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Case Report

Exacerbation of Erythema Nodosum Leprosum Possibly Triggered by COVID-19 Vaccine : A Case Report

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Erythema nodosum leprosum (ENL) is an immune complex mediated type III hypersensitivity reaction seen in patients of borderline lepromatous and lepromatous leprosy. It can be caused by a wide array of triggers and can be seen before, during, or after completion of anti-leprosy therapy. There are multiple well-known triggers for type 2 reactions like the initiation of multidrug therapy, Mantoux testing, vaccination, mental and physical stress, and physiological states like pregnancy. Herein, we report a case of exacerbation of ENL in a middle-aged woman, probably due to COVID-19 vaccine while she was well-controlled on immunosuppressive therapy. The episode was treated with non-steroid anti-inflammatory drugs and oral steroids and the symptoms resolved within 2 weeks. Although causality was highly possible between the occurrence of ENL and COVID-19 vaccine, physicians should be aware that it can be easily managed with proper care and medicines and this should not be a basis for deferring the vaccine.

Keywords : Erythema Nodosum Leprosum, AstraZeneca-Oxford, COVID-19 Vaccine, Leprosy, Vaccination, Type 2 Reaction

Introduction

Erythema nodosum leprosum (ENL)/ type 2 leprosy reaction is a distressing and painful condition seen in borderline lepromatous and lepromatous leprosy. ENL is considered to be a neutrophil-mediated type III hypersensitivity immune-complex reactional state in which there is deposition of immune complexes in the serosa, glomeruli, vessel walls, etc. Histologically, the acute stage of ENL is characterized by a prominent neutrophilic infiltrate throughout the dermis and subcutis and complement C3 and C5 deposition in the lesions (Polycarpou et al 2017). ENL can occur before, during, or after completion of leprosy therapy (Baima de Melo et al 2020). We hereby present a patient with recurrence of ENL while on systemic immunosuppression, likely to be triggered by the AstraZeneca- Oxford COVID-19 vaccination.

Case

A 46-year-old, Asian female was diagnosed with borderline Hansen's with grade 2 deformity in 2019. Her bacillary index (BI) was 5+ and morphological index (MI) was 0 at the time

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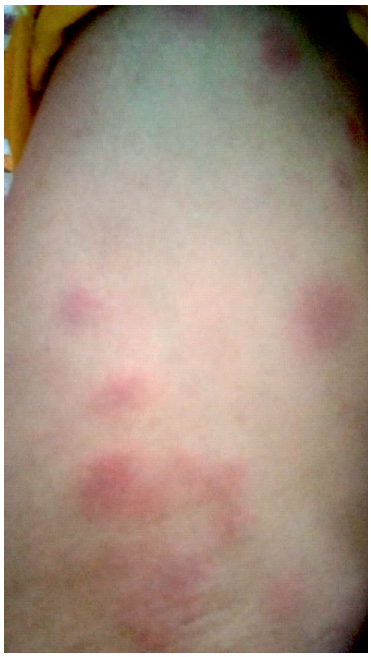

Fig. 1 : Multiple well-defined, dome shaped, dusky-to-erythematous nodules on the anterior aspect of the thigh.

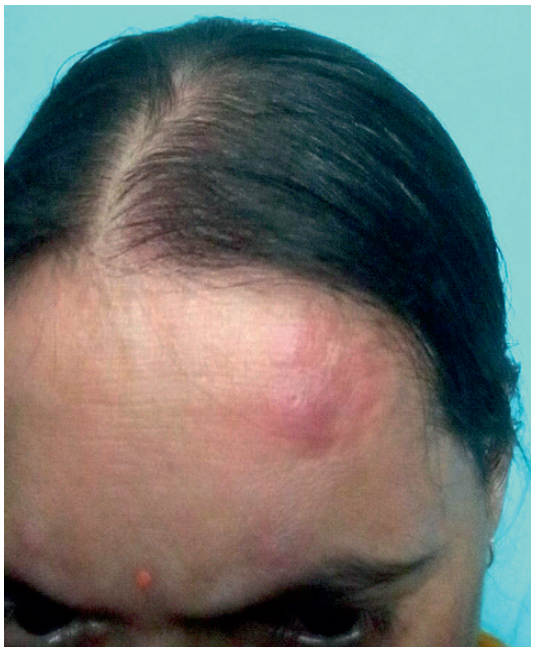

Fig. 2 : Single erythematous dome shaped nodule of size 2x3 cm over the left forehead.

of diagnosis and she was started on WHO multidrug therapy-multibacillary regimen (MDT-MBR). She took this regimen for 4 months, but due to bothersome pigmentation caused by clofazimine she was shifted to dapsone, rifampicin, and moxifloxacin. She completed 12 months of therapy with a BI of 2+ and MI of 0.

Approximately 6 months after completion of MDT, she developed ENL (no triggers could be identified) with skin lesions over her face and extremities along with joint pains and fever, and was started on oral prednisolone. She initially responded well to the treatment, but developed diabetes in January 2021. On tapering prednisolone to 20 mg she experienced a recurrence of ENL along with increasing sensory and motor impairment. She was then administered 30 mg apremilast twice a day along with 40 mg oral prednisolone in a tapering dose. Over the next 4 months, her lesions resolved and her nerve function improved.

She took the first dose of the Covishield vaccine on 30th May 2021; one week later she experienced a recurrence of ENL while on 20 mg prednisolone and oral apremilast 30 mg twice a day. There were no other identifiable triggering factors for ENL. She was prescribed Tab paracetamol 650 mg twice a day and prednisolone was increased to 30 mg following which there was resolution of symptoms over the next 2 weeks.

Discussion

Type 2 lepra reactions are often triggered by initiation of MDT, Mantoux testing, infections, vaccines, physical and mental stress, and physiological states like pregnancy which

stimulates the immune response (Cuevas et al 2007, Manandhar et al 1999). In 1973, a case series of 73 leprosy patients who were vaccinated for small pox demonstrated adverse reactions of which 7% developed new onset ENL and 4% had worsening of preexisting ENL (Saha et al 1973). After successful leprosy therapy new onset ENL, likely to be triggered by a combination of influenza vaccine and upper respiratory tract infection, has been reported (Sandre et al 2019). Similarly, our patient presented with recurrence of ENL which was adequately controlled prior to the vaccination. A delayed inflammatory cutaneous reaction of localized scleroderma was reported in a 68-year-old-woman who presented with pruritic erythematous papular eruptions in her morphea lesions three days after her first dose of ChAdOx1 nCoV-19 vaccine (Bogdanov et al 2021). Recently, Panda et al (2022) reported a case of type 2 reaction causing foot drop following Covishield™ vaccine in a patient who had developed ENL post multidrug therapy and was well controlled on thalidomide. Robello & Pennini (2021) also reported type 2 reaction in the form of ENL in two male patients post first dose of Astra Zeneca-Oxford vaccine which were successfully treated with thalidomide per their guidelines.

ENL and COVID-19 infections have a lot in common as far as neutrophil biology is concerned as supported by transcriptomic analysis revealing neutrophilic-response signature genes and relevant inflammatory networks. Both these infections show neutrophilia, increased absolute neutrophil count, altered neutrophil-to-lymphocyte ratio and high serum levels of neutrophil extracellular traps (NETs) associated markers including free DNA, myeloperoxidase-DNA complexes, and citrunillated histone H3 (Schmitz & Santos JB dos 2021, Sahu et al 2021). All these observations might indicate involvement of a common, precisely orchestrated axis of inflammatory networks regulating the recruitment, activation, or degranulation of neutrophils and relevant cytokine-chemokine production.

In future studies, it will be quite intriguing to investigate if the development of ENL following COVID-19 infection or its vaccination is just coincidental or the infection triggers ENL recurrence, affecting its incidence and severity.

Although a causal relationship between development/recurrence of ENL and COVID-19 vaccination is possible, it should not be a reason to defer the vaccine as ENL can be controlled easily with therapy and physicians in leprosy care should be aware of this possibility so that the patients can be diagnosed, managed, and educated properly, and this does not dissuade them from getting themselves and others vaccinated.

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