

Single Case

Severe Infantile Bullous Pemphigoid Treated with Dapsone after Bridging with Systemic Glucocorticoid

Kenneth Thomsen^a Mette Deleuran^a Christian Vestergaard^a
Mette Holm^b Rikke Riber-Hansen^c Rikke Bech^a

^aDepartment of Dermatology and Venerology, Aarhus University Hospital, Aarhus, Denmark; ^bPaediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus, Denmark; ^cDepartment of Pathology, Aarhus University Hospital, Aarhus, Denmark

Keywords

Bullous pemphigoid · Paediatric dermatology · Dapsone · Treatment refractory

Abstract

We present a case of severe and treatment-refractory bullous pemphigoid in a 3-month-old child. After topical and systemic corticoid treatment proved inefficient, dapsone 0.75 mg/kg was added initially without success. Disease control was reached with dapsone 1.5 mg/kg in addition to both topical and systemic glucocorticoid treatment, leaving the child with several side effects of the glucocorticoid treatment.

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Introduction

Bullous pemphigoid (BP) is an autoimmune disease characterized by tense bullae on an erythematous background, mainly affecting the elderly from the 7th decade [1], with an incidence of 13.4–66 per 1,000,000 [2]. BP has also been reported as an adverse effect of new checkpoint inhibitors, such as pembrolizumab [3]. Although rare, BP occurs in infants with a mean age of 4.5 months at debut [4] and a predominant acral presentation [5].

The diagnosis is confirmed by histopathology of the skin, with dermal infiltration by eosinophils, subepidermal blisters, and linear immune globulin G (IgG) and C3 complement factor alignment at the basement membrane zone. Eosinophils may also be increased in the blood [2]. Initial BP treatment is prednisolone 0.5 mg/kg/day and potent topical steroid therapy [6]. Disease control in adults can be maintained by azathioprine or methotrexate [7], as prolonged treatment with prednisolone is associated with significant adverse events and increased mortality [8].

In a systematic review of 81 case reports of BP in infants [4], monotherapy with prednisolone was the most frequently used treatment for initial disease control. Dapsone was the second most used drug. In 19.8% of the paediatric BP cases dapsone was used in combination with prednisolone, and dapsone was given as monotherapy in 2.5% of cases.

Intravenous immunoglobulin treatment combined with prednisolone has in some cases been reported to be effective in childhood BP [4, 9, 10]. Lastly, macrolides like clarithromycin and erythromycin have also been reported as treatment options [4, 11].

Here, we present a case of infantile BP treated with prednisolone and dapsone.

Case

A 3-month-old boy, of healthy, non-related parents of Middle Eastern descent, developed an erythematous rash on the plantae of his feet. The general practitioner initiated daily topical treatment with hydrocortisone 17-butyrate.

Five days after the onset of rash, the patient was seen at Paediatrics and Adolescent Medicine, Aarhus University Hospital. The infant had now developed a bullous skin rash on an erythematous background located on the plantae of the feet, palms of the hands, the abdomen, and behind the ears. Furthermore, the patient was febrile with a temperature of 39.6°C.

Clinical Presentation/Histology

Initially, a bullous impetigo was suspected. Biochemistry showed a normal CRP and slight eosinophilia at $1.88 \times 10^9/L$. *Staphylococcus aureus* was isolated to one eroded bulla with a yellow crust and treated with amoxicillin and clavulanic acid for 14 days with good response.

The patient was readmitted to the paediatric ward 11 days after the onset of the bullous rash due to progressing skin lesions (Fig. 1). Eosinophilia was increased to $5.12 \times 10^9/L$. Topical treatment was intensified with clobetasol propionate ointment for the trunk and extremities and hydrocortisone 17-butyrate cream for inverse areas and the face.

Two punch biopsies were performed – one formalin-fixed for conventional light microscopy (formalin-fixed, paraffin-embedded) and one unfixed for immunofluorescence microscopy. Light microscopy showed superficial perivascular and interstitial inflammation

dominated by eosinophils and a bulla on the dermo-epidermal border. Direct immunofluorescence microscopy revealed both IgG and compliment C3 linear alignment at the basement membrane as well as eosinophilic inflammation (Fig. 2).

At day 15 progression of skin lesions was observed and systemic prednisolone treatment of 1 mg/kg/day was initiated. Further progression was noted after 4 days, now including the face. Systemic prednisolone treatment was increased to 2 mg/kg/day initially with good disease control.

Re-admission occurred at day 38 with new eruptions of bullae, and therefore at day 40 dapsone 0.75 mg/kg/day was initiated. At day 47 new eruptions were still occurring, and dapsone was increased to 1.5 mg/kg/day and topical treatment to twice daily. This treatment was continued until day 70, resulting in complete control of the disease and regression of symptoms. The patient was now cushingoid, with weight and length decreased from the mean to $-1\frac{1}{2}$ and $-\frac{1}{2}$ SD, respectively, for male infants. First, the topical treatment was steadily reduced and the prednisolone dose was tapered to zero within 3.5 months. Dapsone treatment was stopped after another 3.5 months of treatment. No new eruptions have been noticed after 1.5 years of follow-up. A treatment flowchart is presented in Table 1.

Discussion

In a systematic review of 81 infants with BP [4], dapsone 1–1.5 mg/kg/day was a successful and safe treatment of BP. In our 3-month-old patient we used dapsone as a steroid-sparing agent. The combination of dapsone 1.5 mg/kg/day, topical corticosteroid twice daily, and systemic prednisolone up to 2 mg/kg/day was successful in controlling this severe case of treatment-refractory childhood BP.

The child became cushingoid as a consequence of systemic prednisolone treatment for 2 months. Earlier initiation of dapsone treatment could possibly have cleared the way for tapering the systemic prednisolone treatment before the child became cushingoid. As an oral treatment, dapsone is very easy to administer, whilst intravenous immunoglobulin, an often-used treatment in childhood BP, is administered intravenously. Thus, dapsone is a safer and cheaper choice of treatment, with no discomfort and pain related to obtaining an intravenous access as in immunoglobulin treatment.

We suggest that dapsone be used as a corticosteroid-sparing agent in the treatment of childhood BP. We strongly suggest that dapsone treatment should be instituted immediately after BP diagnosis has been established in order to taper corticosteroid treatment and avoid long-term corticosteroid side effects in the child.

Statement of Ethics

Written informed consent to publish this case was obtained from the parents.

Disclosure Statement

All authors have nothing to disclose, and there is no conflict of interest.

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Fig. 1. Acral presentation of bullae on the soles of the feet.

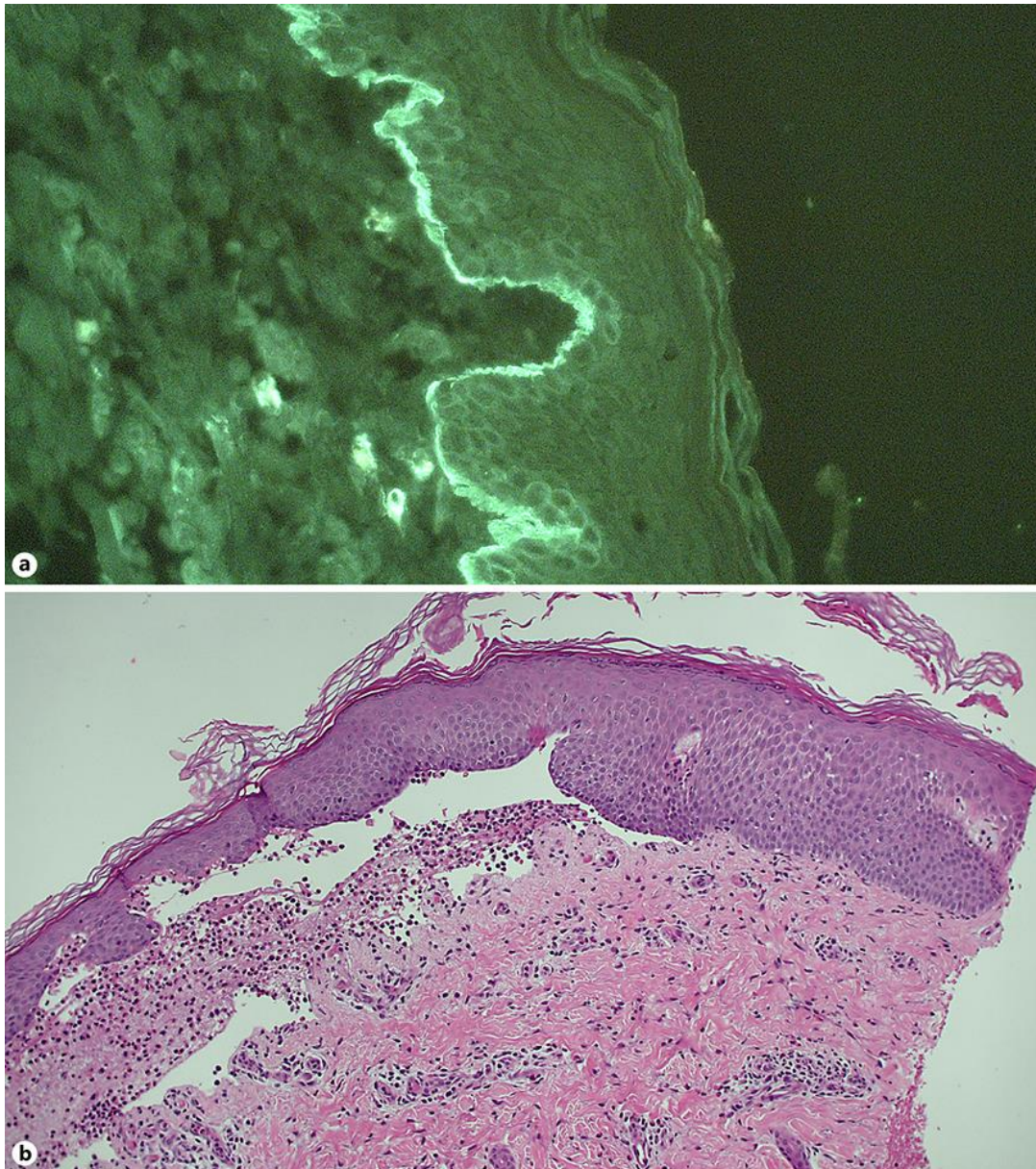


Fig. 2. **a** Indirect immunofluorescence of a biopsy, showing IgG deposition along the dermo-epidermal border along the basement membrane. **b** Haematoxylin-eosin staining of a skin biopsy, demonstrating the split along the dermo-epidermal border as well as eosinophilic inflammation.

Table 1. Treatment flowchart

Day 1	Hydrocortisone 17-butyrate topical treatment once daily
Day 5	Admission to paediatric ward
Day 11	First dermatological visit; topical hydrocortisone 17-butyrate administered inversely and mometasone furoate treatment for the trunk and extremities, once daily
Day 15	Systemic prednisolone 1 mg/kg/day added
Day 19	Systemic prednisolone raised to 2 mg/kg/day
Day 21	Topical mometasone furoate replaced with clobetasol propionate
Day 40	Dapsone 0.75 mg/kg/day added
Day 47	Dapsone raised to 1.5 mg/kg/day
Day 57	Topical treatment increased to twice daily
Day 70	Slowly decreasing topical treatment frequency and prednisolone dose