CASE REPORT

# A Rare Case of Bullous Pemphigoid in an Infant

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## Abstract

Bullous pemphigoid is an autoimmune blistering skin disease, rare in infancy, but increasingly reported. We report on a case of bullous pemphigoid in a 6 month-old infant with an excellent response to topical and oral corticosteroids. In this age group, the dermatosis assumes some particularities which must be recognized by clinicians to prevent an unnecessary diagnostic workup or diagnostic delay and treat appropriately to avoid severe morbidity.

**Keywords:** Skin Diseases, Vesiculobullous/diagnosis; Pemphigoid, Bullous/diagnosis; Pemphigoid, Bullous/therapy; Infant

## Introduction

Bullous pemphigoid is an acquired autoimmune blistering disease that typically affects the elderly, being uncommon in children. The incidence of childhood bullous pemphigoid in Israel is estimated in 2.36 out of 100,000 inhabitants per year.[1] However, in most countries no central registry exists, and the disease might be underrecognized.

Bullous pemphigoid is induced by autoantibodies against two proteins (AgPB230 and AgPB180) that are structural components of the hemidesmosomes in the dermal-epidermal junction.[1-5] The diagnosis is based on clinical features and laboratory findings. Clinically, it manifests with large tense blisters on eczematous or urticarial plaques, with moderate to severe itch. Mucosal involvement is rare. Histological examination reveals subepidermal blisters and inflammatory infiltrates consisting mainly of eosinophils and neutrophils. Direct immunofluorescence represents the gold standard for diagnosis and shows linear deposition of immunoglobin (Ig) G and C3 along the basement membrane zone.[1-5] Indirect immunofluorescence on normal human salt-split skin shows linear IgG deposits at the epidermal side. Enzyme-linked immunosorbent assay (ELISA) is an additional extremely sensitive test for bullous pemphigoid diagnosis.[3]

## Case Report

A 6 month-old boy was admitted to our dermatologic outpatient clinic with a pruritic bullous dermatosis with a three-week duration, characterized by multiple tense blisters on erythematous plaques, with acral distribution. The dermatosis started one week after vaccination according to the national plan of vaccination (diphtheria, tetanus, pertussis, and hepatitis B vaccines). He was otherwise healthy. Pregnancy had been monitored, with no complications. He was born by eutocic delivery. No family history of cutaneous diseases was known. At physical examination, he had multiple tense blisters, with diameters ranging from 1-3 cm, over erythematous plaques on his hands (Fig. 1 A, B) and feet (Fig. 1 C), with palmoplantar involvement. The oral and genital mucosae were spared. The infant was otherwise well and afebrile.

Laboratory studies disclosed peripheral eosinophilia (4,780 x $10^9$ cells/L). Bacteriological test of the blister content was negative.

Skin biopsies were performed for histopathology and immunofluorescence. Histological examination showed a subepidermal blister (Fig. 2 A), filled with eosinophils and some neutrophils (Fig. 2 B). Direct immunofluorescence showed linear deposition of IgG and C3 along the dermo-epidermal junction (Fig. 3). Investigation of the hemidesmosome antigen by ELISA revealed autoantibodies to BP180 > 200 UA/mL (BP230 < 2 UA/mL). The diagnosis of bullous pemphigoid was established.

After drainage of the blister content, he was started on

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the twice daily topical application of clobetasol cream and oral prednisolone for 35 days, with progressive tapering, with an excellent response (Fig. 4), maintaining clobetasol application on the residual erythematous spots. Vaccination was continued according to the national plan without recurrence in four years of follow-up.

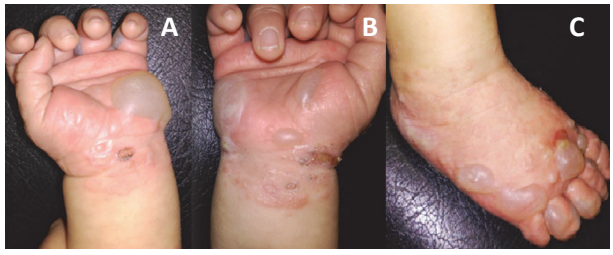


**Figure 1.** Multiple tense blisters on erythematous papules and plaques on the hands (A, B) and right foot (C).

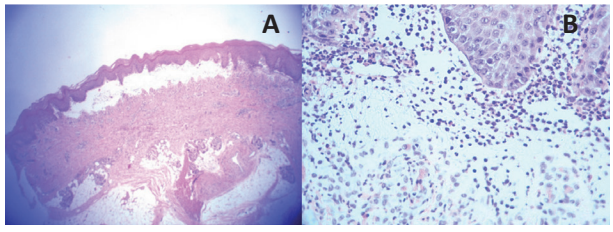


**Figure 2.** Histopathology. A. Subepidermal blister (hematoxylin and eosin, x40). B. In high magnification, the blister is fulfilled by eosinophils and some neutrophils (hematoxylin and eosin, x400).

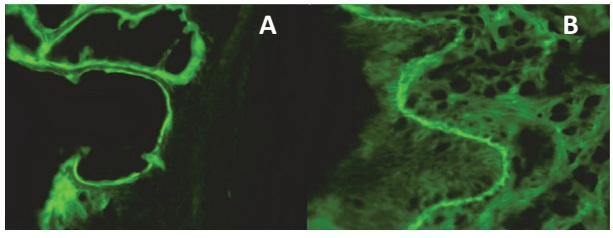


**Figure 3.** Direct immunofluorescence. Linear deposition of immunoglobulin G (A) and C3 (B) along the dermo-epidermal junction on direct immunofluorescence.

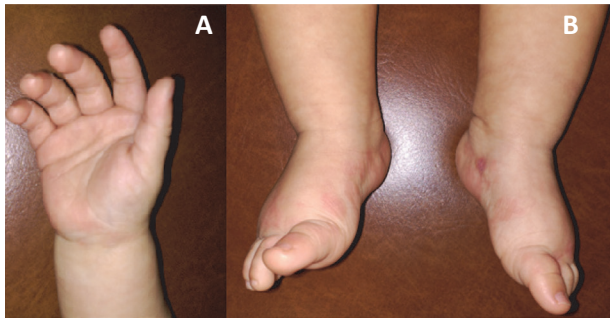


**Figure 4.** Evolution at the 35th day of corticotherapy, with almost no lesions remaining, with only residual spots.

## Discussion

Bullous pemphigoid rarely occurs in children with fewer than 100 cases reported in the literature.[6] About 30.8% of the cases occurred shortly after vaccination.[2] It has been suggested that a one-month latency period from the time of vaccination to the onset of the first lesion may be appropriate for anti-basement membrane antibody induction. Nevertheless, many cases of infantile bullous pemphigoid have a shorter latency period after vaccination as in our case. Although there are several reports of post-vaccination bullous pemphigoid, epidemiological studies demonstrating the association are lacking.[2] The simultaneous administration of multiple vaccinations for different diseases might overload the infant immune system.[3,4] However, a close relationship between vaccination and bullous pemphigoid onset is difficult to prove, considering the widespread use of vaccines in infancy and the frequent absence of bullous pemphigoid relapse after further vaccinations.[2-4]

Infantile bullous pemphigoid manifests with predominant acral involvement with or without generalized blistering and it can be considered as a clinical hallmark and diagnostic clue of infantile bullous pemphigoid.[3-5] Oral and genital mucosae are rarely affected. In the largest published series of 81 cases of infantile bullous pemphigoid[3], the mean age of disease onset was around 4 months, without gender predominance, 98% were healthy children and all had lesion on hands and feet. About 83.9% had moderate-severe disease (> 10% of body surface area). Mucosal membranes were spared. No case of infantile bullous pemphigoid in relation with a malignant neoplasm has been reported.

Infantile bullous pemphigoid (< 1 year) differs from childhood bullous pemphigoid (> 1 year), the latter being not quite different from adult bullous pemphigoid with possible mucosal involvement and the possible generalization of the lesions, lacking the accentuation of the acral lesions typical of infantile bullous pemphigoid.[4] The diagnosis is similar to adult form, based on typical clinical picture (urticarial plaques and blisters, acral distribution), subepidermal blistering with an eosinophil rich inflammatory infiltrate on conventional histology and linear IgG, and/or C3 deposition at the basement membrane in direct immunofluorescence. Further diagnostic pointers are the presence of serum autoantibodies against BP180 and/or BP230.[2,3,7] Even though the ELISA results were only reported in a minority of cases, different test systems used do not allow for direct comparison. However, it seems that reported autoantibody levels in infants are fairly high, compared to adults and higher values at presentation

correlated with the need for more aggressive and longer-term treatment.[3]

The main differential diagnoses are epidermolysis bullosa, linear IgA dermatosis, porphyria, bullous impetigo, pompholyx, bullous mastocytosis, or insect bites.[3,4]

No treatment guidelines for infantile bullous pemphigoid exist. It has been suggested that all of the patients should receive treatment with mid- to high-potency topical corticosteroids.[3] Children with moderately severe or severe disease (>10% body surface area) usually require additional treatment with systemic corticosteroids.[3,6,8] If the treatment response is slow or high doses of corticosteroids are needed for disease control, additional steroid sparing agents should be considered.[6-10] Dapsone seems to be the agent of choice as it is usually well tolerated and effective.[9,11] Other steroid sparing agents used are intravenous immunoglobulin, cyclosporine, and mycophenolate mofetil.[3,6,8,10,11] Little or no experience exists for erythromycin, methotrexate, cyclophosphamide, or azathioprine treatment in infants with bullous pemphigoid. Rituximab is to be reserved as rescue treatment for the most severe cases.[3,12] The role and dosing of omalizumab in infantile bullous pemphigoid warrants further investigation.[13] Complementary measures, e.g. oral antihistamines, blisters drainage, and topical or oral antibiotics for treating bacterial co-infection, are equally important.[3]

After clinical remission, treatment discontinuation can be considered. Autoantibody ELISA values can take a long time to normalize and are, therefore, not always helpful in deciding when to end treatment.[3]

Infantile bullous pemphigoid usually has a favorable prognosis and resolves fairly rapidly with therapy. The number of relapses seem to be very low and eventually can be triggered by infections or when tapering of corticosteroids was started early.[1,3,6] In addition, relapses seem more frequent in patients who did not receive systemic corticosteroids.[3]

**WHAT THIS CASE REPORT ADDS**

- Bullous pemphigoid is a rare autoimmune blistering disease in infancy.
- Infantile bullous pemphigoid manifests with blisters on urticarial plaques with predominant acral involvement, usually with no oral and genital lesions.
- The main differential diagnoses are epidermolysis bullosa, linear immunoglobulin A dermatosis, bullous impetigo, pompholyx, or insect bites.
- The correct diagnosis and treatment enable the avoidance of severe morbidity.
- The treatment is mainly based on high-potency topical corticosteroids with or without systemic corticosteroids. Steroid sparing agents can be necessary.
- The prognosis is favorable and relapses are rare.

## Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.


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## Consent for publication

Consent for publication was obtained.

## Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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**Um Caso Raro de Penfigoide Bolhoso numa Criança**

**Resumo:**
O penfigoide bolhoso é uma doença cutânea autoimune, rara na infância, mas cada vez mais relatada. Descrevemos um caso clínico de penfigoide bolhoso numa criança de 6 meses de idade, que teve uma excelente resposta aos corticosteroides tópicos e orais. Nesta faixa etária, a dermatose tem algumas particularidades que devem ser reconhecidas pelos clínicos para evitar exames de diagnósticos desnecessários ou atrasos no diagnóstico e, assim, tratar adequadamente a doença para evitar uma morbilidade grave.

**Palavras-Chave:** Dermatopatias Vesiculobolhosas/diagnóstico; Lactente; Penfigoide Bolhoso/diagnóstico; Penfigoide Bolhoso/tratamento