Tropical medicine rounds

Rare atypical presentations in Type 2 lepra reaction: a case series

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Abstract

Objectives Type 2 lepra reaction is a Th2-mediated type III hypersensitivity reaction in leprosy, with a characteristic cutaneous manifestation in the form of erythema nodosum leprosum (ENL). We describe unusual presentations of Type 2 lepra reaction in five patients.

Methods Patient data and dermatological findings were analyzed in three men and two women diagnosed with Hansen’s disease.

Results Findings included multiple tender, polycyclic, necrotic lesions distributed over the face in one patient, and painful, fluid-filled lesions on both arms and lower limbs in another. The third patient showed erythematous, tender nodules, bullae, and necrotic ulcers over the back and upper and lower limbs. The fourth showed erythematous tender nodules over the face, neck, back, and extremities, predominantly in sun-exposed areas. The fifth revealed multiple erythematous, severely tender nodules and urticarial plaques mimicking those of Sweet’s syndrome. Diagnosis of borderline or lepromatous leprosy with atypical Type 2 reaction were made in all cases.

Conclusions Type 2 lepra reactions are antigen antibody-mediated immune complex reactions that present with constitutional symptoms and ENL characterized by tender, erythematous, evanescent nodules mainly on the face, arms, and legs. Over 50% of lepromatous leprosy patients and 25% of borderline lepromatous leprosy patients experienced type 2 lepra reactions prior to the advent of multi-drug therapy. Thalidomide is the drug of choice for severe atypical lepra reactions because of its anti-tumor necrosis factor-α action. Awareness of these atypical variants and prompt diagnosis and treatment are essential to prevent mortality and morbidity in potentially treatable patients.

Introduction

Leprosy is a multi-organ infectious disease affecting mainly the skin and nerves.¹ Type 2 lepra reaction is a Th2-mediated type III hypersensitivity reaction, with a characteristic cutaneous manifestation in the form of erythema nodosum leprosum (ENL). Herein, we describe unusual presentations of Type 2 lepra reaction in a series of five patients.

Case reports

Patient 1

A 36-year-old male patient, diagnosed with Hansen’s disease (borderline lepromatous) and maintained on uniform multi-drug therapy (MDT) for the previous eight months, presented with multiple painful, red, raised lesions with ulceration, fever, and arthralgia of three days’ duration. Dermatological examination revealed multiple tender, polycyclic, coalescing, necrotic lesions over the face. Each of the resulting ulcers had a clean base, sharply defined borders, and erythema along the margin (Fig. 1a,b). A final diagnosis of borderline lepromatous leprosy with Type 2 reaction in the form of erythema necroticans leprosum was made.

Patient 2

A 54-year-old male patient, known to have Hansen’s disease (lepromatous leprosy) and maintained on uniform MDT for the previous 18 months, presented with multiple painful, fluid-filled lesions over both arms and lower limbs, which broke down to form ulcers. Dermatological examination revealed bilaterally symmetrical involvement of the face and upper and lower limbs, which demonstrated persistent multiple erythematous, tender nodules and hemorrhagic bullae over an
erythematous base. The patient also had multiple ulcers covered with necrotic slough (Fig. 1c–e). Peripheral smear showed toxic granules suggestive of sepsis. Swabs from the wound grew *Staphylococcus aureus*. A final diagnosis of Hansen’s disease with a Type 2 lepra reaction (erythema necroticans lepromatous with infarct-like triangular ulcer) and associated septicemia was made.

**Figure 1** (a) Patient 1, a 36-year-old man, demonstrates evolving erythema necroticans over the face and (b) erythema necroticans with ulcer formation. (c) Patient 2, a 54-year-old man, exhibits an infarct-like triangular ulcer with central necrotic slough, and (d) hemorrhagic blisters over an erythematous base over the bilateral thighs, legs and (e) right upper limb.

**Figure 2** Patient 3, a 50-year-old man, demonstrates a mitten-like hand resulting from recurrent Type 2 reactions with a crusted ulcer over the dorsum of the left forearm.

**Figure 3** (a) Patient 4, a 39-year-old woman, demonstrates persistent, tender erythematous nodules over photo-exposed areas on the back and (b) forearms. (c) Patient 5, a 50-year-old woman, exhibits grouped and discrete erythematous papules and nodules with apparent pseudovesiculation in a Sweet’s syndrome-like presentation on the face and (d) upper back.
Patient 3
A 50-year-old male patient presented with a history of multiple painful, red, raised lesions and blisters over his body for a period of five days. These blisters had ruptured to form ulcers. Dermatological examination revealed bilaterally symmetrical involvement of the back and upper and lower limbs in the form of multiple erythematous, tender nodules, bullae, and necrotic ulcers. Patchy glove and stocking hypoesthesia was present, along with mitten hands caused by recurrent Type 2 reactions (Fig. 2).

Patient 4
A 39-year-old woman diagnosed with Hansen’s disease (lepromatous) and maintained on MDT for the previous year presented with multiple painful, red, raised lesions over the body, high-grade fever with chills, and body ache of two days’ duration. The lesions were not evanescent. Dermatological examination revealed multiple erythematous, tender nodules over the face, V area of the neck, back, and extremities, predominantly in sun-exposed areas and sparing of covered areas (Fig. 3a,b).

Patient 5
A 50-year-old woman presented with a history of fever and episodes of painful, raised lesions over the body over a period of 15 days associated with constitutional symptoms. Dermatological examination revealed bilaterally symmetrical involvement of the upper back and the extensor aspects of the upper limbs, predominantly in the photo-exposed area, manifesting as multiple erythematous, severely tender nodules and urticarial plaques. The lesions mimicked those of Sweet’s syndrome and took the form of characteristic urticarial plaques studded with pseudovesicles (Fig. 3c,d). A skin biopsy showed intense neutrophilic infiltrate but no evidence of the fibrinoid necrosis seen in Sweet’s syndrome. The patient was diagnosed with lepromatous leprosy with a Type 2 reaction presenting as a Sweet’s syndrome-like manifestation.

Table 1 Clinical and laboratory findings in five patients diagnosed with Hansen’s disease

| Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 |
|-----------|-----------|-----------|-----------|-----------|
| Atypical Type 2 presentation | Noduloulcerative necrotic lesions over face | Hemorrhagic bullae and infarct-like triangular ulcer | Necrotic ulcers with mitten-like hands | Persistent ENL lesions over photo-exposed areas | Urticarial plaques with pseudovesicles presenting as Sweet’s syndrome-like lesions |
| General examination | Febrile, tachypnea, tachycardia, swelling of face, hands and bilateral pedal edema, non-tender lymphadenopathy | Common involved nerves that were tender included the ulnar and common peroneal nerves |
| Investigation | | | | |
| Hb (gm/dl) | 9.6 | 9.0 | 10.0 | 12.0 | 13.5 |
| TLC (x10^3) | 18 400 | 39 400 | 16 000 | 14 500 | 16 400 |
| DLC | N_81L_11E_04 | N_80-L_13M_05E_05 | N_84L_12M_01E_03 | N_90-L_10M_01E_01 |
| ESR (mm/h) | 20 | 24 | 16 | 24 | 24 |
| Serum bilirubin, mg/dl | 1.0 | 1.2 | 1.0 | 0.9 | 0.8 |
| AST (IU/l) | 246 | 850 | 45 | 40 | 35 |
| ALT (IU/l) | 132 | 345 | 36 | 32 | 40 |
| Slit-skin smear | Bi 6+ | Bi 5+ | Bi 5+ | Bi 5+ | Bi 6+ |
| Histopathology | Consistent with lepromatous leprosy in Type 2 reaction | Dermis showed collection of neutrophils superimposed on foamy macrophages |
| Treatment | MDT, prednisolone, thalidomide | MDT, thalidomide, injectable antibiotics | MDT, prednisolone, thalidomide | MDT, prednisolone, thalidomide | MDT, thalidomide |
| Course of illness | Ulcers healed in 2 weeks with post-inflammatory depigmentation | Nodules disappeared in 7 d and ulcers healed in 3 weeks | Nodules disappeared in 3 d and ulcers healed in 3 weeks | All reactional lesions regressed in 1 week |

ENL, erythema nodosum leprosum; Hb, hemoglobin; TLC, total leukocyte count; DLC, differential leukocyte count; ESR, erythrocyte sedimentation rate; AST, aspartate aminotransferase; ALT, alanine aminotransferase; MDT, multi-drug therapy.

Discussion
Type 2 lepra reactions are antigen antibody-mediated immune complex reactions that present with constitu-
tional symptoms and ENL. Erythema nodosum leprosum is characterized by tender, erythematous, evanescent nodules mainly on the face, arms, and legs.2,3 Usually 15–50% of lepromatous leprosy patients develop ENL reactions within the first year of therapy. Over 50% of lepromatous leprosy patients and 25% of borderline lepromatous leprosy patients used to experience ENL reactions in the pre-MDT era.4

In Type 2 lepra reaction, patients show sudden crops of red, tender nodules or plaques, which occasionally become vesicular, pustular, bullous, or necrotic; these were seen in the first three patients in the present series. Erythema necroticans has been reported by Verma and Pandhi.5 It can be fatal, the cause of death being septicemia occurring secondary to skin ulcers and urinary tract infection precipitated by corticosteroids.1,6 Our second patient developed features of sepsis and was managed with broad-spectrum parenteral antibiotics. Sethuraman et al.7 reported a severe bullous variety of ENL in a 35-year-old man, similar to that seen in our second patient, who, in addition, also showed an infarct-like triangular ulcer. A bullous-type reaction mimicking pemphigus in a lepromatous leprosy patient from India was described by Petro.8

Our fourth and fifth patients showed predominantly photodistributed ENL lesions, a manifestation that has rarely been reported in the literature. Kou and Chan reported a patient with ENL simulating Sweet’s syndrome, which responds well to high-dose systemic corticosteroids,9 as our fifth patient demonstrated.

Thalidomide is the drug of choice for severe ENL because of its anti-tumor necrosis factor-α (TNF-α) action.10 Short courses of oral corticosteroids are used in the setting of acute neuritis and involvement of the eyes as thalidomide does not penetrate the eyes.

Awareness of these atypical variants and their prompt diagnosis and treatment are essential to prevent mortality and morbidity in potentially treatable cases.

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