Bullous Pemphigoid in an Infant: A Case Report and Literature Review

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Abstract

Bullous pemphigoid is an autoimmune bullous disease that is rare in children and infants. It seems indistinguishable from the disease in adults although mucous membrane, palms and soles involvement appear more commonly in childhood bullous pemphigoid. There is no association with malignancy. The most reliable diagnostic criterias are the linear deposition of IgG and C_3 along the basement membrane zone and the presence of circulating IgG antibasement membrane zone antibodies. The literature of bullous pemphigoid is reviewed and a case of a 7-month-old girl with typical clinical manifestations and immunofluorescence studies is reported. She responded very well to a high dose of systemic corticosteroid. The disease can be spontaneously resolved and the prognosis for children is good in most cases.

Bullous pemphigoid is a chronic autoimmune blistering disease of the skin and mucous membrane that predominantly affects the elderly, in particular, after the age of 60 years. This disease is rare in children and very rare in infancy with less than 10 cases being reported and the youngest being 3 months old[1,2]. This report presents one of the young juvenile bullous pemphigoid cases with typical characteristics of the disease.

CASE REPORT

A 7-month-old Thai girl from Ayudthaya province was referred to the Department of Pediatrics, Siriraj Hospital in October 1995. She developed multiple blisters on her soles at the age of 5 months. The lesions spread to feet, legs, trunk, arms and face. She had no fever and was in good health. Her parents did not notice the oral ulcer. She was treated with dressing, topical and oral antibiotics without improvement.

On dermatologic examination, there were generalized tense vesicles and bullae with clear fluid on normal appearing skin on the face, scalp, trunk, genitalia and extremities including palms and soles (Fig. 1). Nikolski's sign and bullous spreading sign were absent. There were vesicles

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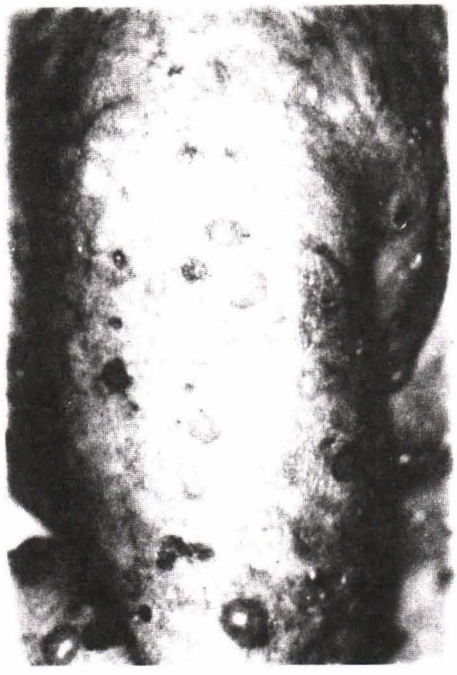

Fig. 1. Multiple vesicles and bullae on the shoulder and arm.

and erosions on the palate and buccal mucosa. General physical examination revealed no abnormality.

Laboratory studies showed leukocytosis with eosinophilia (wbc = 22,800 cells/mm^3 with eosinophils = 1,368 cells/mm^3). She had normal urinalysis, renal and liver function tests. Her G-6PD level was 81.5 IU/ml. The LE, anti-DNA, VDRL and antinuclear antibody tests were negative. Histopathologic examination of biopsy specimen obtained from a new blister exhibited small subepidermal bullae with very little cellular infiltration (Fig. 2). Electron microscopy demonstrated separation of the lamina lucida with well developed attachment plaque and hemidesmosome. Direct immunofluorescence microscopy was strongly positive for IgG and C_3 in linear pattern at the epidermal basement membrane zone (Fig. 3). Indirect immunofluorescence showed circulating IgG antibasement membrane zone antibodies at a titre of 1:80.

The diagnosis of infantile bullous pemphigoid was established. Oral prednisolone 2 mg/kg/day was given with good clinical response in 2 weeks. Most blisters healed with hypopigmentation without scarring.

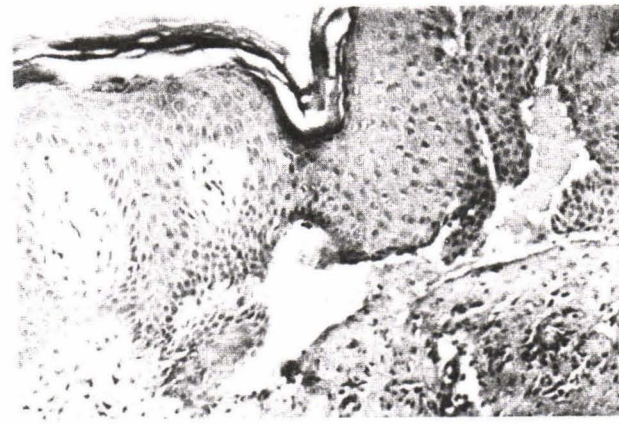

Fig. 2. Histopatholgy shows subepidermal bullae with few cellular infiltration (x100).

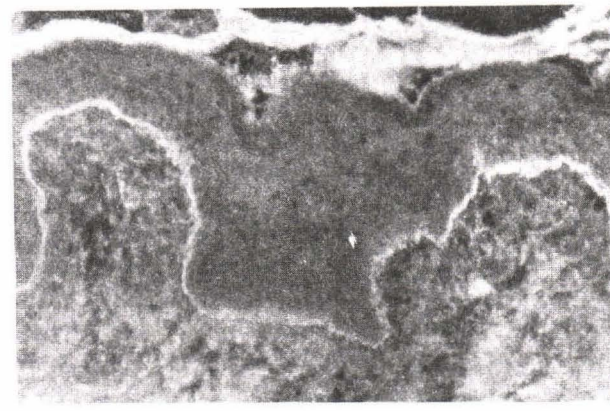

Fig. 3. Direct immunofluorescence shows strongly positive for IgG and C_3 in linear pattern at the epidermal basement membrane zone.

DISCUSSION

Childhood bullous pemphigoid is considered indistinguishable from that seen in adults. The most characteristic clinical feature is the presence of large tense bullae which arise on either an erythematous base or on normal skin. Involvements of the face, palms, soles and mucous membrane especially in the mouth are more common in childhood bullous pemphigoid than those in adults[3]. The lesions are often widespread but may be localized and heal without scarring. Almost all juvenile cases are disseminated although there is a report of localized disease[4]. The prodrome may begin with nonspecific urticarial or dermatitic process with intense pruritus[5]. Diagnosis is

based on clinical presentation and histopathological examination of a fresh blister but the most specific diagnostic procedures depend on direct and indirect immunofluorescence studies on the perilesional or non-involved skin[6]. Our patient was diagnosed as infantile bullous pemphigoid because she had typical cutaneous lesions and the histopathological examination showed subepidermal bullae. Direct immunofluorescence study of her skin demonstrated linear deposit of IgG and C_3 at the basement membrane zone. The deposition of IgG is found in 50-90 per cent and of C_3 in 80-100 per cent of bullous pemphigoid cases[4]. IgG_4 is the predominant IgG subclass[7]. Weak deposits of IgA and IgM are also present in a limited percentage of cases. The amounts of immunoreactant deposits in the skin correlate roughly with the extent of the disease and are less in localized than generalized disease[8]. Circulating IgG antibodies to basement membrane are present in 70 per cent of cases. The antibodies usually detect antigens on the epidermal side of 1 M NaCl split skin[9]. Serum IgE levels tend to be high and eosinophilia may be found as in this case. No correlation exists between peripheral blood eosinophil count and eosinophil infiltration in lesional skin. The peripheral eosinophilia is transient, and disappears when the blisters are controlled[7].

The differential diagnosis includes chronic bullous dermatosis of childhood, dermatitis herpetiformis, pemphigus vulgaris, bullous impetigo, Staphylococcal scalded skin syndrome, toxic epidermal necrolysis, erythema multiforme, bullous contact dermatitis, bullous drug eruption, herpesvirus infection, bullous lupus erythematosus and epidermolysis bullosa acquisita[10].

The etiology of bullous pemphigoid is unknown. Different factors may be involved in the pathogenesis. It can occur after ultraviolet radiation, irradiation, vaccination, drugs, chemical administration or accompany other systemic diseases[10]. It has been reported in association with malignancies of lymphoreticular system, skin, lung, breast, pancreas, kidney, endometrium, ovary, tongue, gastrointestinal and genitourinary tract[7] but there are no reports of particular association with childhood pemphigoid[11]. Our patient had no associated underlying disease and was in good health until the onset of the illness. Bullous pemphigoid is probably an autoimmune disease mediated by the autoantibody directed against a normal antigen in the basement membrane zone, named BP antigen. BP antigen has been detected in sera of the patients. It is shown to be produced by epidermal basal cells and localized in lamina lucida of the basement membrane[12]. Immunoblot analysis identified the BP antigen as multiple antigen molecules, principally 230 and 180 kD antigen[13]. There is considerable evidence suggesting that bullous pemphigoid autoantibodies are pathogenic[14]. The antigen-antibody complexes can activate complement, produce chemotactic activity and activate leukocytes and mast cells to play an important role in mediating the inflammatory event in the disease. These cells produce enzymes and immune-modulating factors whose interaction has been proposed as a mechanism for bullous pemphigoid subepidermal blister formation[15].

Corticosteroids appear to be the mainstay of therapy[10]. They may exert their beneficial effect by influencing local factors related to skin inflammation rather than by suppressing antibody synthesis[15]. Generalized disease requires systemic therapy while localized disease has responded well to topical steroids alone. Intramuscular gold, sulfapyridine, plasma exchange and immunosuppressive agent such as azathioprine, cyclophosphamide and methotrexate have been used either alone or as an adjuvant therapy to minimize the use of steroids[15,16]. Dapsone also produces a good response[17]. In recent years, several reports have claimed the success of tetracycline, erythromycin/niacinamide therapy which suppresses leukocyte chemotaxis[18]. Our patient responded very well to high dose systemic corticosteroid therapy. We avoided using dapsone because she has a heterozygous G-6PD deficiency.

This disease can be spontaneously resolved but usually lasts several months to a year with remissions and exacerbation. Most patients achieve complete remission. Recurrences are often less severe than the initial attack. The mortality rate is extremely low.

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รายงานผู้ป่วยบุลลัส เพ็มฟิกอยด์ ในเด็กทารกและทบทวนวารสาร

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Bullous pemphigoid เป็นโรคผิวหนังเรื้อรังจากการที่ร่างกายมีภูมิต้านทานต่อผิวหนังของตัวผู้ป่วยเอง ส่วนใหญ่โรคเกิดในผู้สูงอายุ พบได้น้อยในวัยเด็กโดยเฉพาะในเด็กทารก การวินิจฉัยนอกจากอาศัยลักษณะทางคลินิก และการตรวจทางพยาธิวิทยาแล้วต้องใช้การตรวจทางอิมมูนพยาธิวิทยาซึ่งจะพบ IgG และ C_3 ติดเป็นเส้นบริเวณรอยต่อระหว่างหนังกำพร้าและหนังแท้บริเวณรอยโรค ผู้ป่วยส่วนใหญ่จะมีแอนติบอดีย์ต่อรอยต่อระหว่างหนังกำพร้าและหนังแท้ในกระแสเลือดด้วย รายงานฉบับนี้เป็นการทบทวนบทความเกี่ยวกับ bullous pemphigoid ในเด็ก และนำเสนอผู้ป่วยเด็กหญิงไทย อายุ 7 เดือน ที่มีอาการและการตรวจพบเข้าได้กับลักษณะของ bullous pemphigoid ทุกประการ เมื่อให้การรักษาด้วยการรับประทาน corticosteroid ก็ได้ผลดี

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