PURE NEURAL LEPROSY, A DIAGNOSIS NOT TO MISS IN PATIENTS PRESENTING WITH POLYNEUROPATHY

Imran Ahmad, Mutaher Zia*, Muhammad Irfan Anwar

Pakistan Naval Ship Shifa Hospital Karachi Pakistan, *Marie Adelaide Leprosy Centre (MALC) Karachi Pakistan

ABSTRACT

Leprosy is a chronic infectious disease, caused by *Mycobacterium leprae*. It mainly affects the peripheral nerves and skin. In pure neural or neuritic leprosy, there are no skin lesions. Hence the diagnosis is delayed, leading to deformities. It is more common in India as compared to other countries, including Pakistan. We are reporting two cases who presented with pure neural leprosy. Their diagnosis was delayed for several months, until a nerve biopsy showed typical changes of leprosy. Due to the delay in diagnosis, both developed visible deformities (grade 2 disabilities). These two cases emphasize the importance of early recognition of this type of leprosy; so as to prevent permanent crippling disabilities.

Key words: Leprosy, Neuritic leprosy, Nerve biopsy, Peripheral neuropathy.

INTRODUCTION

Leprosy is a chronic infectious disease, caused by *Mycobacterium leprae* (M.leprae). It primarily affects the peripheral nerves and skin, followed by other tissues such as the eye, upper respiratory mucosa, muscles, bones and testes[1,2]. However, in pure neural leprosy which comprises 4-8% of all leprosy cases there are no skin lesions, resulting in delayed diagnosis, progression of disease and ultimately deformities[3]. One of the reasons for this delay is that leprosy is considered an ancient disease, with dermatological manifestations only. As the doctors are not exposed to this spectrum of the disease, they do not consider it in their patient work-up. This type of leprosy is frequently seen in other countries especially India, but to our knowledge no such report has been published from Pakistan.

M. leprae can enter nerves either through naked axons, in the epidermis or superficial dermis or they may enter, through endoneural blood vessels. After entering the nerves, *M. leprae* produce nerve damage at superficial sites, where the temperature is low and where nerves are easily traumatized; at entrapment points in fibroosseous canals, at or near joints. Cellular infiltration and edema raise the Intra-neural pressure, leading to ischemia of the nerve tissue.[2] Peripheral neuropathy is the major morbidity in leprosy, resulting in deformities and disability. The mixed, motor and sensory nerves commonly affected are the ulnar, median and radial in the upper limbs and the common peroneal and posterior tibial, in the lower limbs. Swollen nerves can be palpated at the sites of predilection, often causing pain and tenderness. Loss of nerve function leads to anesthesia, wasting and eventually deformities.

We are presenting two cases with features of pure neural leprosy and without any cutaneous involvement. The diagnosis was delayed in both for several months, it was later confirmed by a nerve biopsy and ultimately, treatment was started.

Case 1

A 35-year-old male, laborer was referred to Marie Adelaide Leprosy Centre (MALC), by a dermatologist from Khyber-Pakhtunkhwa (KPK) province. He complained of pain in his left forearm and hand, for past 8 months; This was followed by numbness in both hands, feet, left forearm and lower half of both legs. Later on, he observed weakness in his left hand and foot. He also had low grade fever for the last 2 months without any cough, sore throat, joint swelling or

Correspondence: Dr Imran Ahmad, Neurologist, PNS Shifa Karachi Pakistan (*Email: drimran72@yahoo.com)*
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altered urinary/bowel habit. This was followed by burning, lacrimation and pain in the left eye, for one month. Lately, he accidently got painless burn on his right index finger while working in the kitchen. After which he was referred to MALC for workup.

On examination of his upper and lower limbs, he had a glove and stocking pattern of anesthesia and a burn ulcer was present, on the palmer surface of his right index finger. There was wasting of interossei, thenar and hypothenar muscles, more marked in the left hand and clawing in both hands (fig-1). On lower limb examination, he was having left foot drop (fig-2). Fine touch and pain sensations were impaired in both feet, along with muscle wasting. However, deep tendon reflexes were intact in lower limbs. On cranial nerve examination, he was having a left lower motor neuron, facial palsy. Both great auricular nerves in his neck were enlarged. His ulnar, median, radial cutaneous, common peroneal and posterior tibial nerves were also bilaterally enlarged.

His laboratory investigations were insignificant and skin smear was negative, for acid-fast bacilli (AFB). Electrophysiological tests were found to be abnormal and suggested a chronic, asymmetrical, sensory-motor axonal polyneuropathy with possible secondary demyelination. As he had an asymmetrical, sensory-motor polyneuropathy with a facial nerve palsy along with enlarged, painful nerves, the diagnosis was straightforward for someone familiar with the varied spectrum of leprosy. As there were no visible cutaneous manifestations, we decided to take a nerve biopsy from the right radial cutaneous nerve, to confirm the diagnosis. On histopathology there was an intense lymphocytic, perineural infiltration and focal granulomatous inflammation, around the nerve. Lepra bacilli were seen on lepra stain (fig-4). He was started on standard anti-leprosy treatment, at MALC.

Case 2

A 33-year-old male tailor, presented with a history of fever, off and on for the last one year. This was followed by pain in forearms, hands and feet. Symptoms started in the left hand and in ensuing six months, involved the other side. This was followed by weakness and wasting, due to which he had to leave his job. He consulted a local neurologist who labeled it as a chronic inflammatory, demyelinating polyneuropathy and started him on corticosteroids. He discontinued the treatment after eight weeks, as there was no improvement and no further work-up was done.

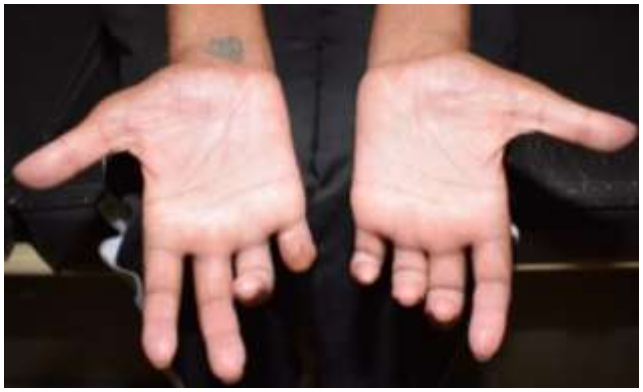

Figure-1: Bilateral muscle wasting and claw hands, due to Median and Ulnar nerve damage.

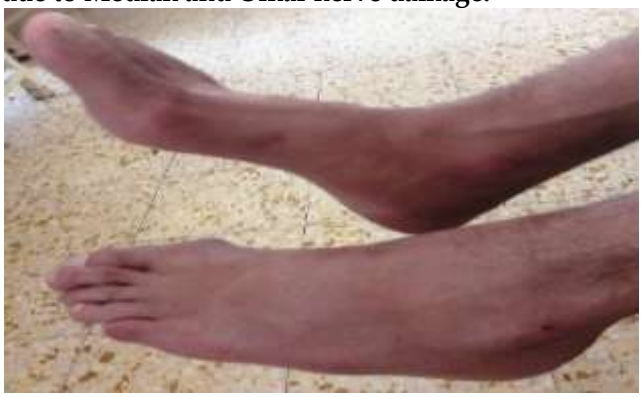

Figure-2: Left foot drop, due to common peroneal nerve Involvement (Case-1).

On examination, he had wasting of the interossei and hypothenar muscles, together with clawing in both hands. He had loss of sensation over the extensor surface of forearms, hands and ulnar side of both palms. Clawing was present bilaterally and both ulnar nerves were enlarged. Surprisingly his peripheral reflexes were present and brisk, but planters were down going bilaterally. Fine touch and pain sensations were

impaired in both feet and up to the level of mid legs, along with muscle wasting.

Magnetic Resonance Imaging (MRI) of the cervical spine done to rule out syringomyelia, was found to be normal. But electrophysiological tests were abnormal and suggested an asymmetrical, sensory-motor axonal polyneuropathy, with secondary demyelination. His skin smear was negative for acid fast bacilli (AFB). But AFB

Figure-3: Left lagophthalmos, due to facial nerve damage.

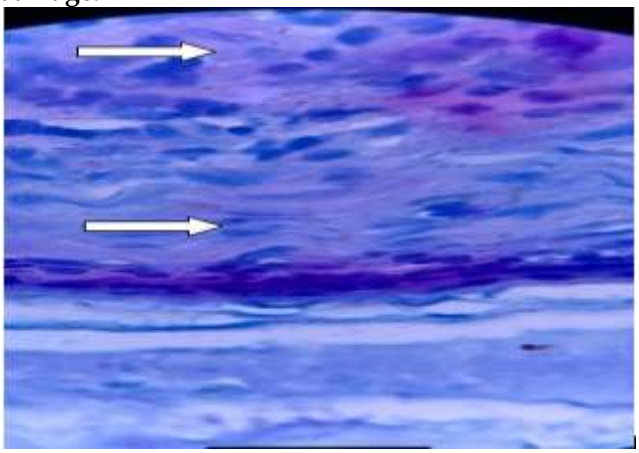

Figure-4: Nerve showing lymphocytic infiltration and around the trunk, with pink leprosy bacilli (Fite stain – Case 1).

were detected in the dermis on histopathology, which showed a perivascular, perineural infiltrate comprising lymphocytes and foamy macrophages; thus confirming the diagnosis of leprosy. He was started on anti-leprosy, multi-drug therapy.

DISCUSSION

According to the WHO leprosy update-2017, the incidence and prevalence of leprosy in Pakistan was 0.2 per 100,000 population and 0.02 per 10,000 population, respectively[4]. Pakistan is therefore a low endemic country. A total of 403 new leprosy cases were detected in the country, during 2017[4]. Out of these, 99 (25%) were detected in the northern province of Khyber-Pakhtunkhwa and 194 (48%), in the southern province of Sindh[5]. Our first case belonged to the former province and the second, to the latter. Currently, no epidemiological data is available on the prevalence of neural leprosy in Pakistan. However, the authors from their experience also do not consider it as common in Pakistan. Ghafoor *et al*. reported 7% cases of neural leprosy, in their study[6]. No cases with a pure neural presentation were reported by Khan *et al*. and Soomro *et al*., in their studies from the northern and southern parts of the country respectively[7,8]. In India, the occurrence varies from 4.2% in North India to 17.7%, in the South[9,10].

Both the cases presented here were adult males, aged 35 and 33 years respectively. In a retrospective analysis from India, the mean age was 36.9 years and 85.4% were males[11]. In a study done in Brazil, the mean age was 42.9 years and 52.9% cases were males[12]. In our patients, the onset of signs and symptoms varied from eight months to one year. Pain in nerves followed by numbness, weakness in hands and feet, were the initial symptoms in the first case. While fever, severe pain in both forearms and hands, followed by weakness in hands were the first symptoms, in the second case. In a prospective, longitudinal study done in Brazil, 38% cases presented with neural pain, 83% had sensory impairment and 88% had muscle weakness[13].

The first case presented with a left eye lagophthalmos, bilateral enlargement of the great auricular, ulnar, median and radial cutaneous nerves. Both common peroneal and posterior tibial nerves were also found to be thickened. All peripheral nerves were tender. The second case had bilaterally enlarged ulnar nerves. Glove and stocking anesthesia was a common feature, in both the cases. Muscle wasting and clawing were more marked in the left hand of the first case, who also had a left foot drop. The second case

had bilateral wasting of interossei and hypothenar muscles, with an ulnar-median clawing in both hands. The first case also had a burn ulcer in right hand. Studies have reported ulnar and common peroneal (lateral popliteal), as the most commonly involved nerves in neural leprosy[14].

Skin smears were negative in both but AFB were found in the dermis, on histopathology of the second case. In patients with pure neuritic leprosy, histological evidence has been found in extra neural tissues, as seen in samples taken from the nasal mucosa and hypoesthetic skin[3]. Nerve biopsy of our first case showed signs of leprosy and electrophysiological tests in both, suggested a sensory-motor, axonal polyneuropathy with secondary demyelination. Shetty & Wakade detected evidence of leprosy, in 97% nerve biopsies and 44% skin biopsies of patients, presenting with purely neural symptoms[15]. In their study on the electrophysiological profiles of leprosy neuropathy, Marahatta et al. found the sensory-motor, axonal type to be the commonest pattern of peripheral neuropathy[16].

There was no history of a household contact in either. But the first case had a relative in the same village, who had been treated for leprosy. The diagnosis was delayed in both the cases, more so in the second case. Zia and Anwar had earlier reported two young males working in the military and paramilitary forces of Pakistan, whose leprosy had manifested with neural signs but the diagnosis was delayed by 5-13 years[17]. Lockwood and Reid reported delayed diagnosis of leprosy in 82% cases in the United Kingdom, with 68% presenting with a disability[18]. Both of our patients were also unable to work, due to ensuing deformity in their hands. One had been working as a laborer and the other was a tailor. Both were facing financial problems and psychological stress, due to their disability.

The ideas behind publishing these cases are manifold. We need to create awareness among our colleagues in neurology and dermatology for early diagnosis of this type of leprosy, in order to prevent deformities and disability. Leprosy should be considered in the differential diagnosis of neuropathy, when there is cutaneous sensory loss with palpable nerves, asymmetrical involvement, painful nerves and predominant upper limb involvement. We also need to emphasize the importance of a nerve biopsy, in the workup of neuropathy cases.

CONCLUSION

We thereby conclude that health care providers should be aware of the presence of the pure neural form of leprosy, which can be difficult to diagnose in the absence of any visible skin lesions but can be easily diagnosed, by a cutaneous nerve biopsy.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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