Treatment of Peripheral Neuropathy in Leprosy: The Case for Nerve Decompression

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Summary: Plastic surgery has a tradition of caring for patients with facial deformity and hand deformity related to leprosy. The approach, however, to the progressive deformity and disability related to chronic nerve compression is underappreciated in the world today. A cohort of patients with leprous neuropathy from an indigenous area of leprosy in Ecuador was evaluated for the presence of chronic peripheral nerve compression, and 12 patients were chosen for simultaneous upper and lower extremity, unilateral, nerve decompression at multiple levels along the course of each nerve. The results at 1 year of follow-up show that 6 patients improved into the excellent category and 4 patients improved into the good category for improved function. Based on the early results in this small cohort of patients with leprous neuropathy, an approach to peripheral nerve decompression, encompassing the concept of multiple crush at multiple levels of each nerve, seems to offer optimism to improve upper and lower extremity limb function. Long-term studies with quality-of-life outcomes would be welcome. *(Plast Reconstr Surg Glob Open 2016;4:e637; doi: 10.1097/GOX.0000000000000641; Published online 17 March 2016.)*

Leprosy (Hansen's disease) is an ancient disease that continues to impose a significant societal burden and is still relevant to peripheral nerve and plastic surgery.[1,2] At least 213,899 new cases globally were last reported,[3] and currently, more than 4 million people worldwide experience disabilities due to Hansen's disease.[4] In the United States, leprosy continues to exist, with 175 new cases in 2014 and a prevalence of 293 as of today.[3] Physical disabilities resulting from Hansen's disease include paresthesias, muscle paralysis (eg, lagophthalmos, foot drop, and claw hands), ulcers, and amputations.

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Before the late 1940s, the cause of paralysis among patients with Hansen's disease was unclear. A major advancement occurred when the late leprologist and hand surgeon Paul Brand (1914–2003) observed that the Hansen's bacilli, *Mycobacterium leprae*, preferentially targeted peripheral nerves; he saw that abnormal "nerve swellings" occurred at specific locations "where the nerve lay close to the skin surface:" "[the tibial nerve] behind the ankle, [the peroneal nerve] just above the knee, […the median and ulnar nerves] at the wrist, […the facial nerve] at the chin and cheekbone, and […the ulnar nerve] just above the elbow."[5] Brand witnessed the cause of leprous neuropathy.

Since Brand's observations in the late 1940s and the introduction of multidrug therapy in 1981, more attention has gradually been placed on understand-

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ing, preventing, and treating nerve damage as the source of the disabilities and deformities, and therefore as the root of the stigma associated with Hansen's disease.[6,7] In 1975, Antia et al.[8] demonstrated that even clinically uninvolved nerves, such as the superficial branch of the radial nerve, could present with definite nerve damage.

At the turn of the century, Ng et al.[9] demonstrated that phenolic glycolipid-1 of *M. leprae* binds specifically to laminin-2 (see Supplementary Digital Content 1, which displays structure of the C-terminal laminin G-like domains 4 and 5 of the laminin alpha-2 chain; ***http://links.lww.com/PRSGO/A179***) within the basal lamina of Schwann cell-axon units, promoting bacterial invasion and, even after bacterial cell death, damage to Schwann cells and nerves. Around the same time, Scollard et al.[10] observed that *M. leprae* extensively colonized epi- and endoneural blood and lymphatic vasculature as well. In 2010, Teles et al.[11] found that *M. leprae* can also bind mannose receptors on Schwann cells via lipoarabinomannan, which, as Bahia El Idrissi et al.[12] recently demonstrated, can also activate complement and promote inflammation. Molecular studies in 2007 revealed that *M. leprae* has a defective heat stress response that restricts the bacterium to superficial and cooler regions of the body, such as the peripheral nerves.[13] Taken together, the evidence seems to support that after bacterial colonization of superficial peripheral nerves via phenolic glycolipid-1 and/or lipoarabinomannan, and/or after immunologic reactions, the nerve is more likely to suffer ischemia from "inflammation, trauma, or mechanical stress [such nerve compression at tunnels and near the joints],"[10] contributing to the development of neuropathy.[14,15]

Despite arising from different mechanisms, nerve compression among diabetics may help us understand the treatment of leprous neuropathy. In diabetics, nerve compression results from narrow anatomic sites, such as tunnels, placing increased external pressure on peripheral nerves predisposed by the diabetes to increased water retention and therefore swelling.[16–18] The resulting compression causes ischemia of the nerve and paresthesias, 2 aspects that diabetic and leprous neuropathies have in common. Surgical decompression has been shown to be effective in treating diabetic neuropathy, when chronic nerve compression is present and using techniques designed to decompress each peripheral nerve at multiple sites along its pathway at known locations for anatomic narrowing.[19,20] Here, we present evidence to support the use of similar nerve decompressions in the upper and lower extremities in the treatment of leprous neuropathy.

PATIENTS AND SURGICAL TECHNIQUE

This is a level IV, retrospective therapeutic study. All patients gave verbal informed consent to having before and after surgery photography and receiving surgical decompression as part of a medical mission trip to Guayaquil, Ecuador. Patients were selected if they satisfied all the following criteria: being more than 6 months without multidrug therapy for Hansen's disease; not having an ongoing type II reaction; having either upper or lower extremity pain, numbness, weakness and/or deformity; and presence of positive Tinel's signs at known sites of entrapment; or tender, thickened peripheral nerves. In total, 51 patients and 120 nerves were measured and analyzed for peripheral nerve dysfunction using the Pressure-Specified Sensory Device (Sensory Management Services, LLD, Baltimore, Md.) (Table 1). The degree of peripheral nerve dysfunction as measured by the Pressure-Specified Sensory Device was not a factor as to whether a patient was included or excluded from surgery.

Twelve patients were selected for the surgery. In each patient, surgical decompression of the 3 nerves in an arm and 3 in a leg was done simultaneously using a 2-team approach and under general anesthesia. Pneumatic tourniquets, bipolar coagulators, and 3.5× loupe magnification were utilized.

M. leprae localizes to superficial nerves, and the host response makes these nerves vulnerable to compression at known sites of nerve compression. Our approach thus emphasized decompression of each nerve at each site in which it could be decompressed in that extremity. The ulnar nerve was decompressed at the elbow and at the wrist. Submuscular transposition by musculofascial lengthening decompressed the ulnar nerve at the elbow; decompression at the wrist included the sensory and motor branches of the ulnar nerve. The median nerve was decompressed at the wrist and forearm. If pronator syndrome was absent, submuscular transposition by musculofascial lengthening also decompressed the median nerve. The superficial sensory branch of the radial nerve was also decompressed in the forearm. The tibial nerve was decompressed at each of its branches in the medial, lateral, plantar, and calcaneal tunnels. The peroneal nerve was decompressed at both the

Table 1. Staging of Peripheral Nerve Dysfunction with the PSSD

Peripheral Nerve (n = 117)	% Mild-Moderate (n)	% Severe (n)	% Anesthetic (n)
Median (n = 29)	41 (12)	24 (7)	35 (10)
Ulnar (n = 40)	35 (14)	37 (15)	28 (11)
Peroneal (n = 30)	10 (3)	13 (4)	77 (23)
Tibial (n = 18)	11 (2)	16 (3)	73 (13)

PSSD, Pressure-Specified Sensory Device.

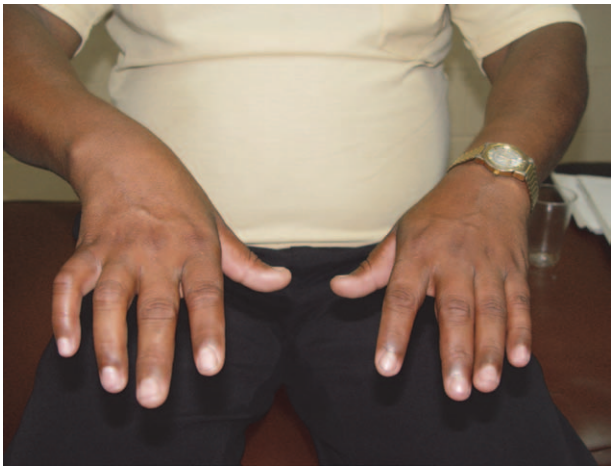

Fig. 1. View of patient 1 year after nerve decompression in the left upper extremity. This patient had bilaterally symmetrical degree of nerve compression before surgery. The improvement in the left side is obvious. For the ulnar nerve, not only was a submuscular transposition with musculofascial lengthening done, plus internal neurolysis, but also, at the wrist level, a neurolysis was done on the motor branch in Guyon's canal.

fibular neck and over the dorsum of the foot. Internal neurolysis was performed as indicated by intraoperative findings of firmness, intraneural fibrosis, and/or loss of perineurial markings.

RESULTS

During the period of this study, all patients healed primarily from surgery, and there were no postoperative complications. With regard to motor function, patients who had paralysis but who did not have fixed joint contractures were observed to recover movement and over the year of follow-up to have improvement in strength and mobility.

Seven patients reported better sensation in the hand and foot that were operated on after than before surgery; they also had better feeling in operated extremities compared with nonoperated extremities. Two patients reported no sensory improvement. One patient had a brain metastasis, and the surgically treated lower extremity became worse. Overall, postoperatively, 6 patients were in the excellent category, 4 in the good category, and 2 did not improve. Figures 1 and 2 illustrate improvement in selected patients.

DISCUSSION

We presented a preliminary report of some of over 100 cases of leprous neuropathy treated with surgical decompression over the past decade. The vast majority of patients have excellent or good improvement in motor and sensory function.

Data on the effects of neurolysis on patients with leprous neuropathy are limited. Neurolysis has been reported to restore sensation in 50% of cases of leprous neuropathy.[21,22] Furthermore, in 2001 and 2003, it was found that neurolysis improved musculature and muscular function.[23,24] Motor recovery rates as high as 89% have been reported.[21] The effects of nerve decompression for leprous neuropathy also include ulcer healing and pain relief.[21] Most recently, nerve decompression was used in the United States to treat ulnar neuropathy in a case of Hansen's disease.[25] The authors report that after surgery, sensation and strength returned in the ulnar distribution.

Studies on the effectiveness of nerve decompression, especially those with high levels of evidence, are lacking. A literature review concluded that the only 2 existing randomized control trials (RCTs), published in 1984 and 1996, were of such low quality that

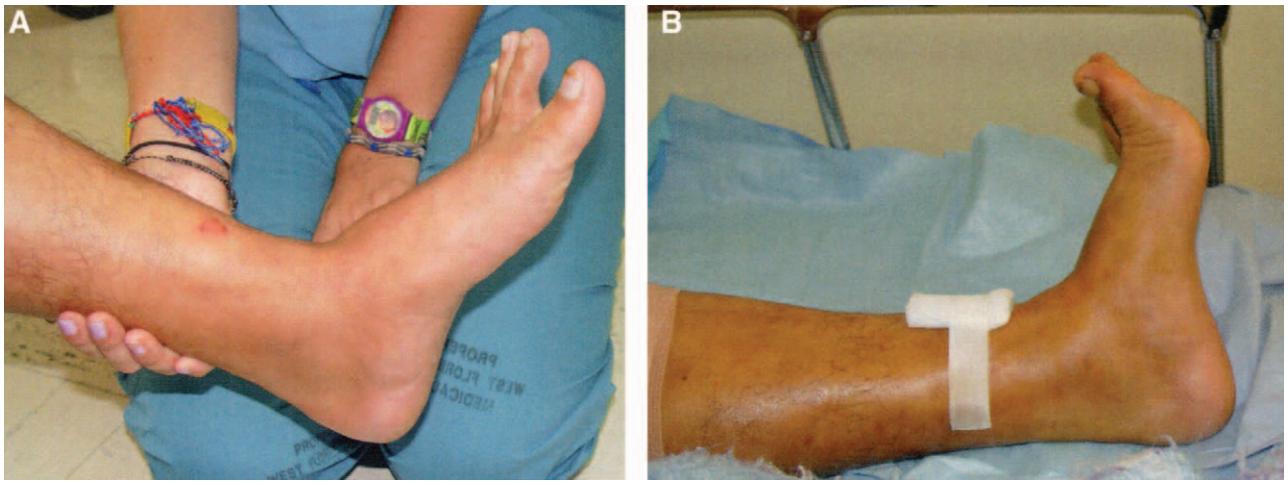

Fig. 2. A, Immediately preoperative view of patient who had inability to extend big toe and dorsiflex ankle. B, Immediately postoperative view of patient after neurolysis of common peroneal nerve at the knee, who had regained ability to extend big toe and dorsiflex the ankle.

robust conclusions could not be made about the efficacy of nerve decompression on leprous neuropathy.[26] The authors and others have called for a high-quality RCT studying surgical decompression in leprous neuropathy.[27] From our experience, nerve decompression brings relief to and rehabilitates patients with Hansen's disease; an RCT would likely be successful in showing the benefits of nerve decompression.

The limitations of this study are that it is a single-center study with a small number of patients. A further limitation of this study is that the follow-up of the small cohort was limited to 1 year. Finally, it was not within the purpose or scope of this study to evaluate the effect of steroids on leprous neuropathy.

CONCLUSIONS

Nerve damage caused by leprosy remains a significant cause of disabilities due to leprosy. It is possible, through nerve decompression, to reverse the nerve damage and improve patient sensation and strength. There is a great potential for a successful RCT in nerve decompression for leprous neuropathy.

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