Intraepidermal neutrophilic dermatosis type of IgA pemphigus with circulating linear IgA disease antibodies associated with ulcerative colitis

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Editor
A 42-year-old woman with ulcerative colitis previously well controlled on mesalazine presented with blistering, crusts and severe itching on her upper body and legs together with painful erosions on her conjunctivae and oral mucous membranes in addition to active bowel symptoms for 2 weeks. Clinical examination revealed multiple lesions consisting of vesiculopustules with circinate distribution and central crusts in sunflower-like configuration on her flanks and legs, a typical characteristic of intraepidermal neutrophilic dermatosis (IEN)-type of IgA pemphigus (Fig. 1a and c).\(^1\) Lips, nasolabial folds and eyelids were affected by yellow crusts and erosions on erythematous base (Fig. 1b).

Lesional histopathology showed a mid-intraepidermal blistering with a predominantly eosinophil and neutrophil infiltrate. Direct immunofluorescence microscopy of perilesional skin revealed discrete IgA depositions along the epithelial cell surface (ECS) in the basal cell layer diminishing towards the mid-sponges layer of the epidermis (Fig. 2). There were no IgG, IgM, C3 or fibrinogen deposits. These laboratory findings fit IgA pemphigus. The serum did not contain detectable circulating IgG or IgA autoantibodies against desmoglein 1 and 3, desmocollins 1, 2, and 3, BP230, or type VII collagen by enzyme-linked immunoassay (ELISA) or by immunoblot with recombinant antigens or keratinocyte extracts, which is common in IEN-type of IgA pemphigus. IgA antibodies against the 120 kDa ectodomain of BP180 could be detected by immunoblot using keratinocyte medium, which is commonly detected in a linear IgA disease (LAD).

A diagnosis of IEN-type IgA pemphigus was made. The patient had been given 20 mg prednisone in addition to mesalazine prior to consultation due to her ulcerative colitis. We changed the systemic glucocorticoid medication to oral methylprednisolone 40 mg per day, and started dapsone 100 mg per day combined with an intensive antiseptic local treatment. The dosage of mesalazine was increased to 1000 mg\(^3\) daily. Within a week, a resolution of blistering and crusts was achieved allowing tapering of oral steroids. Due to the severe and painful involvement of the oral mucosa we supported the therapy with liquid diet and application of topical anesthetic mouthwash products. Furthermore, the patient was given adequate pain reducing therapy. Bowel symptoms improved within two weeks with no recurrence on tapering methylprednisolone.

Here, we present a very rare entity of IEN-type IgA pemphigus with in addition circulating LAD antibodies concomitant with an exacerbation of ulcerative colitis. The coexistence of autoimmune bullous disorders and ulcerative colitis has been previously reported,\(^2\) including epidermolysis bullosa acquisita,\(^3\) linear IgA disease \(^4\) and rarely IgA pemphigus.\(^5\) There is only one case of IEN-type IgA pemphigus with additional circulating

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**Figure 1** (a and c): Multiple lesions consisting of vesiculopustules forming annular lesions with central crusts, appearing as ‘sunflower-like’ lesions on the whole body predominantly on flanks and legs of the patient. (b) Conjunctiva, nasolabial areas and lips with erythema and painful erosions covered with yellow crusts.

**Figure 2** Direct immunofluorescence of perilesional skin shows a discrete intercellular IgA fluorescence in the basal epidermis which is typical for an IgA pemphigus.
LAD IgA antibodies in a patient with ulcerative colitis in the literature similar to our case. Interestingly our patient exhibited the clinical manifestation only of IEN-type IgA pemphigus but in a severe form with an extreme mucosal involvement which is rather rare. Neutrophil infiltration in the histology and IgA ECS depositions by the direct immunofluorescence were compatible with IgA pemphigus. We speculate that the additional IgA antibodies against the 120 kDa ectodomain of BP180 (LAD antigen) may have evoked the mucous membrane involvement.

It is known that patients with autoimmune bullous disorders and inflammatory bowel disease often show autoantibodies to several autoantigens, suggesting that epitope-spreading phenomena might play a role in the pathogenesis. Also, the rare coexistence of IgA pemphigus with LAD antibodies in the same patient as in our case supports this hypothesis. It is supposed that a primary immune response is initiated in inflamed colonic tissue resulting in cross-reactivity with cell surface antigens of the epidermis and its basement membrane zone.

Patients with IgA-mediated autoimmune bullous disease exhibit predominant neutrophilic infiltrates and therefore usually benefit from treatment with dapsone as in our case. Remission of skin disease requires adequate treatment of ulcerative colitis, as we assume that the inflammatory bowel disease elicits and maintains the autoimmune bullous disease.

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