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Assessing nerves in leprosy

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Abstract Leprosy neuropathy is dependent on the patient's immune response and expresses itself as a focal or multifocal neuropathy with asymmetric involvement. Leprosy neuropathy evolves chronically but recurrently develops periods of exacerbation during type 1 or type 2 reactions, leading to acute neuropathy. Nerve enlargement leading to entrapment syndromes is also a common manifestation. Pain may be either of inflammatory or neuropathic origin. A thorough and detailed evaluation is mandatory for adequate patient follow-up, including nerve palpation, pain assessment, graded sensory mapping, muscle power testing, and autonomic evaluation. Nerve conduction studies are a sensitive tool for nerve dysfunction, including new lesions during reaction periods or development of entrapment syndromes. Nerve ultrasonography is also a very promising method for nerve evaluation in leprosy. The authors propose a composite nerve clinical score for nerve function assessment that can be useful for longitudinal evaluation.

Introduction

There are many ways to look at leprosy. Some consider the disease a neurologic affliction, whereas others consider it as a dermatologic affliction. Some observers, to make it easy and comprehensible, have divided it into an infectious disease and an immune-mediated neurologic disease.[1] In fact, it is a multisystemic disease that affects tissues originating from the embryonic ectoderm, affecting specially the skin, mucosa, and the peripheral nerves. It is not seen in the central nervous system. As an infectious disease, it always has both components: The infection and the immune response. These responses vary depending on the agent (*Mycobacterium leprae* [ML] is a peculiar bacterium) and on the host, as we see in other diseases, but they are more complex in leprosy due to the lengthy time of evolution. The following aspects are essential for the comprehension of neuropathy in leprosy (Hansen's disease [HD]): (1) the patient's immune response, which builds the clinical types of the disease and the different reactions undergoing during the treatment; (2) the involvement and extension of nerves and skin, expressed as numbers of nerves and skin areas affected; and (3) the temporal aspect (ie, the long and oscillatory evolution of this highly chronic disease, and its relation to the age of onset and duration of illness to immunologic leprosy reactions).[2]

Leprosy neuropathy usually evolves as a mononeuropathy or a mononeuritis multiplex (MM), and its focal distribution aspect can be seen, even in nerve fascicules and skin terminal branches through microscopy.[3] The clinical

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picture of polyneuropathy is actually confluent multiple neuropathies in multibacillary patients.

The HD/leprosy neuropathy is primarily demyelinating but frequently leads to axonal loss during its evolution. The bacilli specificity to Schwann cell (SC) membrane and its basal laminin is well known,[4,5] and it is not selective to one fiber modality. The involvement of fibers is universal.[6] It seems to predominate, at least in the beginning, in small fibers related to pain and thermal sensation. The HD neuropathy is temperature dependent. The bacilli grow better in areas with lower temperatures, both in skin and nerves. The most affected nerves are in the distal limbs and in the anatomic tunnels (at the elbows, wrists, knees, or ankles), while the skin regions mostly involved are those of the ear lobes, the elbows, and the knees, which are areas where skin smears are routinely done.

The effectiveness of the patient's cellular immune response is directly related to the clinical presentation. According to the immunopathologic spectrum of the Ridley and Jopling classification,[7] just a few nerves are affected in the pole tuberculoid (TT) and borderline tuberculoid (BT), leading to a mononeuropathy or a restricted mononeuropathy multiplex, while patients classified as borderline borderline (BB) and borderline virchowian (BV) will develop a full mononeuropathy multiplex. Patients in the virchowian virchowian (VV) pole usually develop an extensive mononeuropathy multiplex that may simulate a polyneuropathy (polyneuropathy-like pattern presentation of leprosy neuropathy).[8]

The HD neuropathy has three long-lasting phases of evolution: (1) the SC parasitization by ML, in which the clinical expression is poor or asymptomatic, and its estimated duration is from 3-5 to 10 years; (2) the acute and subacute periods, due to type 1 and type 2 reactions, in which symptoms are intense with sensory and motor loss and painful manifestations (up to 10 years); and finally (3) the last phase, which is characterized by late nerve impairments, caused mainly by the intraneural fibrosis, leading to an interstitial neuropathy.[9] During the development of the disease, two *complicating factors* must be mentioned, the development of entrapment neuropathies and neuropathic pain. Due to the extreme chronicity of the disease and the distinct periods of evolution in the patient management, a robust and reliable follow up system should be used.[10] An important problem in clinical practice is to find out if the painful manifestations result from active disease with persistent inflammatory disease or are due to neuropathic pain. The routine assessment of the nerve system should be able to lead insights about all these aspects.

Clinical evaluation

The evaluation of a person with neuropathy should be done in a systematized way, to allow a logical approach to the patient's disease. Leprosy neuropathy (LN) shows a pattern known as mononeuritis multiplex or multiple mononeuropathy, where manifestations are very asymmetric, meaning that the disease process has affected different nerves in different topographies and severities (Figure 1); however, LN has a particular type of mononeuritis multiplex, where nerves are affected in the coolest areas of the body, once ML ideally lives and thrives well below the human body temperature. In addition, ML, in non-myelinated and small myelinated nerve fibers, responsible for the autonomic function, pain, cold and hot sensations, has less impediment to go through the SC membrane than in the gross myelinated fibers.[5] The initial complaints are those of decreased sweat production and lack of pain and temperature sensations in a patchy distribution, concentrating initially at the dorsal aspects of the arms, at the anterior-medial-dorsal aspects of the legs, and at ears and malar aspects of face. In those patients at the tuberculoid spectrum, there is usually just one or only a few relatively small compromised areas, but in untreated patients at the lepromatous spectrum, the compromised area progressively expands to involve the dorsal aspects of the hands and arms, the medial aspects of the arms, and the anterior-lateral aspects of the thighs.

Some patients may notice decreased sweat production and decreased tactile sensations, but the most relevant manifestations from the patient's point of view are the loss of touch sensation and the loss of pain sensation, resulting in injuries and burnings without any unpleasant sensation. While the disease is restricted to the intradermal nerve branches, the vibration, postural sensation, motor function, and tendon jerks are preserved, but at some point in the disease history nerve trunks become clinically affected. Some patients may notice that occasional nerve trunks are enlarged and tender at

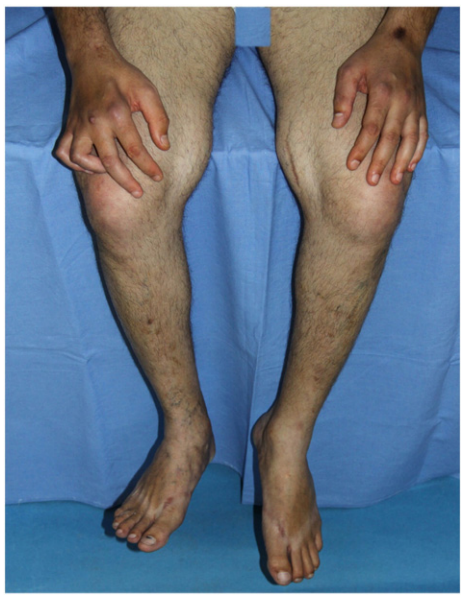

Fig. 1 In a patient with *mononeuropathy multiplex*, the motor involvement is pronounced at the right ulnar (ulnar claw hand) and at the left peroneus (drop foot).