RHEUMATOLOGY

Letter to the Editor (Case report)

Rheumatology 2021;60:e192–e194
doi:10.1093/rheumatology/keaa826
Advance Access Publication 26 December 2020

LABD-like manifestation in a patient with systemic lupus erythematosus

Rheumatology key message

- IgA linear dermatosis might be a rare cutaneous manifestation of SLE.

Dear Editor, A 19-year-old female was admitted to our hospital for facial erythema with eyelid oedema for one week. Physical examination revealed the presence of distinctive 'butterfly' erythema, palpebral oedema and multiple joint and muscle tenderness. Laboratory testing showed leukopoenia (2×10^9/l), anaemia (81 g/l), thrombocytopenia (43×10^9/l), proteinuria (17.9g/24 h), low levels of complement (C3 0.17 g/l, C4 0.03 g/l), increased erythrocyte sedimentation rate (100 mm/h), elevated anti-DNA antibody titre (>800 IU/l) and positive ANAs (IF testing on HEp-2 cells). Thus, the diagnosis of SLE and LN was made and the SLEDAI score was 18 points, suggestive of severe disease activity.

Intravenous methylprednisolone (60 mg daily) and CYC (0.4 g every other week) as well as HCQ, valsartan [an angiotensin II receptor blockage (ARB)] and low molecular weight heparin (LMWH) were prescribed.

However, 5 days after the initiation of treatment, annular erythema and tension blisters erupted over the patient's extremities, especially on the dorsal side of both hands, with severe itching and sharp prickling pain when touched (Fig. 1A). Skin biopsy showed subepidermal blisters, oedema of dermal papillae, and profuse infiltration of neutrophils and eosinophils (Fig. 1B). Direct immunofluorescence (DIF) microscopy demonstrated linear deposits of IgA along the basement membrane zone (BMZ) (Fig. 1C), suggesting Linear IgA bullous dermatosis (LABD) that we considered to be within the spectrum of nonspecific skin lesions associated to SLE. Therefore, high-dose intravenous methylprednisolone (250 mg daily for three days) was administered, with a subsequent dose of 80 mg daily for five days and then tapered gradually. Meanwhile, low-lose intravenous CYC (0.4 qw for 4 weeks), MMF (1.0 bid) and thalidomide (50 mg qn) were prescribed. The patient responded very well and quickly to the treatment. The bullae almost healed up 3 weeks later (Fig. 1D), and other clinical manifestations also improved significantly (Supplementary Table S1, available at *Rheumatology* online).

LABD is a rare autoimmune vesiculobullous subepidermal dermatosis characterized by circulating and tissue-bound IgA antibodies against heterogeneous antigens located in the cutaneous BMZ [1]. Though most cases of LABD are idiopathic and the underlying mechanism remains unclear, some inducing factors such as autoimmune disorders, infections, malignancy or drugs have been reported. In terms of drug-induced LABD, drugs such as antibiotics (especially vancomycin), NSAIDs or antiepileptics (e.g. phenytoin) have been identified as common causative agents [1]. The disease affects people of all ages and has two clinical variants: childhood onset type and adult onset type. The typical lesions are pruritic, annular papules, papulovesicles and tension blisters that are small and negative for Nikolsky's sign. The diagnosis can be confirmed by DIF of a skin biopsy, which shows linear IgA deposits along the epidermal basement membrane [2]. In addition, deposition of IgG, IgM and C3 may be detected.

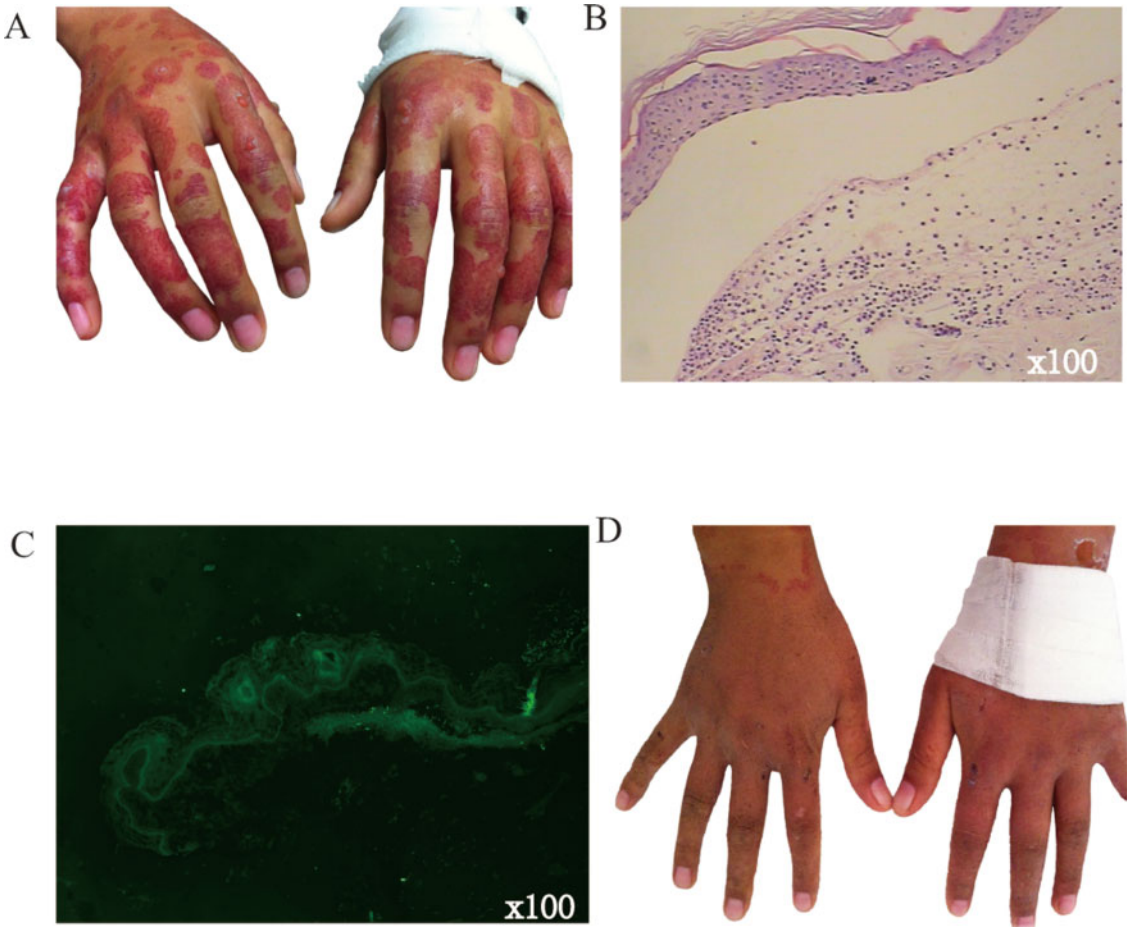
Though LABD may share similar features on immunofluorescence and immunohistology with bullous SLE (BSLE), there are still some crucial differences between these two conditions. For example, linear IgA dermatosis-1 protein (LAD-1) is a unique target antigen for LABD. Besides, the ultrastructural locations of the autoantigens are different: lamina lucida for LABD and anchoring fibrils for BSLE [3–4]. Furthermore, LABD is caused by specific IgA autoantibodies targeting antigenic fragments (e.g. 97-kDa, 120-kDa) of BMZ component (e.g. BP180, BP230 and laminin-5) in skin and mucosa [5]. Recent research also suggested that in comparison to LABD, leukocytoclasis was a hallmark of BSLE and the DIF was polymorphic in BSLE, revealing linear, granular or both linear and granular deposits of IgG, IgA, IgM and C3 at the BMZ [6].

Cutaneous involvement is well recognized in SLE. Among various kinds of skin manifestations, the most typical are butterfly erythema, discoid rash and vasculitis-like lesion. Blisters and bullae were rare in SLE patients, among which only a few presented as LABD-like manifestations [7]. Although the patient we reported here was consistent with the diagnosis of BSLE according to the classification criteria [8], the DIF of skin biopsy identified the presence of linear, but not granular, deposit of IgA and absence of leukocytoclasis, which corroborated a diagnosis of LABD. Meanwhile, as the DIF also demonstrated deposits of C3 and weak IgG (Supplementary Fig. S1, available at *Rheumatology* online) indicative of cutaneous lupus, we considered LABD as a lesion associated with SLE.

Though >30% of LABD cases are drug-induced, the drugs we used for the initial treatment of this patient (i.e. methylprednisolone, CYC, HCQ, valsartan and LMWH) are not the common triggering drugs reported. Therefore, we continued to use the above drugs for better control of the disease. After a combination treatment

LETTER

Fig. 1 Images of the patient's hands



(**A**) The patient presented with annular erythema and pruritic tension blisters over both hands. (**B**) Histopathological examination showed a subepidermal blister with a neutrophil-rich inflammatory infiltrate [hematoxylin–eosin (HE), original magnification ×100]. (**C**) Direct immunofluorescence (DIF) microscopy demonstrated linear deposits of IgA along the basement membrane zone (BMZ) (original magnification ×100). (**D**) The hand bullae almost healed after treatment.

with high-dose methylprednisolone and immunosuppressive agents (including HCQ, CYC, MMF and thalidomide), the patient's skin lesion almost recovered completely within 3 weeks, which also supports that LABD of this patient was rather a manifestation of lupus flare than drug-related adverse effect.

Hereby, we propose to include LABD in the spectrum of nonspecific bullous lesions associated to SLE, which will raise awareness of this condition when rare rashes occur in SLE patients.

Acknowledgements

The patient's written consent was obtained according to the Declaration of Helsinki, and the design of the work was approved by the ethics committee of the Affiliated Hospital of Nantong University.

Funding: This work was supported by the National Natural Science Foundation of China (grants 81671606 and 81601410); the Liaoning Distinguished Professor program (Liao taught 2018–2020); Special Fund for Clinical Medicine, Nantong Science and Technology Bureau (grants HS2014071 and HS2016003); Jiangsu Provincial Commission of Health and Family Planning (grant H201623); and Nantong 226 Talents Project (grant 2017–13).

Disclosure statement: The authors have declared no conflicts of interest.

Data availability statement

Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article.

Supplementary data

Supplementary data are available at *Rheumatology* online.

Zhimin Lu[1,2,*], Dinglei Su[3,*], Xia Li[2,] and Zhanyun Da[1,**]**

[1]*Department of Rheumatology, Affiliated Hospital of Nantong University, Nantong,* [2]*Department of Immunology, College of Basic Medical Science, Dalian Medical University, Dalian and* [3]*Department of Rheumatology and Immunology, Nanjing First Hospital, Nanjing Medical University, Nanjing, People's Republic of China*

Accepted 12 November 2020

Correspondence to: Zhanyun Da, Department of Rheumatology, Affiliated Hospital of Nantong University, 20th Xisi Road, 226001 Nantong, People's Republic of China.
E-mail: dazhanyun@163.com
*Dr Zhimin Lu and Dr Dinglei Su contributed equally to this study.
**Professor Xia Li and Professor Zhanyun Da contributed equally to this study.

References

1 Zone JJ. Clinical spectrum, pathogenesis and treatment of linear IgA bullous dermatosis. J Dermatol 2001;28:651–3.

2 Patrício P, Ferreira C, Gomes MM, Filipe P. Autoimmune bullous dermatoses: a review. Ann N Y Acad Sci 2009; 1173:203–10.

3 Vassileva S, Drenovska K, Manuelyan K. Autoimmune blistering dermatoses as systemic diseases. Clin Dermatol 2014;32:364–75.

4 Saschenbrecker S, Karl I, Komorowski L *et al.* Serological diagnosis of autoimmune bullous skin diseases. Front Immunol 2019;10:1974.

5 Johnson EF, Jacobs MH, Smidt AC. Annular vesiculobullous eruption in a healthy young man. JAMA 2013;310:2559–60.

6 de Risi-Pugliese T, Cohen Aubart F, Haroche J *et al.* Clinical, histological, immunological presentations and outcomes of bullous systemic lupus erythematosus: 10 new cases and a literature review of 118 cases. Semin Arthritis Rheum 2018;48: 83–9.

7 Rutnin S, Chanprapaph K. Vesiculobullous diseases in relation to lupus erythematosus. Clin Cosmet Investig Dermatol 2019;12:653–67.

8 Camisa C, Sharma HM. Vesiculobullous systemic lupus erythematosus. Report of two cases and a review of the literature. J Am Acad Dermatol 1983;9: 924–33.