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LETTER

Pure neural leprosy: a diagnostic conundrum

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Sir,

We read with interest the article by Brandsma *et al.* entitled 'Pure neural leprosy—mind the diagnosis'.[1] The authors describe the demographics, prevalence, and nerve involvement in pure neural leprosy (PNL) from a large cohort of patients recruited originally in the TENLEP study.[2] The study has confirmed once again the existence of this subset of leprosy (PNL). Beyond that the situation is not as foggy as it has been made out to be and presently a lot more is known about the diagnosis and management of PNL.

The authors have proposed a new definition for clinical diagnosis of PNL 'enlarged and/or tender peripheral (incl. cutaneous) nerves with or without sensory and/or motor impairment in the distribution area of the nerves commonly involved in leprosy in the absence of typical skin lesions for leprosy and a negative skin smear'. As per this definition, enlarged nerves alone are sufficient to establish the diagnosis of PNL. This is in contrast to the second cardinal sign of leprosy as per the WHO expert committee, which requires 'thickened or enlarged peripheral nerve with loss of sensation and/or weakness of the muscles supplied by that nerve'.[3]

Nerve thickening is merely a soft-pointer towards the diagnosis of PNL, the inter-observer reliability and specificity of nerve palpation has been shown to be poor in several studies.[4–6] A study from India found only moderate reproducibility among eight experienced paramedical workers.[5] The specificity of ulnar and common peroneal nerve palpation in detecting neural involvement has been reported to be only 34% and 40%, respectively.[6] A palpable nerve is very likely to be recorded as a thickened nerve, especially by less experienced observers. False positive findings may occur because of poor examination technique or because of nonspecific enlargement of a nerve seen in some heavy manual workers. Additionally, several other diseases may present with nerve thickening, such as diabetes mellitus, Refsum's disease,

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hereditary sensory motor neuropathy, Dejerine–Sottas syndrome, amyloidosis, acromegaly and neurofibromatosis.[7] Further, a rise in prevalence of diabetes has been noticed among middle and low-income households in recent years.[8,9] The justification that diabetic neuropathy can be ruled out based on the likely poor socio-economic status of the patient does not seem valid.

The authors justify their definition by stating that most of the tests used in the diagnosis of PNL are not useful 'in the field' as over 95% of patients are diagnosed in low resource settings; the authors suggest a sophisticated investigation like high resolution ultrasonography (HRUS). Although HRUS is a promising and sensitive tool in the hands of experts to investigate 'nerve enlargement' and even neuritis, if we add Doppler, it may not be able to differentiate between the different pathologies associated with nerve enlargement, as no structural abnormalities have been described which are specific for the diagnosis of leprosy on ultrasonography.[10]

The authors mention that two of the centers in the TENLEP study were able to diagnose subclinical neuropathy in PNL. Among 372 patients enrolled in the subclinical neuropathy study, 29 were diagnosed as having PNL. It would be interesting to know how these patients labeled as subclinical neuropathy presented, as by the new definition they would lack both skin and nerve involvement, so how were these cases picked up and categorized as PNL (subclinical)?

The issue of primary neural vs pure neural leprosy has been discussed many times but it may just be a matter of semantics, we all know that every leprosy case begins as primary neural leprosy—the main issue is how long does it stay 'neural'? If it has stayed neural for a sufficiently long time and at the time of diagnosis the manifestations are only neural then we can label it as pure neural. The classification may change when the skin lesion(s) develop but the treatment will remain the same. Contrary to the impression of the authors, the classification and treatment schedules have been clearly defined by WHO where pure neuritis is also classified under 'multibacillary disease' and there is no ambiguity about this fact.[3]

We are of the opinion that the diagnosis of PNL is not, and should not be, simple 'detection of enlarged nerves on palpation'. A valuable axiom that must be remembered is 'when in doubt, never diagnose leprosy'. Usage of a subjective test such as nerve thickening as the sole diagnostic criterion will certainly result in more confusion. Indeed, the diagnosis of PNL is a difficult task. However, the proposed definition may be an over simplification of this rather arduous diagnosis, which may lead to over diagnosis; this must be avoided, bearing in mind the enormous stigma that continues to be associated with the diagnosis of leprosy.

A balanced approach must be followed for the diagnosis of PNL and should include nerve function impairment in addition to nerve thickening.[11] While diagnostic modalities such as nerve biopsy, fine needle aspiration cytology (FNAC) of the affected nerves, nerve ultrasonography and nerve conduction studies may not be available in resource poor settings, combining nerve palpation with monofilament testing and voluntary muscle testing will greatly improve the specificity of the diagnosis of nerve damage at the field level.[6,12]

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