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"COPPER PENNY" OF PATHOLOGY- CHROMOBLASTOMYCOSIS- A CASE REPORT AND BRIEF REVIEW OF LITERATURE.

Pathology

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ABSTRACT

Chromoblastomycosis (CBM) is a chronic, granulomatous, mycosis of the skin and subcutaneous tissue produced by the traumatic implantation of various dematiaceous fungi. The most prevalent species (90%) is Fonsecaea pedrosoi. We report a case of a 29 year male presented with complaints of non- healing ulcer since 6-7 months and underwent exploration and curettage. It was diagnosed as chromoblastomycosis in histopathological examination on identification of characteristic copper pennies/sclerotic bodies. Later on patient responded well to oral antifungal and antibiotic therapy. To conclude, CBM although infrequent, must be considered in the differential diagnosis of chronic skin lesions.

KEYWORDS

Chromoblastomycosis, ulcer, curettage, and copper

INTRODUCTION

Chromoblastomycosis (CBM) is a chronic, granulomatous, non-communicable mycosis limited to skin and subcutaneous tissue produced by the traumatic implantation of various dematiaceous fungi of the order *Chaetothyriales* and family *Herpotrichiellaceae,* and include *Fonsecaea pedrosoi, Fonsecaea monophora, Cladophialophora carrionii, Fonsecaea pugnacius, Rhinocladiella aquaspersa, Cladophialophora samoensis Fonsecaea nubica, Phialophora verrucosa, , Cyphellophora ludoviensis, Rhinocladiella tropicalis, and Rhinocladiella similis*. The most prevalent species (90%) is *F. pedrosoi*.[1-10]

It was first described in 1914, in Brazil by Max Rudolph, a German physician.[11] In 1922, Terra et al. pointed the term chromoblastomycosis to refer to the disease.[12] Seventy years later, in 1992, the term was suggested by the International Society for Human and Animal Mycology (ISHAM) as the official name for the mycosis.[13] CBM is currently categorised by the International Classification of Diseases as follows: ICD-9 117.2 and ICD 10-B43.[14]

These fungi are present in plants, soil, and decomposing wood and is distributed worldwide, but majority of cases have been reported from tropical and subtropical regions.[15,16]

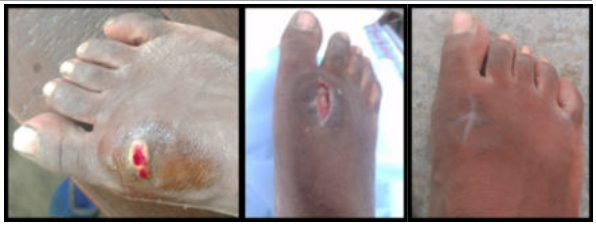
The disease often involves lower extremities of rural men worked barefooted in agricultural field. Other unusual sites of involvement include ala of nose, penile shaft and vulva.[17]

The disease progresses at slow pace, with diverse clinical presentation ranging from ulcer to papulonodular to cauliflower like growth, hence often confused clinically for other lesions. The disease is distinguished by the presence of thick walled, brownish, septate sclerotic bodies (also known as muriform bodies/ medlar bodies/copper pennies) in the tissues. CBM is a continous, damaging, refractory, occupational disease, progressing with episodes of secondary bacterial infections.[18]

The infection is not uncommon in India and many case reports from the sub-Himalayan belt and western and eastern coasts of India have been published.[19] A very few case series describing the clinical manifestations, therapy, and outcome are available from eastern part of India. We herein report a case from our institute.

Case Report

We report a case of a 29 year male, a farmer from Nalanda district of Bihar, and was referred to AIIMS , Patna with complaints of Non-Healing Ulcer since 6-7 months. There was a history of trauma during the field work after which he developed an ulcerated lesion over dorsum of right foot gradually increased in size as shown in Figure 1.



A B C

Fig 1- (A)-Ulcerated lesion over dorsum of right foot. (B)- Post operative wound. (C)- Healed wound with scar tissue.

On examination he had an ulcer measuring 2.5x1x0.3 cm which was covered with exudates and ulcer base was formed by granulation tissue. Surrounding tissue was edematous. There was no constitutional symptoms and inguinal node enlargement .No history of diabetes mellitus, hypertension and tuberculosis. Patient gives history of oral antibiotics given over a period of time but ulcer did not heal. Skin biopsy for histopathological evaluation and swab culture from wound for causative etiology and sensitivity was never done.

Patient was admitted under PMR department. Routine blood investigations was within normal limits and viral markers were negative. Exploration and curettage was performed .

Thorn was isolated and pus was drained and sent for culture and sensitivity. Excised tissues was sent for histopathological examination. Histologically, fibrocollagenous tissue was seen with patchy ,nodular infiltrates of sheets of plasma cells, histiocytes and lymphocytes.

There was presence of intracellular (within macrophages) and extracellularly tiny, round to slightly oval structures (copper penny bodies/ sclerotic bodies) which were strong PAS positive.

Pus which was sent for culture and sensitivity showed growth of Methicillin Sensitive Staphylococcus Aureus. Hence, the nonhealing ulcer of long duration in this patient who was a farmer by occupation with a history of thorn prick injury, with the presence of sclerotic bodies in skin biopsy and even without fungal growth was diagnosed as a case of chromoblastomycosis.

There was no fungal growth. However, patient responded well to oral antifungal and antibiotic therapy. Regular dressing of Post operative wound (Fig 2) was done . Patient was discharged within a week. After two month of discharge, wound has completely healed(Fig 3).

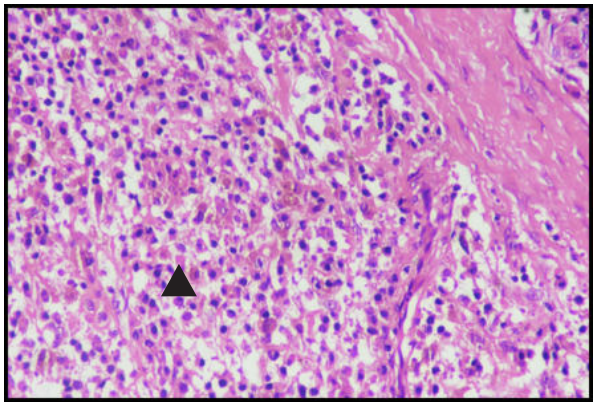


Fig 2- Sheets of inflammatory cells with tiny, round to slightly oval structures (copper penny bodies/ sclerotic bodies, marked with arrow head. (H&E, 400x)

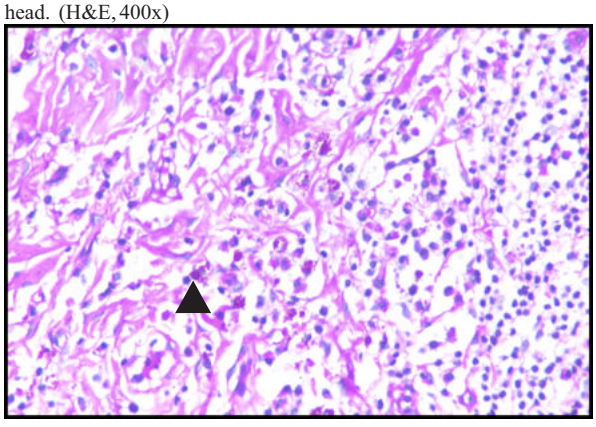


Fig 3- PAS positive copper penny bodies/ sclerotic bodies. Marked with arrowhead. (PAS. 400x)

DISCUSSION

In India, CBM was reported by Thomas E et al. in the year 1957 for the first time from rural areas of Assam.[20] In study done by Agarwal et al., a considerable number of cases had been reported from the western and eastern coasts, southern India, northeastern areas, and the sub-Himalayan belt, namely Karnataka, Kerala, Maharashtra, West Bengal, Assam, and Himachal Pradesh, as fungi thrives in hot and humid climate in the region. A few sporadic cases had also been reported from nonendemic areas such as Bihar, Chattisgarh, Jammu and Kashmir, Rajasthan, and Uttar Pradesh. Thus it is important to keep CBM in differentials for cutaneous lesions, irrespective of the geographical distribution.[17] The disease is more common in males 30-50 years of age, with a male to female ratio ranging from 5:1to 9:1 in various studies.[8,21] CBM presents clinically with minor symptoms or asymptomatic lesions, which explains why patients presents for medical care after months or even years of living with the disease. Exposed areas are usual site of initial lesion, as a papule with centrifugal growth that evolves to any one of the several clinical forms. Classifications of the clinical forms which is still in use is proposed by Carrión in 1950 (Chart 1).[22]

Chart 1: Clinical Classification Of Chromoblastomycosis Types According To Carrión (1950)	
Nodular	Fibrotic, erythematous-violaceous nodules, with smooth or hyperkeratotic surface
Verrucous or warty	Cauliflower-like, dry, hyperkeratotic lesions with black dots
Plaque (infiltrative or erythematous	Erythematous or violaceous plaques, infiltrated, circumscribed, irregular, sharp and elevated edges, with black dots
Tumoral	Isolated or coalescent lobulated lesions, smooth or vegetative-like surface
Cicatricial or atrophic	Cicatricial or atrophic

Histologically, the fungi shows 4-12 microns round/oval bodie which are brownish and thick-walled cells which multiply by septation in two distinct planes, called muriform (sclerotic) bodies (cells) or Medlar's bodies, which represents the invasive form. Polymer dihydroxy naphthalene (DHN) forms melanin of the dematiaceous fungi, and produces the melanin complex by interacting with proteins, lipids, and carbohydrates from the cell wall and constitutes an important factor in the virulence of these fungi.[23]

CBM results from the transcutaneous, traumatic inoculation of propagules from various species of dematiaceous fungi. The main immune response of CBM is cellular, involving macrophages, Langerhans cells, factor XIIIa+ dermal dendrocytes, in addition to the humoral response. In 2003, D'Ávila *et al.* described CBM-spectrum disease, associating the clinical forms to the cytokine profile. Verrucous lesions demonstrated granulomas and prevalence of IL4 and IL10, a Th2 response. In the atrophic forms,well-formed granulomas were seen with more epithelioid and Langhans cells, IFN-gamma, and TNF-alpha, a Th1 response profile.[24]

Gimenes *et al.* demonstrated that patients with the severe form of CBM had inefficient T-cell proliferation and produce high levels of IL-10 and low levels of IFN-γ.[25] The immunohistochemical analysis of 23 biopsies from the untreated verrucous form of CBM demonstrared local immune response with high IL-17 expression and low expression of other cytokines, but this Treg/Th17 disparity can provide proof of decreased immune response to the fungus.[26]

Direct microscopy using potassium hydroxide (KOH) 10- 20% reveals muriform (sclerotic) bodies, diagnostic of CBM regardless of the causative species. Fungal culture in Sabouraud agar is used to isolate and identify species, but the causative agents usually present similar characteristics. *F. pedrosoi* produces velvety, dark-brown, olive-green, or black colonies. *Phialophora verrucosa* produces slow-growing, velvety, moss-green, brown, or black colonies. *C. carrionii* displays colonies very similar to those of *F. pedrosoi.*[27]

Intradermal tests for the disease have not been standardized. Molecular biology techniques and PCR tests are currently essential to complete the diagnostic workup, and have been developed to identify *Fonsecaea* species and *C. carrionii.*[6,28,29]

Histopathologically, In CBM epidermis shows hyperparakeratosis, pseudoepitheliomatous hyperplasia, intracorneal microabscesses, and demonstration of fungi, either inside or outside the microabscesses . The dermis presents dense granulomatous inflammation with mononuclear cells (histiocytes, lymphocytes, and plasma cells), epithelioid cells, Langhans and foreign body types of giant cells, and polymorphonuclear cells along with different degrees of fibrosis. Fungal cells with their characteristic micromorphology – round, dark-brown, thick-walled, 4-12 microns in diameter and with multiplanar reproduction, called copper pennies/sclerotic bodies – are found in microabscesses and in Langhans and/ or foreign body-type giant cells.[27]

In H&E stained tissue sections, sclerotic bodies must be differentiated from hemosiderin or formalin pigment which are irregular, dense brown colored and don't show characteristic division, whereas sclerotic bodies have definite morphology with intracellular division. There is limitation in identifying the genus and exact species, as all of them look similar histologically. Thus we have to rely on culture studies.[30] Sclerotic bodies have been observed in 80-85% cases, and culture has been found to be positive in 70-75% cases as reported worldwide.[31] The most common complication is secondary bacterial infection. As, in our case, culture was negative for fungal growth but was positive for *Staph. Aureus*. The other common complications include lymphatic disruption with elephantiasis. Squamous cell carcinoma may occur rarely in long-standing cases.[32]

Chronic and extensive cases of CBM is difficult to treat and is associated with low cure rates and high relapse rates. Treatment choice vary from case to case and depends on the etiological agent, size and extent of the lesions, topography, and presence of complications. Treatment consists of long periods of antifungal drugs, often combined with physical treatments like surgery, cryotherapy, and thermotherapy. However, studies have reported variable clinical and mycological cure rates, ranging from 15% to 80%..[33] Wide local excision of small and localized lesions along with antifungal agents which can be often used before surgery to downsize the lesion and later to avoid risk of relapse.[27] There is minimal risk of adverse effects with cryotherapy or cryosurgery with liquid nitrogen and thermotherapy (local heat to produce controlled temperatures of 42- 45°C, which inhibit fungal

growth) and however these are more appropriate for single, limited lesions.[34,35]

CONCLUSION

Chromoblastomycosis, although infrequent, must be considered in the differential diagnosis of chronic skin lesions in patients from tropical and sub-tropical regions. Eventhough it spreads very slowly and is rarely fatal, and usually have good prognosis, its early diagnosis is must to institute appropriate treatment and avert rare complication of squamous cell carcinoma.

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

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