

EBA – A DERMATOLOGICAL CHALLENGE. CLINICAL CASE

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Summary

Epidermolysis bullosa acquisita is a rare autoimmune bullous disease, with the development of autoantibodies directed against type VII collagen. Cutaneous manifestations are heterogeneous and may be common to other bullous diseases. The classic presentation is that of a noninflammatory mechanobullous disease characterized by the development of acral blisters that occur with minor trauma and that heal with atrophic scarring, milia formation, and pigmentation changes. Skin biopsy and serologic tests are necessary to confirm the diagnosis and treatment is difficult and often unsatisfactory. We present the case of a 71-year-old female patient who was admitted to our clinic for the presence of erythematous-petechial and vesiculo-bullous lesions, which occur spontaneously or after minor trauma, disseminated throughout the body, with an evolution of over 3 years. Histopathological examinations were not specific to epidermolysis bullosa, although the clinical examination was highly suggestive. After therapeutic failure with Colchicine and Dapsone, it was decided to start treatment with Medrol with a favorable outcome after one month of treatment. Although the diagnostic criteria are not defined the clinical aspects and the evolution under corticosteroid treatment support the diagnosis of epidermolysis bullosa acquisita.

Keywords: epidermolysis bullosa acquisita, diagnosis, corticotherapy.

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Introduction

Epidermolysis bullosa acquisita (EBA) is a rare subepidermal bullous disease, of unknown etiology, with the development of autoantibodies directed against type VII collagen, an important constituent of the basement membrane [1,2,3].

It can be associated with a number of diseases such as systemic lupus erythematosus, amyloidosis, inflammatory bowel disease, lung cancer, multiple myeloma and lymphomas [1,3].

Cutaneous manifestations are heterogeneous and may be common to other bullous diseases. The classic presentation is that of a non-inflammatory mechanobullous disease characterized by the development of acral blisters that occur with minor trauma and that heal with atrophic scarring, milia formation, and pigmentation changes [1,3,4]. Cutaneous blisters may become hemorrhagic with subsequent

erosions. They are localized to trauma-prone surfaces especially the elbows, knees, and dorsal aspects of the hands, feet and toes. Clinically it is characterized by: skin fragility, bullae, post-bullous erosions caused by minor trauma, atrophic scars, milium cysts, nail dystrophies [1,3,5].

Histopathologically, there is a subepidermal cleavage, without acantholysis, with minimal inflammatory infiltrate. Direct immunofluorescence shows IgG deposits distributed in a continuous linear pattern along the epidermal basement membrane. Rarely, linear deposits of C3, IgA or IgM are found [1,2,3].

By standard indirect immunofluorescence, circulating epidermal basement membrane antibodies can be detected in ~ 50% of patients with EBA. These are primarily of the IgG class, but circulating IgA autoantibodies have also been reported [1].

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Immunoelectron microscopy has long constituted the “gold standard” for diagnosing EBA, especially when circulating autoantibodies are absent and therefore cannot be characterized by IIF microscopy, immunoblotting studies, or ELISA [1,3,6].

Electron microscopy studies of fresh vesicles demonstrate that dermal-epidermal cleavage occurs within the sublamina densa zone. In addition, a reduction in the number of anchoring fibrils can be observed [1,2,3,6].

The treatment of EBA is difficult and often unsatisfactory. Systemic corticosteroids and immunosuppressive agents, such as azathioprine, methotrexate, mycophenolate mofetil, cyclophosphamide, or, more recently, rituximab, are sometimes helpful in controlling the BP-like variant of EBA, which may go into remission [1,3,4,5].

Colchicine, dapsone, gold salts and cyclosporine may also have some benefits [1,3,4]. In patients with severe EBA unresponsive to conventional immunosuppressive therapy, IVIg may be helpful [1,7].

Case report

A 71-year-old female patient, with no notable personal pathological history, is admitted to the clinic for the presence of erythematous-petechial and vesiculo-bullous lesions, disseminated

throughout the body, with an evolution of over 3 years. Lesions occur spontaneously or after minor trauma (pressure, friction). Anamnestic, the patient reports erosions in the oral mucosa, but no lesions were found at the time of examination. Familial antecedents fail to reveal a history of any bullous disease. The general clinical examination on admission showed a normal-weight patient, cardio-respiratory normal, without other pathological changes.

Prior to the presentation at the clinic, the patient underwent investigations for possible associated autoimmune diseases that were negative and also for neoplasms and blood dyscrasias - subsequently refuted.

Biologically it was found: normocytic normochromic anemia, low IgG and IgM, low total serum proteins, proteinuria.

Blood tests were taken for other possible autoimmune diseases, including SLE that were negative. Type VII collagen-specific auto-antibodies were negative.

Outpatient histopathological examination showed subepidermal vesiculo-bullous dermatitis, with infiltrates with lymphocytes, histiocytes and rare polymorphonuclear leukocytes in the underlying dermis. The cleavage space spreads to the reticular dermis, which has a hyaline appearance and the roof of the vesiculo-



Figure 1. Erythematous-petechial and vesiculo-bullous lesions localized to trauma-prone surfaces (dorsal aspect of the hand).



Figure 2. Erythematous-petechial and bullous lesions.



Figure 3. Before corticotherapy.



Figure 4. After corticotherapy.

bullous lesion includes the epi-dermis, the basement membrane of the epidermis and fibrin deposits. All these histopathological changes suggested epidermolysis bullosa, but without all the diagnostic criteria.

A new skin biopsy was taken in our clinic, and the histopathological result showed small foci of subepidermal cleavage, minimal perivascular inflammatory lymphocytic infiltrate in the superficial dermis and edema in the papillary dermis, while the direct immunofluorescence tests performed did not show the presence of IgG, IgA, IgM and C3 deposits. In conclusion, histopathological examinations were not specific to epidermolysis bullosa, although the clinical examination was highly suggestive.

The patient underwent previous treatment with Colchicine for 3 months, but without therapeutic benefit, followed by Dapsone, with a favorable evolution, but in which she developed anemia with methemoglobinemia, reason why the administration was interrupted.

It was decided to start treatment with Medrol 32 mg/day, antiseptic and healing dressings with a favorable evolution after 1 month of treatment. The patient also entered the rare disease program for a better therapeutic conduct.

Discussions

Epidermolysis bullosa acquisita may be confused with inherited dystrophic EB, bullous pemphigoid, cicatricial pemphigoid, bullous drug eruption, bullous systemic lupus erythematosus, porphyria cutanea tarda, pseudo-porphyrria or rare variants of porphyria (e.g. porphyria variegata) [1,2,3]. The presence of lesions mainly in the hands may mimic porphyria cutanea tarda, but the latter can easily be excluded by increased urinary uroporphyrin levels [1]. Bullous systemic LE usually presents as a widespread, inflammatory subepidermal blistering condition and less frequently, as a mechanobullous eruption with milia and scarring, located especially in the photoexposed areas. It also has specific immunological changes. EBA in adults has a poor response to treatment, whereas in patients with bullous systemic lupus erythematosus a dramatic improvement is observed after initiation of therapy with dapsone, azathioprine, corticosteroids or plaquenil [1]. Regarding bullous pemphigoid, direct immunofluorescence reveals linear deposits of IgG and C3 in the basement membrane region, on electron immunomicroscopy the pemphigoid antigen is found in the lamina lucida, and ELISA shows

anti-desmoglein I and III antibodies [1,3]. In the case of bullous drug eruption, we find a history of ingestion of drugs and coexistence with simple papular or cockade lesions [1,3].

Although the diagnostic criteria are not defined (type VII collagen-specific auto-

antibodies negative, DIF negative) the clinical aspects and the evolution under corticosteroid treatment support the diagnosis of epidermolysis bullosa acquisita, this being the peculiarity of this case. We are currently supervising the patient in our service.

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Conflict of interest
NONE DECLARED

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