

## Drug Induced Linear IgA Disease with Unusual Features: Koebner Phenomenon, Local Insulin Sensitivity and Annular Blister of the Nipples

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**SUMMARY** Linear IgA disease is an autoimmune subepidermal bullous disease in which linear IgA deposits are found at the basement membrane zone. It is classically idiopathic but may be drug induced. We report on a patient with drug induced linear IgA disease who exhibited certain unusual and interesting clinical features including isomorphic Koebner response, annular blister of the nipples and local insulin sensitivity. To the best of our knowledge, these clinical features have not yet been reported in linear IgA disease.

**KEY WORDS:** linear IgA disease, drug induced linear IgA disease, Koebner phenomenon, local insulin sensitivity, annular blister

### INTRODUCTION

Linear IgA disease is a rare autoimmune vesico-bullous disorder characterized by linear IgA deposits at the basement membrane zone (BMZ) on immunofluorescence. Although idiopathic variant of the disease is common, the occurrence of drug induced linear IgA disease has also been quite frequently reported (1). Clinical presentation of linear IgA disease may be variable and sometimes there is overlap with other bullous dermatoses (2). We report on a case of linear IgA disease induced either by metronidazole or hyoscine-N-butylbromide (Buscopan, Boehringer Ingelheim/Merck Marker) displaying certain unusual and interesting features including isomorphic response of Koebner, blisters at the site of insulin injections and annular blister of the nipples. To the best of our knowledge, these clinical features have not yet been reported in linear IgA disease.

We report this interesting case to highlight that recognizing unusual features of an established disease is important as it may enhance the understanding and management of the disease.

### CASE REPORT

A 30-year-old male presented with a rash on his body which started 12 hours after taking metronidazole and hyoscine-N-butylbromide together, for stomach ailment. The patient could not recall metronidazole and hyoscine-N-butylbromide intake in the past. The rash consisted of erythematous papules scattered over face and trunk, at sites forming targetoid configuration. The rash later spread to the limbs and genitalia with the formation of hemorrhagic and non-hemorrhagic blisters and erosions. The blisters were tense and appeared both



**Figure 1.** Koebner phenomenon in linear IgA disease in scratch marks and along waist line.

on normal and erythematous background. Some of the lesions on the trunk were disposed in linear fashion at the sites of scratch marks and along waist line exhibiting Koebner phenomenon (Fig. 1). Annular blister along the entire circumference of the nipple on both sides was also seen (Fig. 2). Oral mucosa was involved and there was congestion of the conjunctivae. Skin biopsy revealed a subepidermal blister with an intact undamaged epidermis. There was an intense infiltrate of neutrophils and few eosinophils in the subepidermal zone. Immunofluorescence of perilesional skin revealed linear deposits of IgA (+++), IgG (+) and C3 (+) at dermoepidermal junction. On the basis of these findings, he was diagnosed as a case of drug induced linear IgA disease. Metronidazole



**Figure 2.** Single annular blister along the entire circumference of the nipple in linear IgA disease.

and hyoscine-N-butylbromide were stopped forthwith and as he was glucose-6-phosphate dehydrogenase deficient, he was given oral prednisolone at a dose of 60 mg daily for two weeks and then gradually tapered off. During steroid therapy he developed glucose intolerance for which insulin was introduced, but, it had to be stopped because he developed fresh large blisters at the site of insulin injection (Fig. 3). However, such a phenomenon was not observed at the sites of other needle pricks for taking blood samples. The patient was again given subcutaneous insulin injection at a different site but blister appeared at that site too. Then he was administered oral hypoglycemics to control hyperglycemia. While his steroids were being tapered off, scrubbing of his healed skin for cleaning led to the formation of blisters on the scrubbed area. The dose of steroids had to be increased temporarily to control this fresh eruption. Prednisolone was tapered off over the next 6 weeks. Fresh lesions have now ceased to appear and previous lesions have healed with mild scarring.

## DISCUSSION

Many drugs have been implicated (3-5), but it is not easy to differentiate idiopathic linear IgA disease from drug induced variant. Although drug induced autoimmune subepidermal bullous diseases including linear IgA disease usually develop a few weeks after the introduction of the offending drug, there also are cases previously reported in the literature where the onset of linear IgA disease was within 1-2 days of the drug administration (6,7).



**Figure 3.** Localized blistering at the site of insulin injection in linear IgA disease.

Our patient exhibited certain unusual and interesting features. Firstly, koebnerization was observed as ascertained by the disposition of lesions in a linear fashion at the site of scratching on the trunk and along waist line, and by the appearance of lesions on healed skin by scrubbing. Koebnerization has been described previously in autoimmune blistering disorders (8-10), but we were unable to find any literature data on the association of koebnerization with linear IgA disease. It is likely that trauma and friction caused local increase in blood flow, bringing more autoantibodies to the site. The significance of this finding implies that avoidance of trauma and gentle handling of such patients can lead to early recovery from a self-limiting disease. This patient also developed blisters at the site of subcutaneous insulin injection, but this could not be attributed to koebnerization because blisters did not develop at the sites of other needle pricks. This effect may have been due to local sensitivity to insulin in the patient during active phase of the disease. Now that his disease is under control, he is still being treated for glucose intolerance with insulin without developing lesions at insulin injection sites any more. Skin-prick test performed to confirm local allergic reaction to insulin was negative.

Polycyclic erythematous lesions with blisters at the edges of pre-existing lesions are common in childhood variant of the disease. In our patient, there was formation of regular annular blister on each nipple. A likely explanation for this unique and interesting finding could be that the hair follicles containing erector pili muscles are arranged all around periphery of the nipple causing the line of skin tension on the nipple to be circular. The lesions here might have followed these circular lines of tension hence becoming annular.

This interesting case is reported with the purpose to highlight the fact that recognizing unusual features of an established disease is important as it may enhance understanding of the disease and help in its management.

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