BRIEF ARTICLES

An Atypical Presentation of Pemphigus Vegetans in the Umbilicus

Antonio Jimenez, BS[1], Paige Hoyer, MD[2], Michael Wilkerson, MD[2]

[1]The University of Texas Medical Branch, School of Medicine, Galveston, TX
[2]The University of Texas Medical Branch, Department of Dermatology, Galveston, TX

ABSTRACT

Pemphigus is a chronic, autoimmune bullous disease that affects the skin and mucous membranes. Pemphigus vegetans is a rare variant of pemphigus and presents as oral ulcerations with associated verrucous lesions in intertriginous or flexural areas. A 38-year-old African American woman presented to the clinic with a chief complaint of oral ulcers. She carried a diagnosis of Behcet's disease and was referred by rheumatology for evaluation of treatment-resistant mucosal ulcerations. At the time of her dermatology visit, she also reported an enlarging umbilical mass that had been present for several months. Further examination of the umbilical lesion identified an exophytic, vegetative mass. Histologic assessment of the lesion identified acanthosis and acantholysis with dermal eosinophils consistent with pemphigus vegetans. A pemphigus antibody panel was done and resulted positive for IgG desmoglein-3 antibodies.

The patient was treated with prednisone and rituximab with improvement of her lesions. We present an atypical presentation of pemphigus vegetans involving the umbilicus. This diagnosis should be considered in patients who present with oral erosions and concomitant vegetative lesions, regardless of location or prior diagnoses.

INTRODUCTION

The word "pemphigus" is derived from the Greek word "*pemphix*" or blister.[1] Pemphigus is a rare, blistering mucocutaneous disease. The pathogenesis of pemphigus involves the autoimmune destruction of desmosomal proteins–the bullous character of the disease is the result of the loss of intercellular connections. Pemphigus is common in middle-aged adults aged 50-60.[2] Pemphigus vulgaris is the most common type of pemphigus, and it presents with oral erosions and flaccid bullae in the skin. The disease is chronic. A rare variant of pemphigus vulgaris is pemphigus vegetans. In contrast to pemphigus vulgaris, it most often presents with verrucous plaques in intertriginous and flexural areas. The rare presentation of the disease makes it a diagnostic challenge. We present a case of pemphigus vegetans in the umbilicus of a 38-year-old female.

CASE PRESENTATION

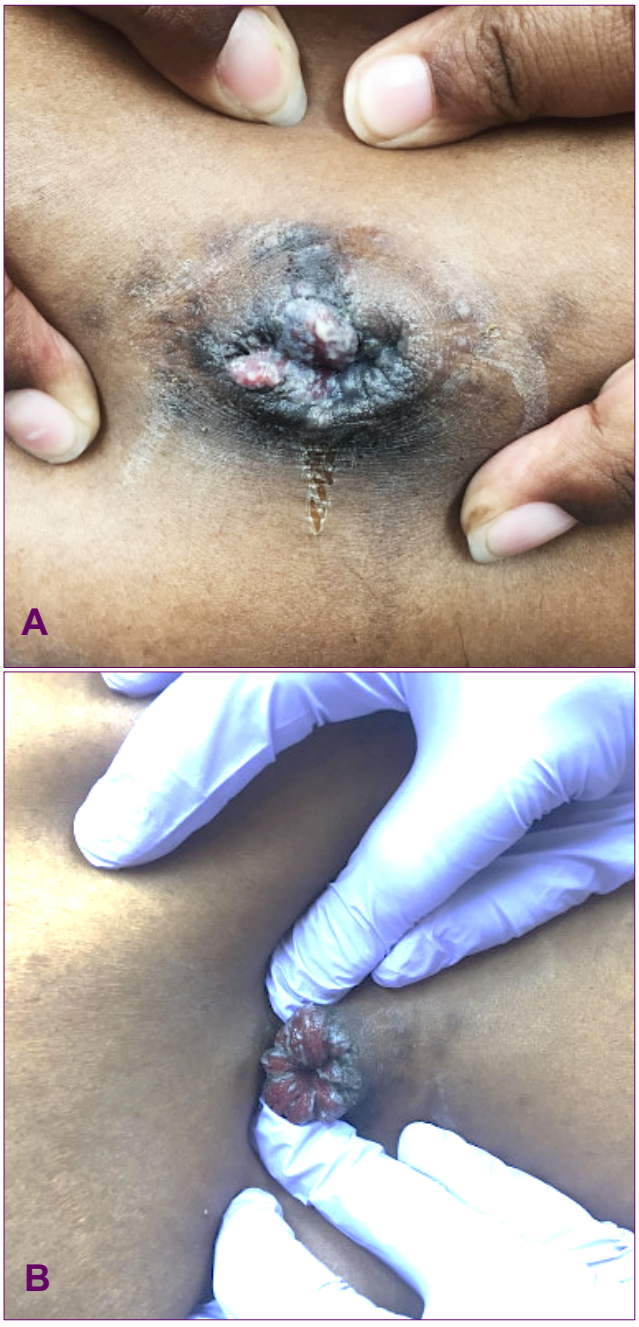
A 38-year-old African American female with a past medical history of Behcet's syndrome, presented to the dermatology clinic with a chief complaint of recalcitrant oral ulcers. She was diagnosed with Behcet's syndrome four years prior by her rheumatologist on the basis of her oral ulcers. At the time of her diagnosis, a full autoimmune serology work-

up was completed and resulted in a positive ANA of 1:80 (anti-snRNP, anti-SSA, anti-dsDNA negative). HLA-B51 was negative. Her flare-ups were previously well-controlled on azathioprine 50 mg and prednisone 10 mg; however, she now reported a 3-4-month history of persistent, painful oral ulcers. She was referred by rheumatology for further evaluation. She had no significant family or social history. At initial presentation to dermatology clinic her treatment regimen consisted of colchicine 0.6 mg three times per day, prednisone 10 mg daily, and adalimumab 40 mg/0.8 ml injections every 2 weeks. Physical examination demonstrated ulcerated lesions along her lower lip, lower gingiva, and tongue.

The patient also reported an umbilical lesion that had been present for several months and had slowly increased in size. The lesion was painful and would drain clear fluid. She denied change in bowel habits, bloating, or hematochezia. She said she had not applied any treatments to the lesion. A colonoscopy completed one-month prior was clear. Physical examination demonstrated a firm, erythematous exophytic mass arising from the umbilicus with erosions throughout (Fig 1A). Serous drainage and fibrinous slough were also noted (Fig 1B). Histopathological evaluation revealed acanthosis and acantholysis with dermal eosinophils consistent with pemphigus vegetans. A pemphigus antibody panel was ordered and resulted positive for IgG desmoglein-3 antibodies. Indirect immunofluorescence demonstrated a cell surface IgG titer of 1:5120 on monkey esophagus substrate and 1:320 on intact human skin substrate which was also consistent with pemphigus.

The patient was treated with prednisone 60 mg daily, and her symptoms remained stable. She then underwent 2 courses of 1,000 mg rituximab infusions given 2 weeks apart and noted significant improvement in the size of the umbilical lesion and the number of oral ulcers. Her prednisone dose was tapered off. After 1 year of clinical improvement, the patient noted worsening in the number of oral ulcers and reappearance

Figure 1. Pemphigus Vegetans. **(A)** A draining, vegetative plaque on the patient's umbilicus. **(B)** The patient's lesion after expression of serous fluid.



of the umbilical lesion. She was re-started on prednisone 80 mg and received 2 infusions of rituximab 900 mg 2 weeks apart. Her oral ulcers had improved 1 week after her second round of infusions. Per oncology, they will plan for another round of rituximab in 1 year if needed.

DISCUSSION

Pemphigus is the result of pathogenic autoantibodies against desmosome cadherins or desmoplakins. There are three main types: pemphigus vulgaris, pemphigus foliaceus, and paraneoplastic pemphigus. Pemphigus vulgaris accounts for 70% of cases and is the result of autoantibodies against desmoglein-3 and/or desmoglein-1.[4] The clinical presentation of the disease is an eruption of eroded, flaccid bullae in the skin often with painful mucosal ulcerations. Pemphigus vulgaris is diagnosed by histology and immunofluorescence, with confirmatory serologic testing. Histopathological assessment of a pemphigus blister demonstrates intra-epidermal acantholysis of the basal layer; the characteristic "tombstone" appearance of keratinocytes can be observed.[5] Direct Immunofluorescence (DIF) demonstrates intercellular deposits of immunoglobulin G (IgG) and/or C3 in a net-like pattern.

A rare, vegetative variant of pemphigus vulgaris is diagnosed in 1-2% of cases.[6] Pemphigus vegetans is described as a heaped-up, papillomatous plaque localized in intertriginous and flexural areas including: axillary, inguinal, peri-anal, and inframammary folds.[7] Oral involvement is also present in a majority of reported cases. The pathogenesis of the disease is similar to pemphigus vulgaris; it is the result of auto-antibodies against desmoglein-3, and/or desmoglein-1 and desmocollin-1, -2, and -3.[8] There are two clinical subtypes of pemphigus vegetans, and they are differentiated by their initial presentation: Neumann variant (flaccid bullae) and Hallopeau variant (pustules); both later develop into vegetative plaques.[9] The Neumann subtype resembles pemphigus vulgaris in its morphological character and relapsing-remitting course. In contrast, the Hallopeau subtype has a benign course with prolonged remission rates; it seldom mirrors the classic clinical presentation of pemphigus vulgaris.[9] There are histopathological differences between pemphigus vegetans and pemphigus vulgaris; however, there are no observed differences between the Neumann and Hallopeau subtypes which are differentiated clinically. On histological examination, there is evidence of the prototypical supra-basal acantholysis and additional epidermal hyperplasia, papillomatosis, and eosinophilic intraepidermal abscesses.[10] There are no differences between pemphigus vegetans and vulgaris on immunofluorescence.

The rare presentation of the disease makes it a diagnostic challenge; thus, it is important to differentiate pemphigus vegetans from other vegetative diseases including pyoderma vegetans and pyodermatitis pyostomatitis vegetans. The mainstay of treatment is systemic glucocorticoids and/or immunosuppressive agents (e.g., rituximab, azathioprine, cyclophosphamide) for treatment-resistant disease.[7]

CONCLUSION

We present a 38-year-old African American female with biopsy-proven pemphigus vegetans on the umbilicus with mucocutaneous involvement. Her oral lesions had been previously misdiagnosed as Behcet's disease in the past. To date, most reported cases of pemphigus vegetans have involved the scalp and intertriginous

areas. This case highlights an atypical presentation of the disease, as the presentation of pemphigus vegetans in non-flexural areas is rare. This diagnosis should be considered in all patients with verrucous plaques and associated mucosal involvement. Additionally, patients diagnosed with pemphigus vegetans should be considered for treatment with rituximab similarly to patients diagnosed with pemphigus vulgaris.

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Corresponding Author:
Paige Hoyer, MD
301 University Blvd
Galveston, TX 77555
Phone: 512-968-5742
Email: pehoyer@utmb.edu

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