First North American Case of IgG/IgA Pemphigus in an Adult
An Unusual Blend of Clinical and Histologic Features

In this case, the antibody response is mediated both by IgG and IgA to Dsg1.

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Pemphigus, an autoimmune mucocutaneous disease characterized by antibodies against desmoglein (Dsg) proteins on the cell surfaces of epidermal keratinocytes, can be sub-classified into its two major forms as vulgaris (PV) and foliaceus (PF). The difference between the two is the antibody target; in PV the antibody response is against Dsg3, whereas in PF the antibodies are against Dsg. Because of the different targets, the clinical presentations are usually somewhat different. Both conditions present as superficial vesicles and bullae, but the vesicles of PF are more superficial, often ruptured, and mucosal involvement is seen less often. The most common histologic findings are suprabasilar or subcorneal acantholysis respectively. Other less common variants of IgG pemphigus include pemphigus herpetiformis, pemphigus erythematosus, pemphigus vegetans, and paraneoplastic pemphigus. The majority (80 percent) of pemphigus is IgG mediated, however IgA has also been described. IgA pemphigus is characterized by a unique histologic pattern, ranging between subcorneal pustular dermatosis (SPD),1-3 to intraepidermal neutrophilic dermatosis (IEN).4-6 SPD typically presents as vesiculopustules in an annular pattern. Direct immunofluorescence demonstrates desmocollin 1 (Dsc1) antigen bound by IgA in the superficial epidermis. IEN manifests as a vesiculopustular eruption but usually has more erythematous plaques. Histology shows intraepidermal pustules. In IEN, the antigen bound by IgA has been found to be Dsg1 or Dsg3.5 Here we present the first North American case in an adult of IgG/IgA pemphigus in which the antibody response is mediated both by IgG and IgA to Dsg1, producing an unusual clinical and histologic picture. To date, there have been only 17 cases in the English literature, mainly in Japan and Europe.6-23

CASE REPORT

A 67-year-old Caucasian female with past medical history of melanoma was referred to dermatology with a two-week history of a recurrent rash. It initially started on her back, and then spread to her upper chest and upper abdomen. The lesions were vesicular and extremely pruritic. When scratched, the lesions would open to form erosions. She did not report any pain, fever, or any other new symptoms related to the rash. She denied any new medications or other new exposures. On physical exam, she had eruptions of erythematous scaly plaques on her back, chest, anterior neck, inframammary folds, and upper abdomen with several 1-2cm open erosions.

Fig. 1. The back of the patient showing superficial erosions with surrounding erythematous scaly plaques and residual crusts.

Fig. 2. Erythematous scaly plaques and macules with erosions on chest and inframammary folds.
and superficial ulcerations, many with eschars and excoriation (Figures 1, 2). There were a few tense bullae on her trunk, with a negative Nikolsky's sign. No erosive lesions were found in the oral mucosa or genital area. A complete metabolic panel was normal.

A biopsy was performed and revealed an intraepidermal pustular dermatosis with both acantholysis and neutrophilic abscesses (Figure 3). Direct immunofluorescence performed on a perilesional site using antibodies for IgG, IgA, IgM, kappa, lambda, C3, and fibrinogen showed an intraepidermal distribution of IgG, IgA, kappa/lambda, and C3 on keratinocyte cell surfaces throughout the epidermis (Figures 4a, 4b). A serum antibody analysis was performed, and the patient's serum demonstrated positive anti-Dsg1 antibodies with negative antibodies to Dsg3. Based on these findings, a diagnosis of IgG/IgA pemphigus foliaceus was made, and the patient was started on doxycycline 100 mg BID, clobetasol 0.05% ointment, and 500mg niacinamide TID. After one month she noted fewer flares, but was still getting sparse new blisters every two to three days. Additionally, her scalp continued to develop pruritic blisters, which were only partially responsive to treatment with clobetasol twice daily. After 12 months, her condition is stable with fewer erosions on her trunk, but she continues to get flares of scalp vesicles, and reports new lesions on the arms, vaginal area, in the nose, and ears. Very recently, dapsone therapy (50mg daily) has been started with the patient with little therapeutic efficacy. However, upon increasing the dose to 75mg daily, the patient reports that the lesions are starting to respond favorably. The patient continues to be followed in clinic and is slowly improving, and the efficacy of the addition of dapsone to her treatment regimen will be continued to be monitored.

**DISCUSSION**

Since the first description of IgG/IgA pemphigus by Nishikawa et al in 1987,17 cases have been reported in the English literature. The clinical characteristics of IgA/IgG pemphigus are often similar to that of IgG pemphigus, however, there is significant amount of variability in the clinical and histopathological features of the disease (Table 1). Seven of the cases describe the erythematous lesions as vesicular,9,11,15,16,19,21,22 while eight described the lesions as predominantly pustular.9,10,12,14,16,17,21,23 Four reports describe oral or genital mucosa involvement.10,13,14,20 Some reports involved a neutrophilic infiltrate8,15,19,20,21,23 whereas others had an eosinophilic infiltrate.14-16,19,23 Acantholysis was found in about half of the reports.8,9,11,14,17,20,21 Furthermore, in many cases, ELISA and immunoblotting studies were performed to determine the presence of antibodies against specific antigens. The results are very diverse, with both IgA and IgG targeting a variety of intraepidermal proteins. IgA antibodies were found against Dsg1 in 10 reports,9,11,12,15,16,18,19,21,22,23 against Dsg3 in five,10,13,14,19,20 against Dsc in three,8,10,17 and in one against desmoplakin (DP).10 Similarly, IgG antibodies were found against Dsg1 in nine reports,9,11,12,15,18,19,21-23 against Dsg3 in five,10,13,14,16,20 against Dsc in five,8,10,12,17,22

![Fig. 3. Histology of a perilesional biopsy demonstrating intraepidermal pustular dermatosis with acantholysis and neutrophilic abscesses.](image)

![Fig. 4. Direct immunofluorescence using normal human skin as a substrate demonstrates IgG (a) and IgA (b) antibodies on keratinocyte cell surfaces.](image)
and in one against DP.\textsuperscript{10} Finally, the therapeutic regimens varied between the reports, but the most popular regimens involved the use of dapsone and/or prednisolone.\textsuperscript{10-23} Some cases also reported using tetracycline,\textsuperscript{23} minocycline,\textsuperscript{11} clomotizone,\textsuperscript{23} minocycline,\textsuperscript{11} clostridial IgG and IgA antibodies,\textsuperscript{24} which has been demonstrated due to the fact that dapsone inhibits neutrophilic adherence in previous IgG/IgA pemphigus cases. This may be because of a good therapeutic effect, especially as her symptoms continue to improve. Dapsone has shown excellent results in previous IgG/IgA pemphigus cases. This may be due to the fact that dapsone inhibits neutrophilic adherence to IgG and IgA antibodies,\textsuperscript{24} which has been demonstrated in this patient’s histology.

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