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Pemphigus Vulgaris Associated with Acquired Hemophilia A due to Factor VIII Inhibitor

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A rare case of pemphigus vulgaris associated with acquired hemophilia A is reported. The presence of factor VIII inhibitor is confirmed, and the co-existence of two autoimmune diseases is discussed.

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Since the first report by Quick & Stefanini (1), 5 patients with pemphigus complicated with an acquired hemorrhagic diathesis have been reported (1–5). Factor VIII inhibitor, an autoantibody against coagulation factor VIII, was proved to be responsible for this condition. We report the first Japanese male with pemphigus vulgaris with acquired hemophilia A, in which the presence of factor VIII inhibitor was confirmed.

CASE REPORT

A 45-year-old Japanese male visited our department on November 5, 1979 with a 1-month history of blister formation on his face and trunk (Fig. 1). He had no previous history of bleeding tendency or blood transfusion. Histological examination of a blister obtained from his lumbar part showed a typical acantholytic bulla just above the basal cell layer. Direct immunofluorescence study demonstrated the deposition of IgG in the intercellular spaces. The serum titer of the anti-intercellular substance antibody was 1:40. No abnormality was found in routine examinations, including anti-nuclear antibody, anti-DNA antibody and LE cell preparation. He was diagnosed as pemphigus vulgaris. His skin lesions rapidly improved with the conventional treatment of dexamethasone, 2.5 mg/day.

On the 16th day after admission, bleeding from the biopsied site was noticed, followed by hematuria and hematoma on his left arm. Hematological examinations revealed a marked prolongation of both coagulation time (more than 30 min) and activated partial thromboplastin time (65.3 s). The bleeding time, the prothrombin time and platelet count were normal. Abnormality in the coagulation cascade was suggested, especially in the internal phase. Assays for specific clotting factors disclosed a decreased activity of factor VIII (3.4%), while activities of other coagulation factors were normal. The addition of patient's plasma prolonged the activated partial thromboplastin time of plasma from normal individuals. Furthermore, the activity of this inhibitor was neutralized with anti-human IgG rabbit serum (κ and λ type).

These results confirmed the presence of factor VIII inhibitor (20 U/ml; new Oxford unit), and thus the diagnosis of acquired hemophilia A due to factor VIII inhibitor was made. We first treated him with a replacement therapy of factor VIII, 400U and 1000U, but it was not effective. A plasma exchange was then introduced, which dramatically decreased the activity of factor VIII inhibitor and improved his clinical symptoms. The dose of dexamethasone was gradually decreased to 0.5 mg/day. He has been in good health without relapsing for 13 years.

DISCUSSION

Autoimmune diseases tend to occur simultaneously in various combinations. Pemphigus groups associated with myasthenia gravis (6) or systemic lupus erythematosus (7) have been reported. To our knowledge, only 5 patients with pemphigus complicated with hemorrhagic diathesis have been described (1–5). However, factor VIII inhibitor was confirmed only in one case (5). As the same condition was recognized in other autoimmune bullous diseases, such as bullous pemphigoid (8) and dermatitis herpetiformis (9), it is less likely that pemphigus antibody has a cross-reactivity to factor VIII. The production of two autoantibodies in the same patient may suggest a common immunological background, such as abnormal function of suppressor T cells (5). Factor VIII inhibitor is the commonest anticoagulant and has been found in four groups (10): 1) patients with hemophilia A who have been treated

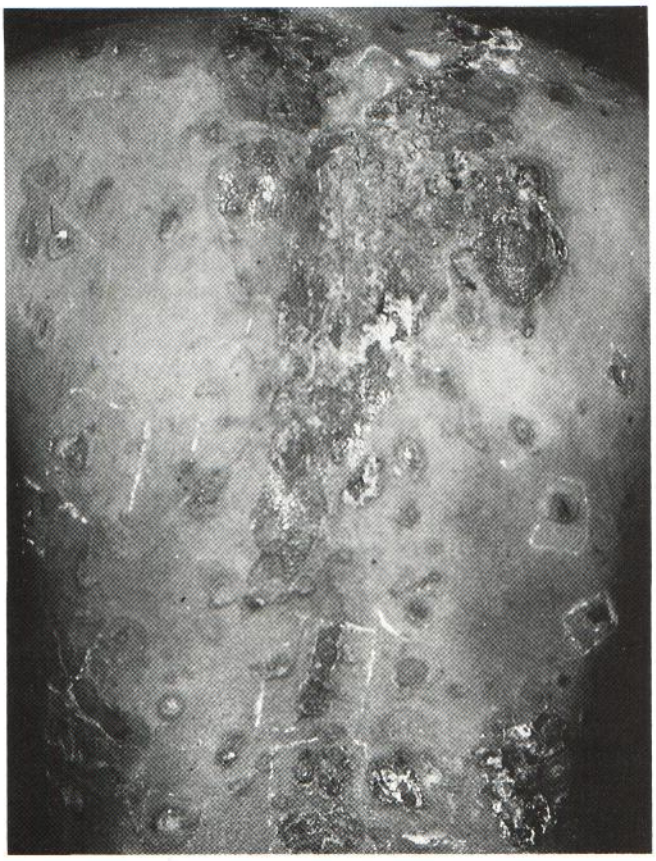

Fig. 1. Blisters and erosions on the patient's back.

with replacement therapy, 2) women after normal delivery, 3) patients with immunologic disorders, and 4) healthy persons without underlying diseases. Spontaneous remission is rare except for the second group. So, in cases of pemphigus vulgaris resistant to conventional immunosuppressive therapy, a hemorrhagic diathesis might be an aggravating factor, and plasma exchange can then be of special value.

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