Frequency of Shifts Over Time in the Profile of Antidesmoglein Antibodies in Pemphigus Vulgaris

The clinical features of pemphigus vulgaris (PV) are related to the presence and profile of desmoglein 3 (anti-dsg3) and desmoglein 1 (anti-dsg1) antibodies. Anti-dsg3 is associated with mucosal PV; the concurrent presence of anti-dsg3 and anti-dsg1, with mucocutaneous disease; and anti-dsg1 alone, with pemphigus foliaceus (PF). Shifts over time in the pattern of anti-dsg antibodies from that associated with PV to that seen in PF have been described in several case reports. How often these serologic shifts occur is unknown. The present study was conducted to examine the frequency and the types of shifts in the profile of anti-dsg3 and anti-dsg1 that occur in patients with PV.

Methods. Thirty-seven sequential patients with PV who satisfied the following criteria were studied: (1) PV diagnosis based on clinical, histologic, and immunologic criteria; (2) intercellular antibodies at baseline assayed by indirect immunofluorescence; (3) at least 2 serum specimens collected at different times during the course of illness; and (4) disease active at both measurement times as evidenced by persisting skin and/or oral lesions. The median interval between the sampling of specimens was 26 months (range, 2-124 months). Anti-dsg1 and anti-dsg3 antibodies were measured by enzyme-linked immunosorbent assay using a commercially available kit (Medical & Biological Laboratories Co Ltd, Nagona, Japan). The cutoff for calling serum results positive was that recommended by the manufacturer: 20 U or higher.

Results. At baseline, 97% of patients (36 of 37) had anti-dsg3, and 59% (22 of 37) had anti-dsg1 antibodies (Table). There was no difference in antibody profile in 60% of patients (22 of 37) between the baseline and end point. In this group, 13 patients had only anti-dsg3 antibodies and 9 had both anti-dsg3 and anti-dsg1 antibodies at both measurement points.

In 41% of patients (15 of 37), a shift occurred in anti-dsg antibody profile over time. The changes varied (Table). Of the 21 patients initially testing positive for both antibodies, 9 had no change in profile, 6 ultimately showed anti-dsg1–negative results, 3 ultimately showed anti-dsg3–negative results, and 3 ultimately tested negative for both antibodies. In 15 patients initially testing positive for anti-dsg3 and negative for anti-dsg1 antibodies, 13 had no change in profile, and 2 ultimately showed anti-dsg1–positive results. No patients showed anti-dsg3–negative results. One patient had only anti-dsg1 antibodies at baseline and tested positive for both antibodies at the final measurement. The reason for these changes was not determined, but possibilities include antigenic drift and changes in the course of the disease (eg, relapse vs continuous disease activity).

At baseline, there was a good correlation between the profile of both anti-dsg3 and anti-dsg1 antibodies with the phenotype of PV: the presence of both antibodies was associated with mucocutaneous disease. The presence of only anti-dsg3 was associated with mucosal disease. In the 22 patients whose antibody profile did not shift, the PV phenotype also did not change. By contrast, in the 15 patients whose anti-dsg profile changed over time, the phenotype also changed in 73% of the patients (11 of 15). However, the changes were not consistent. Among the 6 patients initially testing positive for both antibodies and whose profile then shifted to anti-dsg1 negative, 2 still retained mucocutaneous disease instead of developing only mucosal disease. Both patients initially testing positive for anti-dsg3 and negative for anti-dsg1 whose profile then became positive for both antibodies developed skin lesions but lost their prior oral lesions. The phenotype of the 1 patient whose profile shifted from only anti-dsg1 antibodies to both antibodies shifted from mucocutaneous disease to having only skin lesions. The cause for the lack of correlation between changes in anti-dsg profile and the phenotype of PV is not known. One possible explanation might be intramolecular epitope shifts that are known to occur in patients with PV and PF and that could result in the enzyme-linked immunosor-
bent assay detecting antibodies to desmoglein epitopes that are not pathogenic.

Comment. Shifts over time in the anti-dsg3 and anti-dsg1 antibody profile occur frequently in patients with PV, rather than being exceptional events. A variety of changes can occur. The absence of a consistent relation between changes in anti-dsg profile and changes in PV phenotype indicates that factors in addition to the anti-dsg profile play a role in the clinical manifestations of PV.

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Histologic Cutaneous Modifications After the Use of EMLA Cream, A Diagnostic Pitfall: Review of 13 Cases

While the eutectic mixture of lidocaine and prilocaine (EMLA cream; AstraZeneca International, Sodertalje, Sweden) is the topical anesthetic most widely used before performing a skin biopsy,1,2 EMLA-induced cutaneous histologic alterations have rarely been reported.3,5 We herein report 13 cases where pathological diagnosis was highly complicated by EMLA application.

Methods. We reviewed 13 skin biopsy specimens obtained after EMLA application from children (mean±SD age, 3.6±4.4 years) with erythematous and squamous disease (n=4, patients 1-4), keratinization disorder (n=4, patients 5-8), bullous disease (n=3, patients 9-11), and suspected storage (n=1, patient 12) or connective tissue (n=1, patient 13) disorders.

In addition to histopathologic findings in relation to suspected diagnoses, unexpected striking features were observed in 9 biopsy specimens (Figure 1). A diffuse pallor with swollen upper keratinocytes was seen in 7 specimens (patients 1-3, 5, 7, 9, and 10). Lower keratinocytes displayed a sharp vacuolization in 8 cases (patients 1-7 and 10). Destruction of the basal layer was observed in 8 cases (patients 1, 2, 4-7, 9, and 10). Either focal

Figure 1. Standard histologic analysis (hematoxylin-eosin). A, Focal vacuolization in basal and suprabasal keratinocytes (original magnification ×100). B, Diffuse vacuolization in basal layers associated with swelling and pallor of the upper epidermis (original magnification ×250). C, Subepidermal cleavage (asterisk) and cell vacuolization (original magnification ×100).