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Case Report

A curious case of Lepromatous Leprosy Developing Complete loss of Pigmentation, followed by Reappearance of Pigmentation with Multi Drug Therapy (MDT) alone - A Support for Neural Theory of Vitiligo Pathogenesis?

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Lepromatous leprosy is a multisystem disease characterized by a decline in delayed hypersensitivity to *Mycobacterium leprae* antigens, causing multiplication of bacilli in huge numbers. We herein report a case of an adult male with lepromatous leprosy who was started on adult multibacillary multi-drug therapy. With treatment, the surface of lesions developed depigmented macules and patches. However, on continuation of antileprotic drugs, there was progressive perifollicular as well as inter-follicular re-pigmentation. This case clinically depicts re-pigmentation of depigmented skin following multidrug therapy for leprosy supporting the role of neural system in the homeostasis of melanocytes.

Key words : Lepromatous leprosy, Depigmentation, Multidrug therapy, Vitiligo, Neural theory

Introduction

Lepromatous leprosy (LL) is a multisystem disease in which there is concomitant loss of cell mediated immunity to *Mycobacterium leprae* antigens causing multiplication of bacilli in huge numbers and subsequent infiltration into nerves and skin (Chacko and Desikan 2001). Histopathology reveals large and expansile macrophages with bacilli in the dermis and the adnexa of blood vessels, sweat gland, pilosebaceous unit, sensory and autonomic nerves (Massone et al 2015). Hypopigmentation in leprosy has been attributed to reduced number of normal melanocytes, inhibition of melanogenesis due to lack of Dopa oxidase activity or defective transfer of melanin from melanocytes to keratinocytes and shows a predilection for areas supplied by brachial and lumbar plexus (Shereef and Thomas 1992, Cichorek et al 2013). This case report shows interesting sequence of events pertaining to depigmentation and re-pigmentation in a LL case following therapy; and the damage to nervous

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system and recovery in lepromatous leprosy patients.

Case report

A 28 year old male, presented with numerous reddish elevated lesions distributed all over the body, present for the preceding 1.5 years. To start with, there were pale, flat lesions over the face, arms, buttocks and legs, which progressed to attain the present status. There was a history of nasal congestion, epistaxis and bipedal edema. There was no history of fever, joint pain, trophic ulcers or weakness of muscles. The patient denied any past history of kala-azar. Past medical as well as surgical history was unremarkable. Cutaneous examination revealed bilaterally symmetrical erythematous papules, plaques and nodules over the face, neck, trunk, genitalia, buttocks, upper and lower limbs. Besides, hands were remarkable for fusiform swelling of the digits. There was anesthesia in a glove and stocking pattern up to mid-calf region and elbow in lower and upper extremities respectively. Nerve examination revealed bilaterally symmetrical thick and tender supraorbital, greater auricular, median, superficial radial cutaneous, ulnar, radial, common peroneal and posterior tibial nerves. In addition, there was increased lacrimation of eyes and hoarseness of voice. A slit skin smear from the earlobes, right forehead, chin and left gluteal

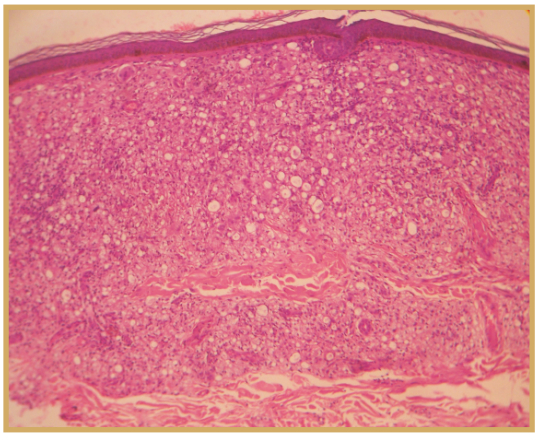

Fig 1a : Atrophic epidermis with a narrow sub-epidermal grenz zone and diffuse infiltration of foamy macrophages in upper dermis (H&E x 100)

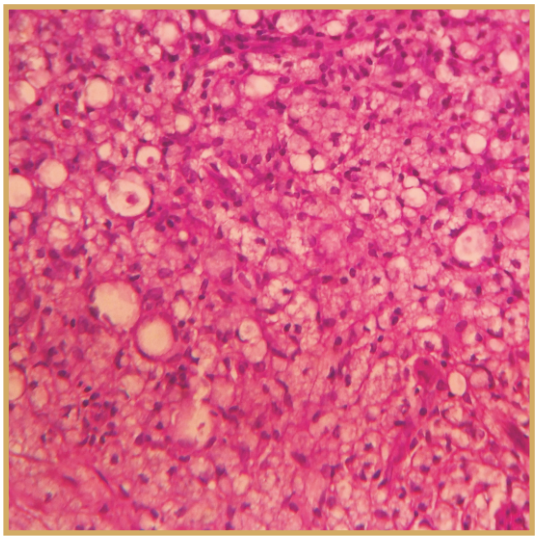

Fig 1b : Higher magnification (H&E x 400)

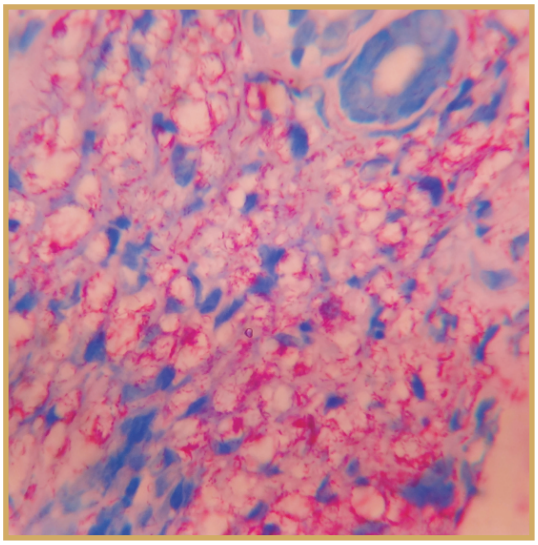

Fig 1c : Fite-Faraco stain showing numerous acid fast bacilli (Fite-Faraco stain X 400)

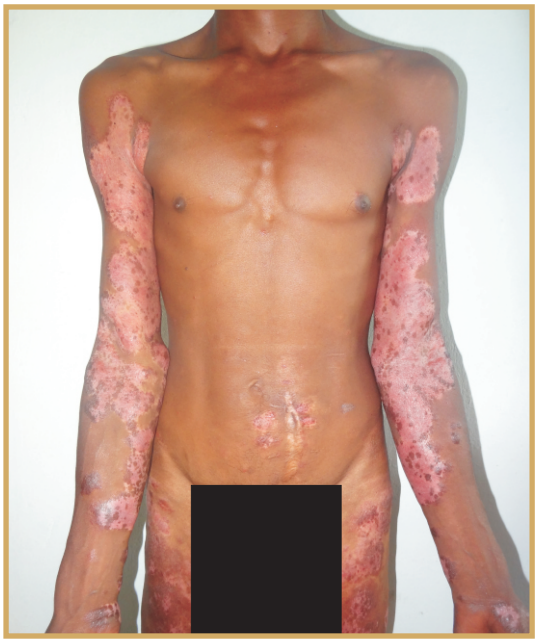

Fig 2a : Lepromatous leprosy lesions developing depigmentation

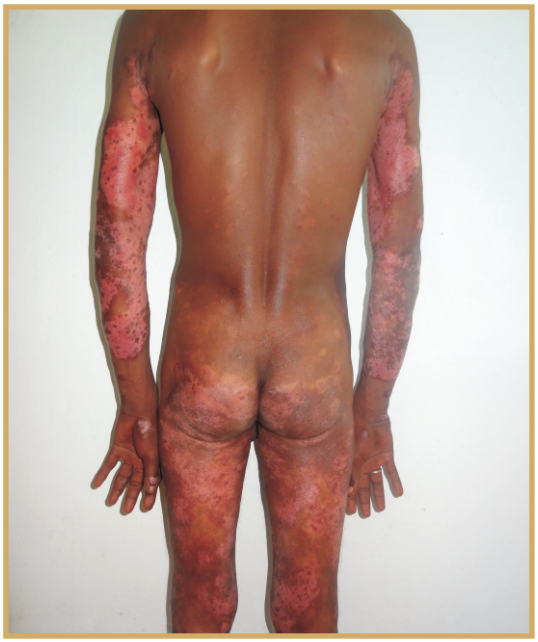

Fig 2b : Lepromatous leprosy lesions developing depigmentation

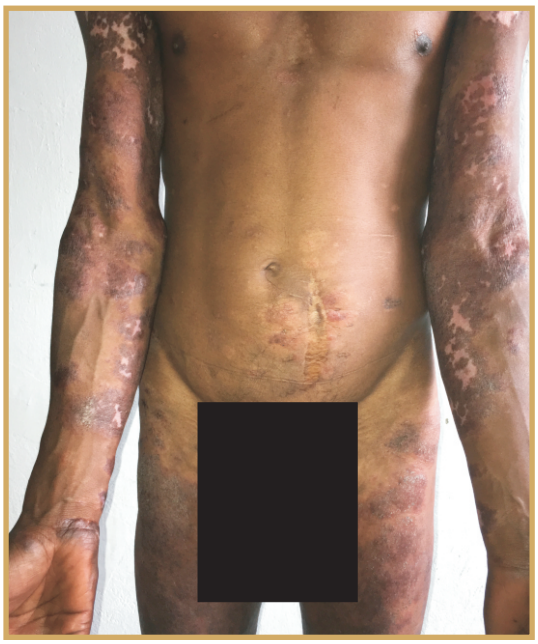

Fig 3a : Near complete re-pigmentation after 6 months of MB multi drug therapy (MDT)

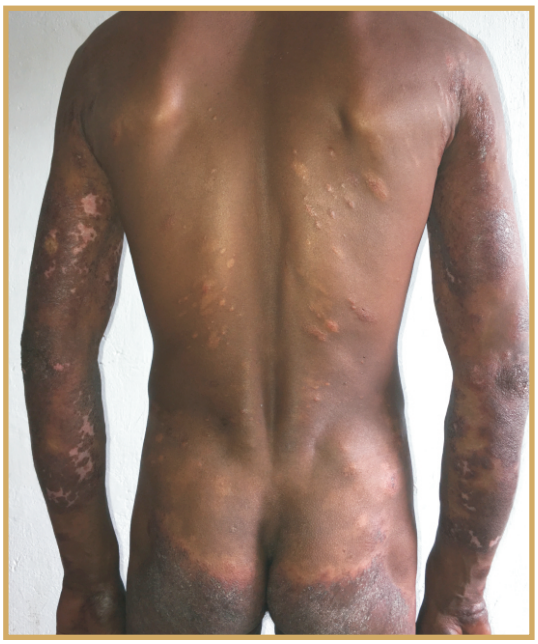

Fig 3b : Near complete re-pigmentation after 6 months of MB multi drug therapy (MDT)

regions showed solid staining acid fast bacilli with a 5+ bacteriological index. Histological examination revealed atrophy of epidermis with a narrow sub-epidermal grenz zone. Diffuse infiltration of foamy macrophages was present in the dermis. Fite-Faraco stain showed enormous number of pink, uniformly stained, rod-shaped, acid fast bacilli within these macrophages (Figs 1a, 1b and 1c).

Following detailed clinical history, examination and histopathological correlation a diagnosis of lepromatous leprosy was made and patient was started on adult type multibacillary multi drug therapy (MDT). After one month of therapy, the previously erythematous lesions became depigmented. These surface changes were confined to the central area of the plaques leaving a narrow erythematous scaly halo at the periphery (Figs 2a and 2b). This depigmentation was associated with further loss of autonomous and sensory functions over the lesions.

The patient was counseled and advised to continue the multidrug therapy. At three months of completing multidrug therapy, the proximal depigmented lesions started showing perifollicuar and interfollicular re-pigmentation. Patient was under periodic follow up and we observed gradual re-pigmentation of depigmented areas with MDT alone (Figs 3a and 3b).

Discussion

Mycobacterium leprae has a predilection for ear lobe, anterior chamber of eye, nasal mucosa, finger tips and peripheral nerves (Massone et al 2015). Organism can also be seen in melanocytes (derived from neural crest) (Van Brakel 2000). In lepromatous leprosy, the depressed cell mediated immunity results in high bacterial and morphological index. The expansile macrophage granuloma leads to irreversible destruction of the nerve. However, there is certain degree of regeneration of Schwann cells and small nerve fibres following treatment (Scollard et al 2015). Pigmentary loss in leprosy has been linked to decreased number and function of melanocytes in the epidermis, dermal hair follicles, sweat glands and nerves respectively. Recently there has been a proposition that cutaneous melanocytes can also arise from neural crest derived schwann cell precursors that are found along the nerves within the skin (Cichorek et al 2013). This partly explains the pigmentation changes in our patient. Another hypothesis for reduced pigmentation in the our case may be put forward as inhibition of melanogenesis from melanocyte rich areas confined to leprosy affected skin secondary to bacillary infiltration and nerve damage. High bacillary multiplication and infiltration in the dermis, hair follicle, and schwann cells may not only inhibit their function but also cause destruction of melanocytes (Van Brakel 2000).

In lepromatous leprosy, there is unchecked bacillary multiplication in large quantity in the schwann cell and perineurium. Infiltration of perinuerium with histiocytes and plasma cells causes incompetence of perineurium to stabilize the intraneural environment (Suneetha and Rao 2010, Scollard 2008). Thus in lepromatous neuropathy there is extensive degeneration because of lack of immunity to react to mycobacterial antigen. Even though there is permanent damage to endoneural fibres, there is some degree of regeneration of schwann cells and small nerve fibres following treatment (Nath et al 2015). These regenerating schwann cell precursors may give rise to formation of cutaneous melanocytes following treatment.

In addition to hypopigmentation, the patient also had areas of depigmentation with leucotrichia distributed over the face, trunk and extremities. We would like to correlate the depigmentation in

this case of leprosy with neural hypothesis of vitiligo, which suggests that destruction of melanocytes may occur due to liberation of some neurochemical mediators or due to gross alteration in the ratio of normal neurotransmitter substances in the lesion. The influx of inflammatory cells in the secondary stage of nerve damage may be associated with release of varied tissue damaging cytokines like transforming growth factor beta (TGF-B). Increased levels of TGF-B have been reported in lepromatous leprosy. TGF-B controls the influx of inflammatory cells by down regulation of tumor necrosis factor alpha, interferon gamma and inhibits inducible nitric oxide synthase induction by macrophages which in turn promote bacterial multiplication (Scollard 2008). These immunologically mediated cytokines might trigger destruction of surrounding melanocytes which may be clinically perceived as depigmentation. The origin, microanatomical feature and behavior that identify melanocytes as nerve cells, and chemical similarity between dopa and noradrenalin which are known products of melanocyte and nerve tissue respectively are additional supports to neural theory of vitiligo (Mohammed et al 2015).

This case highlights the close relation between peripheral nerves and melanocytes. With nerve damage due to lepromatous leprosy, patient starts to lose pigmentation and develop depigmented patches. It is widely accepted that with early diagnosis and treatment (MDT), there is some recovery of nerve damage and there is some improvement in sensory loss. Reappearance of pigmentation in our patient is a visual proof of this recovery due to MDT.

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