BRIEF ARTICLES

A Rare Transition from Pemphigus Vulgaris to Pemphigus Foliaceus Following Rituximab Therapy Confirmed by Antidesmoglein ELISA

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ABSTRACT

The phenotypic expression of pemphigus subtypes is mediated by differences in desmoglein (DSG) autoantibody profiles, a concept that is demonstrated in rare cases of transition between pemphigus subtypes. Diagnosis of transition is made on the basis of changes in classic phenotypic expression in conjugation with changes in immunofluorescence and/or antidesmoglein ELISA.

We report a 54-year-old male with a history of severe mucocutaenous pemphigus vulgaris (PV) brought into remission by treatment with systemic steroids and adjuvant rituximab infusions who re-presented approximately 1 year following steroid discontinuation with new crusted erosions covering the upper trunk and proximal extremities and notable absence of mucosal involvement. Antidesmoglein ELISA profile revealed an isolated rise in DSG-1 antibodies. Previous antidesmoglein ELISA profiles showed dual elevation in both DSG-1 and DSG-3 antibodies during active PV and absence of both DSG-1 and DSG-3 during disease remission.

The current case describes a rare transition from PV to pemphigus foliaceus (PF) following rituximab therapy as suspected clinically by classic phenotypic expression and confirmed serologically by antidesmoglein ELISA. This is only the second reported case of pemphigus transition following rituximab adjuvant therapy, and there are less than thirty cases of PV to PF transition reported in the literature. There is currently not a satisfactory explanation for the autoantibody shifting that is observed in transition between pemphigus types.

INTRODUCTION

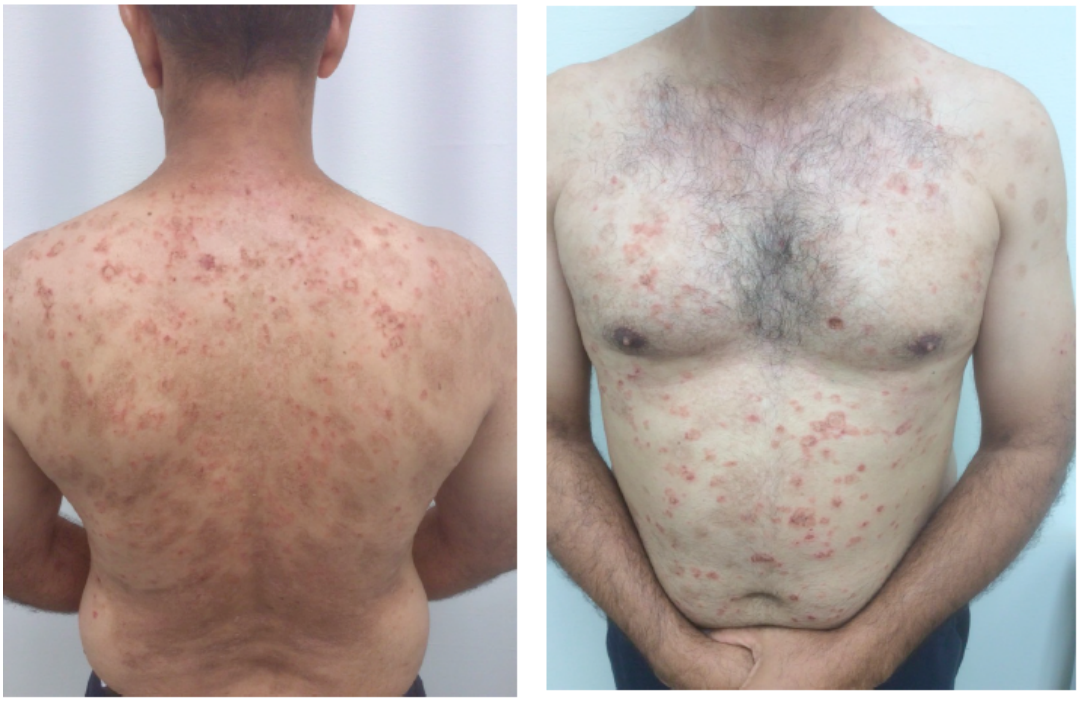
Pemphigus defines a group of blistering diseases characterized by autoimmunity against intraepidermal adhesion proteins and subsequent flaccid blister formation, two major subtypes of which are pemphigus foliaceus (PF) and pemphigus vulgaris (PV). Of these, PF is typically more benign and characterized by IgG autoantibodies against desmoglein-1 (DSG-1) with exclusive cutaneous involvement. In contrast, PV is typically more severe and characterized by IgG autoantibodies against desmoglein-3 (DSG-3) in the mucosal predominant form and against both DSG-3 and DSG-1 in the mucocutaneous form[1].

The phenotypic expression of pemphigus subtypes is mediated by differences in desmoglein autoantibody profiles[2]. This concept is demonstrated in rare cases of transition between pemphigus subtypes. Diagnosis of transition is made on the basis of changes in classic phenotypic expression in conjugation with changes in immunofluorescence and/or antidesmoglein ELISA[3-7]. In this report, we describe a rare case of transition from PV to PF following rituximab therapy confirmed serologically by antidesmoglein ELISA.

CASE DESCRIPTION

We report a 54-year-old male with a history of severe mucocutaneous PV brought into remission by treatment with systemic steroids and adjuvant rituximab infusions who re-presented with a new cutaneous eruption approximately 1 year following steroid discontinuation. Physical examination revealed crusted erosions covering the upper trunk and proximal extremities with notable absence of mucosal involvement, consistent with the PF phenotype (figures 1 & 2). Antidesmoglein ELISA profile revealed an isolated rise in DSG-1 antibodies, confirming the suspected diagnosis of PF. Previous antidesmoglein ELISA profiles showed dual elevation in both DSG-1 and DSG-3 antibodies during active PV and absence of both DSG-1 and DSG-3 during disease remission (figure 3). The patient was stabilized by Dermatology with topical clobetasol and oral doxycycline and underwent a complete four-infusion course of rituximab under the supervision of Oncology, but was ultimately lost to follow-up.

FIGURES



Figures 1 & 2: Scattered crusted erosions covering trunk and proximal upper extremities with no mucosal involvement, suggestive of pemphigus foliaceus.

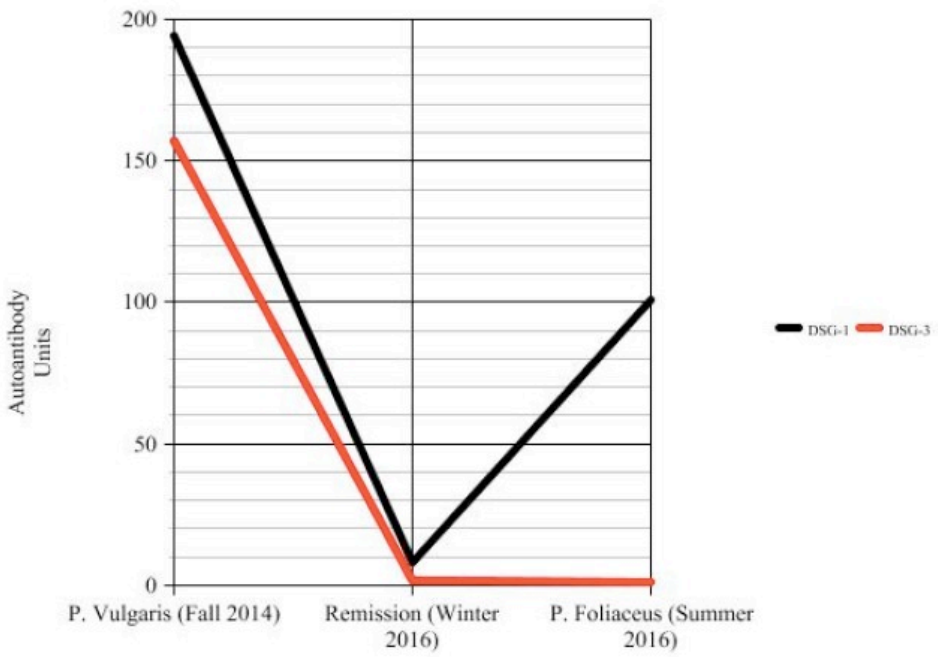


Figure 3: Rise and fall of desmoglein 1 & 3 auto-antibodies as a function of time and clinical disease appearance. Note the present of DSG-1 & 3 autoantibodies during pemphigus vulgaris disease stage, with recurrence of only desmoglein-1 autoantibodies during pemphigus foliaceus.

DISCUSSION

The current case describes a rare transition from PV to PF following rituximab therapy as suspected clinically by classic phenotypic expression and confirmed serologically by antidesmoglein ELISA. The case supports the concept that differences in desmoglein autoantibody profiles mediate phenotypic expression of pemphigus subtypes. The patient displayed the mucocutaneous PV phenotype when both DSG-1 and DSG-3 autoantibodies were expressed, while he displayed the PF phenotype when only the DSG-1 autoantibody was present. The findings in the current case are consistent with the majority of prior case reports which have found dramatic changes in DSG-1 and DSG-3 autoantibody levels upon transition between pemphigus types[3-7].

The occurrence of transition between pemphigus subtypes in the literature is infrequent, with less than 30 cases identified of PV to PF transition and even fewer cases of PF to PV transition[3-7]. Interestingly, the current case is only the second reported case of pemphigus transition following rituximab adjuvant therapy[6].

There is currently not a satisfactory explanation for autoantibody shifting involved in transition between pemphigus types. One proposed explanation is ‘epitope spreading’ in which autoreactive immune cells recognize epitopes on antigens that become exposed by prior autoantibody damage. This mechanism would theoretically support antigenicity gain involed in transition from PF to PV; however, it would not explain antigenticity loss involved in transition from PV to PF. Furthermore, epitope spreading has been shown to be rare in pemphigus patients[7]. More research. Is needed to elucidate the pathophysiology of transition between pemphigus subtypes.

Conflict of Interest Disclosures: None

Funding Sources: None

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