# Linear IgA bullous dermatosis preceding a diagnosis of Crohn's disease

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***Key words:*** blistering disease; Crohn's disease; inflammatory bowel disease; Linear IgA bullous dermatosis; Linear IgA disease.

## INTRODUCTION

Linear IgA bullous dermatosis (LABD) is a rare, autoimmune blistering skin disorder that involves the deposition of IgA at the dermoepidermal junction. This disease presents with widespread tense vesicles and bullae, clustered into rosettes. LABD can occur spontaneously or following drug exposure, and it can be seen in patients with underlying inflammatory bowel disease (IBD), most commonly ulcerative colitis. We report an interesting case of extensive LABD in a healthy patient who subsequently developed Crohn's disease (CD), and whose skin disease cleared on prednisone and azathioprine.

*Abbreviations used:*

| | |
|---|---|
| ALT: | alanine aminotransferase |
| ANA: | antinuclear antibody |
| CD: | Crohn's disease |
| CMV: | cytomegalovirus |
| ENA: | extractable nuclear antigen |
| LABD: | Linear IgA bullous dermatosis |

## CASE REPORT

A previously healthy 41-year-old man presented to the Emergency Department with a 2-week history of a blistering rash. The eruption began suddenly under both axillae and along the waistline and also involved blisters in the mouth. He had previously been treated by a primary care physician for presumed varicella, with a 5-day course of prednisone 10 mg and triamcinolone 0.1% cream that mostly cleared the oral lesions and improved the rash. Shortly after discontinuing prednisone, the rash spread flagrantly to the trunk, upper and lower extremities, scalp, face, acral surfaces including the palms and soles, with involvement of the oral and ocular mucosa as well. He described the rash as severely pruritic and painful when the blisters ruptured.

Examination revealed multiple stages of vesicles and bullae arranged around annular plaques with overlying scale, raising concern for LABD (Fig 1).

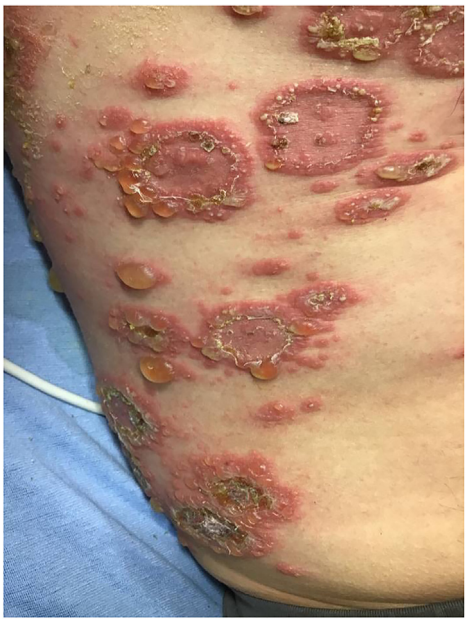

**Fig 1.** Vesicles and bullae arranged around annular scaly plaques on right flank and trunk.

Punch biopsy showed subepidermal vesicle and intraepidermal pustule formation with neutrophils and

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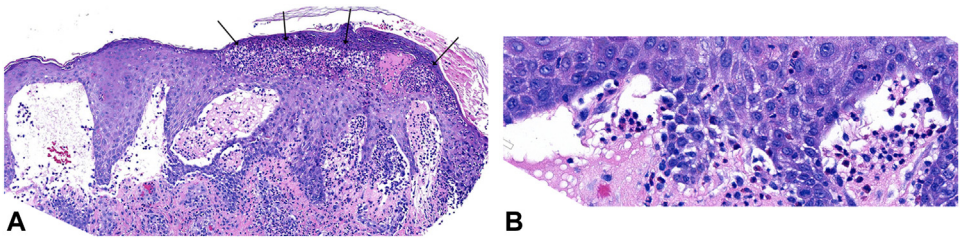


**Fig 2. A,** A biopsy of skin has subepidermal vesicle and papillary dermal neutrophils. Also present are neutrophilic spongiosis and subcorneal pustules (*arrows*). Neutrophils are present in the subepidermal vesicle and along the dermal epidermal junction. (**A** and **B,** Hematoxylin and eosin stain; orginal magnification:**A**, 12×; **B**, 40×).

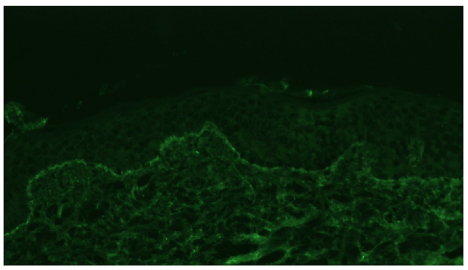

**Fig 3.** Linear 4+ deposition of IgA at the epidermal and follicular basement membrane (direct immunofluorescence, right upper arm).

eosinophils along with neutrophilic spongiosis (Fig 2). Direct immunofluorescence assay resulted with 4+ linear IgA at the epidermal and follicular basement membranes, confirming the diagnosis (Fig 3). Indirect immunofluorescence performed at a later date showed IgA autoantibodies against the epidermal side of salt split skin at a titer of 1:20. Laboratory tests revealed ALT (Alanine aminotransferase) elevation, leukocytosis, thrombocytosis, and negative ANA (antinuclear antibody) and ENA (extractable nuclear antigen) screen. The patient was initiated on prednisone 80 mg, with a planned taper over 8 weeks. He was also started on dapsone 25 mg daily, which was slowly titrated to a maximum dose of 250 mg daily, triamcinolone 0.1% ointment, and hydrocortisone 2.5% ointment.

Four months after the LABD diagnosis, the patient presented to the emergency department for persistent severe abdominal pain and intractable diarrhea and emesis. He had been previously treated for viral gastroenteritis but was ultimately diagnosed with CMV (cytomegalovirus) ileitis and CD following colonoscopy and biopsies. Prednisone was briefly interrupted in the setting of active CMV ileitis but was reinstated following resolution. He began cyclosporine and infliximab, and dapsone and prednisone were tapered. Given his new diagnosis of CD, the patient's treatment regimen was carefully coordinated with his gastroenterologist, and several other therapies, including methotrexate and myfortic acid, were attempted before being discontinued due to the patient's inability to tolerate the side effects. The patient is now being treated with azathioprine 50 mg twice daily and vedolizumab infusions every 4 weeks with excellent control of the LABD and CD; he continues to attempt to taper prednisone from 10 mg daily.

## DISCUSSION

LABD has a known association with IBD. Most cases of LABD occurring in IBD have been described in patients with known ulcerative colitis,[1] and presently there are just 6 reported cases of LABD that developed after CD (Fig 1). Here we describe the case of a healthy patient whose severe presentation of LABD preceded a diagnosis of CD.

The pathogenesis of LABD in association with IBDs is not well-understood, and it is unclear whether LABD occurs in CD by the same mechanisms as in ulcerative colitis. Some reports have hypothesized about the role of immune dysregulation, including the cross-reactivity of intestinal antigens to cutaneous antigens that then stimulate an autoimmune response against cutaneous basement membrane zones.[2] Another hypothesis on epitope spreading posits is that inflammation in IBD releases intestinal epithelial basement membrane zone antigens that then trigger an autoimmune response against LABD antigens.[3] Some have postulated that the course of IBD may trigger the onset of LABD.[4] Indeed, we found that the diagnosis of CD preceded the development of LABD in all reported cases of patients with both LABD and CD (Table I). However, as seen in our patient whose first flare of LABD preceded the symptoms, and diagnosis, of CD, much remains to be known about the temporal association of LABD and CD, and their pathophysiology.

Moreover, LABD typically presents with subepidermal blistering with papillary dermal neutrophilic infiltrate on histopathologic examination. In this patient, microscopic exam revealed typical change of LABD with the additional finding of subcorneal pustules that are not expected in LABD. Subcorneal

**Table I.** Summary of cases of linear IgA bullous dermatosis associated with Crohn's disease

| Case | Age | Sex | From Crohn's to LABD | Treatment for LABD | Progress of LABD | Treatment for Crohn's |
|---|---|---|---|---|---|---|
| Torres et al[3] | 33 | M | 3 y | Prednisolone, dapsone | Remission by dapsone | Prednisolone |
| Ibrahim et al[5] | 40 | M | ~1-2 y | Azathioprine, doxycycline | Spontaneous improvement of LABD free of treatment | Adalimumab, prednisone, Infliximab, and Ustekinumab |
| Nanda et al[6] | 13 | F | 1.5 y | Dapsone | Remission by dapsone | Not specified |
| Williams et al[7] | 36 | M | 6 y* | Dapsone | Remission by dapsone | Infliximab |
| Birnie and Perkins[8] | 55 | F | 5 wk | Prednisolone, dapsone | Remission by dapsone | Prednisolone, mesalazine |

*LABD*, Linear IgA bullous dermatosis.
*Patient received prior diagnosis of ulcerative colitis 6 years prior to LABD, with diagnosis revised to Crohn's at the onset of LABD.

pustulosis has been previously described in IBD.[9] In one case, a patient with a 1-year history of CD developed a pustular eruption with consistent histologic findings.[10] While the precise mechanism of pustulosis in our patient is not well-understood, this finding, taken together with the patient's subsequent diagnosis of CD, highlights that CD-associated LABD may present with intraepidermal pustules histologically as an early microscopic marker of IBD.

Despite existing treatment algorithms, LABD remains difficult to treat and this patient's disease course presented distinct challenges of managing this disease, particularly given the association with CD. This patient's LABD was recalcitrant even after using multiple steroid-sparing agents and thus required creative approaches to treatment. Dapsone is regarded as the first line of therapy, with 82 percent of patients achieving remission on this drug,[2] and it typically generates favorable therapeutic responses at doses of 100 to 200 mg. All but one reported case of LABD in CD achieved remission of skin lesions with dapsone (Table I). Despite being on supramaximal doses of dapsone, our patient faced recurrent flares of LABD and was unable to tolerate a taper off prednisone.

In this patient, several medications were initiated to treat the CD and LABD in tandem. To date our patient has seen skin clearance on low dose prednisone with excellent control of his CD using azathioprine 50 mg twice daily for 8 months and vedolizumab infusions. Ultimately, the care team continues to optimize this patient's azathioprine dosing with a goal of sustaining his remission and reducing his steroid dependence.

**Conflicts of interest**

None disclosed.

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