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Case Report

Progression of pure neural leprosy towards borderline lepromatous leprosy

Aidha Juniar Permatasari Hartono, Hardyanto Soebono

Department of Dermatology and Venereology, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Jalan Farmako, Sekip, Yogyakarta, 55281, Indonesia.

Abstract Pure neural leprosy (PNL) is characterized by the absence of skin lesions and negative slit skin smear, however, several studies found that up to 35% cases will progress to visible skin lesion. A 62-year-old man came with chief complaint of facial edema, wound and deformities. The nerve impairment and deformities started progressively seven years ago followed by the emergence of skin lesion recently. Clinical examination revealed madarosis, earlobe infiltrate, punched-out lesion on the face, hypopigmentation on the trunk and extremities with sensory impairment, nerve enlargement alongside sensory and motor deterioration, claw hand, drop foot and resorption of phalanges. The slit skin smear revealed bacterial index (BI) +4 and morphological index (MI) 15%. Histopathological examination revealed periadenexal granulomas consisting of foamy macrophages, histiocytes, epithelioid cells, with BI +5 on Fite-Faraco stain. This case represents progression of PNL towards Borderline Lepromatous (BL) leprosy with type I reaction (T1R) and second-degree deformities. Neuritis and emergence of new lesion on reaction episodes often lead to confirmation of diagnosis in PNL cases. Another hypothesis regarding silent neuropathy explained a progressive nerve damage without any preceding reactions that may arise on treated and untreated cases resulting in extensive deformities. All leprosy cases probably pass through a neuritic phase before the development of skin lesions either following reaction episodes or indicate the natural progression of the disease. Any delay in diagnosis and treatment potentially lead to further deformities and transmission.

Key words
Pure neural leprosy; Borderline lepromatous leprosy; Deformity; Type 1 reaction; Silent neuropathy.

Introduction

Leprosy is a chronic granulomatous infection due to *Mycobacterium leprae* with predominant involvement of the skin and peripheral nerves. The clinical manifestations are defined by the host immune response and bacillary load, resulting in wide clinical spectrum.[2] Pure neural leprosy (PNL) was initially described by the Indian classification in 1955, which the onset, progress and final evolution are imperfectly understood. Despite the characteristic of PNL such as the absence of skin lesions and negative slit skin smear, several studies found that up to 35% of the cases will developed visible lesions during disease progression.[3] The aim of this case report is to increase the awareness of such manifestations of leprosy to avoid future misdiagnosis and treatment delay.

Address for correspondence
Dr. Aidha Juniar Permatasari Hartono
Department of Dermatology and Venereology,
Faculty of Medicine, Public Health, and Nursing,
Universitas Gadjah Mada, Jalan Farmako, Sekip,
Yogyakarta, 55281, Indonesia.
Ph: +6281211659090
Email: aidhajuniarph@gmail.com

Case report

A 62-year-old man came as referral from orthopedist with chief complaint of facial edema, wounds and deformities. Seven years ago, the patient had numbness of extremities followed by progressive hand joint stiffness.

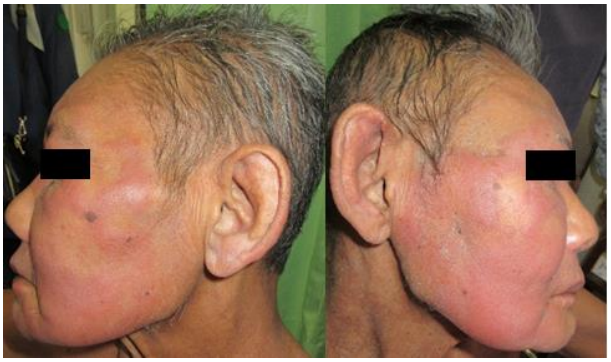

Figure 1 Partial madarosis, ill-defined erythematous plaque and punched out lesion.

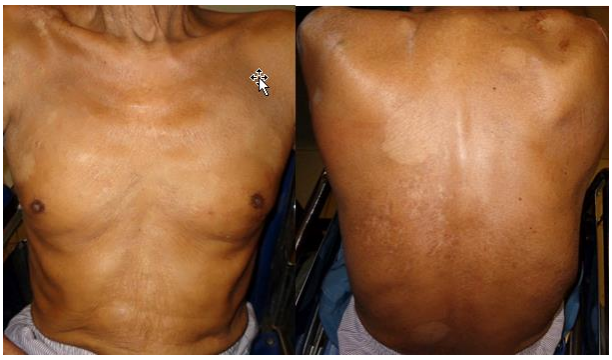

Figure 2 Anesthetic, xerotic, well-defined hypopigmented patches.

Two years later, sudden wound formation of the fingers and weakness of the foot developed. There wasn't any skin lesion until non-pruritic, painless white spots on the chest and the back were emerged seven months ago. One month prior to consultation, skin slit smear from the ears and back revealed zero acid fast bacilli (AFB) thus he was referred to orthopedist regarding the deformities. A week prior to consultation, due to the emergence of facial edema he was referred to Sardjito hospital with suspected leprosy. The patient was born and grew up in Jember, moved for work in Rembang then Kalimantan and Malaysia for a year, back to Rembang until 2003 and moved back to Cepu since then.

Physical examination revealed partial madarosis, ill-defined erythematous plaque and punched out lesion on the face (**Figure 1**), also xerotic, well-defined hypopigmented patches on the trunk and extremities with diminished temperature and touch sensation (**Figure 2**). Claw hand, drop foot, ulceration on palms and soles, fingers resorption with anonychia were also observed (**Figure 3**). On the nerve examination, both ulnar and right tibialis posterior nerve were enlarged without pain on palpation and also deterioration of function of ulnar, median, bilateral tibialis posterior and peroneus nerves.

The slit skin smear from hypopigmented lesion were negative for AFB, but the smear from facial lesion revealed BI +4 and MI 15%. Skin biopsy was taken from two locations, the Haematoxylin Eosin (HE) staining of hypopigmented lesion demonstrated orthokeratosis and flattening of rete ridge with mild periadenexal lymphocytic infiltrate without granulomas and zero AFB on Fite-Faraco (FF) stain. Meanwhile the facial lesion demonstrated numerous periadenexal granulomas consisting of foamy macrophages, multinucleated giant cells, histiocytes, epitheloid cells, with BI +5 on FF stain (**Figure 4**).

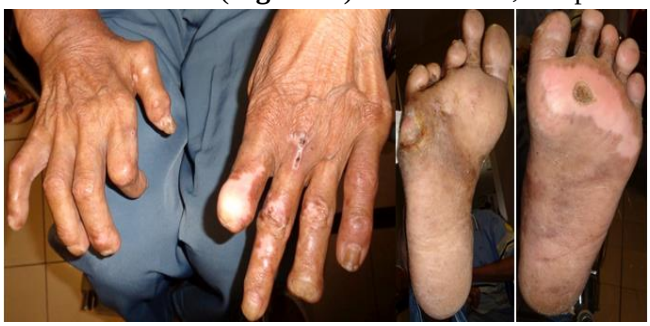

Figure 3 Claw hand, drop foot, ulceration on palmar and plantar, fingers resorption with anonychia.

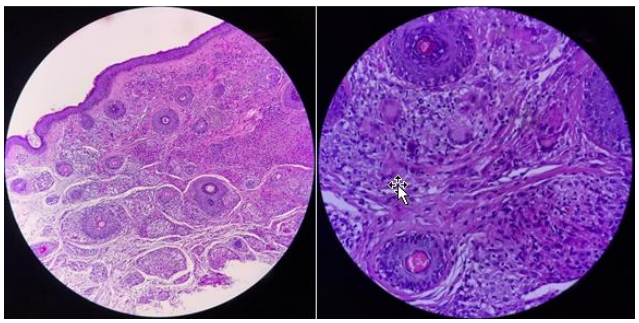

Figure 4 Granulomas peri-adnexal, foamy macrophages, multinucleated giant cells, histiocytes and epitheloid cells.

Thus, we concluded that this case represented a progression of PNL case towards Borderline Lepromatous (BL) leprosy with type 1 reaction (T1R) and second-degree deformities. The multidrug therapy for multibacillary leprosy (MDT MB) and methylprednisolone with starting dose 32mg/day were initiated.

Discussion

Most of the leprosy cases are diagnosed on the basis of classical manifestations such as anesthetic skin lesion however there are also cases with predominantly neurological manifestations that often are confused with other entities which lead them to visit neurologist or orthopedic surgeons instead, thus the diagnosis may be missed or delayed.[5] In this case, the nerve impairment and progressive deformities was already manifested years ago, while the visible skin lesion emerged recently. The history of close contact to person with similar complaint was denied, but approximately 20 years ago he worked as a construction labor in Rembang for years, which is known as one of the highly endemic area for leprosy and even ranked first on deformities cases in Central Java.[6]

Pure neural leprosy (PNL) or primary neuritic leprosy, is a form of leprosy that presents as a peripheral neuropathy without evidence of cutaneous lesions. This entity can only be detected by observation of progressive neurological deficit and regular neurological examination, supported by several diagnostic modalities, such as nerve biopsy.[3] However, present studies found that 15-35% PNL patients will eventually developed cutaneous lesion, irrespective of age, number of nerves involved, or the treatment. Suneetha *et al*. found histopathology evidence of leprosy in apparently normal skin in one-third of PNL cases, and 38% later developed skin lesions, thereby implying that neuritic phase often precedes the cutaneous lesions with features of indeterminate to BL leprosy.[3,7] This case came up with progressive nerve impairment that left untreated for years followed by the emergence of lesions proven pathologically as BL leprosy.

Reaction episodes in which neuritis and new skin lesions are the most frequent manifestations, often lead to confirmation of PNL diagnosis. Type 1 Reaction (T1R) associated with the increase of immunological activity towards the cell-mediated immunity (CMI) response to mycobacterial antigens in both untreated and treated cases.[1] Several studies also tried to correlate nerve damage, reaction and cytokine levels, which come to conclusion that high levels of inflammatory cytokines such as TNF-α that carried myelin-toxic properties are associated with recurrent T1R and acute inflammation in a pre-existing nerve lesion resulting in severe damage. Since peripheral nerves are a good storage for persistent bacilli, it is plausible that it may put the patients at a higher risk of recurrent episodes of reaction neuritis.[9] Another hypothesis about silent neuropathy (SN), explain about progressive nerve damage without any preceding reactions unrelated to MDT. One study found that 33.3% of subjects with SN were later diagnosed as PNL and 66.6% were previously untreated, thus it was concluded that anti-leprosy drugs play definite role in SN prevention.[8] In this case, the symptoms left untreated for years, thus the progressive nerve impairment and the emergence of new skin lesion might be indicated the recurrent episodes of T1R and/or SN phenomenon resulting in extensive deformities.

Conclusion

This case report highlights that all leprosy cases probably pass through a neuritic phase before the emergence of skin lesions, either following reaction episodes or indicates the natural

progression of the disease. In a setting with no advance diagnostic modalities, a thorough history taking and neurological examination should be conducted in establishing early diagnosis of PNL or neuritic phase of leprosy. With the aim of leprosy elimination, early diagnosis and prompt treatment holds the key, since any delay would potentially lead to further deformities and transmission of leprosy.

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