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Bullous pemphigoid in infancy developing after the first vaccination

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A previously healthy 3-month-old boy presented with a 10-day history of a blistering eruption on his hands and feet.

On physical examination, large vesicles and bullae were seen in a acral distribution with a florid, generalized, erythematous, urticated eruption with no mucosal involvement (Fig. 1a,b). Notably, he had received his first set of vaccinations 8 days before developing the skin eruption [diphtheria, tetanus, pertussis, polio, *Haemophilus influenza* B (Pediacel®; Movianto UK, Bedford, UK) and *Pneumoccocus* (Prevenar®; Wyeth Vaccines UK, Maidenhead, Berkshire, UK)]. There was no relevant family history and the mother had no history of a rash during pregnancy.

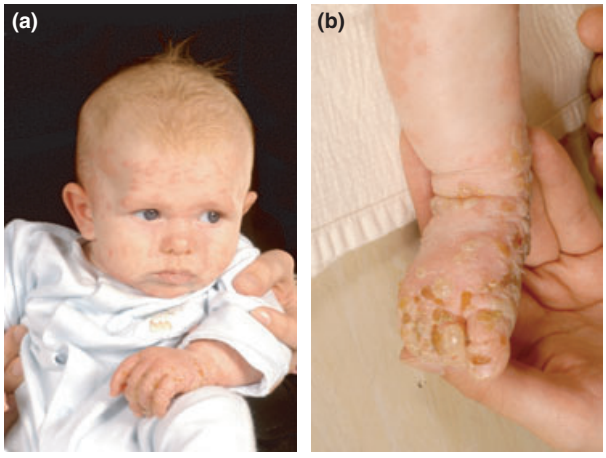

Figure 1 (a) Florid generalised urticated eruption; (b) florid vesiculobullous eruption on a background of urticated erythema in an acral distribution.

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Results of laboratory investigations showed that the patient had eosinophilia (5.3×10^9/L; normal range $0.04–0.4 \times 10^9$/L), thrombocytosis (608×10^9/L; $150–400 \times 10^9$/L) and a marginally increased C-reactive protein level (10 mg/L; < 10 mg/mL) and erythrocyte sedimentation rate (12 mm/h; 0–15 mm/h). Results of tests for anti-pemphigus and pemphigoid antibodies, immunoglobulins, complement, antinuclear antibodies, extractable nuclear antigens and tryptase were all normal or negative.

Histological examination of a diagnostic biopsy found features of a spongiotic epidermis with a mixed inflammatory cell infiltrate including eosinophils. On direct immunofluorescence, positive linear staining for IgG and C3 was seen on the epidermal side of salt-split skin; staining for IgA and IgM was negative. Indirect immunofluorescence (IIF) revealed antibasement membrane antibodies (1 : 10) binding to the roof of salt-split skin. ELISA for bullous pemphigoid (BP)180 was positive and Western blotting against epidermal extract gave positive results for both BP antigen 1 (230 kDa) and BP antigen 2 (180 kDa) bands (Fig. 2), consistent with a diagnosis of BP. IIF using the mother's serum gave negative results.

The infant was managed with oral prednisolone 2 mg/kg with dramatic effect, and he became free of blisters after 4 weeks of treatment. Prednisolone was gradually tapered off over a 5-month period with no evidence of disease relapse. Although we advised the parents to postpone further immunizations only while the infant was taking oral prednisolone, the parents opted to have no further vaccinations for their child (who is now 3 years old) unless medically essential.

BP is an autoimmune blistering skin disorder associated with tissue-bound and circulating IgG autoantibodies directed against BP antigens 180 and 230.[1] BP usually affects the elderly and is rare in infants (from birth up to 1 year of age). Although the precise incidence of BP in children is unknown, there have been only 33 cases of infantile BP reported.[2] In

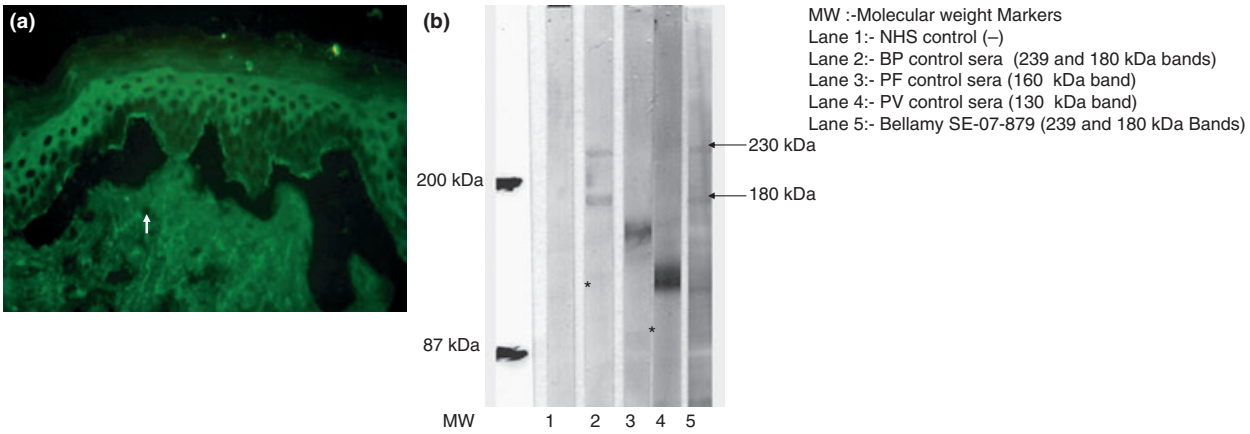

Figure 2 (a) Indirect immunofluorescence showing IgG anti-basement membrane zone antibodies staining the roof of salt-split substrate (1 : 10 dilution). (b) Western blotting against epidermal extract showed bands for both bullous pemphigoid antigens 1 (230 kDa) and 2 (180 kDa).

most cases, the disease started 6 months postnatally. Although one explanation for the development of BP in infants could be due to the transfer of maternal IgG pemphigoid antibody, antibodies have not been detected to date in the serum of mothers of affected patients.

Most infantile BP responds well to conventional treatments, with an excellent prognosis. Agents previously used successfully include corticosteroids, dapsone, sulfapyridine, erythromycin, nicotinamide and mycophenolate mofetil, and in refractory cases, intravenous immunoglobulin.[2] Although the clinical, histopathological and immunological features of childhood BP are indistinguishable from those of adult BP, the clinical presentation of infantile BP seems to differ from that of childhood BP. A recent study found that acral involvement in infantile BP was much more likely in childhood BP, whereas genital and mucosal involvement was found to be very rare.[3] These differences could be attributed to possible age-dependent expression of BP antigen in various bodily sites. However, the autoantibodies in childhood BP target the same antigens as in adult BP.[4]

Numerous possible trigger factors of BP are known, including malignancy, recurrent trauma, some systemic diseases and psoriasis. It is thought that injury and inflammation may disrupt the skin basement membrane locally and enhance the antigenicity of the BP antigen.[5] A further potential trigger is vaccination, with 13 cases of BP having been reported in both infants and adults soon after vaccination.[6] Ten cases were of adult BP; the vaccines were tetanus toxoid booster in three cases and anti-influenza in seven. The appearance of the lesions after vaccination varied from 1 day to 4 weeks.[6] All three cases of infantile BP had a very short period between vaccination and onset of the lesions, as in our case.

The association of BP and vaccination could be entirely coincidental, given that virtually all infants in the UK receive these vaccinations routinely. In our case, although the mechanism of induction is unclear, the close relationship of vaccination and onset of the disease suggests that there may be a true association. This case highlights that BP can rarely occur in infancy and may be associated with vaccinations.

References

1 Kuenzil S, Grimatre M, Krishcher J *et al.* Childhood bullous pemphigoid: report of a case with life-threatening course during homeopathy treatment. *Pediatr Dermatol* 2004; **21**: 160–3.
2 Nobuyuki S, Nagai Y, Matushima Y *et al.* Infantile bullous pemphigoid treated with intravenous immunoglobulin therapy. *J Am Acad Dermatol* 2007; **57**: 1084–9.
3 Waisbourd-Zinman O, Ben-Amitai D, Cohen A *et al.* Bullous pemphigoid in infancy: clinical and epidemiologic characteristics. *J Am Acad Dermatol* 2008; **58**: 41–8.
4 Chimanovitch I, Hamm H, Georgi M *et al.* Bullous pemphigoid of childhood: autoantibodies target the same epitopes within the NC16A domain of BP180 as autoantibodies in bullous pemphigoid of adulthood. *Arch Dermatol* 2000; **136**: 527–32.
5 Venning VA, Wojnarowska F. Induced bullous pemphigoid. *Br J Dermatol* 1995; **132**: 831–2.
6 Baykal C, Okan G, Sarica R. Childhood bullous pemphigoid developed after the first vaccination. *J Am Acad Dermatol* 2001; **44**: 348–50.

