Blistering diseases in Sri Lankan patients

P Angunawela[1], A de Tissera[2], S Rathnayake[3], C Gunasekera[4], D N Athukorala[5] and K Weerasekera[5]

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Summary

Patients with bullous diseases are commonly encountered in primary care practice in young, middle-aged and old patients. The diagnosis of blistering diseases of the skin has been done in the past only by histological methods. However accurate diagnosis cannot be arrived at in most instances by histology alone. This is the first report of the use of immunofluorescence in the diagnosis of immunological blistering diseases in Sri Lanka. Out of 23 cases studied 7 had pemphigus, 3 had dermatitis herpitiformis, 3 had linear IgA disease, another 3 had bullous pemphigoid and one patient had pemphigus gestationis. In 6 patients the diagnosis was not conclusive.

Introduction

The immunologists in particular have contributed a lot to understanding of autoimmune bullous diseases. The differential diagnosis includes nonimmune cases such as contact dermatits, infections and bullous reactions to drugs and insect bites. An autoimmune blistering disease may be distinguished clinically by the age of the patient when the disease first appears, the morphology and the distribution of the lesions and the presence or absence of mucosal lesions and scarring. Because the clinical presentations of blistering disorders are often similar special immunofluorescence tests are used to confirm the specific diagnosis. The presence or absence of circulating antibodies and the level of the antibody titres are helpful not only in the diagnosis, but also in the management and prognosis of patients with autoimmune bullous diseases.

Patients, materials and methods

Immunological studies were done on 23 patients with autoimmune blistering disease who were admitted to the Dermatology ward of the National Hospital of Sri Lanka between May 1994 to November 1994. Skin biopsies were performed under local anaesthesia. The biosies were immediately adhered on a piece of cork with an adhesive, tissue TEK. Then it was frozen in liquid nitrogen at a temperature of -170 degrees. The frozen samples were transported to the Medical Research Institute in a flask containing liquid nitrogen. A sample of blood was also taken from 4 patients for serology. One micron thick sections were cut in the croyostat and one section from every patient was stained with haematoxylin and eosin. Other sections were stained with fluorescein labelled IgA, IgG, IgM, IgE, and C3.

Indirect immunofluorescence of 4 samples of serum was done using IgA, IgG, IgM, IgE, and C3.

Results

7 patients had intraepidermal bullae and showed intercellular IgG. 3 had subepidermal bullae and granular deposition of IgA and C3 at the dermo-epidermal junction (Figure 1). 3 had subepidermal bullae and showed linear deposition of IgA at the dermoepidermal junction (Figure 2.) 3 patients with subepidermal bullae had linear deposition of IgG and C3 at the dermoepidermal junction. One female patient with a subepidermal bullae had only C3 at the dermoepidermal junction. In 6 patients the diagnosis was inconclusive.

[1] *Associate Professor of Pathology, Faculty of Medicine, Colombo.*
[2] *Consultant Pathologist, Medical Research Institute.*
[3] *Medical Officer, Medical Research Institute.*
[4] *Senior Registrar,*
[5] *Consultant Dermatologists, The National Hospital of Sri Lanka, Colombo.*

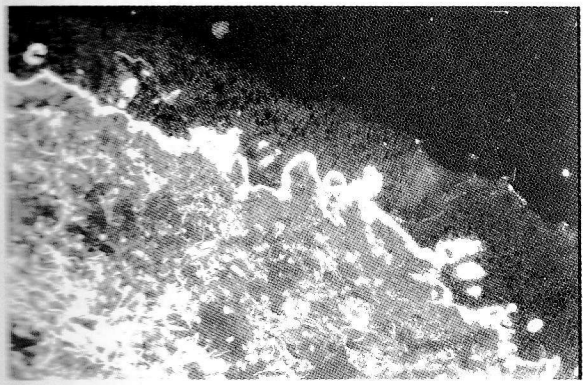

Figure 1. Immunofluorescence staining with IgA shows granular deposition at the dermoepidermal junction in Dermatitis Herpetiformis x200.

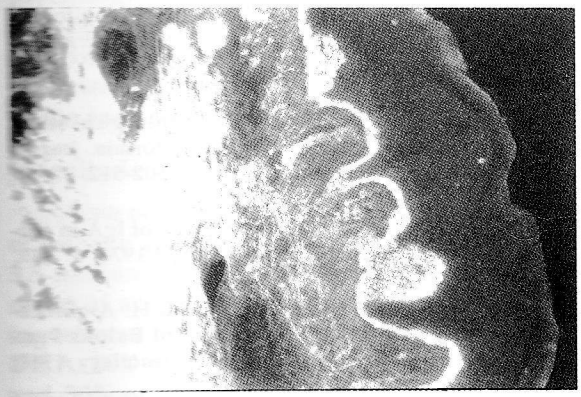

Figure 2. Immunofluorescence staining with IgA shows linear deposition at the dermoepidermal junction in Linear IgA disease x200.

Discussion

7 out of 23 of our patients had intraepidermal bullae with intercellular IgG pattern with immunofluorescence staining and they were diagnosed as Pemphigus group of bullous diseases. These patients have intraepidermal blisters histologically. Immunoglobulins and complement are found bound to the intercellular substance in the perilesional epidermis. Two major variants can be defined by the level of cleavage within the epidermis. Suprababasal clefting is seen in pemphigus vulgaris and its rare vegetating from pemphigus vegetans. More superficial intraepidermal bullae are found in pemphigus folliaceus and its variant pemphigus erythematosus.

Out of our 7 patients except one, all were suprabasilar cleavages and they were diagnosed as pemphigus vulgaris. One patient had very superficial cleavage and the lesion was diagnosed as pemphigus folliaceus. Pemphigus vulgaris has a world-wide distribution and affects both sexes almost equally, although under the age of 20 there is predilection for women[1]. Out of 7 patients 4 were males and the 3 were females, and ages ranged from 32 to 78 years. We did not have any patients below the age of 20 years. The sample size is too small for us to comment on the predilection for any sex group for Sri Lankan patients. Autoantiobodies were first described in patients with pemphigus in 1964 and subsequent research has raised the possibility that there is a correlation between the disease activity and the titre of antibody. We were able to do antibody titres of 2 patients with pemphigus vulgaris and both showed high titres.

3 of our patients who had subepidermal bullae showed granular deposition of IgA and C3 at the dermoepidermal junction and they were diagnosed as dermatitis herpitiformis (DH). This is a rare, intesely pruritic, chronic, recurrent papulo-vesicular disease. HLA studies have shown that 85-90% are HLA B-8 positive and that there is an even stronger association with HLA DW3 and DRW3[2]. In addition the majority of patients often have asymtomatic gluten sensitive enterpathy[2,5]. 2 of our patients were males and one was a female, and none of them had any symptomatic gastrointestinal disease.

Granular deposition of IgA are detected in the dermal papillary tips of lesional and perilesional skin in patients with DH[4].

Ultrastructurally these deposites of IgA appear to be closely associated with the dermal microfibrillar bundles. It has been suggested that IgA binds to part of an abnormal microfibrillar bundle which may be unique to DH.

Whilst most patients with DH have a granular pattern of IgA, a group exists with linear deposition of IgA and we had 3 of such patients who were diagnosed as linear IgA disease. Ultrastructural studies have shown that the immune deposits are either within the lamina lucida or in the subbasal laminar area[5].

Bullous pemphigoid is a blistering disease of the elderly which often starts with urticaria like and pruritic erythematous lesions and later develops large tense blisters. There were 3 males in our study who were diagnosed as bullous pemphigoid. They had IgG and C3 at the dermoepidermal junction in the perilesional skin. All 3 patients were above 60 years of age. In one patient the serum showed a high titre of autoantibodies. About three-quarters of these patients have a circulating antibody to the basement membrane zone. Recent studies have shown that the correlation between the level of antibodies and the disease activity is poor in bullous pemphigoid[6].

One pregnant female with a subepidermal bulla had only C3 at the dermoepidermal junction and it was diagnosed as herpes gestationis. This is an exceedingly uncommon, intensely pruritic bullous eruption that may develop in association with either pregnancy or the trophoblastic tumours such as hydatidiform mole and choriocarcinomas. The most significant HLA association with herpes gestationis is the possession of DR3 and DR4[7]. The histopathology of early lesions of herpes gestationis show epidermal and papillary dermal oedema with occasional foci of epsinophilic spongiosis. The bullous lesions are subepidermal and contain numerous eosinophils. Ultrastructurally, the level of splitting occurs within the lamina lucida. Direct immunofluorescence studies show that in all active cases of herpes gestationis there is C3 deposition at the basement membrane zone. Furthermore, usually a C3 binding serum factor can also be demonstrated.

In 6 patients a definitive diagnosis could not be arrived at with immunofluorescence.

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