# Linear IgA bullous disease in a patient with Crohn's disease

T. Torres, M. Sanches, and M. Selores

SUMMARY

**Linear IgA bullous disease is a rare autoimmune subepidermal blistering disease characterized by linear deposition of IgA along the basement membrane zone. We report a clinical case of a rare association of Linear IgA bullous disease and Crohn's disease. Parallel clinical improvement of both cutaneous and intestinal disease was observed with dapsone treatment.**

KEY WORDS

**linear IgA bullous disease, Crohn's disease, epitope spreading phenomenon**

## Introduction

Linear IgA bullous disease (LAD) is a rare autoimmune subepidermal blistering disease characterized by linear deposition of IgA along the basement membrane zone. LAD has been reported in association with inflammatory bowel disease, particularly ulcerative colitis (1, 2) and in only three reports associated with Crohn's disease (3–5).

## Case report

A 33-year-old man with Crohn's disease of 3 years' duration presented to our dermatology department with a history of generalized, pruritic, vesiculobullous eruption. He also reported the recent onset of non-bloody diarrhea and abdominal pain. On physical examination, there were numerous tense bullae and eroded and crusted lesions localized to his neck, trunk, and extremities (Fig. 1). There were no mucosal lesions.

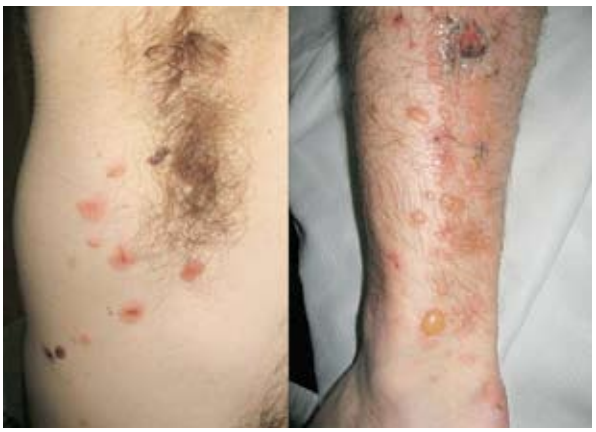

**Figure 1. Tense bullae and eroded, crusted lesions on the trunk and extremities.**

Laboratory tests showed hypochromic microcytic anemia with hemoglobin of 10.3 g/dL, reactive thrombocytosis with a total platelet count of 655 $\times 10^3/\mu L$, an increased erythrocyte sedimentation

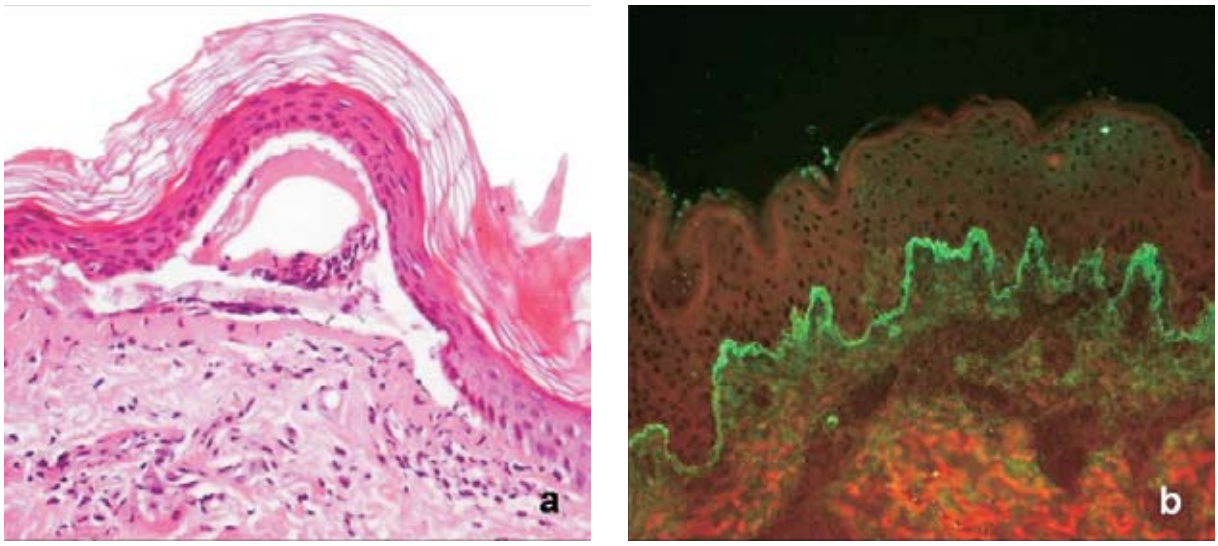


**Figure 2. (a) Subepidermal blister (H&E 20×); (b) Linear deposition of IgA at the dermoepidermal junction (direct immunofluorescence).**

rate of 58 mm/h, and increased C-reactive protein of 331 mg/L. Other routine tests were within normal limits. Histological examination showed a subepidermal blister containing eosinophils and fibrin and a dermal infiltrate comprising neutrophils and eosinophils. Direct immunofluorescence exhibited a linear deposition of IgA at the basement membrane zone, supporting a diagnosis of LAD (Fig. 2). A colonoscopy was performed and the endoscopic and histological results were consistent with active Crohn's disease. The patient was prescribed prednisolone 30 mg and dapsone 100 mg daily and, in 3 weeks, great clinical and laboratory improvement was observed of both cutaneous and intestinal disease. At this time prednisolone was stopped. Presently, at 10 months follow-up, with a maintenance dose of 100 mg dapsone daily and no oral steroids, the patient remains free of the skin lesions and free of intestinal disease symptoms.

## Discussion

LAD is a rare autoimmune subepidermal blistering disease, occurring in both adults and children, associated with linear deposition of IgA along the basement membrane zone. LAD has been reported in association with drugs, malignancy, infections, connective tissue diseases, and inflammatory bowel disease, particularly ulcerative colitis, with just 3 cases of association with Crohn's disease described. In predisposed individuals, the IgA autoantibodies are directed against various antigens at the basement membrane zone, probably as a reaction pattern to various stimuli. A study presented by Paige et al. of 70 adult patients with LAD revealed a 7.1% prevalence of ulcerative colitis in the patients affected by LAD, much higher than the 0.05% prevalence of ulcerative colitis in the general population (2). LAD did not correspond to the disease activity of the ulcerative colitis in any cases and, in some patients, persisted after total colectomy. In this particular case, like in the others reported, we describe a case of LAD associated with Crohn's disease occurring during a flare-up of the bowel disease. The way inflammatory bowel disease influences the course and pathogenesis of LAD remains unclear, and the link with Crohn's disease is probably somewhat different from that with ulcerative colitis. Various mechanisms have been proposed to explain these associations. Abnormalities in colonic mucosal B cells and mucosal IgA production have been reported in patients with ulcerative colitis (6). Moreover, Badr-el-Din et al. showed a dysfunction of transepithelial IgA secretion even in quiescent ulcerative colitis (7), which may allow development of LAD in patients with inactive ulcerative colitis. On the other hand, the phenomenon of epitope spreading has been used to propose that in Crohn's disease the intestinal inflammation could cause the release and exposure of constitutively "sequestered" intestinal epithelial basement membrane zone antigens and consecutively lead to an autoimmune response against the LAD antigens, which probably have some antigenic similarities to intestinal basement membrane zone components (8, 9). This would explain the occurrence of LAD during a Crohn's disease flare. Additionally, in this case, an improvement of the intestinal disease was noted with dapsone therapy. There are some

reports of Crohn's disease improving with dapsone, and one Cochrane review found that antituberculous therapy may be effective in maintaining remission in Crohn's patients (3, 10). On the other hand, there are no reports of dapsone improving ulcerative colitis.

This case appears to be the fourth description of an association of LAD with Crohn's disease and emphasizes that gastrointestinal tract screening should be considered in cases of LAD with no other associations or precipitating factors.

## REFERENCES


1. De Simone C, Guerriero C, Pellicano R. Linear IgA disease and ulcerative colitis. Eur J Dermatol. 1998;8:48–50.

2. Paige DG, Leonard JN, Wojnarowska F, Fry L. IgA disease and ulcerative colitis. Br J Dermatol. 1997;136:779–82.

3. Birnie AJ, Perkins W. A case of linear IgA disease occurring in a patient with colonic Crohn's disease. Br J Dermatol. 2005;153:1050–2.

4. Nanda A, Dvorak R, Al-Sabah H, Madda JP, Anim JT, Alsaleh QA. Association of linear IgA bullous disease of childhood with Crohn's disease. Int J Dermatol. 2006;45:1184–6.

5. Barberis C, Doutre MS, Bioulac-Sage P, Pompougnac E, Beylot C, Quinton A. Linear IgA bullous dermatosis associated with Crohn's disease. Gastroenterol. 1988;12:76–7.

6. MacDermott RP, Nash GS, Scott MG, Nahm MH, Bertovich MJ, Kodner IJ. Altered patterns of secretion of IgA and IgG subclasses by ulcerative colitis and Crohn's disease intestinal mononuclear cells. Adv Exp Med Biol. 1987;216:335–44.

7. Badr-el-Din S, Trejdosiewicz LK, Heatley RV, Losowsky MS. Local immunity in ulcerative colitis: evidence for defective secretory IgA production. Gut. 1988;29:1070–5.

8. Chan LS, Vanderlugt CJ, Hashimoto T, Nishikawa T, Zone JJ, Black MM, et al. Epitope spreading: lessons from autoimmune skin diseases. J Invest Dermatol. 1998;110:103–9.

9. Powell AM, Black MM. Epitope spreading: protection from pathogens, but propagation of autoimmunity? Clin Exp Dermatol. 2001;26:427–33.

10. Prantera C, Kohn A, Mangiarotti R, Andreoli A, Luzi C. Antimycobacterial therapy in Crohn's disease: results of a controlled, double-blind trial with a multiple antibiotic regimen. Am J Gastroenterol. 1994;89:513–8.


## AUTHORS' ADDRESSES


*Tiago Torres, MD, Department of Dermatology, Centro Hospitalar do Porto – Hospital de Santo António, Edifício das Consultas Externas do Hospital Geral Santo António, Ex. CICAP, Rua D. Manuel II, s/n, 4100 Porto, Portugal, E-mail: tiagotorres2002@hotmail.com*

*Madalena Sanches, MD, same address, E-mail: madalenavsanches@gmail.com*

*Manuela Selores, MD, same address, E-mail: dermat@sapo.pt*