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Duhring Brocq Disease: The First Manifestation of Celiac Disease in an Adolescent

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Abstract Dermatitis herpetiformis (Duhring Brocq disease) is an autoimmune inflammatory disease determining polymoprhic pruriginous lesions. It is always associated with a gluten sensitive enteropathy which is most frequently clinically silent. The diagnosis is made on the basis of clinical, serological (IgA antitransglutaminase antibodies and antiendomysial antibodies), hystological and immunollogical (granular immunglobulin A deposits in the papilarry dermis by direct immunofluorescence) data. We present the case of an adolescent with dermatitis herpetiformis associated with atypical celiac disease. The particularity of the case was the abscence of other celiac disease manifestations and the finding of a cutaneous abscess infected with Staphiloccocus aureus, facilitated by the excoriated lesions caused by scratching, which was afterwards complicated with septic arthritis. After 6 weeks of gluten-free diet the cutaneous lesions dissapeared and the pruritus diminished.

Keywords: *dermatitis herpetiformis, celiac disease, gluten-free-diet*

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1. Introduction

Dermatitis herpetiformis (Duhring Brocq disease) (DH) is a chronic autoimmune inflammatory disease determining polymoprhic pruriginous lesions. It is always associated with a gluten sensitive enteropathy, most frequently clinically silent [1,2].

The diagnosis is made on the basis of clinical, serological (IgA type antitransglutaminase antibodies-ATA and antiendomysial antibodies-EMA), hystological and immunollogical (granular IgA deposits in the papilarry dermis by direct immunofluorescence-DIF) data [1]. Duodenal biopsy confirms the intestinal lesions specific to celiac disease (CD). Gluten-free diet (GFD) is the election treatment. Dapsone can be cautiously used, due to its adverse effects, until the regimen becomes efficient [3,4].

A 17 years old adolescent was submitted for a persistent erythemato-vesicular, pruriginous, cutaneous eruption, located on the posterior thorax, sacrate region and symmetrically on the arms, elbows and kneees. There was no family history for autoimmune of cutaneous disease. His personal medical history was insignificant, with the exception of a prerotulian cutaneous abscess infected with Staphilococcus aures, complicated with septic arthritis of the right knee (6 weeks before submission).

2. History of the Present Ilness

The cutaneous eruption had appeared 5 months ago. It was initially erythematous micropapular, afterwards becoming vesiculous, with the aforementioned localisation. He recieved local treatment with steroidal antiinflammatory ointments, with no improvement. After 3 months he had developed a right prerotulian abcess, which was later complicated with septic arthritis of the right knee (Methicillin-sensitive Staphylococcus aureus). He recieved parenteral antibiotherapy in triple association (Cefriaxone + Clyndamicin + Gentamicin). The local outcome was good, but the erythemato vesiculous eruption was not influenced by the antibiotics administered.

On examination, he appeared in a good state of health, with normal body temperature and normal nutrition state (W=84kg, p:91.77; H=197cm, p:99.9; BMI=21.6kg/m^2, p: 55.4), presenting no cardiac, pulmonar, or abdominal anomalies. There was an erythematous vesiculous eruption with excoriations and crusts on the posterior thorax, sacral region and symmetrically on the extensor surfaces of the elbows and knees. The skin of these areas was dry, indurated, with small hyperpygmented stains (Figure 1).

Considering the aspect of the eruptions and its long-lasting history, we suspected DH, which is one of the extradigestive manifestations of CD. ATA and EMA where positive. He was tested positive for the DQ2 heterodimer. The superior digestive endoscopy with duodenal biopsy showed a histological aspect typical for Marsh 3c CD: continuous surface epithelium of the duodenal mucosa, lack of villi, hyperplastic crypts, the high infiltration of the corium with inflammatory cells with patological exocytotic activity, mostly in the surface epithelium.

The biological studies showed low ionic calcium levels, the absence of carential anaemia and of immunological annomalies. There was no humoral immune deficiency, no

complement deficiency and no phagocytosis impairment. He did not test positive for any other autoimmune antibiodies. The total immunglobulin E levels were normal, specific immunglobulin E were negative.

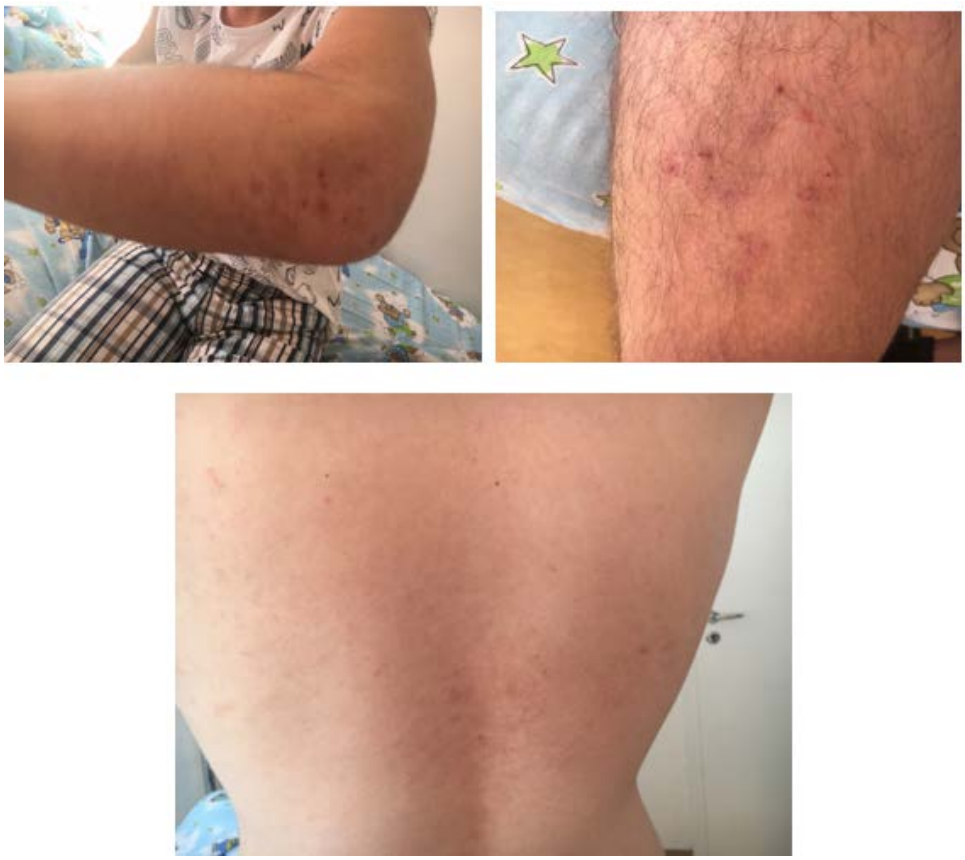

Figure 1. Clinical examination of our patient

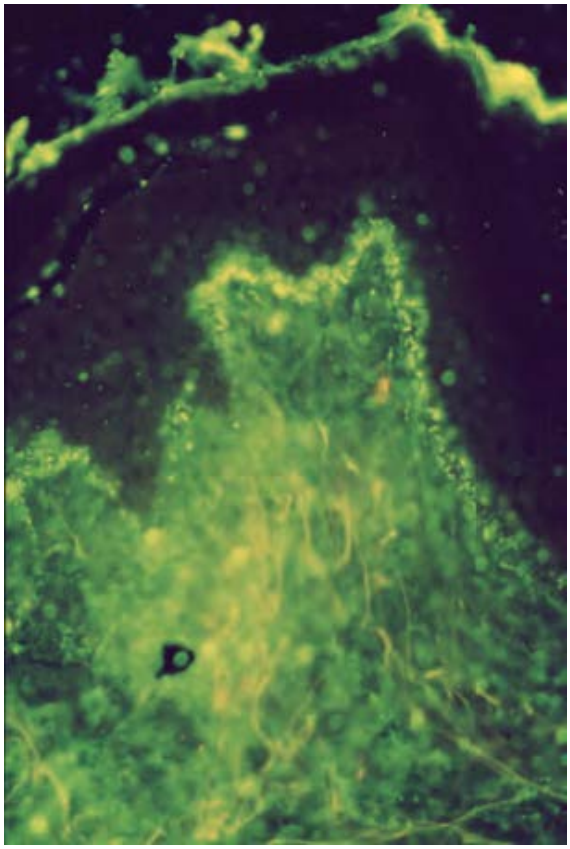

Figure 2. Granular IgA deposits in the pappilary dermis and along the basal membrane, observed by direct immunofluorescence

The perilesional cutaneous biopsy was analysed using DIF, which showed the presence of granular IgA deposits in the dermal papillae (Figure 2). There were no IgG, IgM or C3 deposits.

We interpreted the case as atypical Marsh 3c CD with extradigestive manifestations - DH. The sole therapeutic measure was GFD, initiated immediately after the histological confirmation of CD. During the following 6 weeks the cutaneous lesions had almost completely dissapeared, with the persistance of some erythematous hyperpigmented areas, and the pruritus was slighltly diminished. We have considered administering Dapsone.

3. Discussion

DH is a chronic autoimmune inflammatory disease, characterised by polymorphic bullous-vesiculous pruriginous skin lesions and a series of hystopathological and immunulogical features [1].

DH patiens always associate a gluten sensitive entheropaty, usually clinically silent [2]. DH can be the first sign of CD. Over 80% of the patients have intestinal lesions, especially if their diet contains high amounts of gluten and in the case of 20%, total villous atrophy is present [1]. It appears most frequently in adolescents and young adults [4,5]. Out patient did not have any digestive signs of CD [3].

The pathophysiology of DH implies a genetic predisposition. 10.5% of the patients have a positive family

history for CD or DH [6]. The majority of individuals (over 99%) are positive for the DQ2 or DQ8 heterodimer, only 0.7% showing another HLA (7). Our patient had the DQ2 heterodimer. The tissular transglutaminase (tTG) is the major autoantigen in CD, and the epidermal transglutaminase (located in the basal keratinocytes and dermal capillaries) is the most important autoantigen in DH [3,4,8]. Our patient had ATA, in a 3- fold greater amount than the upper detection limit. These are higly specific serological markers of CD and DH [3,4], with specificity 90% and sensibility 47-95% [9]; also being useful for testing the GFD compliace in CD and DH patients [10].

DH comprises two types of IgA against the epidermic transglutaminase [8]. While one of them exclusivelly binds to this enzyme, with an almost 100% specificity; the other one cross-interacts with tTG (which has similar aminoacid-sequencies in some regions) having a reduced affinity for the epidermal variant; this is found in CD patiens with no cutaneous manifestations [8].

Initally, ATA are synthesised in the intestine. They are realeased in the circulaton and can be deposited in the skin because of a crossed reaction with the epidermal antitransglutaminase antibodies (eTG) [11]. This enzyme is expressed in the epidermis, in the cytoplasm of the keratinocytes in the granullous and spinous layers [3]. The circulating immune complexed formed by IgA and tTG may bind to the dermal papillae as the enzyme can be active. In conclusion, DH can be consideres as a gluten sensitivity of the skin, developed by some CD patiens, with a secretion of eTG [8].

The primary lesions in DH consist of grouped erythematous papulae and vesicules, with a herpetiform apperanace. In our case, the characteristic lesions were symmetrically located on the extensor surfaces of the elbows and knees and on the posterior thorax and sacral region. In these areas the skin was dry, indurated, with crusts and hyperpigmented regions.

The intense pruritus was permanently present. Excorations due to scrathcing were seen and probably were the cause of the bacterial infection, which led to the formation of the prerotulian abscess later complicated with the septic arthritis of the right knee.

We suspected an IgA deficiency, as it is associated with CD in the case of 2% of the patients, with a 16-fold higher frequency compared to the general population [5], but it could not have been confirmed at our patient. Furthermore, he was tested negative for other immunologic anomalies such as Hashimoto tyroiditis, type I diabetes mellitus, IgA nephropathy, colagenosis, psoriazis, vitiligo, Biermer anaemia.

DH patients require constant follow-up, as they are under a higher risk of developing non-Hodgkin lymphoma and intestinal lymphoma [3,5]. The differential diagnosis, in our case, was made with urticaria, atopic and contact dermatitis, scabies, psoriazis and bullous dermatoses [3,4].

The skin biopsy showed the pathognomonic characteristic for DH: granular IgA deposits in the pappilary dermis and along the basal membrane, observed by DIF [13]. The presence of these deposits is a more specific and sensitive diagnostic test than the histological examination [6]. The latter difficultly differentiates DH from other subepidermal bullous diseases (bullous pemphigoid, bullous epidermolysis, erythema multiforme), due to the presence of vesicular neutrophilic microabscesses in the old lesions [3].

The constant association between DH and CD obliged us to confirm the latter. EMA were found in our patient. Because over 90% of the individuals with DH have intestinal lesions the patient underwent an upper digestive tract endoscopy with duodenal biopsy. The histological studies confirmed the specific intestinal lesions, with a 3C Marsh score.

The skin lesions evolved well after the GFD was initiated, with the almost complete dissapearance of the lesions after 6 weeks, but with the persistence of the pruritus. It is known that the IgA deposits form the dermo-epidermal junctions that are cleared after several years of GFD [8]. The persistence of pruritus may require Dapsone, which is the first choice therapy and the only drug approved by the Food and Drug Administration for this disease [4].

The initial treatment with 25mg/kg, followed by a daily dose of 0.5-1mg/kg considerably diminishes the pruritus and improves the skin lesions. However, during the first 3 to 12 weeks of treatment, Dapsone can determine a hypersensibilisation syndrome comprising liver toxicity and 3 types of haematological reactions: haemolysis, methaemoglobinemia, agranulocytosis. In consequence, Dapsone is solely indicated, as a complementary treatment, if GFD does not determine a singificant healing of the skin lesions [3,4].

4. Conclusions

All the individuals with DH must undergo investigations in order to confirm CD, as they are constantly linked, despite the fact that the majority of patiens do not present digestive manifestations. DIF done on skin biopsy is a decisive test for DH diagnosis, by highlighting the granular IgA deposits located in the dermal pappilae. GFD is the therapeutic measure of choice, but the clinical improvement of DH requires a certain amount of time.

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