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Etoricoxib-Induced Linear IgA Bullous Dermatosis

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ABSTRACT: Linear IgA bullous dermatosis is a rare subepidermal bullous disease that can occur idiopathically or to be drug-induced. The disease affects both the skin and mucous membranes in children and adults. Drug-induced linear Ig A bullous dermatosis occurs more often in elderly patients who suffer from various chronic and systemic diseases. Among the most frequently reported medications causing the disease are non-steroidal anti-inflammatory drugs, antibiotics, anticoagulants, statins, ACE-inhibitors. In this report, we present a case of etoricoxib-induced linear Ig A bullous dermatosis in a woman with no known comorbidities at the time of hospitalization.

KEYWORDS: Linear IgA bullous dermatosis, etoricoxib, drug induced dermatosis.

INTRODUCTION

Linear IgA bullous dermatosis (LABD) is characterized by linear deposits of IgA along the dermoepidermal junction seen on direct immunofluorescence (DIF) assay. Very rarely, the test may demonstrate IgG, less often, IgM antibodies or C3 protein in the complement system in the pathologically involved area. It is a relatively rare disease with an incidence of about 0,5 cases per million population (1). Both children and adults can be affected by the disease. In children, the onset of the disease is usually in preschool age - around 4,5 years and is known as “chronic bullous dermatosis of childhood”. In elderly patients, the onset of the disease is usually after 60 years of age. Because of the increased comorbidity in this age group and more frequent medication intake, drug-induced linear Ig A bullous dermatosis (DILABD) should be carefully considered. Polycyclic vesicular lesions with a centrally located crust called “a string of pearls” are more characteristic in children, whereas skin lesions in adults are polymorphic, sometimes mimicking toxic epidermal necrolysis (TEN) (2,3,4,5). Despite the different clinical onset and presentation, it is considered that the pathogenetic processes occurring in the two groups of patients are identical. In an etiological aspect, it is also believed that there are no significant clinical and pathophysiological differences between idiopathic and drug-induced LAD (6). Among the most frequently reported medications causing the disease are antibiotics, non-steroidal anti-inflammatory drugs, anticoagulants, statins, ACE-inhibitors. For the first time, the idiopathic form of the disease was described in the seventies of the last century (7), and the DILABD, which developed after taking diclofenac - in 1981 (8). In this report, we present a case of a DILABD after taking etoricoxib for low back pain after vigorous physical activity in a 65year-old woman with no established comorbidities until the time of hospitalization. In the scientific literature search, we did not find any other case of LABD triggered by etoricoxib.

PRESENTATION

We present a case of a 65-year-old woman who, until the time of hospitalization, had no established chronic diseases. Two weeks before hospitalization, for low back pain after increased physical activity, the woman took an etoricoxib tablet. Two days later, intense itching appeared, initially on the skin of the lower extremities and later on the torso and upper extremities (Fig.1). A small, intensely itchy blister developed on the right lower leg, which the patient interpreted as a thermal burn and treated topically with Deflamol (retinol palmitate/ergocalciferol) ointment without much effect. In the following days, similar changes appeared on the skin of her upper limbs, for which she visited a dermatologist. Therapy with Oxycort (oxytetracycline hydrochloride / hydrocortisone) - topical and levocetirizine once daily for 7 days was started, but therapeutic effectiveness was again lacking and new rashes appeared, on the torso and in the oral cavity. On admission, the patient was in a preserved general condition. The pathological changes were disseminated on the skin of upper and lower limbs, torso and oral mucosa. Multiple extensive, hemorrhagic loose blisters were seen on the extremities, single smaller and more tense blisters were visualized on the chest, one oval erosion was found on both sides of the oral cavity. Fetor ex ore was missing.

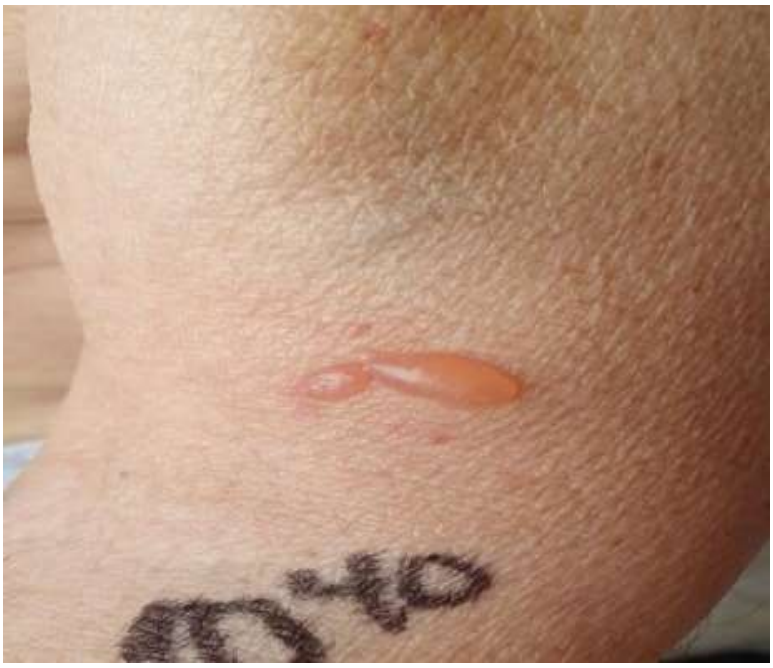

Fig.1 Blister on ventral surface of right antebrachium presenting "string of pearls" symptom.

The blood count revealed iron deficiency anemia (Hb 105,0 g/L, Er 3,81 10*12/L, HCT 0,33 L/L, Fe 11,1 umol/L) for which the patient was referred to a specialist for diagnostic clarification of the condition. No pathological deviations were found during the performed imaging studies - echoscopy of the abdominal cavity, X-ray of the lungs, in order to rule out an underlying malignant process.

A 4 mm punch biopsy was performed from a bullous lesion located on the left forearm. The morphological result of the histological preparation establishes a strip of skin of multilayered squamous epithelium, type of epithelium with a subepidermal bulla, scanty lymphoplasmatic infiltrates in the superficial dermis, solar elastosis (Fig.2). Direct immunofluorescence demonstrated linear deposition of IgA, IgM, and C3 at the dermo-epidermal border (Fig.3).

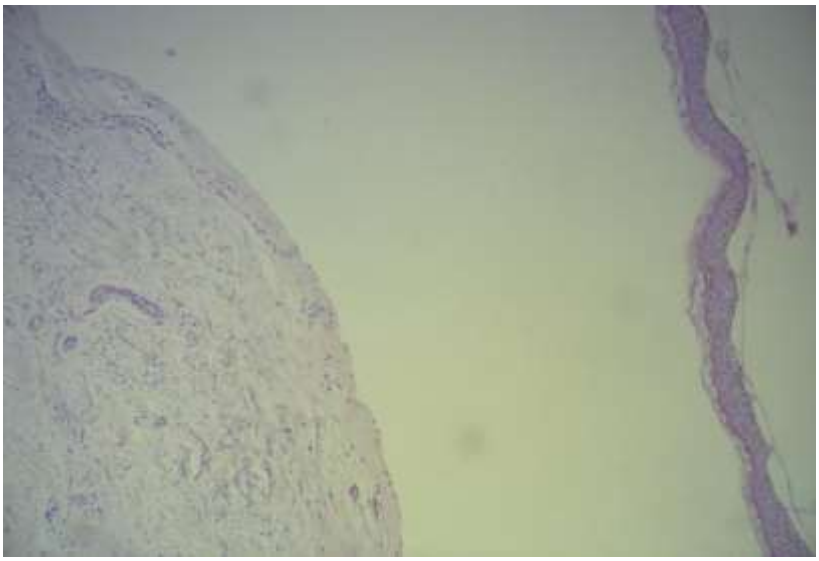

Fig.2 A subepidermal bulla, scanty lymphoplasmatic infiltrates in the superficial dermis, solar elastosis.

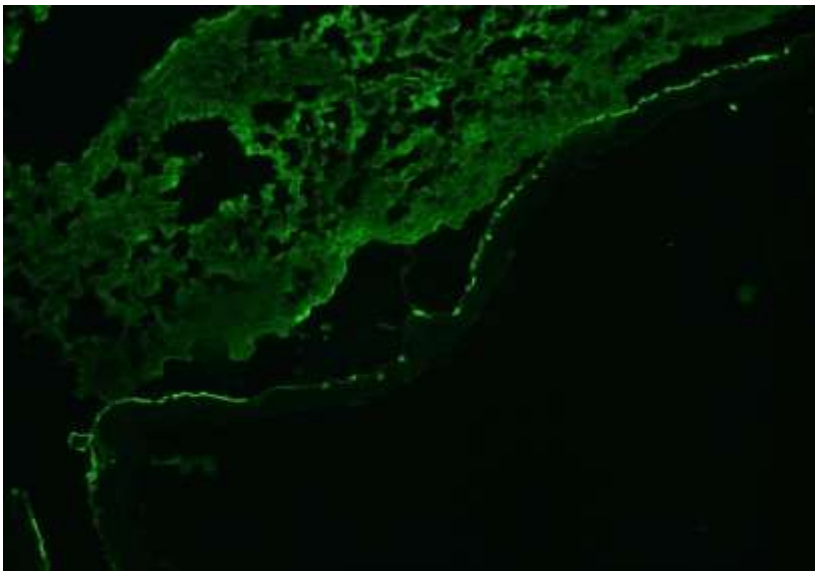

Fig.3 Direct immunofluorescence demonstrated linear deposition of IgA at the dermoepidermal border.

After the diagnosis of linear IgA bullous dermatosis was made, therapy was started with 80 mg of intravenous methyprednisolone daily, H-2 receptor blocker - famotidine 20 mg - twice daily orally, antihistamine - chloropyramine hydrochloride - once in the evening, intramuscularly. Topical therapy included evacuation of the bullous contents without breaking open the blisters, liniment with getnamicin and methylprednisolone. And for the oral mucosa - ex tempore form of nystatin and glycerin - 3-4 times a day for gagging. The therapeutic course lasted 3 weeks, gradually establishing a dose of methylprednisolone 4 mg tablets - 12 mg twice a day for 1 month, levocetirizine - 5 mg daily.

In the course of treatment, the formation of new bullous lesions stopped. The available ones started to soak in and dry out. They covered themselves with delicate squamous crusts and gradually began to peel and the formed shallow erosions to epithelize. At the follow-up visit, residual mildly erythematous tender macules were found in the areas with changes. The dose of methylprednisolone tablets was reduced to 8 mg twice daily for a month, levocetirizine 5 mg daily was continued. The patient is subject to follow-up in order to prevent unwanted lesions.

DISCUSSION

We present a case of a 65-year-old woman diagnosed with DILABD. This is a rare autoimmune bullous disease in which the clinic is dominated by the presence of tense vesicles and bullae, arranged as "a string of pearls" - more often in children or as polymorphic, sometimes mimicking toxic epidermal necrolysis blisters accompanied by itching and pain in adults. The pathogenic substrate of the dermatosis is the formation of autoantibodies (IgA, sometimes IgG, IgM or C3 protein in the complement system) directed against lamina lucida, sublamina densa, or both locations simultaneously (97- and 120-kd antigen fragments of BPAg2) (9). The disease occurs spontaneously or as a result of an inducing factor - a drug. In the medical literature, vancomycin is described as the most common triggering factor, as well as its combined use with penicillins, fluconazole, third generation cephalosporins, quinolones. Non-steroidal anti-inflammatory drugs can also cause the development of DILABD, with diclofenac and naproxen being among the most frequently reported (10, 11). In our case, the patient developed his complaints two days after taking etoricoxib for low back pain.

CONCLUSSION

We presented a case of a rare autoimmune dermatosis confirmed histologically and immunologically, provoked by taking the nonsteroidal anti-inflammatory drug etoricoxib. The severe and prolonged course of the disease is a reason for the medication to be added to the list of potential adverse events in the Summary of Product Characteristics for etoricoxib.

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