Chromoblastomycosis: A Case Series and Literature Review

Abstract

Chromoblastomycosis is a subcutaneous mycosis caused by a variety of dematiaceous fungi. *Fonsecaea (F.) pedrosoi* is the most common causative agent. Majority of cases have been reported from tropical and subtropical regions with rural and agricultural background. It is a chronic disease with low incidence of complications but is very refractory to therapies. This is a case series of 22 cases of chromoblastomycosis from two health-care facilities in India. Information regarding the history, clinical presentations, diagnostic methods, therapy, and outcome of treatment were retrieved. Preponderance was seen among the males and in the age group of 41–60 years. Manual and agricultural laborers were commonly affected. Lower extremities were the most common sites affected. Morphological patterns like verrucous plaque, psoriasiform plaque, and verrucous nodules were seen. Direct microscopy with potassium hydroxide (KOH) mount was positive in all the cases. Histopathology in all cases displayed suppurative granulomatous inflammation with pigmented fungal cells. Fungal culture was positive in 10 cases with *F. pedrosoi* being the commonest agent. Antifungal treatment alone was instituted in 10 cases, cryotherapy along with antifungal therapy was given in 9 cases, and surgical excision was done in 3 cases. Complete clinical cure was achieved in seven cases. Chromoblastomycosis is characterized by chronicity, diverse clinical presentations, and therapeutic recalcitrance. Direct KOH mount of the black dots forms an important bedside tool in the diagnosis. Long-term antifungal therapy along with adjuvant cryotherapy may be the best option for the management.

Keywords: *Chromoblastomycosis, subcutaneous mycosis, verrucous plaque*

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Introduction

Chromoblastomycosisis is also known as "chromomycosis," "cladosporiosis," "Fonseca's disease," "Pedroso's disease," "phaeosporotrichosis," and "verrucous dermatitis". It was first reported in Brazil in 1914 by Max Rudolph, a German physician. Histopathological aspects were first described by Medlar in 1915 ("Medlar bodies").[1,2] Chromomycosis is caused by dematiaceous fungi, which are abundantly found in organic materials like wood, soil, and rotting plant material. The most common causative organisms are *Fonsecaea (F.) pedrosoi*, *F. compactum*, *Phialophora verrucosa*, *Wangiella dermatitidis*, *Cladophialophora (C.) carrionii*, and *Rhinocladiella aquaspersa*. Trauma, penetrating injury, and agricultural occupation are common risk factors. The condition usually flourishes in tropical and subtropical regions.[3] The most common site is extremities and the commonest clinical presentation is a verrucous plaque with surface black dots.[4]

Case Series

All diagnosed, treated, and followed-up cases of chromoblastomycosis from two referral hospitals in a span of 10 years from 2007 to 2017 were analyzed. These hospitals are located within a distance of 1 km and all patients were residents of coastal districts of Karnataka and Kerala states, namely, Mangalore, Udupi, Kannur, and Kasargod. Data pertaining to demography, occupation, history of trauma, cutaneous and systemic examination findings, complications, and instituted therapy were retrieved. Direct microscopy with 10% potassium hydroxide (KOH), fungal culture using Sabouraud's dextrose agar containing cycloheximide and chloramphenicol, and skin biopsy for histopathologic examination with routine hematoxylin and eosin stain were performed in all the cases and the reports were analyzed. Details of instituted pharmacological, surgical, and physical therapies were also retrieved.

There were a total of 22 cases, details of which are summarized in Table 1. The

How to cite this article: Shenoy MM, Girisha BS, Krishna S. Chromoblastomycosis: A case series and literature review. Indian Dermatol Online J 2023;14:665-9.

Received: 16-Apr-2023. **Revised:** 21-May-2023. **Accepted:** 25-May-2023. **Published:** 10-Aug-2023.

Access this article online

Website: https://journals.lww.com/idoj

DOI: 10.4103/idoj.idoj_292_23

Quick Response Code:

Table 1: Demography, clinical presentations, laboratory findings, and therapy details of chromoblastomycosis (*n*=22)

Age	Sex	Occupation	Presentation	Site	Duration (years)	Trauma	Culture	Treatment
45	F	Housewife	Verrucous plaque	Ankle	8	+	Negative	Medical
49	M	Manual laborer	Verrucous nodule	Ankle	3	+	Negative	Medical
30	M	Manual laborer	Scaly plaque	Lower leg	2	+	Positive	Medical + cryotherapy
45	M	Manual laborer	Scaly plaque	Lower leg	4	+	Positive	Medical + cryotherapy
60	F	Housewife	Verrucous nodule	Dorsum of foot	1	−	Negative	Surgery
50	M	Manual laborer	Lupoid plaque	Thigh	3	−	Positive	Medical + cryotherapy
55	M	Manual laborer	Scaly plaque	Dorsum of foot	5	−	Negative	Medical + cryotherapy
70	M	Retired teacher	Verrucous plaque	Dorsum of foot	2	−	Positive	Medical
35	M	Cook	Verrucous plaque	Chest	2	−	Positive	Medical
39	M	Manual laborer	Verrucous plaque	Posterior-aspect of ankle	3	+	Negative	Medical
42	F	Manual laborer	Scaly plaques	Ankle	7	−	Negative	Medical + cryotherapy
29	M	Manual laborer	Verrucous plaque	Ankle	2	+	Negative	Medical
45	M	Businessman	Psoriasiform plaque	Posterior-aspect of ankle	8	+	Positive	Medical
54	F	Housewife	Verrucous plaque	Inner part of elbow	3	−	Positive	Surgery
27	M	Manual laborer	Verrucous nodule	Lower leg	2	−	Negative	Medical
57	F	Manual laborer	Psoriasiform scaly plaque	Lower leg	1	−	Negative	Medical
56	M	Agriculturist	Lupoid plaque	Chest	1	−`	Positive	Medical + cryotherapy
58	M	Agriculturist	Psoriasiform scaly plaque	Lower leg	7	−	Negative	Medical + cryotherapy
38	M	Agriculturist	Verrucous plaque	Thigh	6	−	Negative	Medical
42	M	Agriculturist	Verrucous plaque	Dorsum of foot	4	+	Negative	Medical + cryotherapy
24	M	Student	Eczematous plaque	Foot (toe)	0.75	+	Positive	Surgical
30	M	Agriculturist	Verrucous plaque	Lower leg	1.5	+	Positive	Medical + cryotherapy

youngest patient was 24 years old and the oldest was 70 years old. Thirteen patients belonged to the age group of 41–60 years. Seventeen were male. Manual laborers constituted 10 cases, followed by 5 agriculturists. Other occupations included housewives, retired teacher, student, businessman, and a cook. Ten patients could recall a history of prior trauma at the site of the lesions. The duration of disease at the time of presentation varied from 9 months to 15 years. Sixteen patients had duration of 1–5 years, followed by five patients with duration of more than five years. Only one patient gave history of having the lesion for less than 1 year.

Majority of the patients (20 out of 22, 91%) were asymptomatic. Discharging ulcers were present in two cases (9%). The associated systemic diseases (9 cases, 41%) were diabetes mellitus in six, ischemic heart disease in two, and chronic obstructive pulmonary disease in one case. The most common site of affection was lower extremities, seen in 19 cases (86%). Two other patients had lesions over the chest and one patient had involvement of upper limb (elbow). Most common morphology was verrucous plaque seen in nine cases (41%). Scaly plaques were seen in four, and psoriasiform plaque and verrucous nodule in three cases each. Plaques with central healing along with peripheral extension (lupoid) in two and eczematous plaque in one case were also seen [Figure 1].

Direct microscopy with 10% potassium hydroxide (KOH) was positive in all cases which showed characteristic brown fungal cells [Figure 2a and 2b]. Fungal culture using Sabouraud's dextrose agar medium was positive for 10 cases. Isolated causative agents were *Fonsecaea pedrosoi* [Figure 2c and 2d] in nine cases and *Phialophora verrucosa* in one case. Further mycological work-up, such as antifungal susceptibility testing, was not done. Biopsies were taken from the edge of the lesions in all cases and subjected to routine histopathological examination using hematoxylin and eosin staining. Epidermal hyperplasia with suppurative granulomas were seen in all cases along with pigmented fungal cells [Figure 3].

Surgical excision alone was performed in three cases with small and localized lesions; recurrence was noted in one case after 4 months. Pharmacologic therapy alone was instituted in 10 cases, whereas pharmacologic therapy along with cryotherapy in 9 cases. Cryotherapy was administered once a month for four to eight cycles depending on the response to therapy. Daily application of heat using a non-electrical water bottle for at least few minutes a day was advised as an adjuvant therapy for cases who were not supplemented with cryotherapy. Pharmacologic therapy included itraconazole at a dose of 100 mg BID (12 cases) and terbinafine at a dose of 250 mg OD (7 cases). All treated cases were monitored with regular investigations like liver function tests, renal function tests, and blood counts. Five cases showed complete cure with up to 9 months (range of 4–9 months) of antifungal treatment; they included one case each of terbinafine and itraconazole

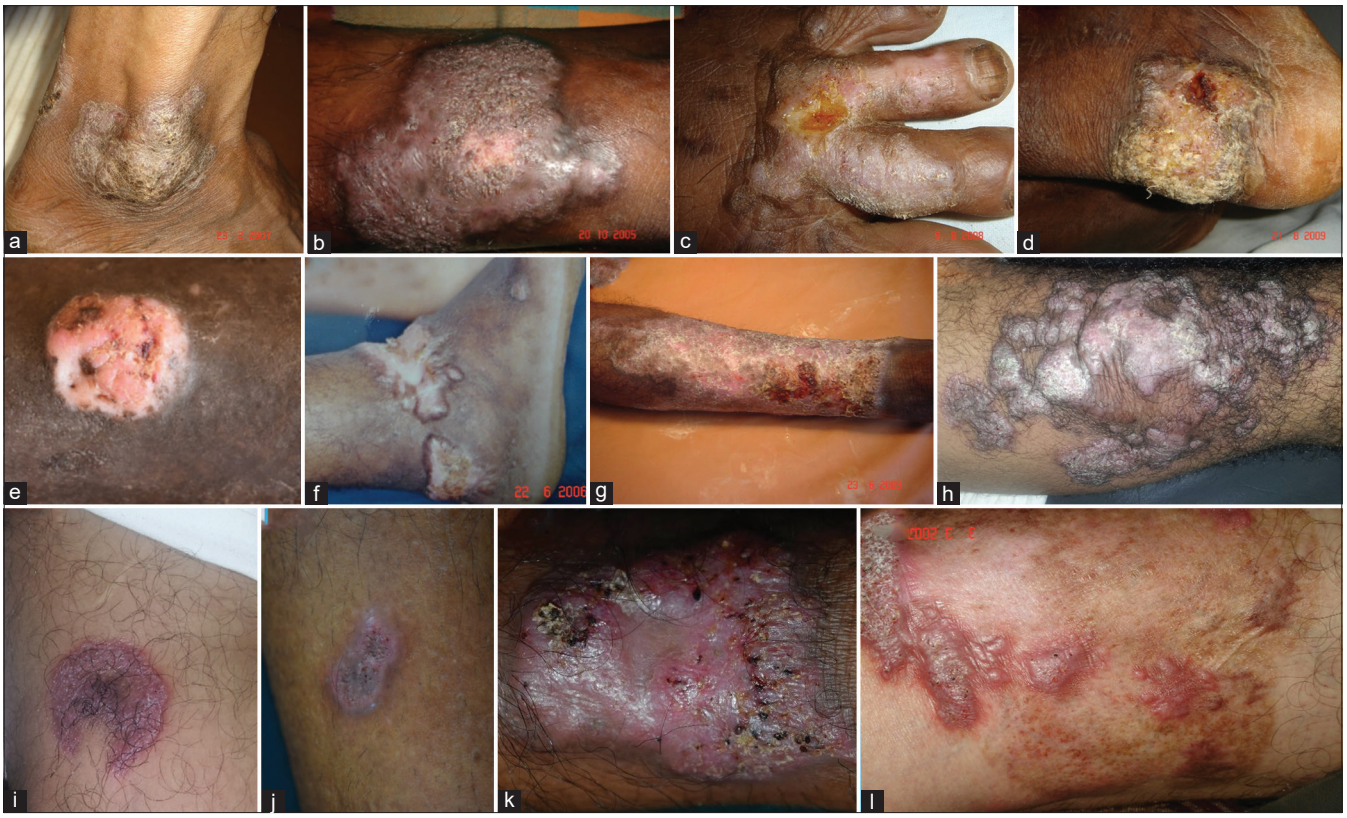

Figure 1: Clinical presentations of chromoblastomycosis. (a) Verrucous plaques over the ankle. (b) Verrucous plaque on the leg. (c) Verrucous plaque on the foot. (d) Verrucous plaque on the back of ankle. (e) Verrucous plaque on the leg. (f) Verrucous plaques on the ankles. (g) Large psoriasiform plaque on the leg. (h) Psoriasiform plaque on the knee. (i) Small psoriasiform plaque on the arm. (j) Small nodular lesion on the leg. (k) Psoriasiform plaque on leg. (l) Large psoriasiform plaque with partial healing after itraconazole combined with cryotherapy

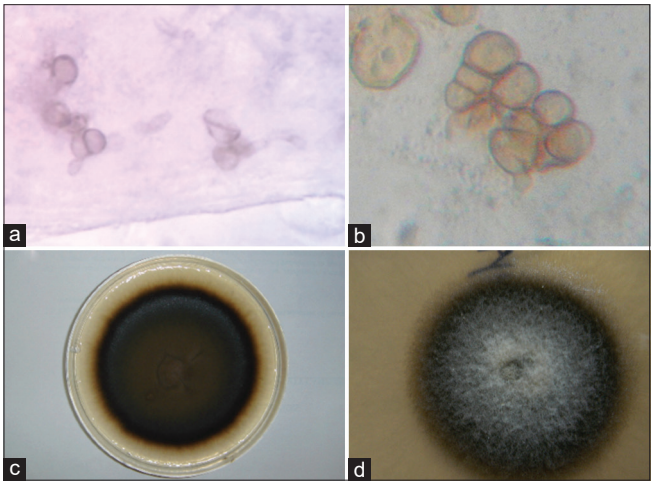

Figure 2: Mycological examination findings of chromoblastomycosis. (a) Direct microscopy under 10% potassium hydroxide mount. 40×. (b) Direct microscopy under 10% potassium hydroxide mount showing characteristic brown fungal cells. 100×. (c) Fungal culture using Sabouraud's dextrose agar medium showing olivaceous to brown-black flat and folded colonies of *Fonsecaea pedrosoi*. (d) Closer view of the colonies of *Fonsecaea pedrosoi* showing velvety surface

with cryotherapy and three cases with itraconazole alone. No recurrence was noted among these patients in the 6-month follow-up. Thus, a total of 7 cases were cured out of 22 cases.

Discussion

Chromoblastomycosis has a higher prevalence in tropical and subtropical regions, which can be explained by the favorable environment for the fungus.[5] The usual clinical presentation is a slowly enlarging exophytic warty plaque with superficial crusting and black dots. The hallmark of chromoblastomycosis is the identification of the sclerotic body or medlar body on direct microscopy which is an adaptive tissue form that helps the organism to escape from host defense mechanisms.[6] Challenges in the diagnosis and treatment along with a scoring system have been studied in the past.[7]

Histopathology depicts constant findings of a granulomatous process and marked epithelial hyperplasia with transepithelial elimination, neutrophils, and the presence of sclerotic bodies.

Although chromoblastomycosis is not a fatal disease, it is chronic, and known for complications due to lymphatic damage and neoplastic transformation.[8] Age group commonly affected in our case series was 40–60 years which does not correlate with other series where it was seen commonly in the age group of 20–40 years.[9,10] Disease occurs 20 times more commonly in men than women. In many studies and in our series too, rural males

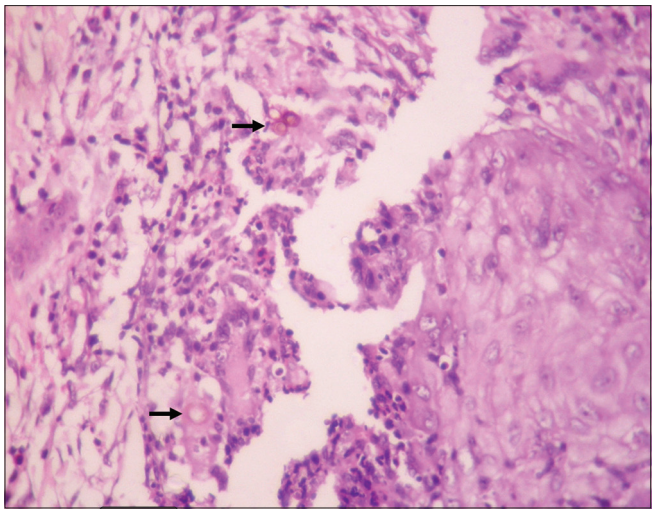

Figure 3: Histopathology of chromoblastomycosis showing suppurative granuloma with epithelioid cells, neutrophils, and eosinophils, along with brown, round, thick-walled fungal cells (black arrows). (H and E 40×)

employed in various agricultural tasks and manual laborers were frequently affected.[5,10-12]

The disease occurs at the site of traumatic inoculation; however, every patient may not recall the history of trauma as seen in our series. Most common area involved as seen in our case series was lower limb which is in accordance with study results of others.[4,5,10-13] The anatomical distribution of lesions of chromoblastomycosis reflects the point of contact with infective material from soil or vegetable matter where the fungus is present in nature. Thus, the feet and legs are the most frequent sites of infection.[14]

Scrapings for microscopic examination using 10% KOH should be taken from a site where black dots are seen on the surface of the lesion. It represents the transdermal elimination of fungal agents.[8] Attapattu reported positivity of KOH mount in 94% of the patients.[14] We found KOH positivity in all cases. KOH mount is the sensitive screening tool based on which therapy can be instituted. *F. pedrosoi*, as found in our study, is the most common etiologic agent isolated.[5,15-17] *F. pedrosoi* is very resistant with no single antifungal agent or regimen providing satisfactory results.[8] The therapeutic response to itraconazole and terbinafine are thought to be better if the causative agent is *C. carrionii*.[5]

Histological examination is a useful tool to establish diagnosis. Hyperkeratosis, pseudoepitheliomatous hyperplasia, mixed-tissue inflammatory response with acute and chronic inflammation, and granulomas with giant cells are consistent features. There can be variation in histopathogical features with suppurative granulomatous reaction with several fungal cells, suggesting a Th2 immunological response in verrucous plaques while tuberculoid granulomatous pattern with reduced number of fungal elements is seen in erythematous plaques.[18]

Complications seen in the present study included persistent ulceration with discharge in two cases. Complications like ulceration and lymphedema may appear when the whole limb is affected. Primary disease can worsen following secondary bacterial infections causing symptoms resulting in itching and foul odor. Scratching may lead to autoinoculation with development of secondary lesions.[4,8]

In our case series, nine patients were put on physical therapy in the form of cryotherapy along with pharmacologic therapy (terbinafine in three and itraconazole in six patients). Surgical excision alone was done in three patients. It is advisable to continue antifungal treatment for a few months to avoid recurrence following excision of chromoblastomycosis; however, we did not recommend due to their inability for follow-up. One patient relapsed in 4 months. Cryotherapy promotes the destruction of the pathological tissue through freezing and alteration of immunologic response. Itraconazole can be used for larger lesions, cryotherapy for small lesions, and the combination may be given in some patients.[19] This study could not arrive at minimum inhibitory concentration (MIC) data and hence our treatment was based on existing regimens. Geometric mean MIC of 10 isolates of *F. pedrosoi* for terbinafine, itraconazole, and voriconazole were 0.0866, 0.1029, and 0.1237 μg/ml, respectively, indicating its *in-vitro* susceptibility to these antifungals.[20] Geometric mean MIC values for *P. verrucosa* clinical isolates for itraconazole, voriconazole, and terbinafine were 0.476, 0.361, and 0.143 μg/ml, respectively.[21] In a case series from Nepal, combination of itraconazole with subsequent cryosurgery showed good response.[12] The prognosis is very good for small lesions.[8] In cases of refractory chromoblastomycosis, photodynamic therapy using 5-aminolevulinic acid and irradiation in combination with antifungal therapy has been successfully used.[22] Antifungals are needed to be given for 6–12 months, often combined with physical therapy such as cryotherapy and thermotherapy for larger lesions. Potassium iodide is found to be a cost-effective drug for patients who cannot afford antifungals.[5]

Conclusion

The most striking features of chromoblastomycosis are its diverse presentation and its refractoriness to treatment. The disease may easily be misdiagnosed by those who are not sensitized to its clinical presentation. Potassium hydroxide mount is a simple, cost-effective bedside tool for the diagnosis. Despite various medical and surgical therapies, complete cure is a challenge, especially in those with multiple and extensive lesions. Results are better when systemic antifungals are combined with physical and surgical therapies.

Acknowledgments

We acknowledge the efforts of Dr. Smitha Prabhu, Additional Professor, Department of Dermatology, Kasturba

Medical College, Manipal, India, for expert inputs in preparing the manuscript.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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