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Clinical aspects of leprosy

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Abstract Leprosy is a chronic, infectious disease caused by *Mycobacterium leprae*. It mainly affects the peripheral nervous system, skin, and certain other tissues such as the reticulo-endothelial system, bones and joints, mucous membranes, eyes, testes, muscles, and adrenals. Leprosy clinical presentation varies from few to widespread lesions. In most patients, early leprosy presents as macular and hypopigmented lesions. This initial clinical presentation is known as indeterminate leprosy and occurs in individuals who have not developed cell-mediated immunity against *M leprae* yet. The number of lesions depends on the genetically determined cellular immunity of the patient. Individuals presenting a vigorous cellular immune response and limited humoral immune responses to *M leprae*, usually present few skin lesions. Without treatment, those patients tend to evolve into the polar tuberculoid or borderline tuberculoid form of leprosy. Due to the inability to mount an effective cellular-mediated response to *M leprae* and the consequent hematogenous spread of the bacilli, some patients may present with numerous and symmetrically distributed hypochromic lesions. Without treatment these patients evolve to a nonresistant form of leprosy, polar lepromatous.

Clinical leprosy

Leprosy is a chronic, infectious disease caused by *Mycobacterium leprae*. It mainly affects the peripheral nervous system, skin, and certain other tissues such as the reticulo-endothelial system, bones and joints, mucous membranes, eyes, testes, muscles, and adrenals. The clinical presentation of leprosy clinical presentation varies from few to widespread lesions.[1] Similarly, histopathology of skin lesions varies from compact granulomas to diffuse infiltration of dermis, which largely depend upon the immune status of the patient and may not be in agreement with the clinical diagnosis.[2–4] Leprosy classification has been a matter of debate for many years.[4] The first classifications were based only upon clinical parameters, generating confusion and controversies. In 1953, during the Madrid congress, a classification based on four main disease groups was proposed: lepromatous leprosy, tuberculoid leprosy, indeterminate leprosy, and borderline or dimorphous leprosy.[5,6]

In 1962 [2] and 1966 [3], Ridley and Jopling proposed a new classification based not only on the clinical features, but also on histopathology, bacterial load and the degree of cell-mediated immune response (CMI) against *M leprae*, which is evaluated by the result of Mitsuda's intradermal test. Based on these immunopathological criteria, patients are divided into a five-group spectrum that extends from tuberculoid leprosy (TT) with heightened CMI (hyperegic pole) through borderline tuberculoid (BT), borderline-borderline (BB), borderline lepromatous (BL), to the poorly resistant (anergic) lepromatous

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type (LL) characterized by increased humoral immunity. Indeterminate (I) leprosy does not fall into this spectrum because there is a lack of correlation between the clinical and histopathological features. This clinical form represents an early stage of the disease in which the degree of CMI is still not clear.[1]

In 1982, the World Health Organization (WHO) advocated the use of two different regimens of multidrug therapy for the treatment of leprosy.[7] Patients are classified as paucibacillary if the bacterial index (BI) is less than 2+ or as multibacillary if the BI is equal or higher than 2+.[7–9] BI is a parameter directly related to bacterial load, being the estimated number of all bacteria, regardless of their shape, present in a smear. The results are expressed on a logarithmic scale: 1+ (at least 1 bacillus in every 100 fields), 2+ (at least 1 bacillus in every 10 fields), 3+ (at least 1 bacillus in every field), 3+ (at least 1 bacillus in every field), 4+ (at least 10 bacillus in every field), 5+ (at least 100 bacillus in every field), and 6+ (at least 1000 bacillus in every field).[7,8]

In this contribution, the authors have decided to describe leprosy clinical manifestations based on Ridley and Jopling classification. One must remember that the first signs that lead leprosy patients to seek for medical attention are most often dermatological. Careful examination of skin is a key element in leprosy diagnosis.

I leprosy

In most patients, early leprosy presents as macular and hypopigmented lesions. This initial clinical presentation is known as I leprosy and occurs in individuals who have not developed cell-mediated immunity against *M leprae* yet.[1,10] The single (Figure 1) or multiple macules have no more than 3–4 cm wide, present with a smooth surface and are not scaling or pruriginous (Figure 2). The lesions may also be red in light-skinned patients or coppery in dark-skinned patients. There is normal sweating and body hairs are present.[11–14]

A very important characteristic of leprosy lesions is the impaired sensation (anesthesia). On I leprosy lesions the patient commonly presents with loss of thermal sensation, not being able to distinguish between a cold and a hot tub of water. Hyperalgesia often precede the detection of skin lesions.[12,13]

The number of lesions depends on the genetically determined cellular immunity of the patient. Individuals presenting a vigorous cellular immune response and limited humoral immune responses to *M leprae*, usually present few skin lesions.[12] Without treatment, those patients tend to evolve into the polar T or BT form of leprosy. Individuals within the tuberculoid pole may present a tendency towards spontaneous healing. Patients presenting with numerous or countless number of hypochromic lesions, without treatment, tend to evolve into BB, BL, or LL forms.[13,14]

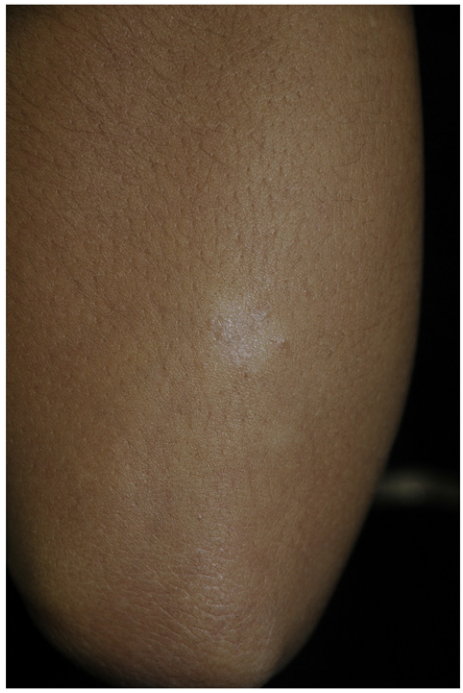

Fig. 1 Indeterminate leprosy. A single, irregular and hypochromic patch on the left elbow.

The diagnosis of indeterminate patients may be difficult. Besides sensory tests already mentioned, the histamine test is a very useful diagnostic tool for light-skinned patients. It consists in the application of one drop of histamine (dilution - 1/1000) within and around the suspected hypochromic lesion. After 1–2 minutes, a triphasic skin reaction known as Triple Response of Lewis will occur: first a red line develops at the site due to histamine release, then a flare develops around the red line, and lastly a wheal is formed as a result of local edema. This triple reaction is only observed in the normal skin or hypochromic lesions caused by other diseases; if the lesion is due to leprosy the response of the skin to histamine will be incomplete once this local reflex depends upon the integrity of sympathetic nerve fibers.[12]

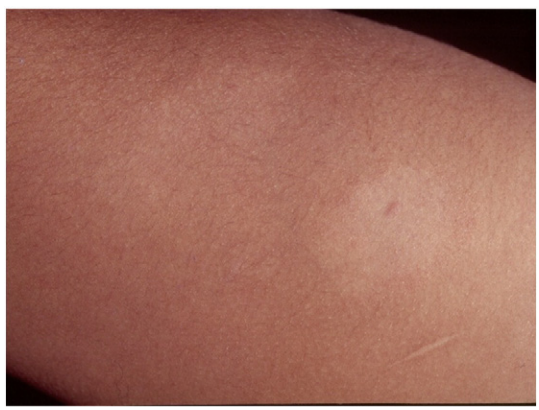

Fig. 2 Indeterminate leprosy. An irregular, hypochromic patch on the lower limb.