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Heat Therapy Intervention and Pulse Dose Itraconazole as Combination Treatment for Chromoblastomycosis: An Unusual Case Report

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Abstract

Chromoblastomycosis (CBM) is a rare chronic fungal infection caused by dematiaceous fungi, presenting a significant challenge in Indonesia. This case involves a 54-year-old man who reported a lump on his right leg persisting for 10 years. Examination revealed multiple erythematous nodules with well-defined borders and a verrucous surface, forming a linear pattern around the ankle, some covered by brownish crusts. The patient denied itching and pain in the lesions. The initial diagnosis of chromoblastomycosis was confirmed through culture and histopathology. Treatment involved pulsed doses of intraconazole and heat therapy. Remarkably, lesions significantly improved after one month, underscoring the efficacy of combination therapy for chromoblastomycosis. Pulsed dose itraconazole enhances treatment compliance with its cost-effectiveness, while heat therapy, as a physical intervention, proves to be an easily administered option with promising efficacy. Considering the prolonged management required for CBM, it is imperative to factor in the patient's socioeconomic condition during treatment planning.

Keywords: chromoblastomycosis, heat therapy**,** itraconazole pulse dose, case report

Introduction

Chromoblastomycosis, a chronic fungal infection affecting the skin and subcutaneous tissue, is primarily attributed to pigmented dematiaceous fungi introduced into the dermis from environmental sources.[1,2] Fungi within the Dermateaceae family are the main culprits behind these infections.[3,4] Notably, this disease exhibits a prevalence exceeding 70% in tropical and subtropical regions, with Madagascar recording the highest prevalence. Additionally, observed cases are notable in Latin America, Asia, Oceania, and select European countries.[5,6,7]

Clinically, the onset of chromoblastomycosis often follows trauma, leading to the inoculation of the causative fungus.[3,8] Manifesting with diverse features, the initial lesion typically presents as a slowly spreading verrucous papule. A definitive diagnosis relies on the presence of muriform cells in the tissue and the isolation of the causative agent through culture examination.[1,2,5,6,7]

Managing chromoblastomycosis poses challenges for clinicians, particularly in severe and recalcitrant cases. Treatment modalities include physical therapy, chemotherapy, and combination therapy.[7] Notably, heat therapy emerges as a conventional yet effective alternative among physical therapies, frequently employed as an adjuvant therapy in chromoblastomycosis.

This paper presents a compelling case of chromoblastomycosis treated with pulsed dose itraconazole in combination with heat therapy. The case not only outlines the diagnostic approach but also underscores the significance of employing appropriate and affordable treatment modalities in managing this challenging fungal infection.

Case Presentation

A 54-year-old Southeast Asian male presented to the outpatient clinic with a chief complaint of a lump on his right leg, a condition persisting for approximately 10 years. Throughout his adolescence and adult life, the patient worked as a farmer in an outdoor setting, often without wearing footwear. Initially attributing his skin condition to minor injuries caused by grass or wood branches during garden work, the patient noted that these scratches would heal but gradually transformed into painless, persistent, small nodules. These nodules progressed in size, thickness, and surface alterations. Notably, the patient denied experiencing significant weight loss, prolonged cough, night sweats, or any other systemic diseases.

Dermatological evaluation of the distal right leg revealed multiple erythematous nodules with well-defined borders, oval to round in shape, measuring 1.5 to 2.5 cm in diameter. The nodules' surface exhibited a verrucous appearance, and several lesions demonstrated a linear pattern around the patient's ankle, as illustrated in Figures 1a-1d. Additionally, scattered dry erosions covered with brownish and dark crusts, measuring 0.1 to 0.3 cm in diameter, were observed in some areas, as depicted in Figures 1b and 1d.

Figures 1a-1d. The lesion on the right ankle appears to form a linear growth pattern towards the patient's healthy skin with a verrucous surface nodule.

The KOH examination of skin scrapings did not reveal sclerotic, muriform cells, or fungal elements. Nevertheless, histopathological examination of the skin biopsy tissue, utilizing hematoxylin and eosin (HE) staining, indicated the presence of golden-brown, thick-walled round cells around the granuloma and abscess area, as illustrated in Figure 2. No evidence of tuberculoid granuloma, characteristic of mycobacterial lesions, or squamous cell carcinoma was found, leading to the exclusion of these possibilities. Consequently, the histological morphological features of the lesions on the patient's right ankle were consistent with the diagnosis of chromoblastomycosis.

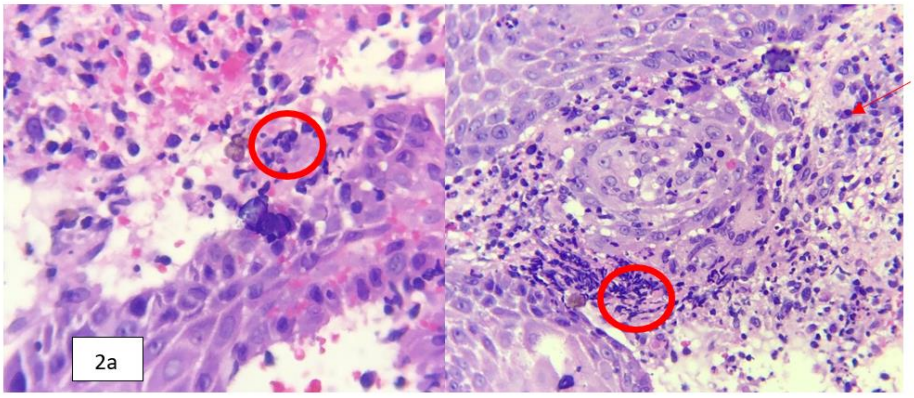

Figure 2a. Showing different magnifications, showing medular bodies

Subsequent culture on SDA media revealed the growth of black fungal colonies with a slightly irregular surface and a velvety greyish layer, as depicted in Figures 3. Microscopic examination using lactophenol cotton blue staining of the colony culture exhibited long, branched hyphae and conidia with a flask shape, known as thin-walled and long phialides, as seen in Figure 4. The suspected causative species was identified as *Fonsaceae pedrosoi*.

Figures 3a,b. Fungal colonies. Figure 3b shows a blackish colony covered with a velvety greyish surface.

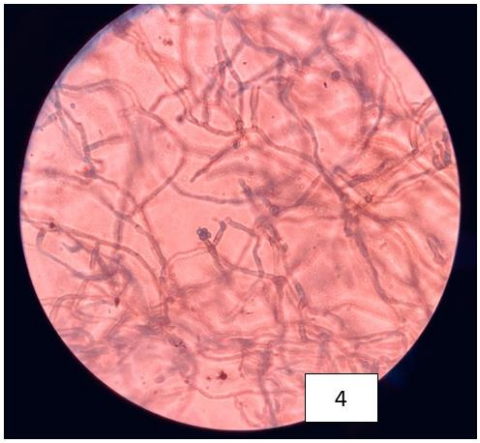

Figure 4. Samples taken from cultures on media

In light of the patient's history, physical examination, and supporting investigations, the working diagnosis was confirmed as chromoblastomycosis. The patient was managed on an outpatient basis with itraconazole 400 mg every 24 hours. Warm compress therapy was advised for home use. Remarkable improvement was observed after one month of this therapeutic regimen, as depicted in Figures 5a-5d.

Figure 5a-d. Shows improvement of the lesion in the form of a smoother nodule surface and reduced black dots.

Discussion

Chromoblastomycosis, a chronic fungal infection affecting the skin and subcutaneous tissue, is primarily caused by pigmented fungi forming sclerotic, muriform bodies within the tissue.[2,5,6] The predominant causative agent is a saprophytic fungus found in soil, wood, and plants.[8] *Fonsecaea pedrosoi* being the most common, followed by *Phialophora verrucosa*, *Cladosporium carrionii*, *Fonsecaea compacta*, and *Rhinocladiella aquaspersa.* In Indonesia, reported cases are notably rare, with only 13 documented from 1930 to 2019, showing a higher prevalence in males aged 30 to 60, possibly linked to occupational factors and a higher risk of inoculation trauma, particularly in agriculture and forestry workers.[9] The primary mode of infection involves traumatic inoculation of the causative agent into the host tissue, often stemming from unnoticed injuries like thorn or wood splinter punctures. In this case, the patient's occupation, involving daily garden work and walking barefoot, likely exposed him to such trauma. Other potential risk factors include age, low socioeconomic status, poor nutrition, and inadequate personal hygiene.

Chromoblastomycosis's pathogenesis is intricate, dependent on factors such as the host's immune response, fungal virulence, and exposure level to the causative agent. Skin lesions are variable, typically initiating at the site of traumatic inoculation, with slow, asymptomatic growth over several years to decades. Lesion types include nodular, tumorous, verrucous, plaque, and cicatricial. In our case, the patient initially presented with a blister that progressed into a persistent nodular lesion spreading to surrounding healthy skin, characterized by nodules with uneven surfaces or reddish-colored verrucose with black dots.[10]

Supporting examinations, including potassium hydroxide (KOH 10%) examination, culture on SDA medium at 25 to 30ºC, and histopathological examination, are crucial for a correct chromoblastomycosis diagnosis. Specific identification relies on culture examination, but in our case, the KOH examination did not reveal muriform bodies, potentially due to improper sampling.[2,5,6,7,11]

Therapeutic approaches encompass physical therapy, chemotherapy, and combination therapy. Physical therapy options include surgery, frozen surgery, and thermotherapy, while

common chemotherapy modalities are indicated for extensive and long-standing lesions. First-line therapies are itraconazole (200-400mg/day) and terbinafine (250-500 mg/day) for 6 to 12 months, with posaconazole for refractory cases. Pulse dose itraconazole, with its advantages of high cure rates, minimal side effects, and improved compliance, has shown success in reported cases.[12] Pulse dose itraconazole, with its advantages of high cure rates, minimal side effects, and improved compliance, has shown success in reported cases.[13]

Combination therapy, an option for refractory or severe cases, can involve physical therapy and chemotherapy or systemic therapy. Reports on the combination of heat therapy, such as warm compress with itraconazole, have shown promising results. Heat therapy inhibits fungal development by restraining pathogen growth at temperatures over 42 to 46°C, making it a favorable consideration for combination therapy. Its application in Japan resulted in clinical improvement and negative microscopic examination and culture results. This cost-effective combination alternative allows patients to administer it themselves.[14]

In our case, the patient received pulsed dose itraconazole (400 mg/day) alongside heat therapy. The therapy choice considered the lesion extent requiring systemic treatment, drug availability, patient compliance, and economic ability. Combining itraconazole with heat therapy aimed to reduce drug side effects and additional costs. The planned therapy duration ranged from 8 to 12 months, aligning with chromoblastomycosis cure criteria. Despite the limitation of a lack of follow-up information after one month due to the patient not returning, the case exhibited improvement characterized by a smoother nodule surface and reduced black dots.

Conclusion

This case represents a rare occurrence in Indonesia. The diagnosis relied on thorough anamnesis, physical examination, and additional investigations. The patient fulfilled the epidemiological, clinical, and supporting criteria for chromoblastomycosis. Treatment involved a pulse dose of itraconazole and daily heat therapy, offering a cost-effective and patient-friendly combination that can be self-administered at home. However, to comprehensively assess clinical and mycological cure, monitor therapy side effects, and evaluate potential disease complications, follow-up observations are essential. Further research and long-term observations will contribute valuable insights into the efficacy and outcomes of this combined therapeutic approach for chromoblastomycosis.

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