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Diagnosis of pure neuritic leprosy

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Abstract

About 4-8% of all leprosy is clinically limited to the peripheral nerves. Diagnosing leprosy in the absence of typical dermatological features is challenging and requires histological confirmation. This is often achieved using nerve biopsy. Limitations of this technique are sampling error, low sensitivity and permanent nerve deficit. Recent improvements in sampling techniques, using fine needle aspiration cytology and specimens from nasal mucosa and dermatologically normal but hypesthetic skin, have resulted in significantly increased diagnostic yield and less side effects. The additional usage of antibodies specific to Myocobacterial antigens further enhances diagnostic accuracy. In view of its potentially debilitating effect, the high prevalence rate in many parts of Asia, and with increasing rates of travel and migration, physicians practicing in both high and low endemic area should have acute awareness of the possibility of leprosy, and be familiar with its' varied presentations.

INTRODUCTION

The WHO "global leprosy elimination by the year 2000" campaign has failed as evidenced by the rising numbers of leprosy in many countries. In the year 2000 alone, 719,330 new patients were registered worldwide.[1] In the 27 top countries where leprosy is endemic, the incidence did not fall between 1985 and 1999 and in the six countries that account for 88% of new cases the numbers and incidence of new cases were rising. Three of the top 6 endemic countries were in Asia. They were: India, Nepal, and Myanmar, all with incidence rate of greater than 20/100,000 population. Cambodia, Indonesia, Laos, Papua New Guinea and the Philippines, were the other countries in Asia having high prevalence rate of more than 1/10,000 population.[1]

Although leprosy is a treatable disease, many patients will continue to experience significant nerve damage. Patients with leprosy have high rates (56%) of established nerve damage at diagnosis, which frequently lead to disability[2] despite prednisolone being able to ameliorate acute nerve damage in about 60% of patients.[3] The corner stone of the effective management of leprosy remains early recognition and treatment of nerve damage with prednisolone. In view of its potentially debilitating effect, the high prevalence rate in many parts of Asia, and with increasing rates of travel and migration, physicians practicing in both high and low endemic area should have acute awareness of the possibility of leprosy, and be familiar with its' varied presentations.

THE DIAGNOSIS OF PURE NEURITIC LEPROSY

Diagnosing leprosy relies on the identification of the typical clinical and histopathological involvement of the skin and nerves.[4] The absence of typical dermatological features greatly decreases clinical diagnostic accuracy and necessitates histological confirmation.[5] Clinical case series estimate that 4-8% of all leprosy is limited to the peripheral nerves.[6,7] This form of leprosy is termed pure neuritic leprosy. The other names given are: neural, pure neural, primary neural, primary neuritic, purely neural, purely neuritic, or polyneuritic.[6]

The clinical features of leprotic nerve involvement include nerve enlargement, tenderness, pain and sensory motor impairment. These are not specific and not always present. The most commonly affected nerves include the posterior tibial, peroneal, ulnar and median nerves. As mentioned above, proof of leprosy as a cause of pure neuritic leprosy needs histological evidence, which is often sought in affected peripheral nerves. This may be problematic as nerve biopsy is limited by sampling errors, low sensitivity and permanent nerve deficit as still functioning nerves often need to be sacrificed and sampling errors occur. Histopathological

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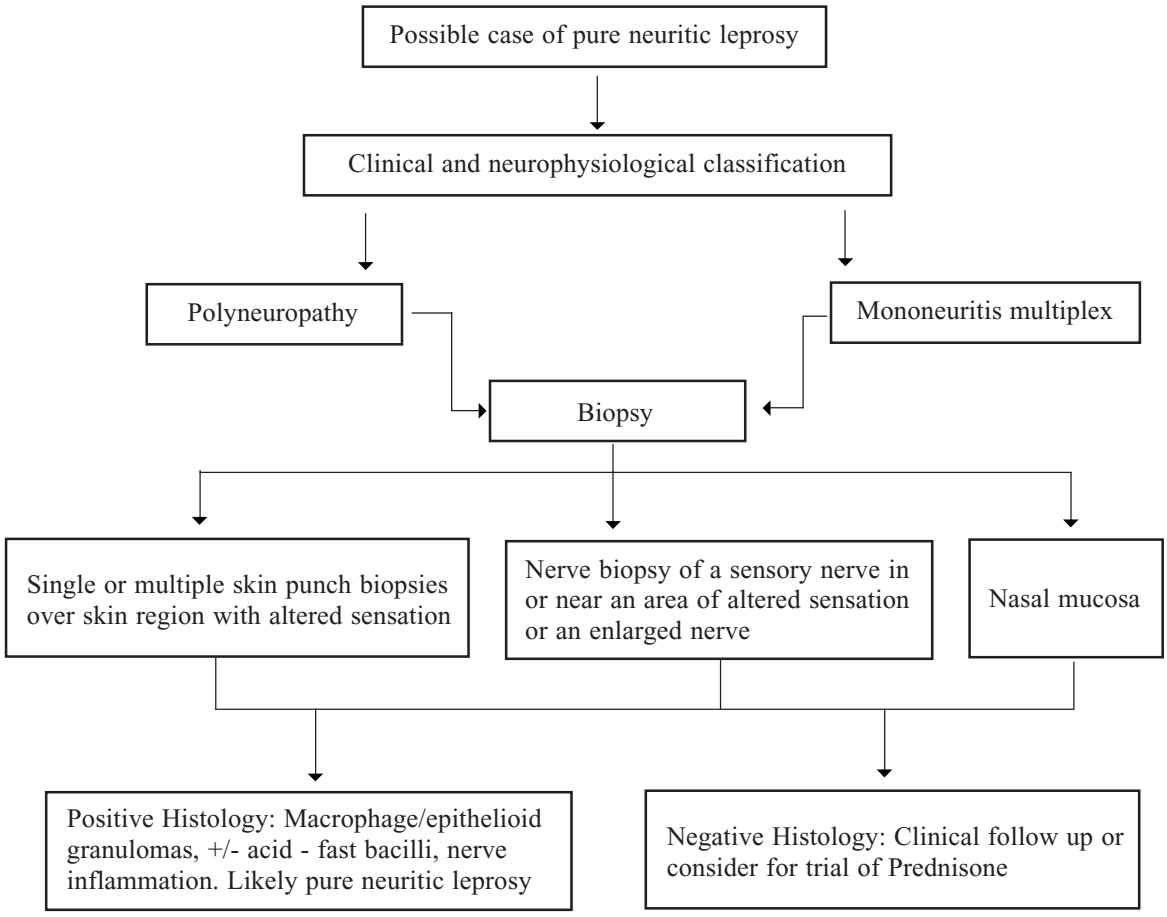
Figure 1: Flowchart for the investigation of pure neuritic leprosy



studies show that the entire spectrum of lepromatous changes with acid-fast bacilli to tuberculoid reaction with epitheloid granuloma can be observed in nerves of pure neuritic leprosy. There is no relation to clinical parameters such as the number and distribution of affected nerves or the type of immune response.[6]

THE RECENT ADVANCES

Leprosy is a disease where Mycobacterium leprae is primarily directed against specific targets in the peripheral nerves.[8-10] Recent research has clearly demonstrated the gap between clinical and histopathological disease definition. The majority of patients with pure neuritic leprosy are now known to have histological evidence of involvement beyond neural tissues. Simple histological examinations of nasal mucosa and dermatologically normal skin from hypesthetic regions may be used to reveal the characteristic changes of leprosy.[11-14] Due to the embedding of nerves in the skin, pathophysiological processes naturally spill over to involve the surrounding tissues even early on in the disease process. In patients with pure neuritic leprosy established on clinical examination, typical histological involvement of extra neural tissues occurs frequently. Samples taken from hypesthetic skin and nasal mucosa, show specific changes of leprosy in more than 50%.[12-14] Abnormalities are typically seen surrounding the deep dermal nerves and the neurovascular complexes.[12] Changes seen in the nasal mucosa range from macrophage granulomas with acid-fast bacilli, to epithelioid granulomas and nerve inflammation.[12]

Nerve sparing techniques such as fine needle aspiration cytology have been shown to maintain a high diagnostic yield when compared with standard biopsy with the added advantage of less side effects.[5] Additional usage of antibodies specific to Myocobacterial antigens has been shown to further enhance diagnostic accuracy.[15] These developments are of considerable practical

importance to the clinician confronted with diagnosing leprosy neuropathy without dermal involvement.

Similar to histopathological investigations, neurophysiological investigations using nerve conduction and vasomotor reflexes, show that neural damage is frequently more widespread than indicated by the clinical examination.[16] Small nerve fibres are affected first. Although neurophysiological tests are useful for uncovering a more widespread neural involvement, histological tests are needed to characterise the underlying etiology.

RECOMMENDATIONS ON DIAGNOSIS OF PURE NEURITIC LEPROSY

Recent epidemiological data reinforces the need for all clinicians to maintain a high index of suspicion for possible leprosy in patients with unclear peripheral neuropathy.[1] The presence of mononeuritis multiplex, tender and enlarged nerves should always raise suspicion towards possible underlying leprosy.[14] If careful dermatological examination cannot identify macules, papules or plaques with hypesthesia, further supportive tests must be utilised to demonstrate or exclude leprosy. Most commonly this involves sensory nerve biopsy, which is usually performed at the superficial sensory radial nerve branch at the wrist or the sural nerve. Motor nerves are generally not biopsied. It is important to ask the pathologist to carefully examine the perineural skin tissues. In the case of negative or non-specific nerve biopsy findings, the most useful additional tissue samples are from skin with sensory changes and the nasal mucosa.[11,12] In the case of diffuse sensory changes, multiple small skin punch biopsies (3 mm diameter) will increase the likelihood of picking up specific changes. Experienced laboratories should be able to recognise the typical features of leprosy from nerve aspirations. Since this is a relatively "nerve sparing" procedure, this may allow examination of motor nerves when sensory nerves are not involved or cannot be sampled. In the face of clinical non-specific features with negative histological findings, the physician will be placed in the difficult position on whether to treat with prednisolone or wait-and-see. For this situation there are no clear guidelines. In either case, initial close follow up (monthly) of the peripheral nerve status is mandatory as new clinical signs may provide diagnostic clarification. Follow-up of unclear cases in a highly endemic region has shown that a minority of cases will show progression to typical dermatological signs.

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