Pemphigus vegetans with Premalatha sign: a case report

Kanawat Kanjanapiboon MD,

Pinnaree Kattipathanapong MD.

ABSTRACT:

KANJANAPIBOON K, KATTIPATHANAPONG P. PEMPHIGUS VEGETANS WITH PREMALATHA SIGN: A CASE REPORT. THAI J DERMATOL 2018; 34: 163-168.

INSTITUTE OF DERMATOLOGY, MINISTRY OF PUBLIC HEALTH, BANGKOK, THAILAND.

Pemphigus vegetans is a rare clinical variant of pemphigus vulgaris, an autoimmune bullous disorder. It is characterized by papillomatous vegetations commonly affecting periorificial and intertriginous areas. The pathogenesis is due to a production of immunoglobulin G (IgG) antibodies against intercellular adhesion protein leading to acantholysis. It is clinically classified into two variants: Neumann type and Hallopeau type. We reported a 42-year-old male patient presented with intractable stomatitis, vegetating lesions over the flexural areas and the typical cerebriform tongue or "Premalatha sign" which led to the diagnosis of pemphigus vegetans.

Key words: Pemphigus vegetans, cerebriform, Premalatha

บทคัดย่อ:

คณวัฒน์ กาญจนพิบูลย์, ปิ่นนรี ขัตติพัฒนาพงษ์ รายงานผู้ป่วยโรค PEMPHIGUS VEGETANS ร่วมกับ PREMALATHA SIGN วารสารโรคผิวหนัง 2561; 34: 163-168.

สถาบันโรคผิวหนัง กรมการแพทย์ กระทรวงสาธารณสุข

From : Institute of Dermatology, Ministry of Public Health, Bangkok, Thailand.

Corresponding author : Kanawat Kanjanapiboon, MD. e-mail: phetpcn29@hotmail.com

Pemphigus vegetans เป็นโรคตุ่มน้ำพองชนิดหนึ่งที่พบได้ไม่บ่อย จัดเป็นโรคในกลุ่มเดียวกับ pemphigus vulgaris อาการแสดงทางคลินิกมักเป็นผื่นนูนหนาตามบริเวณซอกพับและรูเปิดของร่างกาย กลไกเกิดจากการสร้างแอนติบอดี้มาทำลายการยึดเกาะของเซลล์ผิวหนัง ทำให้ผิวหนังแยกชั้นหลุดจากกันโดยง่าย สามารถแบ่งโรคตามลักษณะทางคลินิกออกเป็น 2 ชนิด คือ ชนิด Neumann และชนิด Hallopeau ในรายงานนี้นำเสนอผู้ป่วยที่มีอาการแสดงคือ แผลเรื้อรังในช่องปากร่วมกับมีผื่นนูนหนาบริเวณซอกพับและพบลิ้นย่นริ้วหรือเรียกว่า Premalatha sign ซึ่งเป็นลักษณะเฉพาะที่ช่วยในการวินิจฉัยโรค Pemphigus vegetans ได้

คำสำคัญ: Pemphigus vegetans, รอยหยัก, Premalatha

Case report

A 42-year-old Thai man came to the Institute of Dermatology with intractable stomatitis and itchy rash on perianal area for 1 year. Initially, the cutaneous lesions started with few discrete vesicles and bullae on his face, scalp, right arm and itchy rash on perianal area. Later, the lesions on his scalp and perianal area had gradually progress into jagged mass. The lesions became intensely itchy and occasionally painful without tendency to heal. The patient had no other systemic symptom. He had no underlying disease and denied neither traumatic history nor exposure to chemical compound. Neither similar skin lesions nor malignancy presented in his family members.

Physical examination revealed localized large well-defined papillomatous vegetating erythematous plaques on perianal area (Figure 1) and few discrete tense bullae on the face, scalp, right arm with approximately involved 3% of body surface area (Figure 2). Multiple oral ulcers and erosions with cerebriform tongue (Premalatha sign) were also noticed in his oral cavity (Figure 3). Eye and nail examination were both unremarkable.

Blood examination for complete blood count (CBC) and liver function tests (LFTs) were unremarkable. Serology tests for human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) were all non-reactive. A 4-mm punch biopsy from lower perianal area displays suprabasal separation of the hyperplastic epidermis with acantholysis and neutrophilic infiltration within the blister (Figure 4). The dermis shows a superficial perivascular infiltration with lymphocytes and neutrophils. Direct immunofluorescence at that time showed positive IgG and C3 at intercellular space of epidermis. Indirect immunofluorescence was also positive as low titer (1:80) for pemphigus IgG autoantibody. Anti-desmoglein 3 antibody was positive at level of 483.

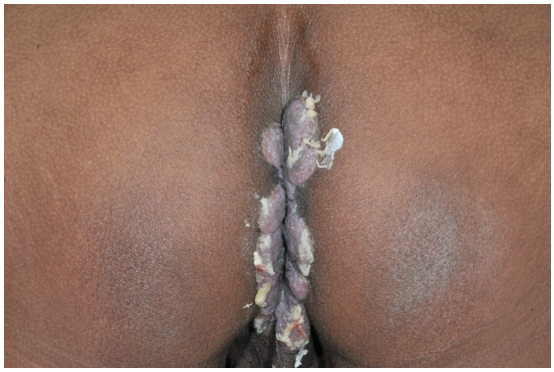

Figure 1 Localized large well-defined papillomatous vegetating erythematous plaques on perianal area

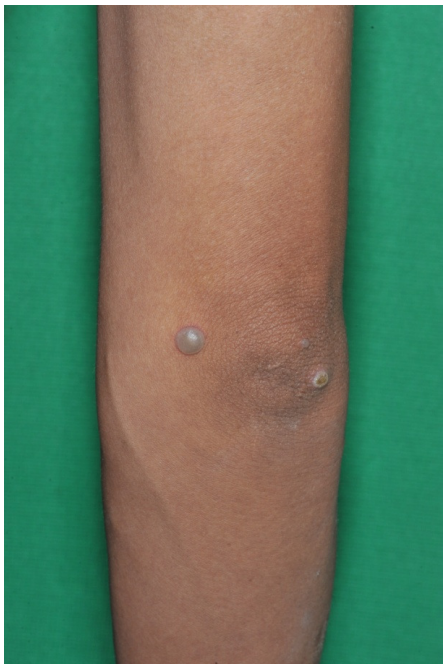

Figure 2 Tense bulla on the right arm

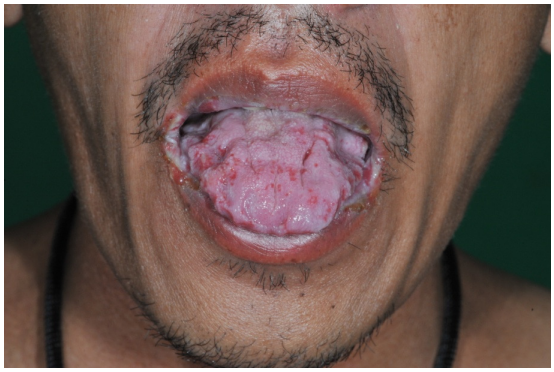

Figure 3 Cerebriform tongue (Premalatha sign)

Discussion

Pemphigus vulgaris is an autoimmune disorder characterized by production of immunoglobulin G (IgG) antibodies against intercellular adhesion protein desmoglein leading to acantholysis.[1] Pemphigus vegetans is a rare clinical variant of pemphigus vulgaris and is characterized by papillomatous vegetations commonly affecting periorificial and intertriginous areas. Cerebriform tongue is a common sign seen in pemphigus vegetans presented with a typical pattern of sulci and gyri over dorsum of the tongue.[2-4] This clinical sign can be used as a clue for the diagnosis of pemphigus vegetans.

Pemphigus vegetans was first described by Neumann in 1876. It is clinically classified as two variants, which are differentiated based on their clinical presentation, disease course and treatment response. 1) Neumann type with periorificial papillomatous vegetations and 2) Hallopeau type with pustular lesions evolving into vegetations preferentially affecting the

intertriginous areas and a benign course with few relapses [5,6]. They can occur over normal skin or over the lesions of pemphigus vulgaris. Half of the patients with pemphigus vegetans have lesions in the oral cavity months preceding cutaneous lesions. Patients with cutaneous lesions will ultimately develop oral manifestations later. The large plaques seen in our patient were typical pattern of sulci, gyri over the flexural lesions seen in pemphigus vegetans. Cerebriform tongue, described as "Premalatha sign", was found in this patient. In a study of 12 pemphigus vegetans cases, 6 cases of Neumann type (50%) showed cerebriform tongue and 2 cases had a cerebriform scalp.[3,4] The papillary hyperplasia could be the cause of the cerebriform morphology on cutaneous lesions over the flexures.[2]

Pemphigus vegetans is caused by intercellular autoantibodies primarily against desmogleins 1 and 3, which are adhesion molecules in the desmosomes of keratinocytes.[7] Previous studies reported autoantibodies against desmoglein 3 in patients with pemphigus vegetans. Occasionally, some previous studies also reported autoantibodies against desmoglein 1, desmocollin 1 and 2, and periplakin.[7-9]

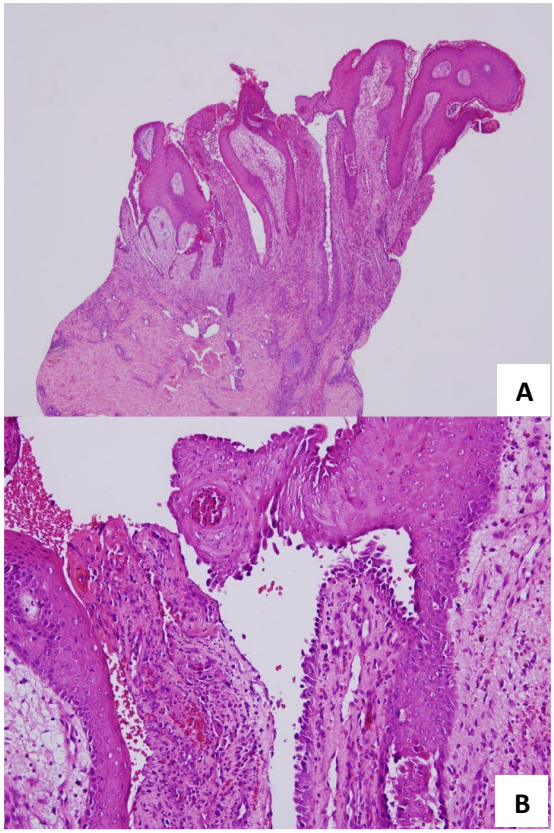

Figure 4 Histologic features of skin biopsy from perianal area; suprabasal separation of the hyperplastic epidermis with acantholysis and neutrophilic infiltration within the blister. The dermis shows a superficial perivascular infiltration with lymphocytes and neutrophils. (H&E; original magnification: **A**. x40, **B**. x200)

The definite diagnosis of this patient was pemphigus vegetans of Neumann, according to clinical presentation and physical examination. The skin biopsy helped to confirm the diagnosis by showing suprabasal separation with acantholytic cells admixed with neutrophils and

prominent papillomatosis and irregular acanthosis of epidermis. Inflammatory cells infiltrated in papillary dermis were mainly lymphocytes and neutrophils. Both direct and indirect immunofluorescences were not different from pemphigus vulgaris, which was the prototype of pemphigus vegetans. Blood test for anti-desmoglein 3 antibody was positive at level of 483, represented the mucosal-dominant lesions in this patient. All of the evidences were clues to our diagnosis.

Treatment of pemphigus vegetans is similar to pemphigus vulgaris, which is normally accomplished with systemic corticosteroid.[10] However, oral corticosteroid administration cannot always induce disease remission. The addition of immunosuppressants, such as azathioprine, cyclosporine or mycophenolate mofetil may improve remission rates and allow a steroid-sparing effect.[10,11] Patients with the Neumann type have a similar course as those with pemphigus vulgaris but may require higher dosages of corticosteroid. Remissions and relapses can be found. Hallopeau patients usually respond to lower dosages of corticosteroid and may have fewer relapses. Some studies show the successful use of dapsone and retinoids.[10-12]

This patient was initially treated with prednisolone 45 mg/day (0.7 mg/kg/day) and azathioprine 100 mg/day (1.5 mg/kg/day). The lesions gradually improved within 3 months and the dosage of prednisolone was slowly decreased. Three months later, the lesions were resolved leaving residual post-inflammatory hyperpigmentation. There was no recurrence after a 6-month follow-up. After 7-month treatment, the medications were gradually adjusted to prednisolone 5 mg/day and azathioprine 50 mg/day to control the symptoms. After 12-month treatment, azathioprine was administered 50 mg on every other day and prednisolone was discontinued. The level of anti-desmoglein 3 antibody was decreased from 483 to 256.

References

1. Dhamija A, D'Souza P, Meherda A, Kothiwala RK. Pemphigus vegetans: An unusual presentation. Indian Dermatol Online J. 2012;3:193-5.
2. Ganapati S. Eponymous dermatological signs in bullous dermatoses. Indian J Dermatol. 2014;59:21-3.
3. Premalatha S, Jayakumar S, Yesudian P, Thambiah AS. Cerebriform tongue-a clinical sign in pemphigus vegetans. Br J Dermatol. 1981;104:587-91.
4. Premalatha S. Cerebriform tongue, the history behind the sign [corrected]. Indian J Dermatol. 2014;59:198-9.
5. Bystryn JC, Rudolph JL. Pemphigus. Lancet. 2005;366:61-73.
6. Becker BA, Gaspari AA. Pemphigus vulgaris and vegetans. Dermatol Clin. 1993;11:429-52.

7. Cozzani E, Christana K, Mastrogiacomo A, et al. Pemphigus vegetans Neumann type with anti-desmoglein and anti-periplakin autoantibodies. Eur J Dermatol. 2007;17:530-3.
8. Morizane S, Yamamoto T, Hisamatsu Y, et al. Pemphigus vegetans with IgG and IgA antidesmoglein 3 antibodies. Br J Dermatol. 2005;153:1236-7.
9. Torok L, Husz S, Ocsai H, Krischner A, Kiss M. Pemphigus vegetans presenting as acrodermatitis continua suppurativa. Eur J Dermatol. 2003;13:579-81.
10. Ichimiya M, Yamamoto K, Muto M. Successful treatment of pemphigus vegetans by addition of etretinate to systemic steroids. Clin Exp Dermatol. 1998;23:178-80.
11. Werth VP, Fivenson D, Pandya AG, et al. Multicenter randomized, double-blind, placebo-controlled, clinical trial of dapsone as a glucocorticoid-sparing agent in maintenance-phase pemphigus vulgaris. Arch Dermatol. 2008;144:25-32.
12. Lin MH, Hsu CK, Lee JY. Successful treatment of recalcitrant pemphigus vulgaris and pemphigus vegetans with etanercept and carbon dioxide laser. Arch Dermatol. 2005;141:680-2.
13. Heaphy MR, Albrecht J, Werth VP. Dapsone as a glucocorticoid-sparing agent in maintenance-phase pemphigus vulgaris. Arch Dermatol. 2005;141:699-702.