# Chromoblastomycosis in China

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**= Abstract =**

Medical mycology has gone through five distinct eras: 1) Fungi causing dermatophytoses, 2) Discovery of rare and fatal systemic mycoses, 3) Realization that fungi cause common and subclinical diseases, 4) AIDS and the era of the compromised host, 5) Broad-spectrum antifungals with few side effects. Chromoblastomycosis caused by a group of dematiaceous fungi is a common disease in china. To date almost 500 cases have been repoted. This article aims to introduce epidemiology, microbiology, clinical features, laboratory diagnosis and treatment of chromoblastomycosis in china.

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**Key Words:** Chromoblastomycosis, China

Chromoblastomycosis is a long-term fungal infection of the cutaneous and subcutaneous tissue caused by a group of dematiaceous fungi. Clinically, the disease is characterized by the development of verrucous, dyschromia, scaly plaque as well as hypertrophic patches and ulcerative lesions[1]. Most cases progress slowly over many years and sometimes decades. Chromoblastomycosis is caused mainly by *Fonsecaea pedrosoi*, and *F. monophora* which was defined by de Hoog according to ITS rDNA sequence diversity in 2004[2], as well as *Cladophialophora carrionii* and *Phialophora verrucosa*. These pathogens exist in the soil and emarcide vegetation, and can infect persons through abrasions of the skin or mucosa. The disease is found throughout the world, but such patients are most common in tropical and subtropical regions.

In china, the first case of Chromoblastomycosis was reported in 1951. Almost 400 patients had been found by the end of 1999, more than 300 of them coming from Shandong province and others scattering in 14 provinces. Another 73 cases have been reported from 2000 to 2011. About 86% of all the patients were engaged in farming. Most of them were men (the male-to-female ratio is 4:1) and at the age of 20~60 with the youngest of 11 months and the oldest of 85 years. The pathomycete mainly involved was *C. carrionii* in north China, especially in Shandong province. An investigation showed that *C. carrionii* had been isolated from wild toads in endemic aera of Shandong province, but not from non-endemic area. The results suggested that wild toads might be associated with endemicity of chromoblastomycosis[3]. In south China, *F. pedrosoi* was once quite common, while in 2008, Xi LY re-evaluated 24 Fonsecaea isolates from symptomatic patients by morphology, ITS rDNA sequence diversity and randomly amplified polymorphic DNA (RAPD) typing partly. Twenty strains, including a morphological mutant, were *F.*

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*monophora*, while only 4 strains were *F. pedrosoi*. This result demonstrated that *F. monophora* was the predominant etiologic agent of chromoblastomycosis in south China[4]. Only six cases were caused by *P. verrucosa* in China. Most patients suffered from the disease with long duration of 5 to 20 years, the shortest one was 1 month, and the longest one lasted 50 years. Hands and arms were the most frequently infected sites (about 67.4%). Next sites involved were feet and legs (27.1%). Faces, shoulders, trunks and buttocks were involved in few cases.

Lesions usually arose as small scaly papules or nodules which were painless but a little itchy. Satellite lesions may arise due to autoinoculation or the spread through lymphatic vessels. The lesions gradually enlarged and became raised irregular plaques, often scaly or verrucous. Lesions in some cases with long duration became large, tumorous and even cauliflower-like in appearance.

In most patients in China, the lesions remained localized in the area of the initial infection and peripheral spread. In some cases, lesions disseminate through the local lymphatic channel and became grouped. In few cases, lesions involved whole limbs. In a word, the clinical manifestations of chromoblastomycosis in china can be divided into five forms: (1) papillomatous plaque, (2) psoriasis-like plaque, (3) warty tuberculosis-like lesion, (4) nodule-ulcerative tumor, (5) Elephantiasis-like lesion. Squamous cell carcinoma occurred in the infected lesions of four cases with long duration.

Histopathology, the inflammatory infiltrate in infected tissue with pseudo-epitheliomatous hyperplasia, granulomatous reaction and microabscess as well as typical brown sclerotic cells can be found in histological sections stained with HE. A single or a pack of thick-walled spores with brown color can be seen by direct microscopic examination. Culture on SDA produces velvety colony with deep green in color initially and black latterly. Species identification has traditionally been made by morphology of the asexual reproduction structures. *F. pedrosoi* can produce conidia by three forms: *Fonsecaea* morph, *Rhinocladiella* morph and *Phialophora* morph. The conidiophors of *C. carrionii* bear long, branched conidial chains. *P. verrucosa* forms conidia from phialides of conidiogenous cells with cup-like collarettes. Recently, molecular biology techniques have gained increasing importance in defining precise taxonomy.

In recent 10 years, researches on chromoblastomycosis in China are as follows: Loop-mediated isothermal amplification (LAMP) was successfully developed by Sun for rapid detection of pathogenic or allergenic fungi in the environment[5]. In 2004, experimental mice model of *F. pedrosoi* was successfully made[6], and in 2010, mice models of *C. carrionii* and *F. monophora* were successfully constructed[7,8]. Recently, Liu WD, observed the level of expression of Th cytokines using mice model of *C. carrionii*, and found that the clonal diversion of Th1/Th2 cells might play an important role in the pathogenesis of chromomycosis by examining the level of IL-10 and IFN-γ in the mice lesion tissue[8].

Treatments include: (1) Operation. Fifty-six cases were cured by removing the lesions. (2) Topical drug treatment. Fifty-nine cases were cured with local application of 30% glacial acetic acid. Other drugs used included 0.2 mg/ml amphotericin B, 10% potassium iodide ointment and infusion of medicinal herb. (3) Physiotherapy included electrocautery, laser, X-rays and liquid nitrogen cryotherapy as well as thermotherapy. (4) Systemic antifungal drugs. In recent years, most of patients of chromoblastomycosis in china were treated with itraconazole, generally 400 mg/d for the first week and then 200 mg/d. The course of treatment for the patients with localized lesion in early stage was 2 to 4 months, but for those with disseminated lesions or in prolonged stage, a 6- to 12-month course

was needed. Most of them cured and the incured patients were often with thick scars. The other common used antifungal product was terbinafine (250~500 mg/d). Amphotericin B, 5-FC, clotrimazole, fluconazole and ketaconazole were also used in some cases.

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