CASE REPORT

CHROMOBLASTOMYCOSIS MASQUERADING AS DERMATOPHYTOSIS, WITH THE DESCRIPTION OF A NEW OPPORTUNISTIC SPECIES

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Abstract. An unusual case of chromoblastomycosis is reported, it resembled dermatophytosis, tinea faciei due to the presence of a well-demarcated scaly erythematous patch on the face. The patient was a 63-year-old farmer from central Thailand, who had the skin lesion for 10 years. Mycological and histopathological investigations of scales and skin biopsy specimen revealed a granulomatous infiltrate with sclerotic bodies, the hallmark of chromoblastomycosis. The infection showed only localized superficial expansion with a scaly patch suggesting a new clinical type of the disease. The causative organism was identified by DNA sequencing as *Rhinocladiella phaeophora*. *R.phaeophora* originally was a saprophytic dematiaceous fungus recovered from maize field soil from Colombia. The case was unusual in its clinical presentation and this is the first case of chromoblastomycosis reported to be caused by a new opportunistic species of the genus *Rhinocladiella*. The disease was not responsive to itraconazole, but was later treated successfully with terbinafine.

Keywords: chromoblastomycosis, dermatophytosis mimick, *Rhinocladiella phaeophora*, new opportunistic species

INTRODUCTION

Chromoblastomycosis is a chronic subcutaneous infection caused by various dematiaceous fungi (Hay, 2012). Infections occur primarily in immunocompetent individuals whose limbs exposed to traumatic implantation of fungal elements into the subcutaneous tissue (Hay, 2012). The fungus multiplies in the tissue producing muriform cells (Hay, 2012). The tissue proliferation results in the production of warty papules eventually leading to extensive verrucous plaques (Queiroz-Telles *et al*, 2009). The most common etiological agents of chromoblastomycosis are the dematiaceous fungi namely *Fonsecaea pedrosoi*, *F.monophora*, *Cladophialophora carrionii* and *Phialophora verrucosa,* all members of the ascomycete order Chaetothyriales in the family Herpotrichiallaceae (Queiroz-Telles *et al*, 2009).

Rhinocladiella sp is usually a saprobe in the soil. There have been reports of chromoblastomycosis caused by *R. aquaspersa*

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(Badali *et al*, 2010a). We report a patient with chromoblastomycosis with an atypical rash mimicking dermatophytosis of the face caused by *R.phaeophora*, a new opportunistic species originally recovered from maize field soil from Colombia (De Hoog *et al*, 2000).

CASE REPORT

A 63-year-old Thai female farmer from Ratchaburi Province, presented to the Institute of Dermatology with a red patch on her cheek for 10 years. She gave no history of penetrating injury to her right cheek. She had been treated with several topical medications over the years without improvement. The skin lesion was slowly expanding. She reported no systemic symptoms. She has no underlying illnesses, except dyspepsia.

Her physical examination was unremarkable except for a solitary erythematous patch on her right cheek which had a slightly elevated border (Fig 1). No black dots were seen on the surface of the patch. The cutaneous sensation in the lesion was intact. A KOH preparation of the rash revealed no hyphae. A skin biopsy of the lesion was performed, and the histopathology showed a diffuse inflammatory infiltrate with lymphocytes and neutrophils, multinucleated giant cells and round pigmented fungal elements in the upper dermis (Fig 2). A KOH preparation of the lesion was repeated 3 weeks after her first visit that showed multiple sclerotic bodies. A skin tissue was inoculated onto Sabouraud's dextrose agar supplemented with chloramphenicol (0.5 mg/l) and incubated at 27-30ºC for six weeks.

The culture grew velvety, elevated colonies with olive-black upper surfaces (Fig 3). Microscopic examination of the colonies showed pale olive colored,

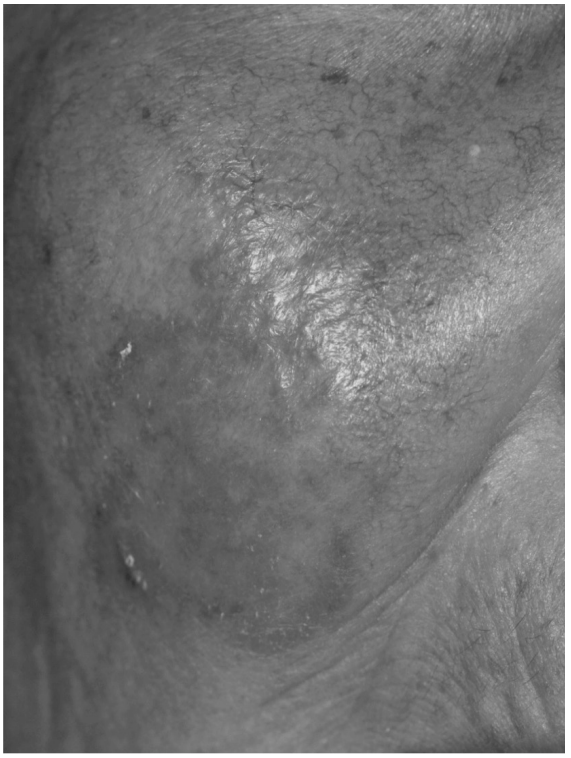

Fig 1–Figure showing a solitary erythematous patch with a slightly elevated border on the right cheek.

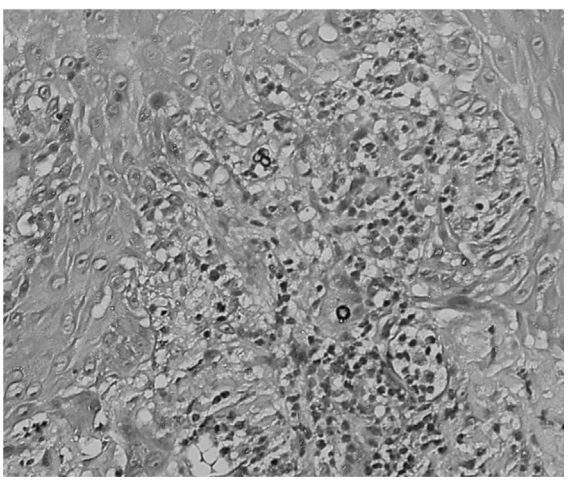

Fig 2–Diffuse inflammatory cell infiltrate of lymphocytes mixed with neutrophils, multinucleated giant cells and round pigmented fungal elements in the upper dermis (H&E x40).

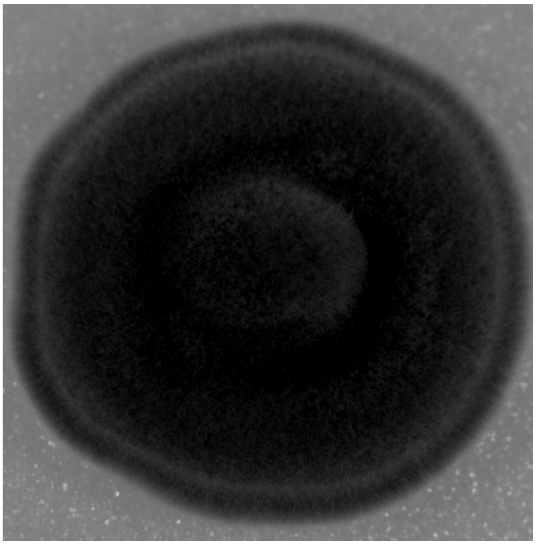

Fig 3–Colony of *R.phaeophora*; velvety, elevated, olivaceous-black upper surfaces and reverses.

Fig 4–Microscopic examination of the slide culture showing pale olivaceous, smooth- or slightly rough-walled hyphae. The conidiophores are straight, upright, unbranched, thick-walled and dark-brown. The conidiogenous cells are terminal, cylindrical, with crowded, slightly prominent denticles and dark scars with hyaline centers. The conidia are subhyaline, smooth- and thin-walled, one- or occasionally two-celled, ellipsoidal to clavate.

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To identify the responsible species, a voucher strain was deposited in the culture collection of First BASE Laboratories, Malaysia (accession number 1741). The strain was subjected to DNA sequencing of the 18S small subunit rRNA gene internal transcribed spacer 1 (ITS 1), 5.8S rRNA gene, ITS 2, and 28S large subunit rRNA gene. Those sequences were then compared with selected sequences at the GenBank + EMBL + DDBJ + PDB sequences (http://blast.ncbi.nlm.nih.gov/Blast.cgi). The strain isolated was identified as *R.phaeophora* by all the genes sequences (maximal identity 99%).

The disease was not responsive to itraconazole due to taking a proton pump inhibitor along with itraconazole, reducing absorption of itraconazole. Itraconazole was then changed to terbinafine since the proton pump inhibitor had to be continued, and the treatment was successful.

DISCUSSION

Chromoblastomycosis is one of the most frequently encountered subcutaneous mycoses (Lupi *et al*, 2005). The organisms causing chromoblastomycosis are saprophytic fungi found in soil and decaying vegetation in high-prevalence areas (Hay, 2012). Several species of dematiaceous fungi cause chromoblastomycosis. The chaetothyrialean fungus genus *Rhinocladiella* is a rare cause of chromoblastomycosis with cases generally confined to Latin America (Badali *et al*, 2010b). The infections caused by species of the genus *Rhinocladiella* are clinically diverse. *R.aquaspersa* is associated with subcutaneous infections (Badali *et al*, 2010a), while *R.mackenziei* causes brain infections in otherwise healthy individuals which are associated with high mortality (Badali *et al*, 2010b).

This case shows *R.phaeophora* can also cause chromoblastomycosis. This infection was probably acquired by accidental inoculation from soil or leaves into the subcutaneous tissues of the subject's cheek. This subject's skin lesion resembled dermatophytosis of the face. The verrucous plaques are characteristic of chromoblastomycosis (Queiroz-Telles *et al*, 2009). Most skin lesions are localized, but disseminated disease has been reported in < 5% of patients (Minotto *et al*, 2001). Lesions continue to evolve, often over many years, and given time may result in morphological characterizable into one or more of 5 types (Carrion, 1950), with nodular, tumorous and verrucous types being more frequent than cicatricial and plaque-type lesions. Pires d'Avila *et al* (2002) found the type of lesion was affected by a cell-mediated tissue reaction. Patients with verrucous plaques have a type Th2 immunological response, whereas patients with erythematous atrophic patches have a type Th1 response. Esterre and Queiroz-Telles (2006) opined relative to cell-mediated immunity, humoral immunity does not offer as much protection against chromoblastomycosis. The *R.phaeophora* infection in our patient might have only induced a Th1 response, resulting in a thin skin lesion. Muriform cells may be detected easily even by direct examination of scales from the skin. A KOH preparation is a simple laboratory investigative technique that may be useful to exclude dermatophytosis-lookalikes, and can confirm the diagnosis of chromoblastomycosis. It is possible to identify the responsible species by examining the microscopic morphologic characteristics of the fungal culture. The genus *Rhinocladiella* demonstrates purely asexual reproduction through the denticulate forms, formerly known as acrotheca (Badali *et al*, 2010a). Morphologically, *R.phaeophora* has sympodial, brown conidiophores which are arranged in a more profusely branched conidial apparatus than other *Rhinocladiella* spp (De Hoog *et al*, 2000).

In general, chemotherapy for chromoblastomycosis has been minimally successful, and prolonged therapy is required. The treatment of choice for chromoblastomycosis caused by *R.phaeophora* is itraconazole. Treatment should continue for at least 1 year, until complete healing. Itraconazole inhibits CYP3A4 and is metabolized by CYP3A4 and has several significant drug interactions (Jacob and Konnikov, 2012). Terbinafine is a fungicidal allylamine related to its blocking of squalene epoxidase (Jacob and Konnikov, 2012). Terbinafine may have an antifibrotic effect on chromoblastomycosis lesions, as was seen in our patient. As with itraconazole, terbinafine has good *in vitro* activity against dematiaceous fungi (McGinnis and Pasarell, 1998). There are few reports of successful treatment of chromoblas-

tomycosis at a low dosage (250 mg/day) (Hay, 1999; Tanuma *et al*, 2000); 500 mg/day is considered to be more appropriate (Queiroz-Telles *et al*, 2009). Esterre *et al* (1996) achieved 74.2% clinical and mycological cure of chromoblastomycosis by 12 months with terbinafine with good patient tolerance. Terbinafine is one of the drugs with the best reported efficacy for treating subcutaneous mycoses and safety results, mainly due to its fungicidal activity and the fact it does not involve the human cytochrome P450 3A4 metabolizing enzyme resulting in fewer drug-drug interactions (Bonifaz *et al*, 2005).

Our case represents a new clinical presentation of chromoblastomycosis masquerading as dermatophytosis of the face. The chromoblastomycosis was caused by a new opportunistic species of the genus *Rhinocladiella*: *R.phaeophora*, which was originally recovered from maize field soil in Colombia.

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