

Squamous cell carcinoma arising from a chromomycosis lesion caused by *Rhinocladiella aquaspersa* with postsurgical recurrence of chromomycosis



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INTRODUCTION

Chromomycosis is a chronic granulomatous infection of the skin and the subcutaneous tissue that often follows traumatic injury and inoculation of the agent, which belongs to the group of dematiaceous fungi.

The main genera associated with the condition are *Fonsecaea*, *Cladophialophora*, *Phialophora*, and *Rhinocladiella*. In Brazil, although 80% of the cases result from *Fonsecaea pedrosoi* infection, only 3% are related to the genus *Rhinocladiella*.¹

Chromomycosis is characterized by hyperproliferation of the tissues involved and by the presence of muriform cells on histopathologic examination. The disease classification, by Arturo Carrión (1950), is based on the different types of dermatologic lesions that may appear: nodular, tumoral, verrucous, scarring, and plaque.²

Chromomycosis lesions may undergo malignant transformation into squamous cell carcinoma that often leads to amputation.³ We report a case of chromomycosis, caused by a rare agent, in Manaus (Amazonas, Brazil). The chronic infection transformed into squamous cell carcinoma and culminated in amputation of the affected limb. Later, chromomycosis recurrence was observed in the stump.

CASE REPORT

A 79-year-old man was referred to our department, in Manaus (Amazonas, Brazil), in January of 2017. He presented with chronic chromomycosis for

the last 20 years and had been irregularly treated with itraconazole. His chief complaint, however, was a fetid odor that started to emanate from his injury in December of 2016. Upon examination, a verrucous exophytic plaque affecting the dorsal side of his right hand was observed, including proximal phalanx of fingers, preventing their flexion (Fig 1). The patient reported intense local pain.

The biopsy result showed a proliferation of cells with hypertrophic, hyperchromatic nuclei, eosinophilic cytoplasm, and keratin pearls, which indicated a well-differentiated squamous cell carcinoma (Fig 2).

The patient had multidisciplinary follow-up, including orthopedic, surgical, and dermatologic evaluation. The medical team, along with the patient, unanimously decided to amputate the affected limb. One month after the procedure, in a follow-up visit to our department, new verrucous lesions on the stump appeared (Fig 3).

Dermoscopy testing found regular linear vessels, crusts, and several black dots above an erythematous background. The black dots, characteristically present in chromomycosis, corresponded to a defense mechanism of the host: the transepithelial elimination of dematiaceous fungi.⁴

Histopathologic examination of the lesion was performed because of the possibility of squamous cell carcinoma recurrence; nevertheless, it showed hyperkeratosis and hyperplasia of the epithelium and dense dermal infiltrate (lymphocytes,

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Fig 1. Verrucous exophytic plaque in the right hand with an evolution of 20 years with irregular medical care.

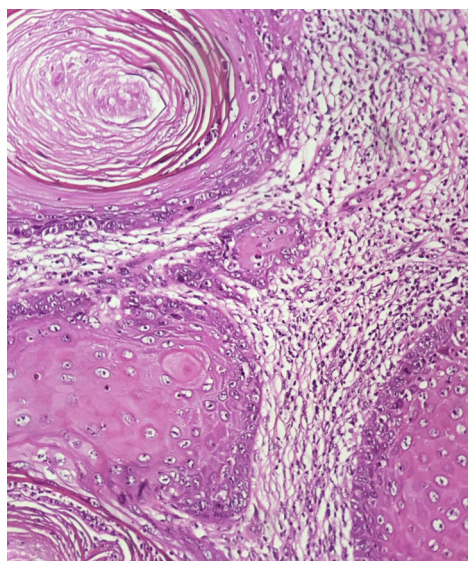


Fig 2. Proliferation of cells with hypertrophic, hyperchromatic nuclei; eosinophilic cytoplasm; and keratin pearls, which indicate well-differentiated squamous cell carcinoma. (Hematoxylin-eosin stain; original magnification: $\times 20$.)

histiocytes, eosinophils, and plasma cells) and muriform cells, confirming the diagnosis of chromomycosis (Fig 4).

Mycological culture was performed. Portions of skin biopsies were inoculated onto culture media Sabouraud dextrose agar supplemented with chloramphenicol (0.5 g/mL) and incubated at 25°C and 37°C for two weeks. Microscopically, the fungus was identified as *Rhinocladiella aquaspersa* based on morphological characteristics.

The patient underwent a combined therapy with both pharmacologic and physical treatment. First-line medication for chromomycosis, itraconazole 100 mg twice daily,² was combined with cryotherapy.

DISCUSSION

The association between squamous cell carcinoma and chromomycosis infection has already been demonstrated in several studies.⁵ In 7 cases

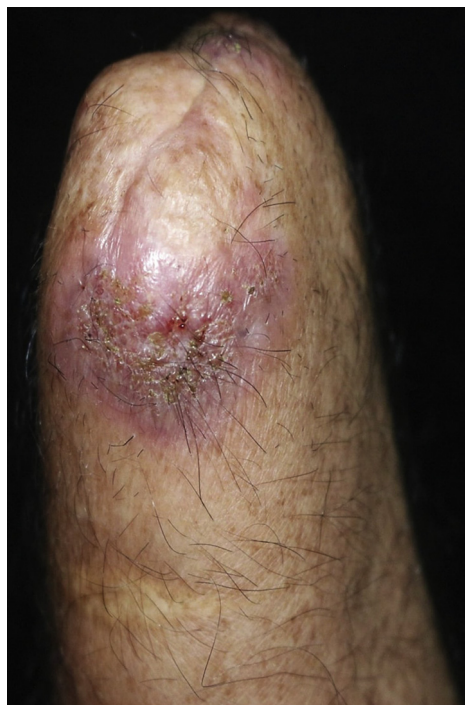


Fig 3. Stump with new lesions 1 month after the surgery.

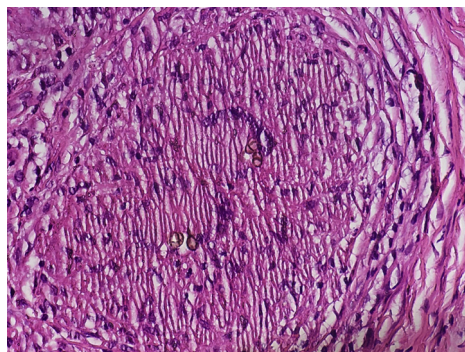


Fig 4. Presence of muriform cells, confirming the diagnosis of chromomycosis. (Hematoxylin-eosin stain; original magnification: $\times 100$.)

described by Jamil et al,⁵ malignancy occurred between 20 to 30 years after the infection.

Although the pathogenesis of squamous cell carcinoma resulting from a lesion of chromomycosis is still not fully understood, it is believed that the chronic inflammation, with enzymes, free radicals, and cytokines release may trigger carcinogenesis.³

According to the skin cancer foundation, anyone who has had squamous cell carcinoma has an increased chance of getting it again, especially in the same skin area or nearby, and typically within the first 2 years after surgery.⁶ On the other hand, recurrence of chromomycosis after resection is less common. The infection can spread contiguously, with rarely reported lymphatic and hematic dissemination.⁷

Azevedo et al³ found that 3 of 7 patients in his study experienced recurrence of chromomycosis after amputation; however, not many other studies support these findings. Possible causes for recurrence of chromomycosis are inadequate treatment, chronicity of the disease, and a deficient immune system.

Chromomycosis has a low cure ratio because the agents have different patterns of sensitivity to antifungals and have a high relapse ratio, especially in extensive infections as our case.⁸ Complications such as skin fibrosis and edema decrease the drug availability in the tissues, jeopardizing the treatment.⁸

The therapeutic options include physical methods, such as cryotherapy, surgery, and laser therapy and chemotherapy with itraconazole, 5-fluorouracil, amphotericin B, ketoconazole, fluconazole, itraconazole, terbinafine, and/or posaconazole.

According to Queiroz-Teles et al,² itraconazole is not only the best but also the most used therapy for chromomycosis, with cure rates ranging from 15% to 80%. Regarding *R aquaspersa*, Daboit et al⁹ found that terbinafine and itraconazole have better in vitro responses.

On the other hand, cryotherapy, which is recommended for small lesions (<15 cm²), induces inflammatory reaction and necrosis and is responsible for the destruction of fungi in chromomycosis lesions.²

Another option is to combine both therapies, which was our choice in this case, as itraconazole and cryotherapy is the recommended approach for extensive cases.¹⁰

We decided to write this report because of the unusual agent involved as well as the severe presentation. The importance of this report is also justified by the uncommon recurrence of the chromomycosis

infection on the amputation stump. Because chromomycosis has recently been added to the list of neglected tropical diseases of the World Health Organization, we strongly recommend further research on this disease to prevent cases like this from occurring again.

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