Erythema gyratumrepens-like eruption in a patient with epidermolysisbullosaacquisita associated with ulcerative colitis

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SIR, Epidermolysisbullosaacquisita (EBA) is an acquired auto-immune bullous disease of the skin and mucous membranes characterized by IgG autoantibodies to type VII collagen, the main constituent of the anchoring fibrils of the dermal– epidermal juction.[1,2] Inflammatory bowel diseases (IBD) may be associated with autoimmunity to type VII collagen.[3,4] Erythema gyratumrepens (EGR), an obligate paraneoplastic syndrome, may occur in patients with pemphigoid diseases.[5–9] To the best of our knowledge, EGR has not been previously described in EBA. We report a most unusual clinical manifestation of EGR-like lesions in a patient with EBA and ulcerative colitis (UC).

A 35-year-old woman presented with 2-year history of bullous skin lesions on the trunk and extremities and erosions on the oral mucosa. In addition, 6 months before her first visit to our department, she developed progressive diarrhoea and asthenia. Following further investigation by endoscopy with biopsy of colonic mucosa a diagnosis of UC was made. A computed tomographic scan ruled out the presence of a neoplastic process. Physical examination revealed widespread blistering, erosions, scarring and milia

formation on her hands (Fig. 1a), feet (Fig. 1b), legs and arms. In addition, erythematous lesions with a wood-grained appearance were observed on the thighs and trunk (Fig. 1c). Bullous lesions were associated with figurate erythematous lesions on the knees and legs (Fig. 1d). Examination of the oral cavity revealed erosions and scarring of jugal and lingual mucosa. Histopathological examination of a blister showed a subepidermal split and a massive infiltrate mainly consisting of neutrophils in the upper dermis (Fig. 2a). Direct immunofluorescence (IF) of the perilesional skin demonstrated linear deposits of IgG and C3 at the basement membrane zone. Indirect IF on NaCl-split skin revealed circulating IgG autoantibodies binding to the dermal side (titre 1 : 320). These antibodies belonged to the IgG1, IgG3 and IgG4 subclasses (Fig. 2b). By immunoblotting using a recombinant form of the noncollagenous (NC) 1 domain of type VII collagen,[10] our patient's serum demonstrated type VII collagen-specific IgG4 autoantibodies (data not shown). Serum tumoral markers, including s-CA 19.9, s-CA 125 and s-CEA, were within the normal range. Enzyme-linked immunosorbent assay analysis using recombinant antigen did not reveal reactivity against the immunodominant XVII NC domain of BP180. Our patient was started on a regimen of prednisone 40 mg daily, oral sulfasalazine 2 g daily and mycophenolate mofetil 2 g daily. Under this treatment, an important clinical and serological improvement was noted at the follow-up visit 3 months later.

Several clinical manifestations of EBA are described, including the classic mechanobullous, the generalized inflammatory, and the cicatricialpemphigoid-like types.[2] Interestingly, our patient presented features of both the mechanobullous and the inflammatory forms of EBA, with acral lesions, scarring, milia formation and an erythematous inflammatory eruption on the trunk. Nevertheless, the Fgurate eruption resembling EGR rep-resents a particular clinical feature of this patient that has not yet been reported in patients with EBA. EGR may be very rarely associated with pemphigoid diseases.[5–9] Although EGR usually represents an ominous sign heralding an associated neoplasm, our patient as well as several previously reported cases[6,7,9] clearly demonstrate that in patients with autoimmune blistering diseases such figurate erythema may occur in the absence of neoplasia.

Irrespective of its clinical manifestation, EBA is associated with autoantibodies to type VII collagen.[1,3] Patients' autoantibodies belonging to different IgG subclasses mainly target epitopes within the NC1 domain of type VII collagen.[1] IgG autoantibodies to type VII collagen mainly belong to the IgG1 and IgG4 and to the IgG3 subclasses in EBA and IBD, respect-ively. Consistent with these findings, our patient presented IgG1, IgG3 and IgG4 autoantibodies to type VII collagen. While the blister-inducing potential of autoantibodies to type VII collagen is established,[2] their contribution to the pathogenesis of IBD and EGR-like lesions is still unclear. IBD occur in approximately 30% of patients with EBA. Thus EBA is mainly associated with Crohn's disease, but

rarely with UC.[4,7] The causes and pathomechanisms underlying the association of EBA with IBD are poorly understood. The detection of type VII collagen expression in the colonic mucosa led to the hypothesis that, in the context of chronic inflammation and damage to the overlying mucosa, antigenic epitopes of the type VII collagen molecule are exposed. These newly exposed antigenic epitopes may invoke production of autoantibodies, which, in some patients, also cross-react with type VII collagen and trigger blister formation in the skin.[7] Why EBA associates more often with Crohn's disease compared with UC is even less clear.

When IBD and EBA are associated, the onset of IBD usually precedes by several years the first manifestations of the blister-ing disease. Interestingly, in our patient, the onset of EBA clearly predated the manifestations of UC.

In conclusion, we report that an EGR-like eruption may occur in EBA associated with UC. Our results emphasize the notion that EBA is clinically a heterogeneous disease and suggest EGR to be one of its possible manifestations. Therefore, the differential diagnosis in patients with EGR-like eruptions should also include EBA and other autoimmune blistering skin diseases.

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Conflicts of interest: none declared.

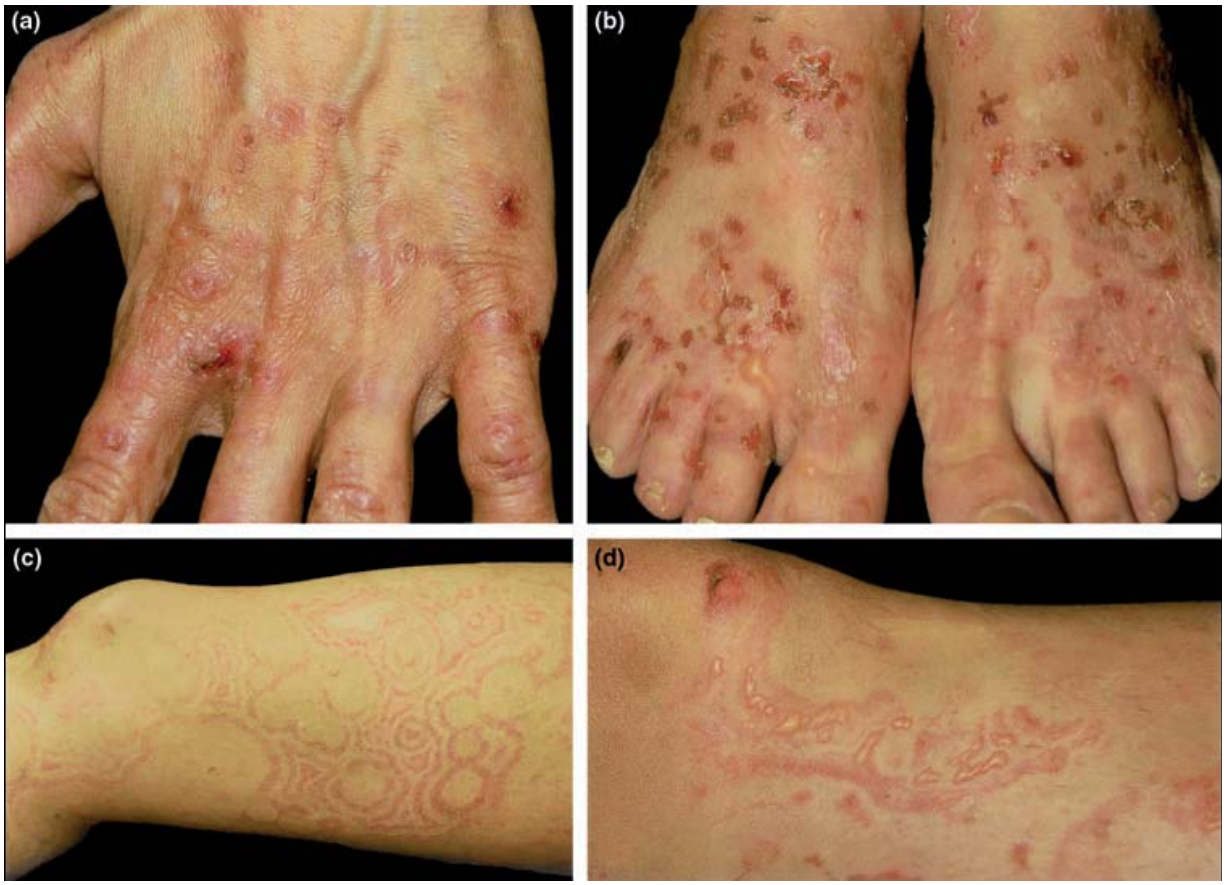

Figure 1. Blisters, erosions, scarring and milia formation on (a) patient's left hand and (b) feet. (c) On thighs, erythematous lesions with a wood-grained appearance were observed. (d) Figurate erythematous lesions accompanied the bullous eruption.

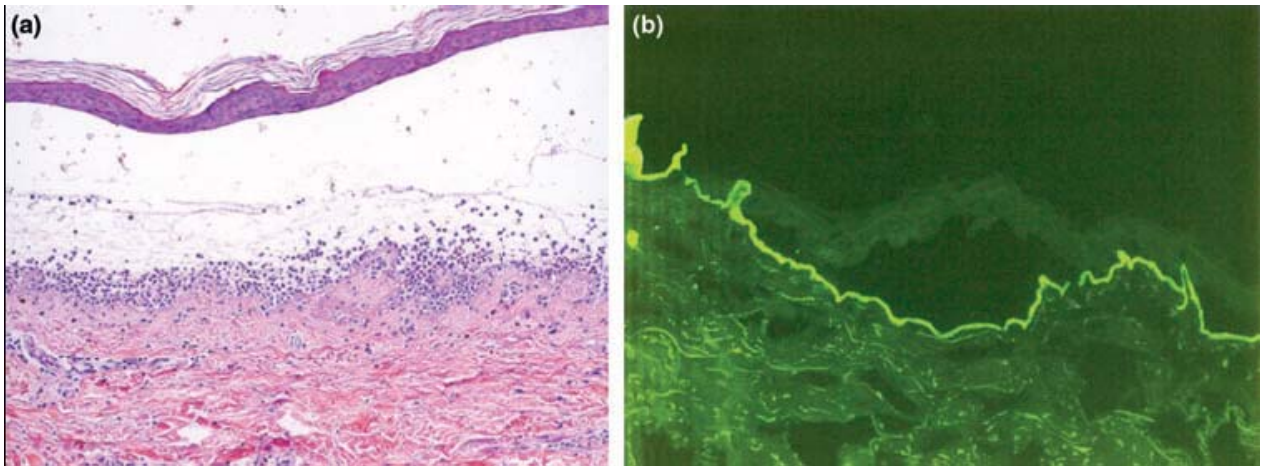

Figure 2. (a) Subepidermal blistering and a neutrophil-rich inflammatory infiltrate were observed within the upper dermis (haematoxylin and eosin; original magnification x 40). (b) Circulating autoantibodies of IgG1, IgG3 and IgG4 subclasses binding to the dermal side of 1 mol L^{-1} NaCl-split skin were detected by indirect immunofluorescence microscopy.