Lobomycosis is a chronic dermal infection that presents a wide spectrum of clinical-dermatological manifestations, mainly characterized by the development of keloid lesions as well as nodular, verrucoid and sometimes ulcerous forms. The etiological agent at an international level, according to the consensus nomenclature, has been called Loboa loboi, even though recently it has been accommodated as Lacazia loboi. The present review extensively covers the clinical-epidemiological aspects as well as the most outstanding historical aspects, including the Venezuelan experience and the presentation of two new cases, which substantiate the Amazon basin as an endemic area for the disease.

Introduction

The first description of this strange pathology occurred in 1931, when in the population of Recife, Brazil, Jorge Lobo identified the development of severe skin lesions with a keloid aspect, multinodular, located in the lumbar region of a 52-year-old patient from the Amazon region.1

The appearance of this new cutaneous mycosis described by Lobo, and named keloidiform blastomycosis by Lobo, echoed in the medical community, and the identification of new cases increased rapidly both in Brazil and in other South and Central American countries, even including a case in Europe of an aquarium worker infected by manipulating a dolphin; the only known species until now capable of being affected by this agent apart from humans, even though other species have been successfully infected experimentally.1

The first case in Venezuela was described by Campo-Aasen in 1952.2 By 1958 the agent, at that time known as Lobomyces, had not been successfully isolated, and existing strains such as Glenosporella loboi and Glenosporopsis amazonica turned out to be known as Paracoccidiodes brasiliensis and Aspergila-cea, with an aberrant aspect that probably had intervened in the original inoculations as vulgar contaminants.1

Studies carried out by Dr Dante Borelli gave Venezuela a pioneering role within experimental Lobomycosis, especially regarding transmission aspects. Curiously, an outstanding aspect comprised successful reproduction of the disease through the inoculation of extracts of the dermis of the knee of a laboratory technician who volunteered for the experiment.3 By 1986 the total number of cases described at a world wide level was 418, and Venezuela occupied the fifth place in the incidence of the disease with 17 cases.1 Of these 17 cases, 13 were confirmed. By 1993 only one new case had been reported, and it was only in 1999 when Brun described three new cases. To date, Venezuela has reported 23 cases, including the two new cases described in this paper.

Efforts to characterize taxonomically this agent have been extensively debated; its denomination has varied constantly through time owing to the diverse criteria employed. We present them successively:

• Glenosporella loboi; Fonseca-Leão: 1940.4
• Blastomyces loboi; Vanbreuseghem: 1952.5
• Glenosporopsis amazonica; Fonseca: 1943.6
• Paracoccidiodes loboi; Almeida-Lacaz: 1948–49; Carneiro: 1956.7
• Loboa loboi; Ciferri, Azevedo, Campos-Carneiro: 1956.8
• Lobomyces; Borelli-Pradinaud: 1968.7
• Loboa loboi, F.C. Odds: 1992.9
• Lacazia loboi, Taborda- 1999.11

Nevertheless, today many authors prefer to maintain the denomination of Paracoccidiodes loboi, based on the morphological characteristics and the relationship and antigenic similarity shared by this agent with Paracoccidiodes brasiliensis.12

From the Laboratorio de Estudio de Antígenos, Instituto de Biomedicina, Universidad Central de Venezuela/Ministerio de Salud y Desarrollo Social, Caracas, and CENASAI, Ministerio de Salud y Desarrollo Social/Gobernación del Estado, Bolivar, Venezuela

Correspondence
Alberto E. Paniz-Mondolfi, MD
Laboratorio de Estudio de Antígenos
Instituto de Biomedicina
Sótano I. San Nicolás a Providencia
Área del Hospital Vargas
San José. Caracas
Venezuela
1010 A. Apartado 4043
E-mail: albertopaniz@yahoo.com
Case Report

Case 1
During a medical team expedition in 2003 covering the Amer Indian community of Sabana Cardona, Bolivar State, a 48-year-old man presented with multiple keloid lesions at the posterior region of the outer ears that had evolved insidiously during the last 6 years. The patient stated that he had never left the area and that he worked in agriculture. At the physical examination the patient showed multiple firm keloid lesions with a confluent tendency, and regions with alternating hypo and hyperchromy. Initially, as he lived in a Leishmaniasis endemic area, the diagnosis was Cutaneous Leishmaniasis, and the patient received a cycle of pentavalent antimonials (meglumine antimoniate) without improvement. When the histopathological diagnosis was confirmed the lesions were partially surgically excised with otoplasty with no remission (Fig. 1).

Case 2
A 60-year-old man belonging to the Yanomami ethnic group, nomad, born in the High Orinoco region. Since adolescence the patient had worked in mining activities, and frequented the Yapacana area in the Middle Orinoco, and the Casiquiare River which joins the Orinoco with the Rio Negro River at Amazon State, where he had resided during the last few years. The patient’s disease began 3 years previously with a papular lesion on one knee that progressed to form a tense and firm zone, at times with a keloid aspect and disperse nodules with a confluent tendency, which occasionally ulcerated. The patient stated that he had been diagnosed, a year previously in Brazil, and had been treated with ketoconazol and itraconazol several times without improvement. The patient was treated with amphotericin B associated with surgical excision of the nodules with partial remission. Nevertheless, the patient was not again consulted and there was no possibility for a follow up (Fig. 2).

Epidemiology of Lobomycosis

Geographic distribution and climatic aspects
Human lobomycosis has been reported until now in nine South American countries (Brazil, Colombia, Surinam, Venezuela, Peru, French Guyana, Guyana, Ecuador and Bolivia) and three Central American countries (Costa Rica, Panama and Mexico); and only one case has been reported in Europe which, as mentioned earlier, resulted from manipulation of a dolphin. It is important to indicate that another infected dolphin (Turciups truncatus) was captured on the coast of Florida. Even though the infection has also been described in the dolphin species (Turciups truncatus and Sotalia guianense) in Venezuela, no cases apart from the human species have been reported. Recently a case was described in France in a patient from Guyana, as well as the first case of a human infection in the United States, where the patient remained for more than 7 years with a keloid lesion on the thorax after visiting Angel Falls in Bolivar State, Venezuela. Curiously, the last case described in the world literature corresponds to a Canadian geologist who worked and lived in the Guyana and Venezuelan forests for 2 years, spending most of her time in the Cuyuni, Esequibo and Rupununi river areas, as well as in other areas of Bolivar State known as endemic zones for this disease.

Of the 23 cases described in the country to date, including those in this paper, only eight have been presented in detail clinically and epidemiologically. Of the total cases, six come from Bolivar State (Santa Elena de Uairen, La Paragua, El
Callao, Santa Maria del Erebato and Sabana Cardona), one case comes from the South-East of Maracaibo Lake, and one from Amazon State, specifically from the Rio Negro region. The geographic distribution of these cases characteristically corresponds to the areas of ecologic reserve of the causative agent. Infection by *Lacazia loboi* occurs in neotropical systems, generally at 200–250 m over sea level heights, with 2000 mm of annual precipitation and with a mean temperature of 24 °C.

Most of the cases described in Venezuela (Fig. 3) geographically come from the South Orinoco River bioregion, which covers half of the national territory and is dominated by humid forests, sharing some of the climatic characteristics of other bioregions such as the Maracaibo Lake, the Central Mountain Chain and the Deltaic System.

**Sex, age and occupation**

There is a clear preponderance of the male sex (90% of cases presented in the literature), which coincides with the cases studied in Venezuela where all are males. Nevertheless, it is important to point out that gender is directly related to the occupational factor. It has been described that in the Amerindian community of the Cayabi in the Brazilian Amazon (population in which the highest incidence has been described) the prevalence is greater in adult women (32%), as they carry out agricultural activities, which constitute one of the main risk factors for exposure to contagion.

Another important epidemiological aspect to consider is the occupation of those affected, since, as has been mentioned previously, most of the cases correspond to persons who carry out agricultural activities, as well those dedicated to fishing, hunting and mining. Of the cases documented exhaustively in Venezuela, it can be seen that five were dedicated to mining and three to agricultural activities, emphasizing the nomadic character of these individuals.

Regarding age, generally the patients present a wide age range between 12 and 70 years, even though cases have been described in 1-year-old children. The disease is of an insidious character and generally, at the moment of diagnosis, has been present for many years. No ethnic predominance has been described and all races seem to be equally susceptible to contagion.

**Pathogenesis**

At present, water, earth and vegetation are considered ecologic habitats of the fungus and the agent accesses the skin by penetration or accidental trauma. Once in the dermis, it is phagocytized, initiating a slow growth and multiplication process which explains the prolonged incubation period. The mycotic granulomas that have been found in regional lymph nodes near the lesions in some patients suggest the occurrence of lymphatic dissemination; although, hematogenous and contiguity are not discarded.

According to some authors, the profuse extension of cutaneous lesions supports the theory of hematogenous dissemination. On the other hand, it has been mentioned that in Lobomycosis there is a depression of cell-mediated immunity, which becomes clinically evident by chronic, insidious and slow evolution. To date, only one case of visceral compromise has been observed in a patient, reported in Costa Rica, who presented with a lesion at the level of the maleolus, leg and knee, with later development of a testicular tumor when the patient was 47 years old.
Immunological aspects

There appears to be a partial deficiency of cell-mediated immunity in these patients, as there is an absence of response to dinitrochlorobenzene and a delayed reaction response to Staphylococci, Streptococci, Trycophyton and Candida antigens. Nevertheless, reactivity towards mycobacterial antigens is very high. Additionally, humoral immunity does not show any signs of alteration.18,20

On the other hand, a relationship and antigenic similarity between Lacazia loboi, Histoplasma capsulatum and H. duboisii, B. dermatidis, Candida spp., Paracoccidioides spp. and mycelial forms of Coccidiodes immitis has been described.11 In fact, an antigen known as Lobina has been developed to measure intradermal reactivity for evaluating carrier cases; however, it was found to be nonspecific, as there was positivity also in paracoccidioides cases as well as in mycetomas produced by Nocardia brasiliensis.14

Clinical aspects

Lesions predominantly appear in exposed areas.22 Areas of occurrence in order of frequency: lower limbs, outer ears, upper limbs and face; their topographical distribution: lower limbs 32%, outer ears 25%, upper limbs 22%, face 7%, disseminated 8%, sacrum 3%, thorax 2% and neck 1%.3 Of the six patients adequately documented in Venezuela, four presented with outer ear lesions, two lower limb lesions, one upper limb lesions and one head lesion.1,19,20

Generally patients refer having suffered a previous traumatic lesion: snake bites, insect bites,14 ray poisoning, wounds owing to penetrating elements, splinters, etc.23,24 Usually, lesions appear as plaques, papules or nodules, initially single but later becoming multiple and disseminated. The kelodan nodule form is the most frequent.25-33 There is evidence of a clinical pleomorphism in the same patient where a variety of lesions can occur, from those already described to others such as verrucous, scar like, sclerodermiform and even ulcerations,25,33,34 as shown in one of the cases presented in this paper.

Regarding color, lesions can be normal, hyper or hypochromic, nonerithematous and with a noninflammatory aspect. They are generally nonpruriginous, even though in some cases slight itching has been described.1,22

Pathologically, there is a diffuse non-necrotic granulomatous process. The lymph nodes are replaced by a massive infiltrate. The histopathology of the lymph nodes is identical to the findings described for the granulomas.25,26

Differential diagnosis

Aspects related to the differential diagnosis are specially important because, for example, the initial clinical diagnosis of the patient we observed in 1999 was cutaneous leishmaniasis (owing to the endemic area) and the similitude of the clinical characteristics (location of lesion on outer ear); nevertheless, a simple and rapid method for differentiation comprises practicing a scraping or biopsy of the lesion to detect Leishmania amastigotes.

Plaque-form lesions can be confused with lepromatous leprosy, or this disease in its reactive tuberculoid form; more so if we add to the clinical picture anesthesia or hypoesthesia in the area of the lesions.24,32 Irregular plaque-form lesions can also be similar to chromomycosis or sporothrychosis, as well as cutaneous manifestations of Paracoccidioides spp.33,34 In cases which the patient we observed in 1999 was cutaneous leishmaniasis (owing to the endemic area) and the similitude of the clinical characteristics (location of lesion on outer ear), other cases also with dermato-phites. Spinocellular epitheliomas or cutaneous metastasis of deep epidermoid carcinomas should also be included in the differential diagnosis, as well as the development of squamous cell carcinomas.5,35

Histopathological diagnosis

Histopathology constitutes the gold standard of the diagnosis on a clinical-epidemiological basis. A small sample of the lesion (biopsy or curettage) prepared with saline or 20% KOH can show abundant uniform round and/or oval cells 6–12 µm in diameter, with refringent cell walls. These cells multiply by simple gemation forming chains, being multiple gemation – as found in Paracoccidioides brasiliensis – unusual in L. loboi.34 Histological sections can be stained with hematoxylin-eosin or Gomori-Grocott (Figs 4 and 5).

Pathologically, there is a diffuse non-necrotic granulomatous lesion formed by foreign bodies, macrophages and multinucleated giant cells. There is a notable epidermal atrophy separated from the granuloma by the thin Unna bands.22 Occasionally the formation of pseudo hyphae has been described,27,28 as well as the presence of asteroid bodies in the multinucleated giant cells.39,40 There is a minimal lymphocytic infiltration in which all cells are T cells.40 Generally, cutaneous annexes and nerves are replaced by a massive infiltrate.35

If the lesion is ulcerous, the plasmocytic and neutrophilic infiltrate is evident. The histopathology of the lymph nodes is identical to the findings described for the granulomas.41,42

Treatment

As yet there is no effective treatment, ketoconazol has been proved without satisfactory results, as well as myconazol.43 Trimethoprin, amphotericine B and 5-fluorocytosine have not given significant benefits.44,45 Nevertheless, clofazamine, an effective drug tested in a large variety of mycoses, and especially in Nocardias, which has a known anti-inflammatory effect in granulomatous processes, has shown certain therapeutical...
activity at a 100–200-mg/day dose. However, there is still a need to study the follow up of cases to determine its complete effectiveness.

Cryosurgery has been practiced with effective results; nevertheless, surgical excision with wide margins remains as the optimal solution.

**Conclusion**

Many aspects of this disease remain unknown. All cultivation efforts have been unfruitful and many pathogenic aspects remain uncertain, including treatment.

Surely the use of up-to-date molecular techniques will contribute to clarify many of these aspects. Nevertheless, it is necessary to strengthen clinics and epidemiology; tools that are already within our reach and that still hold many voids.

**American Trade Names**

- Pentavalent antimonials (meglumine antimoniate): Glucantime, Rhone Poulenc, France.
- Amphotericin B: Fungizone, Bristol-Myers Squibb, France.
- Itraconazol: Sporanox, Janssen Pharmaceutica, Belgium.
- Ketoconazol: Nizoral, Janssen Pharmaceutica, Belgium.
- Miconazol: Miconazol, Janssen Pharmaceutica, Belgium.
- Trimethoprim: Proloprim, Teva, USA.
- Clofazimine: Lamprene, Novartis Pharmaceuticals, USA.

**Acknowledgments**

We greatly appreciate contributions by Professor R. Pradinaud, whose work constitutes an endless source of knowledge and incentives to whoever intends to investigate this fungus, which he himself has called “enigmatic”.

We would like to thank Mrs Maria Eugenia Gallinoto for her kind support and advice.

**References**


---

**Figure 4** Haematoxylin-eosin ×100. Chains of yeast cells in the dermis surrounded by a clear halus. Note the characteristic double refraction of the membrane and connection between cells.

**Figure 5** Gomori-Grocott ×100. Numerous tissue form cells of *Lacazia loboi* in branched clusters with thick walls and a clear center in which some internal structures can be evidenced. Note the process of budding.