Psoriasis Vulgaris Developing in Healed Pemphigus Vulgaris: A Rare Case of Epitope Spread or Isotopic Response?

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Abstract

Although psoriasis and autoimmune blistering diseases are considered to be disorders with completely different etiopathogenesis, literature has documented a few cases of psoriasis associated with bullous diseases, particularly bullous pemphigoid. Here, we report the case of a 30-year-old male presenting with multiple flaccid blisters and erosions, clinically and histopathologically consistent with the diagnosis of pemphigus vulgaris. Although all these lesions resolved after two doses of dexamethasone cyclophosphamide pulse therapy, he returned 3 weeks later with multiple erythematous scaly plaques developing over the postinflammatory areas, compatible with the diagnosis of psoriasis vulgaris, which necessitated a modification in the treatment protocol. This rare case highlights the diagnostic and therapeutic challenges accompanying this unique scenario and attempts to elucidate the probable pathogenic mechanisms underlying the co-existence (simultaneous or sequential) of these two apparently unrelated dermatoses.

Keywords: Epitope spreading, pemphigus vulgaris, psoriasis, Wolf's isotopic response

Introduction

Autoimmune bullous diseases and psoriasis are dermatoses in which immune reactions target the epidermis and induce the development of skin lesions following failures in epithelial cell contacts or defects in epithelial cell proliferation and differentiation. Since the first report of Bloom in 1929, a few cases of psoriasis coexistent with autoimmune bullous diseases have been documented.[1] Bullous pemphigoid is the most frequently observed association, while pemphigus foliaceus has been reported in a few cases. We report the extremely rare occurrence of psoriasis over sites of healed preexisting pemphigus and attempt to elucidate the probable pathogenic mechanisms underlying the co-existence of these two apparently unrelated dermatoses.

Case Report

A 30-year-old male presented with multiple fluid-filled lesions and raw oozing areas over the trunk, extremities, scalp, and oral mucosa. Clinical examination revealed multiple flaccid bullae and extensive erosions with positive Nikolsky's sign [Figure 1]. We made a provisional diagnosis of pemphigus vulgaris (PV). His laboratory parameters were unremarkable.

Histopathological examination revealed suprabasal split and acantholysis with a row of tombstone appearance of basal layer which confirmed PV [Figure 2]. Direct immunofluorescence was not done due to financial constraints.

He was administered intravenous Dexamethasone – Cyclophosphamide-Pulse (DCP) with MESNA (Pasricha regimen) along with daily tablet cyclophosphamide 50 mg once a day (OD) and tablet prednisolone(0.75 mg/kg/day). After completing two pulses, all mucocutaneous erosions resolved with hyperpigmentation.

Within 3 weeks, he developed new itchy raised lesions over areas of postinflammatory hyperpigmentation.

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We noted multiple, well-defined erythematous plaques with silvery-white scaling over the scalp, trunk, and upper and lower limbs [Figure 3]. Nails showed Beau's lines with onycholysis and longitudinal melanonychia.

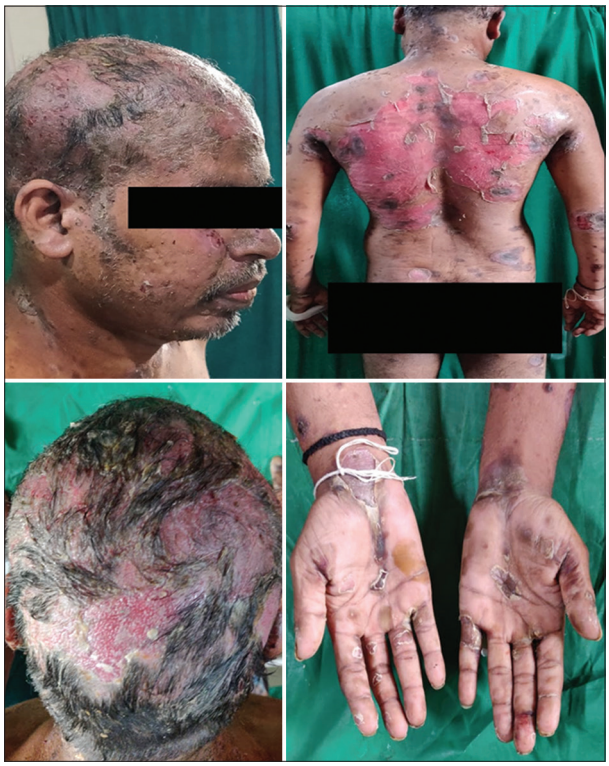

Figure 1: Multiple erosions over the scalp, back, face, and palms, with few areas showing crusting

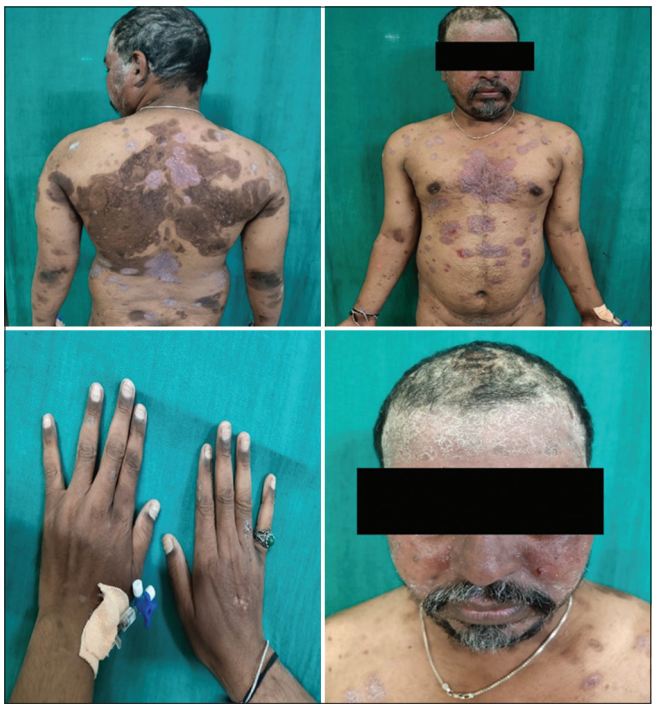

Figure 3: Multiple erythematous scaly plaques over the scalp, trunk, and back. Beau's lines over the finger nails

A histopathological examination showed parakeratosis, Munro's microabscesses, hypogranulosis, and regular elongation of rete ridges with sparse dermal perivascular mononuclear infiltrate, consistent with the clinical diagnosis of psoriasis vulgaris [Figure 4]. This necessitated a modification in the treatment protocol. DCP pulse was withheld and plain monthly cyclophosphamide (500 mg) pulse therapy (Gokhale regimen) was continued with tablet cyclophosphamide 50 mg OD.

For psoriasis (>30% body surface area involvement with Psoriasis Area Severity Index [PASI] 10.4), tablet apremilast 30 mg twice a day (BD) was started along with antacids, anti-emetics, and topical liquid paraffin.

Currently, both dermatoses are well controlled after three cycles of cyclophosphamide pulse therapy and 4 weeks of tablet apremilast without any adverse effects.

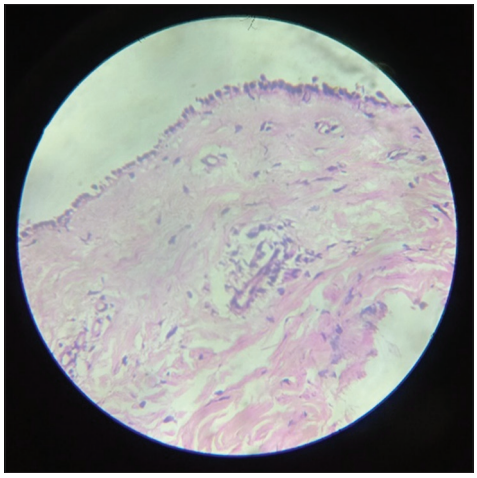

Figure 2: Histopathology (H and E, ×40) of flaccid blister showing suprabasal split with "row of tombstone" appearance and acantholysis, characteristic of pemphigus vulgaris

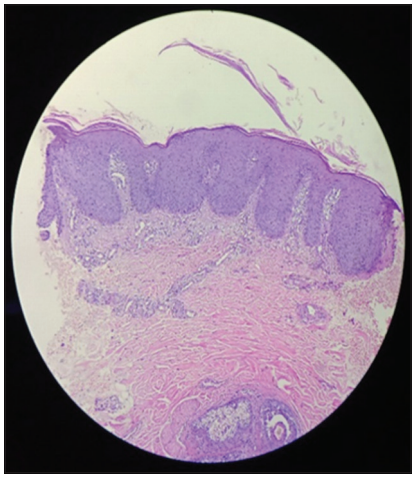

Figure 4: Histopathology (H and E, ×40) of the erythematous plaques showing parakeratosis, thinning of granular layer, and regular elongation of rete ridges with sparse dermal perivascular mononuclear infiltrate, consistent with psoriasis vulgaris

Discussion

PV is an autoimmune blistering disease caused by anti-desmoglein (Dsg1 and/or 3) IgG that leads to acantholysis, resulting in chronic, progressive blistering of mucous membranes and skin. Likely hypotheses include alterations in intracellular transduction signaling and cytoskeleton rupture with keratinocyte shrinkage; spatial impediment for desmoglein adhesion; and formation of desmoglein-deficient desmosomes.

Psoriasis is a chronic inflammatory disorder with pathologic collaboration of T lymphocytes (CD41T cells, CD81T cells, and natural killer T [NKT] cells [double negative and/or CD41NKT-cell subsets]), dendritic antigen-presenting cells such as Langerhans cells, plasmacytoid dendritic cells (DCs), and mature myeloid DC subsets. These DC subsets are responsible for the activation of infiltrating T cells with antigen recognition.

The coexistence of psoriasis vulgaris and bullous diseases (mainly bullous pemphigoid) has been described in literature.[2-5] In most cases, the bullous eruption has been thought to be related to anti-psoriatic treatment. Pemphigus foliaceus was reported in preexisting psoriasis in six cases (duration varying from 8 months to 52 years).[6]

In most cases, psoriasis was the initial event which unmasked the sequestered antigen leading to vesiculobullous disorders. This is defined as the phenomenon of "epitope spreading," characterized by tissue damage from a primary inflammatory process causing release and exposure of a previously sequestered antigen culminating in a secondary autoimmune response against the newly released antigen.[7] Epitope spreading can result from injuries due to cutaneous and systemic inflammatory diseases. Our case is rare wherein PV was the initiating inflammatory dermatoses that might have led to the exposure of sequestered keratinocyte antigens, which were subjected to T cell autoimmune responses, leading to the development of psoriatic plaques. To support this theory, an Israeli study demonstrated a significantly higher prevalence of psoriasis in pemphigus patients than in controls.[8] However, no shared susceptibility human leukocyte antigen alleles have been reported between psoriasis and bullous diseases.

The development of psoriasis in our patient can also be attributed to "Wolf's isotopic response" which describes the occurrence of a new skin disorder at the site of another, unrelated, and already-healed skin disease.[9] The proposed etiology includes viral, immunological, neural, vascular, and *locus minoris resistentiae* (site of lessened resistance). Most previous cases have been described in healed lesions (scars) of herpes zoster or erythema multiforme.[10] There is growing evidence that immunologic factors (atypical and exaggerated hypersensitivity to viral or tissue antigens or immune complex deposits) are involved in the pathogenesis of the second disease. The dermatoses presenting as a consequence of isotopic response are classified as granulomatous reactions, malignant tumors, leukemic infiltrates, dermatoses secondary to immunologic dysfunction, infections, comedonic reactions, and miscellaneous conditions.

In the present case, perhaps, the apparently healed primary disease (pemphigus) may have caused long-lasting immunologic changes, rendering the skin vulnerable to a second disease (psoriasis) in the same area.

Concurrent management of these two dermatoses with different etiopathogenesis was challenging. Systemic steroids (frontline drugs for PV) were relatively contraindicated in psoriasis vulgaris owing to the risk of exacerbation of lesions or precipitation of pustulation upon withdrawal. Hence, we tapered off oral prednisolone and altered the intravenous pulse therapy protocol from DCP pulse to plain cyclophosphamide pulse by omitting the steroid component. In addition, apremilast served as an effective adjuvant for psoriasis. Currently, after 3 months, the patient is off systemic steroids with both dermatoses in partial remission. We have planned to complete a total of 12 cyclophosphamide pulses and continue tablet apremilast until PASI 90 is achieved.

Conclusion

This case illustrates the occurrence of psoriasis vulgaris over healed lesions of PV and highlights the diagnostic and therapeutic hurdles associated with this unique scenario. More research is warranted to clarify the possible role of Wolf's isotopic response or Epitope spreading theory in the co-existence of two such unrelated dermatoses.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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