COMUNICATION

Chromoblastomycosis associated with a lethal squamous cell carcinoma

Carcinoma epidermoide como complicação letal de lesões crônicas de cromoblastomicose

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Abstract: Chromoblastomycosis is a subcutaneous mycosis caused by the dermatophytic fungi Fonsecaea, Phialophora and Cladophialophora. Usual complications include secondary infection, lymphedema and elephantiasis. Associated malignancies have been found in chronic cases. This case report describes a 72 year-old male with a 30 year history of chromoblastomycosis in the gluteal region, who went on to develop a squamous cell carcinoma.
Keywords: Carcinoma, Squamous cell; Chromoblastomycosis; Chronic disease

Resumo: A cromoblastomicose é uma micose subcutânea, ocasionada por fungos dermatófitos, dos gêneros: Fonsecaea, Phialophora e Cladophialophora. As complicações habituais são: infecções secundárias, linfedema e elefantíase. Em lesões crônicas, tem-se documentado malignização. Relatamos um caso de um homem de 72 anos de idade, com cromoblastomicose de 30 anos de evolução, em região glútea, com desenvolvimento de carcinoma epidermoide.
Palavras-chave: Carcinoma de células escamosas; Cromoblastomicose; Doença crônica

INTRODUCTION

Chromoblastomycosis, also known as chromomycosis, Pedroso and Lane's disease or Fonseca's disease, is a subcutaneous mycosis caused by pigmented fungi of the Dematiaceae family, principally of the genera *Fonsecaea, Phialophora* and *Cladophialophora*. It affects the skin and subcutaneous tissue of the lower extremities and feet.

The disease is found worldwide and affects all ethnic groups. There have been reports of the condition in India, Burma, Sri Lanka, Indonesia, Australia, Finland, East Germany, Romania, the Czech Republic and Slovakia, Russia and in Gabon. In Asia, it has been found in Japan, China, the Philippines and Malaysia [1], as well as in numerous European countries. The most significant endemic focus of the disease worldwide may be in Madagascar, with one case for every 480 inhabitants. It is predominant in tropical and subtropical climates (80%), but has also been found in semi-desert regions of southern Africa.

In the Americas, the principal endemic zones are in northwestern Venezuela, the eastern Andes, between Caracas and Cali, Cuba, the Dominican Republic, Costa Rica, [2] Mexico and Brazil.

The most common etiological agent is *F. pedrosoi*; however, in Venezuela, the most common agent is *C. carrionii.* Other agents are *F. compacta* and *P. verrucosa.* [3] In Latin America, four out of every five sufferers are male, whereas in Japan there is no difference in the incidence of this condition between men and women, and in southern Africa the disease affects predominantly women. The condition affects individuals of 30 to 60 years of age (67%) and is rare in individuals under 15 years of age. Most of the individuals affected (80%) live in rural areas and walk barefoot and/or use sandals. [3]

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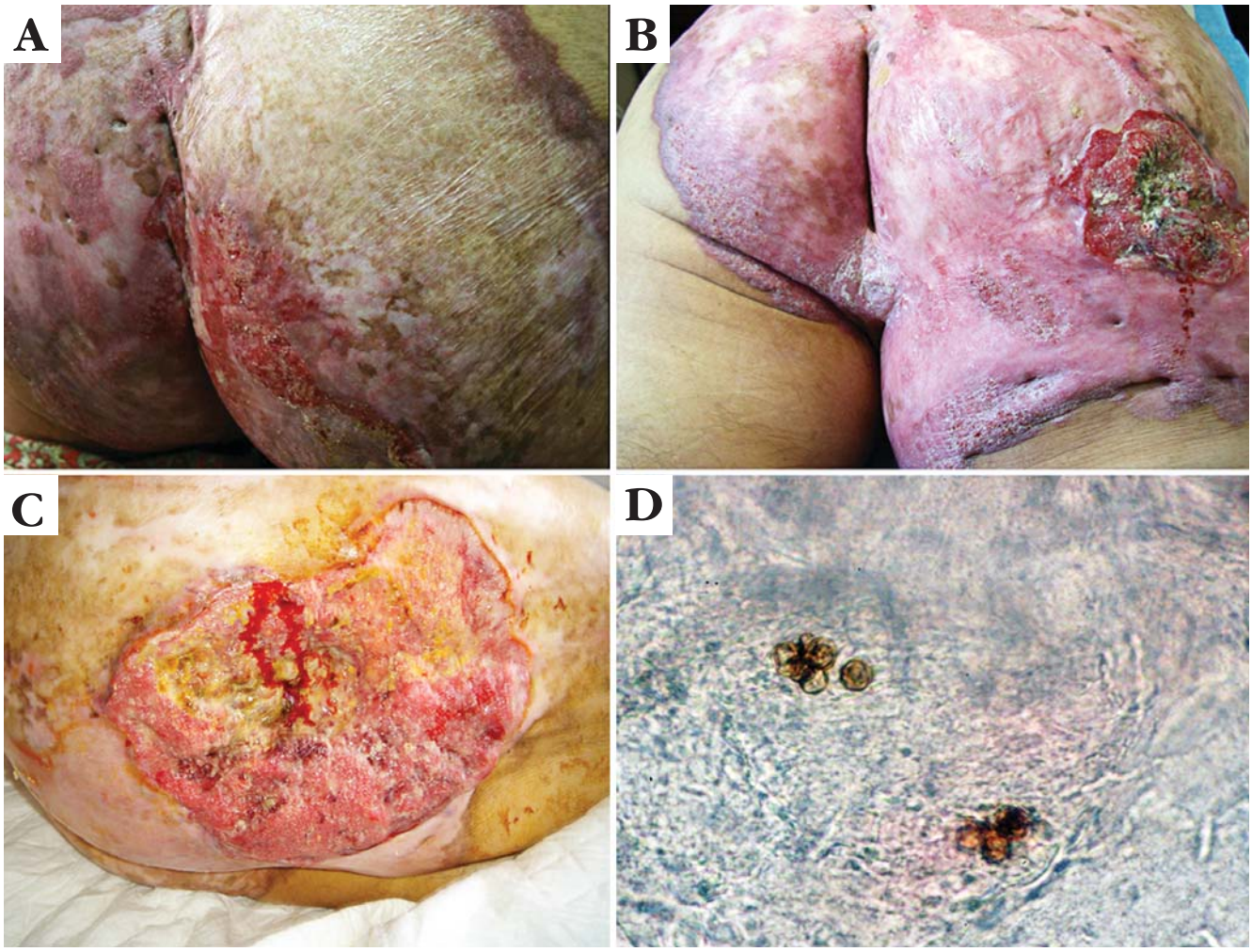

Figure 1: A. Verrucous plaque with areas of keratosis, ulceration and atrophy; **B.** Chronic ulcers with an inflammatory reaction; **C.** Exuberant granulation tissue where the carcinoma developed; **D.** Direct examination, showing Medlar bodies

CASE REPORT

An unemployed 72-year old male patient, formerly an agricultural worker from Puebla, now residing in Mexico State, presented with a dermatosis affecting the lumbosacral region, groin, buttocks and perineum, and consisting of a well-limited, 20 cm verrucous plaque with areas of keratosis. In some ulcerated sites, there was granulation tissue, while in others atrophy was present with areas of hypo- or hyperpigmentation (Figure 1). The patient reported an injury to the area caused by wire 31 years previously, the resulting lesion increasing progressively in size over time. He reported previous treatment with itraconazole. Fluconazole and topical antifungal medication resulted in no improvement.

The diagnosis of chromoblastomycosis was made at this institute by mycological evaluation that confirmed the presence of fungal cells, identified following culture as *F. Pedrosoi* (Figure 1). Biopsy showed keratinocytes with granular eosinophilic cytoplasm, keratin cysts and Russel bodies. An inflammatory reaction was found, with lymphocytes, histiocytes, monocytes and multinucleated cells. Thick collagen rods were arranged parallel to the epidermis from the reticular to the deep dermis, with increased vascularization. Medlar bodies were found, as detected by periodic acid-Schiff (PAS) and Gomori-Grocott trichrome stain (Figure 2).

Treatment was initiated using cryosurgery and potassium iodate 2 grams/day for several months after which itraconazole 300 mg was administered daily for 10 months. As the lesions improved, the patient stopped attending follow-up consultations. He was later hospitalized in another institute with fever, poor general health and pallor (Figure 1). Laboratory tests showed hemoglobin 7-8 mg/dL and neutrophilic leukocytosis. Endoscopy and abdominal tomography showed no abnormalities. Fluid replacement and blood transfusion were given, and treatment was initiated with broad-spectrum antibiotics. The patient's condition improved.

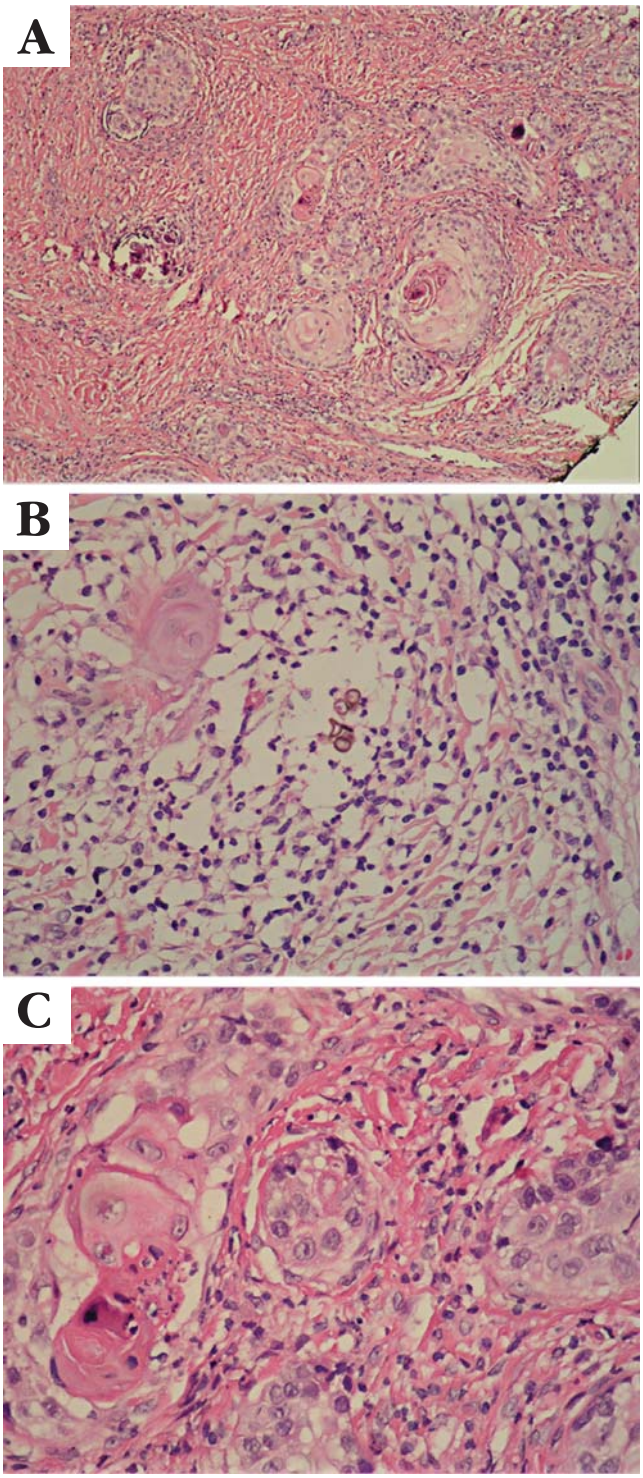

Figure 2: A. Pseudoepitheliomatous hyperplasia and irregular acanthosis. Also note the intense inflammatory infiltrate with giant multinucleated cells (hematoxylin-eosin, magnification 10x); **B.** Biopsy, presence of Medlar bodies (hematoxylin-eosin, magnification 40x). **C.** Proliferation of atypical keratinocytes arranged in sheets and cords with an infiltrative pattern (hematoxylin-eosin, magnification 20x and 40x)

A further biopsy revealed a proliferation of atypical keratinocytes in sheets and cords with large, pleomorphic, hyperchromatic nuclei and one or more prominent nuclei; keratinization in the form of keratin pearls and squamous whirlpool-like patterns, with 4-5 mitoses per field, some of which were atypical. The tumor had infiltrated the collagen rod. Surrounding the tumor, there was an area of inflammatory infiltrate and zones of calcification. Diagnosis: moderately differentiated, infiltrative squamous cell carcinoma (Figure 2).

The patient died, very probably due to the advanced stage of the tumor.

DISCUSSION

All the etiological agents of chromoblastomycosis consist of black fungi with low pathogenicity that are thermosensitive at 40-42^{o}C and live as saprophytes in the soil and in vegetables. They have also been isolated in transported wood and in saunas. Malnutrition may be a predisposing factor. The infection has also been related to an HLA-determined genetic susceptibility (human leukocyte antigen-A29 [HLA-A29]), and to partial immunosuppression.

The microorganisms penetrate the skin following trauma, develop locally and spread by contiguity or, rarely, by means of the blood or lymphatic vessels.

Dermatosis is normally unilateral and asymmetrical. It affects the lower extremities in 54-80% of cases and rarely disseminates (2%).[1] Other possible affected sites are the face, chest, back, buttocks and, in rare cases, the mucosa. [4] In the present case, the buttocks were affected by contiguity; however, there have been other reports of cases in which this was the primarily affected area, particularly in users of saunas in Finland.

The lesions may appear as plaques of psoriasis or tumoral plaques. The course of the infection is chronic, slowly progressive or asymptomatic.[5] Dissemination through the blood or lymphatic vessels is rare. Six clinical variants have been identified: nodular, verrucous or vegetative (53%); tumoral, plaque (41%); psoriasiform; cicatricial; elephantiasic; in addition to occasional other, atypical forms. [1] The present case represents a keratinous form of the condition, which, without a doubt may be similar in clinical appearance to a squamous cell carcinoma, making histopathology obligatory, particularly in cases of prolonged progression.

Known complications include associated infections leading to lymphedema and elephantiasis.[1] There have been reports that prolonged progression and the presence of chronic inflammation and fibrous scarring may predispose to degeneration in malignant neoplasias such as malignant melanoma and squamous cell carcinoma. [6-7]

Some papers have reported squamous cell carcinoma in patients with chronic ulcers that fail to heal (Marjolin), [8-9] varicose ulcers, decubitus ulcers, traumatic ulcers or those resulting from diabetic neuropathies or from burns [10], with a rate of metastasis that ranges from 14 to 58%. The pathogenesis remains unclear. The scarring process is believed to act as a persistent tumor promoter and Fas gene mutations may also be involved. [8,11] There have been few reports of this complication in chronic chromoblastomycosis lesions. In one study carried out in Brazil in 100 patients who had verrucous lesions over a mean duration of 14 years, two patients developed highly aggressive squamous cell carcinomas with metastases. [7] One study carried out in Madagascar reported malignant transformation in 12 out of 1400 cases and reported 2 new cases. [12] In a series of 51 cases in Mexico in which the condition was present for an average of 8 years, only one case of malignancy occurred. [5] The patient in the present case report had all the previously mentioned conditions, verrucous lesions of over 30 years' duration and no adequate treatment during this entire time.

Treatment is complicated and at times ineffective. In advanced cases, a combination of medical and surgical treatment is recommended, including Mohs micrographic surgery. [1] In the present case, appropriate treatment was delayed for a long period of time. Finally, despite the combination of cryosurgery and itraconazole, a squamous cell carcinoma developed as a consequence of the progression of the disease, resulting in the patient's death.

The development of malignant neoplasias in chronic lesions of chromoblastomycosis is rare. To the best of our knowledge, only 17 such cases have been documented worldwide. Without doubt, the conditions of the affected tissue, which involve inflammation and chronic reparatory processes, are significant predisposing factors. The importance of histological follow-up in reaching an early diagnosis of the development of these tumors should be strongly emphasized, since they tend to be more aggressive. This type of surveillance would result in timely treatment and a reduction in mortality. ❑

REFERENCES

1. Arenas R. Micología médica ilustrada. 2 ed. México: Interamericana-McGraw-Hill; 2003. p.140-7.
2. Grigoriou D, Delacrètaz J, Borelli D. Traité de mycologie medicale. Toronto: Hans Huber Publishers, 1987. p.333-9.
3. Rippon J. Medical Mycology. Toronto: Saunders; 1974. p.231-7.
4. Tyring S, Lupi O, Hengge U. Tropical Dermatology. Houston: Elsevier; 2006. p.204-6.
5. Bonifaz A. Chromoblastomycosis: clinical and mycologic experience of 51 cases. Mycoses. 2001;44:1-7.
6. dos Santos GA, Minelli L. Melanoma in a long-standing lesion of chromoblastomycosis. Int J Dermatol. 2006;45:1331-3.
7. Minotto R, Bernardi CD, Mallmann LF, Edelweiss MI, Scroferneker ML. Chromoblastomycosis: A review of 100 cases in the State of Río Grande do Sul, Brazil. J Am Acad Dermatol. 2001;44:585-92.
8. Bolognia J, Jorizzo J, Rappini R. Dermatología. Madrid: Elsevier; 2004. p.1186-8.
9. Bauer T, David T, Rimareix F, Lortat-Jacob A. Marjolin's ulcer in chronic osteomyelitis: seven cases and a review of the literature. Rev Chir Orthop Reparatrice Appar Mot. 2007;93:63-71.
10. Diehl ES, Fleury RN, Ura S, Opromolla DV. Exuberant verrucous carcinoma arising from a burn scar. Cutis. 2007;79:133-5.
11. García-Morales I, Pérez-Gil A, Camacho FM. Marjolin's ulcer: burn scar carcinoma. Actas Dermosifiliogr. 2006;97:529-32.
12. Esterre P, Pecarrère JL, Raharisolo C, Huerre M. Squamous cell carcinoma arising from chromomycosis. Report of two cases. Ann Pathol. 1999;19:516-20.

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