A case of herpes gestationis: Follow-up study of autoantibodies using enzyme-linked immunosorbent assay and immunoblotting

Sir,

Herpes gestationis (HG) is a rare autoimmune-mediated bullous disease that occurs during pregnancy and post partum, and may exacerbate after delivery.[1] IgG autoantibodies in HG bind to the 16th noncollagenous domain (NC16a) of bullous pemphigoid antigen 180 (BP180), which is also recognized by bullous pemphigoid (BP).[2] We herein present a case of HG in which we examined the correlation among the results of enzyme-linked immunosorbent assay (ELISA), immunoblotting and disease activity along the time course.

A 27-year-old Japanese female in the 36th week of her first pregnancy had a pruritic infiltrative erythema on the extremities. After delivery in the 38th week of her pregnancy, she developed widespread infiltrative erythema with small tense vesicles on the extremities and back [Figure 1a]. The patient also showed pruritic vesicles on the palms and soles, resembling dyshidrosis. The skin of her newborn baby was normal. A skin biopsy specimen taken from a lesion on the thigh revealed subepidermal blisters with perivascular eosinophilic and lymphocytic inflammatory infiltrate [Figure 1b]. Direct immunofluorescence of the perilesional skin showed linear IgG and C3 deposits along the basement membrane zone (BMZ) [Figure 1c]. Indirect and complement immunofluorescence using normal human skin as a substrate revealed circulating IgG anti-BMZ autoantibodies at a titer of 1:10. Indirect and complement immunofluorescence of the normal human skin split by 1 mol/L NaCl showed positive reaction (1:10) on the epidermal side of the split for IgG antibodies and C3 [Figure 1d]. Immunoblotting using normal human epidermal extract revealed IgG antibodies to BP180 (data not shown). Immunoblotting using the recombinant protein of BP180 NC16a demonstrated that circulating IgG antibodies reacted with this protein. The BP180 ELISA index was positive (index: 79.42). These clinical and immunologic features lead us to the diagnosis of HG.

Initial treatment with topical steroid for a week was not effective. At that time, antihistamine was not added because the patient refused to take it. Subsequently, a combination therapy with topical steroid and oral antihistamine (the patient agreed to take this) was started, and this modality was effective: new vesicles discontinued to develop and eruptions resolved gradually. At the 50th day after delivery, the patient went into remission. The BP180 ELISA index decreased along with the improvement of skin lesions (index: 41.09 at the 50th day after delivery), and became negative (index: 5.79) at the 120th day after delivery [Figure 2a]. On indirect immunofluorescence, the antibody titer gradually turned negative over the course of the improvement of skin lesions (IgG anti-BMZ antibody titer on indirect immunofluorescence using normal human skin became negative at the 21st day after delivery, while that on indirect immunofluorescence using salt-split skin was still positive at a titer of 1:10 at the 21st day after delivery, but became negative at the 50th day after delivery). On immunoblotting, IgG antibodies against the BP180NC16a recombinant protein were clearly detected at the 5th, 12th and 50th days after delivery but were not detected at the 120th day after delivery [Figure 2b].

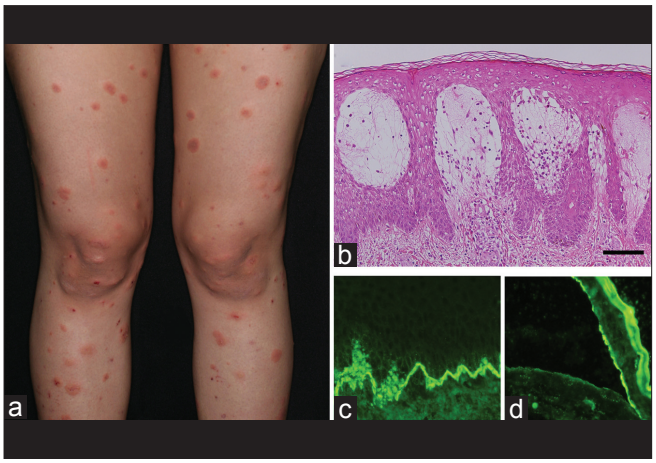

Figure 1: (a) Clinical features of the patient. Infiltrative erythema with tense vesicles on the lower extremities. (b) Histopathology revealed subepidermal vesicles with perivascular eosinophilic and lymphocytic infiltration (hematoxylin and eosin stain, Bar: 100 μm). (c) Direct immunofluorescence showed linear C3 deposits at the basement membrane zone. (d) Complement immunofluorescence using 1 mol/L NaCl split-skin demonstrated a positive C3 reaction on the epidermal side of the split

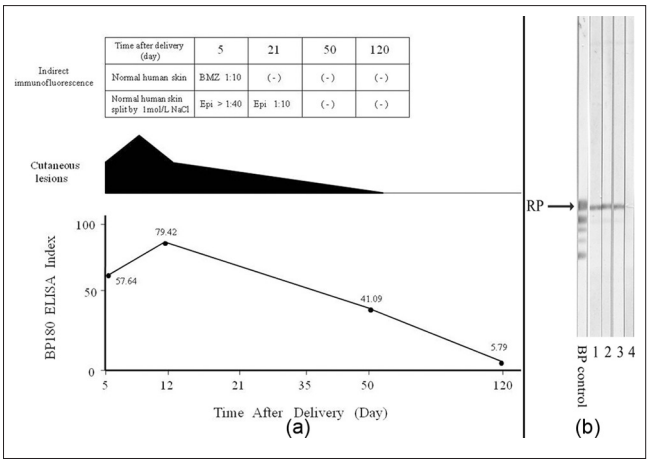

Figure 2: (a) Results of indirect immunofluorescence of the patient's serum obtained over the disease course (upper column). Cutaneous lesions were gradually improved by the treatment with topical steroid and oral antihistamine (middle column). Results of BP180 enzyme-linked immunosorbent assay (lower column). (b) Immunoblotting for BP180 NC16a. Sera from the patient at the 5th (lane 1), 12th (lane 2) and 50th day (lane 3) after delivery reacted with recombinant protein. Serum from the 120th day (lane 4) after delivery was negative

HG is a rare autoimmune bullous disease typically characterized by the onset of pruritic vesiculobullous lesions during the latter period of pregnancy or the puerperium. The onset of HG is usually in the second or third trimester, but could also be in the first trimester. Exacerbation with delivery occurs in 75–80% of HG cases.[1] To date, there is no therapeutical consensus for HG. Mild cases of HG are usually treated with topical steroids in combination with antihistamines. Refractory HG cases have been successfully treated by systemic steroids, cyclosporine, intravenous immunoglobulin or plasmapheresis.

Several studies demonstrated that the BP180 ELISA titer was a sensitive monitoring measurement of disease activity in BP patients.[3] Recently, the ELISA titers of antibodies to BP180 NC16a were reported to fluctuate in parallel with the disease activity in HG patients.[4] In our patient, the BP180 ELISA scores also correlated with the disease activity. To further verify the ELISA results, we also performed immunoblotting of BP180 NC16a recombinant protein, which was a prototype method before the development of BP180 ELISA.[5] The immunoblotting clearly showed positive reactivity at the 5th, 12th and 50th day after delivery, which disappeared completely at the 120th day after delivery. Thus, results of both ELISA and immunoblotting correlated well with the disease activity along the disease course.

In summary, we present a case of HG in which the disease activity correlated well with anti-BP180 antibody levels measured by ELISA. We suggest that BP180 NC16a ELISA is a useful tool for monitoring the disease activity not only in BP but also in HG.

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