Possible rabbit breeders’ *Trichophyton mentagrophytes* infection characterized by Majocchi’s granuloma in immunocompetent host: Case report

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**ARTICLE INFO**

**Keywords:**
- Child
- Rabbits
- Trichophyton
- Granuloma
- Anti-inflammatory agents

**ABSTRACT**

We report on a family of three in a rabbit farm, especially children with Majocchi granuloma as the main clinical feature of cross-infection of *Trichophyton mentagrophytes*, provides experience in reducing the rate of clinical misdiagnosis. Based on the pathological features of Majocchi’s granuloma, taking into account that severe inflammatory reactions are also responsible for the damage of the body. In Majocchi’s granuloma treatment strategy, we recommend the use of anti-inflammatory Chinese medicines that have a hormonal effect and have no side effects.

1. Introduction

*Trichophyton mentagrophytes* is considered to be a zoophilic fungus with a worldwide distribution and a wide range of animal hosts including mice, guinea-pigs, kangaroos, cats, horses, sheep and rabbits [1]. According to this most recently suggested classification and new taxonomy of dermatophytes, the former *T. mentagrophytes-complex* is differentiated into *T. mentagrophytes* (zoophilic strains) and *T. interdigitale* (anthropophilic strains) [2]. From a clinical point of view, however, it should pointed out that *T. interdigitale* is generally isolated from non-inflammatory tinea pedis and tinea unguium, while zoophilic *T. mentagrophytes* is isolated from other variants of tinea (tinea corporis, tinea cruris, tinea faciei and tinea capitis), which lead to mild or inflammatory infections [3]. Of the numerous cases recently reported from outbreaks in South Asia under the name *T. mentagrophytes*, an animal source of infection was mostly not identified [4,5]. Re-evaluation of the taxonomy and ecology of both dermatophytes is urgent. One of the rare infection types ascribed to *T. mentagrophytes* involves hair follicles and is known as Majocchi’s granuloma (MG). With general dermatophyte etiology, this disorder is mainly seen in patients with low immune function or patients treated with topical glucocorticoids [1,6]. Clinical manifestations of MG are diverse. In addition to subcutaneous nodules, perifollicular and papular involvement may be observed. In the absence of known risk factors for fungal infections, MG may be difficult to recognize, and delayed diagnosis may result in painful scarring and hair loss [6–8].

We report on a family managing a rabbit farm, with familial infection by a novel genotype of *T. mentagrophytes* that possibly originated from symptomatic animals. The child developed Majocchi’s granuloma as the main clinical feature in addition to cutaneous lesions, while infections by the same genotype in the parents were mild and superficial.

2. Case

A 7-year-old male patient presented (day 0) with a 4-month history of pruritic eruptions on both head and limbs. At onset of the infection, patient had developed a coin-sized, ring-shaped erythema on the left calf (day -112), accompanied by itching and scaling, and a rash with similar appearance on the head, back and right elbow (day -91). Three weeks before presentation (day -21) his parents used dexamethasone acetate cream topically twice daily on the kid’s skin lesions to relieve itching without doctor’s advice; symptoms did not improve significantly, while the area with head lesions including papulopustules, pustules and abscesses were further enlarged.

The child (day 0) was in general good health; consequently, no special physical examination was judged necessary. He had received traditional monthly shaving of the head. Physical examination of the
head revealed infiltrating erythema with papulopustules, pustules, abscesses, hair loss, some bleeding and yellow crust formation on the infiltrating erythema (Fig. 1A). Multiple erythematous scaly papules and plaques were seen on the right wrist, left forearm and left lower leg (Fig. 1B and C).

The child’s parents managed a rabbit farm, where some of the animals showed lesions of variable size (Fig. 2A), sometimes with loss of fur. Both parents presented with skin lesions similar to those on the child’s left leg six months ago (day -180). The father had a patch of about 2 × 1.5 cm size on the left cheek and of 2 × 2 cm on the right rear arm; the latter was slightly elevated and covered with scales (Fig. 2B). The mother also had a patch about 1 × 1.5 cm on the right arm (Fig. 2C). These lesions remained untreated and had a tendency to spontaneous healing.

Direct examination (KOH 10%) showed disarticulating hyphal elements (Fig. 3A) in samples from lesions on the child’s scalp and from scales of the left lower leg. Cultures from lesions of the child’s head and arm, and from parent’s lesions were performed on Sabouraud glucose agars incubated for two weeks at 28 °C. From all samples identical colonies were obtained that were powdery, cream-coloured, approximately star-shaped, with an ochraceous reverse (Fig. 3B). Macroconidia were sparse, 3–8-celled, smooth- and thin-walled, clavate to cigar-shaped. Microconidia were spherical, sessile, arranged in dense, grape-like clusters or alongside the hyphae. Spiral hyphae were present (Fig. 3C).

Production of urease was determined in Christensen’s urea broth (Oxoid) after incubation for 7 d at 30 °C; a positive response with a color change from yellow to pale pink within 48 h and purple red in 4 d was obtained in all isolates. On purple-milk solids-glucose agar (BCP-MS-G) medium, strains showed profuse growth with a violet colour reaction. Optimal growth (34 mm/7d) was observed at 33 °C, with limited growth (14 mm/7d) at 40 °C and no growth at 45 °C. Genomic
DNA was extracted from cultures grown on MEA following a cetyltrimethyl ammonium bromide protocol as described earlier [9]. PCR amplification and sequencing of the rDNA Internal Transcribed Spacer region (ITS) was done with primers ITS5 and ITS4 [9]. The three isolated strains (head child JYP18-3, arm mother JYP18-24, arm father JYP18-25) had identical sequences in a subclade close to the type strain of Trichophyton mentagrophytes strain IHEM 4268NT. On the basis of these characteristics, the isolates were identified as Trichophyton mentagrophytes, representing an as yet unreported genotype.

Histological examination of a punch biopsy taken from the child's head lesion revealed agranulomatous infiltration of neutrophils, lymphocytes, histiocytes and giant cells was seen in the perifollicular area (Fig. 4A and B), numerous arthrospores and hyphae within the hair follicles, which stained positively with D-periodic acid-Schiff (D-PAS) (Fig. 4C and D). Judging from clinical, pathogenic and histopathological examinations, Majocchi's granulomatosis caused by Trichophyton mentagrophytes was diagnosed in the head of child's skin lesions. Skin lesions on the child's limbs and on the parent's arms and cheek were diagnosed as tinea corporis by the same fungus.

Treatment regimen of the child was initiated on day 4 and consisted of oral itraconazole at a dose of 100 mg per day (5 mg kg⁻¹ p.o. every 24 h) for 12 weeks. To prevent anaphylaxis, oral glycyrrhizin tablets (100 mg/d p.o. every 12 h) for 4 weeks, and daily topical 1% butenafine hydrochloride cream were additionally administered for the large erythematous lesions on head and arm with pustules. Parents only treated with butenafine hydrochloride cream without oral itraconazole. After about two weeks (day 16) a significant improvement of all skin lesions was seen in all family members. Twelve weeks later (day 90), the skin lesions of the child showed complete regression and healing, but several superficial, red, atrophic scars remained with new hair growth (Fig. 1D, E, F). No relapse occurred after six months (day 184) of follow-up, the entire family having complete resolution of the condition.

Antifungal susceptibility testing was performed by the Clinical and Laboratory Standards Institute (CLSI) broth microdilution and demonstrated that the fungus had low minimum inhibitory concentrations (MICs) of 0.0315 μg/ml against terbinafine and 0.125 μg/ml against itraconazole; other drugs demonstrated low MICs as well, i.e. amphotericin B (0.25 μg/ml), voriconazole (0.0625 μg/ml), and posaconazole (0.0625 μg/ml).

### 3. Discussion

Trichophyton mentagrophytes is known as a member of a series of closely related species that comprising some of the major pathogens causing dermatophytosis [1]. Most commonly identified are a supposedly zoophilic species, T. mentagrophytes and an anthropophilic species, T. interdigitale [10]. The ecological concept of zoo-versus anthropophil has been challenged by epidemics on humans where no animal source could be detected [11]. Microscopically, the typical characteristic of zoophilic strains T. mentagrophytes is the presence of grape-like clusters of microconidia and distinctive spiral hyphae. Although numerous anthropophilic strains of T. interdigitale show absence of sporulation (‘var. nodulare’), colonies of this species are very similar to T. mentagrophytes in being fuzzy to cotton-hairy, on average producing fewer conidia and spiral hyphae [12]. From a perspective of pathogenicity, zoophilic strains are more likely to cause more severe inflammation [3].

Our diagnosis of Majocchi's granuloma in the head lesions of our patient was based on (i) histopathological proof of perifollicular granulomatous inflammation; (ii) lesions resulting from infections by dermatophytes; and (iii) dermatophytes being present not only in the superficial layer but also in the dermis [7,8]. The child had a history of contact with rabbits at the farm, and some rabbits showed signs of hair loss. Unfortunately, we were unable to isolate the same pathogen from the rabbit’s skin lesions due to massive growth of contaminants, and we have no direct evidence to prove a rabbit transmission route.

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**Fig. 3.** Direct examination showed disarticulating hyphal elements (A); colony were powdery, cream-coloured, approximately star-shaped, with an ochraceous reverse (B); Microconidia were spherical, sessile, arranged in dense, grape-like clusters or alongside the hyphae. Spiral hyphae were present (C), Scale bar = 10μm.

**Fig. 4.** Histological examination from the child's head lesion revealed agranulomatous infiltration of neutrophils, lymphocytes, histiocytes and giant cells was seen in the perifollicular area (A, B); Numerous arthrospores and hyphae within the hair follicles, which stained positively with D-periodic acid-Schiff (D-PAS) (C, D).
contrast, both parents harboured the same genotype in their skin lesions. Consequently, human-to-human familial transmission without animal interference is an alternative explanation of our observations.

Notably, the child’s Majocchi’s granuloma on the head, appearing despite the host’s intact immunity, differed significantly from cutaneous lesions in the same patients and in his parents. Possible reasons are: (1) break of the skin barrier due to monthly shaving, while the child’s ability of motortic self-control is poor, leading to abrasions [13]. In addition (2), repeatedly scratch due to itchy skin, which is thinner than adult skin, may cause additional damage and local inflammation. Trauma may induce follicular disruption with passive invasion of dermatophytes into the dermis [14]. (3) Topical corticosteroid ointment provides a portal of entry for dermatophytes into hair follicles [13] and deeper into the dermis [15]. (4) The sebaceous glands of the child are not fully mature, and the less secretion of unsaturated lipids may provide an opportunity for invasion of pathogenic fungi. (5) Thermophility of the clinical isolate is an additional virulence factor for invasion deep into the dermis. The strain grows well at 40 °C, with 33 °C as a maximum.

Treatment recommendations for MG are not consistent, application periods ranging from 3 weeks to 1 year [16]. Terbinafine is mostly preferred, but in this case we administered itraconazole capsules orally for 12 weeks, resulting in healing without recurrence during one-year follow-up. Additionally, we used the Chinese traditional medicine glycyrrhizin to strengthen the anti-inflammatory response, which not only protects the liver, but also delays the metabolism of glucocorticoids in the body [9]. Based on the pathological features of Majocchi’s granuloma, infiltration of lymphocytes, neutrophils and histiocytes in the superficial dermal layer surrounding the hair follicle, in addition to the virulence of the pathogen, leads to severe inflammatory reactions and tissue damage. As an adjuvant therapy in MG, we therefore applied anti-inflammatory Chinese medicine known to have a slight hormonal effect and has not been described to have side effects.

Funding source

None.

Competing Interests

None.

Guardians

Written informed consent was obtained from the patient or legal guardian(s) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgements

The authors thank Ping Zhan from Jiangxi Provincial People’s Hospital, Nangchang, China, for her important contributions to the antifungal susceptibility testing.

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