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Chromoblastomycosis due to *Fonsecaea monophora* misdiagnosed as sporotrichosis and cutaneous tuberculosis in a pulmonary tuberculosis patient

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ABSTRACT

Chromoblastomycosis is caused by dematiaceous fungi. It develops after inoculation of the organism into the skin. We report a case of chromoblastomycosis in a pulmonary tuberculosis patient without known history of trauma. The lesions were initially diagnosed as sporotrichosis and skin tuberculosis. Histopathology of scales and skin biopsy specimen revealed sclerotic bodies, the hallmark of *chromoblastomycosis*. The causative organism was identified as *Fonsecaea monophora* by rDNA ITS sequencing. The lesions recovered markedly after two month treatment with oral terbinafine 250 mg daily according to drug sensitive test *in vitro* in combination with local thermotherapy

1. Introduction

Chromoblastomycosis is a chronic subcutaneous fungal infection in immunocompetent individuals, clinically characterized by verrucous skin eruptions, most commonly on lower extremities [1]. Among factors affecting clinical outcome, etiological agents have an important position. To date, several species have been proven as a causative agent of the disease, of which *Fonsecaea pedrosoi, F. monophora, Fonsecaea nubica, Cladophialophora carrionii, Phialophora verrucosa* and *Rhinocladiella aquaspersa* are common agents. Several *Exophiala* species (*Exophiala jeanselmei, Exophiala spinifera* and *Exophiala dermatitidis)* have been confirmed as occasional agents of the disease [2]. A history of mechanical trauma or injury to the site of infection marks the prevalent portal of entry.

In southern China, *Fonsecaea pedrosoi* and *F. monophora* are main causative agents causing chromoblastomycosis, and patients generally are immunocompetent [3]. Here, we present a case caused by *F. monophora* in a pulmonary tuberculosis patient without known history of trauma. The agent was isolated from skin scrapings and identified by phenotypic and molecular markers. The patient was managed successfully with oral terbinafine in combination with topical thermotherapy.

2. Case

A 63-year-old male farmer from Jiangxi Province, southern China presented with asymptomatic verrucous plaques covered with scales on the back side of right hand and a small erythematous was on right forearm on 3 January 2016 **(at day 0)**. The lesion had started as an asymptomatic, red papule on the back of his hand, and slowly enlarged over a period of 10 years. Concomitantly, a similar maculopapule appeared on his left forearm. A history of trauma or inoculation was not recalled. Patient was diagnosed with pulmonary tuberculosis at the beginning of the skin infection in a local hospital **at day-10 years**. He was given with intravenous injection levofloxacin at 0.4 g per day plus oral rifampicin at 0.6 g per day for ten months. The pulmonary tuberculosis healed completely. However, there was no improvement in skin lesion, which recovered slightly in summer and enlarged in winter.

One year ago **(at day-1 years)**, the patient's lesion was diagnosed as sporotrichosis in a local hospital; however, no response was achieved to a 2-month routine course of potassium iodide treatment. Then, because of a suspicion of cutaneous tuberculosis, treatment with intravenous injection of levofloxacin at 0.4 g per

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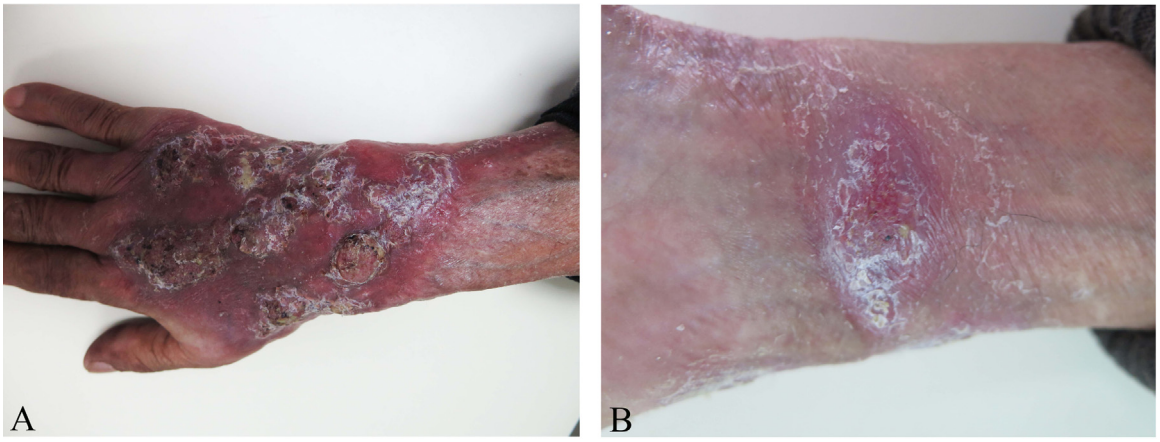

Fig. 1. Lesions caused by *Fonsecaea monophora* on the patient's right wrist and the back side of right hand, even after treatment with 10% potassium iodide solution for 2 months.

day plus oral rifampicin at 0.6 g per day was resumed for one month (**during day-10 months to day-8 months**). However, there was no improvement of the lesion.

Physical examination revealed purple, verrucous plaques covered with scales on the back of his right hand. A small (2 × 2 cm) erythematous was seen on right forearm **(at day 0)** (Fig. 1A and B). Results of routine hematological examination and urine analysis were within normal limits. Serological tests for HIV and anti-nuclear antibodies (e.g., anti-dsDNA antibody and anti-ssDNA antibody) were negative and chest radiography was unremarkable. Histopathology with haematoxylin and eosin staining of the epidermis showed irregular acanthosis, and a granulomatous response with histiocytes, plasma cells, polymorphonuclear cells and giant cells including muriform cells in the dermis (Fig. 2). These results led to a clinical diagnosis of chromoblastomycosis. Direct examination of 10% potassium hydroxide wet mounts from the lesion debris revealed brown muriform cells (Fig. 3A) confirming the clinical diagnosis.

Mycological culture was performed **(at day 0)**. Portions of both skin biopsies and skin debris were inoculated onto culture media attempting to recover the etiologic agent. Primary isolation of the fungus was performed on agar slants of Sabouraud's glucose agar (SGA) containing chloramphenicol (CMP, 0.125 g/l) and incubated at 25 °C and 37 °C for two weeks. Colonies (OA) were restricted, slightly heaped, powdery to velvety or hairy, olivaceous black; colony reverse olivaceous black. The strain was tolerant to cycloheximide (CHX) and grew well at 25 °C and 37 °C on CHX-containing SGA. Microscopically, conidiophores were suberect, olivaceous brown, apically densely branched. Conidiogenous cells were in dense clusters, with broad, flat, pale pigmented scars. Conidia were barrel-shaped, clustered, often remaining attached, smooth-walled, brown, or falling off as short branchlets. Phialides were occasionally produced (Fig. 3C). The fungus was identified as a *Fonsecaea* species based on these morphological characteristics.

The isolated agent was reconfirmed by sequencing of ITS 1 and ITS 4 region of rDNA and compared with sequences deposited in GenBank by Blast program and to an edited research database on black fungi maintained at CBS. Based on these analyses, the fungus was identified as *Fonsecaea monophora*. The isolated agent was deposited in the Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College in Nanjing, Jiangsu, under accession number *CMCCf* 2160004.

At day +10, the *in vitro* susceptibility of the strain to eight antifungal agents was determined using the microdilution method in accordance with the guidelines of the Clinical and Laboratory Standards Institute (CLSI) M38A [4]. The minimum inhibitory concentrations (MICs) were defined as the lowest concentration at which no growth occurred which led to the following results: itraconazole, 0.06 μg/ml; ketoconazole, 0.5 μg/ml; fluconazole, 16 μg/ml; miconazole, 2 μg/ml; voriconazole, 0.06 μg/ml; anidulafungin, > 4 μg/ml; amphotericin B, 16 μg/ml; terbinafine, 0.06 μg/ml.

The patient received empirical treatment with oral itraconazole 200 mg and terbinafine 250 mg daily for 2 weeks **(during day**

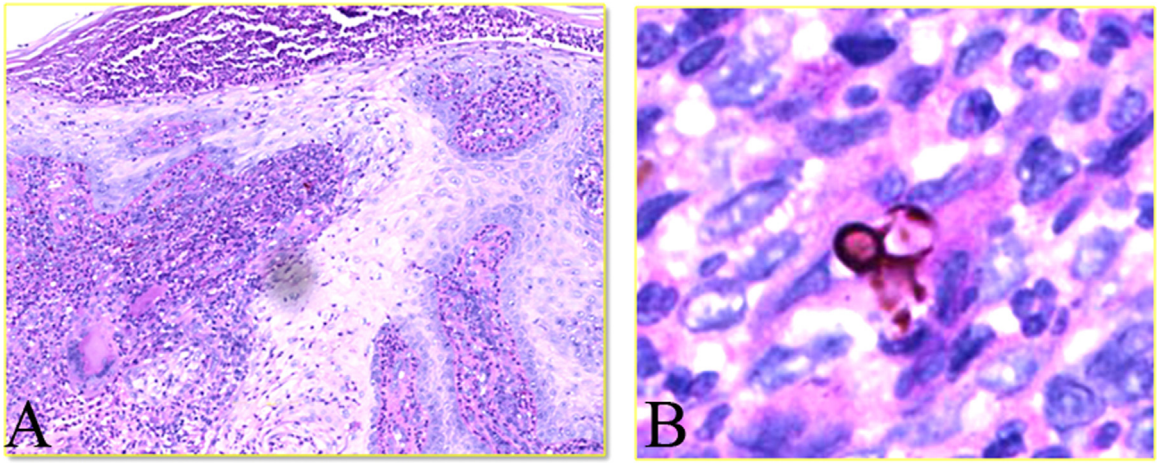

Fig. 2. Chronic granulomatous inflammation: epidermis with irregular acanthosis; dermis consisting of lymphocytes, plasma cells, neutrophils, eosinophils, macrophages, and multinucleated giant cells. Some giant cells containing muriform bodies (periodic acid–Schiff stain; original magnification, × 400).