CASE REPORT

Leprosy and Lobomycosis: First report from the Amazon Region

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Accepted for publication 14 May 2015

Summary Leprosy is still a relevant health problem in Brazil with 31,044 new cases diagnosed in 2013, of which 781 new cases diagnosed in the State of Amazonas. Lobomycosis is a cutaneous-subcutaneous mycosis caused by Lacazia loboï, an in vitro uncultivable fungus. Lobomycosis has been mainly reported in the Amazon region of Brazil and Colombia affecting mainly male farmers and workers in extraction of rubber. Lobomycosis is clinically characterised by keloid-like lesions and chronic evolution. Even if lobomycosis does not represent a major public health problem, it remains a serious condition for patients due to unsatisfactory treatment. We report a case of an old man with lepromatous leprosy diagnosed in 1983, treated with multidrug therapy until 1989 and presenting a leprosy relapse 15 years after treatment. At this time a lobomycosis was also diagnosed in a keloid-like lesion evolving for more than 30 years. This co-infection has been only rarely reported and this is the first detailed case report in the English literature.

Keywords Leprosy; Lobomycosis; keloidal blastomycosis; Paracoccidioides loboï; Jorge Lobo’s disease

Introduction

Leprosy is still a relevant health problem in Brazil with 31,044 new cases diagnosed in 2013, of which 781 new cases diagnosed in the State of Amazonas. Lobomycosis is a subcutaneous mycosis caused by Lacazia loboï (L. loboï) an in vitro uncultivable fungus that was firstly described by Jorge Lobo in 1931. Lobomycosis has been reported mainly in the Amazon region of Brazil and Colombia. Clinically, lobomycosis
presents mainly with polymorphic, nodular or keloid-like lesions that may be localised or disseminated. Usually, lobomycosis occurs on exposed areas and mucosae are spared. The diagnosis of lobomycosis is established by direct mycological examination or by a skin biopsy. The treatment is still unsatisfactory.3,4

We present a patient affected by relapsing multibacillary leprosy and lobomycosis; this association has not yet been reported in the English literature.

Case Report

An 89 year old man presented in 2013 to the Alfredo da Matta Foundation (FUAM) with a 30 year history of slowly enlarging nodule on the skin over his left collarbone (Figure 1).

The patient had a previous diagnosis of lepromatous leprosy in 1983 treated with multibacillary multidrug therapy (MDT) until 1989. In 2005 he experienced a relapse that was again treated with 12 months multibacillary MTD. In 2006 he developed erythema nodosum leprosum and was treated successfully with a short period of prednisone together with thalidomide 100 mg/day that he was still continuing. He did not develop leprosy sequels. Slit-Skin smear examination showed a bacteriological index (BI) of 4,25 in 2007 and a BI of 1,0 in 2009.

At physical examination he presented an 8 x 3 cm large not ulcerated, keloid-like nodule on the skin over his left collarbone. The skin of his chest, extremities and ears was dry and atrophic without signs of active leprosy lesions (Figures 2a and b).

General examination did not show any gross alteration. Neurological status was normal. Laboratory examination showed normal results of complete blood count, urinalysis, hepatic and renal function tests, serum glucose and erythrocyte sedimentation rate. HIV testing was negative. Regional lymph nodes were not enlarged. Chest X-ray was normal.

Figure 1. Keloid-like plaque- nodule on the left collarbone evolving for 30 years.
Histopathologic examination of skin biopsy of the nodule showed an atrophic epidermis and a diffuse granulomatous infiltrate involving the entire dermis constituted by histiocytes and few giant cells. Only few focal lymphocytes were present. The histiocytes’ cytoplasm contained rounded yeast-like hyaline cells with a thick double birefringent membrane. These cells were forming chains of multiple organisms. The Grocott-Gomori methenamine-silver nitrate stain allowed the better visualisation of chains of darkly pigmented, spheroidal, yeast-like organisms (Figure 3).

Slit-Skin smear examination of his right earlobe showed only few fragmented Acid-fast bacilli (BI 1,0) (Figure 4).

Figure 2a,b. The skin of his chest, extremities and ears was dry and atrophic without signs of active leprosy.

Figure 3. The Grocott-Gomori methenamine-silver nitrate stain allowed the better visualisation of chains of darkly pigmented, spheroidal, yeast-like organisms (original magnification 500x).
A skin biopsy of the skin of his trunk showed a normal epidermis with a sparse mainly perivascular and periadnexal infiltrate of foamy macrophages and few lymphocytes. Wade staining showed only fragmented bacilli (‘bacillary dust’) compatible with a multibacillary leprosy in involution (Figure 5).

The diagnosis of keloidal lobomycosis in a patient with a previous relapsing lepromatous leprosy and leprosy reaction Type 2 was made. He refused any treatment for the lobomycosis.

Discussion

We describe a patient with relapsing multibacillary leprosy affected also by a keloid-like lobomycosis. To our knowledge, this co-infection has not yet been reported in the English literature.
Lobomycosis was first described by Jorge Lobo in 1931 and is a deep chronic cutaneous mycosis typical of the Amazon’s areas and is the most common deep mycosis in Manaus.\textsuperscript{3–9} Few cases have been described in Mexico, North America and Europe.\textsuperscript{3,10–12} The pathogen is *Lacazia loboi*, a spherical homogenous yeast of 8-12 mm diameter, residing singly or in chains, predominantly in macrophage vacuoles. The melanin-containing birefringent 1-nm-thick cell wall resists to macrophages digestion and plays a central role in the chronic evolution of the infection. The precise natural reservoir of *L. loboi* is presumed to be in the rural environment, because the disease classically involves male farmers in rural areas and workers in extraction of rubber. Because also two different subspecies of dolphins are frequently infected by lobomycosis, and because most infected human beings live near river borders and watercourses, it is also supposed that *L. loboi* is a hydrophilic pathogen. This fungus has never been cultivated. *L. loboi* is localised in the cutaneous and subcutaneous tissues and do not disseminate elsewhere in the body.\textsuperscript{3–9}

The direct inoculation to the dermis through i.e. a thorn prick or an insect bite is probably the way of transmission. The incubation period goes from several months to many years. The lesions often begin as small asymptomatic slowly growing papules or pustules. The typical keloid-like skin lesions with well defined lobulated margins appear only after several months and the typical appearance is ‘keloids over keloids’. Ulceration is infrequent, but verrucous lesions are often seen. The disease may remain localised with one or few lesions or disseminate with multiple lesions on the trunk and extremities. The most frequent affected area is the pinna of the ear (50%), followed by the lower limbs (29%) and the upper limbs.\textsuperscript{3–9} Clinical differential diagnosis includes the nodular variant of chromoblastomycosis, keloids, xanthomas, fibromas, Kaposi’s sarcoma, neurofibromas and dermatofibrosarcoma protuberans. Differentiation of keloidiform lesions on the ears from lepromatous leprosy is difficult, but the unilaterality is characteristic of lobomycosis.\textsuperscript{3–9}

The diagnosis is based on direct mycological examination of material obtained by scarification, shaving, curettage or tape of the lesion and skin biopsy.

Histopathology shows a diffuse granulomatous dermatitis involving the entire dermis and extending to the subcutaneous fat. Vacuolated histiocytes, histiocytes forming irregular group of cells assuming syncytial aspects, foreign body giant cells and Langhans giant cells with only few lymphocytes may all be observed. *L. loboi* presents as a characteristic bulbous chain of yeast-like cells, 9-10 μ in diameter, with thick (double) birefringent walls in the cytoplasm of the histiocytes as well as outside. The Grocott-Gomori methenamine-silver nitrate stain will allow the visualisation of chains of darkly pigmented, spheroidal, yeast-like organisms.\textsuperscript{3–9,13}

Lobomycosis does not represent a public health problem, however patients with disseminated disease represent a therapeutic challenge. Treatment is difficult and usually consists of total surgical excision, preferably with wide margins but relapses are common. Electrodessication is useful in early stages of the disease. Systemic therapy with clofazimine at 300 mg per day has been used with good results in some patients.\textsuperscript{14} This drug must be continued for at least 2 years at 100 mg/d in responsive patients. Antifungal drugs such as ketoconazole, itraconazole, amphotericin B, and 5-fluorocytosine are ineffective.\textsuperscript{3} No deaths from lobomycosis have been reported.\textsuperscript{3–14}

Currently, Brazil contributes to 93% of all leprosy cases recorded in the Americas with 31,044 new detected cases in 2013 on a total of 215,656 detected worldwide. In the State of Amazonas Manaus 781 new cases were detected in 2013. In Brazil, in 2013 alone, there were
1603 cases of recurrence, an increasing number compared with the 1,483 cases in 2009 while between 2006 and 2013, there were 3,196 cases of leprosy recurrence on a global level.\textsuperscript{1,2}

The co-infection between leprosy and lobomycosis seems to be unusual. Several papers reporting series of patients affected by lobomycosis did not describe the co-infection with leprosy.\textsuperscript{3–14} We performed a search in Pub Med, Ovid and Web of Science and were not able to find case reports of leprosy and lobomycosis in the English literature.\textsuperscript{3–16} We found only a retrospective study in the Portuguese literature by Woods et al. performed in 2010 in Rio Branco reporting among a series 249 patients affected by lobomycosis 10 patients co-infected also by leprosy.\textsuperscript{17} Unfortunately, no further details concerning the type of leprosy, treatment and other clinical data were reported. Interestingly, Woods et al. reported that these 10 patients showed the best results of treatment. The authors speculated that clofazimine is effective in the treatment of both leprosy and lobomycosis, and it is possible that clofazimine had a limiting effect on the progression of the keloid–like lesion in Woods’ patients as well as probably had in ours.\textsuperscript{17}

In conclusion, our patient is the first detailed report in English literature of a patient affected by both lobomycosis and leprosy. It is not possible to speculate on one single case report whether the co-infection leprosy and lobomycosis is rare or not. From the literature review it seems infrequent but more epidemiological studies are needed to better understand this co-infection.

Authors’ contribution
GABRIEL MAROJA IHARA: looked after the patient, wrote the manuscript.
CESARE MASSONE: wrote and edited the paper.
ANTONIO PEDRO SCHETTINI: looked after the patient and provided histopathology.
MARIA DE FATIMA MAROJA (Corresponding author & guarantor): looked after the patient, prepared figures, supervision.

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