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Epidermolysis Bullosa Acquisita Mimicking Linear IgA Bullous Disease in a 5-year-old Child

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ABSTRACT We present a case of a 5-year-old child with epidermolysis bullosa acquisita, clinically resembling linear IgA bullous disease. The case demonstrates that autoimmune bullous dermatoses in childhood may show a clinical overlap, which makes the diagnosis based on clinical features highly unreliable. Specific immunofluorescence and immunoserological tests are crucial for precise diagnosis – in our case circulating antibodies against collagen VII were detected using ELISA and indirect immunofluorescence on transfected cells. The disease was treated with systemic and topical steroids with excellent results.

KEY WORDS: epidermolysis bullosa acquisita, childhood, linear IgA dermatosis, immunofluorescence

INTRODUCTION

Autoimmune bullous dermatoses (AIBDs) in childhood show a significant clinical overlap, which makes the diagnosis based on clinical features highly unreliable. Immunofluorescence and immunoserology tests to determine autoantibody specificity are therefore essential in establishing the correct diagnosis.

Epidermolysis bullosa acquisita (EBA) is an acquired autoimmune bullous dermatosis characterized by subepidermal bullae formation, mediated by autoantibodies against type VII collagen (Col VII). EBA is very rare in childhood and can exhibit variable clinical phenotypes, mimicking other AIBDs such as linear IgA dermatosis (LAD)(1-3), bullous pemphigoid (BP) (4), or even mucous membrane pemphigoid (MMP) (5). The unlikelihood of EBA in childhood makes the clinical diagnosis in such cases almost impossible.

CASE REPORT

A 5-year-old girl presented with a pruritic blistering eruption lasting 2 months that had not responded to previous therapy with antiviral and antibiotic agents. No trigger of the condition could be identified. She was otherwise healthy and had not been on any medications prior to the onset of the skin disease.

Physical examination revealed widespread polymorphic vesiculo-bullous lesions forming plaques with an annular, concentric, and serpiginous pattern of distribution over the face, trunk, and extremities (Figure 1). The blisters ruptured, leaving behind erosions and crusts. There was no mucosal involvement. Based on the patient's age and the clinical picture with a characteristic "string of pearls" sign, a preliminary diagnosis of LAD was established.

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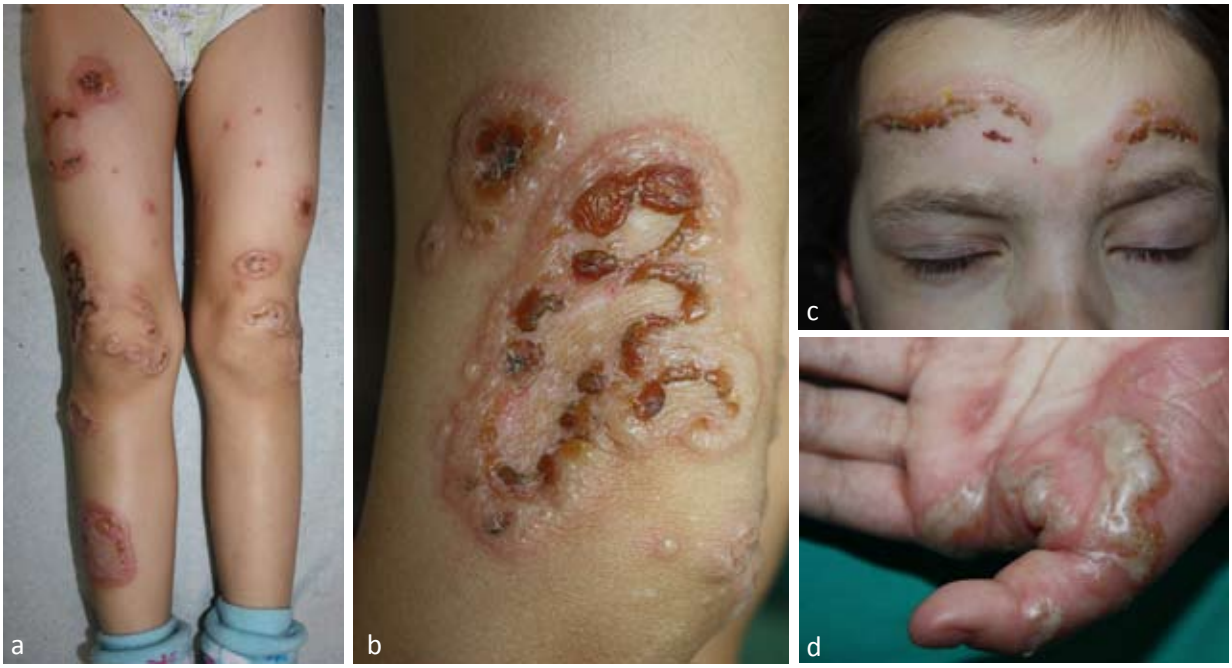

Figure 1. Widespread polymorphic vesiculo-bullous lesions forming plaques with an annular, concentric, and serpiginous pattern of distribution over the face and extremities.

Histology of a vesicle showed a subepidermal blister with dense mixed inflammatory infiltrate in the upper dermis. Direct immunofluorescence on perilesional skin revealed linear deposits of IgG (+++), IgM (+), and C3 (+++) along the basement membrane zone (BMZ) (Figure 2). U-serrated pattern of IgG and C3 deposition could be observed. The patient's serum was positive for dermal type IgG anti-BMZ antibodies by indirect immunofluorescence on salt-split skin substrate (IIF SSS). Circulating antibodies to the non-collagenous (NC1) domain of type VII collagen were detected using ELISA (44 RU/mL; cut-off value 20 RU/mL) and IIF on transfected cells (BIOCHIP, Euroimmun, Medizinische Labordiagnostika AG, Lübeck, Germany). ELISA for detecting circulating antibodies to BP180 was negative. Based on these findings, the diagnosis of EBA was established.

Treatment with oral methylprednisolone at an initial dose of 12 mg once daily and subsequent reduction over a period of 3 months, plus topical steroids, lead to complete resolution of the eruption with transitory milia formation and residual hyperpigmentation. One year later, the child was clinically healthy, without any cutaneous or systemic complaints.

DISCUSSION

EBA is a rare condition. The average age of onset is around 40 years, and women are more commonly affected (6). The condition is even rarer in childhood, although several cases have been reported in recent years (7-12).

Classical EBA presents with formation of spontaneous or trauma-induced non-inflammatory vesiculo-bullous skin lesions, which resolve with atrophic scars and milia. Skin fragility is a typical feature with distribution of the blisters on the extensor surfaces of the arms and hands, as well as on the elbows, knees, sacrum, and soles of the feet. Childhood EBA can be clinically indistinguishable from other subepidermal AIBDs, requiring a combination of diagnostic methods to provide a sensitive and reliable diagnostic algorithm in routine practice.

Direct IF is the "gold standard" test to diagnose subepidermal AIBDs by demonstrating linear deposition of immunoglobulins and C3 at the BMZ. IgA at the BMZ is found in LAD, which is the most common AIBD in childhood. IgA-mediated EBA has also been described in children (5,13), which further highlights the need for more specific tests to establish the correct diagnosis in subepidermal AIBDs. In our case, despite the clinical resemblance to LAD, the immunological process was found to be IgG-mediated. Deposition of IgG points to a diagnosis of BP or EBA without differentiating between the two conditions.

Different immunodeposition patterns have been suggested to distinguish collagen type VII targeting bullous diseases from other AIBD (14). An n-serrated pattern was found in BP, MMP, anti-laminin 332 pemphigoid, anti-p200 pemphigoid, and LAD, corresponding with depositions located in hemidesmosomes, the lamina lucida, or lamina densa. However, the u-serrated staining pattern was detected in EBA

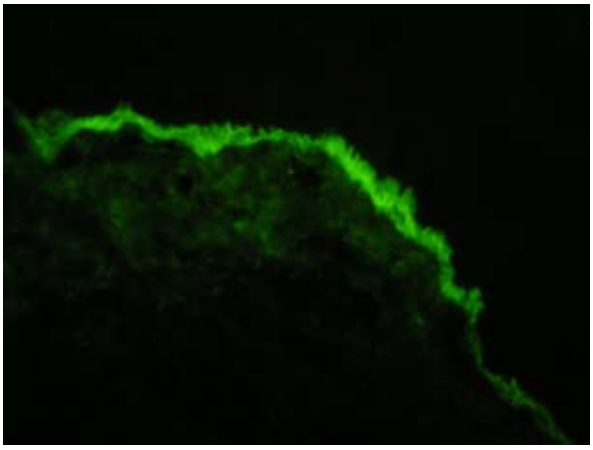

Figure 2. Direct immunofluorescence – linear deposits of IgG (+++) along the basement membrane zone (BMZ).

and bullous systemic lupus erythematosus, corresponding with the ultralocalization of type VII collagen in the sublamina densa zone (14). Nevertheless, these patterns are often difficult to interpret and other methods are needed for more precise diagnosis.

On IIF SSS, patients with EBA demonstrate immune deposits on the dermal side of the artificial blister ("floor pattern"), whereas the deposits are found on the epidermal side ("roof pattern") in BP and LAD (10). This technique, however, does not distinguish EBA from other "floor" binding diseases such as anti-p200 pemphigoid and anti-laminin 332 pemphigoid (10).

A sensitive enzyme-linked immunosorbent assay (ELISA) has been developed using recombinant proteins to detect autoantibodies against collagen VII (15). The main antigen epitopes in EBA are located on the non-collagen domain 1 (NC1) of collagen VII, but other potential antibody targets have been found. ELISA has been accepted as an alternative to immunoelectron microscopy in the diagnosis of the disease. Despite the high sensitivity of the method, most ELISA kits show some limitations in detecting antibodies against the NC1 domain of collagen VII, which can lead to false negative results when other regions of the molecule are targeted.

A new diagnostic method for IIF on Col VII transfected cells is also available. We used both this test and ELISA to find circulating anti-collagen VII NC1 antibodies in our patient.

CONCLUSION

Adult EBA is a chronic condition, and treatment is sometimes difficult and disappointing. In more resistant cases, systemic steroids, often in combinations with cyclophosphamide, azathioprine, or methotrexate, can have little effect on the condition. Similarly to our case, childhood EBA is characterized by better overall prognosis and responds well to dapsone or/and lower doses of prednisolone (3,14).

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