A 9-YEAR-OLD girl was referred to the Pediatric Dermatology and Cutaneous Laser Center, Baltimore, Md, for evaluation of a blistering rash on the thighs and perineum (Figure 1). The eruption was mildly pruritic and resembled herpes simplex virus type 1. However, the results of a previous examination for sexual abuse, including multiple viral cultures, were normal.

The child appeared healthy and afebrile. The results of the examination showed nontender, tense vesicles and bullae, which were confined to the inner thighs, labia, and perineum. No crusts or excoriations were present.

A Gram stain, Tzanck test, and bacterial and viral cultures of the blister fluid were negative for viruses and bacteria. Complete blood cell count with differential cell count was normal. The histologic condition of a skin biopsy specimen demonstrated subepidermal blister formation (Figure 2). Immunofluorescence revealed a linear pattern of IgA deposition along the basement membrane zone (Figure 3).

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Diagnosis and Discussion

**Chronic Bullous Disease of Childhood**

Figure 1. Bullae appeared on the vulva and extended onto the suprapubic area and thighs.

Figure 2. A biopsy specimen of a vesicle reveals a mixed dermal infiltrate of mononuclear cells, neutrophils, and eosinophils associated with subepidermal blister formation (hematoxylin-eosin, ×100).

Figure 3. Direct immunofluorescence shows a linear band of IgA at the dermoepidermal junction (hematoxylin-eosin, ×100).

Chronic bullous disease of childhood (CBDC) is an immunobullous disease that presents with variably pruritic vesicles and bullae. The lesions are usually located on the perineum, thighs, buttocks, and lower abdomen, and less commonly on the arms, face, and legs. The blisters of CBDC are described as "sausage shaped" and may be as large as 2 cm. The tendency for blisters to cluster around the periphery of older, resolving lesions has led to the use of the term "a string of pearls" to describe expanding bullae. Blistering and subsequent erosions of oral mucosa, which occur in up to 50% of patients with CBDC, may lead to decreased oral intake in infants and toddlers.1

Chronic bullous disease of childhood generally begins before age 10 years. Wojnarowska et al1 found the age range in one series to be between 6 months and 10 years (mean age at onset, 4½ years).1 The immunobullous disease is slightly more common in girls, with a female-male ratio of 3:2.

The differential diagnosis of CBDC includes a number of common dermatologic conditions. Bullous impetigo usually presents with extensive superficial crusted blisters filled with cloudy fluid on an erythematous base. These lesions may be easily distinguished from CBDC based on a positive Gram stain and culture. Chronic bullous disease of childhood may be mistaken for genital herpes simplex virus, which is characterized by painful blisters and erosions on the genitals, perineum, and perianal area. However, herpes simplex virus can be excluded by a negative Tzanck test and herpesvirus culture. Chickenpox and herpes zoster may also be differentiated based on the clinical characteristics and a positive Tzanck test.

In acute contact dermatitis, intense edema may result in blister formation. However, a linear pattern is evident and, when necessary, a skin biopsy specimen demonstrates spongiosis, exocytosis, and acanthosis of the epidermis, consistent with acute dermatitis. Chronic bullous disease of childhood must also be distinguished from other immunobullous diseases such as bullous pemphigoid and dermatis herpetiformis. These conditions may overlap clinically, but CBDC can be defined by the characteristic immunofluorescence pattern. Direct immunofluorescence, in which fluorescein-tagged antihuman anti-bodies are reacted with the patient's skin, shows a linear IgA deposition in the basement membrane zone. In addition, indirect immunofluorescence may detect circulating IgA anti–basement membrane zone antibodies. In this technique, a normal skin sample is incubated first with serum from a patient, followed by fluorescein-labeled antihuman antibodies.

Treatment of CBDC is directed at reducing the severity and duration of outbreaks. Numerous reports support the effectiveness of sulfapyridine in the treatment of CBDC.3-5 Side effects of sulfapyridine include agranulocytosis, aplastic anemia, and hepatic toxicity. Dapsone is an effective therapeutic alternative to sulfapyridine.6 However, patients should be observed for methemoglobinemia, hemolysis, and peripheral neuropathy, which are related to dose. Both sulfapyridine and dapsone may trigger hemolytic anemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Consequently, clinicians should check a G6PD level before therapy is begun. Patients who fail to respond to sulfonamides alone may improve with the addition of prednisone.7 Medication may be required for 6 months to 3 years.

The prognosis of CBDC is generally favorable. While recent reports have shown a subset of patients with episodic recurrences that persist until adulthood,8,9 the eruptions resolved in most patients between 3 and 5 years.6 Chronic bullous disease of childhood should be considered in any child who develops a persistent bullous eruption that fails to respond to traditional measures. Early recognition will result in prompt therapeutic intervention and prevention of a costly, anxiety-provoking diagnostic evaluation.


**REFERENCES**


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