รายงานผู้ป่วย

Juvenile pemphigus vulgaris : a case report

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Wananukul S, Pongprasit P. Juvenile pemphigus vulgaris : a case report. Chula Med J 1995 Apr;39(4): 291-297

Pemphigus vulgaris is extremely rare in children. Only 47 cases of juvenile pemphigus vulgaris have been reported. We report an 11 year old Thai girl who presented with skin blisters prior to oral mucous membrane involvement. Biopsy of the skin lesion demonstrated suprabasilar separation. Direct immunofluorescence showed deposition of immunoglobulin G(IgG) and C3 at the intercellular space of the epidermis. Indirect immunofluorescence showed a circulating antiepidermal cell surface antibody titer at 1:640. Treatment with high-dose oral corticosteroid and azathioprine produced a good clinical response. This is first case report of juvenile pemphigus in Thailand.

Key word: *Juvenile pemphigus vulgaris*

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Received for publication. March 15,1995.

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ศิริวรรณ วนานุกูล, ประไพ พงษ์ประสิทธิ์. เพมฟิกัส วัลการิส ในเด็ก: รายงานผู้ป่วย 1 ราย. จุฬาลงกรณ์เวชสาร 2538 เมษายน; 39(4): 291-297

Pemphigus vulgaris ในเด็ก เป็นโรคที่พบได้น้อยมาก ยังไม่พบรายงานในประเทศไทย พบผู้ป่วยเพียง 47 ราย จากวารสารต่างประเทศ คณะผู้เขียนขอเสนอรายงานผู้ป่วยเด็กหญิงไทย 1 ราย อายุ 11 ปี มาด้วยมีตุ่มน้ำใสขึ้นที่ลำตัวก่อน ต่อมาจึงมีในช่องปาก ลักษณะทางจุลพยาธิวิทยาของตุ่มน้ำใสพบผิวหนังแยกที่เหนือชั้น basal cell การตรวจ direct immunofluorescence จากผิวหนังใกล้เคียงตุ่มน้ำใสพบ immunoglobulin G(IgG) และ C3 ติดที่บริเวณ intercellular space ของชั้น epidermis การตรวจเลือดโดยวิธี indirect immunofluorescence พบ antibody ต่อ epidermal cell surface สูง 1:640 ให้การรักษาด้วยคอร์ติโคสเตียรอยด์ขนาดสูงจึงได้ผล ตามด้วย azathioprine เพื่อลดขนาดคอร์ติโคสเตียรอยด์ลงผู้ป่วยตอบสนองดีต่อการรักษา รายงานนี้เป็นผู้ป่วย pemphigus vulgaris ในเด็กรายแรกที่รายงานของประเทศไทย

Pemphigus is an autoimmune intraepidermal blister disease that involves the skin and mucous membranes. It usually occurs during the fourth through the seventh decades of life and is rarely observed before the age of 20.[1] Until the present report, only 47 cases of juvenile pemphigus vulgaris had been reported.[2-9] We present here the first case of juvenile pemphigus vulgaris in Thailand.

Report of a case

An 11 year old girl was healthy until 1 month prior to admission when blisters were noted on the anterior chest wall. Diagnosed by a local physician as having chicken pox, she was first treated with antihistamine and then ampicillin was later added. The skin lesions spread over the body and also involved tongue. She was seen by another physician who prescribed her prednisolone 15 mg per day for 6 days with partial improvement. Her skin lesions got worse after discontinuation of the drug. Examination revealed small erosions (many of which were hemorrhagic and necrotic slough) on the lips, buccal mucosa and tongue (Fig.1). There were some intact as well as numerous ruptured bullae with raw oozing surfaces scattered over the chest wall, abdomen, back and extremities (Fig. 2-4). Bulla spreading sign and Nikolsky's sign were positive. The remainder of the physical examination findings were unremarkable. Results of admission laboratory studies were within normal limits. A Tzanck test showed acantholytic cells. A skin biopsy revealed suprabasilar separation resulting in intraepidermal vesicles that contained few acantholytic cells. In the dermis, there were superficial perivascular mixed cell infiltrations composed of lymphocytes and eosinophils (Fig.5). Direct immunofluorescence of perilesional skin revealed deposition of IgG,C_3 at the intercellular space of the epidermis. Indirect immunofluorescence (using normal human skin as a substrate) revealed the presence of antiepidermal cell surface autoantibodies through a titer of 1:640.

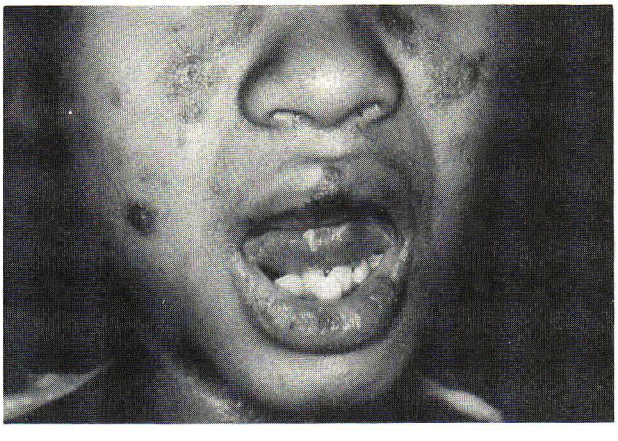

Figure 1. Multiple erosions on tongue and lips.

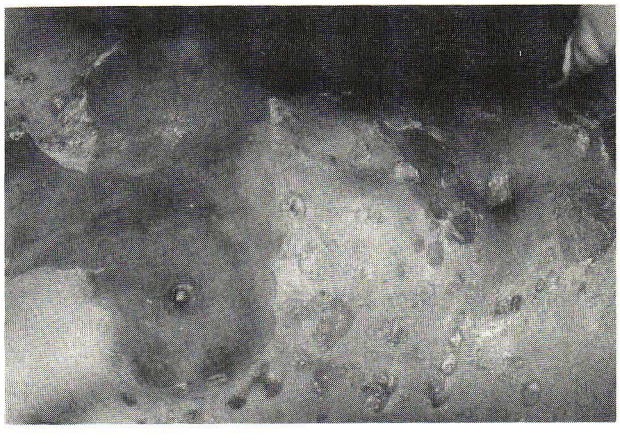

Figure 2. Vesicles, bullae and large denuded raw oozing surfaces at trunk.

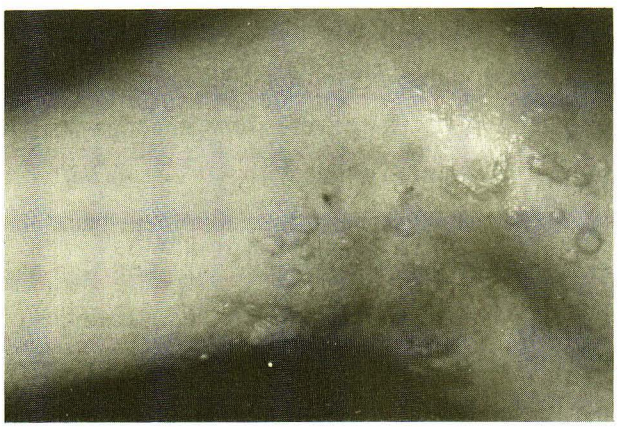

Figure 3. Many vesicles and flaccid bullae on left arm and axilla.

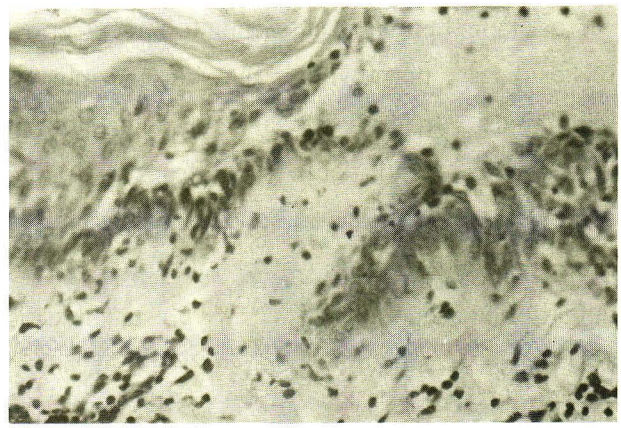

Figure 4. Biopsy of new vesicle on left forearm showing suprabasilar separation with acantholytic cells.

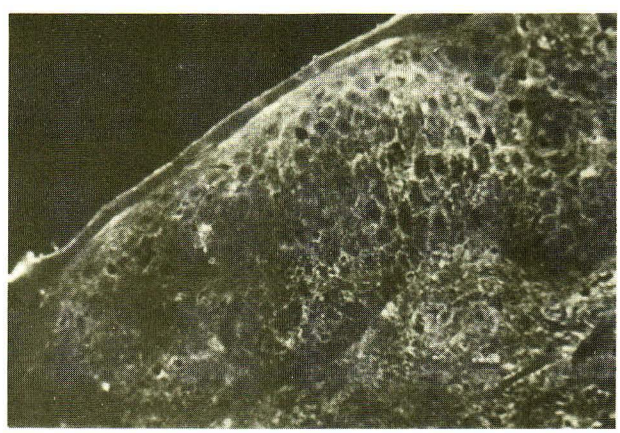

Figure 5. Direct IF showing the intercellular deposit of IgG in the epidermis.

Treatment was strarted with 60 mg oral prednisolone per day (2 mg/kg body weight) but new lesions still developed. The dose of prednisolone was increased by 1 mg/kg body weight weekly until up to 5 mg/kg body weight per day. The patient developed steroid acne, obesity, striae distensa and mild hirsutism. With the cessation of new blister formation, azathioprine at the dose of 2 mg/kg body weight per day was added for steroid sparing effect. Pemphigus antibody titer declined to 1:20 in 4 weeks after treatment. With further improvement the patient's drug dosage was gradually reduced. After 12 months of therapy, she was receiving 15 mg (0.25 mg/kg body weight) of prednisolone every other day and 25 mg (0.5 mg/kg body weight) of azathioprine. She was healthy and free from active skin lesions, only postinflammatory hyperpigmentation was noted. There were no other side effects of the steroid and azathioprine except striae distensa and mild hirsutism.

Discussion

The clinical picture of juvenile pemphigus vulgaris is similar to adult pemphigus vulgaris.[2] Of 47 patients reported to date,[2-9] 25 were male and 22 were female. The youngest patient was 3 years of age. Onset is usually insidious and oral lesions invariably precede skin changes. Cutaneous lesions usually become generalised a few months after the onset of oral changes, but in this case, cutneous lesions preceded oral lesions.

The diagnosis can be established by skin biopsy with histopathologic changes showing suprabasal intraepidermal bulla formation with acantholysis.[10] Demonstration of IgG deposits in the intercellular space by direct immunofluorescence is considered to be a requisite for the diagnosis of pemphigus.[10,11] The circulating antibodies directed against the intercellular substance is correlated with the degree of disease activity.[12,13]

The drug of choice for treatment of pemphigus vulgaris is systemic corticosteroids, prednisolone or its equivalent at 2 to 6 mg/kg per day and is recommended until blistering is brought under control.[14] In childhood pemphigus vulgaris[2] 28 of 31 cases were given systemic corticosteroid in dosages ranging from 0.5 to 8 mg/kg body weight.[2] In this case we started prednisolone at 2 mg/kg per day and the dosage was steped up to 5 mg/kg body weight to completely suppress new blister formation. This patient developed steroid acne, obesity, striae distensa and mild hirsutism, so azathioprine was started for its steroid-sparing effect. Azathioprine is the most commonly used the immunosuppressive agent in the treatment of pemphigus vulgaris.[10] In juvenile pemphigus vulgaris, azathioprine was reported to be effective in 5 cases.[2,13,15] Other adjuvant therapies that have been reported include cyclophosphamide in 2 cases,[2,5] cyclosporine in 2 cases,[6] methotrexate in 2 cases,[2] gold in 1 case [2] and dapsone in 1 case. Dapsone is safer than other adjuvant agents, but it's effect has not been satisfactorily evaluated in either children or adults.[16] Methotrexate is now rarely used for 2 reasons : firstly, it produces rapid granulocytopenic response[17] and thus prone to cause infections and secondly, it has marked effects on the early stage of wound healing in rats.[18] Cyclophosphamide can induce sterility in both men and women and hemorrhagic cystitis.[17] Azathioprine has no inhibitory effect on wound healing in rats[19] and it produces less hematologic toxicity than methotrexate[17] so it is now the immunosuppressive agent most commonly used in the treatment of pemphigus patients.[10]

The prognosis of juvenile pemphigus vulgaris is considerably variable.[2] During the pre-steroid era, pemphigus vulgaris was often a fatal disease. With the introduction of glucocorticoids, the mortality rate decreased dramatically from 60% - 80% to 15% - 45%.[20] In the review of juvenile pemphigus vulgaris,[2] 2/31 died of sepsis and 1/31 died of respiratory insufficiency. Eighteen children lived with maintenance oral therapy, 3 children lived with topical corticosteroid, only 4/31 children were free of disease without treatment.

We emphasize that although juvenile pemphigus vulgaris is rare, it should always be considered in the differential diagnosis of chronic vesiculobullous diseases in children. As the diagnosis cannot always be established by clinical examination alone, Tzanck's test, and histopathologic and immunofluorence studies

are essential for confirmation. Prednisolone should be started promptly because early diagnosis and early treatment influence the course of the disease toward better prognosis. Immunosuppressive agents or other adjuvant therapy should be used only in severe widespread juvenile pemphigus vulgaris that is unresponsive to high dosage of corticosteroid or in case the high dosage of corticosteroid cannot be tapered off.

Acknowledgement

The authors would like to thank Associate Professor Wiwat Kokij for performing and interpreting immunofluoresce studies and Miss Kasemsuk Kuntong for her help in preparing the manuscript.

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