Majocchi’s granuloma in a liver transplant recipient caused by a *Trichophyton* spp., phenotypically consistent with *Trichophyton rubrum* var. *raubitschekii*

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The authors report a case of Majocchi’s granuloma and onychomycosis in a liver transplant recipient caused by a *Trichophyton* spp., phenotypically consistent with *Trichophyton rubrum* var. *raubitschekii*. A 48-year-old female patient who had undergone liver transplantation nine months earlier, presented with red papules and nodular lesions on her back, buttock and thigh of two months duration. She also had onychomycosis of toe nails for a few years, which worsened post transplant. Two fungal isolates were derived from her infected toe nails and nodular tissue. Physical, pathological and mycological examination, including KOH preparation, fungal culture and DNA sequencing of the internal transcribed spacer (ITS) of rRNA were performed. The clinical diagnosis was Majocchi’s granuloma and onychomycosis caused by the *Trichophyton rubrum* var. *raubitschekii*. This is the first case report of this organism from China.

Keywords *Trichophyton rubrum* var. *raubitschekii*, tinea, granuloma, Majocchi

**Introduction**

Majocchi’s granuloma (nodular granulomatous perifolliculitis) is described as a dermal and subcutaneous tissue infection caused by dermatophytes which usually limited to the superficial epidermis. The most common cause is *T. rubrum* [1].

While *Trichophyton raubitschekii* was previously described as a species [2], it is currently recognized as a variant of *T. rubrum* (*T. rubrum* var. *raubitschekii*) [3]. This organism differs from the typical *T. rubrum* in epidemiology, morphology and physiology. It has been considered to be a rare dermatophyte, found worldwide, and causing thus far approximately 50 cases of human infections [4]. The distribution of skin lesions it causes differs from *T. rubrum* in that it is primarily associated with tinea corporis and tinea cruris, and rarely causes tinea pedis and tinea unguium.

In the present study, we report on a case of Majocchi’s granuloma and onychomycosis caused by a *Trichophyton* spp., phenotypically consistent with *Trichophyton rubrum* var. *raubitschekii*. This case is also unusual in that the etiologic agent was isolated from a deep cutaneous granuloma.

**Case report**

A 48-year-old female office worker, born and living in Beijing all her life, presented to the outpatient department of the China-Japan Friendship Hospital, Beijing, China, in May 2007. She had received a liver transplant for primary biliary cirrhosis nine months earlier, and received since her operation combined immunosuppressive treatment with tacrolimus 8 mg/d and prednisolone 10 mg/d. Two months prior to admission, she developed few red papules and itchy nodular lesions on her back, buttock and thigh. The nodules got smaller with topical terbinafine treatment, but soon relapsed. She had developed onychomycosis of the toe nails a few years previously, which worsened...
after the transplant. Again, two months prior to examination she had developed tinea cruris which visually subsided with topical terbinafine therapy.

On physical examination, the patient was in good condition. She had a few erythematous papules and nodules on the left side of the back, buttock and thigh (Fig. 1a). Nine toenails were impaired in the distal areas with some discolouration of the nail plates, dystrophy and accumulation of subungual hyperkeratosis debris. Lymph nodes were not enlarged. A complete blood count revealed: WBC, 2.92 × 10^9/l; platelet, 90 × 10^9/l; and all other values inclusive of cardiopulmonary, liver and renal problems, as well as T-cell status were within normal range.

Excision of a nodular lesion for pathological examination and fungal culture, together with KOH preparation of subungual debris and scrapings from the surface of nodules were performed.

Histopathology of tissue biopsy revealed hyperkeratosis and acanthosis in the epidermis, along with epithelioid cell granuloma formation in dermis, with diffuse inflammatory cells infiltration consisting of lymphocytes, plasma cells, histiocytes and giant cells. Follicular disruption was present with neutrophilic microabscesses. PAS stains demonstrated fungal elements within the stratum corneum, granuloma and polynuclear giant cells (Fig. 1b).

Microscopic examination with 20% KOH demonstrated the presence of septate, hyaline, fungal hyphae.

From these data the diagnosis was Majocchi’s granuloma and onychomycosis.

Because the patient had been receiving immuno-suppressive treatment for her transplant, we were concerned about using therapy for systemic mycoses. Thus we elected to use topical terbinafine for the papules, and noted gradual improvement. Nodular lesions were all excised and no relapse was seen at 1-year follow up.

**Mycological study**

Two fungal isolates from nails and tissue were studied in the Department of Dermatology/Research Center for Medical Mycology, at the Peking University First Hospital, Beijing, China.

Material was cultured on Sabouraud glucose agar containing cycloheximide (SAB) and potato glucose agar (PDA) and incubated for 20 days at 27°C. Colonies were 33–38 mm diameter on SAB agar and the surfaces were fine, velvety to granular in appearance with radial folds and elevated centers. The reverse of the colony was a yellow-brown (Fig. 2a, b). On PDA at 27°C, the isolates formed granular colonies with a central folded elevation, and a faint red color on the surface and a dark-brown color on the reverse.

Slide culture on SAB revealed abundant macroconidia and microconidia. The macroconidia were long, cylindrical, cigar-shaped, 43–52 μm in length by 4.8–6.2 μm in width. A few longer macroconidia (75 μm) were seen. The microconidia varied in shape from pear-shaped to rounded or club-shaped, 4.6–6.2 μm long by 3.0–4.6 μm wide (Fig. 2c, d, & 3).

Growth of both isolates on bromocresol purple casein glucose agar (BCPCG) medium was restricted and failed to produce alkaline substances.
Both stains showed restricted growth on SAB augmented with 3% NaCl.

A urease reaction was performed on Christensen's urea agar, with both isolates positive after 7 days incubation. The *in vitro* hair perforation test was negative.

**DNA sequencing in internal transcribed spacer (ITS) of rRNA**

DNA sequencing was performed in the Department of Dermatology/Research Center for Medical Mycology, at...

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**Fig. 2** (a) Colony on SAB at 27°C after 20 days incubation. (b) Reverse of the colony. (c,d) On slide culture, numerous microconidia and macroconidia of *Trichophyton rubrum* var. *raubitschekii*.

**Fig. 3** On slide culture, numerous microconidia and macroconidia of *Trichophyton rubrum* var. *raubitschekii*. 
the Peking University First Hospital, Beijing, China. Fungal DNA was extracted from the two isolates recovered from the tissue and toe nails, respectively. A segment of ribosomal DNA (rRNA) was amplified by PCR using primers BMB-CR (5'-GTACACACCG CCCGTCG-3') and ITS4 (5'-TCCTCCGCTATTGA TATGC-3'). Amplification was performed in 25 μL containing 50 mM KCl, 10 mM Tris-HCL (pH 8.3), 1.5 mM MgCl2, 100 μM each dNTP, 0.4 μM each primer, 50ng of genomic DNA and 1U of Taq DNA polymerase. The amplification was done at 95°C for 5 min, followed by 30 cycles of 95°C for 30 sec, 58°C for 30 sec, and 72°C for 1min, with a final extension at 72°C for 10 min.

Direct sequencing of the PCR products was performed. The sequences were aligned with those in GenBank by BLAST analysis, and the sequences can be found in GenBank (Tissue- Bankit1112715, Nails-Bankit1116917). The DNA sequencing of both strains displayed 100% identities to that of *T. rubrum* (ATCC 28188) and *T. raubitschekii* (ATCC 42631).

The morphological pattern combined with physiological test and analyses of the DNA sequencing confirmed that these two isolates were *T. rubrum var. raubitschekii*.

**Discussion**

The most common dermatophyte causing Majocchi’s granuloma is *T. rubrum*, but *T. mentagrophytes*, *T. violaceum*, *Microsporum gypseum*, *M. audouinii* or *M. canis* may also be the causative agents [1]. The agents gain entrance by physical trauma that may lead either directly or indirectly to disruption of hair follicles and passive introduction of the fungal elements. These with keratinous material forced into the dermis, which may provide a substrate for survival of the organism [5]. There are two types in Majocchi’s granuloma, a perifolliculitis type secondary to trauma and a subcutaneous nodular type in immunosuppressed hosts [6]. The skin lesions of the latter type are seen as purplish infiltrates of neutrophils. Fungal hyphae can be seen in the stratum corneum [7]. The clinical and histopathological characteristics of the patient described in this report conform to this type. Majocchi’s granuloma may occur in healthy individuals with chronic dermatophytosis and in immunodeficient individuals who may develop systemic pancytopenia, including those receiving transplant and immunosuppressive treatment. If the patient presents with a chronic dermatophytosis of the skin, the individual may be at increased risk of dermal invasion by dermatophytes. With this patient, further investigation by molecular typing on the relationship between the deep infection and superficial dermatophytosis demonstrated the two strains isolated from the deep and superficial areas were identical and of the same origin (data not shown).

Kane et al. in 1981 [2] reported on a new anthropophilic dermatophyte with close affinities to *T. rubrum*. They named it *T. raubitschekii* which had some distinct features differentiating it from a typical *T. rubrum*. These characteristics included velvety or granular colony texture, brown pigment, abundant micro- and macro-conidia, positive urease reaction, as well as the distribution of the skin lesions. Recent molecular studies including the sequence analysis of internal transcribed spacer(ITS) of rRNA and other key molecular markers, have lead mycologists to consider the fungus to be a genotype of *T. rubrum*. (Notes: it should be a phenotype variety of *T. rubrum*, but the genetic homogeneity has made mycologists consider it to be a genotype of *T. rubrum*).

Epidemiological studies revealed that most of the patients with *T. rubrum var. raubitschekii* infection immigrated from or resided in subtropical and tropical areas such as south or east Asian including Hong Kong, Vietnam. Africa, North America [3,10,11]. In addition, the distribution of infections it caused were primarily tinea corporis and tinea cruris, rarely tinea unguium. This dermatophyte has not been previously reported from a native Chinese resident.

Though Majocchi’s granuloma associated with this fungus has not been previously reported anywhere, it does not necessarily mean that this organism has not been associated with this disease. This could be due to the fact the identity of the causative agents is carried to the species rather than the variety levels.

*T. rubrum var. raubitschekii* has been reviewed as the cause of tinea found in seven German patients [3]. Because of unusual aspects of the isolates, the author emphasized the necessity to collect further information about infections caused by this dermatophyte in different countries in order to track its future spread and correlate it with features that may relate to pathogenicity. In our study, morphological and physiological tests demonstrated unique features, e.g., numerous *T. rubrum*-like macroconidia and microconidia especially rounded microconidia that are rarely seen in *T. rubrum* [11]. These combined with the DNA sequencing analysis of the internal transcribed spacer(ITS) of rRNA, demonstrated these two strains were consistent with *T. raubitschekii* [11]. Combined with the clinical appearance, laboratory data and pathological findings, the diagnosis was
confirmed as a Majocchi’s granuloma caused by *T. rubrum* var. *raubitschekii*, which is the first case reported in China.

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References


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