

Pemphigus vegetans: A case report and review of the literature.

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ABSTRACT:

SOMBATMAITHAI S, SOMBATMAITHAI A. PEMPHIGUS VEGETANS: A CASE REPORT AND REVIEW OF THE LITERATURE. THAI J DERMATOL 2012; 28: 169-175.

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Pemphigus vegetans is a very rare variant of pemphigus vulgaris, which is an autoimmune blistering disease of the skin and mucosal membrane. Pemphigus vegetans initially manifests as pustules or vesicles but these primary lesions subsequently develop into vegetating plaques. Typically, these are located in intertriginous areas and the oral mucosa. The histopathological findings of pemphigus vegetans are suprabasal acanthosis, epidermal hyperplasia, papillomatosis, and intraepidermal eosinophilic abscess. Immunofluorescence tests results are indistinguishable from those of pemphigus vulgaris. Pemphigus vegetans has been divided into 2 clinical subtypes, the Neumann type and the Hallopeau type. The Neumann type has a similar course to pemphigus vulgaris, and requires treatment with a high dose of corticosteroids. The Hallopeau type, by comparison, has a more benign course. This report describes a case of pemphigus vegetans Neumann type where the patient presented with typical manifestations and responded to treatment with corticosteroids alone.

Key words: pemphigus vegetans, vesiculobulous disease

บทคัดย่อ:

สรณชัย สมบัติไหมไทย, อลิตา สมบัติไหมไทย. รายงานผู้ป่วย PEMPHIGUS VEGETANS ร่วมกับทบทวนวารสาร วารสารโรคผิวหนัง 2555; 28: 169-175.

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Pemphigus vegetans เป็นโรคที่พบน้อยมากในกลุ่มย่อยของโรค pemphigus vulgaris ซึ่งจัดอยู่ในกลุ่มโรคตุ่มน้ำพองใสที่เกิดจากความผิดปกติของระบบภูมิคุ้มกันที่บริเวณผิวหนังและเยื่อเมือก โดยลักษณะผื่นในระยะแรกจะเป็นตุ่มหนองหรือตุ่มน้ำเล็กๆ โดยทั้งสองชนิดจะกลายเป็นปื้นนูนหนาสีเข้มขึ้นในเวลาต่อมา ตำแหน่งที่พบบ่อยคือ บริเวณซอกพับ เช่น รักแร้ ขาหนีบ และเยื่อในช่องปาก ผลการตรวจทางพยาธิวิทยาโดยในระยะแรกพบ การแยกชั้นเหนือต่อ basal layer ต่อมาชั้น epidermis มีการหนาตัวขึ้น มีการรวมตัวของ eosinophils ในชั้นหนังกำพร้าตามเวลาของการเกิดโรค ผลการตรวจทางพยาธิภูมิคุ้มกัน ไม่สามารถแยกออกจากโรค pemphigus vulgaris ได้ โรคนี้ได้รับการจำแนกออกเป็นสองชนิด ชนิดแรกคือชนิด Neumann ชนิดที่สองคือชนิด Hallopeau การรักษาและการดำเนินโรคของชนิด Neumann จะคล้ายกับโรค pemphigus vulgaris ซึ่งต้องการขนาดของยา corticosteroids ที่สูงเป็นระยะเวลานานและมีโอกาสกลับเป็นซ้ำสูง ต่างจากชนิด Hallopeau ที่รักษาได้ง่ายกว่า การดำเนินโรคสั้นกว่า เรารายงานผู้ป่วยซึ่งเป็นโรค pemphigus vegetans ชนิด Neumann ที่เป็นแบบฉบับและตอบสนองต่อการรักษาด้วย corticosteroids เพียงชนิดเดียว

คำสำคัญ: pemphigus vegetans, โรคตุ่มน้ำพองใส

Introduction

Pemphigus vegetans, a rare form of pemphigus, is characterized by verrucous plaques surrounded by flaccid bulla or pustules on the intertriginous area and oral mucosa. There are 2 types of this disease, Hallopeau type and Neumann type, with the former seeming to have a more benign course than the latter.

Case report

A 65-year-old Thai man presented with a 5 year history of malodorous vegetating plaques with scattered flaccid bulla on the neck, axilla, groin, scrotum and buttocks. He had no symptoms of any systemic disease and was not on any medication. There was no family

history of a vesiculobullous disease. On physical examination, there were foul smelling whitish papillomatous verrucous plaques surrounded by flaccid vesicles and bulla on the neck, axilla, groin, scrotum and buttocks. (Figures 1-5) His tongue showed cerebriform-like changes. (Figures 6) The oral mucosa, hair and nails were unremarkable.

A biopsy specimen obtained from a vesicle on the left axilla revealed suprabasal separations with acantholysis and few dyskeratotic cells with some area of scale crust formation. There were superficial perivascular lymphoplasmacytic infiltrations without eosinophils. Direct immunofluorescence study of the

perilesional skin showed intercellular deposits of C3. (Figures 8) Laboratory testing showed complete blood count and liver function to be normal.

Treatment was started with oral prednisolone 30 mg/day without topical treatment. Within 2 weeks, the verrucous vegetations on both axillae improved dramatically without appearance of skin bullae. (Figures 9) No malodorous smell was detected after 1 month. The dose of prednisolone was tapered to 20 mg/day, without the appearance of new lesions.



Figures 1 Physical examination revealed some minute vesicles and erosions on erythematous bases at nape of the neck.



Figures 2 Physical examination revealed groups of flaccid bullae with hyperkeratotic papules at the center.



Figures 3A, 3B Physical examination reveals bilateral whitish vegetating verrucous plaques surrounding with vesicles on both axilla.



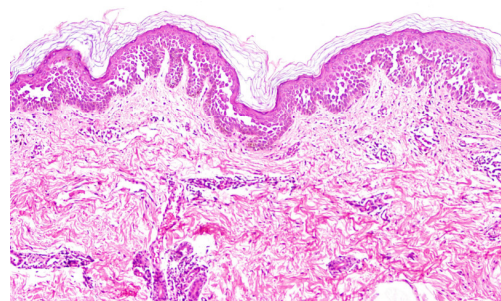
Figures 4 Physical examination revealed whitish vegetating verrucous plaques on both groin and scrotum.



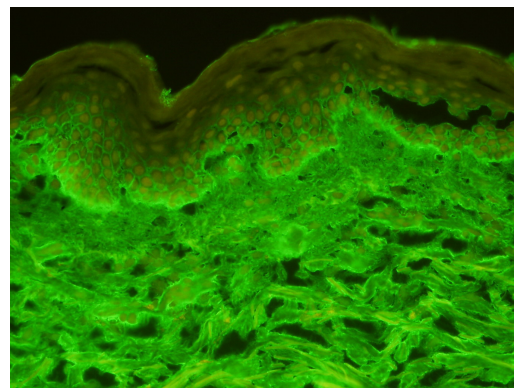
Figures 5 Physical examination revealed flaccid bulla and eroded skin on the buttocks



Figures 6 Physical examination revealed a cerebriiform-like change at dorsal of the tongue.



Figures 7 Histopathology from vesicle showed suprabasal separations with elongated dermal papillae showing so-called villi and acantholysis.



Figures 8 Direct Immunofluorescence study showed intercellular deposits of C3.



9A



9B

Figures 9A,9B Improvement in the clinical appearance of the lesions after 2-weeks of systemic corticosteroids treatment.

Discussion

Pemphigus vegetans is a rare vegetating variant of an autoimmune blistering skin disease, pemphigus vulgaris. Its incidence has been suggested to be 2% of patients with this class of disease in Croatia¹, and Sicily.² Pemphigus vegetans can occur in people of all age groups including children, with the median age of disease onset being 40-50 years.³ The disease is caused by autoantibodies against desmogleins, proteins which play an important role in cell-cell adhesion of keratinocytes. IgG autoantibodies are responsible for the blister formation.⁴

Patients with pemphigus vegetans usually presented with flaccid blisters which became eroded forming fungoid vegetations or granulomatous proliferations. This was particularly dominant in intertriginous areas and the oral mucosa, and sometimes on the scalp or face. Involvement of the vermillion border of the lips is the clinical hallmark of oral lesions.⁵ The tongue may show cerebriform like changes.^{4,6} Nail involvement are characterized by dystrophy and verrucous paronychia.^{7,8,9} There are a few reports of patients with solitary lesions limited to the oral cavity, scalp and feet.^{5,6,10,11,12} Pemphigus vegetans has been classified into 2 subtypes. The first Hallopeau type starts with circumscribed pustules, and has a relatively benign course. This is in contrast to the second Neumann type, which has vesicles and bullae as primary lesions, is more frequently seen, and develops into extensive lesions that are often refractory to therapy.¹³

The diagnosis of pemphigus vegetans is based on clinical findings correlated with histopathology and immunofluorescence. Histopathological examination of skin lesions show suprabasal acantholysis in the early lesions, epidermal hyperplasia, papillomatosis, and intraepidermal eosinophilic abscesses as lesions age. Eosinophilic responses, characterized by the formation of microabscess and vesiculation, are features which help to differentiate this disease from the vulgaris type.¹⁴

Immunofluorescence findings in pemphigus vegetans are indistinguishable from those of pemphigus vulgaris. Direct immunofluorescence demonstrates deposition of IgG and C3 in the intercellular space of keratinocytes. Indirect immunofluorescence reveals circulating IgG on the cell surface.¹⁵

Previous publications consistently reported autoantibodies against desmoglein 3 in patients, while autoantibodies against desmoglein 1, desmocollin 1 and 2 and periplakin were occasionally detected.^{16,17,18} Autoantibodies were generally classified as IgG, and in one instance IgA.¹⁹

It may be difficult to diagnose pemphigus vegetans because of the varieties of clinical presentation and the histopathological resemblance to other conditions. Pyodermitis- pyostomatitis vegetans (PD-PSV) should be included in the differential diagnosis because it shows similar clinical and histopathological features but has a negative result on immunofluorescence. However, most patients with PD-PSV have underlying

ulcerative colitis and some have Crohn's disease.²⁰ Because of mucosal involvement, Stevens-Johnson syndrome and a severe expression of erythema multiforme may be included in the differential diagnosis also.²¹ Paraneoplastic pemphigus (PNP) may also presents with vegetans-like plaque on the oral and perineal area.^{7,20,22} Moreover, there is a case report of childhood pemphigus vegetans variant of intraepidermal neutrophilic IgA dermatosis.²³ Vegetating plaques may present in chronic lesions that resist therapy in one location.⁴

As with pemphigus vulgaris, systemic glucocorticoids are the treatment of first choice for pemphigus vegetans. However, administration of corticosteroids alone does not always induce disease remission. Addition of immunosuppressive agents such as azathioprine, dapsone, cyclophosphamide and cyclosporine may improve remission and allow a steroid-sparing effect. Rackett *et al.* reported that pemphigus vegetans with treatment-resistant scalp lesions can be controlled well with methotrexate, oral corticosteroids and periodic intralesional corticosteroid injection.²⁴ Ichimiya *et al.* reported that treatment with a combination of corticosteroid and etretinate resulted in healing of the persistent verrucous vegetations.²¹ Complete remission of recalcitrant pemphigus vegetans in a patient was achieved with extracorporeal photopheresis.²⁵ Another recalcitrant case was successfully treated with etanercept and carbon dioxide laser.²⁶

Nowadays, there are many case reports of pemphigus vegetans associated with infection, cancer and drug use. These include cases in association with HIV-1 infection,²⁷ and cases associated with exposure to the drugs captopril, penicillamine and intranasal heroin.²⁸ In addition, pemphigus vegetans has been associated with gastric cancer, colon cancer, and lung cancer.^{22,29,30}

Acknowledgements

We would like to thank Professor Kanokvalai Kulthanan and Dr. Tim Cushnie for their kind support.

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