



## Successful treatment of chromoblastomycosis using cryosurgery in association with low-dose itraconazole

*Tratamento bem-sucedido da cromoblastomicose pela associação entre criocirurgia e itraconazol em dose baixa*

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### ABSTRACT

Chromoblastomycosis is a chronic granulomatous infection caused by dematiaceous fungi with varied clinical presentations, which may represent a therapeutic challenge. In this report, we present a case of chromoblastomycosis in a localized form, with a long evolution, in an elderly patient, resistant to previous drug therapies, successfully treated by the association of a physical method with systemic pharmacological treatment, which allowed the use of a reduced dose of the drug.

**Keywords:** Chromoblastomycosis; Cryosurgery; Itraconazole

### RESUMO

Cromoblastomicose é uma infecção granulomatosa crônica causada por fungos dematiáceos, com apresentações clínicas variadas, que podem representar um desafio terapêutico. Neste relato, apresentamos um caso de cromoblastomicose em forma localizada, de longa evolução, em paciente idoso, resistente a terapêuticas medicamentosas prévias, tratado com sucesso pela associação entre um método físico e um tratamento farmacológico sistêmico, o que permitiu o uso de dose reduzida do medicamento.

**Palavras-chave:** Cromoblastomicose; Criocirurgia; Itraconazol

## Case Report

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## INTRODUCTION

Chromoblastomycosis is a chronic granulomatous infection that affects the skin and subcutaneous tissue, caused by dematiaceous fungi (brown pigment-producing). In endemic areas, the prevalent species are *Fonsecaea pedrosoi* and *Cladophialophora carrionii*.<sup>1</sup> The lesions appear as slow-growing verrucous plaques, with the possibility of atrophy or formation of nodules and tumors. It can be considered an occupational disease, frequently occurring in rural workers. Most lesions occur on exposed areas, as the fungus is usually inoculated by trauma.<sup>2,3</sup>

In many cases, chromoblastomycosis treatment still represents a challenge due to the chronic and recurrent nature of the lesions, whether in the localized or extensive forms of the disease. Several reports have demonstrated the usefulness of associating pharmacological treatments with physical procedures to obtain better results.<sup>1</sup>

We report the successful treatment of a case of long-standing chromoblastomycosis using cryosurgery and low-dose itraconazole.

## CASE REPORT

A 71-year-old man presented pruritic lesions on his abdomen for 20 years with no improvement after several treatment attempts with topical agents and systemic antifungals. When the lesions appeared, the patient lived and worked in a rural area, where he reported, as a routine activity, the habit of carrying firewood in contact with the abdomen without any protection. Upon dermatological examination, the patient presented papules and verrucous plaques, well delimited, in the periumbilical region, more to the left, in a corymbiform arrangement (Figure 1). Histopathological examination defined the diagnosis of chromoblastomycosis, showing a chronic granulomatous reaction and epithelial hyperplasia, with the presence of brownish refractive fungi. Tissue culture isolation obtained by biopsy of the fungus *Fonsecaea pedrosoi* confirmed the diagnosis. The

patient underwent two cycles of application of liquid nitrogen in an open spray. Due to the extension, the lesions were divided by areas and treated sequentially until reaching freezing and halo formation (60 seconds). The second cycle was performed after the complete thawing of the lesions (10 minutes). Itraconazole, at a dose of 100 mg per day orally, was prescribed for continuous use until return. After 45 days, the patient showed significant improvement and partial regression of the lesions (Figure 2). He underwent a second cryosurgery session, and itraconazole was maintained at the same dosage. At 90 days, he presented complete regression of the lesions, and treatment was suspended (Figure 3). Follow-up was conducted for five years, with no recurrence of the condition (Figure 4).



**FIGURE 2:** Aspect of the lesions 45 days after the first cryotherapy session and use of itraconazole



**FIGURE 1:** Papules and verrucous plaques in the periumbilical region



**FIGURE 3:** Residual macular lesions after 90 days of itraconazole and two cryotherapy sessions



**FIGURE 4:** Final appearance, no signs of recurrence

## DISCUSSION

Patients with long-standing chromoblastomycosis, both in localized and extensive forms, require prolonged treatment with high-dose systemic antifungals, sometimes associated with physical methods.<sup>4</sup>

In a recent systematic review on the *in vitro* action of oral antifungal drugs available for chromoblastomycosis treatment, based on the minimum inhibitory concentration, the most effective drugs were, in descending order, posaconazole, terbinafine, itraconazole, and voriconazole.<sup>5</sup> However, in clinical practice, itraconazole can be considered the standard drug among the antifungals used. Its use has been recognized for a long time through reports of clinical and biological cures in about 40% of patients when applied for prolonged periods at dosages ranging from 200 mg to 400 mg per day.<sup>6</sup> During treatment with itraconazole, more significant tissue responses were recorded in the dermis, observing a reduction in the thickness of the epidermis, a partial or total decrease in the granulomatous

infiltrate, an increase in fibrosis, and quantitative/morphological alterations.<sup>7</sup>

Cryosurgery with liquid nitrogen has been described as an effective method to treat chromoblastomycosis for several decades.<sup>8-10</sup> Although it is accepted as an effective treatment modality, the mechanism that leads to the cure of the disease is still unknown. Exposure of cultures of the causative microorganisms to temperatures as low as  $-196^{\circ}\text{C}$  did not cause the agents to die.<sup>11</sup> These results demonstrate that cold alone cannot be responsible for their destruction. It is believed that late biological phenomena, such as necrosis with tissue destruction and alterations in the host's immune response, are responsible for eradicating fungi in the lesions.<sup>12,13</sup>

A strategy to increase cure rates and reduce recurrences is the association between different drugs, such as itraconazole and terbinafine, and combining physical methods with oral antifungals. Among these, the association between an oral antifungal and cryosurgery with liquid nitrogen has been one of the most described methods.<sup>14-16</sup> However, oral antifungals, in high doses and for prolonged periods, have their use limited by the high cost and the risks of major adverse events.

In this patient, performing surgery to remove the lesions was considered impractical due to the location and extent of the lesions. Because of the size of the resulting surgical defect, primary closure by approximation of the edges was unlikely, which would imply the need to use more complex techniques such as grafts or flaps. Another aspect considered, in the case of an elderly patient, was to avoid using drugs with potential adverse events in high doses and for a prolonged period.

Thus, the therapeutic approach adopted was to combine cryosurgery with liquid nitrogen, in a non-aggressive way, with oral antifungal, in a lower dosage than that recommended in the literature. This strategy proved to be effective, reducing costs and potential adverse events, providing clinical cures, and, consequently, a better quality of life for the patient. ●

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