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Case Report

Hypothalamo-Pituitary Axis Suppression : A Risk Factor for Late Onset Bullous ENL ?

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A 46 yr old man, diagnosed as a case of lepromatous leprosy in 2010, was put on MB-MDT for a period of 1 year and then released from treatment following the completion of its course. However, the patient suffered from recurrent Erythema nodosum leprosum (ENL) towards the end of the MDT regimen with an exacerbation recorded once every few months. Patient was on long term treatment with a combination of thalidomide, corticosteroids, clofazimine and occasionally colchicine for the same. The patient's current exacerbation had ENL lesions, some of which were studded with clear fluid filled bullaes suggestive of bullous ENL. Histopathology from the lesions confirmed the diagnosis of bullous ENL. These bullous lesions developed suddenly, 2 weeks after withdrawal of oral corticosteroids. During the hospital stay he was diagnosed as a case of Hpothalamo Pitutary (HPA) axis suppression due to his chronic steroid use. He was restarted on the earlier regimen of thalidomide, corticosteroids and clofazimine and his reaction subsided within 4-5 days. He has not developed any similar bullous lesions since then. Bullous ENL is a rare form of type 2 reaction, which usually manifests during the period of MB-MDT therapy, or sometimes in untreated cases. HPA axis suppression due to dependence on steroids may be a key feature as was observed in this case.

Key words : ENL, T2R, MB-MDT, HPA axis suppression

Introduction

Leprosy is a chronic inflammatory mycobacterial disease. Its clinical presentation depends on the host's ability to induce cell mediated immunity against the lepra bacilli. Bullous Type 2 reaction (T2R) is not very common in everyday practice, especially in patients who have completed the full course of MB-MDT. This is a case report of a patient who had completed his MB-MDT 4 years ago, but continued to get recurrent ENL reactions about 4-5 times each year. He therefore, was on intermittent steroid therapy and currently reported with several clear fluid filled bullae present over the ENL lesions on his arms, chest and lower back. He had voluntarily refrained from using corticosteroids (on advise of a local practitioner, due to side effects of steroids) for a period of 2 weeks, prior to the present admission.

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During the course of his hospital stay the patient was diagnosed as a case of HPA axis suppression.

Case History

A 46 year old man, was diagnosed as a case of lepromatous leprosy in 2010. At that time his slit skin smear showed a Bacterial index (BI) and Morphological index (MI) of 6+ and 10% respectively. He completed his 12 month course of MB-MDT and was released from treatment, but kept on suffering from recurrent ENL which were usually not associated with other features of T2R (Type 2 lepra Reaction). Most of the episodes occurred towards the end of his therapy and in the period following his release from treatment. He was given a combination of thalidomide, clofazimine and tapering doses on prednisolone during this period to which he responded well. Patient was lost to followup for a period of 6 months prior to the current admission, as he had gone back to his hometown. During this period he self medicated by consuming tablets of prednisolone 10 mg at every episode of ENL reaction. Twenty days prior to his present admission, patient developed fever and generalised body pain associated with the presence of multiple ENL lesions over his body. He went to a local doctor who advised immediate complete

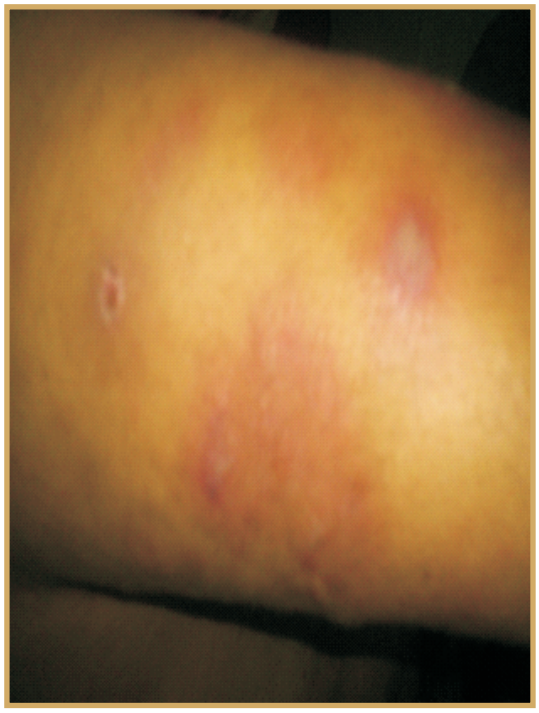

Fig 1 : Showing the clinical photograph of bullous ENL lesions on upper arm

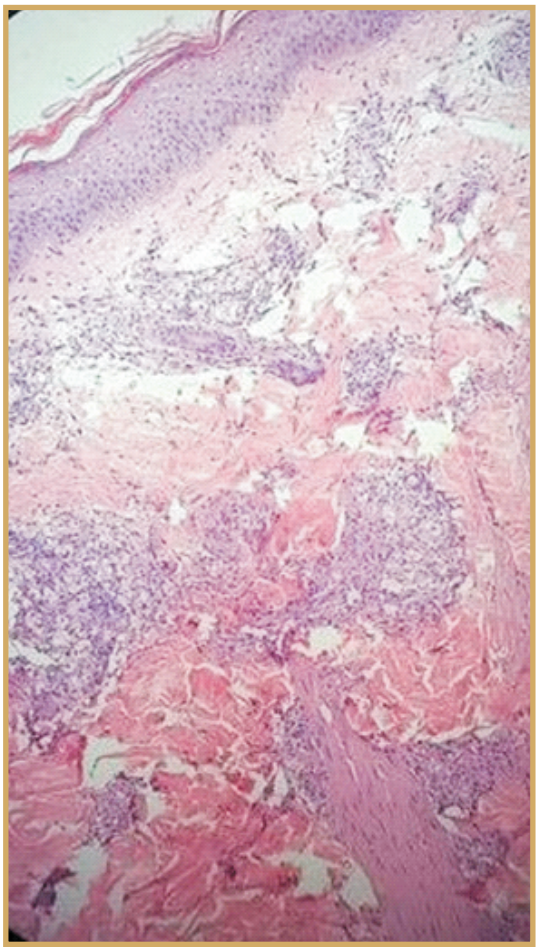

Fig 2 : Showing the histological picture of bullous ENL lesion under High power with 100 magnification with AFB, Fite Farraco staining

withdrawal of oral corticosteroids on account of its side effects. Two weeks after withdrawal of prednisolone, he experienced another episode of ENL reaction with some of the lesions filled with clear fluidbullae over the arms, lower back and chest (Fig 1). Patient visited the hospital and was admitted for the above complaints and was evaluated in detail.

Patient showed no signs of neuritis, iridocyclitis, arthritis and lymphadenitis. Cutaneous examination revealed multiple evanescent erythematous tender subcutaneous nodules suggestive of ENL over the chest, back and limbs with the lesions over the arms filled with clear fluid bullae. Nikolskysign and bullae spread sign were negative. Face, palms and feet were relatively spared. No mucosal involvement was seen. Sensory examination revealed persisting symmetrical sensory loss over the lower legs. The slit skin smear (SSS) showed a BIof 2+, and MI was zero. Other routine investigations were normal. Bacterial culture from the fluid of the bullae showed no growth. Histopathological examination revealed a collection of foamy macrophages, in the dermis. Both superficial and deep dermis showed perivascular periadnexal large granulomas composed of epitheloid cells, lymphocytes and neutrophils with karyorrhectic debris which were also seen infiltrating the arrector pili muscle and nerve twigs (Fig 2). AFB staining showed many fragmented and beaded AFB in the foamy macrophages. The histological picture was consistent with ENL. A final diagnosis of bullous ENL was made. In addition, the patients serum fasting cortisol level was found to be low, i.e. (3.2 mcg/dL), and he was diagnosed to be a case of HPA axis suppression.

Patient was restarted on the earlier combination of thalidomide 100mg tid (thrice a day), Clofazimine 50mg tid, Prednisolone 40 mg daily in the morning with other supportive therapy. His ENL with the vesicobullous lesions subsided after a period of 5-6 days. He was discharged on the same medications. He was followed up after a period of two weeks and had not developed any new episodes of ENL during the period.

Discussion

In leprosy, bullae may occur in lucio phenomenon /lazarine leprosy (Choon and Tey 2009), necrotic ENL (Vandana and Balachandran 2009), heat exposure associated autoimmune bullous disorder (Thappa et al 1996), drug induced bullous reactions (Dutta 1980), trophic ulcers and other causes of necrotizing vasculitis (Choon and Tey 2009).

In multiple case studies (Thappa et al 1996, Dave et al 2003, Kar et al 2009, Agarwal et al 2013), the observed BI of the patients in the respective studies varied from 2+ to 4+, during bullous ENL reaction. Several case reports mention the occurrence of the bullous ENL either during MDT therapy (Agarwal et al 2013), or in new untreated cases of leprosy (Kar et al 2009). The occurrence of bullous ENL, 4 years after stoppage of MDT has not been reported as of yet to the best of our knowledge.

When ENL does occur after the completion of MB-MDT then a provisional diagnosis of bacterial resistance has to be considered (Dave et al 2013). However, with a declining BI and zero MI, this patient was not considered as a case of resistant leprosy.

The usual triggers associated with ENL reaction include surgical operations, pregnancy, parturition, lactation, menstruation, trauma, intercurrent illness, virus infections, vaccination, physical or mental stress, and in the earlier days, sometimes anti leprosy therapy (Meyerson 1996). The patient described in the present report gave no such history, and was off treatment from the last 4 years.

History of unsupervised chronic steroid usage for a variable period, and abrupt steroid withdrawal, prior to the exacerbation can be a triggering factor, and has been reported earlier also (Sethuraman et al 2008).

Chronic steroid usage, does result in HPA axis suppression, due to which an inadequate amount of endogenous steroid is produced. It is also postulated that the normal steroid response which takes place during inflammatory episodes like T2R is suppressed in these patients and this leads to a much severe manifestation of ENL in the form of bullous ENL. This possibility, needs be considered as an important factor in patients with recurrent ENL, who are on long term treatment with varying doses of steroids. In such patients steroids should not be stopped abruptly but slowly and gradually tapered off. This will prevent sudden crisis associated with HPA axis suppression. Steroids along with thalidomide (Theophilus 1980) and daily higher doses of Clofazimine (Schreuder and Naafs 2003) have been suggested for therapy of recurrent ENL reactions, especially in cases who have become steroid dependent. It is also important to closely and regularly follow up the patients with ENL and T2R and monitor their progress. The side effects of drugs need to be monitored closely so as to prevent suppression of HPA which may also be fatal.

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