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CASE REPORT

An unusual presentation of painless penile erosions of pemphigus vulgaris: A case report

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ABSTRACT

INTRODUCTION Pemphigus vulgaris is a life-threatening, autoimmune bullous disease caused by desmogleins (Dsg) 1 and 3 autoantibodies. It is a rare disease with an incidence rate of 0.5 to 3.2 per 100,000 per year. It typically presents as painful, flaccid blisters and erosions on both the skin and mucous membranes.

CASE REPORT We present a 43-year-old male with painless penile erosions of 1-month duration. He was evaluated for sexually transmitted infections, but laboratory tests yielded negative results. Subsequently, vesicles and bullae on the back and hyperkeratotic lesions on the malar area appeared, leading to the differential diagnoses of bullous diseases. Skin biopsy was done revealing intraepidermal suprabasal blisters with acantholytic cells. Direct Immunofluorescence demonstrated positive intercellular deposits of IgG and C3. ELISA Dsg 1 and Dsg 3 were positive (ratio of 1.857 and 4.580, respectively). A final diagnosis of pemphigus vulgaris (PV) was made. The patient has remained in remission after a 3-month course of prednisone and azathioprine.

CONCLUSION This is a unique case of PV presenting with an unusual manifestation of painless penile erosions. There have been limited reports of PV with penile skin involvement and all cases presented with painful lesions. Because painless penile lesions as presenting feature is rare, the diagnosis may be easily missed. This case demonstrates that thorough dermatologic examination and early diagnosis despite atypical findings are crucial to provide timely and appropriate treatment as this determines the clinical outcome of the disease.

KEYWORDS pemphigus vulgaris, desmoglein, azathioprine

INTRODUCTION

Pemphigus vulgaris (PV) is a potentially life-threatening, chronic autoimmune bullous disease affecting the mucosa and the skin. It is characterized by the production of autoantibodies targeting desmogleins (Dsg) 1 and 3, leading to acantholysis and epidermal bullae formation. In most patients, PV affects the oral mucosa, although involvement of other mucosae may also occur. Mucosal involvement is commonly described as painful erosions. There are only few reports of involvement of the penile skin and none of which are described as painless penile erosions. We present a unique case of PV in a 43-year-old male with an initial presentation of painless penile erosions. Presence of this confers a poor prognosis, hence, aggressive intervention should be implemented to achieve early remission and improvement of quality of life.[1]

CASE REPORT

A 43-year-old male, Filipino, presented with painless penile erosions of 1-month duration. The patient has no known comorbidities. Sexual history revealed engaging in unprotected sex with multiple sexual partners. On dermatological examination, there were multiple erythematous painless erosions on the glans penis and upper part of the penile shaft (Figure 1).

An initial working impression of herpes simplex virus-2 (HSV-2) vs Primary Syphilis was made. The initial laboratory work-up included HSV polymerase chain reaction (PCR), human immunodeficiency virus (HIV) immunoassay test, rapid plasma reagin (RPR), and treponema pallidum particle agglutination assay (TPPA). Results were all negative. Upon follow-up, there were no oral mucosal lesions noted, however, the patient reported appearance of brownish-red hyperkeratotic crusted plaques on the malar area accompanied with multiple well-defined erythematous plaques and erosions, some with hemorrhagic crusting on the neck and upper chest (Figure 2-A). Subsequently, there were new eruptions of few flaccid and tense vesicles and bullae on the central back (Figure 2-B). During this time, a diagnosis of bullous disease was entertained specifically, Bullous Lupus Erythematosus, Bullous Pemphigoid, and Pemphigus Vulgaris. Antinuclear antibody (ANA), skin punch

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biopsy, direct immunofluorescence (DIF), and enzyme-linked immunosorbent assay (ELISA) Dsg 1 and 3 were done. ANA showed negative results (<1:1 ratio).

Histology of the skin taken from the upper back revealed intraepidermal, suprabasal blister with acantholytic cells, and red blood cells within the lumen. DIF demonstrated positive (++) intercellular deposits of IgG and positive (+) intercellular deposits of C3, consistent with pemphigus. ELISA Dsg 1 (ratio of 1.857) and ELISA Dsg 3 (ratio 4.580) were both positive (Figure 3). A final diagnosis of Pemphigus Vulgaris was made.

Assessment of disease activity was done using Pemphigus Disease Area Index (PDAI) where the patient scored 9.88% (26/263, moderate disease activity). Prior to treatment, quality of life (QoL) was measured using Autoimmune Bullous Disease Quality of Life (ABQoL) and Treatment of Autoimmune Bullous Disease Quality of Life (TABQoL) where he scored 27.45% (14/51, moderate QoL) and 17.65% (9/51, moderate QoL), respectively.

Prednisone was initiated at 1 mg/kg body weight/day for two (2) weeks which provided control of disease activity (i.e., established lesions begin to heal and new lesions cease to form). After achieving control of disease activity, azathioprine 50mg/day and slow-tapering prednisone regimen (i.e., dose was decreased by increments of 10mg every two (2) weeks followed by decrease in increments of 5 mg every two (2) weeks after 20mg/day dose was reached) were given. At three (3) months of therapy, a repeat ELISA test revealed negative Dsg 1 (ratio of 0.269) and decreased Dsg 3 (ratio of 4.184). At this time, repeat ABQoL score decreased to 17.65% (9/51, moderate QoL) while TABQoL remained at 17.65% (9/51, moderate QoL). PDAI score decreased from 9.88% (26/263, moderate disease activity) to 1.9% (5/263, mild disease activity) indicating good control of disease activity. Clinical improvement was noted as skin and penile mucosal lesions have resolved leaving only post-inflammatory hyperpigmentation (Figure 4).

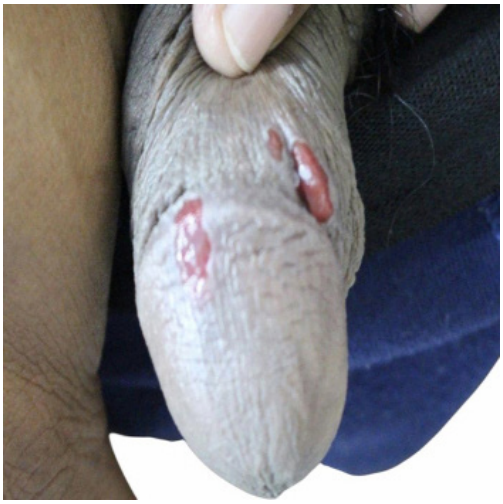

Figure 1. Penile lesions prior to treatment. Few erythematous painless erosions on the glans penis and upper part of the penile shaft.

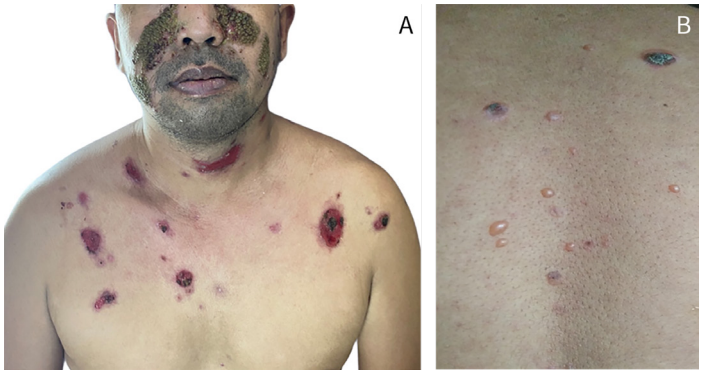

Figure 2. Skin lesions prior to treatment. (A) Multiple well-defined brownish-red hyperkeratotic crusted plaques on both malar areas; erythematous papules, plaques, and erosions with hemorrhagic crusting on the neck and upper chest; (B) Few flaccid and tense vesicles and bullae on the central back.

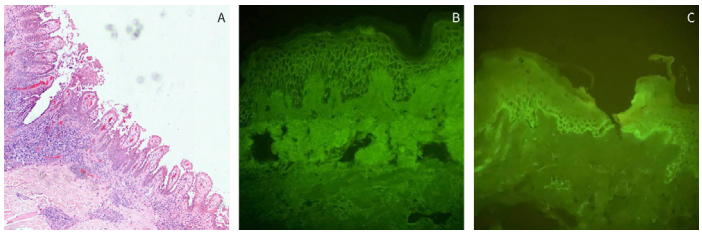

Figure 3. Photographs of biopsy specimen. (A) Skin biopsy from edge of the bullae of the lower back showing an intraepidermal, suprabasal blister with acantholytic cells and red blood cells within the lumen and row of tombstone appearance (H&E, 10x magnification). Positive DIF showing intercellular deposits of (B) IgG and (C) C3.

At six (6) months of therapy, the disease activity score was even lower (PDAI score of 2/263 from 5/263) and quality of life was markedly improved with significant clinical improvement. However, repeat ELISA Dsg 3 remained positive (ratio of 3.50) making our patient serologically active warranting continuous monitoring and treatment with azathioprine.

DISCUSSION

Pemphigus vulgaris is an autoimmune bullous disease affecting the skin and mucous membranes, with an incidence of 0.5 to 3.2 per 100,000 per year. In Asian countries, PV is the most prevalent type, with a sex ratio of 1:1 to 1:2, affecting patients 40 to 60 years old.[2]

Nearly all patients with PV have mucosal involvement. Cutaneous lesions may precede other symptoms by months or may be the only feature. In a retrospective study, Chams-Davatchi et al. reported involvement of the oral cavity, conjunctiva, nasal, vaginal, laryngeal/esophageal and perineal mucosae in 81%, 16%, 11%, 9%, 8% and 2% of cases, respectively.[3] Common to

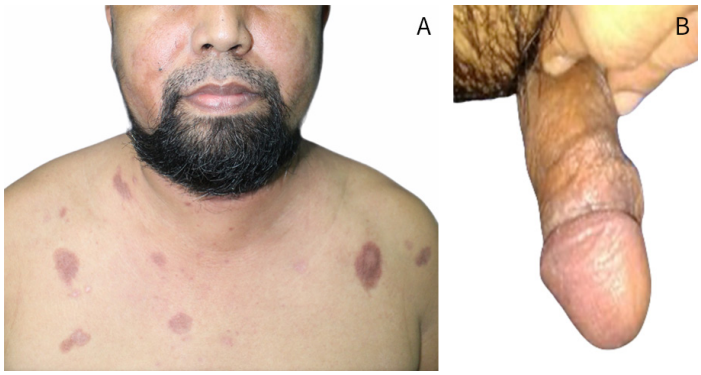

Figure 4. Lesions after three months of treatment with prednisone and azathioprine. (A) Marked improvement of lesions leaving only hyperpigmented macules and patches on the face, neck, and upper chest; (B) Resolution of penile lesions.

these mucosal involvement is the presence of painful erosions that often result in significant discomfort and limitation to an individual's activities of daily living.

Genital involvement in males is rare. Sami et al. reported penile skin involvement of 12 male patients diagnosed with PV. Of these, 10 patients had concomitant cutaneous lesions.[4] Stieger et al. reported two (2) cases of penile erosions as the initial presenting sign of PV.[1] All cases presented with painful penile erosions, and all responded to 1mg/kg/body weight of prednisone and azathioprine. This was the similar treatment given to our patient.

Painless penile erosions are most frequently related to infectious etiologies such as HSV and Syphilis.[5] Our patient presented with painless penile erosions but had a negative result in HSV PCR, RPR, and TPPA tests. The presence of genital lesions in PV is indicative of resistance to treatment and patients may require high doses of systemic steroids and immunosuppressive regimen should be started early in the course of disease.[6]

Pemphigus vulgaris can severely affect the patient's quality of life. The chronicity of the disease poses a significant burden to the physical, emotional, economic, and social well-being of the patient. Scoring systems to assess the quality of life and the clinical disease severity should be used at baseline and at intervals during treatment. To measure health-related quality of life (HRQoL) before and after treatment, ABQoL and TABQoL were used.[7] Both are 17-item questionnaires that are reliable and valid in measuring HRQoL in Autoimmune Bullous Disease (AIBD). QoL during treatment is important to evaluate to establish risk-benefit balance of therapy.[7] A score above 20 points is considered a high score and indicates poor QoL and below 7 points is considered low. In our patient, baseline ABQoL and TABQoL were moderate. Assessment on the 3rd month showed a decrease in ABQoL while TABQoL remained unchanged. At six (6) months of treatment, both ABQoL and TABQoL further improved.

PDAI was assessed to measure clinical disease activity. The optimal points of pemphigus disease severity score in PDAI were: mild (0-15), moderate (15-45) and severe (≥45).[8] In this patient, baseline PDAI score was 9.88% (26/263, moderate disease activity). At three (3) months of treatment, clinical improvement was noted as lesions have resolved leaving only post-inflammatory hyperpigmentation, associated with a decrease in PDAI score to 1.9% (5/263, mild disease activity) with a further decrease to 0.76% (2/263, mild disease activity) after six (6) months.

ELISA detects IgG autoantibodies to serologically diagnose and monitor the disease activity in PV. In this patient, ELISA Dsg 1 and 3 titers decreased from 1.857 and 4.580 to 0.269 and 4.184, respectively. At six (6) months of therapy, ELISA Dsg 3 was still positive at ratio 3.50. A cut-off of 1.0 is used to detect a positive or negative result. Patients with high titers of ELISA Dsg 1 and 3 indicate serological non-remission which would require continuation of immunotherapy.[9] Continuous treatment is warranted despite clinical improvement and increase in QoL. This validates the role of ELISA as an important tool in determining treatment response and duration.

At the third and sixth months of treatment, our patient was in clinical remission. Remission is defined as the absence of new or established lesions for at least two (2) months while on minimal therapy.[10] However, follow-up visits are still recommended every four (4) to eight (8) weeks until oral steroids have been discontinued and until serum anti-Dsg antibodies have normalized.[8]

In conclusion, we present a 43-year-old male with histopathologically proven diagnosis of PV presenting initially with painless penile erosions with subsequent eruption of bullae on the posterior trunk and hyperkeratotic plaques on the malar area. In this case, a diagnostic delay of more than one (1) month may occur from the first manifestation of mucosal lesion. Since mucosal lesions are common in PV and may even be the sole manifestation, a thorough dermatological examination of all mucosal sites is warranted and must include the genital area. This may be of value at present, where online consultation may make examination of certain body areas a challenge. Furthermore, a presentation of painless erosions on the penile organ should not rule out a diagnosis of PV. Genital involvement in PV is associated with treatment resistance and is regarded as a poor prognostic factor and marker of disease severity. Therefore, immediate treatment using a combination of oral steroid and azathioprine is recommended. Finally, this study highlights the importance of incorporating to the standard of care the scoring systems such as the PDAI, ABQoL, and TABQoL. These tools together with ELISA play an important role in providing treatment success.

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