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CASE REPORT

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Invasive Squamous Cell Carcinoma Arising in Long-Standing Chromoblastomycosis Requiring Limb Amputation: A Case Report

Uzun Süreli Kromoblastomikoz Zemininde Gelişen İnvaziv Skuamöz Hücreli Karsinom: Olgu Sunumu

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ABSTRACT
Chromoblastomycosis is a chronic granulomatous infection of the skin and subcutaneous tissue caused by melanized fungi introduced through traumatic implantation. Although typically indolent, long-standing lesions may undergo malignant transformation into squamous cell carcinoma (SCC). We report a 77-year-old man with a 10-year history of a verrucous lesion on the right foot, which progressively enlarged and evolved into a non-healing ulcer. Histopathological examination revealed a well-differentiated invasive SCC infiltrating the reticular dermis, associated with dense fibrosis, chronic granulomatous inflammation, and numerous muriform bodies consistent with chromoblastomycosis. Due to extensive tissue destruction and functional impairment, lower limb amputation was performed. This case highlights the carcinogenic potential of chronic inflammatory dermatoses and underscores the critical role of histopathological evaluation and long-term surveillance in persistent chromoblastomycosis.

Keywords: Chromoblastomycosis, squamous cell carcinoma, chronic inflammation, malignant transformation.

ÖZET
Kromoblastomikoz, travmatik inokülasyon yoluyla deriye giren melanin içeren mantarların neden olduğu, deri ve subkutan dokunun kronik granülomatöz bir enfeksiyonudur. Genellikle yavaş seyirli olmakla birlikte, uzun süreli lezyonlar skuamöz hücreli karsinom (SCC) gelişimine dönüşebilir. Bu yazıda, sağ ayakta kronik verrüköz lezyonu bulunan ve zamanla iyileşmeyen ülser haline ilerleyen 77 yaşında bir erkek hasta sunulmaktadır. Histopatolojik incelemede, retiküler dermisi infiltre eden iyi diferansiye invaziv SCC; buna eşlik eden yoğun fibrozis, kronik granülomatöz inflamasyon ve kromoblastomikoz ile uyumlu çok sayıda muriform cisim saptanmıştır. Geniş doku destrüksiyonu ve fonksiyon kaybı nedeniyle alt ekstremite amputasyonu uygulanmıştır. Bu olgu, kronik inflamatuvar dermatozların karsinojenik potansiyelini vurgulamakta ve persistan kromoblastomikoz olgularında dikkatli histopatolojik değerlendirme ile uzun dönem izlem gerekliliğine dikkat çekmektedir.

Anahtar Kelimeler: Kromoblastomikoz, skuamöz hücreli karsinom, kronik inflamasyon, malign dönüşüm.

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INTRODUCTION

Chromoblastomycosis (CBM) is a chronic granulomatous infection of the skin and subcutaneous tissue caused by melanized fungi of the order Chaetothyriales, primarily Fonsecaea and Cladophialophora species (1,3). Infection occurs through traumatic inoculation of fungal elements and predominantly affects rural populations in tropical and subtropical regions (1–3). Clinically, CBM typically begins as papules or plaques that gradually progress into verrucous, hyperkeratotic, cauliflower-like lesions, which may persist for decades (2,3). Histopathologically, the disease is characterized by the presence of muriform (sclerotic) bodies within a granulomatous inflammatory background (1,3).

Chronic lesions frequently exhibit fibrosis and pseudoepitheliomatous hyperplasia, which may mimic squamous cell carcinoma (SCC) (3). Although uncommon, malignant transformation into SCC has been consistently reported in long-standing, untreated cases (4,5). Herein, we report a case of invasive SCC arising in chronic chromoblastomycosis requiring limb amputation.

CASE

A 77-year-old man presented with a 10-year history of a verrucous lesion on the right foot, with progressive enlargement and eventual evolution into a chronic, non-healing ulcer. The patient reported irregular use of oral antifungal therapy (itraconazole) over several years, without sustained clinical response. Given the progressive growth and ulceration, malignant transformation was suspected, and the patient underwent lower limb amputation. Gross examination revealed an extensive verrucous and ulcerated lesion involving the skin and underlying soft tissues (Fig. 1).

Figure 1. Gross specimen of a transtibial (below-knee) amputation showing an ulcerated and verrucous cutaneous lesion involving the foot in a background of long-standing chromoblastomycosis.

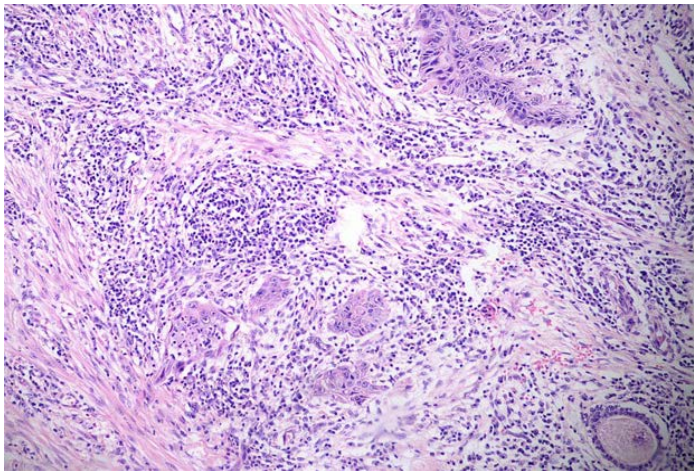

Figure 2. H&E, X20; Area of the neoplasm characterized by irregular squamous nests infiltrating the deep dermis with an associated inflammatory response.

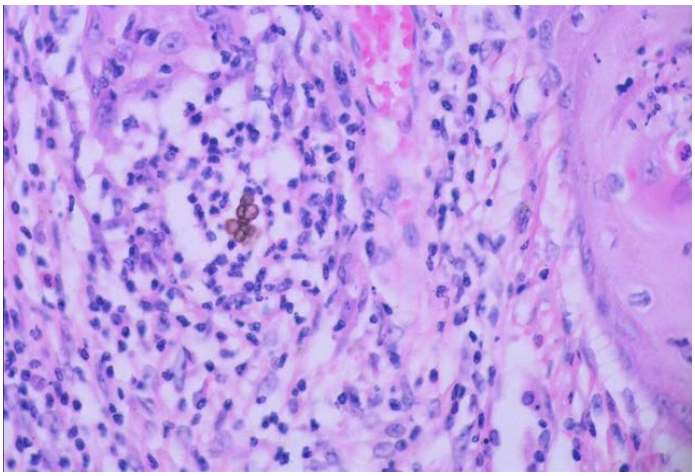

Figure 3. H&E, X40; Dermal granulomatous inflammation containing characteristic pigmented muriform (sclerotic) bodies, consistent with chromoblastomycosis.

Microscopic examination showed a well-differentiated invasive squamous cell carcinoma composed of irregular nests and cords infiltrating the reticular dermis to a depth of 4 mm, with prominent keratin pearl formation (Fig. 2). No angiolymphatic or perineural invasion was identified. The adjacent epidermis exhibited pseudoepitheliomatous hyperplasia. The dermis showed marked fibrosis, chronic granulomatous inflammation, and neutrophilic aggregates. Numerous pigmented muriform (sclerotic) bodies were identified within the inflammatory foci, confirming chromoblastomycosis (Fig. 3). Given the characteristic pigmentation of these fungal elements on hematoxylin–eosin staining, additional histochemical stains

were not required. Surgical margins, including skin, soft tissue, and bone, were free of carcinoma. After two years of follow-up, the patient remains disease-free. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

DISCUSSION

Malignant transformation of chromoblastomycosis into squamous cell carcinoma, although uncommon, is well documented, particularly in long-standing lesions. In a Brazilian series of seven cases, all patients developed SCC after more than 10 years of disease duration, frequently requiring amputation due to extensive local invasion (4). Similarly, individual reports have described malignant transformation in chronic, often inadequately treated infections, highlighting the role of persistent inflammation and suboptimal treatment (6). Chronic inflammation and sustained epithelial regeneration are key drivers of inflammation-associated carcinogenesis. In chromoblastomycosis, persistent infection creates a microenvironment characterized by fibrosis, immune dysregulation, and continuous epithelial proliferation, promoting genomic instability and ultimately facilitating malignant transformation (4).

Histopathological examination remains the cornerstone for distinguishing pseudoepitheliomatous hyperplasia from true invasive carcinoma. This reactive epithelial proliferation may closely resemble well-differentiated SCC, particularly in superficial or limited biopsy specimens, making the identification of dermal granulomatous inflammation and muriform bodies essential to avoid misdiagnosis (3). In contrast, true SCC is defined by destructive stromal invasion, cytologic atypia, and keratin pearl formation, as observed in the present case.

Clinically, features such as rapid growth, ulceration, or lack of response to therapy should raise suspicion for malignant transformation (4). The present case is consistent with prior reports and further supports the role of chronic inflammation, fibrosis, and sustained epithelial regeneration in carcinogenesis associated with chromoblastomycosis. Management remains challenging due to fibrosis and chronic tissue damage resulting from long-standing infection. In advanced cases, radical surgical interventions, including amputation, may be required (4,5). Early recognition and close surveillance of chronic chromoblastomycosis lesions are essential to prevent delayed diagnosis of malignant transformation.

DECLARATIONS

Conflict of Interest: *The authors declare that they have no conflict of interest.*

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