Lobomycosis: a therapeutic challenge*

Marcelo Grossi Araújo[1,2]
Soraya Neves Marques Barbosa dos Santos[2]
Antonio Carlos Martins Guedes[1]
Nathalie Silva Cirilo[3]
Claudemir Roberto Aguilar[1,2]

DOI: http://dx.doi.org/10.1590/abd1806-4841.20187044

Abstract: Lobomycosis or lacaziosis is a chronic granulomatous fungal infection caused by *Lacazia loboi*. Most cases are restricted to tropical regions. Transmission is believed to occur through traumatic inoculation in the skin, mainly in exposed areas. It is characterized by keloid-like nodules. There are only a few hundred cases reported. The differential diagnoses include many skin conditions, and treatment is difficult. The reported case, initially diagnosed as keloid, proved to be refractory to surgical treatment alone. It was subsequently approached with extensive surgery, cryotherapy every three months and a combination of itraconazole and clofazimine for two years. No signs of clinical and histopathological activity were detected during follow-up.
Keywords: Cryosurgery; Keloid; Lacazia; Lobomycosis; Mycoses;

INTRODUCTION

Lobomycosis or lacaziosis is a chronic fungal infection caused by *Lacazia loboi*. The precise mechanisms for inoculation are still unclear, but traumatic inoculation of the fungus in the skin is probably the route that humans acquire the infection.[1]

Most cases are found in tropical regions, with hot and humid climates. More than 550 human cases have been reported, mainly in patients with travel history to or living in endemic areas (Central and South Americas, particularly Brazil).[2]

It is a chronic condition that presents with multiple types of cutaneous lesions on exposed areas, mainly keloid-like lesions. The lesions are restricted to the skin and subcutaneous tissue, with no systemic involvement. The diagnosis is confirmed by the triad: fungus identification on direct microscopy, on histopathology, and no culture growth.[1]

Antifungals, commonly effective in other subcutaneous mycoses, are not successful in lobomycosis. Currently, there is no therapeutic approach fully satisfactory.[3]

CASE REPORT

A 36-year-old male, farmer, born Northern Brazil and living in Minas Gerais state, presented with keloid-like lesions on his left ear that had been present for 6 years (Figure 1). When the lesions first appeared, he was working in the Amazon region with lumbering. Previously healthy, he had no systemic symptoms, mucosal lesions or lymph node enlargement.

He reported surgeries for the removal of keloids in 2008 and 2009, but no biopsies were carried out. When the lesions recurred, in 2012, a biopsy was performed in another medical center, and was consistent with lobomycosis. He reported treatment with itraconazole (200mg/day) associated to cryotherapy sessions for 7 months, with initial improvement, but with no complete resolution of the lesions.

A new histopathology revealed the presence of round hyaline yeasts, with birefringent membrane, budding and linear chains, consistent with active lobomycosis (Figures 2 and 3). Fungal culture was negative. A wide surgical excision of the lesions was performed, associated to concomitant treatment with itraconazole

Received on 18.02.2017.
Approved by the Advisory Board and accepted for publication on 23.06.2017.
* Study conducted at the Dermatology Unit, Hospital das Clínicas, Universidade Federal de Minas Gerais (HC-UFMG) – Belo Horizonte (MG), Brazil.
Financial support: None.
Conflict of interest: None.

1 Department of Internal Medicine, Faculdade de Medicina. Universidade Federal de Minas Gerais (UFMG) – Belo Horizonte (MG), Brazil.
2 Dermatology Unit. Hospital das Clínicas, Universidade Federal de Minas Gerais (HC-UFMG) – Belo Horizonte (MG), Brazil.
3 Medical Specialty Clinic, Medical Work Cooperative, Hospital das Clínicas, Universidade Federal de Minas Gerais (HC-UFMG) - Belo Horizonte (MG), Brazil.

Mailing address:
Marcelo Grossi Araújo
E-mail: mgrossi@medicina.ufmg.br

©2018 by Anais Brasileiros de Dermatologia
CC BY-NC

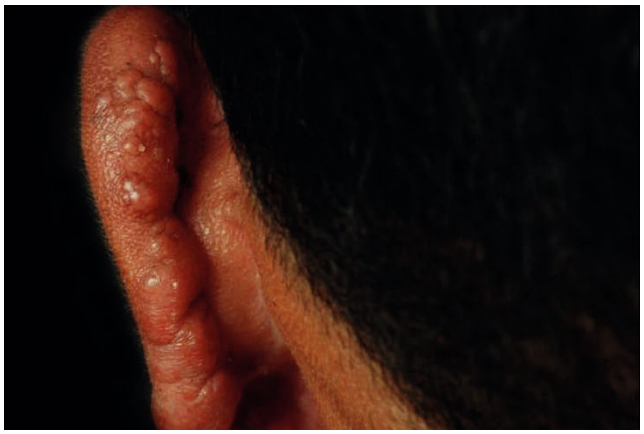

Figure 1: Keloid-like lesions and diffuse infiltration on the earlobe and posterior helix

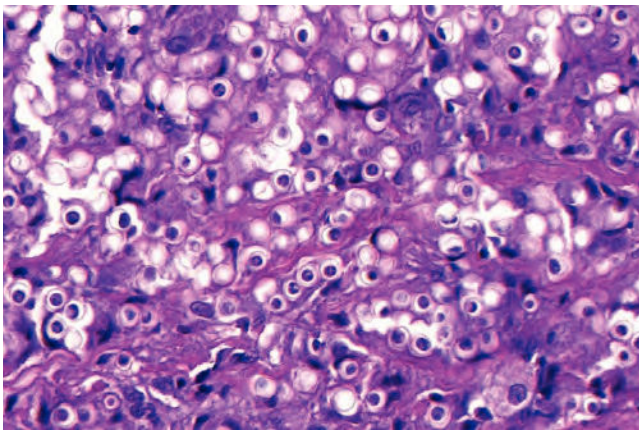

Figure 3: Chain formation, isolated and budding fungi (Hematoxylin & eosin, X400)

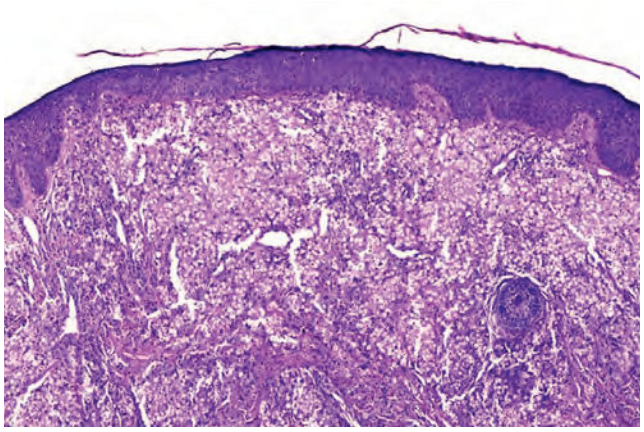

Figure 2: Acanthosis of the epidermis. All through the dermis, amidst a fibrous stroma, a large number of round structures with mild interspersed inflammatory lymphocytic infiltrate can be seen (Hematoxylin & eosin, X100).

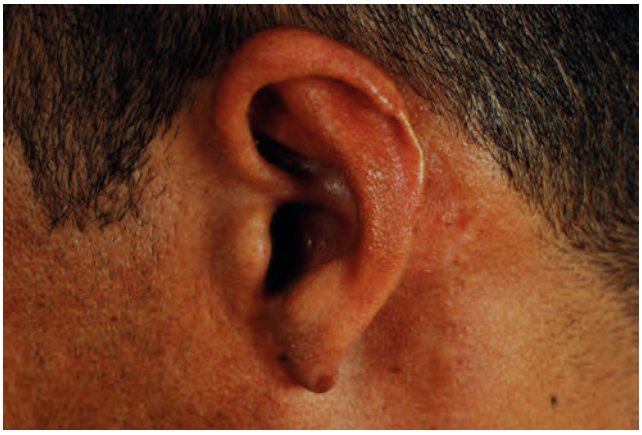

Figure 4: Two years after drug and surgical treatment.

(200mg/day), clofazimine (100mg/day) and cryotherapy with liquid nitrogen (double 1-minute cycles) every 3 months, for 2 years. There was complete regression of the lesions and a new biopsy of the earlobe did not show any fungus (Figures 4 and 5). The patient is still on drug-free follow-up for cure control.

DISCUSSION

Lobomycosis was described by the Brazilian dermatologist Jorge Lobo in 1931. The etiological agent is *L. loboi*, a spherical yeast with a diameter of 8μm to 12μm.[4]

The traumatic implantation of the fungus in the skin is supposedly how humans acquire the infection. The incubation period is not well defined, but there are evidences that it ranges from 1 to 2 years.[5]

The clinical expression is polymorphic, especially in chronic cases, with dyschromic plaques, papules, nodules, gumma, nodular and verrucous plaques, scars and ulcers, with a predominance of keloid-like nodules.[1]

The organisms are found mainly inside macrophage vacuoles and reproduce by budding, forming linear chains with a birefringent cellular wall that contains melanin. They are resistant to digestion by the macrophages, what contributes to the chronicity of the infection.[5] It is suspected that regulatory abnormalities of the immune response, probably specific, contribute to the multiplication of the agent in the infected organism.[6] The ability for phagocytosis could be affected by the cytokine TGF-β, suppressor of the macrophage response, expression of nitric oxide and IFN-γ, thus affecting the cellular immunity response.[6,7]

Diagnosis can be made via direct microscopy or histopathology. On microscopy, a small sample of the lesion with saline or KOH will show round structures, with birefringent cellular walls, isolated or in a linear chain. On histopathology, the epidermis usually appears atrophic and the microorganisms can be seen in the stratum corneum, since transepidermal elimination of the fungus is common; irregular hyperplasia, sometimes pseudoepitheliomatous, is common in vegetating-verrucous lesions and in the borders of ulcers.[1] In the dermis, there can be a light band (grenz *zone*) of variable thickness, separating the epidermis from the granulomatous infiltrate containing macrophages, giant cells, lymphocytes

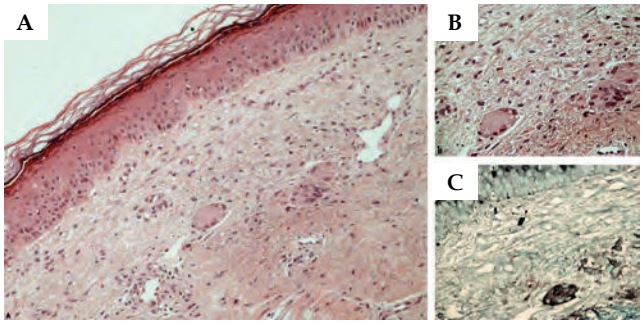

Figure 5: A -Control histopathology shows a young fibrovascular proliferation, rare focal foreign body-type giant cells and mild perivascular and interstitial lymphohistiocytic inflammatory infiltrate (HE, 200x). No fungus could be detected (B- PAS and C- Grocott 400x)

and plasmocytic cells; foamy histiocytes with multiple microorganisms in the cytoplasm are seen. Spores are round, with birefringent capsules under polarized light, and stain with periodic acid Schiff (PAS), methenamine silver (Grocott-Gomori) and Gridley stain for fungus.[8] In lobomycosis, budding is simple, with the aspect of a chain, and should be differentiated from paracoccidioidomycosis, which has the characteristic aspect of a mariner's wheel.[9]

Regarding the differential diagnosis, the infiltrative and nodular lesions on the ears resemble lepromatous leprosy, keloids, and anergic American tegumentary leishmaniasis. The verrucous, vegetating and nodular lesions can resemble sporotrichosis, chromomycosis, paracoccidioidomycosis, keloids, and tumors such as dermatofibrosarcoma, squamous cell carcinoma, and basal cell carcinoma.[9]

Recurrences are common, even with surgical treatment, possibly due to insufficient resection. Treatment with clofazimine and itraconazole was reported in 1 case,[9] leading to an 8-year clinical and histopathologic remission, but the authors subsequently reported recurrence.[7] Despite this, due to the lack of therapeutic options, this combination was adopted in our case, together with cryotherapy with liquid nitrogen and wide surgical excision. Cryotherapy is described as an option in many subcutaneous mycoses and, in lobomycosis, the association of cryotherapy with itraconazole was already reported.[10] Surgical approach is the main treatment recommended in the literature, but the difficulty in defining the lesion, the functional/aesthetic limitation by the frequent location on the head, and even inoculation with surgical instruments are implicated in the compromised final results.[9]

It is accepted that characteristics of the fungus *L. loboi* itself and the fibrosis that develops in long standing cases make the medication action difficult. To date, there are no antifungals available with proven action against this agent. Hence, whenever possible, the association of methods can be the most interesting option. In the reported case, the medication-free follow-up period is still insufficient, but we highlight that the response until now has been completely satisfactory.

Internal migrations and international travels predispose the occurrence of cases of lobomycosis in non-endemic areas. Diagnostic delays and mistakes can occur due to the rarity of the disease and by not performing histopathology examination. ❑

REFERENCES

1. Brito AC, Quaresma JAS. Lacaziosis (Jorge Lobo's disease): review and update. An Bras Dermatol. 2007;82:461-74.
2. Papadavid E, Dalamaga M, Kapniari I, Pantelidaki E, Papageorgiou S, Pappa V, et al. Lobomycosis: A case from Southeastern Europe and review of the literature. J Dermatol Case Rep. 2012;6:65-9.
3. Paniz-Mondolfi A, Talhari C, Sander Hoffmann L, Connor DL, Talhari S, Bermudez-Villapol L, et al. Lobomycosis: an emerging disease in humans and delphinidae. Mycoses. 2012;55:298-309.
4. Taborda PR, Taborda VA, McGinnis MR. Lacazia loboi gen. nov., comb. nov., the etiologic agent of lobomycosis. J Clin Microbiol. 1999;37:2031-3.
5. Lupi O, Tyring SK, McGinnis MR. Tropical dermatology: Fungal tropical diseases. J Am Acad Dermatol. 2005;53:931-51.
6. Vilani-Moreno FR, Belone AF, Soares CT, Opromolla DV. Immunohistochemical characterization of the cellular infiltrate in Jorge Lobo's disease. Rev Iberoam Micol. 2005;22:44-9.
7. Talhari S, Talhari C. Lobomycosis. Clin Dermatol. 2012;30:420-4.
8. Fernandez-Flores A, Saeb-Lima M, Arenas-Guzman R. Morphological Findings of Deep Cutaneous Fungal Infections Am J Dermatopathol. 2014;36:531-53.
9. Fischer M, Chrusciak Talhari A, Reinel D, Talhari S. Sucessful treatment with clofazimine and itraconazole in a 46 year old patient after 32 years duration of disease. Hautarzt. 2002;53:677-81.
10. Carneiro FP, Maia LB, Moraes MA, de Magalhães AV, Vianna LM, Zancanaro PC, et al. Lobomycosis: diagnosis and management of relapsed and multifocal lesions. Diagn Microbiol Infect Dis. 2009;65:62-4.

How to cite this article: Araújo MG, Cirilo NS, Aguilar CR, Santos SNMB, Guedes ACM. Lobomycosis: a therapeutic challenge. An Bras Dermatol. 2018;93(2):279-81.