CASE REPORT

Annular bullous lesions with atypical erythema multiforme in leprosy

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Summary  Erythema nodosum leprosum (ENL) is an immune complex–mediated reaction that may complicate the course of multibacillary leprosy. Bullous lesions in TypeII reaction, though reported, are exceedingly rare. We report the case of a 32 year old female patient who presented initially at our OPD with erythema nodosum. Cutaneous examination revealed impaired sensation over dorsum of right foot and thickened right lateral popliteal nerve. Slit skin smear (SSS) from ear lobes revealed AFB with a bacteriological index of 2+ . She was started on MDT, tablet ofloxacin 200 mg twice a day, and 30 mg oral prednisolone. Two months later, she presented with generalised pruritus, large target lesions over the back, and hemorrhagic bullae over lower extremities and annular pattern of bullae, over both arms. A SSS was repeated which was positive for AFB. Histopathology from bullous lesions was consistent with ENL. Direct Immunofluorescence (DIF) study was negative. Our patient improved rapidly after she was started on thalidomide 100 mg twice daily, with withdrawal of ofloxacin. Erythema Multiforme (EMF) and annular bullous lesions have been reported in patients on treatment with ofloxacin. This case is being presented due to the unusual and varied manifestation of Type II lepra reaction in a 34 year old female patient.

Introduction

Leprosy is a chronic disease caused by Mycobacterium leprae. It affects the peripheral nervous system, the skin, and certain other tissues. The most common institutional classification is the Ridley-Jopling classification. The clinical course of leprosy is often interrupted by reactions which are acute inflammatory episodes that can be classified as Type I (‘Upgrading reaction’ or ‘Downgrading reaction’) and Type II reaction. The most common Type II reaction (T2R) is ‘Erythema Nodosum Leprosum’ (ENL). There are several reported...
atypical manifestations of T2R such as, Lucio’s phenomenon, erythema nodosum necroticans, Vesiculobullous lesions, and Erythema Multiforme (EMF) like lesions.¹

Vesiculobullous lesions in leprosy have rarely been described. There are few published papers from India on bullous lesions in T2R.²,³ These types of lesions are of importance as they can be easily confused with various other vesiculobullous lesions of pemphigus, bullous pemphigoid and drug reactions.

Herein we are reporting an unusual manifestation of T2R with annular bullous lesions and EMF.

**Case report**

A 32 year old female patient presented to our outpatient department with multiple erythematous nodules over legs, along with fever and joint pain of 15 days duration. Examination revealed erythema nodosum, scattered ulcers with crusting (Figure 1), loss of pain, temperature and fine touch sensation over both lower limbs.

The right lateral popliteal nerve was uniformly thickened and moderately tender. A complete blood count (CBC) revealed anaemia (Hb-8 gm %), leukocytosis (13000 cells/cumm) and raised ESR (60 mm/hr). Slit skin smear (SSS) revealed a bacillary index (BI) of 3+. Acid fast bacilli (AFB) were seen on Fite Faraco staining. Thus the patient was diagnosed as borderline lepromatous leprosy with T2R. The patient was started on WHO Multidrug therapy (MDT) for Multibacillary (MB) leprosy comprising of Rifampicin 600 mg once a month, Dapsone 100 mg

![Figure 1. Erythema nodosum with necrotic ulcers over the leg.](image-url)
once daily, Clofazimine 300 mg once a month supervised and 50 mg daily, along with tablet ofloxacin 200 mg twice daily and tablet prednisolone 40 mg in tapering doses.

Twenty days later she presented to us with the complaint of severe itching over her back, along with fluid filled lesions over both her upper and lower limbs of 4 days duration associated with recurrence of fever and joint pain. There was no history of mucosal involvement or epistaxis. Cutaneous examination revealed multiple vesiculobullous lesions arranged in an annular pattern over extremities, large targetoid lesions (EM) lower back,
scattered necrotic ulcers with eschar formation over both upper and lower limbs (Figure 2). Nikolsky’s sign was negative.

She was re-subjected to routine investigations which revealed anaemia, leukocytosis and a raised ESR. Tzanck smear was negative for acantholytic cells. SSS once again revealed a BI of 3+. Antinuclear antibody test, Direct Immunofluorescence study, and *Herpes simplex virus types 1&2* antibody tests were negative. Histopathology from the bulla revealed an intraepidermal bulla, dermal perivascular lymphocytic infiltrate, diffuse irregular granulomas and a few foamy macrophages (Figure 3).

Her treatment was modified by stopping ofloxacin and increasing the dose of clofazimine to 300 mg/day. WHO-MDT was continued along with tablet prednisolone 30 mg/day. After proper counselling thalidomide 300 mg/day was started. She responded dramatically to treatment within a period of 2 weeks (Figure 4).

She has been on MDT with thalidomide 200 mg for the last 6 months with no recurrence of lesions.

**Discussion**

T2R is a Type 3 hypersensitivity reaction occurs exclusively in lepromatous leprosy occasionally in borderline lepromatous leprosy. In severe T2R, ENL lesions may become vesicular or bullous and breakdown to form necrotic ulcers called as Erythema Nodosum Necroticans.2

Bullous lesions in leprosy are very rare.4 Generalised bullous eruptions during treatment with Rifampicin and Dapsone have been reported in the past.3 There are reports of annular bullous eruptions after use of Ofloxacin (a known bactericidal drug) when used concomitantly in treatment of Urinary tract infections.5 Similar lesions are also seen in patients having a high bacillary load, due to sensory neuropathy or as bullous drug reaction.6

Although bullous lesions have been described in literature, atypical presentation of bullae in an annular pattern with tender, erythematous plaques as in our case is extremely uncommon. Until 2009 there were only two such case reports.5 EMF is another atypical manifestation associated with leprosy even in leprosy endemic regions such as Asia and...
South America. One study describes a case of EMF as the first clinical manifestation of leprosy. Clinicians should be alerted to this rare presentation of leprosy.

Histopathologically bullous T2R may show intraepidermal or sub epidermal bulla, dermal oedema or leucocytoclastic vasculitis with diffuse polymorphonuclear infiltrate and few foamy histiocytes. Secondary acantholysis has also been reported (Table 1).

Immunofluorescence is of importance to rule out various autoimmune blistering causes to whom leprosy patients are not immune.

Figure 4. Healed lesions following Thalidomide.
Our patient was started on ofloxacin due to the high bacillary load. Over 99–99.99% killing of viable *M. leprae* is observed within less than 1 month therapy. However, as there is evidence suggesting ofloxacin as the offender for bullous lesions in leprosy, it was discontinued.

Thalidomide is described as the drug of choice for recurrent and severe ENL. It is a steroid sparing drug and shows clinical response within 48–72 hours. It has to be given under strict supervision and is not used in females planning a family, due to its teratogenic effect.

Our patient was counselled regarding the teratogenic side effect of thalidomide. After four consecutive negative pregnancy tests, thalidomide therapy was started in the aforementioned dose. She was admitted with us for the initial month of thalidomide treatment, and has been on follow up ever since.

Newer Treatment of Recurrent ENL include Infliximab, Pentoxifylline and Leukotriene Inhibitors.

**Conclusion**

In this case the lesions were probably related to the use of ofloxacin, which is not a standard component of MDT. Adding extra drugs to standard regimens exposes the patient to additional risks and should be used cautiously.

Varied manifestations of T2R continue to baffle dermatologists worldwide, the incriminating causes of which cannot be predicted with accuracy. Annular bullous lesions and EMF are very rare presentations of T2R. Clinicians should be alerted to this rare presentation of leprosy. It needs to be differentiated from other common causes of blistering. Thalidomide and corticosteroids continue to be the mainstay of treatment.

**References**

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