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Lucio's leprosy: A clinical and therapeutic challenge

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Abstract Leprosy has been a challenge in different areas of medicine; in underdeveloped countries it remains a public health problem, in which the social and economic problems facilitate the disease persistence. The diagnosis and consequently the treatment are delayed due to the clinical polymorphism of leprosy, which especially at the beginning the manifestations are not as evident, as is the case of diffuse lepromatous leprosy. This favors the disabilities and the development of the reaction episodes. Fortunately, reaction episodes have decreased with the use of multidrug therapy, and better control of the type 2 reactions has been managed with the use of thalidomide, as in Lucio's phenomenon.

Introduction

Leprosy is considered an infectious systemic disease of chronic evolution caused by *Mycobacterium leprae*, acid-fast bacilli identified in 1873 by Gerhard Armauer Hansen. It affects mainly the skin and peripheral nerves, and without treatment it can be progressive and can cause permanent sequelae, especially in lepromatous cases.[1,2]

The clinical expression of the disease depends on the host immune response against *M leprae*. Patients with effective T-cell mediated immunity develop polar tuberculoid type with few bacilli (paucibacillary); instead patients with ineffective humoral response develop polar lepromatous type with numerous bacilli (multibacillary).[1,3] In polar lepromatous, there are two main clinical forms: nodular lepromatous leprosy and diffuse lepromatous leprosy or Lucio's leprosy. In the first form, the nodules are on the diffuse infiltration, while in the second, there is only a generalized infiltration without nodules. In addition to this essential difference, Lucio's leprosy has a special type of lepra reaction, which histopathologically corresponds to necrotizing vasculitis with thrombosis, named Lucio's phenomenon or necrotizing erythema by Latapi.[4,5]

For many years, Lucio's leprosy was considered exclusive of Mexico with strong effect on the Northeast of the country, particularly in Sinaloa; however, other cases have been observed and published in different countries like Costa Rica, Argentina, Brazil, and India.[4,5]

The first effective therapy for leprosy was born with the use of sulfones in 1941, and leprosy became curable, but it gave rise to a new problem: drug resistance. To avoid this problem, the World Health Organization (WHO) introduced the multidrug therapy (MDT) in 1981; from this moment reaction episodes like Lucio's phenomenon have decreased considerably, as well as the endemic and disabilities. There are very few new cases of leprosy in developed countries and it is mostly seen in immigrants from endemic countries, although it remains a public health problem in underdeveloped countries.[1,6]

The origin of the concept

Lucio's leprosy is a well-defined clinical form of polar lepromatous and throughout its history has received diverse names. The most popular names are the Spotted or Lazarine

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Leprosy, Lucio's Leprosy or Diffuse Leprosy, Pure and Primitive Diffuse Lepromatous Leprosy, and Leprosy of Lucio and Latapi, which was proposed by Frenken in honor to Prof. Fernando Latapi who identified it in 1936.[2,4,7]

The first to mention this case was Ladislao de la Pascua, and his observations were published in 1844 with the title 'Elefanciasis de los Griegos.' He says: "… and the third one, not referred to or described by any known authors, consists mostly of the production of red and painful spots that become ulcerated, this last patients are what we called in Mexico Lazarine." In this contribution, de la Pascua points out his purpose to describe it more accurately, which apparently he could not do. Rafael Lucio, in collaboration with Alvarado, was considered to be the first to make the description of this "spotted" or "lazarine" clinical form in his "Opúsculo sobre el Mal de San Lázaro o Elefanciasis de los Griegos," published in 1852 (Figure 1).[4,8,9]

This form of leprosy was ignored and misunderstood by the leprologists for 84 years, until 1936 when Latapi identifies this form, describes its main clinical manifestation as the generalized diffuse non-nodular infiltration, and calls it 'pure or primitive diffuse lepromatous leprosy.'[4]

M leprae and *M lepromatosis*

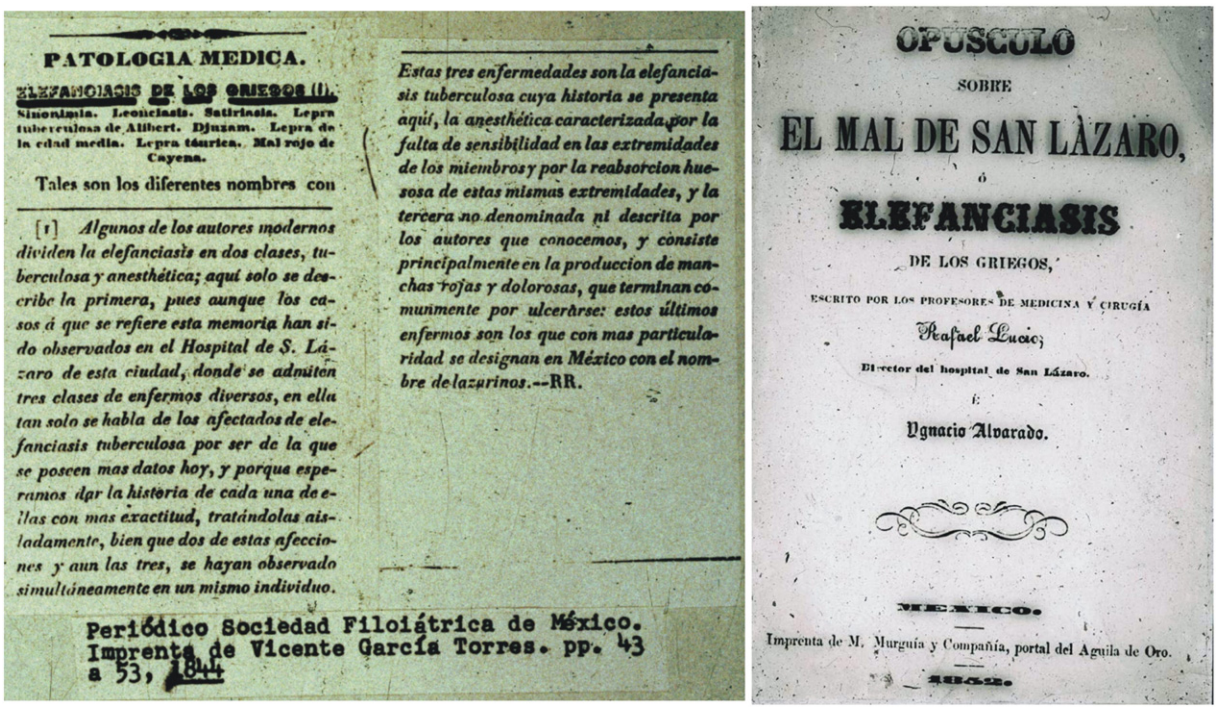
Leprosy was considered the first bacterial disease until 1873, when Armahuer Hansen, a Norwegian doctor, identified the etiological agent of *M leprae,* intracellular bacillus, gram-positive, acid-fast bacilli (AFB), with the capacity to group in globi shape or packs of cigarette in the microphages. It does not grow in artificial culture, but can be cultured in nine-banded armadillos, in the plantar cushion of the mouse, and in the mangabey monkey.[1]

The genome analysis suggests that the bacteria most likely originated in Africa and later spread into Asia and South America.[10,11]

From the wall components of *M leprae* the most important, from an immunological point of view, are lipoarabinomannan and phenolic glycolipid-I because both are able to cause degression of suppressor T cells or inhibit the macrophage bactericidal capacity. The phenolic glycolipid-I has a terminal trisaccharide, which gives specificity and induces production of IgM antibodies. It favors the entry of mycobacteria into the nerves when is united to laminin 2 of the Schwann cell.[10–12]

M leprae was considered as the only etiological agent of leprosy until 2008, when Hans et al, Texas University researchers published their findings in two Mexican immigrants deceased by sepsis with necrosis cutaneous and internal organs vasculitis diagnosis. When the bacterial agent search was done, they found multiorgan infiltration with acid-fast bacilli and concluded that it was diffuse lepromatouse leprosy (DLL) with Lucio's phenonmenon.[13]

Six of the genes were amplified through molecular clinical trials of the AFB and using the polymerase chain reaction (PCR). Significant genetic differences were found with *M leprae,* including a 2.1% divergence of the 16S ribosomal RNA a highly conserved marker of bacterial evolution. Phylogenetic analyses of the genes of 16S rRNA, rpoB, and hsp65 indicated that both organisms evolved from


PATOLOGIA MEDICA.

ELEFANCIASIS DE LOS GRIEGOS (1).

Sinonimia. Leonciasis. Satiriasis. Lepra tuberculosa de Alibert. Djuzam. Lepra de la edad media. Lepra táurica. Mal rojo de Cayena.

Tales son los diferentes nombres con

Estas tres enfermedades son la elefanciasis tuberculosa cuya historia se presenta aquí, la anesthética caracterizada por la falta de sensibilidad en las extremidades de los miembros y por la reabsorcion huesosa de estas mismas extremidades, y la tercera no denominada ni descrita por los autores que conocemos, y consiste principalmente en la produccion de manchas rojas y dolorosas, que terminan comunmente por ulcerârse: estos últimos enfermos son los que con mas particularidad se designan en México con el nombre de lazarinos.--RR.

[1] Algunos de los autores modernos dividen la elefanciasis en dos clases, tuberculosa y anesthética; aquí solo se describe la primera, pues aunque los casos á que se refiere esta memoria han sido observados en el Hospital de S. Lázaro de esta ciudad, donde se admiten tres clases de enfermos diversos, en ella tan solo se habla de los afectados de elefanciasis tuberculosa por ser de la que se poseen mas datos hoy, y porque esperamos dar la historia de cada una de ellas con mas exactitud, tratándolas aisladamente, bien que dos de estas afecciones y aun las tres, se hayan observado simultáneamente en un mismo individuo.

Periódico Sociedad Filoiátrica de México. Imprenta de Vicente García Torres. pp. 43 a 53, 1844

OPUSCULO

SOBRE

EL MAL DE SAN LÀZARO,

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ELEFANCIASIS

DE LOS GRIEGOS,

ESCRITO POR LOS PROFESORES DE MEDICINA Y CIRUGÍA

Rafael Lucio;

Director del hospital de San Lázaro.

Y

Ygnacio Alvarado.

MEXICO.

Imprenta de M. Murguía y Compañía, portal del Aguila de Oro.

1852.

Fig. 1 (left) Text of Ladislao de la Pascua 1844. In Elefanciasis de los Griegos. (right) Cover of the booklet about "El Mal de San Lazaro" of Rafael Lucio.