Detection of IgG Autoantibodies against Desmocollin-3 in Greek Patients with Pemphigus

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Received: January 12, 2018
Accepted: February 11, 2019

ABSTRACT Pemphigus is an autoimmune bullous disorder caused by autoantibodies against desmosomal cadherins. The most common clinical forms are pemphigus vulgaris (PV) and pemphigus foliaceus (PF). Among the numerous proteins that are considered responsible for the cohesion of keratinocytes in epidermis, desmocollin-3 (Dsc-3) has been initially reported to participate in epidermal blistering in mice. There have been reports in which autoantibodies against Dsc-3 have been detected. In PV, a limited number of studies found no presence of IgG or IgA autoantibodies against Dsc-3. In this study we examined sera from Greek patients with PV and PF for the presence of IgG autoantibodies against Dsc-3. In this study we examined sera from Greek patients with PV and PF for the presence of IgG autoantibodies against Dsc-3. Immunoblotting for the detection of autoantibodies against Dsc-3 was performed in sera from all cases. Dsc-3 autoantibodies were not detected in either group (PV and PF). Our results confirm the hypothesis that the pathogenic role of Dsc-3 in epidermal blistering in PV and PF remains controversial.

KEY WORDS: pemphigus, desmocollin

INTRODUCTION

Pemphigus represents a spectrum of autoimmune bullous disorders caused by autoantibodies against desmosomal cadherins with subsequent acantholysis. The main target antigens in pemphigus vulgaris (PV) are desmoglein-1 (DSG-1) and desmoglein-3 (DSG-3), while in pemphigus foliaceus (PF) it is DSG-1 (1). Desmocollins (Dsc) are another group of transmembrane proteins of the Ca2+-dependent cadherin family, including three different isoforms of Dsc (Dsc1-3) (2). Dsc3 is a major molecule of the adhesion complex of epidermal keratinocytes (3). The aim of this study was to examine sera from Greek patients with PV and PF for the presence of IgG autoantibodies against Dsc-3.

PATIENTS AND METHODS

Sera were obtained from patients with PV, PF, and healthy subjects, in order to identify any reactivity to Dsc-3. Diagnosis of PV or PF was established with histology, immunofluorescence techniques, and commercial ELISAs (anti DSG-1, anti DSG-3).
Analysis of the epidermal protein extracts was performed with electrophoresis in polyacrylamide 7.5% gel using the Laemmli method. The epidermal extract proteins separated were by SDS-page and transferred to nitrocellulose membrane. Immunoblotting for the detection of autoantibodies against Dsc-3 was performed in all sera.

RESULTS

Presence of autoantibodies against Dsc-3 was not detected in any of the 45 patients with PV and of 8 patients with PF (Figure 1).

DISCUSSION

Dsc-3 is among the numerous proteins considered to be responsible for the cohesion of keratinocytes in epidermis and has been reported to participate in epidermal blistering in mice. There are reports showing autoantibodies against Dsc-3 (4-6) in case series of patients with pemphigus herpetiformis or paraneoplastic pemphigus and pemphigus cases with atypical immunological profile (4-6). Additionally, there is published data supporting the hypothesis that Dsc-3 participates in PV pathogenesis, whereas other data indicate that Dsc-3 does not constitute an immunological target. Chen et al. reported that loss of function of Dsc-3 in the epidermis of mice causes disorders similar to those observed in patients with PV (3). Spindler et al. demonstrated the important role of Dsc-3 in the integrity of the epidermis and concluded that desmocollin-3 is probably involved in PV pathogenesis (2). It has been suggested that anti-Dsc3 may be pathogenic in cases of dual reactivity against Dsg-3 and Dsc-3 (6).

However, there have been studies demonstrating opposing results. Hisamatsu et al. did not find autoantibodies against Dsc-3 in the serum of patients with PV and PF (7). Muller et al. also reported that existing evidence on the pathogenic role of anti-desmocollin IgA or IgG autoantibodies are probably circumstantial and need to be verified by future research (8).

In the present study we did not detect anti-Dsc-3 antibodies in Greek patients with PV or PF using immunoblotting. Our results support the hypothesis that there is no pathogenic role of Dsc-3 in epidermal blistering in classic PV and PF. Very recently, Mindorf et al. concluded that, based on state-of-the-art assay systems, detection of serum IgG and IgA against Dsc has no significant role in the routine diagnosis of PV, pemphigus foliaceus, or paraneoplastic pemphigus and is only useful in patients with atypical pemphigus (9).

As reported by Duker et al., the pathophysiology of pemphigus is much more complicated than what it was believed in the past and its complexity should be further evaluated. IgA antibodies against Dsc-1, 2, and 3 could be produced separately and are not necessarily involved in the pemphigus cascade of immunological events (10).

CONCLUSION

Studies in separate ethnic groups could also contribute to thoroughly clarifying whether a possible causative role of Dsc in pemphigus may be attributed to environmental or genetic factors.

References:

Figure 1. Detection of IgG antibodies against the desmocollin-3 antigen by immunoblotting using human epidermal extract. Lane 1: anti-desmocollin-3 IgG (PROGEN, GERMANY); lanes 2, 3, 4: sera of patients with pemphigus vulgaris diluted 1:50; lane 5: sera of patients with pemphigus foliaceus diluted 1:50; and lane 6: anti-desmoglein-1 IgG (PROGEN, GERMANY).


