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QUIZ CASES

A man with a widespread bullous eruption

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CASE PRESENTATION

A 50-year-old man presented with a 1-month history of diffuse blisters and erosions on the trunk, limbs, hands, and feet, as well as painful erosions on the tongue and hard palate (Figure 1a–c). The patient was in good general health with no relevant past medical history. The lesions started on the hands and feet, and then spread to the mouth and to the trunk. No trigger could be identified. The routine laboratory examinations were all within normal limits. A skin biopsy was done (Figure 2a) with direct immunofluorescence (Figure 2b) and type IV collagen immunostaining (Figure 2c).

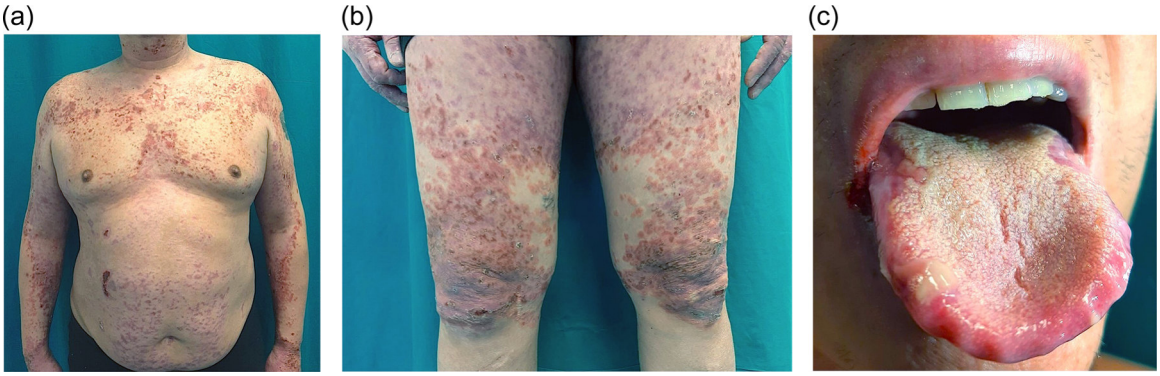

FIGURE 1 (a) Inflamed blisters and erosions on the trunk and upper arms. (b) Inflamed blisters and erosions on lower limbs. (c) Vesicles and erosions on the lateral surface of the tongue.

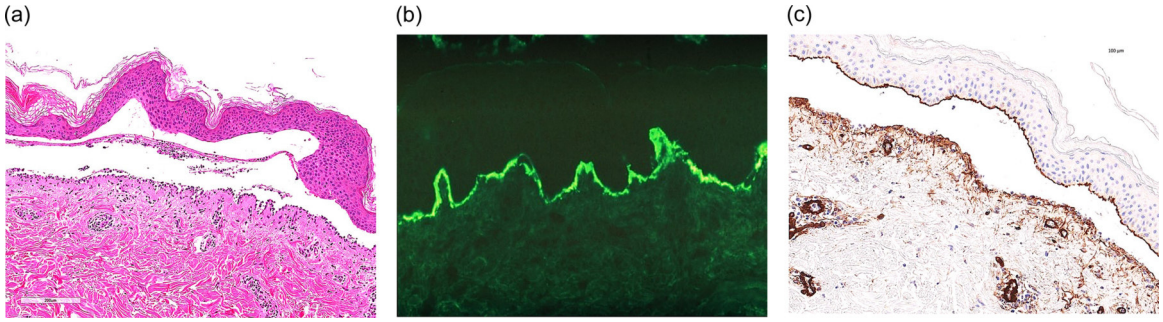

FIGURE 2

WHAT IS THE DIAGNOSIS?

Epidermolysis bullosa acquisita.

DISCUSSION

Histological examination showed the presence of a subepidermal blister with fibrin and sparse neutrophils and neutrophils in linear distribution along the dermo-epidermal junction adjacent to the blister. A mild lymphohistiocytic infiltrate in the superficial dermis with perivascular and interstitial neutrophils, was present (Figure 2a). Direct immunofluorescence showed linear deposits of IgG and C3 along the dermo-epidermal junction (Figure 2b). Moreover, type IV collagen immunostaining decorated the blister roof, consistent with a dermo-epidermal split deep into the lamina densa region (Figure 2c). The patient had high titres of serum anti-collagen VII antibodies (217.13 RU/ml; normal <20 RU/ml) detected by enzyme-linked immunosorbent assay (Euroimmun), whereas anti-BP180, anti-BP230, anti-desmoglein 1 and 3 were absent.

Epidermolysis bullosa acquisita (EBA) is an autoimmune disease, generally occurring in adulthood, characterized by a range of clinical manifestations of variable severity. The classic form of EBA is the mechano-bullous; other types are the inflammatory type, bullous pemphigoid-like EBA, mucous membrane-EBA, Brunsting-Perry type EBA and IgA-EBA.[1] The same patient may have different EBA phenotypes during the course of the disease. The involvement of the oral mucosa is common and can occur in the mouth, upper digestive and respiratory tracts, conjunctiva, and genitalia. Both on the skin and mucosae blisters tend to be localized on areas subjected to trauma, due to cutaneous and mucous fragility.[1,2] Diagnosis of EBA is based on the presence of deposits of Ig and C3 at the dermo-epidermal junction and serum auto-antibodies against collagen VII.[1]

The therapeutic approach to EBA may be challenging and the combination of different drugs is often required.[1–3] Systemic corticosteroids are the first-line treatment, with a starting dose of 0.5–2 mg/kg daily. Besides corticosteroids, colchicine and dapsone are often used to treat mild cases of EBA, while for recalcitrant, or severe cases of EBA, immunosuppressive drugs such as methotrexate, cyclosporine, azathioprine, mycophenolate mofetil or cyclophosphamide are employed.[1,2,4] Minocycline was effective in one case unresponsive to corticosteroids and cyclosporine.[5] In cases not responsive to the combination of corticosteroids and immunosuppressive drugs, IVIg can be used at a dosage of 2 g/kg/cycle for 3 days or 0.4 g/day for 5 consecutive days.[1,4,6] Rituximab is also used in monotherapy or combined with immunosuppressive drugs in severe cases of multidrug-resistant EBA.[4,7] To date, there are two protocols for the infusion of rituximab, one based on 4 weekly infusions of 375 mg/m^2 of rituximab and the other in which two infusions of 1000 mg/day are administered 14 days apart.[1] In addition, multidrug-resistant cases successfully treated with both IVIg and rituximab have also been reported.[8] Response to therapy may be different among the various types of EBA. In particular, colchicine seems to be effective in patients with classic mechano-bullous form and inflammatory variants of EBA. Systemic corticosteroids and immunosuppressive drugs may be effective in bullous pemphigoid-like EBA and in general in inflammatory forms. Dapsone has been reported to have some benefits, especially in patients with neutrophilic infiltrates.[9] IVIg success has not been correlated to EBA subtypes, whereas rituximab seems to be more effective in the mechano-bullous variant.[1]

Our patient presented with a bullous pemphigoid-like EBA with several inflammatory lesions on the skin as

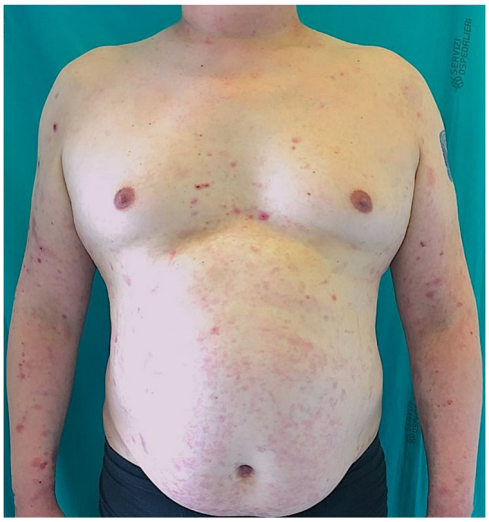

FIGURE 3 Clinical remission six months after treatment with rituximab.

well as oral lesions. Initial treatment with prednisone (0.5 mg/kg/day) plus colchicine (2 mg/day) plus IVIg (0.4 g/day for five consecutive days) was not enough to stop the emergence of new bullous lesions. Thus, rituximab intravenously was started (1 g on two consecutive administrations 15 days apart) with marked improvement after 3 months; prednisone was tapered to 5 mg/day and later withdrawn. After 6 months, the patient was in good remission (Figure 3) with only residual erythematous atrophic scars and milia. Serum anti-collagen VII antibodies dropped to 37.96 RU/ml at 3 months and were no longer detectable thereafter. Antibody levels may correlate with the clinical severity and appear to be useful to monitor disease activity.[10]

ACKNOWLEDGEMENT

None

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The patient in this manuscript has given written informed consent to publication of his case details and for images publication.

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