CONTINUING MEDICAL EDUCATION

LEPROUS NEURITIS : A DIAGNOSTIC DILEMMA

M Madhusudanan

Introduction

Throughout history, Hansen's disease (HD) has been associated with the greatest stigma of any disease and the stigma is primarily due to its neurological complications. Patients with Hansen's disease may seek medical treatment for a long time before the correct diagnosis is made. Patients with mutilating deformities may be incorrectly believed to have hereditary neuropathies, syringomyelia or vascular insufficiency. Mononeuropathy multiplex may be incorrectly ascribed to underlying collagen vascular disease or vasculitis. Skin lesion may have been treated previously be dermatologists and nasal complaints and iritis may have been treated by otolaryngologists and ophthalmologists. Hence it is absolutely necessary that the treating physician should understand the various neurological presentation of this treatable disease and be able to make an exact diagnosis clinically often without the need for laboratory tests.

Clinical manifestations

There are two characteristics of the leprosy bacillus which is responsible for its typical clinical features. First, leprosy bacilli infect peripheral nerves, primarily Schwann cells. Second, *M, leprae* requires a temperature of 28^0 to 32^0 C for growth. As a result, bacilli reproduce in the cooler tissues of the body, primarily in the skin , anterior one third of the eye, and the testes while sparing organs and tissues at core body temperature of 37^0 C. Vital organs such as the heart, brain, liver and kidneys are not clinically affected. Leprosy causes nerve damage in three ways. (a) by destruction of intracutaneous nerve network (b) by involvement of larger nerves in cooler locations and (c) during the course of leprosy reactions where acute inflammatory processes occur within the large nerves.

Becacuse the process involves only the coolest regions of the body, the central nervous system is unaffected. Cranial nerves are affected only where they become superficial and cool, resulting in patchy loss of functions in patterns specific for leprosy. Deep modalities mediated by peripheral nerves such as muscle stretch reflexes, vibration and position sense and most motor functions tend to be unaffected because these nerves are embedded deep in tissues, which keeps them warm. Motor deficits are most often in the distribution of nerves close to the body surface and in cool locations. The nerves so affected may be thickened, hardened and at times even visible.[1]

The most prevasive neurological involvement in leprosy is via destruction of nerves in skin, producing a temperature - linked pattern that is specific for leprosy and that differentiates leprous neuritis from any other

From the Department of Neurology, Medical College Hospital, Kottayam-686008, India

Address correspondence to :

Dr M. Madhusudanan
E-Mail; raju @md 3, vsnl.net.in

neuropathy.[2] The cardinal symptom of leprosy is sensory loss : the loss is often discovered by the occurrence of painless injury. Many patients have sensory loss before other evidence of the disease. Paraesthesias do not always precede sensory loss. Less often patients complain of radiating pains similar to the root pains of radiculopathy.

Sensory abnormalities precede paralysis in all types of leprosy. The order of sensory loss is first warmth, followed, by pain and touch.[3] Position and vibration sensations are entirely normal except in the very advanced cases in which multiple major nerves in extremity are affected. The evolution, pattern and extent of sensory loss and paralysis are determined by the type of leprosy. Leprosy of all types is characterized by sensory loss that is primarily intracutaneous and therefore not in the pattern of any peripheral nerve or nerve root distribution.

Tuberculoid leprosy

In tuberculoid leprosy there may be only one or at most only a few patches of intracutaneous sensory loss. Although the portal of entry is not known, it is thought that the bacteria entered the host at the affected area and the cellular response of the host limits the lesion to the localized area. The skin lesion and the sensory loss develop pari passu, so the sensory loss is present by the time patient is seen. Nerve damage, thus appears to be an inherent part of the host response to the bacilli and not related to the massive proliferation of bacilli. The sensory loss is sharply delimited and coterminous with the skin lesion.[1] A nerve trunk courisng beneath such a tuberculous patch may also be affected and the sensory motor deficits of that nerve will then be superimposed. This combination of an anesthetic patch with affection of a subjacent nerve trunk gives rise to the concept of transaxonal bacillary spread.[4] The major mixed nerves that are commonly affected include the ulnar, median, peroneal and facial. Subcutaneous nerves particularly those near the tuberculoid patch are usually palpably enlarged, sometimes forming skeins of firm nerves. The superficial cutaneous radial, digital, posterior auricular and sural nerves are the commonly affected sensory nerves. The intense response to bacilli within nerves in high resistance leprosy may lead to necrosis with formation of "cold" nerve abscess. Autonomic function is lost and the skin is dry and hairless within the lesion.

Lepromatous leprosy

Sensory deficits

The sensory loss in lepromatous leprosy is not confined to the area of skin lesion in the precise manner noted in tuberculoid leprosy. Skin lesions may have normal sensation in lepromatous disease. Palpably enlarged nerves may be functioning well. Although organisms may be present very early in cutaneous nerves , there may be remarkable little sensory loss because the virtual absence of any immune response to the organism. The infiltrated nerves in low resistant leprosy may eventually fail. Since *M.leprae* reproduce in cooler areas of the skin, a unique pattern of neurologic deficits appears. Hematogeneous spread of the bacilli in low resistant leprosy causes symmetry in the distribution of neurologic deficits. At all stages, the evolution of the temperature linked sensory loss of lepromatous leprosy can be distinguished from the classical "glove and stocking" sensory loss that is characteristic of other peripheral neuropathies.[5]

Cutaneous sensory loss appears first in the pinnae of ears, then dorsomedial surfaces of the forearms, the dorsal surfaces of the feet and the anterolateral aspects of the legs. The lobe and helices of the ears are most affected. As disease progresses, the sensory loss extends over the dorsal forearms, the elbow region and over the medial leg and the anterior knee areas. Sensory loss then starts appearing over the nose, the malar areas, breasts, central abdomen and buttocks. At this stage sparing of the palms and soles is often present even when there is profound cutaneous sensory loss over the dorsa of the hands and feet. This is because of the greater warmth of the palms and soles due to the insulating effect of the thickened cuticle in these areas. Sensory loss progresses in the upper extremities with

completion of insensitivity in the palms.

Extension of the sensory loss of "less cool" areas continues in the untreated case of lepromatous leprosy. Corneal sensation is reduced. When there is insensitivity of the forehead there is abrupt return to normal sensation at the hair line. This highly diagnostic "hair line" sign is an elegant demonstration of the intracutaneous nature of the sensory loss and is the result of an increase of 1.5 to 3°C in temperature under scalp hair.

The lower extremities in untreated case show a similar progression of neurologic deficits. The sensory loss spreads over the trunk, the temperature linked sensory loss is readily identified by detecting certain islands of preserved sensation. The inguinal creases, the popliteal fossa, the perineum, the axillae, the sternal area and a stripe of variable width up the center of the back from the intergluteal fold to the neck are areas that show consistent sparing.

Motor deficits

When sensory loss has progressed to the second stage, paralysis appears. Those motor fibres, which lie closest to the surface of the body, are affected. The deficits are more stereotyped in lepromatous leprosy than in the high resistant types of the disease. Paralysis in the ulnar distribution appears first. The ulnar nerve is most affected over a 10 to 15cm segment proximal to the olecranon groove. The nerve is greatly thickened in this segment than other parts of the nerve. The superficial segment of the peroneal nerve coursing laterally around the fibular head is infiltrated and enlarged. Foot drop is the second most frequent of the obvious paralytic deformities in leprosy. There is also affection of the segment of the posterior tibial nerve in the distal third of the leg, which results in paralysis of the intrinsic muscles of the plantar surface of the foot.

As the sensory loss becomes more profound in the palm and the median nerve-innervated intrinsic muscles of the hand show atrophy and paralysis,[1] an established paralysis of the ulnar nerve-innervated hand muscles is present in lepromatous leprosy before the median deficits appear. Radial nerve motor deficits are less common in lepromatous leprosy.

Autonomic fibers are damaged along with sensory and motor fibers. Loss of sweating occurs in insensitive areas. The extremities become cool and dusky. Since the autonomic fibres that lie more deeply within the body are not involved, postural hypotension, nocturnal diarrhea, abdominal crises, bladder dysfunction and impotence that characterize some other neuropathies and radiculopathies do not occur in leprosy.

Cranial nerve involvement

When facial sensory loss is wide spread a unique paralysis in the distribution of the seventh cranial nerve appears. The facial nerve involvement is patchy and bilateral, totally unlike other disease of facial nerve. The branches are affected where they assume a superficial course, i.e. the forehead, the zygomatic arch and the mandible. The initial dysfunction is usually weakness of eye closure due to damage to the branches coursing over the zygoma and the orbital rim. The medial segments of the frontalis muscle are paralysed before the lateral. When such a patient attempts eye brow elevation, only the lateral aspects rise, resulting in a characteristic V configuration-so called 'devilish appearance'. With progression of the facial nerve lesion, complete lagophthalmos and ectropion of the eye lids develop and eye lashes may turn inward, abrading the cornea and leading to scarring and ulceration.

Involvement of the small twigs to the orbicularis oris muscle results in localized outpouching of the lips at the corners of the mouth. The superficial muscles forming the nasolabial fold may be affected while the tone of the intact deeper cutaneous buccinator causes a series of concentric creases extending out from the corners of the mouth[6] (buccinator smile). Total facial paralysis is not present even in the advanced cases of the lepromaous leprosy. These unique defects in the fifth and seventh nerve are the only

common cranial nerve signs seen in lepromatous leprosy. Hoarseness occurs when the bacilli invade the upper airways tissues and enlarge the vocal cords, but it is not due to recurrent laryngeal nerve palsy.

Dimorphous leprosy

The patient with dimorphous leprosy may present with neurologic deficits characteristic of both high and low resistance disease. These cases are characterized by a degree of host resistance sufficient to result in prompt nerve dysfunction, but tissue response inadequate to preclude hematogeneous dissemination of the disease, and they show wide spread nerve damage early in the course of the disease.[7] There is paucity of the bacilli, but vigorous epithelioid cell response, and sharply circumscribed nature of skin lesion and neural deficits. Furthermore, caseous necrosis of nerves (nerve abscesses) is far more common in high resistance than in low resistance leprosy.

Polyneuritic leprosy

Normally neural involvement in leprosy is an ascending neuritis from the nerve involvement in the dermal lesions. However, in some cases neural involvement is seen in the absence of any dermal lesions. In some of these pure neuritic cases, dermal lesions appear sometimes later. It is therefore, more appropriate to designate such cases as 'primary neuritic cases". Pure neuritic type of Hansen's occurs in about 5% of cases. The clinical presentation is usually as mononeuritis or mononeuritis multiplex. The nerve deficits are in the distribution of nerve in cool locations. Skin lesions may appear only after treatment is begun or may not appear at all while on treatment.[8] The commonest nerve affected is ulnar nerve. Some cases present with foot deformities. In some cases, only facial nerve is affected. Rarely involvement may be of nerve plexus.

BT and TT forms of leprosy have been recognized in this pure form of pure neuritic type of leprosy. The diagnosis is confirmed by nerve biopsy. The nerve trunk in BT variety may show lymphocytes, epitheloid cells, and giant cells. There is destruction of nerve fibres and fibrosis. Acid fast bacilli are seen in the BL pure neuritic disease.

Neuritis in leprosy reactions

The slow evolution of neurologic deficits in uncomplicated progressive leprosy contrast with acute or

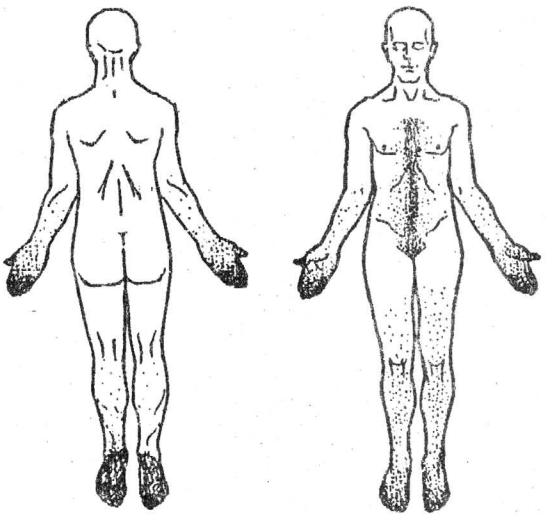

Fig. 1. Length dependent glove - stocking polyneuropathy. The intensity of stippled area reflects the degree of sensory loss.

subacute affection of peripheral nerves in leprosy reactions. The nerves affected in the reactional leprosy are the same as in progressive leprosy. In erythema nodosum leprosum, the manifestations of reactions, including neural involvement are most intense areas of greatest bacillary density. The severe reaction leads to nerve enlargement, pain and tenderness and paralysis. Nerve abscesses requiring drainage may form. In addition to the nerves in the extremities, the intraocular nerves may be involved leading to acute iritis, one of the major causes of blindness in leprosy. In tuberculoid and intermediate leprosy reversal reactions result from a sudden increase in cell-mediated immunity, producing erythema and edema in the lesions. Leprosy reactions with

nerve involvement must be recognized and treated promptly for these deficits are often entirely reversible.[9]

Differential diagnosis

Hansen's disease can have very many confusing neurological presentations, where in one has to differentiate it from other neurological conditions mimicking the same. Hansen's disease may present with an area of sensory loss without a patch, painless trophic ulcers in the feet or in the hands, mononeuropathy or mononeuropathy multiplex or nerve thickening with or without other neurological features.

1. A patient presenting with a patch of sensory loss

There are certain characteristics of Hansen's patch of sensory loss which help to differentiate from other causes. In HD, not only there is an area of sensory loss, but there is loss of sweating and hair. This is because of the atrophy of hair follicles and sweat glands. If there is associated hypopigmentation and nerve thickening, then the diagnosis becomes easy. There are the other situations where we can find such localised area of sensory loss. For e.g.: early radiculopathy and conditions affecting cutaneous nerve twigs. (a) In HD, sensory loss is confined to the skin, where propioceptive sensations are spared, where as in the case of radiculopathy, the joint and position sense are also affected in the area of sensory loss. Pressure paresis of nerve produces localised area of sensory loss:for e.g: a localised area of sensory loss can occur on the dorsum of hand after wearing a tight wristwatch or over the toes after wearing a tight shoe. Numbness over the chin can occur after wearing a tight cervical collar. Lateral cutaneous nerve of forearm, which is a branch of musculocutaneous nerve, may be affected in the cubital fossa of forearm. This sensory branch may be injured by compression, venipuncture or cut down procedure because it lies directly under the medial cubital vein in the centre of the cubital fossa.[10] Sensory loss and paraesthesia over the lateral part of the palm is typically seen in carpal tunnel syndrome. In the cubital tunnel syndrome, the ulnar nerve is compressed in the cubital tunnel. Early compression may produce only sensory symptoms with minimal or no motor weakness.[11] The superficial radial nerve entrapment occurs usually with crush or twisting injuries to the wrist or forearm or may follow repetitive pronation and supination movements required in certain occupations, with sensory loss over dorsolateral aspect of wrist.[12] Paraesthesia and sensory loss confined to the radial side of the thumb (cheiralgia paraesthetica) occurs with a lesion of the distal dorsal digital nerve.

In the lower limb similarly many compression syndromes are known; The most common sensory compressive neuropathy is meralgia paraesthetica due pressure on the lateral cutaneous nerve of the thigh, due to pressure on the nerve by the inguinal ligament. This occurs especially in obese individuals who wear constricting garments. Genitofemoral nerve can be compressed in the inguinal canal or under the inguinal ligament (femoral branch) producing sensory loss either in the skin of the scrotum or in the upper thigh over the femoral triangle.[13] The saphenous branch of the femoral nerve can be compressed as it pierces the aponeurotic roof of the adductor canal above the knee. In this syndrome, the only sign is sensory disturbance that affects the medial side of the lower leg. Damage to the infrapatellar branch of the saphenous nerve results in numbness and paraesthesias in the skin over the patella (gonyalgia paresthetica). The sensory portion of the superficial peroneal nerve may also be affected in isolation (where it emerges from the facia) due to inversion injury or compression injury or compression (by wearing high lace up boots) causing a pure sensory syndrome.[14]

Thus many compressive neuropathies can present with localised sensory loss. Hence one must always ask about any precipitating factors for the likely compression of the nerve. The clue may be obtained in the occupation.

Migrant sensory perineuritis[16]

In this disease of unknown aetiology, there are tingling paraesthesias and dysasthesia in small restricted

areas of skin, usually over an extremity. The nerve branch supplying the area of skin is enlarging due to hyperplasia of epineurium and perineurium. Symptoms may be transient and there may be lesion in other areas. A nerve biopsy may be necessary to define the distinctive pathological changes and to ensure that the leprosy bacilli are not present.

II A patient presenting with distal sensory loss and trophic ulcer

Peripheral neuropathy produces symptoms and signs in distal symmetrical fashion first affecting lower limbs, with later affection of upper limbs. When lower limbs alone are affected as in early peripheral neuropathy, the question arises to differentiate it from cauda equina lesion, which, if long standing, can also result in trophic ulcers. The usual differentiating features are dermatomal sensory loss. Hence in any patient with long standing distal sensory loss with trophic ulcers confined to lower limbs, one should ask for affection of bladder and look for any perianal sensory loss.

Similarly when HD presents first in upper limbs producing mutilating acropathy of fingers, a central cord lesion like syringomyelia comes in the differential diagnosis. In syringomyelia there is dissociated sensory loss, with affection of pain and temperature, but sparing touch sensation. Absence of deep tendon reflexes, long extend dissociated anesthesia in jacket-like distribution distinguishes this condition from HD.

Certain peripheral neuropathies affect only pain, temperature and autonomic fibres - so called "small fibre neuropathies" and spare posterior column sensation, deep reflexes, as they are mediated by large fibres.

So when patient presents with features suggestive of small fibre neuropathy, the first possibility to be considered is HD. But one should also remember that there are other neuropathies which can present with similar features. They are :

1. Hereditary sensory neuropathy - type I and III
2. Tangier's disease
3. Amyloidosis
4. Some cases of diabetic neuropathy

How to differentiate HD from these neuropathies? In general, in polyneuropathies the sensory affection is classically in glove and stocking pattern" -this is due to the "dying back phenomenon". They produce length dependant pattern of nerve involvement beginning in the toes and ascending to involve shorter and shorter nerves as the disease progresses. In peripheral neuropathy, not only there is distal sensory loss, there is graded sensory loss ie: maximal sensory los distally, less severe affection little more proximally and least affection still more proximaly (Fig.1).

Polyneuropathy due to HD has certain characteristics. As opposed to other neuropathies, HD affects cooler areas of the body. Hence affection in leprous neuritis is not truly distal: for eg; the first affected area is over the shin and dorsal part of the foot and not over the toes. Similarly the first affection in upper limb in HD is over the dorsal aspect of forearm, sparing hands. Also sensory loss begins to affect facial promontories which is extremely rare in other polyneuropathies.

3. Patients presenting with mononeuropathy/ mononeuropathy multiplex

One of the common presentation of HD especially the TT and BT variety is as mononeuritis or mononeuritis multiplex. There are many other diseases, which can present in the same fashion. They include : 1. Vasculitis, 2. Diabetes mellitus, 3. Sarcoidosis, 4. Cryoglobulinemia, 5. Hereditary liability to pressure palsy, 6. Lyme's disease, 7. HIV infection, 8. Neoplastic invasion of nerves or roots, 9.Lymphamatoid granulomatosis, 10. Neurofibromatosis.

However, in HD lesions of named nerves occur in selected areas related to temperature rather than the usual entrapment sites or areas of blood supply to nerves. Secondly, in addition to the major nerve involvement in

leprosy, the superimposed intracutaneous nerve loss is diagnostic. Polyneuritic leprosy may cause a problem because there may not be cutaneous sensory loss out side the distribution of the affected nerves. In such situations where cutaneous nerves are not affected, it will be extremely difficult to distinguish HD from other conditions. One clinical point which can help sometimes is the nerve thickening. The other conditions producing mononeuritis multiplex with nerve thickening include hereditary liability to pressure palsy and neurofibromatosis.

4. Patients presenting with nerve thickening

Hypertrophic neuropathies include Hereditary sensory motor neuropathy (HSMN type I), Dejerine - Sottas disease, Neurofibromatosis, Refsum's disease, neoplastic infiltration and chronic inflammatory demyelinating neuropathy. They may be mistaken for HD. But in these diseases, the nerves are not as large, and the hypertrophy is more diffuse than the localised temperature linked pattern in leprosy.

In leprous neuropathy, in the lepromatous, tuberculoid and borderline forms enlargement of nerves is often a conspicuous feature. In lepromatous leprosy, there tends to be a firm smooth enlargement limited to the most superficial nerve trunks. In tuberculoid leprosy, the enlargement may be uniform or nodular. Rarely a localised cystic swelling develops along a nerve related to casseous abscess formation. Nerves may be locally enlarged in the vicinity of cutaneous lesions in tuberculoid leprosy. A diagnostic point that may be helpful in the differentiation from a simple entrapment neuropathy of the ulnar nerve at the elbow is that in HD, the enlargement may extend for a greater distance up the arm or may be maximal some distance proximal to the elbow. In borderline HD, widespread enlargement of nerves is also present before any neuralgic symptoms or cutaneous lesions appear.

Understanding the different types of neurological affection of Hansen's disease is of paramount importance because the disease is eminently treatable. Perhaps, in no other neurological disease are the clinical findings so diagnostically specific and reaffirm the importance of meticulous neurologic examination.

References

1. Sabin TD, Swift TR, Jacobson RR. Leprosy in : Dyck PJ, Thomas PK, Griffin K, et al. (editors). Peripheral Neuropathy.3rd ed. Philadelphia: WB Saunders. 1992:1354-1379.

2. Sabin TD. Temperature - linked sensory loss: a unique pattern in leprosy. Arch Neurol 1969;20:257-262.

3. Dastur DK. Cutaneous nerve in leprosy ; the relationship between histopathology and cutaneous sensibility. Brain 1955;78:615.

4. Dehio K. On the "lepra Anaesthetica" Proceeding of the International Scientific Leprosy Conference, Berlin, October 1987. Reprinted in part in Leprosy in India.1952;24:78;1-2.

5. Sabin TD. Neurological features of lepromatous leprosy. Am Fam Physician 1971;4:84.

6. Monrad-Krohn GH. The neurological aspects of leprosy. Christiana, Denmark : Jacob Dybwad, 1923.

7. Browne SG. Some less common neurological findings in leprosy. J Neurol Sci 1965;2:253.

8. Talwar S, Jha PK, Tiwari VD. Neuritic leprosy; epidemiology and therapeutic responsiveness. Lepr Rev 1992;63:263-268.

9. Naafs B, Pearson LMH, Baar ALM. A follow up of nerve lesions in leprosy during and after reaction using motor nerve conduction velocity. Int J Lepr 1976;44:188.

10. Nunley JA, Basset FH. Compression of the musculocutaneous nerve at the elbow. J Bone Joint Surg 1982;64A: 1050.

11. Campbell WW, et al. Variations in anatomy of the ulnar nerve at the cubital tunnel : pitfalls in the diagnosis of ulnar neuropathy at the elbow. Muscle and Nerve 1991;14:733.

12. Dellon AL MacKinnon SE. Radial sensory nerve entrapment. Arch neurol 1986;43:833.

13. Dawson DM, Kramp C. Perioperative nerve lesions. Arch Neurol 1989;46:1355.

14. Banerjee T, Koons DD. Superficial peroneal nerve entrapment. J Neurosurg. 1981;55:991.

15. Ashbury AK, Picard EH, Baringer JR. Sensory perineuritis. Arch Neurol 1972;26:302-312.