Case Report

Lepra Reactions: Mimickers and Mirror to Unmask Complex Cases of Leprosy

Abstract

Leprosy is a silent disease with protean manifestations, especially during lepra reactions (LRs). Cases with atypical leprosy or LR simulate a number of conditions misdiagnosed frequently. Here, three classical cases of leprosy are reported for their complex presentation. Leprosy was hidden in Case 1 due to co-existing diabetes. COVID vaccination induced LR unmasked all leprosy lesions, which were extensive, large, bizarre and spreading to various immune zones. Case 2 presented with high-grade fever, tachycardia, generalized erythema and body aches. A detailed workup unveiled his leprosy with a rare presentation of Type 1 lepra reaction (T1LR) with erythroderma and severe systemic symptoms. Case 3 mimicked sarcoidosis and lupus erythematosus (LE) on routine workup. She had facial lesions in the malar area, photosensitivity, joint pains, raised angiotensin-converting enzyme (ACE) levels and positive anti-nuclear antibodies. Peri-appendageal granulomas on histopathology and therapeutic response to multidrug therapy helped in the early diagnosis of leprosy.

Keywords: *Atypical, leprosy, mimicker*

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Introduction

Leprosy and Type 2 diabetes mellitus (T2DM) are neuropathic disorders, and incidentally, both can co-exist. Leprosy patients are prone to hyperglycaemia, and co-existing T2DM masks leprosy and increases neuropathic complications.[1] Besides neuropathies, leprosy frequently camouflages various autoimmune disorders like lupus erythematosus (LE) and granulomatous diseases like sarcoidosis. Similarities in granulomas, systemic manifestations and auto-antibodies expression are confounding factors for camouflage.[2] Lepra reactions (LRs) are vital because they complicate 30–50% of quiescent leprosy cases.[3] Approximately 95% of patients seek medical attention for the first time with type 1 lepra reaction (T1LR).[3] So LRs act as a mirror to unveil atypical and hidden cases of leprosy.

Case 1

A 67-year-old diabetic male presented with post-COVID vaccination-induced multiple red raised painful lesions all over the body. Detailed workup revealed numbness, tingling, spontaneous blistering and subsequent ulcers over his extremities for ten years, which were attributed to diabetic neuropathy. On examination, multiple, large, annular and punched-out plaques were distributed extensively in geographic patterns over the trunk and limbs [Figure 1a]. Atypical sites (immune zones) like the scalp, beard [Figure 1b], palms [Figure 1c], scrotum, the tip of the penis and pubic region [Figure 1d] were also involved. All skin lesions were acutely inflamed, neuritis was evident in thickened nerves, and Grade 2 disabilities (G2D) were present in hands, feet and eyes (HFE). Acid-fast lepra bacilli (AFB) were detected on slit skin smear (SSS) with Bacteriological Index (BI) 5+ and Morphological Index (MI) 25% [Figure 1e], indicating a rapid progression of the disease towards the lepromatous pole, and classical features of leprosy were found on Histopathological examination (HPE) [Figure 1f]. The diagnosis of Borderline borderline (BB) downgrading to Borderline Lepromatous (BL) leprosy was easy, but management was challenging due to concurrent unresponsive neuritis and poor glycaemic control (GC). The patient was already on metformin 1 gm twice daily and vildagliptin 50 mg once daily

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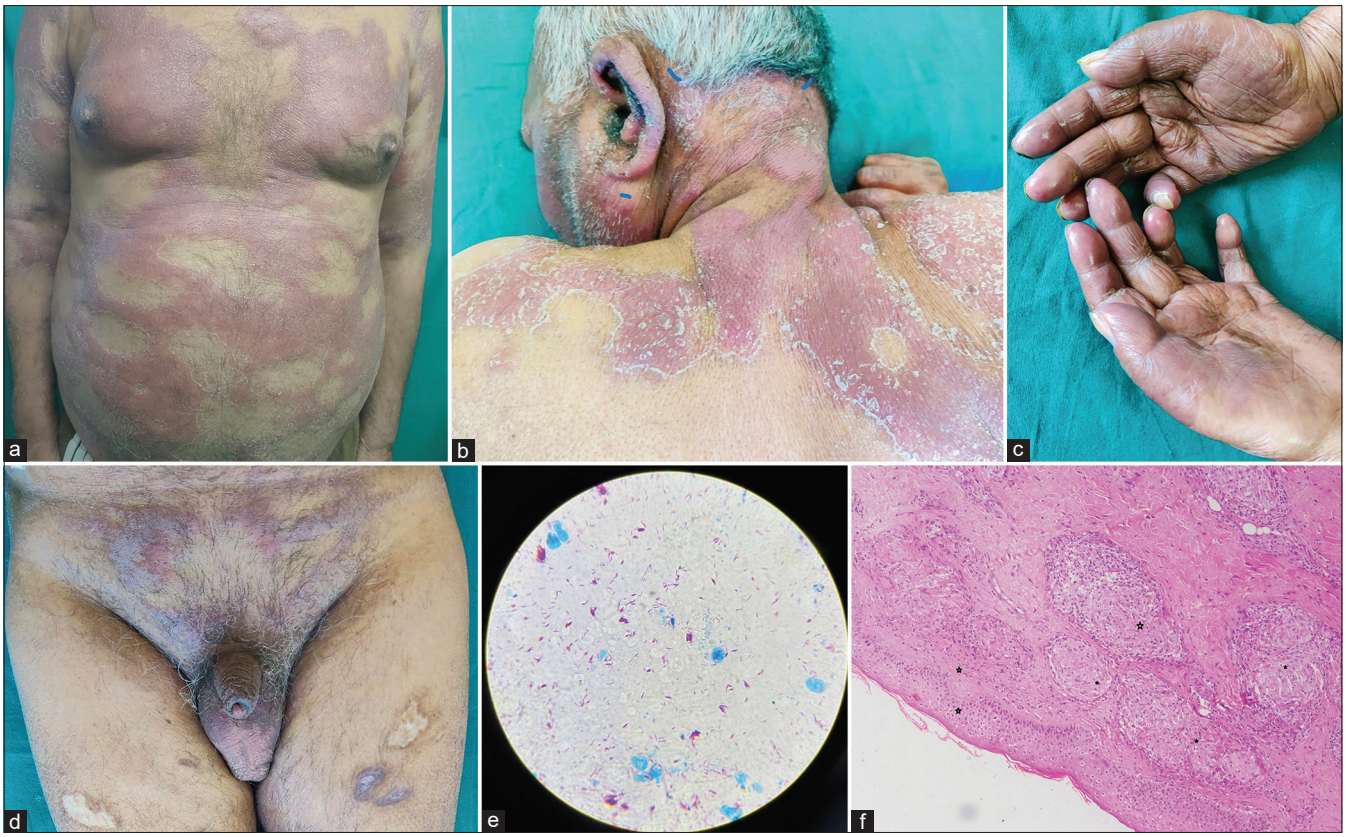

Figure 1: (a) Extensively distributed multiple, annular and punched-out erythematous plaques in geographic pattern over the trunk and upper limbs (b) Presence of erythematous plaques over upper back, neck, ear, scalp margin and beard region (c) Well to ill-defined erythematous plaques over palms and partial ulnar clawing in both hands (d) Erythematous plaques over the pubic region, scrotum and penis and healed atrophic scars over thighs (e) Slit skin smear from ear lobule showing live and fragmented acid-fast bacilli on modified ZN staining (100×) (f) Normal epidermis, well-formed Grenz zone and multiple epithelioid cell granuloma in the dermis; revealing BT downgrading to BL leprosy (H and E 100×)

with good GC (FBS-100 to 110 mg). After the diagnosis of leprosy, MDT-MB (Multidrug therapy - Multibacillary) along with deflazacort (DC) 45 mg was started. Due to the worsening of neuritis and development of facial nerve palsy, DC was increased to 60 mg (40/20) after the 7th day, and 12 units of short-acting insulin (SAI) were also added. Neuritis remained unresponsive, so on the 3rd day, DC was substituted with 60 mg (40/20) of prednisolone (PS) which controlled neuritis but FBS levels reached up to 350 mg–400 mg/dl. It took two weeks to achieve GC with insulin therapy (short-acting 16 units + long-acting 14 units) and four weeks to control neuritis with tapering doses of steroids and 15 mg weekly methotrexate.

Case 2

Sixteen-year-old male presented with fever, generalized erythema, hand, feet and facial swelling for the last 2.5 months. He was sick with high-grade fever, tachycardia and generalized body aches. On examination, the patient was in erythroderma with evident ichthyosis in the upper and lower extremities [Figure 2a and b]. Multiple well to ill-defined plaques of size 0.5 × 0.5 to 10 × 15 cm were palpable over the trunk and upper limbs. He had anaesthesia, motor weakness and Grade 2 disabilities (G2D) in his HF. Infra-orbital, ulnar, radial cutaneous and lateral popliteal nerves were thickened bilaterally in an asymmetric fashion (1+ or 2+). Though AFB couldn't be seen on SSS, HPE from plaque lesion suggested Borderline Tuberculoid (BT) leprosy [Figure 2c]. A diagnosis of BT downgraded to BL leprosy with G2D in HFE and severe T1LR was made, and MDT-MB along with oral steroid (WHO protocol) were started. The patient was discharged after two weeks of clinical improvement and didn't get any episodes of LRs during and nine months post-MDT period. T1R with systemic features is uncommon, and erythroderma-like generalized involvement is unreported.

Case 3

A 37-year-old female presented with red, raised, painless facial lesions for the last three months. She had photosensitivity in facial lesions and joint pains for the previous two months. On examination, multiple plaques of size 2 × 2 cm to 2 × 3 cm were present over the nose, cheeks and left shoulder [Figure 3a]. Besides SSS and skin biopsy, all routine and specific investigations were sent with clinical possibilities of LE and lupus pernio. We found raised ACE levels (136 nmol/ml), a negative Mantoux test, normal serum calcium levels and a chest X-ray (workup for sarcoidosis). The positive ANA with 1:320 titres, speckled pattern, photosensitivity and joint pains were

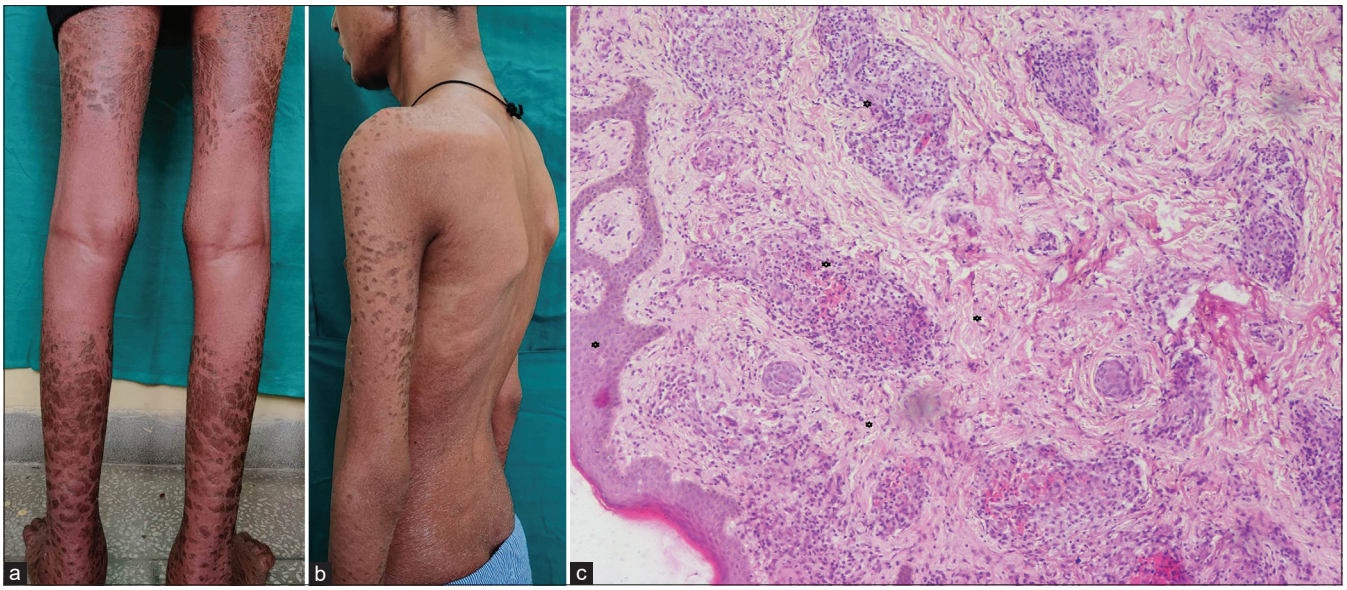

Figure 2: (a) Diffuse erythema over lower limbs and ichthyosis on legs and thighs (b) Generalized body involvement by erythema admixed with ichthyosis on upper limbs (c) Multiple well-formed epithelioid cell granulomas, interspersed lymphocytes and oedema in the dermis diagnostic of BT leprosy with T1LR (H and E, 100×)

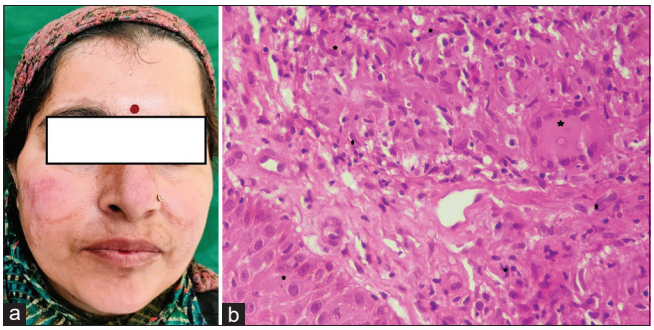

Figure 3: (a) Three well to ill-defined erythematous and elevated plaques over the nose and both cheeks (b) BT leprosy showing sheets of epithelioid cells and Langhans giant cells in dermis (H and E, 400×)

suggestive of LE. But her blood counts, urine routine microscopy/24-hour urinary proteins (not detected), and complement levels were normal. VDRL (Venereal Disease Research Laboratory) test and anti-ds DNA antibodies were also non-reactive. HPE demonstrated peri-appendageal tuberculoid granulomas (without AFB) suggestive of BT leprosy [Figure 3b], so the patient was put on MDT- MB and NSAIDS. Marked clinical improvement in skin lesions and joint pains was observed between 12–16 weeks of MDT-MB without steroids. But further biopsies or follow-up examinations could not be done due to the shifting of the patient to regional health centre.

Discussion

Leprosy is a 'great imitator', so it is always prone to misdiagnosis. T2DM can co-exist with leprosy, and almost 40% of leprosy patients can have impaired glucose or T2DM.[1] Nigam *et al*. (14.2%) and Saraya *et al*. (13.3%) reported a significantly higher incidence of T2DM in leprosy patients.[4,5] Steroids and other factors like disease-related stress and LR-induced catabolic state secrete stress hormones (epinephrine, glucagon and cortisone) to raise the blood sugar level. Secondly, TNF-alpha down-regulates insulin receptors and induces insulin resistance.[4,5] The co-existing T2DM not only masks leprosy, as in Case 1, but also increases neuropathic complications and disabilities to an advanced stage. In Case 1, lesions were extensive, and multiple atypical sites were involved. A delayed diagnosis due to co-existing T2DM can be the leading cause of such a presentation. Though leprosy runs its course still, diabetic immune suppression (like in HIV (Human Immunodeficiency Virus)) may be the additional factor for the extensive involvement of both typical and atypical sites in such cases.[6]

Leprosy and sarcoidosis are granulomatous diseases with multisystem involvement and characteristic epithelioid cell granulomas on HPE. Our case of BT leprosy was a diagnostic challenge due to intact sensations over facial lesions and absent AFB as expected at the upper pole. Furthermore, she had mixed features of LE (ANA positivity) and sarcoidosis (raised ACE levels). Calcium levels were normal, but granulomatous disorders are also rarer because of hypercalcemia due to overproduction of vitamin D.[7] In our set-up, with a lack of auxiliary tests, a high index of clinical suspicion and meticulous HPE examination can help in the final diagnosis. Still, a diagnostic dilemma remains, and a long-term follow-up is recommended in such cases.

Years back, in 1987, Azulae *et al*. described auto-aggressive hanseniasis (in lepromatous and borderline leprosy cases) as a syndrome with clinical and immunopathological manifestations resembling autoimmune connective tissue disorder (CTD).[8] Since then, a wide range of CTD

manifestations and various auto-antibodies expressions has been seen in leprosy patients. Our patient had an SLE-like presentation with positive ANA and later has been reported in 0–37.5% of leprosy cases.[9] Molecular mimicry between the pathogen and self-antigens, stimulation of B cells by these immune complexes and dysfunction of suppressor T lymphocytes explain CTD manifestations in leprosy.[8]

Around 20–50% of all leprosy patients can have either reactional states of type 1 or 2. Constitutional symptoms and systemic manifestations are often seen with Type 2 Lepra reaction (T2LR) (mild and severe), but rarely, they may be a part of T1LR. An unusual and unreported presentation of T1LR with erythroderma and severe constitutional symptoms was found in Case 2. Kar *et al*. reported a case of T1LR with severe constitutional symptoms like high-grade fever, malaise, vomiting, joint pains and tenosynovitis.[10] As per the literature, systemic manifestations can occur in T1LR, but they are infrequent, and unlike in T2LR, they are only seen in a severe form of T1LR, not in a mild type.

Conclusion

Leprosy is a well-known mimicker and has several atypical presentations. Co-existing co-morbidities and initial presentation to non-dermatologists can delay the diagnosis till the stage of disabilities. A high index of clinical suspicion can help in early diagnosis and disability prevention.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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