Two infants with blistering rashes originating on acral sites as a presenting sign of infantile bullous pemphigoid

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INTRODUCTION
Bullous pemphigoid (BP) is a rare autoimmune bullous disorder caused by IgG autoantibodies against hemidesmosomes at the dermoepidermal junction. BP typically occurs in elderly patients but is rarely reported in infants and children. In infants, associations with infection and vaccinations have been proposed.1,2 Topical and systemic steroids are considered first-line treatment options. Disease severity and clinical course vary significantly between patients, and steroid-sparing medications may be necessary.3,4

CASE 1
A 4-month-old boy with a history of eczema and no vaccinations in the previous 2 months presented with a 25-day history of a pruritic blistering rash. The rash started on the hands and feet and then spread to the back. Physical examination found erythematous, polycyclic papules and plaques on the hands, feet, and back (Fig 1) with no mucosal involvement. There were numerous tense bullae filled with serous fluid on the dorsal and ventral surfaces of the hands and feet (Fig 2).

Punch biopsy from the abdomen for hematoxylin and eosin found eosinophilic spongiosis, superficial perivascular inflammation, and numerous eosinophils within the papillary tips. A perilesional punch biopsy for direct immunofluorescence showed linear IgG and C3 along the dermoepidermal junction. Enzyme-linked immunosorbent assay of the patient’s serum showed BP180 IgG antibody (BP180) greater than 150 U (normal <9) and normal BP230 IgG antibody (BP230) (normal <9). Additionally, indirect immunofluorescence testing of the patient’s serum on human salt-split skin substrate showed IgG antibodies along the basement membrane in an epidermal staining pattern.

The patient was treated with 3 days of intravenous methylprednisolone and then transitioned to oral prednisone, 1 mg/kg/d. No new blisters were observed at 3-week follow-up, and he tapered off prednisone over 14 weeks. The patient remained free of disease at 9 months.

CASE 2
A 2-month-old healthy girl presented with a widespread blistering rash that began on her feet the day after her 2-month vaccinations (DTap, Hib, Rotavirus [RV5], PCV13, and Polio [IPV]). On examination, she had erythematous, edematous, polycyclic plaques distributed over the face, trunk, extremities, hands, and feet (Fig 3), including involvement of both the dorsal and ventral surfaces of the hands and feet. There were numerous overlying tense and ruptured bullae (Fig 4). No mucosal lesions were observed.

Skin biopsy for hematoxylin-eosin stain found eosinophilic and neutrophilic spongiosis with small clusters of neutrophils in the papillary dermal tips. Perilesional biopsy for direct immunofluorescence testing showed linear IgG and C3 along the dermoepidermal junction.
showed linear IgG and C3 along the dermoepidermal junction and weak linear IgA. Serum enzyme-linked immunosorbent assay showed BP180 greater than 100 U and normal BP230. Indirect immunofluorescence performed with the patient's serum showed basement membrane zone IgG antibodies in an epidermal pattern on human salt-split skin substrate. Complete blood count (CBC) was notable for white blood cell (WBC) count of 27.8 K/\mu L (normal, 6-18 K/\mu L), platelets of 1,022 K/\mu L (normal, 150-400 K/\mu L), and absolute eosinophil count of 4.6 K/\mu L (normal, 0-0.9 K/\mu L).

She was treated with intravenous methylprednisolone for 3 days followed by oral prednisolone titrated up to 2 mg/kg/d. Given ongoing new lesions,
DISCUSSION

The inciting factors of infantile BP are not fully understood, but stimulation of the immune system by vaccination has been proposed as a trigger. As the presented cases and previous literature demonstrate, a history of recent vaccination is not universal, and the time from vaccination to disease manifestation varies greatly. In one study, the clinical characteristics of 81 infantile BP patients were analyzed, and it was determined 25 patients (30.8%) recently received vaccinations with recent being defined as within the previous 4 weeks. The number and type of vaccines received varied among patients. In case 2, the patient received vaccinations 1 day before her rash started, which suggests the vaccines may have been a trigger.

The presented cases of infantile BP show common clinical and laboratory features of the disease. Both manifested as a blistering rash on acral skin surfaces followed by widespread skin involvement sparing the mucosae. Infantile BP has near-universal involvement of acral sites often followed by a generalized spread and infrequent mucosal involvement.  The elevated BP180 levels with normal BP230 levels in both cases is representative of infantile BP, which manifests with elevation of BP180 and rarely BP230.

The patient in case 2 showed prominent and persistent eosinophilia on her CBC that only decreased once she stopped getting new skin lesions. Previous case reports similarly show eosinophilia on CBC, suggesting eosinophil counts as a possible marker for disease activity and treatment response.

These cases show differing responses to initial corticosteroid treatment. The patient in case 1 responded quickly, whereas the patient in case 2 required a longer course of corticosteroids and additional steroid-sparing agents. Most infantile BP cases respond quickly to systemic corticosteroids, but dapsone is often given with systemic corticosteroids in refractory cases. Intravenous immunoglobulin may also be considered in infantile BP treatment, especially in recalcitrant disease.

Although infantile BP is considered a rare disease, its incidence has been growing. Whether this is caused by increased disease incidence or better diagnostic techniques is uncertain, but clearly defined diagnostic and treatment guidelines would aid clinicians in identifying and treating patients.

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