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Linear IgA Bullous Dermatosis Associated with Ulcerative Colitis in a 14-Year-Old Boy: A Case Report

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Abstract

Introduction: Linear immunoglobulin A bullous dermatosis (LABD) is a rare, heterogeneous, autoimmune blistering skin disorder that can be associated with other autoimmune conditions.

Case presentation: We describe the case of a 14-year-old Italian boy with previously diagnosed ulcerative colitis who presented a severe LABD well controlled after appropriate medical therapy and in total remission after a follow-up of one year.

Conclusion: Our case shows that LABD can occur in adolescent with ulcerative colitis and can be successful treated with appropriate medical therapy avoiding bowel surgery. A longer follow-up and a larger sample of patients would be of critical importance to detect long-term efficacy of dapsone and to identify responders and non-responders LABD patients.

Keywords: Linear IgA bullous dermatosis (LABD); Ulcerative colitis (UC)

Abbreviations: LABD: Linear Iga Bullous Dermatosis; UP: Ulcerative Proctitis; GCS: Glasgow Coma Scale; CRP: Reactive Protein C; ESR: Erythrocyte Sedimentation Rate; metHB: Methemoglobin

Introduction

Linear immunoglobulin A bullous dermatosis (LABD) is a rare, heterogeneous, autoimmune blistering disorder. The etiology of LABD is not fully understood and international accepted diagnostic criteria are lacking [1]. However, diagnosis is mainly based on a combination of clinical, histopathological and immunologic parameters.

Different disorders have been associated with LABD, malignant diseases as non-Hodgkin lymphoma, lymphocytic leukaemia and bladder cancer but also ulcerative colitis and systemic lupus erythematous [2]. The coexistence of malignancy and LABD cannot be defined as a true paraneoplastic syndrome since the two pathologies seldom follow a parallel course. Ulcerative colitis (UC) may present with gastrointestinal symptoms and skin involvement mostly related to pyoderma gangrenosus and eythema nodosum. The first case of LABD in a patient with dates back to 1992 [3]. Since then nearly 20 cases have been published with improvement reported in a few cases only after colectomy. Recently, a case of a 13-year-old male patient, with an 11-month history of ulcerative colitis, who developed linear IgA dermatosis have been reported [4]. The patient experienced unsatisfactory partial control of skin lesions and intestinal symptoms despite the use of adalimumab, mesalazine, prednisone and dapsone. After total colectomy, he presented complete remission of skin lesions with no need of medications during two years of follow-up.

We describe the case of a teen-ager with ulcerative colitis and LABD, not responsive to steroid treatment but well controlled after dapsone and in total remission after six-month of follow-up.

Case Report

A 14-year-old Italian boy with a previous diagnosis of distal UC (with only rectum involvent) was admitted to our department for the appearance of mild painful, tense and flaccid bullae and tense vesicles filled with clear fluid, with a haemorrhagic component in a few lesions, diameter ranging from 1 cm to 10 cm covering nearly the total surface of the body skin. There was neither hitchy nor involvement of oral/anal mucosae and conjunctiva. The patient's hands and feet were spared, as well as oral mucosa and conjunctiva. Lower extremities were edematous. Blood pressure, cardiac and respiratory rate, Glasgow Coma Scale were normal. Weight 54 kg (50°P), height 165 cm (50°P to 75°P) and body temperature was 38.8°C. Blood tests showed neutrophilic leucocytosis WBC (15950/mmc, N 10110/mmc), thrombocytosis (PLT 863000/mmc), increased inflammatory markers (CRP=105.2 mg/L, ERS=74 mm/h), hypoalbuminemia (albumina 1.98 g/dL).

The first skin lesion appeared on his neck reported in association with aftous stomatitis, three weeks before. Cutaneous lesions worsened progressively and based on suspicious of viral and bacterial skin infection, a treatment with amoxicillin-clavulanic acid and acyclovir had been started. His UC was diagnosed 4 years before and was controlled with topical enemas at onset and oral mesalazine, no gastrointestinal symptoms were currently present or reported in the previous year but blood traces were occasionally found in stools.

Clinic was suggestive for a blistering disorder and differential diagnosis included dermatitis herpetiformis, bullous pemphigoid, bullous systemic lupus erythematosus, Stevens-Johnson syndrome and toxic epidermal necrolysis.

Throat swab, blood culture, serology for HIV, Hepatits B and C virus were negative, antineutrophil cytoplasmic antibodies (C-ANCA, P-ANCA) and extractable nuclear antigen (ENA) were negative, anti-nuclear antibodies (ANA) were positive 1:180. The search for fecal occult blood was positive in one out of three samples.

At admission, an antibiotic therapy with teicoplanin was started in association with acetaminophen, fluid hydration and albumin. Based on the concomitant presence of UC and clinical outcome. The more likely diagnosis appeared LABD which was confirmed, after 3 days, by a

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cutaneous biopsy and direct immunofluorescence assay. Corticosteroids were started i.v., (methylprednisolone 500 mg per day for 8 days), then orally (prednisone 50 mg/day) with only partial benefit [5].

After 16 days, given the persistence of skin lesions, dapsone was started at a dose of 25 mg per day. Dapsone has been recently identified as the most effective drug for LABD with both excellent initial responses and long-term remission.

Dapsone is a sulfonamide antibiotic which blocks the synthesis of dihydrofolic acid, firstly, used for the treatment of leprae. It is mostly used for its therapeutic efficacy in skin diseases with abnormal accumulation of neutrophils. However, its mechanism of action in antibody-mediated diseases remains unclear [6,7]. It may cause, with frequent dose-related effect, hemolysis in subjects with G-6PDH deficiency or methemoglobin reductase deficiency or hemoglobin M. Other known adverse effects are represented by peripheral neuropathy, vomiting, nausea, vertigo, pancreatitis, abdominal pain, headache, fever, psychosis, tachycardia and nephrotic syndrome [8].

In our patient G6PDH and methemoglobin were normal (G6PDH: 26.3 U/gHB with normal range between 11 and 35 U/gHB, metHB 0.9% with normal rate ≤ 1%) (Figures 1-4).

In addition to dapsone fatty gauze with diprosone dressings were placed on his arms, legs and abdomen. After one month of hospitalization the patient was discharged with minimal active skin lesions.

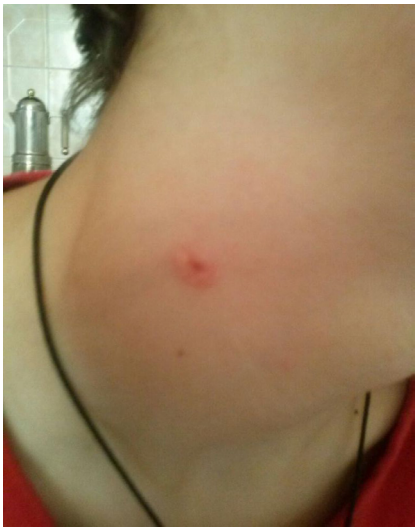

Figure 1: The first lesion on the neck.

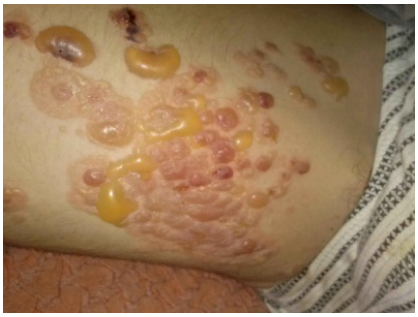

Figure 2: Two weeks after the first lesion.

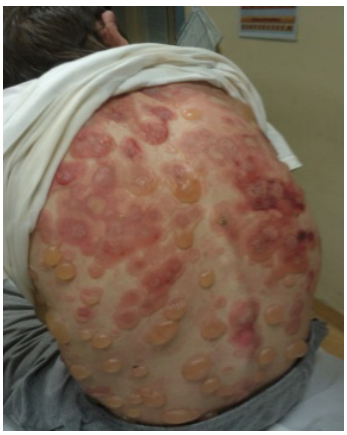

Figure 3: Three weeks after the first lesion, at admission to the hospital.

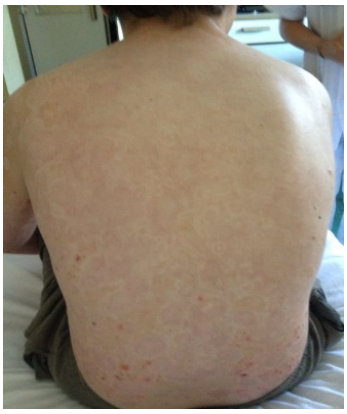

Figure 4: At discharge from the hospital.

Oral steroids were progressively tapered and stopped after 6 months. Dapsone treatment was also continued for 6 months but with half dosage after 5 months from starting therapy because of a transient increase of metHB up to 2% (normalized after 2 weeks).

Neither reappearance of skin lesions nor relapse of UC occurred during the follow-up of 12 months.

Discussion

Approximately one-third of patients with inflammatory bowel disease (IBD) develop skin lesions [9,10]. The prevalence of UC in LABD is three times more than in general population (7.1% compared to 0.05%) [11-13]. Whilst the risk of LABD in UC is currently unpredictable due to the lack of population studies. UC usually precedes the onset of the skin disease, although the opposite may also occur [13,14].

The etiopathogenicity of the association between IBDs and LABD is still unclear although an immune dysregulation may represent a common background. Patients with UC have an increased number of IgA and IgG-producing lymphocytes in the mucosa of the colon. *In vitro* studies revealed that B-lymphocytes from the bowel mucosa of UC patients produce less total IgA than controls, but secrete more monomeric IgA (specially IgA-1) [15,16]. LABD is a disease mediated by monomeric IgA-1. It has been suggested that the immunologic disturbance in patients of UC reflects an alteration in the process of antigenic presentation, resulting in an abnormal production of IgA-1

with cross-reactiveness to antigens of lamina lucida and sub-lamina densa in genetically susceptible patients. Despite the lack of populational studies calculating the relative risk of LAD in patients with UC, the available evidence strongly suggests a significant association with UC playing an important role in the development of LAD.

Conclusion

Our case shows how severe LABD can occur in young patients with distal and well-controlled UC and is unrelated to gastrointestinal relapse. LABD can be unresponsive to steroid treatment but can be successful treated with dapsone therapy avoiding bowel surgery. A longer follow-up and a larger sample of patients would be of critical importance to detect long-term efficacy of dapsone in this condition and to identify responders and non-responders LABD patients.

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