Rowell Syndrome with Palmoplantar Involvement and Suspected Epitope Spreading

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Sir,

We describe here a 20-year-old woman with erythema multiforme-like lesions that were diagnosed as Rowell syndrome. We also discuss the overlap between bullous lupus erythematosus (BLE) and other auto-immune blistering diseases.

CASE REPORT

During her summer holidays a 20-year-old female patient developed severe erythema, itching and small blisters in the face, on the chest, palms and soles. The peri-oral region was spared (Fig. 1A). On examination, target-like lesions were noted on the neck, chest and, strikingly, the palms and soles (Fig. 1B). The Nikolski sign was negative. Some lesions also showed scaling. She had aphthous lesions in the mouth, up to 10 mm in size. Her medical history was remarkable for recurrent Herpes simplex virus (HSV) infections (genital and mouth), retinal vasculopathies and acral Raynaud’s disease. At age 18 years, systemic lupus erythematosus (SLE) with lupus nephritis was diagnosed that was henceforth well controlled with azathioprine (100 mg/day). No other medication was taken.

Several histology specimens showed an interface dermatitis with lymphocytes and neutrophils, necrotic keratinocytes, small subepidermal blisters and cytoid bodies (Fig. 2). IgG and C3 were deposited in a lupus band-like pattern in peri-lesional skin, as evidenced by direct immunofluorescence (DIF) (data not shown). She had axillary lymphadenopathy. A chest X-ray, abdominal ultrasound and gynaecological examination were unremarkable. Haemoglobin 9.9 mg/dl, white blood cells (WBC) 3.75×10⁶/µl, differential complete blood count revealed 93% neutrophils and 4% lymphocytes. Serum chemistry and C-reactive protein were unremarkable. Viral swabs were negative for HSV-, varicella zoster virus (VZV)-, human herpes virus (HHV)-6- and HHV-7-DNA. Candida albicans was detected on the cervix, throat and stool.

Given the patient’s history, erythema multiforme in association with recurrent HSV infection was suspected with regard to the distribution pattern. Furthermore, phototoxic dermatitis, drug reaction (the patient took aspirin for menstrual pain) viral rash and BLE were also considered.

Antinuclear antibodies were positive (1:10.240) with a speckled pattern. Anti-DNA antibodies: 34 U/ml (positive). The serum contained antibodies against the extractable nuclear antigens RNP70, RNPc, SmB, SmD and Ro60. Serum was also tested for auto-antibodies against the dermo-epidermal junction by indirect immunofluorescence (IIF) and enzyme-linked immunosorbent assay (ELISA). IIF with salt-split human skin showed IgG reactivity with the nuclei of epidermal cells and weak reactivity with the epidermal portion of split skin. By ELISA there was reactivity against several BP180 epitopes: the NH₂-terminal domain (aa490–812) and the COOH-terminal domain (aa1048–1465), and extracellular portion of the BP180 antigen (BPAG2, collagen XVII). Antibodies to collagen type VII were negative.

As the patient had no immediate history of HSV infection and HSV-DNA analysis was negative, treatment was performed with systemic corticosteroids (prednisolone 80 mg/day) and with oral amphotericin B as well as fluconazole (200 mg/day). Local treatment consisted of topical mometasone furoate cream and wet dressings (NaCl). The oral ulcers were treated with topical 0.1% trimcinolone ointment. Mometasone furoate under occlusion was applied.
Immune subepidermal blistering skin diseases can be antigens described above (7, 9). Auto-antibody reactivity against various epidermal anchoring fibrils and type-VII collagen (1). However, (7). Moreover, coexisting bullous pemphigoid and SLE (7). Furthermore, coexisting bullous pemphigoid and SLE. Evidence that anti-basement membrane zone antibodies in bullous erosion of systemic lupus erythematosus recognize epidermolysis bullosa acquisita autoantigen. J Invest Dermatol 1985; 84: 472–476. Shirahama S, Furukawa F, Yagi H, Tanaka T, Hashimoto T, Takigawa M. Bullous systemic lupus erythematosus: detection of antibodies against noncollagenous domain of type VII collagen. J Am Acad Dermatol 1998; 38: 844–848. Barton DD, Fine JD, Gammon WR, Sams WM Jr. Bullous systemic lupus erythematosus: an unusual clinical course and detectable circulating autoantibodies to the epidermolysis bullosa acquisita antigen. J Am Acad Dermatol 1986; 15: 369–373. Chan LS, Lapiere JC, Chen M, Traczyk T, Mancini AJ, auto-immune disease against the basement membrane zone that is provoked by systemic auto-immunity, a hallmark of SLE; (ii) “epitope-spreading” describing an immunological event, in which a primary auto-immune or inflammatory process causes tissue injury, releasing previously “sequestered” antigenic epitopes (10). The deposition of immunoglobulins may cause injury to adjacent components such as BP180 (11). Auto-antibody-mediated loss of hemidesmosomal adhesion may facilitate a secondary auto-immune reaction against the second auto-antigen, BP230. In the patient described here, bullous lesions were associated with IgG auto-antibodies against the 2 major antigenic epitopes of BP180. A recent study suggested that this pattern is associated with involvement of the mucous membranes (11). To our knowledge, this is one of the first cases of bullous SCLE with IgG reactivity against BP180. We consider this immunological finding as a secondary auto-immune response (epitope spreading).

Rowell syndrome has to be differentiated from photosensitive eruptions of SCLE and classical BLE. In the original publication by Rowell, 4 of 120 patients with discoid LE also had erythema multiforme-like lesions. All patients suffered from Raynaud’s syndrome and presented with positive rheumatoid factors (12). They also presented a similar pattern of immunological abnormalities with antinuclear antibodies of the speckled type. However, none of the patients had involvement of the palms and soles. We would therefore like to add our case with target-like lesions and prominent involvement of the palms and soles to the features of Rowell syndrome (erythema multiforme-like LE).

**REFERENCES**

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