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Mycetoma-like chromoblastomycosis: a diagnostic dilemma

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Abstract

Mycetoma and Chromoblastomycosis are subcutaneous fungal infections caused by pigmented fungi. They are common in the tropics and subtropics and are usually acquired through minor trauma or abrasion in the skin. Here, we report a pregnant woman who presented with an indurated swelling around the ankle joint with multiple discharging sinuses which was clinically diagnosed as a case of mycetoma. But on further investigating, histopathology and fungal culture were suggestive of Chromoblastomycosis caused by *Fonsecaea pedrosoi.* This unusual mycetoma like presentation of chromoblastomycosis has not been previously reported in literature and may be attributed to the altered immune status in pregnancy. Treatment was initiated with Terbinafine 250 mg daily and patient showed excellent response within 6 months of therapy.

Conclusion This unusual clinical scenario should alert physician about the need to be vigilant of the atypical presentations of well-known dermatological conditions, especially in special situations like pregnancy.

Introduction

Mycetoma is a chronic suppurative granulomatous disease affecting the skin and subcutaneous tissue which is common in the tropics and subtropics. It was John Gill who first described the clinical features of the disease in the year 1842 in Madurai[1], the city after which it was named Maduramycosis. It includes two main groups – Actinomycetoma caused by aerobic actinomycetes and Eumycetoma caused by true fungi[2]. We report a very rare and unusual case of mycetoma-like presentation caused by *Fonsecaea pedrosoi* which is a common causative agent of chromoblastomycosis.

Case report

A 24-year-old primigravida in her 7th month of gestation attended the dermatology outpatient clinic with a rapidly enlarging painful swelling on the right ankle of 2 months duration. There was no history of any preceding trauma or surgical procedures. Patient had no comorbidities. The lesion continued to increase in size causing considerable discomfort to the patient despite antibiotic therapy and surgical debridement.

Examination revealed a diffuse indurated swelling around the ankle joint with sparing of the anterior part (Fig. 2a,b). There were multiple papules and nodules with sinuses draining serosanguinous and purulent material on the surface. Regional lymph nodes were not enlarged. Systems were within normal limits. Based on the above clinical picture, we made a presumptive diagnosis of Mycetoma and did further investigations.

Routine blood and urine examinations, radiograph of right ankle and chest showed no abnormalities. No grains were identified from the discharge obtained from a saline dressing kept overnight and a KOH smear showed no organisms. Pus culture revealed no bacterial growth. Biopsy from the area showed numerous neutrophilic microabscesses and tuberculoid granuloma with giant cells and lymphocytes. Numerous thick-walled brownish spherical sclerotic bodies were present both inside and outside the giant cells suggesting the picture of chromoblastomycosis (Fig. 1a). No grains or fungal hyphae could be seen. Specimens were also sent for fungal and mycobacterial culture. Within 3 weeks, culture in Sabouraud's dextrose agar showed olive gray colonies with jet black in reverse (Fig. 1b); and lactophenol cotton blue mount of the same showed septate branching hyphae with sympodial (*Rhinocladiella*) and acropetal (*cladosporium*) type of conidiation typical of *Fonsecaea pedrosoi* (Fig. 1c).

Discussion

Dematiaceous or pigmented fungi cause a variety of subcutaneous fungal diseases – Mycetoma, chromoblastomycosis, and pheohyphomycosis being important among them. Mycetoma presents as a chronic indurated swelling with discharging sinuses usually involving the lower extremities. The hallmark

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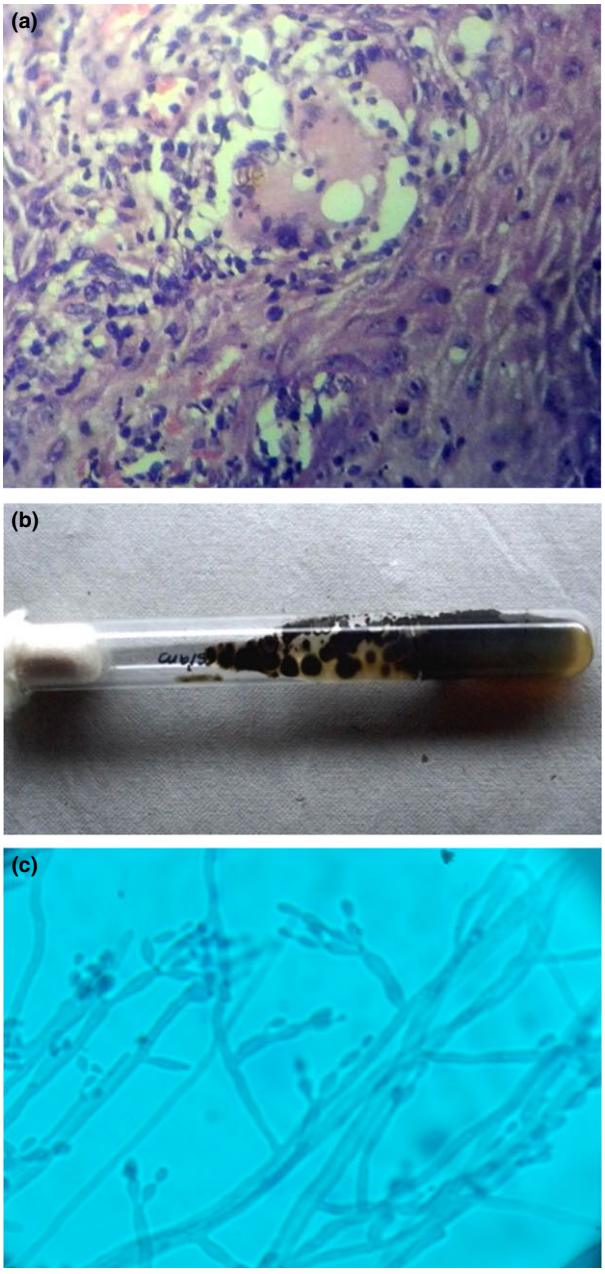

Figure 1 (a) Skin biopsy showing granuloma in the dermis with Langhans Giant cell containing sclerotic body (H&E; × 40). (b) Gray-black velvetty colonies on tube culture with a jet black reverse, (c) microscopy showing septate hyphae with sympodial and acropetal type of conidiation (lactophenol cotton blue mount, ×40)

triad of the disease is tumefaction, fistulization of the abscess and extrusion of colored grains[3,4]. Grains, also known as sclerotia, are aggregates of the fungal hyphae or bacterial filaments, sometimes embedded in tough, cement-like material[5]. It extends slowly invading the subcutaneous tissue, fat, ligaments, muscle, and bone. The infection is not self-curing and, if untreated, leads to massive lesions, which may in the end necessitate surgical amputation[6]. *Madurella mycetomatis, Madurella grisea, pseudallescheria boydii, leptosphaeria senegalensis, and Acremonium* are some of the important fungal agents causing eumycotic mycetoma, whereas *Nocardia, Actinomadura, and Streptomyces* are common agents causing actinomycotic mycetoma. Histologically, there is chronic inflammatory reaction with suppurative granuloma formation and granules containing either thick-walled septate hyphae as in eumycotic mycetoma or fine branching interlacing filaments as in actinomycotic mycetoma.

Chromoblastomycosis, on the other hand presents as a hypertrophic verrucous plaques at sites prone to trauma commonly on feet, legs, arms, face, and neck[7]. It may ulcerate or develop atrophy and scarring. Satellite lesions are produced by scratching and there may be lymphatic spread to adjacent areas. It can also present in varied morphologies like nodular, tumoral, cicatritial, plaque, and verrucous.[8–10] The common causative agents include *Fonsecaea pedrosoi, Cladophialophora carrionii, Phialophora verrucosa*, *Rhinocladiella aquaspersa,* and *Fonsecaea compacta*. Irrespective of the species, the pathogen can be demonstrated as deeply pigmented thick-walled muriform or sclerotic bodies. They are seen either in giant cells or neutrophilic abscesses in histopathology[11]. Demonstration of muriform body in scrape smear, histopathology or in aspiration cytology is diagnostic of Chromoblastomycosis.[12]

In our case, although the clinical presentation showed close resemblance to mycetoma, typical granules were not demonstrated which pointed against a diagnosis of mycetoma. Diagnosis of chromoblastomycosis was confirmed through histopathology which showed sclerotic bodies and fungal culture which demonstrated the causative agent *Fonsecea pedrosoi.*

The reason for such an altered presentation may be related to the underlying immunological mechanism. It is assumed that genetic susceptibility of the host, virulence of the organism, and host immunity are important factors determining the clinical and histological presentation of the disease. Tsuneto et al.[13] have enumerated the role of HLA-A29 A in susceptibility to Chromoblastomycosis. Though the first line of defense against fungi are the dendritic cells, studies have shown that the immunological response in chromoblastomycosis is primarily T-cell mediated. In 2003, D'Ávila et al.[14]suggested that patients presenting with verrucous plaques have Th2 immunological response characterized by suppurative granulomas with several fungi cells, while those with erythematous atrophic plaques have a Th1 response associated with tuberculoid granulomas and few fungi cells within the lesions. According to Mazo etal[15], severe forms of the disease are associated with high levels of IL-10 and low IFN-γ, whereas mild forms are associated with low levels of IL-10 and higher IFN-γ, thereby indicating a crucial role of IFN-γ and CD4 + T lymphocytes in the immune response against chromoblastomycosis.

Pregnancy is associated with immunosuppression often subjecting the patient to increased risk of infection. There is a shift

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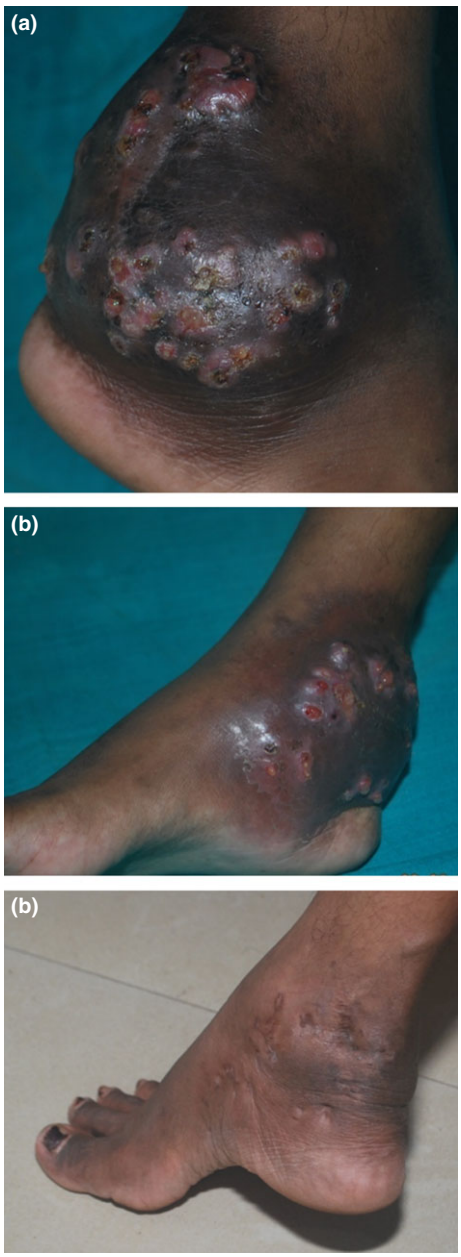

Figure 2 (a & b) Indurated swelling with multiple discharging sinuses around right ankle. (c) After 6 months of treatment with Terbinafine

in the immunological profile toward Th2 response in pregnancy with elevated IL-10 levels[16] and it would be reasonable to postulate that this shift in immunological profile accounted for the severe form of the disease with deeper tissue involvement and rapid progression of the condition.

Dematiaceous fungi are increasingly being recognized as an important pathogen in human infections especially in the past few decades. A case of Disseminated Phaeohyphomycosis because of *Exophiala spinifera* during pregnancy was reported by Ricardo et al.[17] and a case of concurrent mycetoma and chromoblastomycosis was reported by Murthy et al.[18], but a mycetoma-like presentation of chromoblastomycosis is yet to be reported. It is said that Chromoblastomycosis and pheohyphomycosis represent two poles of a spectrum of disease caused by pigmented fungi[19]. So, we assume that the spectrum of diseases caused by dematiaceous fungi has no strict boundries and a mycetoma-like presentation may be induced by F.pedrosoi during immunosuppression. Interestingly, *Exophiala jeanselmei* is a black fungi which is known to cause all the three conditions[6].

Both itraconazole and terbinafine have been used successfully in the treatment of chromoblastomycosis. Potassium iodide is another effective drug for chromoblastomycosis caused by *F.pedrosoi*. The therapeutic responses to Itraconazole and Terbinafine are thought to be better if the causative agent is *C.carrionii*[15]. Other options include surgical excision, cryotherapy, local application of heat, and CO_2 laser vaporization. They are useful only in smaller lesions. Our patient was treated with terbinafine 250 mg daily in the postnatal period and she showed an excellent response within 6 months (Fig. 2c).

Conclusion

This unusual clinical setting reiterates the need to be vigilant about the atypical presentations of well-known dermatological conditions, especially in special situations like pregnancy. It also emphasizes the need for appropriate investigations in every case even if the diagnosis seems straight forward. Being a case report, our findings have limitations and we need further reports to confirm the new findings.

References

1 Narayanan AS, Kasliwal MK, Suri A, *et al.* Eumycetoma presenting as a cerebellopontine angle mass lesion. *Clin Neurol Neurosurg* 2007; **109**: 516–519.
2 Zijlstra EE, van de Sande WW, Welsh O, *et al.* Mycetoma: a unique neglected tropical disease. *Lancet Infect Dis.* 2016; **16**: 100–112.
3 Davis JD, Stone PA, Mc Garry JJ. Recurrent mycetom of the foot. *J of Foot ankle Surg.* 1999; **38**: 55–60.
4 Merrcut D, Tita C, Lanosi S, *et al.* Madurai's Foot (Mycetoma). *Chirurgia* 2003; **98**: 261–264.
5 Ahmed OAA, Leeuwen WV, Fahal A, *et al.* Mycetoma caused by Madurella mycetomatis: a neglected infectious burden. *Lancet infect Dis* 2004; **4**: 566–574.
6 Boiron P, Locci R, Goodfellow M, *et al.* Nocardia, nocardiosis and mycetoma. *Med Mycol* 1998; **36**: 26–37.
7 Hay RJ, Ashbee HR. Mycology. In: *Rook's textbook of dermatology* (Burns T, Breathnach S, Cox N, Griffiths C, eds), 8th ed. **Vol. 2**. West Sussex: Wiley-Blackwell; 2010:36.75–36.76.
8 Minotto R, Bernardi CD, Mallmann LF, *et al.* Chromoblastomycosis: a review of 100 cases in the state of Rio Grande do Sul, Brazil. *J Am Acad Dermatol* 2001; **44**: 585–592.

9 Krzyściak PM, Pindycka-Piaszczyńska M, Piaszczyński M. Chromoblastomycosis. *Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii* 2014; **31**: 310–321.
10 Queiroz-Telles F, Esterre P, Perez-Blanco M, *et al.* Chromoblastomycosis: an overview of clinical manifestations, diagnosis and treatment. *Med Mycol* 2009; **47**: 3–15.
11 Vicente VA, Attili-Angelis D, Pie MR, *et al.* Environmental isolation of black yeast-like fungi involved in human infection. *Stud Mycol* 2008; **61**: 137–144.
12 Chavan SS, Reddy P. Cytological diagnosis of chromoblastomycosis. *J Cytol.* 2013; **30**: 276–277.
13 Tsuneto LT, Arce-Gomez B, Petzl-Erler ML. HLA-A29 and genetic susceptibility to chromoblastomycosis. *J Med Vet Mycol* 1989; **27**: 181–185.
14 D'Avila SC, Pagliari C, Duarte MI. The cell-mediated immune reactions in cutaneous leisons of chromoblastomycosis and their correlation with different clinical forms of the disease. *Mycopathologia* 2003; **156**: 51–60.
15 Mazo FGV, Da Gloria DS, Ferreira KS, *et al.* Cytokines and lymphocyte proliferation in patients with different clinical forms of chromoblastomycosis. *Microbes Infect* 2005; **7**: 708–713.
16 Cunningham FG, Leveno KJ, Bloom SL, *et al.* Infectious Diseases. In: ???? ???? ed. *Williams Obstetrics*. 24th edn. New York: McGraw Hill Education; 2014: 1239.
17 Negroni R, Helou SH, Petri N, *et al.* Case Study: Posaconazole treatment of disseminated phaeohyphomycosis due to *Exophiala spinifera*. *Clin Infect Dis* 2004; **38**: e15–e20.
18 Murthy R, Swain JP. Concurrent mycetoma and chromoblastomycosis. *Indian J Med Microbiol* 2011; **29**: 437–439.
19 Son Y-M, Kang H-K, Na S-Y, *et al.* Chromoblastomycosis Caused by *Phialophora richardsiae*. *Ann Dermatol* 2010; **22**: 362–366.
20 Chandran V, Sadanandan SM, Sobhanakumari K. Chromoblastomycosis in Kerala, India. *Indian J Dermatol Venereol Leprol* 2012; **78**: 728–733.