *M. audouinii*. However, the positive hair perforation test (although only after 4 weeks) and the relatively good growth and sporulation on rice grains after 2 weeks, are inconsistent with this species. The sequence of the internal transcribed spacer (ITS) region provided unambiguous evidence that the strain was *M. audouinii*. We therefore believe that our isolate is an unusual strain of *M. audouinii* with the ability to perforate hairs *in vitro* and sporulate on rice grains. Recently, the first report concerning a hair perforation-positive strain of the fungus was published in a German case report [8].

While *M. audouinii* is most prevalent in Africa, a general increase of anthropophilic tinea capitis has been noted in Europe [1]. However, few outbreaks with *M. audouinii* have been described from the developed world in the last years. Viguie-Vallanet *et al*. reported in 1997 two outbreaks in France involving African children [19]. Weill *et al*. described in 1999 an epidemic in a French school involving 28 cases of children of African and European background [20]. Haedersdal *et al*. reported in 2003 an outbreak of tinea capitis in 12 children at a kindergarten in Denmark originating from Danish/African siblings [21]. McPherson *et al*. described an outbreak of tinea capitis in an English-language school in 2008 in Australia involving 23 children who were mostly migrants of African or Arab ethnicity. The infections of six of the children involved *M. audouinii*, with others caused by *T. soudanense* and *T. tonsurans* [22]. Interestingly, the three patients presented here were from families originating from South and Western Asia but it is not known where the infections originated.

Systemic therapy is required for treatment of tinea capitis because topical antifungals do not penetrate the hair follicle [9]. In our three patients, different systemic antimycotics were prescribed along with topical treatment. However, patients 1 and 2 were clinically and mycologically cured through the use of only griseofulvin. Patient 3 was successfully treated with oral itraconazole. Traditionally, griseofulvin has been the treatment of choice for tinea capitis [10] and it is licensed for this application in most countries, excluding Switzerland. There is evidence that newer antifungals including terbinafine, itraconazole and fluconazole may provide similar results as griseofulvin in the treatment of tinea capitis caused by *Trichophyton* species [10]. These antifungals may be preferred because shorter duration of treatment may improve adherence. While the role of fluconazole for *Microsporum* tinea capitis has not been fully elucidated, itraconazole proved to be effective against *Microsporum canis* [11,12] with a good safety profile even in the treatment of infants [13]. Unfortunately, efficacy of itraconazole against *M. audouinii* was not mentioned in these studies. Terbinafine is less effective against *Microsporum* species as compared to members of the genus *Trichophyton* [14] and in randomized trials it has been shown that there was a better response to griseofulvin than to terbinafine in patients with infections caused by *M. audouinii* [15] or *M. canis* [16]. Therefore, griseofulvin remains the treatment of choice for *Microsporum* tinea capitis [10]. The paediatric dosage often described is 10–25 mg/kg/day for 6–8 weeks [17]. Some patients with *Microsporum* infections may require longer courses of treatment depending on clinical and mycological findings, sometimes for as long as 12 weeks [18].

Anthropophilic dermatophytes have been associated with high rates of asymptomatic carriage [7]. Most cases have been observed in African, African-American, African-Caribbean, Anatolian, and Arab populations. The majority of reports observed that asymptomatic carriage is more common in boys than in girls [7]. This is consistent with our investigation in that of the five classmate carriers, three were boys belonging to African immigrant families, one was a Tamil boy and one a Swiss boy. There is some debate in the literature as to whether the spread of anthropophilic infections occurs primarily in schools or in households [7]. As all three patients of our study attended the same after-school care facility, we assume this was the place where transmission took place, with secondary spread to family members. Carriers can become symptomatic themselves. In a study following 19 carriers of *M. audouinii* [23], 21% became symptomatic, 42% had persistent carriage and 37% became culture-negative after 4 months. Based on other reports, Sogair and Hay [18] have estimated that approximately 10% of carriers become clinically apparent over a 6-month period and that carriers may act as vectors in the transmission. For these reasons, screening the social environment of index cases is important. If possible, all household members of an anthropophilic scalp ringworm patient should also be examined and screened with the hairbrush or toothbrush methods. Additionally, parents should be asked about other possibly infected class-mates. It is proposed that students in the entire school be screened if more than two class-mates are infected [18]. There is no agreement on whether carriers should be treated with systemic or topical or both types of antifungals or if any form of treatment is required [7]. However, as carriers can become symptomatic (see above), it seems reasonable to treat them. In our experience, topical ketoconazole for class-mate carriers efficiently prevented symptomatic infections.

The case presented here exemplifies the high epidemic potential of *M. audouinii*, reminding us of the importance of social environment screening and treatment of asymptomatic carriers. The effectiveness of griseofulvin in *Microsporum* tinea capitis has been corroborated, while newer antimycotic drugs like fluconazole or terbinafine failed. For the mycologist, it is important to note that *M. audouinii* may have the ability to perforate hair *in vitro* and form conidia on rice grains.

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