A progressive cicatricial plaque on the face with nasal destruction, an uncommon presentation of chromoblastomycosis

Panod Chinpipat MD,

Oraya Kwangsuksatid MD.

ABSTRACT:

CHINPIPAT C, KWANGSUKSATID O. A PROGRESSIVE CICATRICIAL PLAQUE ON THE FACE WITH NASAL DESTRUCTION, AN UNCOMMON PRESENTATION OF CHROMOBLASTOMYCOSIS. THAI J DERMATOL 2019; 35: 55-61.

INSTITUTE OF DERMATOLOGY, DEPARTMENT OF MEDICAL SERVICES, MINISTRY OF PUBLIC HEALTH, BANGKOK, THAILAND.

Chromoblastomycosis is a chronic subcutaneous fungal infection caused by dematiaceous fungi. It is normally found in soil, decayed plants and woods especially at tropical and subtropical regions. It commonly occurs in male agricultural workers who were inoculated with the organism via contaminated thorns or wood splinters. We reported a case of 70-year-old man who presented with progressive cicatricial plaque at right ala of the nose associated with nasal destruction. Diagnosis was made by using polymerase chain reaction (PCR) technique and reported *Fonsecaea nubica*. In Thailand, no evidence of this species has been reported. The patient's clinical symptoms were responded to oral itraconazole after 6-month course of treatment.

Key words: Subcutaneous mycoses, Chromoblastomycosis, *Fonsecaea spp.*, *Fonsecaea nubica*, Cicatricial

From: Institute of Dermatology, Department of Medical Services, Ministry of Public Health, Bangkok, Thailand

Corresponding author: Panod Chinpipat, M.D., email: panod_biopc@hotmail.com

Received: 9 October 2018 Revised: 24 October 2018 Accepted: 29 December 2018

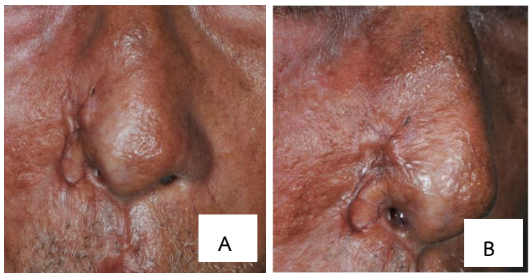
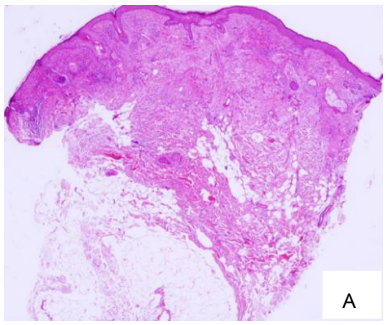


Figure 1 A Solitary ill-defined cicatricial atrophic plaque at right ala of the nose with nasal destruction, extending to upper lip (A). A cicatricial atrophic plaque with indurated border at right lateral nasolabial fold (B)

Introduction

Chromoblastomycosis is a chronic subcutaneous fungal infection caused by dematiaceous fungi normally found in soil, decayed plants and woods[1,2]. Although this condition has been reported worldwide, it is more common in tropical and subtropical regions[1,2]. Both *Fonsecaea spp.* and *Cladophialophora spp*. are the two common causative pathogens[2-4]. Infection usually occurs in male agricultural workers with history of puncture wound from contaminated thorn or wood splinter[5]. Typically, the rash starts with papule or nodule at the traumatic site. Then, it slowly progresses and expands to verrucous plaque. Satellite lesions resulting from scratching or lymphatic spreading can be found[1,2]. The predilection site is lower extremities, but facial lesion is rarely reported. There were a few reports of chromoblastomycosis presented with intranasal mass at nasal septum. Neither traumatic wound nor tissue destruction of the nose was reported[6,7].



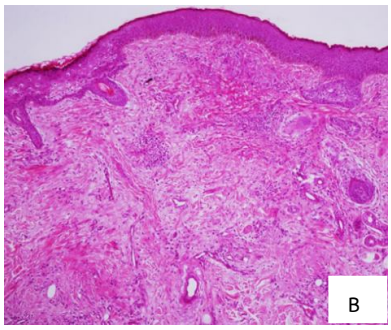


Figure 2 A Histopathological examination shows unremarkable epidermis with hyperkeratosis.(H&E,X40) (A). The dermis shows a superficial perivascular infiltration of lymphocytes and fibrosis. (H&E,X100) (B)

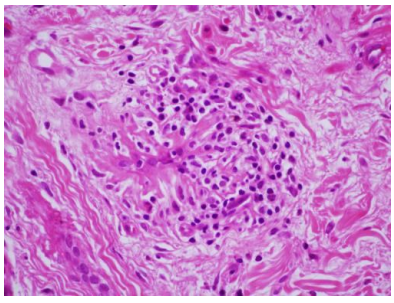
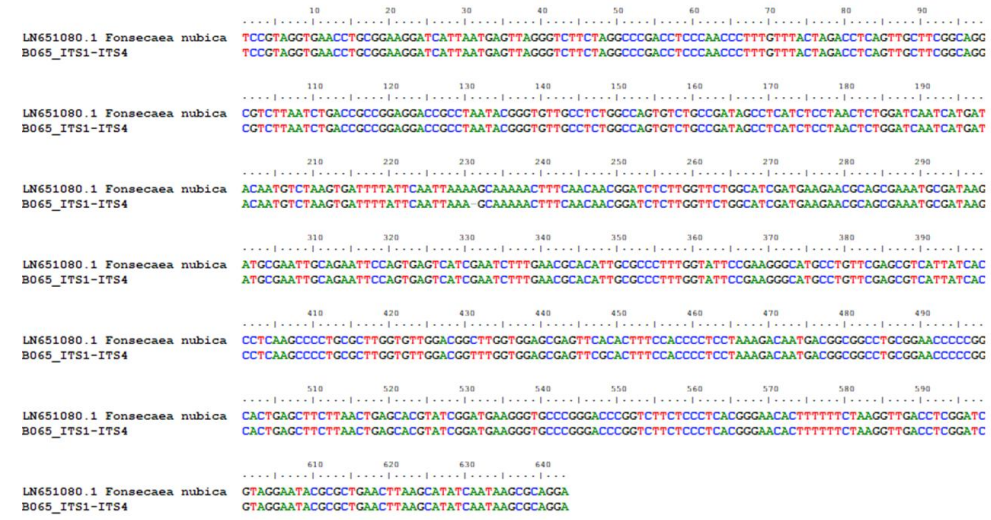


Figure 3 Histopathological examination shows an aggregate of histiocytes and multinucleated giant cells forming granuloma. (H&E,X600)

Case report

A 70-year-old male farmer from central Thailand presented with a cicatricial atrophic plaque at right ala of the nose for 3 months. At this time, he was accidentally penetrated by a small tree splinter at right ala of the nose. He went to a local hospital and treated with a course of intravenous antibiotics for a week without significant improvement. One month later, he started to develop an erythematous rash adjacent to the traumatic site which was slowly expanding and evolving into atrophic plaque with slightly elevated border. The clinical symptom was not responsive to antibiotics, antivirals and intralesional steroid injection from multiple clinics. The rash progressed and, as a consequence, led to the destruction of his right ala of the nose. Apart from the numbness at the rash, there was neither a systemic symptom nor any abnormal discharge from the nose. A dermatological examination showed solitary ill-defined erythematous atrophic plaque with indurated border expanding from the right ala of the nose to the nasolabial fold and vermillion border at same site of the face (Figure1A&B). Right nasal lumen was distorted with scar. Pinprick sensation was lost at the plaque. The cervical lymphadenopathy could not be palpated. A skin biopsy was performed at the erythematous border of the plaque closed to the right upper cutaneous lip and the result revealed unremarkable epidermis with hyperkeratosis. Neither spongiosis nor interface change was seen. The dermis showed a superficial perivascular infiltration of lymphocytes (Figure2A&B). In addition, a single aggregate of histiocytes and multinucleated giant cells forming granuloma were seen in upper dermis (Figure3). Central degeneration of collagen was seemly present. No medlar bodies were found in the tissue biopsy specimen. Tissue culture for mycobacterium and fungus reported no growth. Then, the tissue PCR for fungus was done. First, we obtained the specimen from tissue biopsy and identified a part of the internal transcribed spacer (ITS) by ribosomal DNA sequencing and amplification with PCR technique. After that, we compared the base pair sequence against the ITS of rDNA by reference database from international society of human and animal mycology (ISHAM).The results from the ITS of rDNA method showed similarity by percentage of matched fungal species. The result of our patient was nearly a hundred percentages in similarity of *Fonsecaea nubica* (reported from China). (Figure 4A&B)



A

Pairwise Results | Clustering results

#	Reference description	Score	Probability	Similarity%	Fragments	Overlap%	Direction	Rating
1	MITS1785, Fonsecaea nubica, CBS 121720, Clinical, China, n437: ITS sequence ITSSeq	897.089	0	99.824	1	87.635	+/+	****
2	MITS3072, Fonsecaea nubica, ITS region; from TYPE material, CBS 269.64, NR_111333.1, Clinical, Cameroon, n437: ITS sequence ITSSeq	868.559	0	99.296	1	87.635	+/+	****
3	MITS1784, Fonsecaea nubica, CBS 444.62, Clinical, Suriname, n437: ITS sequence ITSSeq	865.39	0	99.12	1	87.635	+/+	****
4	MITS1786, Fonsecaea nubica, CBS 121733, Clinical, China, n437: ITS sequence ITSSeq	840.03	0	98.77	1	87.635	+/+	****
5	MITS1804, Fonsecaea pedrosoi, dH 12660, Bonifaz 51201, NA, Mexico, n437: ITS sequence	824.181	0	97.842	1	85.781	+/+	****

B

Figure 4 Similar base pairs from the ITS (compared between index case and standard reference). (A) ISHAM barcoding database (http://its.mycologylab.org) showed the result of ITS in similarity of matched fungal species by percentage.(B)

The overall findings are compatible with chromoblastomycosis from *Fonsecaea nubica*. In order to evaluate deep tissue invasion, Magnetic resonance imaging (MRI) of head and neck region was requested and displayed neither deep tissue

invasion nor brain/bone involvement. No abnormality of air sinuses was seen.

Discussion

Chromoblastomycosis is a chronic fungal infection causing a verrucous papule that may progress to an extensive verrucous plaque in many cases. Five clinical manifestations have been reported including nodular lesion covering with cauliflower-like scabs, tumoral lesions, verrucous hyperkeratotic lesions, cicatricial atrophic lesions and erythematous scaly plaques[3]. The verrucous type is the most common presentation, whereas the cicatricial atrophic lesion is rarely reported. Most reported cases have been infected at the traumatic areas especially at the extremities. Our patient presented with a progressive atrophic plaque on right ala of the nose which was an uncommon presentation of chromoblastomycosis. Unfortunately, the delay in diagnosis had led to tissue scarring and nasal destruction. However, the history of a penetrating wound from a traumatic wood splinter was the clue for diagnosis. Differential diagnoses include other mycobacterium and parasitic infections such as leishmania. Otherwise, discoid lupus erythematosus, cutaneous squamous cell carcinoma and basal cell carcinoma are differential diagnosis of non-infectious cause.

Diagnosis of chromoblastomycosis is based on direct mycological examinations with 10% potassium hydroxide and/or histopathology. Demonstration of fungal pathogen, characterized by dark brown, thick wall, 5-12 microns in diameter, round cells which presented as single or a cluster in chestnut-like structure, is also known as medlar bodies[4]. The diagnostic sensitivity of this test is approximately 90%[2]. Fungal culture is another useful method that gives more specific information on the pathogen; however the morphology does not differentiate between species. Recently, the molecular techniques are widely used to identify the pathogen[8]. Inferring epidemiology, there are two most common species of chromoblastomycosis including *Fonsecaea spp.* and *Cladophialophora spp.*[2-4] The most common pathogen in Thailand that has been reported is *Fonsecaea pedrosoi* similar to Japan and China[2, 9]. In 2010, a new species of *Fonsecaea nubica* was introduced by molecular techniques in South China and South America[10,11]. No evidence of chromoblastomycosis caused by *Fonsecaea nubica* has been reported in Thailand before. Its species was identified by molecular technique using sequence markers, for example, amplified fragment length polymorphism (AFLP), internal transcribed spacer(ITS) of ribosomal DNA, partial beta-tubular (BT2) gene or Translation elongation factor1- alpha (TEF1-α). The ITS of rDNA is widely used for identification of *Fonsecaea spp*[11, 12].

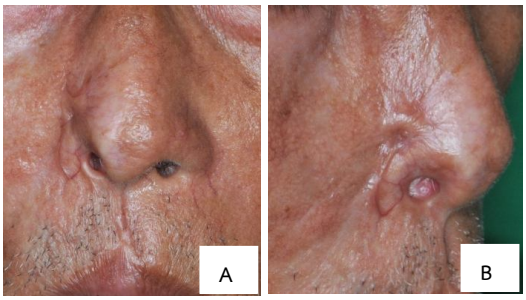


Figure 5 After treatment with oral itraconazole for 4 months, There was no progressive cicatricial plaque.(A) The indurated border at right nasolabial fold was gradually resolved. (B)

Chromoblastomycosis is a chronic condition that is refractory to treatment. Surgical excision may be helpful in a small lesion. Antifungal agents, such as itraconazole 200-400 mg/day or terbinafine 250-500 mg/day, have been used successfully as a monotherapy or combined with other treatment. Topical imiquimod/5-fluouracil or physical modalities such as surgery, cryotherapy, thermotherapy, laser or photodynamic therapy have been reported as a combination regimen[2, 3].Duration of treatment varies from 8-10 months[2]. Some literatures have shown cure rates of up to 80-90% for at least 6 months[13]. In case of invasive or refractory mycosis, more than two systemic antifungal agents (e.g. itraconazole, terbinafine or 5-fluorocytosine) are recommended at least 6-month of duration. Therapeutic outcomes depend on multifactorial factors including site of infection, size of lesion, pathogen and host immune status[14]. In this patient, the lesion was responded to oral itraconazole 200 mg/day for 6 months. (Figure5A&B)

We reported a case of chromoblastomycosis presented with progressive cicatricial plaque at right ala of the nose associated with nasal destruction. Histopathology was compatible with chronic granuloma. Tissue culture failed to demonstrate the pathogen. The diagnosis of *Fonsecaea nubica* was made by PCR technique. This method is very useful especially when histopathology and tissue culture fail to demonstrate the pathogen. Clinician should aware of this condition especially if the patient has the history of traumatic injury by decayed plants or woods.

Reference

1. Martinez RL, Mendez Tovar LJ. Chromoblastomycosis. Clin Dermatol 2007; 25: 188-94.
2. Queiroz-Telles F, De Hoog S, Santos DWCL, et al. Chromoblastomycosis. Clin Microbiol Rev 2017; 30: 233-76.
3. Queiroz-Telles F, Esterre P, Perez-Blanco M, Vitale RG, Salgado CG, Bonifaz A. Chromoblastomycosis: an overview of clinical manifestations, diagnosis and treatment. Med Mycol 2009 ; 47: 3-15.
4. Krzysciak PM, Pindycka-Piaszczynska M, Piaszczynski M. Chromoblastomycosis. Postepy Dermatol Alergol 2014; 31: 310-21.

5. McDaniel P, Walsh DS. Chromoblastomycosis in Western Thailand. Am J Trop Med Hyg 2010; 83: 448.
6. Nakamura T, Grant JA, Threlkeld R, Wible L. Primary Chromoblastomycosis of the Nasal Septum. Am J Clin Pathol 1972; 58: 365-70.
7. Granato L, Gonçalves ÍRD, Barrese TZ, Takara CK. Primary chromohifomycosis of the nasal septum. Braz J Otorhinolaryngol 2014; 80: 86-7.
8. Najafzadeh MJ, Gueidan C, Badali H, Van Den Ende AHGG, Xi L, De Hoog GS. Genetic diversity and species delimitation in the opportunistic genus Fonsecaea. Med Mycol 2009; 47: 17-25.
9. Ungpakorn R. Mycoses in Thailand: current concerns. Jpn J Med Mycol 2005; 46: 81-6.
10. Najafzadeh MJ, Sun J, Vicente V, Xi L, Van Den Ende AHGG, De Hoog GS. *Fonsecaea nubica* sp. nov, a new agent of human chromoblastomycosis revealed using molecular data. Med Mycol 2010; 48: 800-6.
11. Fransisca C, He Y, Chen Z, Liu H, Xi L. Molecular identification of chromoblastomycosis clinical isolates in Guangdong. Med Mycol 2017;55:851-8.
12. Deng S, Tsui CKM, Gerrits van den Ende AHG, et al. Global Spread of Human Chromoblastomycosis Is Driven by Recombinant *Cladophialophora carrionii* and Predominantly Clonal Fonsecaea Species. PLoS Negl Trop Dis 2015; 9: 1-15.
13. Tuffanelli L, Milburn PB. Treatment of chromoblastomycosis. J Am Acad Dermatol 1990; 23: 728-32.
14. Yang YP, Li W, Huang WM, Zhou Y, Fan YM. Chromoblastomycosis caused by Fonsecaea: clinicopathology, susceptibility and molecular identification of seven consecutive cases in southern China. Clin Microbiol Infect 2013; 19: 1023-8.