

Clinical and mycological spectrum of chromoblastomycosis

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Abstract Diagnosis of chromoblastomycosis is often delayed for multiply reasons; poor degree of clinical suspicion or confusion with similar condition due to its polymorphic features and difficulties of confirmed laboratory examination. The case series aims for describing clinical appearance and mycological examination variation of chromoblastomycosis. We reported four cases of chromoblastomycosis with different type of clinical appearance. Each case appeared with different morphology; verrucous-type, tumor-type, plaque-type and mixed type. All patient had history of contact with soil, multiple trauma and chronic course of disease. Diagnosis of chromoblastomycosis in all cases were confirmed by finding sclerotic bodies in either potassium hydroxide or histopathology examination, the fungal of culture of all cases are suitable of the growth of *Fonsecaea pedrosoi*. All cases were treated by pulse dose itraconazole 400mg daily for a week every month. Chromoblastomycosis is fungal infection caused by pigmented fungi acquired usually by inoculation of the skin as part of occupational or environmental hazards. It is found in immunocompetent host; all cases had no history of comorbidity. As the verrucous-type is the common type, chromoblastomycosis often misdoubt with tuberculosis cutis verrucosa, as like our first case. Microscopic detection of sclerotic bodies is important and four cases here confirmed the diagnosis by its finding. *Fonsecaea pedrosoi* is the most common cause of chromoblastomycosis, detected in the first three cases. Itraconazole and terbinafine are the choice anti-fungal either pulse dose or daily dose.

Key words

Chromoblastomycosis; Dematiaceous fungi; Muriform cell.

Introduction

Chromoblastomycosis (CMB) is a chronic deep mycosis caused by pigmented (dematiaceous) fungi that enter the dermis through the skin.¹ Several fungal species have been identified as CBM pathogens, the most common being the *Fonsecaea* and *Cladophialophora* genera. CBM has also been linked to the *Exophiala*, *Phialophora*, and *Rhinocladiella* genera. These fungi are originated from plant debris and soil.

Infections are typically started by traumatic inoculation into the human body, most notably in the extremities.¹⁻²

The incidence according to epidemiological estimates are based on published case reports and surveys. Chromoblastomycosis occurs worldwide, with a higher prevalence in tropical and subtropical region. Brazil, Mexico, Venezuela, Madagascar, India, China, and other countries in Latin America, Africa, Asia, and Australia have the highest documented rates of cases. The estimated incidence rate for this disease in Brazil is 3/100,000. Later research revealed that Japan had the highest incidence of CBM among Asian populations (1/416,000).³⁻⁴ In Indonesia, Yahya S *et al.* (Jakarta, 2016)

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reported three cases of CMB from sixteen cases of cutaneous mycosis in the Dermatology and Venereology Department of Dr. Cipto Mangunkusumo National Hospital between 1989 and 2013. Sukmawati *et al.* reported six cases of CMB in total 16 cases of subcutaneous mycosis (40%) at Soetomo Hospital in Surabaya from January 2010 to December 2014.⁵ From 2016 to 2020, nine cases of CMB were reported at Dr. M. Djamil Hospital in Padang. (unpublished information).

The first lesion typically develops as a warty or pink smooth-surface papule that expands slowly over months or years on the feet, legs, arms, or upper trunk in solitary and unilateral lesions.^{1,6} It may develop into a polymorphic clinical aspect. The modified Carrion's categorization divides the lesions into five categories: nodular, tumoral (cauliflower-like), verrucous, cicatricial, and plaque.⁷ Verrucous-type is the common type, tuberculosis cutis verrucosa often become differential diagnosis in several cases.

Chromoblastomycosis requires laboratory confirmation through direct mycological examination and histopathology. The presence of sclerotic bodies (also known as muriform cells, medlar cells, or copper-pennies) in clinical specimens can confirm the diagnosis of this disease.¹⁻⁷ Dermoscopy may aid in diagnosis, and fungal culture may be used to identify the species of dematiaceous fungi.⁸

Lesions of CMB are clinically polymorphic, and if not detected early, they can become resistant to therapy and extremely difficult to eradicate. There is no spontaneous remission in the course of CMB disease.¹ The therapy of CMB is quite challenging. Some risk factors may play a role to affect the treatment. The time of evolution, the site involved, the patient's hygiene habits, adherence to antifungal therapy, and compromised host innate immune mechanisms

are the key factors influencing this disease's severity. The major treatments for CMB are oral itraconazole (200 mg daily), oral terbinafine (250 mg daily), and, in severe instances, intravenous amphotericin B (up to 1 mg/kg daily). In any case, treatment is continued until the lesions are clinically resolved, which usually takes several months. Antifungal medication combinations like amphotericin B and flucytosine or itraconazole and terbinafine are typically ineffective for treating extensive lesions. In addition, CMB offers additional therapeutic modalities like traditional surgery, cryotherapy, heat therapy, and photodynamic therapy.^{1,4}

Case reports

Case 1 We reported that a 53-year-old man presented to the outpatient clinic department of dermatology-venereology Dr. M. Djamil Hospital on November 24th, 2018 with the chief complaint of a rough greyish patch that had grown in size on his left ankle over the previous year. The lesion began two years ago as an asymptomatic small pimple, similar to a wart. The pimple grew in size gradually, eventually becoming a large patch with a rough and warty surface. He frequently picked at the lesion until it bled. He tried callusol[®] (salicylic acid 0.2g, lactic acid 0.05g, polidocanol 0.02g) to treat the lesion, but there was no improvement. After that, the patient stopped treating the lesion. There was no other lesion on his body. Patient worked as a palm farmer, there was no history of trauma on his leg before the lesion appeared, and he always wore rubber shoes and socks while working. The patient had no comorbidities. Physical examination revealed normal vital signs and a general state of well-being. Clinical finding a greyish-pinkish plaque measuring 12cmx7cmx0.2cm was discovered on his left ankle, with a verrucous surface, small brownish-blackish dots on the surface, yellowish crusts,



Figure 1 depicts the first case from various perspectives. A) For a year, the patient complained of a rough greyish patch that had grown in size on his left ankle, surrounded by erythematous skin. B) The surface of the greyish plaque was verrucous, with black dots (red arrows) visible even with the naked eyes. C) A sclerosing body was discovered during a KOH 20% examination. D) Fungal culture, with brownish-blackish colonies and a downy surface. E) Fungal culture morphology; erected conidiophore at hyphae end site (red circle).

and excoriation (**Figure 1A,1B**). On the upper side of the lesion, the surrounding skin appeared erythematous. The patient was suspected of having CMB but was also diagnosed with tuberculosis verrucosa and squamous cell carcinoma.

Sclerotic bodies were found in histopathology as well as potassium hydroxide 20% examination (**Figure 1C**). In fungal culture, there were brownish-blackish color colonies with downy surfaces (**Figure 1D**), microscopically septate hyphae with erected conidiophores, and ovoid conidia located either at the end or at the side of conidiophores (**Figure 1E**); both morphology cultures were suitable for *Fonsecaea pedrosoi* development. Based on anamnesis, clinical features, and further examination, the patient was diagnosed with verrucous chromoblastomycosis and was prescribed pulse itraconazole 400mg daily for a week every month until the clinical appearance resolved.

Case 2 Sixty-one-year-old man was referred to the Department dermatology-venereology

outpatient clinic of Dr. M. Djamil hospital on December 12th, 2019 with a chief complaint there was a rough surface lump with debris on his middle left toe which smell bad. The lesion began five years ago as a solitary wart-like papule the size of a corn kernel. Because the initial lesion was itchy, the patient scratched it unconsciously. The warty papule was getting bigger, he went to general practitioner and got topical treatment meanwhile the lesion still was getting bigger. The warty papule had transformed into a rough surface lump with debris, was wet, and smelled foul after three years. There were no new skin lesions. The patient has been a palm farmer for over 30 years and frequently forgets to wear his boots. Physical examination was within normal limits. Clinical finding revealed a 7cmx4.5cmx1.5cm reddish cauliflower-like tumor on the middle left toe, with crusts and a few blackish dots on the surface (**Figure 2A**). At first, the patient was suspected of chromoblastomycosis and differential diagnosis with squamous cell carcinoma. Dermoscopy revealed blackish dots as well as yellowish ovoid structure (**Figure 2B**).

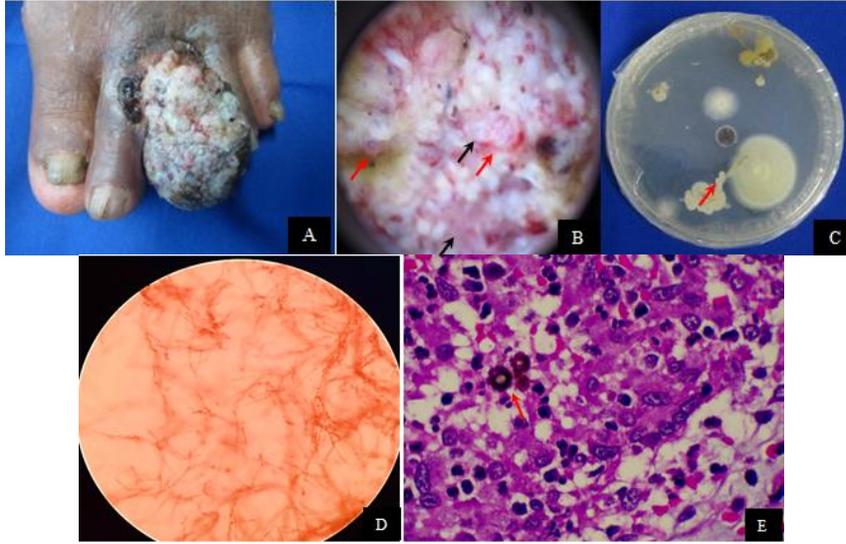


Figure 2 Features of case 2 examinations. A) Dermatological state which reddish cauliflower-like tumor sized 7cmx4.5cmx1.5cm with crusts and few blackish dots on the surface. B) Dermoscopy gives clearer view of blackish dots (red arrows) and yellowish ovoid structures were also found (black arrows). C,D). *Fonsecaea pedrosoi* was confirmed as aetiology by fungal culture and its morphology. E) Sclerotic bodies (red arrows) were found in histopathology (H&E, 40x).

The culture revealed a black colony with several contaminants after four weeks (**Figure 2C**). Both potassium hydroxide and histopathology revealed typical sclerotic bodies (**Figure 2E**). No atypical keratinocytes were infiltrating the dermis, excluding the possibility of squamous cell carcinoma transformation. We took x-rays of the left foot, and the results were normal. Finally, patient was diagnosed with CMB tumor-type and was treated with pulse itraconazole 400mg daily for a week every month. We intended to administer the regimen until the clinical appearance resolved.

Case 3 A 57-year-old man referred to the dermatology-venereology outpatient clinic of Dr. M. Djamil Hospital with the chief complaint of a slightly painful reddish patch and yellowish crusts on his right heel. The patient initially complained about a reddish patch the size of a coin on his right heel that had been there for fifteen years. The reddish patch was itchy at times, so he scratched frequently, and the reddish patch grew in size. He attempted to treat the lesion by seeing a general practitioner, but he saw no improvement. He also tried traditional topical medications like turmeric applied to the reddish patch, but the lesion remained. He stopped treating the lesion until he experienced

minor pain in his right heel while walking, which prompted him to visit a dermatologist. During those fifteen years, multiple traumas such as rubbing and scratching and it occasionally bled and yellowish crusts appeared on the surface of the reddish patch. On the other side of his body, no other reddish patch, wart papule, or nodule was visible. The patient worked as a farmer and a greengrocer. He frequently plants while barefoot. The patient had no comorbidities. The physical examination, the right heel had an erythematous plaque with hyperkeratotic yellowish scales measuring 12cmx7cm (**Figure 3A,3B**). The working diagnosis for the third case was suspected CMB with tuberculosis cutis verrucosa as a differential diagnosis.

Dermoscopy revealed a pink-white background with a yellowish-orange ovoid structure, as well as black dots and scales. On potassium hydroxide 20% examination, a group of sclerotic bodies was discovered microscopically (**Figure 3C**). Sclerotic bodies were also discovered in histopathology image granuloma (**Figure 3E**). After six weeks, there were black colonies with downy surfaces growing on fungal culture (**Figure 3D**). We took an x-ray of his right pedis and found it to be normal. Finally, the patient

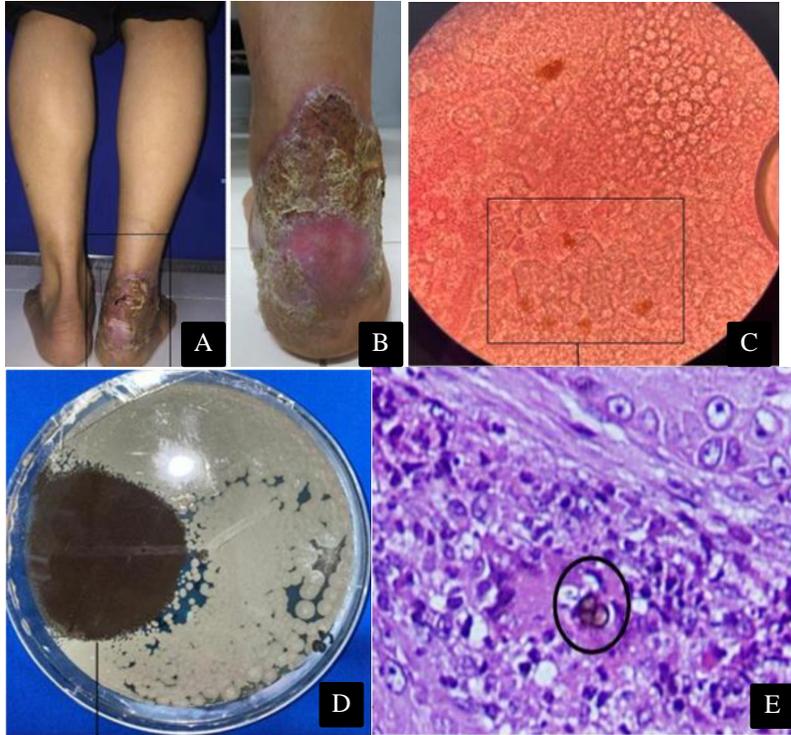


Figure 3 Several case perspectives A,B) Dermatological condition on the right heel with an erythematous plaque and hyperkeratotic yellowish scales. C) 20% potassium hydroxide; positive sclerotic bodies (the red box was a magnification of the black box). D) Fungal culture produces black colonies with a downy surface. Histopathology confirmed the presence of granuloma formed by macrophages and epithelioid cells (red box) and sclerotic bodies (black circle) (H&E, 40x).

has diagnosed with *Fonsecaea pedrosoi*-caused plaque-type chromoblastomycosis and was treated with a pulse dose itraconazole 400mg daily for a week every month.

Case 4 A sixty-year-old man was referred to the Department dermatology-venereology outpatient clinic of Dr. M. Djamil Hospital from Pasir Pangaraian hospital with the chief complaint of a painful reddish patch with a rough surface around his right ankle toward the instep. The initial lesion was a reddish patch the size of a corn kernel that grew slowly over fifteen years. The initial lesion was a reddish patch the size of a corn kernel that grew slowly over fifteen years. As he worked as a palm farmer, the reddish patch was frequently scratched, and it grew outwards. When the reddish patch appeared, the patient rarely wore boots while working. After twelve years the surface became rough and warty in several places. One week before referred he complained painful right foot while walking. Actually patient had already been diagnosed as deep mycosis by dermatologist and

got treated for two months but stopped the medication as he felt no improvement. Appearance of other skin lesion was denied. Patient had diabetes but never controlled routinely. Clinical finding showed erythematous plaque with verrucous surface toward edge of plaque around right ankle and instep, there was atrophic scar in the middle of erythematous plaque, yellowish crusts and reddish-blackish dots (**Figure 4A**). The working diagnosis for the case was suspect CMB and differential diagnosis was tuberculosis cutis verrucosa.

Dermoscopy revealed multiple black dots with a yellowish-orange ovoid structure (**Figure 4B**). On potassium hydroxide 20% examination, a group of sclerotic bodies was discovered microscopically (**Figure 4C**). Sclerotic bodies were discovered in histopathology images as well (**Figure 4D**). After six weeks, the fungal culture produced black colonies. The patient was diagnosed with mixed-type chromoblastomycosis and was prescribed pulse dose itraconazole 400mg daily for a week every



Figure 4 Patients' images in various examinations on the fourth case. A) Erythematous plaque with the verrucous surface (red arrows) toward plaque edge, atrophic scar (black arrows), yellowish crusts, and reddish-blackish dots around right ankle and instep. B) Dermoscopy; red arrows point to black dots and yellowish ovoid structures (black arrows). C,D) Examination with potassium hydroxide 20% and histopathology revealed typical sclerotic bodies (black arrows) (H&E, 20x).

month. Furthermore, the patient was referred to the internal medicine department and was treated for diabetes with oral metformin and glimepiride.

Case 5 A 54-year-old woman presented to Dermatology and Venereology Out Patient Clinic M. Djamil Hospital with the chief complaint that there. Itchy reddish patches with rough surfaces on her left lower arm have increased in number and size over the last 6 months. The complaint was filed 15 years ago. The patient had previously been diagnosed with deep mycosis and did not continue treatment. The patient has been a rice farmer for 20 years.

The physical examination was within the normal range. On her left lower arm, dermatology discovered an erythematous and verrucose plaque with yellowish crusts, blackish-red crusts, and black dots. The working diagnosis, in this case, was suspect chromoblastomycosis plaque type, with tuberculosis cutis verrucose and squamous cell carcinoma as differential diagnoses. Dermoscopy revealed numerous irregular black dots (yellow circles) and yellowish-orange ovoid structures (black circles) over the pink and white areas. Direct light

microscopy of a skin-scraping sample treated with 20% potassium hydroxide revealed sclerotic bodies (**Figure 5**). The fungal culture produced black aerial hyphae, and microscopic examination revealed *Fonsecaea pedrosoi*. Histopathology resulted was hyperplasia, acanthosis, papillomatosis, hyperkeratosis, and parakeratosis. In the dermis, there was lymphosit cell, plasma cell, epitheloid, histiocyte and 1-2 of datia cell. There was PMN cell, on the upper dermis and contain a round-oval thing with thick wall (like copper-pennies appearance). Patient was diagnosis with chromoblastomycosis plaque type and got itraconazole 2x200mg p.o and cetirizine 1x10mg as a treatment.

Discussion

Chromoblastomycosis also known as chromomycosis, is one of the most prevalent implantations fungal infections, accounting for the majority of mycoses caused by melanized or brown-pigmented (dematiaceous) fungi. Lesions of CMB are clinically polymorphic, and if not detected early, they can become resistant to therapy and extremely difficult to eradicate.^{1,4} This case series focused on the various clinical forms and mycological spectrum of CMB that

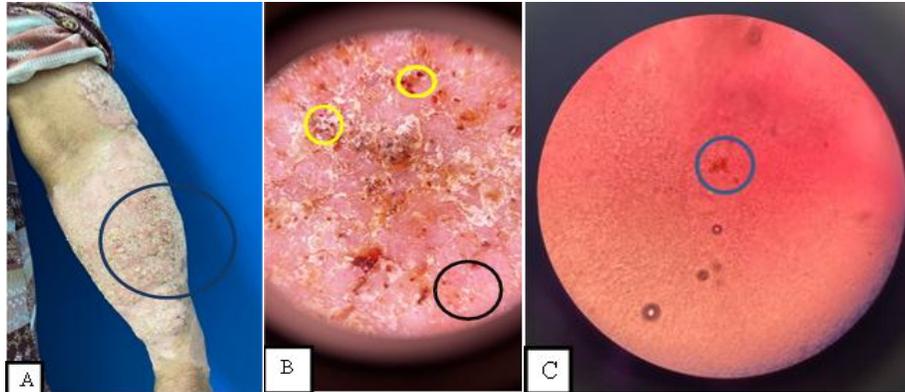


Figure 5 A) An erythematous and verrucous plaque with yellowish crusts, blackish red crusts and black dots (black circle) on her left arm B) Dermoscopy showed multiple irregular black dot (yellow circle) Yellowish orange ovoid structures (black circle) over pink and white areas. C) Direct light microscopic of skin scraping sample using potassium hydroxide 20 % (KOH) showed sclerotic bodies/copper pennies (blue circle).

were reported between 2016 and 2020.

Chromoblastomycosis (CMB) is generally a tropical or subtropical disease that can afflict anyone anywhere in the world who have certain risk factors. The main risk factors for CMB are adult age, male gender, rural labor or outdoor activities, a lack of protective shoes, gloves, or clothing, poor diet, and inadequate hygiene practices. In a study of 325 instances in the Brazilian Amazon region, the condition mostly afflicted people between the ages of 41 and 70; 86.1% of the patients were agricultural laborers; and 93.2% of the cases were male.^{1,4} All of our patients in this case series were men who had been farmers for more than twenty years. Because they rarely wear boots or shoes while working, their lower extremities are frequently subjected to multiple micro traumas. The infection of CMB may occur in any body part; however most frequently it affects limbs especially lower limbs (foot).¹

Our patients had an expanding CMB lesion on their feet. An initial lesion is an erythematous papule or a warty papule that gradually enlarges from the site of infection, taking on various shapes and sizes. It may form a scaly surface. With diverse clinical polymorphism, the initial lesion may progress and evolve. Several

classifications have been developed since the 1900s, but Carrion's classification is the only one that is still in use today.¹¹

Table 1 describes each type of CMB and compares it to the literature and our patient's characteristics. Besides determining the type of lesion, The clinical manifestations of CBM exhibit varying levels of severity, and it is crucial to rank the severity as follows; (1) Mild form: a single lesion of the plaque or nodular type, less than 5 cm in diameter; (2) moderate form: a single or multiple lesions of the plaque, nodular, or verrucous (verruciform) type, when multiple, the presence of one or various types of lesions located on one or two adjacent skin areas; and (3) severe form: any type of single or multiple lesions, adjacent or otherwise, covering extensive areas of the skin. When there are several lesions present in combination with one or more different types of lesions (**Figure 6**).¹⁰ Four cases that were reported display different type of CMB but the degree of severity are similar; all cases rate as moderate form of CMB.

A mycological exam and/or histology are always required to confirm the presence of CMB because the disease's complex morphology leads to an equally diverse differential diagnosis. Muriform (sclerotic) bodies, pathognomonic of

Table 1 Clinical type of lesion chromoblastomycosis and its comparison between literature and patient's feature

Lesion type		Pictures from literature	Our patient
Nodular type	Moderately elevated, fairly soft, dull-to-pink violaceous growth. Surface smooth, verrucous or scaly. With time lesions may gradually become tumorous.		-
Verrucous or warty	Hyperkeratotic is the outstanding features in this type, dry lesion. Frequently encountered along the border of the foot.		
Plaque	Slightly elevated, with variously sized and shaped areas of infiltration. Reddish to violaceous in colour presenting a scaly surface, sometimes shows marked lines of cleavage. Generally found on the higher portions of limbs.		
Tumor-type	Tumor-like masses, prominent, papillomatous, sometimes lobulated; "cauliflower like". Surface partly or entirely covered with epidermal debris and crusts. More exuberant on lower extremities.		
Cicatricial or atrophic	Non-elevated lesions that enlarge by peripheral extension with atrophic scarring, while healing takes place at the centre. Usually with annular, arciform or serpiginous outlines. Tends to cover extensive areas of the body.		
Mixed type	Two or more type of lesions found in one individual		



Figure 6 CBM lesions according to severity criteria. A - mild; B - moderate; C – severe. [10]

CBM independent of the pathogenic species, are shown by direct microscopy using potassium hydroxide (KOH) 10–20%. The samples with the greatest chance of being positive come from lesions that have what are known as "black dots". It is visible on the surface of the lesion, which signify the fungus has been eliminated transdermally. The direct mycological examination has a sensitivity between 90% and 100%. Although the causative agents frequently exhibit remarkably similar macromorphological traits, fungi can be isolated and identified using fungal culture in Sabouraud agar. A velvety, dark-brown, olive-green, or black colony is produced by *F. pedrosoi*. Colonies of *Phialophora verrucosa* develop slowly and are velvety, moss-green, brown, or black in color. Colonies of *C. carrionii* resemble those of *F. pedrosoi* quite a bit. Colonies of *R. aquaspersa* are moss-green to black in color and silky.^{4,6,10} Our cases showed similar growth in fungal culture; black colonies with downy surfaces. We

concluded that the etiology of CMB in our patients are *F. pedrosoi*.

Dermoscopy, as non-invasive technique, helps clinician both in establishing diagnosis and clearer visual to select the best side for direct microscopy specimen. The dermoscopic findings in our instances are consistent with past reports. Dermoscopy-observed pink and white spots correspond to the lesion's rough, uneven clinical surfaces. The presence of numerous reddish black dots, which are attributed to the process of transepidermal clearance of inflammatory cells, foreign fungal components, and bleeding and are clinically recognized as black dots, is the most distinctive dermoscopic observation. Although they can also be seen in other granulomatous disorders, the yellowish ovoid structures are mycotic granulomas and are not unique to chromoblastomycosis. **Table 2** has been discussed in relation to the dermoscopic results of CMB and its differentials.⁸

Table 2 Dermoscopic findings on chromoblastomycosis and its differentials.

Disorders	Dermoscopic findings
Chromoblastomycosis	Yellowish orange ovoid structures (black arrows) over pink and white areas, along with scales and crusts. Multiple, scattered reddish black dots are the most characteristic finding.
Sporotrichosis	Generalized erythema, yellowish structureless areas with clustered pustules at the periphery. White scar-like areas and yellowish structureless area surrounded by arborizing telangiectasias are also present.
Lupus Vulgaris	Structure-less focal or diffuse orange areas and focused linear or branching vessels are seen. In addition, milia-like cysts can also be observed.
Cutaneous Leishmaniasis	Erythematous papular lesion shows generalized erythema, yellow tear drop structures, and vascular structures (comma-shaped vessels and linear irregular vessels). More advanced lesions show central erosion, white starburst pattern, and peripheral vascular pattern (comma-shaped vessels, dotted vessels, and hairpin vessels).

Table 3 Impact factors playing a role in the therapy of patients with chromoblastomycosis. [11]

The host	<p>Wrong or delayed diagnosis</p> <p>Severity of the disease: lymphedema, excessive fibrosis, hardened tissue and low vascularization are barriers for therapeutic response. Drug bioavailability at the site of infection is low</p> <p>Secondary bacterial infection and malignant transformation</p> <p>Long duration therapy with systemic antifungal may cause non-compliance to therapy</p> <p>Individual immune response: Patients with mild forms develop Th1 response and patients with severe forms Th2 response. High levels of INF-γ and low levels of IL-10 are important in the control of CBM infection</p>
The etiologic agent	<p><i>Fonsecaea</i> spp. infections are more difficult to treat than <i>C. carrionii</i>.</p> <p>Treatment discontinuations may lead to fungal resistance.</p> <p>Muriform cells are difficult to eradicate</p>
The antifungal drugs	<p>No standardized in vitro tests for melanized fungi</p> <p>Muriform cells were not tested in vitro for the antifungal drugs.</p> <p>There is no animal model for CBM therapy</p> <p>Triazoles, mainly itraconazole may present an erratic absorption</p> <p>Therapeutic drug monitoring for itraconazole is usually unavailable</p> <p>Itraconazole may present several drug-to-drug interactions and toxicity</p> <p>Posaconazole is still an expensive drug and mostly unavailable in endemic areas</p> <p>There is no good quality comparative clinical trial on this disease</p>
Social factors	<p>Chromoblastomycosis is an orphan and neglected disease mainly affecting the low socioeconomic groups who live in rural environments of the endemic areas</p> <p>Chromoblastomycosis is relatively neglected by researchers</p> <p>Diseases linked to poverty likewise offer little incentive to industry to invest in developing new or better products for a market that cannot pay</p>

We tried to find any case reports or reviews about the dermoscopic feature in tuberculosis cutis verrucosa as the main differential diagnosis of CMB but could not find.

Chromoblastomycosis is characterized histopathologically by pseudoepitheliomatous proliferation of the epidermis. The dermis exhibits a dense granulomatous inflammation with varying degrees of fibrosis, composed of Langhans and foreign body types of giant cells, epithelioid cells, mononuclear cells (histiocytes, lymphocytes, and plasma cells), and polymorphonuclear cells. Hematoxylin-eosin staining makes it simple to identify fungal cells with their distinctive micromorphology—round, dark-brown, thick-walled, 4–12 microns in diameter, known as the sclerotic bodies—inside intraepidermal microabscesses, multinucleated

Langhans and/or foreign body-type cells, suppurative or tuberculoid granulomas.¹⁰ The histopathologic features of our patients showed the sclerotic bodies, confirmed our diagnosis of CMB. The sclerotic bodies mostly found inside the granulomas.

The therapy of CMB is quite challenging. Some risk factor may contribute the failure of the treatment (**Table 3**).¹¹ Based on **Table 3**, all our cases, working as farmer, mostly palm farmer. The delayed diagnosis and the poor compliance may contribute to the treatment failure. This may cause the lesion become more extensive. Our fourth case never complete the treatment before went to M. Djamil Hospital. He first was diagnosed as deep mycosis 3 years ago and never complete the medication after diagnosed.

Low cure rates and high relapse rates are common in chromoblastomycosis cases, especially those that are chronic and severe. There are various available treatments for chromoblastomycosis, notwithstanding the lack of a "gold standard" therapy. The majority of cases of chromoblastomycosis necessitate long-term, ongoing systemic antifungal medication. Therapy sessions might last from a few weeks to many years, or even longer. Itraconazole (200-400mg/day) and terbinafine (500-1000mg/day) for at least 6-12 months, preferable at greater doses if tolerated, are the antifungals that have demonstrated the best efficacy. The aforementioned doses has been accepted by the Indonesian Dermatovenereological Society (*PERDOSKI*) as a Clinical Guideline of CMB Treatment in Indonesia.^{9,10} Both medications showed significant in vitro action against the CBM-causing substances. Itraconazole pulse therapy (400 mg/day for 7 days/month) has been reported and has proven to be more cost-efficient, effective, and linked to higher treatment compliance. Itraconazole and terbinafine, two drugs with separate targets and synergistic effects, have also been used in combination.¹⁰ Our patients were treated by pulse itraconazole 400mg daily for a week every month. Proper explanation to patient and family are pivotal for successful treatment in CMB as the duration of therapy will be in long-term. The cure criteria that is important for clinician in term to stop the treatment are:

1. Clinical: the pain and itchy disappear and total healing on the lesion that become scar
2. Mycology: there were no fungi found on direct examination and culture
3. Histopathology: performed every month for 3 months, and on every histopathologic examination show no fungi, atrophy epidermis, no micro abscess and granuloma, chronic inflammation and fibrosis.

Conclusion

Chromoblastomycosis is a deep cutaneous mycosis that continues to remarkably impair afflicted people. Treatment of CMB is quite challenging, especially for the more severe clinical manifestations. We reported fourth cases of CMB with clinical variation and mycological examination spectrum. Diagnosis was established by finding of sclerotic bodies either on direct microscopy of potassium hydroxide or histopathology examination. *Fonsecaea pedrosoi* was the most common cause of CMB, proven by fungal culture.

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