Clinical and Serological Transition From Pemphigus Vulgaris to Pemphigus Foliaceus Demonstrated by Desmoglein ELISA System

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Several cases in which the disease course has undergone a transition from pemphigus vulgaris (PV) to pemphigus foliaceus (PF) or vice versa have been reported in the literature. The disease transition in these cases was determined by means of clinical and histopathological observations and immunoblot analysis. To our knowledge, the case described herein represents the first report to clearly demonstrate the serological transition from mucous PV to mucocutaneous PV to PF using a desmoglein (Dsg) enzyme-linked immunosorbent assay (ELISA) system.

**REPORT OF A CASE**

A 55-year-old Japanese man presented to our outpatient clinic in March 1997 with a 3-month history of intractable oral erosions (Figure 1A). Clinical, histopathological, and immunological findings led to the diagnosis of PV. Using a Dsg ELISA system (Dsg1/3 ELISA kit; Medical & Biological Laboratories Co Ltd, Nagoya, Japan), only anti-Dsg3 autoantibodies (index, 214.07) were detectable (Figure 2A); the oral lesions had been well controlled with a dexamethasone gargle.

In March 1999, the patient presented with newly developed oral lesions as well as bullae and erosions on the trunk and extremities (Figure 1B). Histopathological analysis and immunofluorescence studies of his skin blisters showed findings that were the same as those observed at his first presentation. He was diagnosed as having mucocutaneous PV. At this time, ELISA of his serum samples demonstrated both anti-Dsg1 (index, 163.76) and anti-Dsg3 (index, 173.45) autoantibodies (cutoff index value, Dsg1, 9.78; Dsg3, 9.79) (Figure 2B). He was treated with a combination of 1000 mg of methylprednisolone sodium succinate pulse therapy, plasmapheresis, and 8 mg/d of betamethasone. When the dosage of betamethasone therapy was reduced to 3.5 mg/d after the PV lesions had cleared, flaccid bullae and macerated crusts developed on his face and trunk, while he was completely clear of oral lesions (Figure 1C). Clinical and pathological findings led to a diagnosis of PF. At this point, his serum sample contained only anti-Dsg1 autoantibodies (Figure 2C).

The dosage of betamethasone therapy was increased to 6 mg/d, and 150 mg of azathioprine was added to the regimen. The lesions were gradually epithelialized, and no new blister formation was observed.

**COMMENT**

It has been clearly demonstrated that serum samples from patients with the mucosal dominant type of PV contain only anti-Dsg3 autoantibodies, while those of patients with mucocutaneous PV contain both anti-Dsg1 and anti-Dsg3 autoantibodies. Therefore, the anti-Dsg autoantibody profile defines the clinical phenotype of pemphigus. In the present case, the patient experienced a clinical transition from the mucous dominant type of PV to mucocutaneous PV to PF. We...
performed Dsg ELISA 15 times during the course of the disease (Figure 2), and the ELISA titers and pemphigus phenotype as well as disease activities proved to be closely correlated.

The course of disease in most patients with PV begins with mucous lesions; subsequently, cutaneous lesions develop. In such cases, epitope spreading from Dsg3 to Dsg1 might occur, but the reason for the reduction in anti-Dsg3 autoantibodies during the disease course, as seen in our case, is still unknown.

Ding et al demonstrated that anti-Dsg1 autoantibodies in PV serum samples are pathogenic and that they induce typical PF lesions in neonatal mice. In case of transition, some immunological mechanism may cause the reduction of anti-Dsg3 autoantibodies during the mucocutaneous PV stage, and then the remainder of anti-Dsg1 autoantibodies cause PF lesions.

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REFERENCES


Figure 1. A, Oral erosion of mucous pemphigus vulgaris. B, Erosions of mucocutaneous pemphigus vulgaris on the upper chest area. C, Flaccid bullae and macerated crusts of pemphigus foliaceus.

Figure 2. Desmoglein (Dsg) enzyme-linked immunosorbent (ELISA) index of mucous pemphigus vulgaris (A), mucocutaneous pemphigus vulgaris (B), and pemphigus foliaceus (C).