# Unrecognized vegetative plaque: Pemphigus vegetans

**Chuda Rujitharanawong MD,**

**Penvadee Pattanaprichakul MD.**

## ABSTRACT:

**RUJITHARANAWONG C, PATTANAPRICHAKUL P, UNRECOGNIZED VEGETATIVE PLAQUE: PEMPHIGUS VEGETANS. THAI J DERMATOL 2018; 34: 200-206.**

*DEPARTMENT OF DERMATOLOGY, FACULTY OF MEDICINE SIRIRAJ HOSPITAL, MAHIDOL UNIVERSITY, BANGKOK, THAILAND.*

Vegetative plaques on intertriginous areas are a classic characterization of Pemphigus vegetans (P veg). By clinical presentations, two subtypes of P veg are demonstrated including (i) Neumann type that initially presents with flaccid bullae and erosions, (ii) Hallopeau type that originally characterized by pustular lesions, then rupture to form granulating erosions. Consequently, vegetative plaques with peripheral hypertrophic granulation tissue develop with a centrifugal expansion. The P veg typically affects intertriginous regions, nevertheless, it may occur at any site of body.[1] To our knowledge, very few studies have been reported about P veg. Therefore, this case was presented as a solitary vegetative lesion in atypical area, right preauricular region that was initially mistaken diagnosis due to its unusual presentation of P veg.

**Key words:** pemphigus vegetans

From: Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Corresponding author : Chuda Rujitharanawong MD., email : maichudaruji@gmail.com

**บทคัดย่อ:**

**ชุดา รุจิธารณวงศ์, เพ็ญวดี พัฒนปรีชากุล รายงานผู้ป่วยโรค PEMPHIGUS VEGETANS**
**วารสารโรคผิวหนัง 2561;34: 200-206.**

*ภาควิชาตจวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล*

ลักษณะรอยโรคที่สำคัญของโรค pemphigus vegetans คือเป็นปื้นหนาที่บริเวณซอกพับต่างๆ (intertriginous area) โดยจากลักษณะรอยโรคเริ่มแรกสามารถแบ่งโรค pemphigus vegetans ออกเป็น 2 กลุ่มดังนี้ (1) ชนิด Neumann เริ่มแรกพบเป็นตุ่มน้ำแตกง่ายกลายเป็นแผลถลอกตื้น (2) ชนิด Hallopeau เริ่มแรกเป็นตุ่มหนองแล้วแตกออกกลายเป็นแผลถลอก ซึ่งการดำเนินโรคต่อมาของทั้ง 2 ชนิดนั้นแผลถลอกมักจะขยายออกไปจนกลายเป็นแผ่นใหญ่ พบมีการสร้างเนื้อเยื่อแกรนูเลชัน (granulation tissue) และปกคลุมด้วยสะเก็ดทำให้แผลหนาตัวขึ้น โดยทั่วไปโรค pemphigus vegetans มักเกิดที่บริเวณซอกพับต่างๆ แต่ก็มีรายงานการเกิดที่บริเวณอื่นๆ ของร่างกายได้เช่นกัน จากการรวบรวมข้อมูลก่อนหน้าพบว่ารายงานเกี่ยวกับโรค pemphigus vegetans ยังมีน้อย ด้วยเหตุนี้จึงขอนำเสนอเคสผู้ป่วยชายที่มีลักษณะรอยโรคเริ่มแรกเป็นปื้นหนาที่บริเวณหน้าต่อใบหูข้างขวาเพียง 1 ตำแหน่ง ซึ่งไม่ใช่ตำแหน่งที่พบบ่อยของโรค pemphigus vegetans จึงทำให้เกิดความผิดพลาดในการวินิจฉัยในตอนแรก

**คำสำคัญ:** โรค pemphigus vegetans

**Introduction**

Pemphigus vegetans (P veg) is an unusual clinical presentation of pemphigus vulgaris (PV) that is only 1-2% of all pemphigus.[1,2] The prevalence of P veg ranges from 2-7% and affects predominantly middle-aged adults.[3-8]

**Case report**

A 66-year-old, never-smoker male, presented with progressive dyspnea for 1 year without fever, chronic cough, hemoptysis, nor pleuritic chest pain. Chest x-ray demonstrated right pleural effusion. Pleural aspiration with pleural fluid analysis and computed tomography of the chest were performed and confirmed the diagnosis of pleural tuberculosis. Antituberculosis drugs were initiated but the symptom of dyspnea was worsening, so he was admitted to the hospital for reevaluation by pleuroscopy. Meanwhile, the patient mentioned a gradually progressive plaque on his right preauricular area, which began as a pruritic brownish verrucous plaque with oozing for over 18 months. He had no other cutaneous lesions nor mucosal involvement. He had previously applied several topical antibiotics such as mupirocin and neomycin, but the lesion was not improved. No family history of an autoimmune or blistering dermatologic disease was recorded.

On physical examination, there was a well-defined, approximately 3 × 5 cm in size, irregular, hypertrophic, crusted brownish plaque over the right preauricular area (Figure 1).

Cervical lymphadenopathy or other systemic findings were not identified. Laboratory investigation of complete blood count, liver function test, and renal function test were within normal range. Chest X-ray revealed persistent right pleural effusion with pulmonary infiltration. The diagnosis of pleural tuberculosis was re-confirmed by the pleural effusion analysis showing exudative pleural profile. Therefore, the standard regimen of antituberculosis drugs were continued. Regarding to the cutaneous lesion, the differential diagnosis for dermatologic diseases including autoimmune disease and malignancy was reconsidered. Therefore, the elliptical skin biopsy at lesion was performed and demonstrated eosinophilic microabscesses and intraepidermal clefts with acantholytic cells with background of marked epidermal hyperplasia (Figure 2). Direct immunofluorescence (DIF) was positive for immunoglobulin G (IgG) and complement 3 (C3) at intercellular space (Figure 3). In addition, the tissue culture showed *Pseudomonas aeruginosa*, whereas, the results of fungal and mycobacterial culture were negative. Thus, the diagnosis of P veg with colonization of *Pseudomonas aeruginosa* was confirmed. The patient was then treated by topical corticosteroid; 1% mometasone furoate cream along with several courses of broad-spectrum antibiotics. Although the lesion was persisted, the vegetative plaque stopped progression and was significantly decreased the thickness and size of the lesion in 4-week duration. There had been no new lesions occurred on the skin or mucosal membrane elsewhere.

**Discussion**

P veg is considered a rare clinical variant of PV that firstly described by Neumann in 1876.[9] The disease can occur in all age groups with preponderance in middle-age patients. Additionally, P veg is noticeable in patients with history of enalapril, intranasal heroin abuse, and immunocompromised host including HIV infection, and organ transplantation.[9-12] The typical presentation of P veg is verrucous and vegetative plaques that are usually limited to intertriginous area. The oral mucosa is commonly affected, and cerebriform or scrotal tongue is a diagnostic clue of early involvement.[13] P veg is classified into 2 types, based on initial clinical presentation and disease progression, consisted of Neumann and Hallopeau types. For Neumann type, erosive blisters on intertriginous areas and mucosa are firstly observed, then progress to be vegetations. Whereas Hallopeau type develops from pustular lesions over typical affected location, then gradually evolve into verrucous and papillomatous vegetation.[1] Due to lack of clinical resemblance to a vesiculobullous disorder, the Hallopeau variant is difficult to diagnosed. To

compare between 2 types, Hallopeau type is a relatively benign severity with preferable response to treatment.[1] Hence, the prognosis of Hallopeau type assumes to be better than another one and higher opportunity of remission.

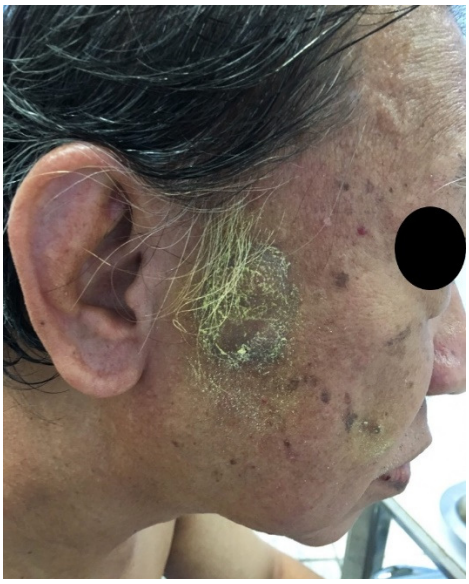

**Figure 1.** The well-defined solitary brownish hypertrophic plaque with verrucous surface and thick crusted formation located on right preauricular area. No vesicle, bullae or pustular lesion was noticed on the surface of this plaque.

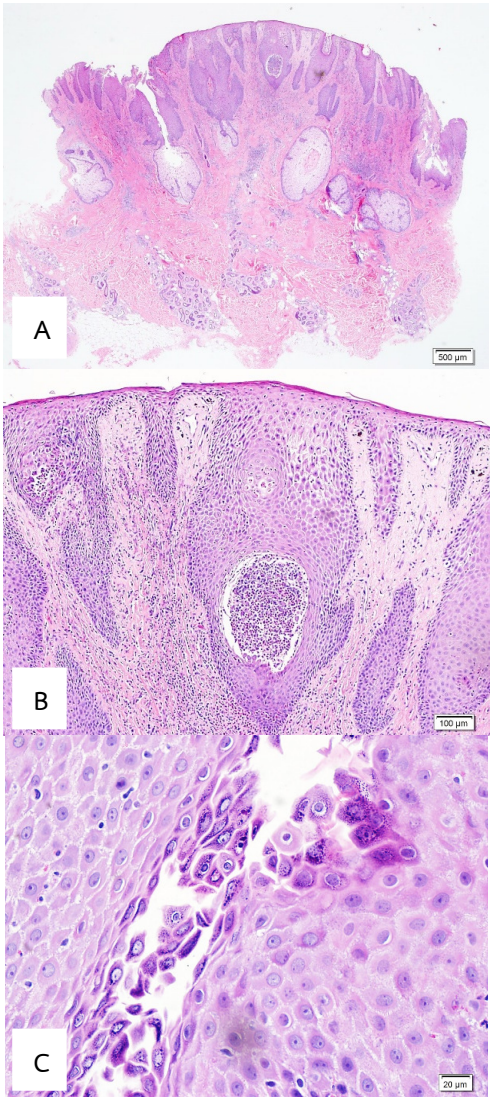


**Figure 2.** (A) A biopsy of the vegetative plaque from right preauricular area demonstrated a papillomatous epidermis with parakeratosis and erosion. (B, C) The typical evidence of suprabasal sepeartion with scattered acantholytic cells was detected within epidermis. Moreover, epidermal spongiosis with exocytosis of eosinophils and eosinophilic microabscess were revealed and a sparse infiltration of mixed inflammatory cells was observed. (A; H&E x2, B; H&E x40, C; H&E X100)

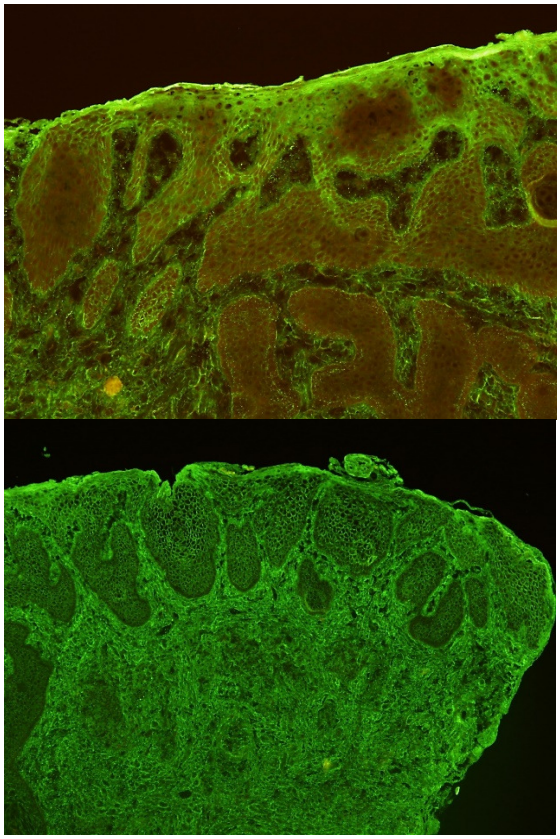

**Figure 3.** Direct immunofluorescence demonstrated intercellular immunoglobulin G and complement 3 deposition at the skin lesion.

In the aspects of P veg pathogenesis, the immunological factors including helper T-cell mediated immune reaction with autoantibody and cytokines is assumed to play a principal role in abnormal epithelial proliferation and eosinophil chemotaxis. Referring to previous studies, anti-desmoglein 1 and 3 autoantibodies are reported to initiate P veg. Additionally, other autoantibodies as desmocollin1, desmocollin2 and periplakin, are also associated with the cause of this disease.[14] Nevertheless, the exact pathogenesis of P veg is still indefinite. Interestingly, other dermatologic diseases such as paraneoplastic pemphigus and pyostomatitis vegetans can exhibit similar lesions to P veg. Owing to rare condition and lack of familiarity with clinical theory, the diagnosis of P veg is often failed to notice. Therefore, histologic examination and immunofluorescent study should be performed. The evidence of pseudoepitheliomatous, verruciform, epidermal hyperplasia with intraepidermal eosinophilic abscesses is an essential clue of P veg.[2] The deposit of IgG and C3 on the surface of keratinocytes is the most common feature of P veg on DIF.[1] According to indirect immunofluorescence (IIF), positive circulating anti-epithelial cell-surface IgG is demonstrated. For other laboratory tests, eosinophilia is observed in previous reports and sometimes rise up to 5400/mm$^3$, however, this data is limited and needed further studies.[11, 13]

Of this present case, P veg is unrecognized at the beginning owing to atypical location and unusual presentation with superimposed Pseudomonas infection. Relying on repeated clinical reviews, histological evaluation and immunofluorescent study, we can accomplish a correct diagnosis. The pathologic examination and DIF strongly support the diagnosis of P veg. From the review of literature, P veg is previously

observed as a solitary lesion that occurs over non-intertriginous areas such as scalp and face, and later on the vegetative plaques turn to be drying out and transform into warty, fissured, painful, seborrheic keratosis-like lesions. Although there was no initial pustular lesion, the Hallopeau types is suspected in the present case due to benign progression with mild disease severity. The importance to determine P veg subtype is due to the prognosis and treatment outcome. Based on previous studies, young age of onset is related to worsening treatment outcome. Moreover, the mucosal involvement is indicative for poor prognosis.[3]

The treatment of P veg is similar to PV. Both of topical and systemic corticosteroids play role as the main treatment of P veg. Topical and/or intralesional corticosteroids are recommended to treat localized from of P veg with previous reports of significantly improved outcomes. Nevertheless, many cases require other immunosuppressive drugs including azathioprine, cyclosporine, cyclophosphamide, mycophenolate mofetil and methotrexate to achieve complete remission. For therapy-refractory patients, TNF $\alpha$-blockers, extracorporeal photopheresis, and carbon dioxide laser are proposed for successful outcomes.[15] The potent topical corticosteroid; 1% mometasone furoate cream, was chosen to apply in this case due to localized lesion. The disease was well-controlled without further progression.

In conclusion, this case is a representative case of the unrecognized P veg on the atypical location. These interesting morphology and physical characteristics are important and help to encourage physicians to recognize the P veg as one of differential diagnoses in vegetative lesions on the head and neck region. Finally, the successful treatment is accomplished by careful follow-up observation in each patient.

**Acknowledgement**

In our respects, the authors would like to thank Associated Professor Chanisada Wongpraparut, MD. for her advice during treatment.

## *References*

1. Stanley JR. Pemphigus. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick's dermatology in general medicine. 8th ed. New York: McGraw Hill, 2011:591.
2. Lever WF: Pemphigus and Pemphigoid. Springfield, IL: Charles C. Thomas: 1965.
3. Zaraa I, Sellami A, Bouguerra C, et al. Pemphigus vegetans: a clinical, histological, immunopathological and prognostic study. J Eur Acad Dermatol Venereol 2011; 25: 1160-7.
4. Micali G, Musumeci ML, Nasca MR. Epidemiologic analysis and clinical course of 84 consecutive cases of pemphigus in eastern Sicily. Int J Dermatol. 1998; 37: 197-200.

5. De Almeida HL, Pereira Neugebauer MG, Guarenti IM, Aoki V. Pemphigus vegetans associated with verrucous lesions: expanding a phenotype. Clinics. 2006; 61: 279-82.
6. Lubojevic S, Lipozencic J, Brenner S, Budimcict D. Pemphigus vulgaris: a review of treatment over a 19 year-period. J Eur Acad Dermatol Venereol. 2002; 16: 599-603.
7. Arya SR, Valand AG, Krishna K. A clinic-pathological study of 70 cases of pemphigus. Indain J Dermatol Venereal Leprol. 1999; 65: 168-71.
8. Benchikhi H, Ghafour S, Disky A, Janati K, Bichra L, Lakhdar H. Pemphigus: treatment and outcome in 122 cases. Ann Dermatol Venereol. 2006; 133: 1012-4.
9. AdrianoI AR, NetoII AG, Hamester GR, Nunes DH, Giunta GD. Pemphigus vegetans induced by use of enalapril. An. Bras. Dermatol. 2011; 86: 1197-200.
10. Morelli JG, William M, Weston MD. Childhood immunobullous disease following a second organ transplantation. Pediatr Dermatol. 1999; 3: 205-7.
11. Downie JB, Dicostanzo DP, Cohen SR. Pemphigus vegetans-Neumann variant associated with intranasal heroin abuse. J Am Acad Dermatol. 1998; 39: 872-5.
12. Lateef A, Packles MR, White SM, Don PC, Weinberg JM. Pemphigus vegetans in association with human immunodeficiency virus. Int J Dermatol. 1994; 33: 168-71.
13. Sawai T, Kitazawa K, Danno K, et al. Pemphigus vulgaris with esophageal involvement: successful treatment with minocycline and nicotinamide. Br J Dermatol. 1995; 132: 668-70.
14. Cozzani E, Christana K, Mastrogiacomo A, Rampini P, Drosera M, Casu M, et al. Pemphigus vegetans Neumann type with anti-desmoglein and anti-periplakin autoantibodies. Eur J Dermatol. 2007; 17: 530-3.
15. Son YM, Kang HK, Yun JH, Roh JY, Lee JR. The Neumann type of pemphigus vegetans treated with combination of dapsone and steroid. Ann Dermatol. 2011; 23: S310-3.