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Case Report

# A Curious Case of Neurofibromatosis Type-1 Coexisting with Borderline Lepromatous Leprosy

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Leprosy and Neurofibromatois are distinct diseases both of which cause nerve thickening yet they have specific cutaneous as well as clinical manifestations. Further, the aetiology and pathophysiology of both of these diseases is different. While leprosy is caused by infection with *Mycobacterium leprae* the neurofibromatosis is a genodermatosis. Neurofibromatosis has earlier, also, been reported to co-exist different clinical forms of leprosy. It is important to distinguish both of these diseases, specially so in the post elimination era when leprosy is completely curable and does not lead to disabilities if treated early and efficiently. We report a case neurofibromatosis and leprosy coexisting together. This case was initially thought to be coexistence of Lepromatous and Histoid leprosy manifestations and only after further clinical, bacteriological and histopathological evaluation, the case was confirmed as that of Neurofibromatosis type -1 along with Borderline Lepromatous Leprosy. High index of suspicion followed by use of appropriate techniques is required to solve such cases.

**Key words** : Leprosy, Neurofibromatosis, Schwann Cells, Coexisting

## Introduction

Leprosy and Neurofibromatosis-1 (NF-1) are neurocutaneous disorders that affect Schwann cells and skin. Peripheral nerve enlargement is a feature of both the entities, but cutaneous lesions seen in the conditions are clearly distinct. However, the aetiology and pathophysiology of both these diseases is different. Leprosy is caused by infection with *Mycobacterium leprae* and neurofibromatosis is a genodermatosis. (Swift 1971). Whether the co-existence of neuro-fibromatosis and leprosy will be more damaging because of the nerve involvement in both of them is still unclear. Neurofibromatosis has been reported to coexist with different types of leprosy including Borderline Lepromatous forms (Angoori et al 2010).

We report a rare case of Borderline Lepromatous leprosy with NF-1.

## Case Report

A 22-year-old male patient presented with asymptomatic skin patches over both the legs since the last 10 months. He complained of tingling & numbness over the hands and feet. He

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also had noticed the presence of nodules and brown patches over the body since the age of 10 years. The nodules were painless, skin coloured, of varying size, present over trunk and extremities. Family history revealed similar skin lesions in his father. There was no history of seizure, deafness or visual problem.

Cutaneous examination revealed few soft, non-tender, dome shaped nodules of variable size, ranging from 1 to 1.5 cm in diameter, over the above mentioned sites (Fig. 1). These nodules had characteristic 'button holing' features i.e. application of pressure to these nodules caused them to herniate into the underlying tissue. There were few hyper pigmented patches with intact sensation (café-au-lait spot) on trunk and extremities, which were 1-2 cm in diameter (Fig. 1). Both palms showed freckling (Patrick Yesudian sign) (Fig. 2). In addition erythematous patches with loss of tactile and pain sensation were seen, which were distributed over both the thighs extending up to the middle of the leg (Fig 3). On peripheral nerve examination grade 1 thickness of bilateral greater auricular, ulnar, median, and posterior tibial nerves as well as the left common peroneal nerve was observed. Grade 1 tenderness of ulnar and median nerves was present bilaterally. Sensory examination to pain and temperature (cold and hot) was done which showed impaired sensation over the dorsum of both hands and soles. Crude touch was done with Semmes Weinstein monofilament and was found to be intact. Oschner clasp test, pen test and book test were negative. Card test was positive indicating weakness of adduction of fingers between the1$^{st}$, 2$^{nd}$ and 3$^{rd}$ web spaces of both hands suggesting bilateral ulnar involvement. Wartberg's sign was also positive. There was no pain or fingertip ulcerations. Egawa test was negative. Systemic examination did not

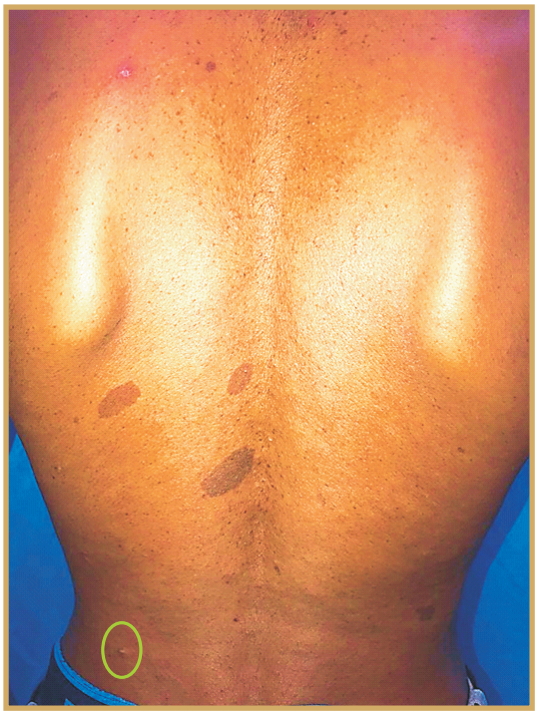

**Fig. 1 : Cafe au lait macules (Hyperpigmented ovoid macules of size > 15 mm with smooth borders) with neurofibroma (green circle)**

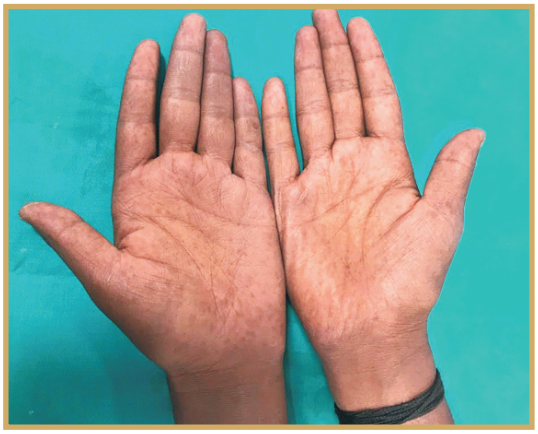

**Fig. 2 : Palmar Freckling (Patrick Yesudian sign) (Multiple hyperpigmented macules over both the palms)**

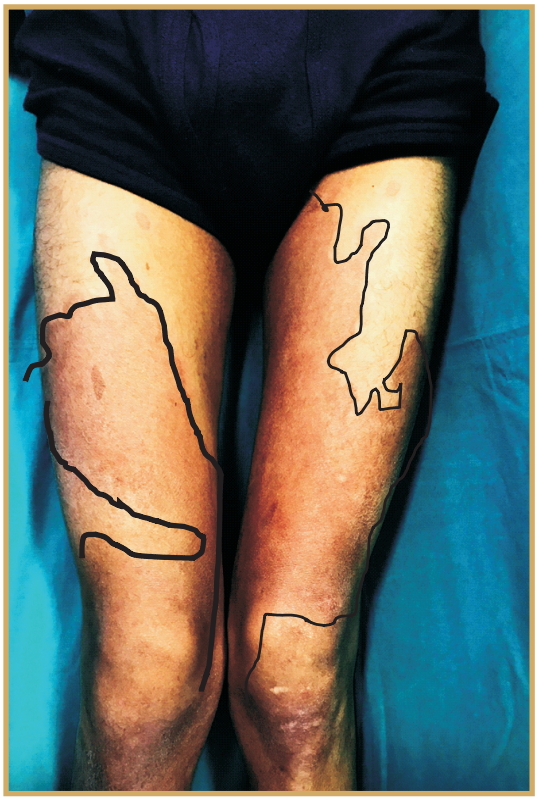

**Fig. 3 : Erythematous patches over the bilateral thighs**

reveal any abnormalities. Ocular examination on inspection was normal and on slit lamp examination showed the presence of Leisch nodules.

Initially, the provisional diagnosis of Lepromatous leprosy with Histoid nodules was suspected, after carefully eliciting the history, clinical examination and investigations like slit skin smears and histopathology (Ridley & Jopling 1966) the diagnosis of Neurofibromatosis type-1 (NF-1) (NIH 1988) coexisting with Borderline Lepromatous leprosy was made.

Slit-skin smears from earlobes, forehead and hypopigmented patches for acid fast bacilli (AFB) showed the average bacteriological index (BI) of 2+. Skin punch biopsy from nodules on the back showed features of neurofibroma – non encapsulated circumscribed neoplasam with multiple spindle shaped cells and wavy collagen bundles (Fig. 4). Skin punch biopsy from erythematous patches from thigh showed features of granulomatous infiltrate of lymphocytes, epithelioid cells and foamy macrophage suggestive of Borderline Lepromatous (BL) Leprosy (Fig. 5).

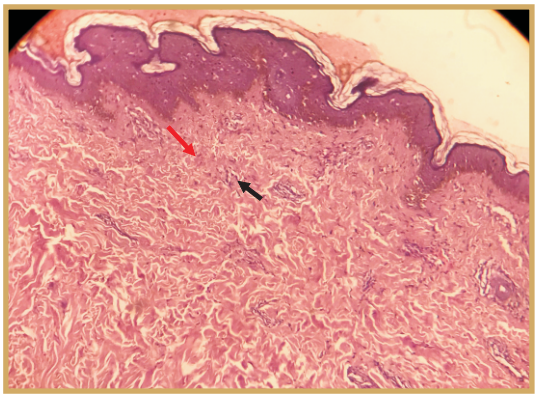

**Fig. 4 : Histopathology of neurofibroma showing non encapsulated circumscribed neoplasm in dermis with multiple spindle shaped cells (black arrow) with wavy collagen fibres (red arrow) (H & E 100x)**

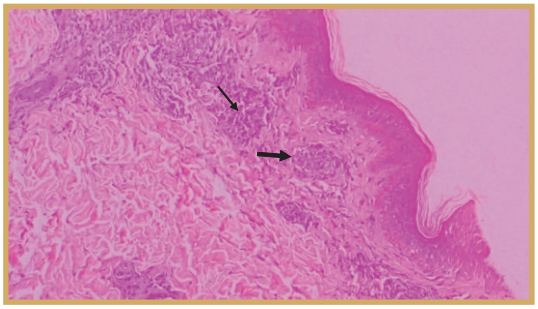

**Fig. 5 : Histopathology of borderline lepromatous leprosy showing granulomatous infiltrate (lymphocytes, epithelioid cells and foamy macrophages) in the dermis (H & E 100x)**

The patient satisfied the criteria of National Institute of Health Consensus (1988) for Neurofibromatosis Type 1 which included presence of cafe au lait macules, neurofibromas and leisch nodules. These findings confirmed the diagnosis of NF1and BL leprosy. The patient received standard treatment for multibacillary leprosy (MB-MDT) and was counselled about NF. He had been on regular follow-up monthly during the treatment period of 12 months and showed a gradual disappearance of leprosy lesions, nerve tenderness reduced to grade 0. Motor weakness improved after physiotherapy exercises but there was no improvement in sensations to temperature and pain.

## Discussion

It is well known that Neurofibromatosis is a neurocutaneous syndrome while on the contrary Hansen's disease is of infectious origin. The simultaneous occurrence of Leprosy and Neurofibromatosis can be a diagnostic puzzle due to the rarity of the existence of both the diseases in the same patient (Angoori et al 2010). Both the diseases affect Schwann cells and the electron microscopic studies have demonstrated that in NF most cells are derived from Schwann cells and in leprosy Schwann cells are predominantly invaded by *M. leprae* and this leads to sensory and motor impairments due to the disease. AFB have been demonstrated in the cytoplasm of the Schwann cells in leprosy. However, these have not been seen in the axon.

Some workers have earlier also reported the co-existence of these two diseases in the same patient. A case of neurofibromatosis with enlargement of all peripheral nerve trunks simulating leprosy was reported by Mittal et al (1997). Similarly an unusual case of hypopigmentation confined to the neurofibromas with symmetrical nerve enlargement with coexistent lepromatous leprosy has also been described by Khandpur et al (2004). Clinical suspicion of leprosy was solved by microbiological, histopathological, and electrophysiological investigations in various studies. In non-endemic areas, leprosy may be mistaken for neurofibromatosis as the two conditions present with nodules and nerve thickening which delayed the appropriate treatment. Numerous such instances of diagnostic dilemma have been reported (Naik et al 1985, Somani et al 1993). Nerve biopsy is suggested to confirm the cause of nerve enlargement whether caused by leprosy or neurofibromatosis. High resolution sonography can also be done to differentiate the nerve enlargement caused by leprosy or NF, in the former there will be increase in the cross sectional area, fusiform enlargement, loss of fascicles and increased vascularity in contrast to multiple fascicles in NF (Lawande et al 2014). In the present case the diagnosis of both the disease were clinically and histopathologically confirmed (Ridley & Jopling 1966, NIH 1988). Besides typical histopathological features present, immunohistochemical markers such as S-100, GAP43, Aldehyde dehydrogenase 1 (ALDH1), Ki-67, calretinins can serve as diagnostic markers for neurofibromas to differentiate malignant and benign proliferations (Liesche et al 2019).

To conclude, as Leprosy and NF are two distinct disorders involving skin as well as the nerves, difficulty in diagnosis can be resolved by careful clinical examination as well as investigations like skin smears, histopathology and other investigations like ultrasonography.

**Informed Consent** : Written informed consent to publish the findings anonymously including images was obtained from the patient.

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