Lepr Rev (2012) **83,** 93–97

CASE REPORT

Leprotic neuropathy misdiagnosed as chronic inflammatory demyelinating polyneuropathy

SE HOON KIM*, HA YOUNG SHIN**,
SEUNG MIN KIM**, KI-HAN KWON***
& YANG KI MINN***
**Department of Pathology, Yonsei University College of Medicine, Seoul, Korea*
***Department of Neurology, Yonsei University College of Medicine, Seoul, Korea*
****Department of Neurology, Hangang Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Korea*

Accepted for publication 30 November 2011

Introduction

Leprosy is a disease characteristically involving the skin and peripheral nerves. Leprosy is diagnosed typically by observation of representative skin lesions and the presence of acid-fast bacilli (AFB) in a skin smear or a skin biopsy; deep nerve biopsies such as a sural nerve biopsy are not routine procedures. Therefore, very few reports of sural nerve biopsies that yield a pathologic finding of leprosy are available; moreover, electron microscopic studies are still rarer.

A nerve conduction study (NCS) and sural nerve biopsy are the gold standards for the diagnosis of chronic inflammatory polyneuropathy (CIDP). NCS findings that indicate leprosy are known as mononeuropathy pattern or mononeuritis multiplex pattern[1] and these findings distinguish leprosy from demyelinating polyneuropathies such as CIDP.

In non-endemic areas such as Korea, leprosy is not the most likely diagnosis to account for subacute peripheral nerve lesions. We report a case of lepromatous leprosy neuropathy that was misdiagnosed as CIDP after a nerve conduction study and a sural nerve biopsy.

Case Report

A 49-year-old woman was admitted to our hospital because of slow, progressive sensory changes with motor weakness. She had no erythematous skin lesions, except for multiple burn scars on her right arm (Figure 1).

Correspondence to: Yang-Ki Minn, M.D., Ph.D., Department of Neurology, Hangang Sacred Heart Hospital, 94-200 Yeungdeungpo-dong, Yeungdeungpo-gu SEOUL, KOREA 150-719 (Tel: +82-2-2639-5690; Fax: +82-22635-5827; e-mail: yangki2@unitel.co.kr

0305-7518/12/064053+05 $1.00

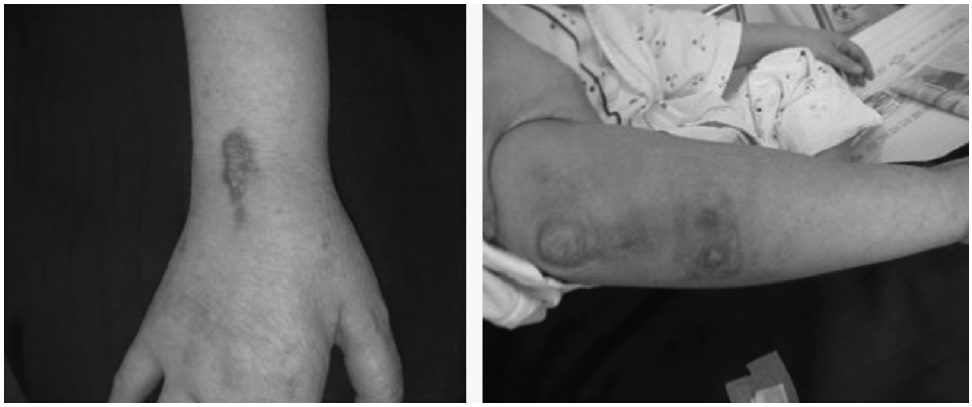

Figure 1. Multiple burn scars on the right arm.

No enlarged nerves were observed, even along the ulnar and posterior auricular nerves. Deep tendon reflexes were preserved. A nerve conduction study revealed a pattern of sensory-motor polyneuropathy. Bilateral ulnar, tibial, and sural nerve function abnormalities were observed. Left ulnar nerve-conduction block was apparent at the elbow segment. These findings were compatible with CIDP. A high positive titer of IgM anticardiolipin antibody and a negative titer of IgG type in serum were obtained. A sural nerve biopsy was performed to confirm the diagnosis. On routine histopathologic examination, scattered mononuclear inflammatory cell infiltration with mild fibrosis was observed (Figures 2a and 2b).

Neither multinucleate giant cells nor granulomatous inflammation were evident. Immunohistochemistry revealed that most inflammatory cells were CD68-positive cells (Figure 2c).

Teased fibre preparation test and semithin sections showed marked myelinated nerve fibre losses with some remyelination (Figures 2d and 2e).

Some lymphocytes with CD3 and CD20 positivity were scattered throughout the perineurium, and a few were identified inside the nerve parenchyma. The patient was subsequently diagnosed with CIDP and treated with a high dose of steroids. However, we could not explain the retention of deep tendon reflex. One month later, when biopsy specimens were re-stained, Ziehl-Neelsen staining revealed many scattered AFB in the nerve parenchyma (Figure 2f). Electron microscopic (EM) examinations revealed many electro-dense oval-shaped bacilli, compatible with *Mycobacterium leprae* (*M. leprae*), in unmyelinated Schwann cells (Figure 3).

Discussion

Based on the initial evidence in this case, the patient's symptoms could reasonably indicate a diagnosis of either leprosy or CIDP. Electrophysiological findings and routine biopsy findings point to CIDP; the only feature which would probably rule out CIPD was preserved deep tendon reflex. Because autoimmune diseases are often the cause of peripheral neuropathy, we determined various autoantibody levels. IgM type of anticardiolipin antibody titer was high, but this was not a concern because she had frequent abortion history. Antiphospholipid antibodies (aPL) have been reported not only in autoimmune disorders but also in various

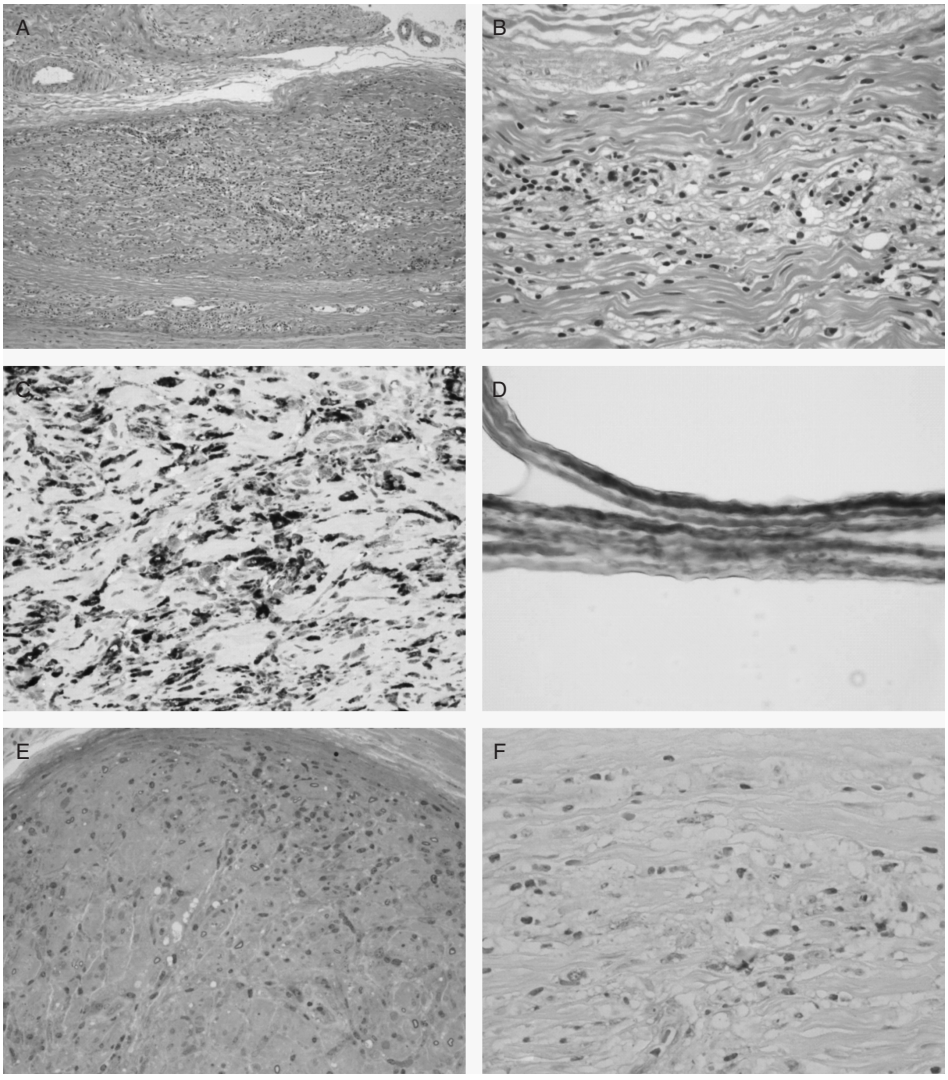

Figure 2. Histopathologic findings of this case. a) Low-power view shows diffusely infiltrative inflammatory cells in the nerve fibre and perineurium (hematoxylin-eosin [H-E], 100×). b) High-power view shows pale foamy macrophage infiltration with fibrosis in the nerve fibre (H-E, 400×). c) Immunohistochemistry for CD68 shows macrophage infiltration (CD68, 400×). d) and e) Teased nerve fibre preparation (d, osmium tetraoxide, 100×) and semithin-section (e, toluidine blue, 400×) show marked loss of myelinated nerve fibres (less than 1,000/mm^2). f) Ziehl-Neelsen staining reveals many scattered acid-fast bacilli (Ziehl-Neelsen, 600×).

infectious diseases. Other investigators reported the cases of 51 outpatients with leprosy without any clinical features of antiphospholipid syndrome (APS), 35 with lupus anticoagulant, and 31 with anticardiolipin antibodies. Leprosy-related aPL resemble those found in patients with APS, but the immunoglobulin isotype is different, and IgM much more prevalent in leprosy patients.[2]

The electrophysiological findings and initial pathological findings were compatible with demyelinating disease. The clinical feature of this disease is a granulomatous reaction to

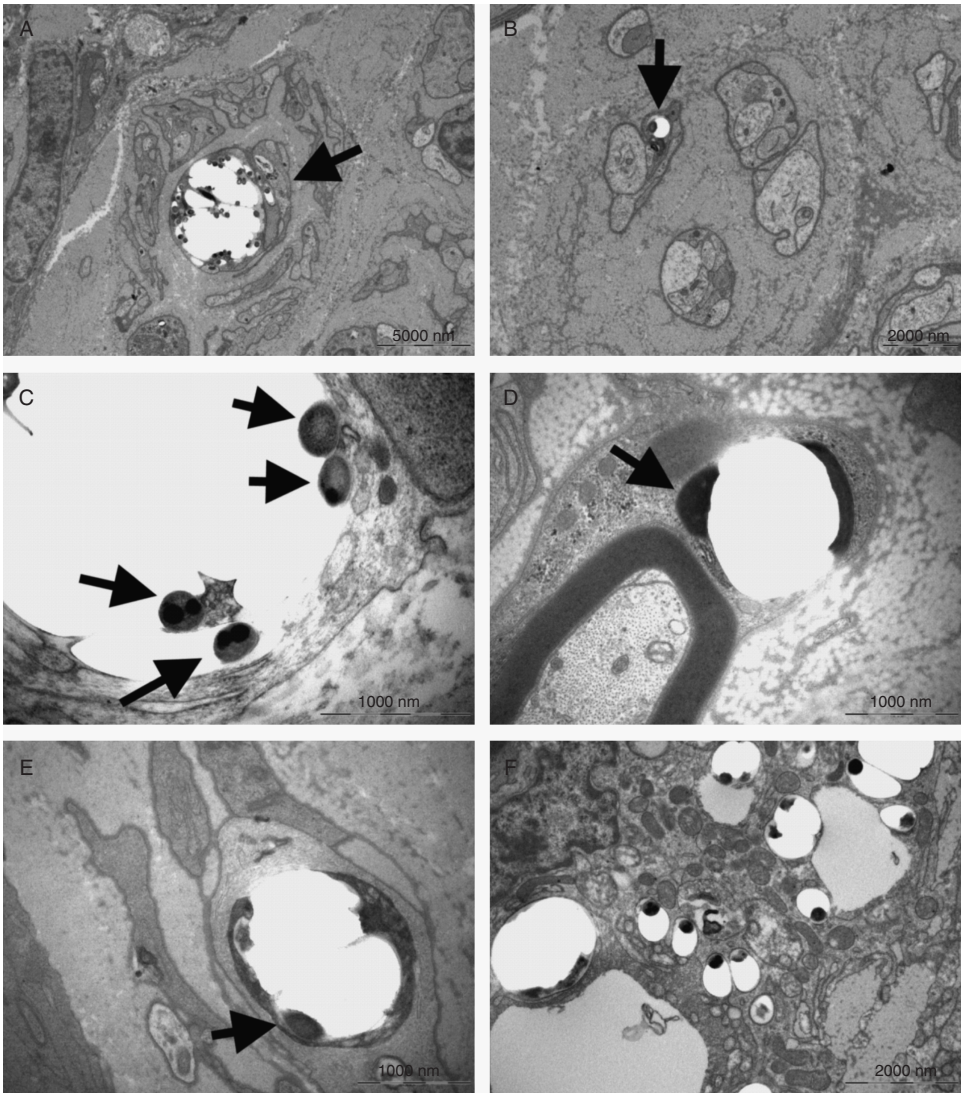

Figure 3. Ultrastructural findings in this case. a) Many scattered electron-dense oval-shaped bacilli (arrow) are seen in the unmyelinated nerve fibres (×5K). b) A bacillus (arrow) is seen in the unmyelinated Schwann cell (×10K). c) High-power view of electron-dense oval-shaped bacilli (arrows) (×40K). d) and e) Bacilli (arrow) in the myelinated Schwann cell (×30K) and axon (×30K). f) Many bacilli are seen in a macrophage (×15K). Many organelles can be seen in the macrophage cytoplasm.

bacilli living inside phagocytes; the host, therefore, depends on cell-mediated immunity for bacterial elimination,[3] and host immune response depends on host genomic background.[4] Unlike in skin lesions, *M. leprae* can destroy Schwann cells without an immune response. Severe nerve damage without immune cell infiltration or caseating granuloma is well reported.[5,6] *M. leprae* proliferates in unmyelinated Schwann cells; however, demyelination is a common pathological finding in leprosy neuropathy. In recent years, *M. leprae* capable of inducing demyelination was found in *in vitro* studies. *M. leprae* interacts with ErbB2

receptors on the surface of myelinating Schwann cells and causes myelinated Schwann cells to dedifferentiation into an unmyelinated cell via an internal signaling process.[7–9] We obtained images in which *M. leprae* appears to attach to the myelinated fibre (Figure 3d).

In *in vitro* studies, *M. leprae* cannot survive in macrophages at 37 °C.[10] Unlike cutaneous nerves, sural nerves are located deep. Some authors reported that leprosy is a superficial condition rather than a peripheral neuropathy, because *M. leprae* proliferates most actively in tissues with a temperature between 27 °C and 30 °C.[11] We believe that *M. leprae* can survive and proliferate in Schwann cells at high temperatures.

Conclusion

Leprotic neuropathy can be misdiagnosed as other peripheral neuropathies, especially in non-endemic areas. Through this case we emphasise that a clinical clue (preserved Deep Tendon Reflexes) is more important than biopsy findings (demyelinated feature with scattered inflammatory cells) in the diagnosis of leprosy.

References

1 Chaurasia RN, Garg RK, Singh MK *et al.* Nerve conduction studies in paucibacillary and multibacillary leprosy: a comparative evaluation. *Indian J Lepr*, 2011; **83**: 15–22.

2 de Larranaga GF, Forastiero RR, Martinuzzo ME *et al.* High prevalence of antiphospholipid antibodies in leprosy: evaluation of antigen reactivity. *Lupus*, 2000; **9**: 594–600.

3 Trindade MA, Benard G, Ura S *et al.* Granulomatous reactivation during the course of a leprosy infection: reaction or relapse. *PLoS Negl Trop Dis*, 2010; **4**: e921.

4 Behr M, Schurr E, Gros P. TB: screening for responses to a vile visitor. *Cell*, 2010; **140**: 615–618.

5 Massa R, Morello M, Sancesario G, Bernardi G. Sural nerve without nerve fibers in leprous neuropathy. *Arch Neurol*, 2002; **59**: 306.

6 Ooi WW, Srinivasan J. Leprosy and the peripheral nervous system: basic and clinical aspects. *Muscle Nerve*, 2004; **30**: 393–409.

7 Rambukkana A. *Mycobacterium leprae*-induced demyelination: a model for early nerve degeneration. *Curr Opin Immunol*, 2004; **16**: 511–518.

8 Rambukkana A, Zanazzi G, Tapinos N, Salzer JL. Contact-dependent demyelination by Mycobacterium leprae in the absence of immune cells. *Science*, 2002; **296**: 927–931.

9 Franklin RJ, Zhao C. Tyrosine kinases: maiming myelin in leprosy. *Nat Med*, 2006; **12**: 889–890.

10 Fukutomi Y, Maeda Y, Matsuoka M, Makino M. Temperature dependency for survival of *Mycobacterium leprae* in macrophages. *Nihon Hansenbyo Gakkai Zasshi*, 2009; **78**: 7–16.

11 Sabin TD. Neurologic features of lepromatous leprosy. *Am Fam Physician*, 1971; **4**: 84–94.