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Casos Clínicos

Linear IgA dermatosis induced by captopril

Dermatosis IgA lineal

N. Menezes[1], P. Varela[1], A. Furtado[2], G. Mota[1], A. Baptista[1]
[1]Serviço de Dermatologia e Venereologia. [2]Serviço de Anatomia Patológica. Centro Hospitalar de Vila Nova de Gaia/Espinho

Correspondencia:
N. Menezes
Serviço de Dermatologia e Venereologia
Centro Hospitalar de Vila Nova de Gaia/Espinho
Rua ConceiÇão Fernandes
4430 VN Gaia
Tel.: +351936262253
Fax: +351227832755
e-mail: nuno.menezes.dermatologia@gmail.com

Summary
Linear IgA dermatosis is an auto-immune bullous disease characterized by linear IgA deposition in the basement membrane. Most cases are idiopathic but some are drug-related. These lack mucosal involvement, have spontaneous remission and IgA deposition clearance at the basement membrane after drug cessation.
A 89 year-old patient presenting with symmetric, itchy, tense and translucent bullous lesions located on the upper limbs and abdomen with 2 weeks evolution is reported.
The patient had started captopril regimen two months before.
The diagnosis was histologically confirmed. The patient started prednisolone and changed the hypertension medication from captopril to amlodipine. After 4 weeks an almost complete resolution of the lesions was observed. Prednisolone was slowly tapered and there have been no relapses for almost 2 years.
Skin autoimmune diseases are almost always idiopathic. However some cases can be induced or aggravated by exogenous factors including drugs, trauma, infections, vaccinations, radiographs and UV radiation[1]. Linear IgA bullous dermatosis (LABD), a rare, acquired, autoimmune, heterogeneous subepidermal blistering disorder, is no exception[2]. Patients may present with combinations of annular or grouped papules, vesicles, and bullae. Typically, these lesions are distributed symmetrically on extensor surfaces including elbows, knees, and buttocks[2].

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Key words: *Linear IgA dermatosis, captopril.*

Resumen
La dermatosis IgA lineal es una enfermedad ampollosa autoinmune caracterizada por la presencia de depósitos IgA lineales en la membrana basal de la epidermis. Muchos casos son idiopáticos sin embargo otros están relacionados con fármacos, no afecta a las mucosas. Así se ha visto que al dejar dichos fármacos se produce una remisión espontánea de los depósitos de la membrana basal.
Hemos tenido ocasión de estudiar un varón de 89 años que presentaba lesiones ampollosas traslúcidas y tensas, pruriginosas, y de distribución simétrica, en extremidades superiores y abdomen. Pocos meses antes había comenzado tratamiento con captopril.
El estudio histológico confirmó el diagnóstico y fue tratado con prednisona sustituyendo el captopril por amlodipina. Cuatro semanas mas tarde se observó una remisión prácticamente completa de sus lesiones. La prednisolona fue retirada de forma paulatina y no ha presentado recidivas después de dos años.

Palabras clave: Dermatosis IgA lineal, captopril.

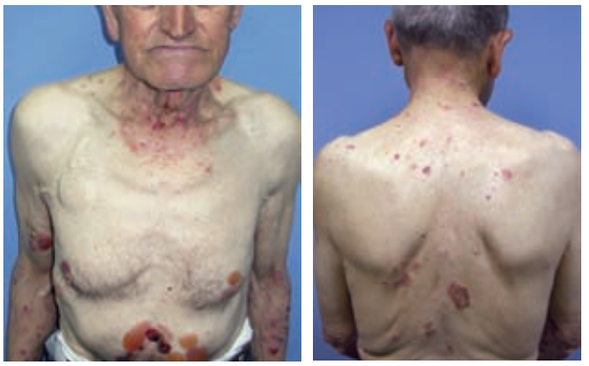

Figure 1. *Bullous lesions involving the upper limbs and the trunk.*

Case report

A 89 year-old patient presuming by symmetric, itchy, tense and translucent bullous lesions located on the upper limbs and abdomen with 2 weeks evolution is reported. The lesions first started around the umbilicus and distal parts of upper limbs with progressive spreading to the back and thoracic region (Figure 1). An intense burning sensation was described by the patient preceding the appearance of new lesions. The patient was taking captopril for 2 month due to hypertension.

Biopsy specimens were obtained from lesional and perilesional skin for histopathologic examination with hematoxylin-eosin staining and direct immunofluorescence (IF). A subepidermal blister with abundant fibrine and eosinophils in the blister fluid was observed. In the papillary dermis a sparse mixed inflammatory infiltrate (neutrophils and eosinophils) was present (Figure 2).

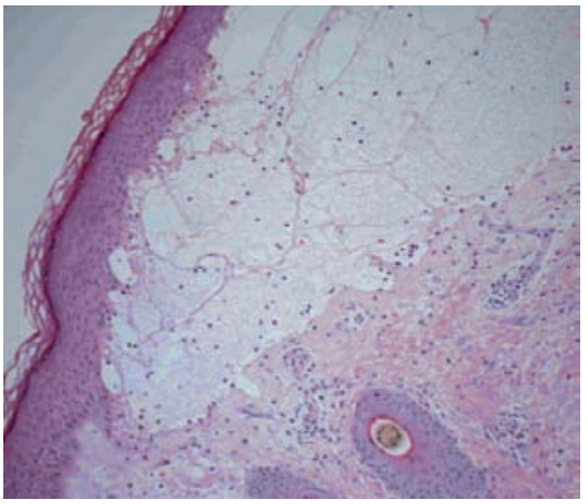

Figure 2. *Subepidermal blistering with abundant fibrine and eosinophils in the blister fluid. A sparse mixed inflammatory infiltrate (neutrophils and eosinophils) was present in the papillary dermis. (Hematoxilin-eosin 4x).*

Sections 4μm-thick were prepared and stained with fluorescein isothiocyanate-labeled antibodies to human IgG, IgM, IgA and C3. The direct IF showed continuous linear deposits of IgA at the basement membrane but no evidence of IgG, IgM and C3 (Figure 3).

Therapy with prednisolone (1 mg/kg/day) was started, suspecting of a bullous disease and the hypertension medication was changed from captopril to amlodipine.

After 4 weeks an almost complete resolution of the lesions was observed and prednisolone was slowly tapered for three month period.

After complete resolution and prednisolone withdrawal a new skin biopsy was performed which revealed a normal skin with a negative direct IF. After 2 years of follow-up the patient is without lesions and had no new flares (Figure 4).

Comment

LABD is a rare subepidermal autoimmune bullous dermatosis almost always idiopathic but several drugs medications were implied as etiologic factors. Vancomycin is the most frequent agent reported[3-5], but other drugs with the potential to induce LABD include diclofenac , furosemide , captopril, lithium, cefamandole, somatostatin[3] phenytoin, trimethoprim-sulfamethoxazole, rifampicin, IL-2, interferon gamma, amiodarone, penicillin G, carbamazepine, piroxicam, atorvastatin and topical iodine[3, 6-19].

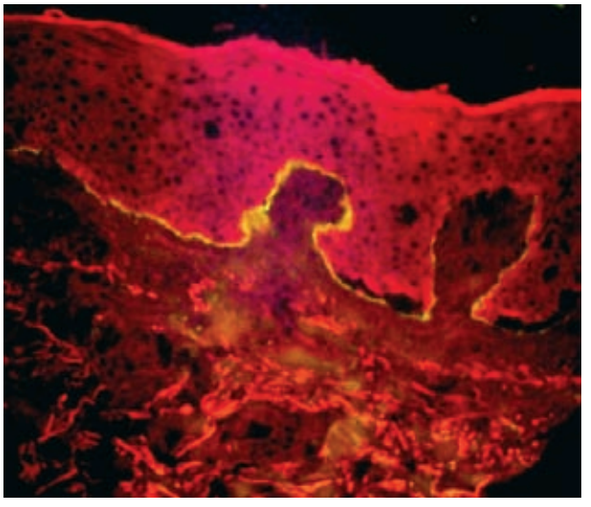

Figure 3. *Direct IF showed continuous linear deposits of IgA at the basement membrane but no evidence of IgG, IgM and C3.*

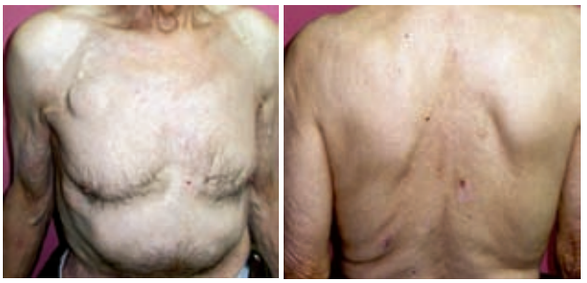

Figure 4. *The patient without lesions.*

Captopril, an angiotensin-II-converting enzyme inhibitor, is a largely used antihypertensive agent that has been associated with a wide variety of cutaneous reactions, including angioedema, urticaria, lichenoid eruptions and pityriasis rosea-like rash. Despite being already established as an etiologic factor to pemphigus, it's role as an inducer of other bullous disease has not been frequently reported[20-25]. There are very few case reports from LABD induced by captopril, the last one being from 1996.

Both idiopathic and drug-induced LABD are heterogeneous in clinical presentation[26].

A spectrum of clinical presentations has been described regarding this disease; patients have lesions similar to dermatitis herpetiformis or bullous pemphigoid, but the unique immunofluorescence pattern with linear IgA deposition along the basement membrane allow the diagnosis[3]. Most typically, tense vesicles are arranged in herpetiform, sausage-like, rosette-like or arciform patterns on erythematous or normal-appearing skin. Histology usually reveals subepidermal bullae and an inflammatory infiltrate of the upper dermis, sometimes with microabscesses. Direct IF is a useful tool to allow the differential diagnosis between bullous diseases. Indirect immunofluorescence in LABD only occasionally reveals circulating IgA anti-basement-membrane-zone antibodies[21].

There are reports of unrelated antibodies in LABD (detected by indirect IF), to a 285 Kd antigen in the lamina densa and sublamina densa regions, a 250 Kd dermal antigen corresponding to collagen VII of anchoring fibrils, BP230 antigen and a 97 kd antigen in the upper lamina lucida which is believed to be an ectodomain of the BP230 antigen produced by proteolysis[3, 27-29], but direct IF remains the gold standard for diagnosis.

However, drug-induced LABD, according to Kuechle et al. appears to differ from idiopathic cases in some aspects, namely lack of mucosal involvement, spontaneous remission after drug cessation and IgA deposition clearance at the basement membrane once the cutaneous lesions resolve[3]. However these clues for a drug-induced IgA bullous dermatosis can't be viewed in a dogmatic way, because in a literature review conducted by Palmer, 13 of 29 patients with LADB drug-induced had mucosal involvement[27].

Our case lacked mucosal involvement and had a significant improvement of the lesions after suspicious drug withdrawal. We also performed a skin biopsy after dermatosis resolution which was normal, with a negative direct IF to all antibodies tested. This together with the time relationship between start of captopril intake and the appearance of the lesions, despite the absence of a drug rechallenge, make us believe this is a case of drug induced LABD.

In drug-induced cases the withdrawal of the offending agent normally induces rapid resolution of the dermatosis. However some authors treat actively the disease with the objective of a more rapid remission[3, 28]. In our case due to the pemphigoid-like presentation corticosteroids were started and slowly tapered. After that there were no flairs, being without lesions for three years now.

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