Triple therapy approach for treating chromoblastomycosis in a Lebanese patient

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Key clinical message:

Chromoblastomycosis, though rare in non-endemic regions like Lebanon, should be considered in patients presenting with chronic, verrucous skin lesions unresponsive to conventional therapies. Multimodal treatment combining oral antifungals, cryotherapy, and adjunctive topical therapies like 5-Fluorouracil demonstrates efficacy in managing refractory cases.

Introduction

Chromoblastomycosis is a chronic granulomatous infection of the skin caused by several pigmented fungi, resulting in the formation of slow growing verrucous plaques and nodules 2. In this article we present the first documented case of chromoblastomycosis in Lebanon, a region not previously associated with this infection.

Case History/Examination

A 70-year-old female with diabetes and heart failure presented with asymptomatic plaques and nodules on her left hand over six months, treated unsuccessfully with oral steroids and antibiotics. Physical examination revealed three cauliflower-like hyperkeratotic nodules with secondary ulcerations and pustules on the left forearm, without lymphadenopathy (Fig. 1 – a, b). The patient denied any insect bites, occupational exposure, or travel history, but reported spending time gardening.

Methods

Differential Diagnosis, Investigations, and Treatment:

The differential diagnoses included tuberculous and non-tuberculous mycobacterial skin infection, neutrophilic dermatosis, sarcoidosis, deep fungal infection of the skin, sporotrichiosis, and leishmaniasis. Multiple biopsies were taken for histopathologic examination, mycobacterial PCR analysis, acid-fast culture, bacterial, and fungal cultures.

Histopathology showed hyperkeratotic skin with parakeratosis, pseudo-epithiliomatous epidermis and marked mixed interstitial inflammation with granulomatous and abscess formation in the dermis in favor of an infectious process. Special stains, mycobacterial PCR and acid fast cultures were negative. Bacterial culture was positive for Streptococcus agalactiae and the patient was started on amoxicillin/clavulanic acid. However, lesions kept growing and became more exophytic and verrucous in appearance with overlying black dots (Fig. 1- c,d). A deep fungal infection of the skin was highly suspected, specifically chromoblastomycosis. Potassium Hydroxide examination of the black dots from the surface of the lesion showed numerous spherical spores, characteristic of muriform bodies (Fig. 2) and fungal culture on sabouraud dextrose agar grew brownish colonies confirming chromoblastomycosis. The patient was started on oral terbinafine 500 mg daily and once weekly sessions of cryotherapy without improvement after 6 weeks, then switched to oral itraconazole at 200 mg daily with no improvemen after 4 weeks.

Results

After two therapy regimens failure, she was initiated on a combination of triple therapy consisting of 6 sessions of cryotherapy using liquid nitrogen once weekly, and oral itraconazole 100 mg twice daily with topical 5-Fluorouracil (5-FU) five times per week. Six weeks later this multidrug regimen resulted in significant lesion regression and was maintained on this regimen for an additional 6 months. At follow-up patient shows almost 90% clearance in her lesions.

Discussion

Chromoblastomycosis is a tropical skin infection caused by various dematiaceous fungi, such as *Fonsecaea spp* . and*Cladophialophora spp* . Clinically, it manifests as slow-growing, warty plaques and nodules that can ulcerate[2,3]. As a neglected tropical disease, chromoblastomycosis can lead to serious complications, including secondary bacterial infections, chronic lymphedema, deep tissue fibrosis, and squamous cell carcinoma[4]. In our case, Streptococcus agalactiae was identified as a superinfection, marking the first reported association between these two infectious agents. Diagnosing chromoblastomycosis is challenging due to its ability to mimic various infectious and inflammatory disorders[3,4]. The fungus induces a granulomatous response in

the dermis, with pseudoepitheliomatous hyperplasia of the epidermis. The fungal elements, often visible as sclerotic or muriform bodies, are brown and extruded transepidermally, appearing as black dots on the lesion's surface, which is characteristic of chromoblastomycosis[3]. Potassium hydroxide examination of these black dots, revealing muriform bodies, provides a simpler, less invasive diagnostic method, especially when these bodies are not seen on histology[4]. The antifungal drugs of choice are itraconazole or terbinafine, administered alone or together for a year or more. Other treatment options include oral potassium iodide solution, cryotherapy, posaconazole, voriconazole, photodynamic therapy, and excision of solitary lesions. In our case, terbinafine and itraconazole monotherapies were ineffective, and other treatment modalities, such as voriconazole or photodynamic therapy, were unavailable. The patient showed significant improvement with a combination of cryotherapy, topical 5-Fluorouracil (5-FU), and oral itraconazole[2–4]. To our knowledge, this is the first case of chromoblastomycosis reported in Lebanon[1], highlighting a novel therapeutic approach for treatment-resistant cases where broader-acting antifungals like voriconazole and posaconazole are not available.

Conclusion

Chromoblastomycosis is a neglected tropical disease presenting as slowly growing verrucous lesions. Dermatologists should consider this diagnosis, even in non-endemic regions, and recognize the efficacy of a multidrug regimen involving cryotherapy, topical 5-Fluorouracil, and itraconazole in managing treatment-resistant cases.

Figures Legend:

Figure 1: a, b) Hyperkeratotic erythematous nodular lesions with secondary ulceration and pustules. c) Evolution over time, the lesion became more hyperkeratotic and exophytic. d) black dots on the surface of the lesion, representing sclerotic bodies.

Figure 2: Numerous muriform/sclerotcic bodies seen on KOH examination

Author Contributions: Joe khodeir conceived the study, diagnosed and managed the patient, and drafted the manuscript. Paul ohanian conducted the literature review and contributed to the manuscript writing. Hala Megarbane contributed to the diagnosis and treatment discussion. All authors critically reviewed and approved the final manuscript

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