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Case Report

Managing a Case of Steroid Dependant Erythema Necroticans in a Severely Immune-compromised Patient: Case report

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Erythema necroticans is a severe manifestations of type 2 lepra reaction manifested as painful, ulcerated nodules distributed over limbs & trunk, associated with systemic symptoms. Oral glucocorticoids are used as first line therapy to arrest the progression. However, due to relapsing & remitting course of disease, chronic steroid use land up into many dreadful complications. Here we are reporting a case having chronic steroid dependent erythema necroticans with tuberculosis which can be a therapeutic challenge in the field of dermatology. History revealed that the patient had self-administered steroids and thalidomide for one and half year which was earlier prescribed for an episode of severe ENL and tapered off. During the course of disease, she developed tubercular arteritis leading to stroke which proved fatal. There is immense need for adequate and appropriate counselling of such patients suffering from recurrent episodes of lepra reactions.

Keywords: Erythema necroticans, Steroid Dependent, Tuberculosis, Type 2 Lepra Reaction

Introduction

Erythema nodosum leprosum (ENL) is an immune complex mediated inflammatory reaction seen in nearly 50% of lepromatous leprosy patients and 5–10% of borderline lepromatous leprosy (BL) patients especially those having bacterial index above 4 (Pocaterra et al 2006, Walker et al 2015). Cutaneous manifestations of ENL are characterized by crops of evanescent, erythematous inflamed nodules, that wean off within 48-72 hour. Severe ENL may present as ulcerated, necrotic, pustular, sweet's syndrome like and bullous lesions (Alakad et al 2021). As per study conducted in India, less than 10% of patients had a single episode of ENL whereas approximately 62.5% had chronic ENL (Pocaterra et al 2006).

The management of ENL is a challenge with patients those who have become steroid dependent. Multiple recurrences were seen in 39%-77% of cases when steroid withdrawal was attempted (Sachdeva et al 2021). Here, we are presenting a case of recalcitrant recurrent severe type 2 reaction who developed uncontrolled type 2 diabetes mellitus (DM), extra pulmonary tuberculosis, cataract, hypothalamic pituitary axis (HPA) suppression after chronic systemic steroid use posing a treatment challenge.

Case report

A 60-year-old female patient presented with

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chief complaints of multiple painful nodules, ulcers with profuse purulent discharge, severe joint pain and headache since 15 days. On dermatological examination, there were multiple erythematous tender nodules of size varying approximately from 1*1 cm to 2*3cm over right shoulder (Fig. 1), bilateral thighs (Fig. 2), right buttock. Most of these nodules ruptured to form multiple sinus openings over an indurated base mimicking carbuncle and few developed into large ulcer having undermined edge with floor containing purulent slough mimicking pyoderma gangrenosum. However, all the ulcers were invariably painful and extremely tender that made patient functionally handicapped. On general examination, the patient was febrile (101^0F), irritable and not cooperative to time place and person. She had also tachycardia, hypotension, tender non-matted significant inguinal and axillary lymphadenopathy and bilateral pitting pedal oedema. On nerve examination, peripheral nerves were neither enlarged nor tender. There was no glove and stocking anaesthesia. Meanwhile the patient also complained of severe persistent throbbing headache which was not relieved with conventional analgesics.

As per history, the patient was previously treated with multidrug therapy (MDT) for 12months for BL Hansen's disease. After 2 months of completion of MDT, patient developed multiple evanescent reddish tender nodules, fever and arthralgia which was continued as on and off episodes for further 8months, as a manifestation of severe ENL, which was managed with oral

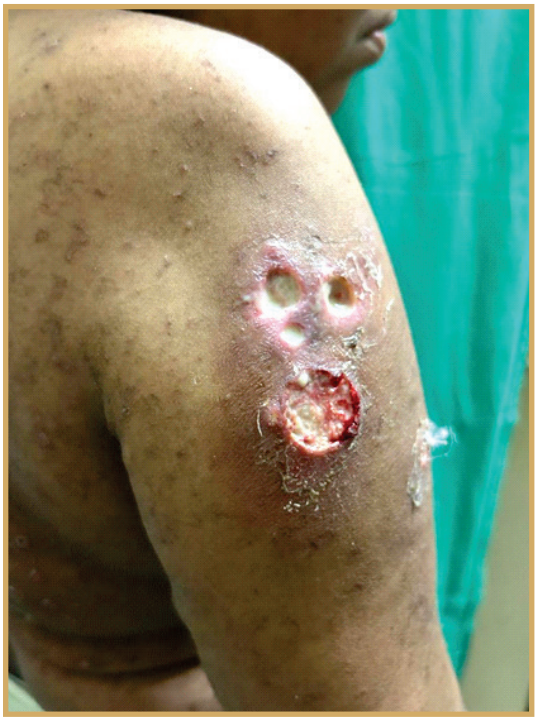

Fig. 1: Carbuncle like ENL on right arm.

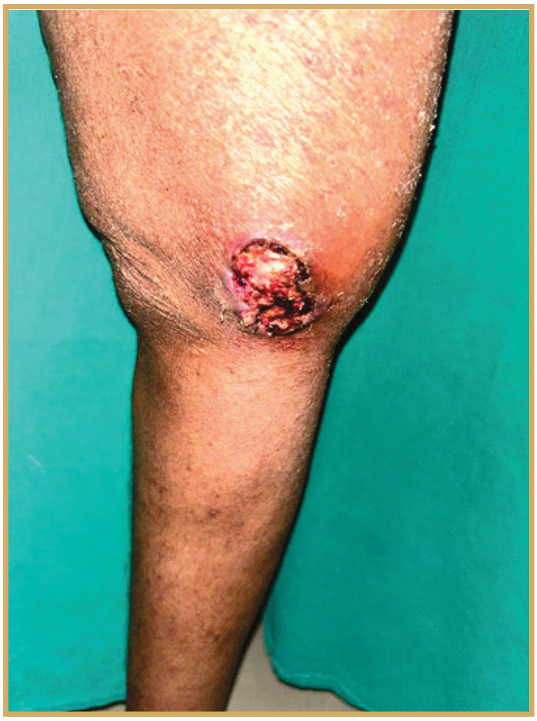

Fig. 2: Pyoderma gangrenosum like ENL over posterior aspect of right thigh.

steroid, started at the dose of (1mg/kg) followed by tapering and thalidomide 300mg. However, patient continued the above medications without consulting any physician for 1.5year. Eventually patient developed cataract, type 2 DM and hypertension and was started on subcutaneous insulin.

In this episode patient had no signs of active Hansen's disease clinically. Slit skin smear showed fragmented bacilli. On histopathology, dense inflammatory infiltrate comprised of predominantly neutrophils, lymphocytes, histiocytes, in superficial dermis extending up to subcutis (Fig. 3) suggesting erythema necroticans. Wade Fite stain showed multiple fragmented and granular bacilli (Fig. 4). No organism growth was found in pus culture. So, we started managing the case with final diagnosis of erythema necroticans and type 2 DM having low serum cortisol. After that patient was managed with low dose oral steroid as per endocrinology consultation. However, after tapering of oral steroid, within a week, patient again developed new nodules with ulceration and purulent discharge.

During this course the general condition of patient also deteriorated with increased irritability and severity of headache. Therefore, CECT was planned which showed multiple rim enhancing lesions with surrounding white matter oedema suggestive of tuberculoma. Then patient was further evaluated for any other active focus of tuberculosis (TB). Meanwhile patient was started high dose injectable dexamethasone and mannitol to manage CNS TB after neurologist opinion with which there was significant improvement in both skin lesions and general status of the patient.

The HRCT thorax revealed fibrotic changes and atelectatic bands of right lower lobes of lungs. So anti tubercular therapy was started for pulmonary tuberculosis.

During this period, patient was found to have thrombocytopenia, so thalidomide was stopped but clofazimine and apremilast (30mg twice daily) were initiated as steroid sparing agents for erythema necroticans. Though there was initial control of ENL episode, but again new lesions reappeared that were later unresponsive to above

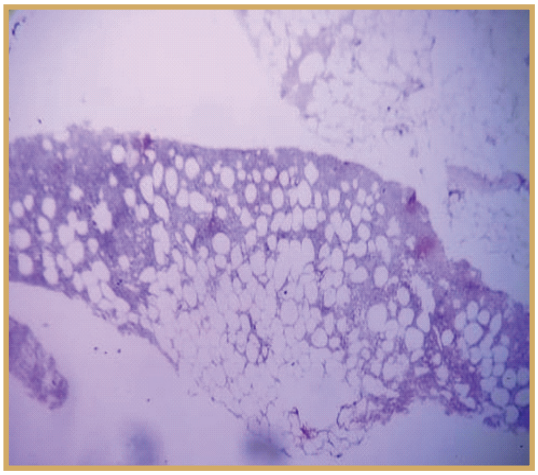

Fig. 3: Neutrophilic infiltrates in lower dermis extending to lobules of subcutis. (H &E, 10X)

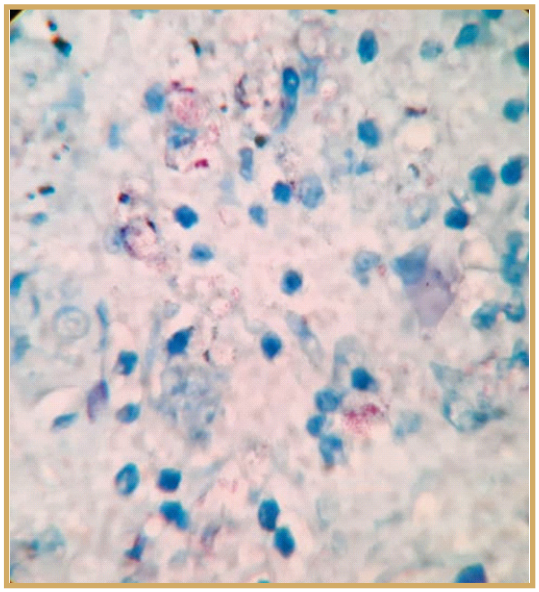

Fig. 4: Wade Fite stain showing granular & fragmented bacilli.

medications. Therefore, biologics were planned but could not be started due to concomitant active tuberculosis. There was great dilemma whether treatment with high dose systemic steroid is to be continued to control erythema necroticans or other steroid sparing agent should be considered to address HPA axis suppression. But deciding the safe steroid sparing agent in patient having active TB was also a difficult task for us as we had already stopped thalidomide, cyclosporine due to thrombocytopenia.

Eventually in due course of illness, patient developed tubercular arteritis which led to stroke. Patient was shifted to ICU, intubated and finally patient could not be extubated and succumbed to death within few days.

Discussion

There are two types of leprosy reactions: type 1 reaction or reversal reaction, and type 2 reaction, in which the most frequent manifestation is ENL. Although most ENL patients respond well to conventional therapeutics, few have severe morbidity or mortality as they are refractory to treatment. Antimicrobial resistance (AMR) may be a predisposing factor for chronic and recurrent ENL (Narang et al 2022) and it was found that rifampicin resistance can be a cause behind chronicity of ENL (Sardana et al 2020). Therefore, we had also thought for doing drug resistance study but couldn't go ahead as there was lack of resources in our setting.

Mycobacterium lepromatosis causes diffuse non nodular infiltrated skin lesions causing lucio leprosy and lucio phenomena which usually manifests as angular jagged purpura, ulceration and necrosis, which resolves with atrophic scarring, having no constitutional symptoms like fever. Contrary to this, in our case, all lesions evolved as nodules without a background of purpuric and necrotic skin, associated with fever. Also in histopathology, there was no findings of bacillary infiltration of endothelial wall of vessels. However, *M lepromatosis* can cause severe prolonged ENL reactions in case of LL Hansen's treated with MDT (Sotiriou et al 2016). Therefore, genomic studies could play an essential role in determining the causative organism (Singh et al 2023). But due to unavailability of infrastructure and expertise we were unable to perform genomic sequencing.

Due to chronic, recurrent ENL, patients develop steroid-dependence and fatal adverse effects. Previous studies have shown that prolonged corticosteroids therapy in ENL patients lead to immunosuppression and results in septic shock, pneumonia, diabetic ketoacidosis (Sugumaran 1998).

There is a report of a case of ENL who died of an intracranial infection due to chronic steroid use (Zhu et al 2017). Other reports have stated that steroid dependant ENL patients may develop severe infections, such as Nocardia farcinica pleuritis, (Arunthathi et al 2001), Strongyloides hyperinfection syndrome (De souza et al 2014). Although a retrospective study suggested a significant proportion of ENL deaths occur due to adverse effects of chronic steroid use, but this is yet to be confirmed with epidemiological data (Walker et al 2014). Occasionally leprosy and tuberculosis may also coexist as both are chronic granulomatous disease with aerosol route of transmission and both are endemic in India. Due to chronic immunosuppressive use in Hansen, TB may develop during management of reactions.

Our case was a challenge of managing severe steroid dependant Type-2 reaction along with the coexisting immunosuppression possibly because of unsupervised chronic steroid use. There is a need of adequate and appropriate counselling for the cases of lepra reactions who require long term steroid use.

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