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Neuropathic pain in leprosy

Irina Raicher, MD[a], Patrick Raymond Nicolas Andre Ghislain Stump, MD[a], Rosemari Baccarelli, PT, PhD[b], Lucia H.S.C. Marciano, OT, MSc[b], Somei Ura, MD, MSc[b], Marcos C.L. Virmond, MD, PhD[b], Manoel Jacobsen Teixeira, MD, PhD[a], Daniel Ciampi de Andrade, MD, PhD[a,c,*]

[a]*Department of Neurology, Clinics Hospital of the University of Sao Paulo Medical School, Av.Dr. Éneas de Carvalho Aguiar, 255, 05403-900 Sao Paulo, Brazil*
[b]*Instituto Lauro de Souza Lima, Bauru, Brazil*
[c]*Pain Group, Cancer Institute of the State of Sao Paulo, Av. Dr. Arnaldo, 251, 01246-000 Sao Paulo, Brazil*

Abstract Nerve impairment is a key clinical aspect of leprosy and may present the distribution of mononeuropathy or multiple nerve trunks, small cutaneous nerve fibers, and free nerve endings. The clinical range of leprosy is determined by individual cell-mediated immune response to infection that also may play a role in different types of pain syndromes in leprosy. Previous studies reported a high prevalence of neuropathic pain in leprosy. In an Ethiopian study with 48 patients, pure nociceptive pain was experienced by 43% of patients and pure neuropathic pain (NeP) by 11% of patients. In an Indian study, 21.8% of leprosy patients had pain with neuropathic characteristics. These rates underlie the need to develop tools for the early diagnosis and detection of infection and its complications, such as nerve damage and pain. In a larger sample with leprosy-associated NeP (n = 90), we have applied the *Douleur Neuropathique en 4 questions* (DN4) and found sensitivity = 97.1% and specificity = 57.9%. The high sensitivity of this tool in leprosy patients suggests that it could be a valuable tool to screen for neuropathic pain in this population and could be used as part of health care programs aimed at detecting, treating, and rehabilitating leprosy in endemic areas.

Neuropathy in leprosy

Leprosy (Hansen's disease) is a chronic infection caused by the intracellular infection of *Mycobacterium leprae*.[1] Its global prevalence has fallen substantially in the past five decades; however, incidence continues to be high in more than 80 countries within Asia, Africa, and Latin America.[2] Prevalence in Brazil is 4.4/10,000 population.[3] A survey done in Maharashtra, India, found rates of three to nine cases per 10,000 population, and 30% of these newly diagnosed cases were in children.[4] These data indicate that despite huge efforts for its control, leprosy continues to pose a heavy burden on a large part of the world's population due to active infection and side effects of treatment. *Mycobacterium leprae* is ominously present in the environment, but only part of the population is susceptible to infection due to hosts' individual immunologic response. Leprosy affects skin, eyes, upper respiratory tract, testes, and peripheral nerves[5] and may be associated with systemic features. Different segments of the peripheral nerves can be affected by the direct effect of infection or after multidrug therapy (MDT).

* Corresponding author. Tel.: +55 11 3069 6000.
E-mail address: Ciampi@usp.br (D. Ciampi de Andrade).

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Isolated or multiple nerve trunks, small cutaneous nerve fibers, and free nerve endings can be differently affected, leading to different degrees of autonomic, sensory, and motor dysfunction.[6–10]

The clinical range of leprosy is determined by individual cell-mediated immune response to infection. The different presentations may be categorized according to the Ridley-Jopling classification, which is based on skin lesion type and bacterial load.[11] Nerve impairment is a key clinical aspect of leprosy and is an important cause of disability and poor quality of life in affected individuals.[12] This underlies the need to develop tools for the early diagnosis and detection of both the infection and its complications, such as nerve damage. Sensory damage in leprosy includes early loss of pain and temperature perception, followed by increase of tactile and pressure detection thresholds.[6] The anatomic distribution and onset of neuropathy can vary according to the type of leprosy, being more insidious and widespread in lepromatous cases, localized and with acute onset in tuberculoid, and with an overlapping pattern in borderline types. In the indeterminate phase of the disease, cutaneous nerve endings are preferentially injured and nerve trunk damage has not yet developed,[6–10] leading to localized patterns of nerve injury that affects terminal branches in the skin. Peripheral nerves can be affected in its cutaneous branches, in a single (mononeuropathy) or in multiple (multiple mononeuropathy) nerve trunks. A diffuse pattern caused by the presence of a spatially extensive multiple mononeuropathy is also recognized, resulting in a pattern of nerve involvement that is similar to a polyneuropathy, wherein length-dependent involvement of the limbs is more pronounced distally than proximally (glove and stocking pattern).[1] In such instances, it is challenging to clinically individualize each different nerve trunk affected by the disease (Figure 1). This "confluent" presentation is more often seen in the lepromatous leprosy.[6–10]

Leprosy neuropathy is a chronic condition in which acute and subacute flares occur during its insidious evolution. Its rate of development depends mainly on three factors:

1. The individual's immune response to infection, which determines the types of immunologic reactions that lead to neuritis (ie, type 1 reaction, present in borderline-borderline, borderline-tuberculoid, and tuberculoid patients; and type 2 reaction, present in lepromatous and borderline-lepromatous patients).
2. The spatial dimension of the infection, which is related to the number and preferential part of the peripheral nerve affected.
3. The temporal dimension, which is related to the time profile of disease progression (slow and chronic evolution or acute flares).

Classical neurologic syndromes are described in the leprosy literature as depending on the interplay between these previously enumarated factors and are called: neuritis associated or unassociated with reactions,[8] compression syndromes,[13] silent neuritis,[14,15] and mononeuropathy. These clinical presentations may or may not be accompanied by neuropathic pain.[16,17] Nociceptive pain can also be present in instances of

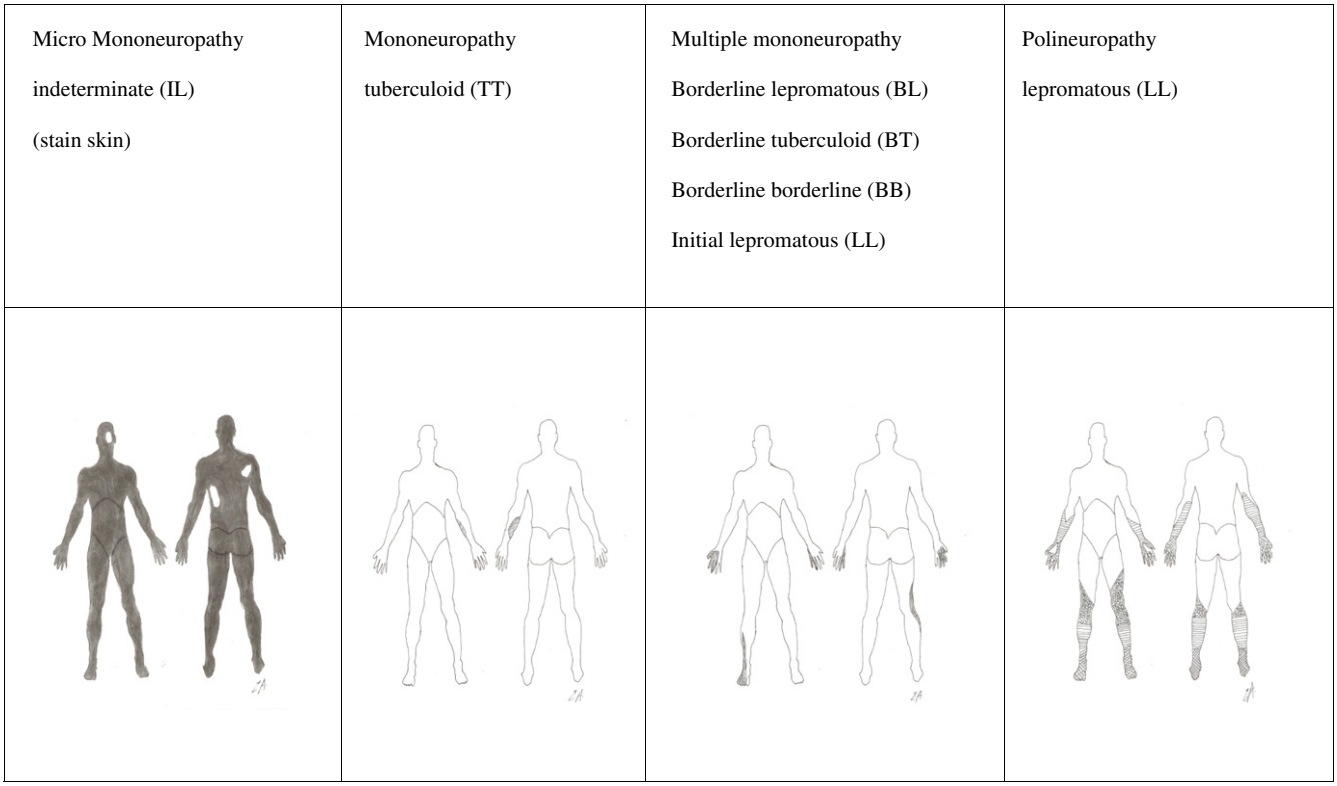

Fig. 1 Anatomic pattern of neuropathy in leprosy.