*L*ibyan *M*edical *J*ournal
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Case report

Rifampicin and Terbinafine in the Treatment of Chromoblastomycosis: A Case Report

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Citation. Lagha S, Musbah F. Rifampicin and Terbinafine in the Treatment of Chromoblastomycosis: A Case Report. Libyan Med J. 2024;16(2):164-167.

Received: 12-08-2024
Accepted: 02-10-2024
Published: 05-10-2024

Funding*: This research received no external funding.*

Conflicts *of Interest: The authors declare no conflict of interest.*

Abstract

Chromoblastomycosis, a deep fungal infection, is recognized as a rare neglected tropical disease predominantly affecting individuals residing in impoverished conditions. Its clinical presentation is often chronic and early diagnosis can be missed due to the nonspecific clinical features in the early stages. Only four cases have been documented in Libya, where deep fungal infections are uncommon, with a particular suspicion of occurrence in the rural southern areas. This report presents a fifth case identified at Tripoli Central Hospital, of a 43-year-old female patient who experienced a relapsing-remitting course over two decades. She presented with a progressively enlarging erythematous warty plaque characterized by pus discharge, a yellowish thick crust, scales, and micro erosions on the dorsal side of her left forefoot, the patient was treated with rifampicin and terbinafine, resulting in significant symptom improvement and subsequent remission.

Keywords: *Chromoblastomycosis, Rifampicin, Terbinafine, Case Report.*

Introduction

Chromoblastomycosis is a rare chronic granulomatous disease affecting the skin and subcutaneous tissue, resulting from pigmented dematiaceous fungi with 7,740 cases documented worldwide moreover it's considered to be endemic in tropical and subtropical regions [1,2]. This fungus has the ability to infiltrate the cutaneous tissue by entering through an inoculation site, typically through skin trauma with contaminated soil [3]. with chronic course and different clinical presentations that vary from verrucous papules to ulcerative tumor-like masses, initial diagnosis can be misleading, and histopathological studies are needed [4]. In this case report, we present a case of chromoblastomycosis that was diagnosed over twenty years ago. The patient has gone through a relapse-remission course, and rifampicin and terbinafine are the mainstays of treatment for achieving remission. While four cases have been reported in Libya, we report a fifth case from Tripoli Central Hospital.

Case report

A 43-year-old housewife has been diagnosed with chromoblastomycosis on the right foot since 1993 in Tripoli Central Hospital after sustaining an injury from walking barefoot on contaminated soil. Although She initially achieved remission through topical treatment, she encountered a more aggressive relapse in 2012. In 2023, the patient presented with a lesion that had progressively developed at the same site. on examination, a large erythematous warty plaque was observed, characterized by pus discharge, yellowish, thick crust, scales, and micro erosions on the dorsal aspect of the left forefoot, with swelling in the second and third toes. Furthermore, the leg had notable swelling, exhibiting a shiny and erythematous appearance (Figure 1). A systematic review revealed symptoms of a dry cough, vomiting, fatigue, and headaches. Routine investigations indicated a hemoglobin level of 10 g/dL, and a white blood cell count of 18.7 x 10^3 cells/µL, predominantly consisting of neutrophils 16.7 x 10^3 cells/µL, (89.3%). A Doppler ultrasound examination showed a subcutaneous fluid collection in the lateral aspect of the right foot, accompanied by multiple reactive lymph nodes in the popliteal and inguinal regions, which suggests the presence of cellulitis (Figure 2). All other diagnostic tests and imaging studies were within normal parameters.
The clinical diagnosis was confirmed through skin biopsy with a PAS stain, which showed epidermal hyperplasia, spongiosis with neutrophil exocytosis, and the formation of an intraepithelial microabscess. The dermis showed dense mixed inflammatory cell infiltrate and

the presence of epitheloid granulomas with giant cells. Brown-pigmented spores arranged in clusters with septations were also detected (Figure 3). Unfortunately, culture wasn't available and couldn't be requested.

Throughout her month-long hospitalization, she was administered rifampicin at a dosage of 300 mg twice daily, terbinafine at 500 mg once daily, ciprofloxacin intravenously at 200 mg, potassium permanganate diluted to 1/8000, and fusidic acid cream for topical application. The treatment led to the alleviation of symptoms and a significant reduction of the lesion, which was sustained at both 1-month and 3-month follow-ups. The treatment plan involves the continuation of rifampicin while discontinuing terbinafine after two months (Figure 1).

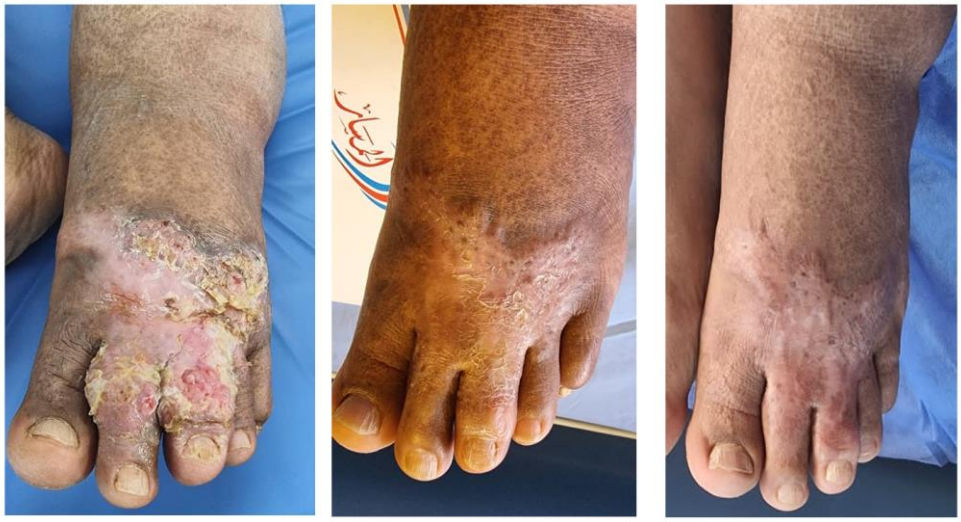

Figure 1. Left shows a lesion at the time of admission; erythematous warty plaque with a yellowish, thick crust, scales, and erosions on the dorsal aspect of the forefoot, with swelling in the second and third toes. Middle shows marked improvement after one month of treatment. Right shows maintenance of remission after 3 months.

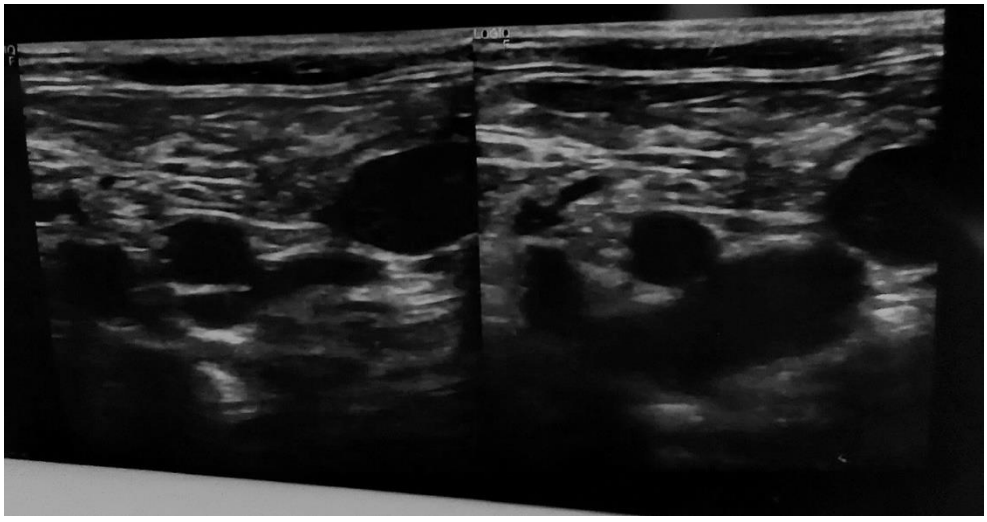

Figure 2. Doppler ultrasound revealed Subcutaneous fluid collection.

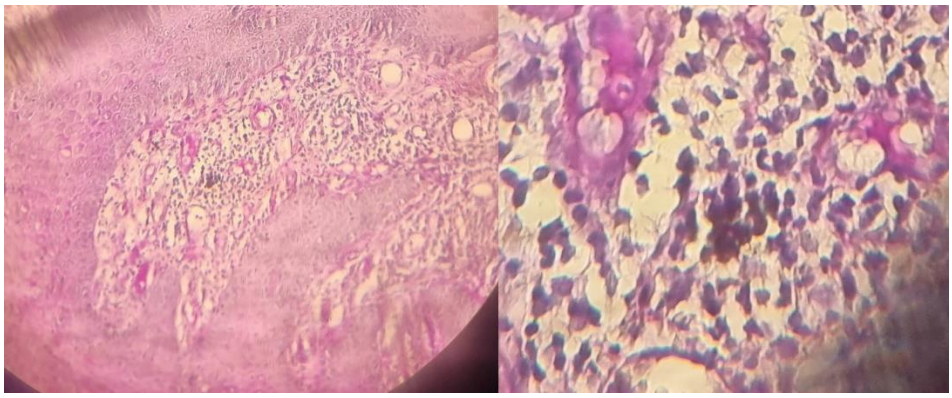

Figure 3. Left Hematoxylin and eosin and Periodic acid-Schiff stain; epidermal hyperplasia spongiosis with neutrophil. The right dermis shows dense mixed inflammatory cell infiltration and the formation of epitheloid granulomas with brown-pigmented spores.

Dissection

Chromoblastomycosis (CBM) is recognized as a rare neglected tropical disease predominantly affecting individuals residing in impoverished conditions, The precise geographical spread of this disease remains unclear, although a recent study documented 7,740 cases spanning from 1914 to 2020, It is primarily prevalent in tropical and subtropical regions, In Africa, 1,875 cases were reported, with only 4 cases identified in Libya, where Phialophora spp was the most commonly isolated organism, resulting in a lower incidence rate compared to other East African countries. For instance, Madagascar reported 1,323 cases [1,5]. Chromoblastomycosis is a rare chronic granulomatous disease affecting the skin and subcutaneous tissue, resulting from pigmented dematiaceous fungi with Fonsecaea pedrosoi, Fonsecaea monophora, and Cladophialophora carrionii being the most prevalent causative agents, and it's endemic in tropical and subtropical regions [2]. This fungus has the ability to infiltrate the cutaneous tissue by entering through an inoculation site, typically through skin trauma with contaminated soil [3]. With different clinical presentations; verrucous papules and nodules, scaly plaques, exophytic or ulcerative tumor-like masses, and cicatricial plaques of varying sizes. Chromomycosis typically follows a slow and chronic progression and seldom leads to mortality [4].

The initial lesion can be misdiagnosed and nonspecific, thus diagnosis relies on the histopathological identification of aggregation of pigmented thick-walled fungal cells in the dermis, referred to as medlar bodies, muriform bodies, or sclerotic bodies [3]. Initiating treatment at an early stage is crucial as it yields the most favorable outcomes within a span of approximately three to six months. Many treatment options can be considered according to the patient clinical condition including oral anti-fungal, cryotherapy, and surgical interventions. Patients with extensive lesion and limb swelling often need treatment for over a year, regardless lymphedema may persist [5]. Supposing it was left untreated it may result in; tissue fibrosis, the formation of squamous cell carcinoma in the area of the original infection, lymphedema, or secondary bacterial infections [6].

In Libya, the occurrence of the infection is rare, but suspected particularly in the rural southern region, with four cases reported in Libya, Hofmann et al. and Siala et al. both reported the growth of Phialophora verrucosa. While Bhaktaviziam et al. and Ellabib et al. found Fonsecaea compacta and Cladophialophora carrionii respectively, with variation in age from 12 to 60 years old and involvement different sites including face upper limbs and lower limbs with or without history of trauma, and all four cases shared chronic presentation with relapse remission course ranging from 6 to 15 years with good response to oral antifungal, Although CBM complication are usually limited to scarring and local spreading Hofman et al. reported lymphadenopathy paranasal sinuses involvement and x-ray changes indicating osteomyelitis [7-10].

The patient in this instance had two previous relapses following the cessation of antifungal treatments. During her latest hospitalization, she received rifampicin and terbinafine. rifampicin exhibited considerable effectiveness over a one-month period. After her discharge, the ongoing administration of this treatment resulted in a successful remission, with a reduction in lesion size and an improvement in symptoms.

Rifampicin serves as a powerful inducer of CYP3A4 and is an FDA-approved treatment for tuberculosis. It functions by inhibiting DNA-dependent RNA polymerase, which contributes to its efficacy as a bactericidal agent against a broad spectrum of pathogens, including rare fungal infections in individuals with compromised immune systems [11,12].

Our main disadvantage was the lack of culture media can make identifying the causative organism challenging. It's crucial for enhancing our understanding of the disease and improving its management without missing the diagnosis. Increased case reporting is essential to address concerns about missing cases and to establish a solid background to the prevalence of this disease.

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