Haemorrhagic erythema nodosum leprosum precipitated by Measles–Rubella vaccination

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Introduction

Type 2 lepra reactions are not uncommon in patients being treated with anti leprosy treatment. There are various precipitating factors. We report a girl who was on treatment for multibacillary leprosy and prednisolone for type 2 lepra reaction who developed a severe exacerbation of Haemorrhagic erythema nodosum leprosum following Measles-Rubella vaccination.

Case report

A 18-year old girl, a diagnosed patient with lepromatous leprosy who had completed a one year's course of multibacillary treatment without any sequelae and declared 'cured' three years back, presented again seven months ago with a relapse of leprosy and MB treatment was restarted and she was tolerating the drugs well. The skin lesions had faded away after three months of treatment. After about a month she developed erythema nodosum leprosum and was started on prednisolone, after which the reaction improved but she was continuing with low dose preadnisolone and MB treatment. Her ENL was stable on 10 mg/day prednisolone. Then, on her own, she had stopped prednisolone, but the ENL condition had not flared up. Later she had had vaccination under the Measles-Rubella Catch-up Immunization programme without disclosing her situation, to the medical authorities.

One day after she received the vaccination she developed acute onset painful skin lesions, fever and arthalgia and facial swelling. On examination she had multiple polymorphic erythematous macules, which were tender on her face, and both upper and lower limbs sparing the trunk and mucosal surfaces. There was central blistering and some were like typical target lesions. Subsequently these lesions underwent central necrosis with eryhtema. She was feeling ill and had high grade fever, facial oedema and asymmetrical arthritis involving both ankles, left knee and right elbow joints. She was not pale or icteric and there were no abnormal examination findings related to abdomen, cardio-vascular, respiratory, or genito-urinary systems.

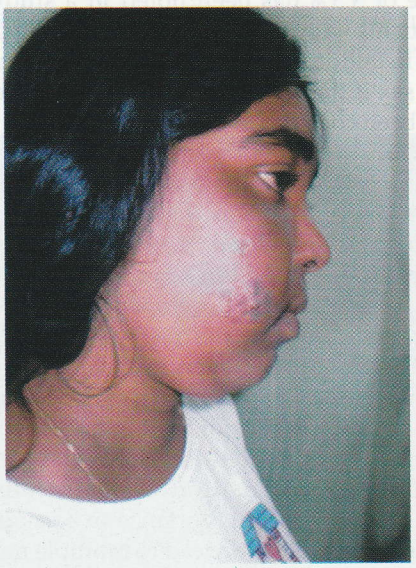

Figure 1. *Necrotic eryhtema nodosum leprosum lesions on the face.*

On admission her white blood cell count was 42000 per mm^3 with 89% neutrophils and her Hb was 8.3% with MCV of 83 fl and a retic count of 4%. ESR was 35 mm in the first hour and her urine microscopy and liver function tests were normal.

Our differential diagnoses were erythema multiforme, severe ENL reaction triggered by vaccination and Lucio phenomenon. Skin biopsy showed a flattened epidermis, papillary dermis showed oedema and a mixed dermal infiltrate of neutrophils with lymphocytes superimposed on a collection of macrophages and features of small vessel vasculitis. Some areas of dermis showed granulomas suggestive of leprosy. Sub cutaneous fat showed septal panniculitis with necrosis of blood vessels suggestive of erythema nodosum leprosum.

The patient was started on intravenous cefuroxime and prednisolone 20 mg twice a day while continuing on MB treatment without Dapsone since she had features of a haemolytic anaemia. While in

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the ward she developed septic arthritis of left elbow joint probably from an overlying necrotic infected skin lesion and arthrotomy was done where pus was removed and irrigation was done with normal saline. The Gram stain revealed pus cells but no organisms and pus culture was repeatedly sterile, probably due to prior antibiotic therapy. Thereafter she made a full recovery gradually over next two weeks and was discharged on MB treatment and a low dose prednisolone (15mg) with plans to tail off very slowly.

Discussion

Lepra reactions are immunological phenomena which occur usually when the patient is started on treatment, but they can occur even before starting treatment at the first presentation or several months after stopping the treatment[1]. There are two types of lepra reactions. Type 1 reaction is due to rapid change in cell mediated immunity, either for better or for worse. It is a type IV hypersensitivity which typically occurs in borderline tuberculoid and mid borderline areas of the disease spectrum. About 35% of borderline patients will experience Type 1 reactions[2]. The existing skin lesions rapidly swell and redden and may ulcerate. Nerve swelling, and pain are invariable and constitutional symptoms are unusual. Intraneural oedema and cellular infiltrates may cause serious nerve dysfunction such as facial palsy or foot drop. There may be oedema of face, hands and feet. Reactions often occur within the first six months of treatment, and in the puparium, due to rapid regaining of cell mediate immunity following its depression during pregnancy[2,3]. It causes a rapid destruction of bacilli.

The type 2 lepra reaction or erythema nodosum leprosum (ENL), the more severe one of the two, is a type 2 hypersensitivity reaction, an immune complex syndrome in which antigens, provided by dead bacilli and their products, react with antibodies in the tissues or in the circulation occurring in the lepromatous end of the spectrum. It has been reported that over 50% of patients with lepromatous leprosy and 25% of patients with borderline leprosy develops ENL but it has reduced to 15% after multi drug therapy with clofazamine is started[1,3]. This type of reaction most commonly occurs when majority of leprosy bacilli are fragmented or granular, and therefore in the early stages of treatment. Usually 15-20% of lepromatous leprosy patients develop ENL within the first year of therapy but it can occur even later in the course of the illness. Classically ENL is a systemic disorder, presents as a few, to hundreds of crops of tender, warm, erythematous papules, plaques or nodules from few millimeters to 4 or 5 cm, lasting few weeks or recurrences over several months or years. In contrast to type 1 reaction the actual leprosy lesions appear unchanged clinically. There is intermittent fever, nerve swelling and pain which is worse at night; Oedema of the face, hands and feet is common. Bone pain due to periosteitis, swollen joints, myelgia are often there as in our patient. Less commonly erythema multiforme like lesions, hemorrhagic, vesicular, bullous and ulcerated lesions may occur[2,4] as in our case. The skin lesions usually involve face, trunk and extremities. Extra cutaneous manifestations are common including constitutional symptoms, mental depression, iridocyclitis, rhinitis, epistaxis, stridor due to glottic oedema, painful dactilitis, tender lymphadenitis and glomerulonephritis and proteinuria and hypoalbuminemia. However these complications were not there in our patient. In addition epididimo-orchitis, and rarely, and amyloidosis may occur[2,4]. Blood count in Type 2 reaction is characteristic: a polymorphonuclear leucocytosis and a raised sedimentation rate, as in our case[1]. The usual histologic features are formy granulomas in the dermis and sub cutanious tissue with increased number of lymphocytes and a variable number of neutrophils from none to many. The infiltrate preferentially involves the deeper dermis and subcutis (as a lobar panniculitis) with relative sparing of the upper dermis with or without vasculitis or fibrosis. Acid fast bacilli are usually found[1,5].

ENL can be precipitated by several triggers. Effective treatment, trauma, surgical operations, intercurrent illness, for example, sepsis, typhoid, malaria, dysentery[6], tuberculine skin testing[7], pregnancy, parturition, lactation, menstruation, physical and mental stress, some drugs such as iodides and bromides, highly bactericidal drugs such as Ofloxacin[4] are some known causes. As in our case protective immunization is also a recognized precipitating factor, though rare. ENL has been reported following vaccination against smallpox[6]. ENL in a setting of one day after Measles-rubella vaccination, as in our case has not been reported.

ENL is treated with steroids, clofazamine, specially important in chronic cases as steroid sparing agent[7], asprin and in resistant cases with thalidomide. Use of Pentoxifylline[8] and ciclosporin[9] has also been described. Our patient made a rapid recovery with prednisolone.

Lucio's phenomenon is one of our differential diagnoses. It is very rare in Asia. It may occur in patients with diffuse lepromatous leprosy[1]. The lesions are shallow, often large polygonal, triangular or irregular macules occurring on the skin in crops, which are tender, often on the legs. They rarely affect the face, a region commonly involved by ENL and ocular sparing is the rule[1]. Later sloughing ulcers occur and they heal poorely. Then a scab forms and falls

leaving a hypo pigmented scar. They are frequently recurrent and may be generalized. When generalized it is frequently fatal due to bacterial infection and septicemia. Histologically these lesions appear to be a variant of ENL or a result of arteriolar infraction. Nither thalidomide nor corticosteroids has proved effective. In severe cases exchange transfusion may be effective. Good wound care and appropriate antibiotics are also recommended. The clinical course of our patient's condition, histopathological findings as well as it's rarity in the Asian region made Lucio phenominan unlikely in our case.

Our case highlights several important factors. Firstly patients can develop severe ENL following vaccinations. Secondly as she was on prednisolone she should not have taken live attenuated Measles-Rubella vaccination. Fortunately she did not develop Measles or Rubella, otherwise it would have further complicated the management. This case also highlights a common problem associated with long term medications, the non compliance or discontinuation of drugs without medical advice, which may lead to severe consequences, and hence the importance of futher stressing on the compliance specially when taking the drugs like steroids.

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