

LETTER

Case of a severe vulgaris and foliaceus pemphigus in a young patient treated with rituximab, with subsequent development of chronic urticaria

Dear Editor,

We are going to describe the case of a 19-year-old Caucasian girl who had been suffering from a generalized form of pemphigus since May 2017. Before this date, the patient was in good health and she was not taking any medication.

The clinical aspect of our patient was of painful scaly and crusted erosions diffused on the patient's chest, trunk, arms, and face, with no mucosal lesions. Histology showed intraepidermic, both subcorneal and suprabasal, acantholysis; IFD showed a strong positivity of the IgG autoantibodies against keratinocytes (Figure 1). These elements, the enzyme-linked immunoassay test (antibodies (AB) anti-desmoglein [DSG]-1 was 226.43 U/mL; Ab anti-DSG-3 was 115.58 with a positive cutoff of ≥ 20 U/mL) and the Western blot on serum confirmed the dual diagnosis of a cutaneous form of pemphigus vulgaris (PV) and pemphigus foliaceus (PF), justified, respectively, from the absence of mucosal involvement, from suprabasal acantholysis, the presence of both Ab anti-DSG-1 and anti-DSG-3 (cutaneous form of PV¹) and for the scaly and crusted clinical aspect with the presence of also superficial blister and subcorneal acantholysis to the histological examination (PF).

Moreover, molecular typing at medium-high resolution of locus DRB1 highlighted the presence of the DRB1*14:54 allele, belonging

to the DRB1*14:01P group, which is involved in the predisposition to pemphigus in Italian patients² and others alike, as shown by previous studies.

We know from the literature that the two main subtypes of pemphigus, PV and PF, can transit from one form to the other or vice versa and, more rarely, it is possible to find features both of PV and PF, as in the case of our patient. In 1998, Izumi et al³ described the first case of this coexistence and only four other papers involving patients with cutaneous lesions were published ever since⁴; the remaining literature (four papers more) shows patients with both cutaneous and oral mucosal involvement.⁴

The pemphigus of our patient was resistant to corticosteroid therapy (ev dosage between 0.5 and 1 mg/kg) and therapy with two repeated cycles of immunoglobulins.

Due to the severity of the clinic (Figure 2), on January 2018, the patient underwent therapy with rituximab (RTX), a monoclonal antibody targeting CD20 and increasingly used for its effectiveness on pemphigus.⁵ Two different dosing protocols of RTX are used in the literature⁶: a traditional oncologic protocol (4 weekly infusions, 375 mg/m² of body surface) and a more recent rheumatoid arthritis protocol (a single 1000 mg infusion repeated after 15 days); we chose the latter. This therapy allows a fast and complete healing from pemphigus in just a few weeks (Figure 3), with autoantibody negativization. No additional doses of RTX were administered to the patient, only a low dosage of corticosteroid therapy was maintained, as suggested by the literature.⁷

To the best of our knowledge, of all the patients described in literature with this coexistence of the two variants,⁴ our case is the first one which has been successfully treated with RTX. Moreover, at the 24-month follow-up, the patient is still in clinical and serological remission. This successful clinical outcome and the lack of relapse in a patient treated with RTX for an aggressive pemphigus could be justified by the absence of mucosal involvement.⁸

Unfortunately, in the last 6 months the patient has developed chronic urticaria (CU). The association of pemphigus or pemphigoid with autoimmune disorders in adult patients has been studied.⁹ More than 72 million of hospitalizations for pemphigus or pemphigoid were analyzed; these data show the link between pemphigus and 9 of the 29 autoimmune disorders examined. According to this paper,⁹ CU seems to be more connected with pemphigoid than pemphigus, but the authors admitted that some autoimmune comorbidities may have

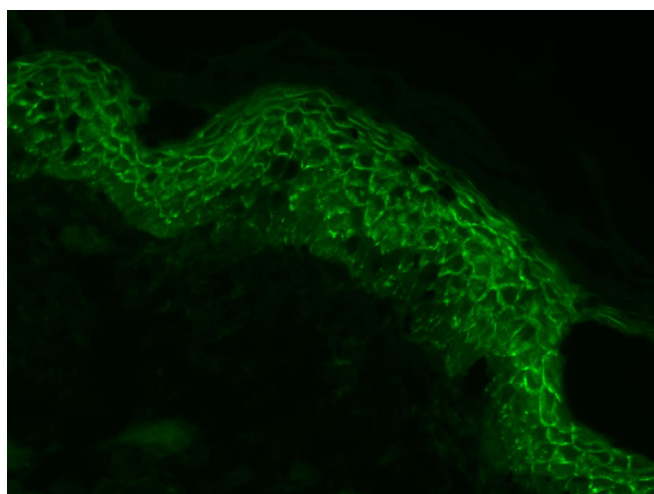


FIGURE 1 Direct immunofluorescence (DIF) showed a strong positivity of the IgG autoantibodies on keratinocyte cell surfaces in all layers of epidermis



FIGURE 2 December 2017: foliaceus and vulgaris pemphigus on the whole body, complicated by a staphylococcus infection



FIGURE 3 February 2018, 2 weeks after the beginning of rituximab: complete resolution of the disease

been misclassified (eg, urticarial pemphigoid may have been classified as CU). In conclusion, further investigations are required to better explore the link between bullous diseases and other autoimmune comorbidities. Regarding the treatment of CU, our patient is responding to H1-antihistamine. However, in the case of recurrence

of pemphigus or no longer response to H1-antihistamine, RTX may play a role in the treatment of CU by eradicating the autoantibodies produced by B cells.¹⁰

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CONFLICT OF INTEREST

none.

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