Juvenile Bullous Pemphigoid – a Case Report

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UDC 616.527-08-053.2

Abstract
Bullous pemphigoid is an autoimmune blistering disease that predominantly affects elderly persons and rarely children. We present a 12-year-old girl with sudden appearance of tense blisters on an erythematous base on the trunk, neck, hands and legs with intense pruritus. Standard laboratory test results were within the normal range except for blood eosinophilia of 12% of the total white cell count. Skin biopsy specimens showed evolving subepidermal blisters with perivascular lymphohistiocytic, eosinophil and neutrophil infiltrations in the papillary dermis. Direct immunofluorescence of perilesional skin showed linear, continuous deposits of IgG and C3 along the dermoepidermal junction. Indirect immunofluorescence showed circulating anti-basement membrane zone IgG autoantibodies at a titer of 1:80. We started treatment with systemic corticosteroids, methylprednisolone 0,5 mg/kg per day and 500 mg erythromycin 4 times a day during 10 days. After 3 days 50 mg dapsone (DDS, 4,4-diaminodiphenylsulphone) per day was added. After a few days, there were no new changes on the skin and pruritus disappeared completely.

Key words
Pemphigoid, Bullous; Autoimmune Diseases; Child; Pruritus; Fluorescent Antibody Technique, Indirect; Dapsone; Treatment Outcome

Bullous pemphigoid (BP) is an autoimmune blistering disease that predominantly affects elderly persons and rarely children. It is an immune-mediated disease that is associated with a humoral and cellular response directed against the two well-characterized self-antigens: bullous pemphigoid antigen 1 (BPAG1) and bullous pemphigoid antigen 2 (BPAG2), both components of hemidesmosomes – junctional adhesion complex in the skin and mucosa. The cutaneous manifestations of BP may be extremely polymorphic. In the non-bullous phase of the disease, signs and symptoms are frequently non-specific, from mild to severe intractable pruritus. The bullous stage of BP is characterized by the development of vesicles and bullae on apparently normal or erythematous skin (1).

The first well-documented report of childhood BP was published in 1970 (2). The diagnostic criteria are the same as in adults: appearance of tense bullae, histopathological findings of subepidermal blisters with eosinophilia, direct immunofluorescence (DIF) showing linear deposition of IgG or C3 as the major immunoreactants at the basement membrane zone and presence of circulating IgG anti-basement membrane zone autoantibodies (3). The course of childhood BP is usually indolent with rare relapses (4). Even so, the disease may be life threatening, particularly if appropriate management is delayed (5).

Case report
We present a 12-year-old girl, with sudden appearance of tense blisters on an erythematous base on the trunk, neck, hands and legs (Figure 1, 2) with intense pruritus. Mucous membranes were not involved. The family history showed no evidence of autoimmune diseases. Standard laboratory test results were within the normal range except for blood eosinophilia of 12% of the total white cell count. Histopathological analysis of lesional and perilesional skin samples revealed subepidermal blisters with perivascular
Figure 1. Tense blisters on an erythematous base on the legs

Figure 2. Annular distribution of blisters, typical for juvenile bullous pemphigoid
lymphohistiocytic, eosinophil and neutrophil infiltrations in the papillary dermis (Figure 3). Direct immunofluorescence (DIF) test of perilesional skin demonstrated linear, continuous deposits of IgG and C3 along the dermoepidermal junction (Figure 4). Indirect immunofluorescence (IIF) microscopy demonstrated circulating anti-basement membrane zone IgG autoantibodies at a titer of 1:80.

The diagnosis of juvenile bullous pemphigoid was established based on clinical manifestations (tense bullae on an erythematous base, pruritus), characteristic histopathological findings (subepidermal splits with dominant eosinophils in the cavity and in dermal infiltrations), direct immunofluorescence (DIF) microscopy (linear IgG and C3 deposits along the basement membrane zone) and positive IIF test 1:80.

Treatment with systemic corticosteroids, methylprednisolone 0.5mg/kg per day and 500 mg erythromycin 4 times per day was initiated. However, after 3 days the disease was not under control, so 50 mg dapsone (DDS, 4,4-diaminodiphenylsulphone) per day was added. After a few days, there were no new changes on the skin and pruritus disappeared completely and the therapy with methylprednisolone and dapsone was not discontinued after discharge. The therapy was well tolerated. Hypertension was not recorded during therapy, while laboratory findings, including glucose as well as arterial blood pressure, were within reference values. Two months later, the disease was in complete remission. During a 6 months follow up, methylprednisolone was tapered to 4 mg per week, until the daily dose of 4 mg was achieved in combination with 50 mg dapsone per day.

**Discussion**

Autoimmune bullous diseases with subepidermal split are very rare in children. The first case of juvenile bullous pemphigoid (JBP) was published in 1970 (1). In 1993, Fisler and al. analyzed 53 collected cases of juvenile bullous pemphigoid, where the age of onset ranged from 2.5 months to 14 years (4). Female patients accounted for 60% of cases.

The disease most often occurs in children older than 8 years. None of the children had any form of malignancy or any other associated disease (3). We presented a 12 year-old girl, with no evidence of other acute or chronic disease. Sudden appearance of bullous

**Figure 3.** Histopathological analysis of lesional and perilesional skin samples reveals subepidermal blisters with eosinophilic spongiosis and perivascular lymphohistiocytic, eosinophil and neutrophil infiltrations in the papillary dermis (HE, x400)
eruptions was not accompanied by deterioration of the general condition. Skin eruption was generalized, but there was no involvement of mucous membranes. In case series from the Pediatric Dermatology Unit, University Clinic of Dermatology, Belgrade, three of six children with BP had changes on the oral mucosa (6).

In our case, histopathology and DIF analyses were characteristic of BP: subepidermal blistering with perivascular lymphohistiocytic, eosinophil and neutrophil infiltrations in the papillary dermis, while DIF showed linear, continuous deposits of IgG and C3 along the dermoepidermal junction. In a study including six cases with JBP, three showed deposits of IgG, C3 and IgA (6). We did not find deposits of IgA in the perilesional skin. About 60 - 80% of patients present with circulating antibasement membrane IgG autoantibodies, and there is no difference between adults and children considering that matter.

Bullous pemphigoid may coexist with lichen planus in both adults and children (7). Immunopathologically, the disease is identical to bullous pemphigoid. However, it is usually possible to differentiate bullous pemphigoid from lichen planus pemphigoides on clinical base alone: in bullous pemphigoid there is no evidence of associated lichen planus (8). In our case, positive direct DIF test helped to exclude bullous lichen planus (9).

Systemic corticosteroids are the best choice for the initial treatment of JBP. In children, as in adults, a minimal dose of drugs that controls the disease is recommended (2, 10). Powell et al. analyzed immunobullous disease in children and its good response to sulfa drugs and macrolides (11). Macrolide antibiotics, including erythromycin, have anti-inflammatory effects similar to those of tetracyclines. It has been shown that they exhibit not only a steroid-sparing effect when used in conjunction with steroids, but also an inhibition of neutrophil chemotaxis (11). All patients responded well to the therapy with dapsone, sulphonamides and systemic erythromycin (11). In our patient, we initiated therapy with a systemic corticosteroid methylprednisolone 0.5 mg/kg daily and oral 500 mg erythromycin 4 times a day. After 3 days the disease was still not under control, so we added dapsone 50 mg per day. Prompt therapeutic effect with reduction of pruritus was obtained, and there were no new blisters. Spontaneous remission of JBP may be achieved within 5 years and it has a good prognosis, although in some children the course is less benign. The average time to achieve control of BP was about 1 month in the study of Gajić-Veljić et al. (6), which was shorter than in the study reported by Weston et al. (12), where remission with systemic corticosteroids and dapsone was achieved after 2
months. Complete remission was achieved in all JBP patients in both studies, as well as in our patient.

**Conclusion**

In general, children with BP have a good prognosis. Remission is achieved within several weeks to a few months. In most children the response to treatment is rather fast and ranges between a few days to several months, as in our patient. In juvenile bullous pemphigoid relapses are very rare, which is opposite to much slower remission and higher rate of relapses reported in adults suffering from BP.

**Abbreviations**

BP - Bullous pemphigoid
BPAG1 – Bullous pemphigoid antigen 1
BPAG2 – Bullous pemphigoid antigen 2
IgG – Immunoglobulin G
C3 – Complement component C3
DIF - Direct immunofluorescence
IIF - Indirect immunofluorescence
JBP – Juvenile bullous pemphigoid

**References:**

Opšte stanje je obično nepromenjeno, a ni kod jednog deteta do sada nije utvrđen prateći malignitet. Promene mogu da zahvate i vidljive sluznici, opisani su slučajevi sa promenama na orofaringealnoj sluznici. Presudni dijagnostički značaj ima patohistološki nalaz i direktna imunofluorescencija kojom se duž zone bazalne membrane dokazuje prisustvo kontinuiranih linearnih depozita sastavljenih iz IgG i C3 antitela. Opisani su depoziti sastavljeni i od IgA. Kao i kod odraslih, u 60−80% slučajeva indirektnom imunofluorescencijom potvrđuje se prisustvo u serumu cirkulišućih IgG antitela usmerenih protiv bazalne membrane, koji su bili prisutni i kod našeg pacijenta.

**Ključne reči**

Bulozni pemfigoid; Autoimune bolesti; Dete; Pruritus; Indirektna imunofluorescentna metoda; Dapson; Ishod lečenja