

CASE REPORT

Bullous erythema nodosum leprosum manifesting in the post partum period with unusual features

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Summary A 30 year old woman who presented with multiple numb patches on the body was initially diagnosed as borderline lepromatous leprosy and started on multidrug therapy for leprosy. She had an episode of Type 1 reaction during the fifth month of pregnancy. After delivery, she stopped therapy fearing harm to her child and developed an episode of Type 2 reaction. The reaction was unusual in that bullous lesions developed over previous leprosy patches which had initially become indurated, with associated neuritis. Histopathology revealed bullae with intense neutrophilic reaction and strong positivity for acid fast bacilli. There was no response to steroid therapy which was started for the reaction. Thalidomide had to be prescribed after stopping lactation by medical means. She responded dramatically to Thalidomide with regression of cutaneous lesions and neuritis. This patient is being reported as a very unusual manifestation of bullous erythema nodosum leprosum in the postpartum period responding dramatically to thalidomide.

Keywords: Erythema nodosum leprosum, bullous, thalidomide, lactation, post-partum

Introduction

Erythema nodosum leprosum (ENL) is a Type 2 reaction characterised by the appearance of bilaterally symmetrical crops of erythematous tender nodules or plaques. It is associated with a host of extra-cutaneous features, including fever, neuritis, lymphadenopathy, iridocyclitis and other constitutional symptoms. Vesicular or bullous lesions have been reported rarely in severe forms of Type 2 reactions, mainly from Brazil, other parts of South America and India.¹ We are reporting a bullous Type 2 reaction in a post-partum woman with atypical features rarely described in the literature before.

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Case Report

A 30 year old woman presented with a 1 year history of light colored numb lesions over neck and upper limbs. There was no history of similar complaints in close contacts. Dermatological examination revealed multiple polymorphic, hypopigmented, hypoaesthetic macules with multiple thickened peripheral nerves. The Bacteriological Index was 5+ and the skin biopsy showed multiple epithelioid cell granulomas with foamy macrophages in the dermis (Figure 1).

She was diagnosed as a case of Hansen's disease (Borderline lepromatous) and started on multi drug therapy (MDT) in the form of rifampicin 600mg once monthly, dapsone 100 mg daily and clofazimine 100 mg on alternate days. She was counselled regarding all aspects of leprosy, including dosage and duration of medicines, methods of transmission, side effects and regular visits to the hospital. After 8 weeks of taking MDT, the patient returned to her hometown and found that she was pregnant. She discontinued MDT on the advice of her relatives thinking that the drugs would harm the fetus. However at her next antenatal visit to the hospital, she was referred to us by the obstetrician. MDT was re-started and within a month she developed a Type 1 reaction in the form of redness and swelling of pre-existing lesions, along with a left ulnar neuritis. Skin biopsy revealed dermal edema and disintegrating granulomas with a predominantly lymphocytic infiltrate. She was given tapering doses of prednisolone (starting with 1 mg/kg daily) for a total duration of 10 weeks and her lesions completely regressed.

Following her delivery, she again discontinued her MDT during the period of lactation. She then reported with a history of fever and multiple red, raised, painful lesions within a month of her delivery. Lesions appeared over her pre-existing patches of leprosy in both arms. Subsequently, over the next 24 hours multiple fluid filled painful lesions appeared over

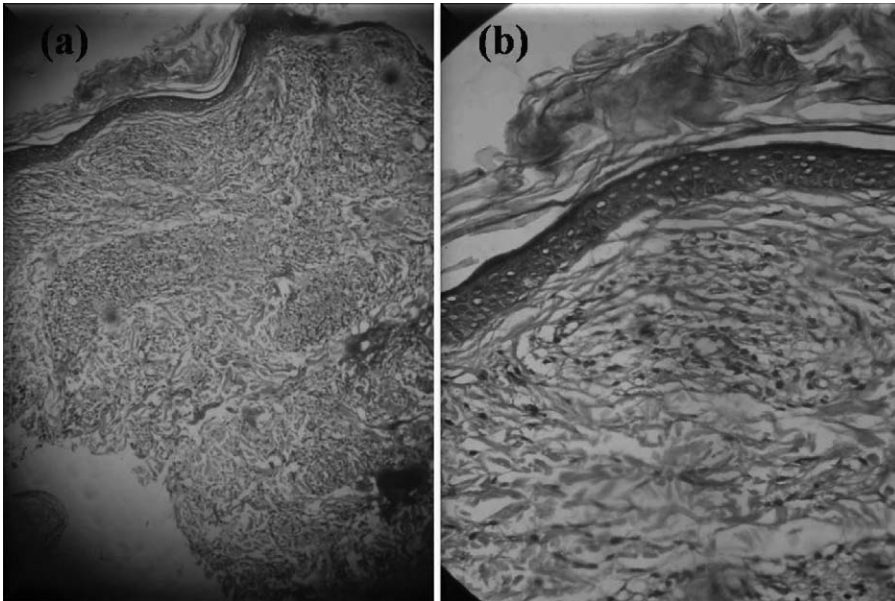


Figure 1. Histopathology of the initial clinical manifestation of borderline lepromatous leprosy: (a) Macrophage filled granulomas with clear grenz zone [10x: H & E stain] (b) AFB positivity [100x: Fite Faracco stain].

the raised borders of these lesions. Lesions had clear fluid and were tense. The patient also had generalised swelling of hands and feet. She continued to get fresh crops of painful, red, raised lesions over the next few days. She had sharp shooting pain across her left forearm, associated with generalised malaise and body ache. There was no history of physical trauma.

On examination she was found to have pallor and was febrile with pitting edema over hands and feet. Dental and gynaecological examination did not reveal any focal infection. Her systemic examination was essentially within normal limits. Dermatological examination revealed multiple erythematous plaques with tense bullae on their surfaces over both forearms and neck (Figure 2).

There were multiple tender, erythematous nodules on both legs (Figure 3).

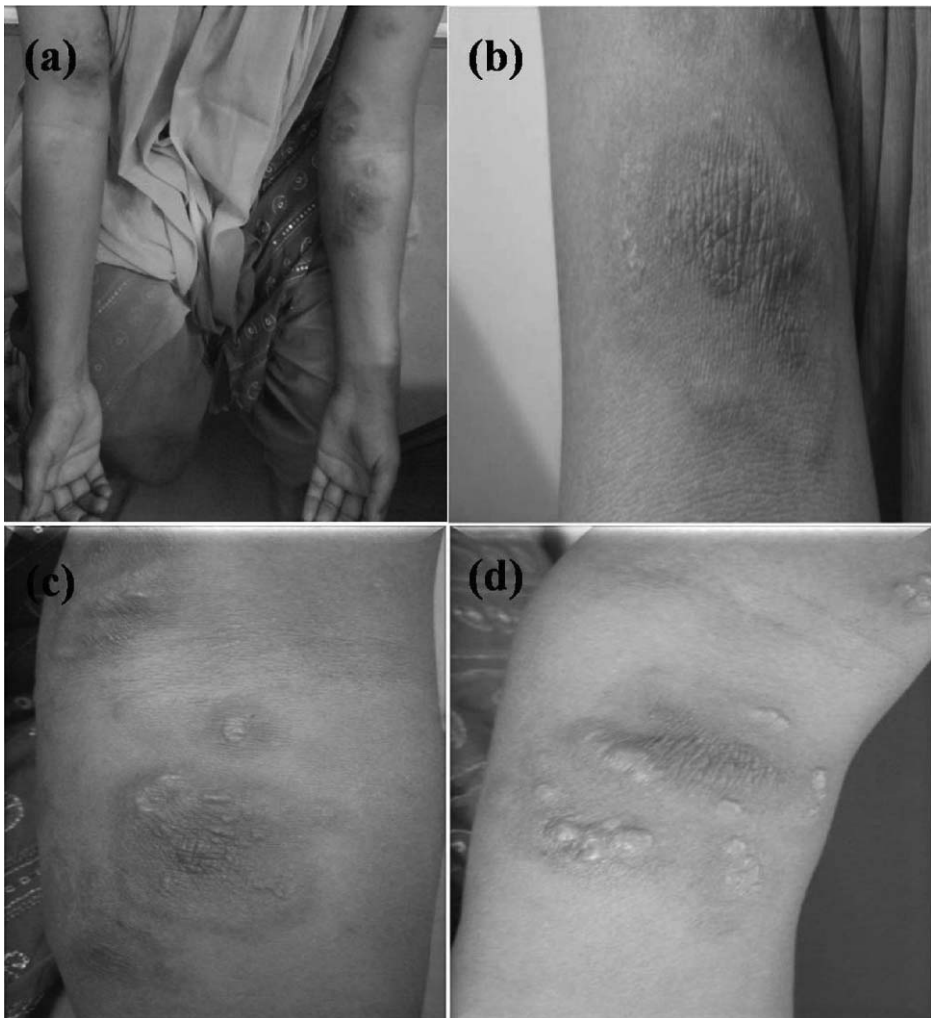


Figure 2. Clinical evolution of bullous erythema nodosum leprosum: (a) Raised erythematous lesions on both arms and forearms (b) Central clearing in few lesions (c) Bullae developing on periphery of plaques (d) Well defined tense bullae on the underlying plaques.

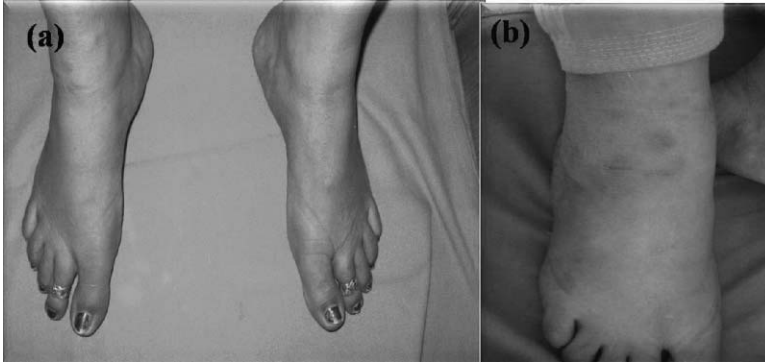


Figure 3. (a) Erythema nodosum leprosum lesions on both legs (b) Close up view of the same.

The left ulnar nerve was uniformly thickened and tender, while the right ulnar and both common peroneal nerves were uniformly thickened and non-tender.

Investigations revealed a normocytic normochromic anaemia with neutrophilic leukocytosis. Blood sugar and urine examination were normal. She had no evidence of any infection or parasitic infestation. Skin biopsy from the bullous lesions revealed multiple subepidermal bullae with ill defined macrophage-filled granulomas and a dense neutrophilic infiltrate (Figure 4).

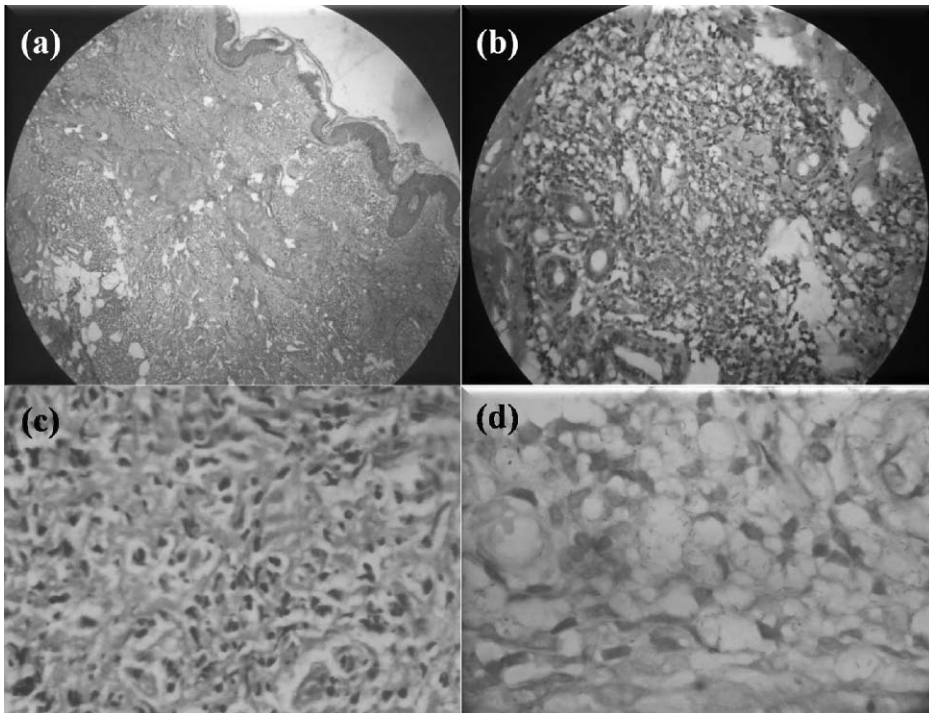


Figure 4. Histopathology of the bullous lesions (a) Bulla formation in low power [10x: H & E stain] (b) Bulla formation in high power with intense neutrophil infiltration [40x: H & E stain].

Based on the clinical and histological findings she was diagnosed as Hansen's disease (borderline lepromatous) with bullous ENL lesions and neuritis. She was initially managed with three drug MDT, oral prednisolone at 1mg/kg daily, oral haematinics and NSAID's. Even after 2 weeks therapy she continued to be symptomatic and new crops of bullous lesions kept on appearing. With very few therapeutic options left, she was started on thalidomide 100mg QID with the advice that she should immediately stop breast feeding. Her lactation was suppressed medically with Cabergoline 0.5 mg BD for 2 days and the child was put on bottle feeding. She was also advised to maintain barrier contraception throughout the entire period.

Within 48 hours of starting thalidomide, the tender, red lesions over the legs disappeared and within the next 4 days all her bullous lesions subsided. The neuritis completely subsided over a period of 1 week. She became afebrile and her general condition stabilised. Thalidomide was tapered over the next 4 months and then stopped. She has presently completed her course of MDT and continues to be free of relapse and reactions.

Discussion

Less than 10 cases of bullous ENL have been reported in literature.² The mechanism of bulla formation has been described as due to leukocytoclastic vasculitis or severe dermal oedema. Sethuraman *et al.* reported severe bullous ENL in a 35 year old male which was controlled by intra-venous hydrocortisone.³ A bullous reaction mimicking pemphigus in a lepromatous patient was described by Petro; in this patient, constitutional features and neuritis were absent, and histopathological examination from the lesion was not done, so the final diagnosis is uncertain.⁴

A systematic literature review of the interaction between leprosy and pregnancy highlighted an association between the development of Type 1 reactions and neuritis in the post-partum period, when cell-mediated immunity returns to the pre-pregnant level.⁵ ENL reactions can occur throughout pregnancy, but are rarely reported post-partum. One case of annular bullous ENL has been described in pregnancy, which was controlled by treating the concomitant urinary tract infection.⁶ There are no previous reports of bullous ENL in the immediate post-partum period.

Another interesting manifestation was the occurrence of bullous ENL lesions in pre-existing patches. Initially with the raised edges of the pre-existing lesions and neuritis, it was thought to be a Type 1 reaction. The patient had constitutional symptoms in the form of fever and myalgia. Tender evanescent nodules were present on the lower limbs and histopathology from the bullous lesions confirmed features of Type 2 reaction. This led to the diagnosis of ENL in this case.

In most reported cases, bullous ENL lesions were recurrent and responded better to thalidomide than corticosteroid.^{7,8} There are no available studies of thalidomide during lactation in humans because of the major problem associated with teratogenicity in pregnancy. Animal studies have shown transmission of the drug through breast milk. Studies in animals have also shown reduced viability of young ones, increased abortions, reduced body weight gain, alterations in learning and memory, decreased fertility and reduced pregnancy index when the lactating mother was given thalidomide.⁹ The consensus is therefore that it is better avoided in lactation. We had to stop breast-feeding in our patient and start her child on bottled feeds so that she could take thalidomide. In many countries,

thalidomide is available only to those physicians and pharmacists who are registered with the system for thalidomide education and prescribing safety (STEPS) programme. In India, thalidomide can be accessed through various projects and institutes like the Bombay Leprosy Project and the Central Leprosy Research Technical Institute, Chennai. However vigilance needs to be extremely high because of the availability, to prevent adverse effects.

Because MDT was started prior to delivery, the risk of transmission of leprosy to the child is low. Our patient was informed, however, regarding the clinical features of leprosy in children, so that she can seek medical help as early as possible on detecting such features in her child. The family was also counseled regarding financial issues if the child was not breast fed. The family was ready to face any financial issues in this case and the child has been healthy throughout the follow-up period.

The therapeutic challenges faced in our patient were the non-responsiveness to oral corticosteroids and the use of thalidomide in a post-partum woman during lactation. We observed that thalidomide is helpful not only in resolving the bullous ENL lesions, but it was very effective in treating the peripheral neuritis which had not responded to oral steroids.

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