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Pemphigus Vulgaris: Case Report and Review of Current Treatment Algorithms

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ABSTRACT: **Background:** Pemphigusvulgaris (PV)is a rare autoimmune blistering disorder affecting the skin and mucous membranes. It is mediated by pathogenic IgG autoantibodies against desmoglein 3 and desmoglein 1—key components of desmosomes responsible for keratinocyte adhesion.

Case Summary: We report a case of a **45-year-old female** with a history of hypothyroidism who presented with painful, flaccid blisters and oral erosions. **Clinical examination**, supported by histopathology and direct immunofluorescence, confirmed the diagnosis of PV. The patient was treated with high-dose intravenous prednisolone and azathioprine, which led to clinical stabilization, cessation of new lesions, and progressive healing.

This case highlights the importance of early recognition and timely initiation of systemic therapy to prevent complications such as infection, dehydration, and nutritional deficiency. While corticosteroids remain the mainstay of treatment, adjunctive immunosuppressants help reduce steroid burden. In severe or refractory cases, biologics such as rituximab are now established as effective first-line agents. Long-term remission requires a multidisciplinary and individualized approach.

KEYWORDS: Pemphigus vulgaris, autoimmune disorder, desmoglein, corticosteroids, azathioprine, rituximab, mucocutaneous lesions.

I. INTRODUCTION

Pemphigus vulgaris (PV) is a chronic autoimmune illness that mostly affects the mucous membranes and skin**.** It is characterized by intraepithelial blistering due to the loss of cell-cell adhesion among keratinocytes. The disease is caused by circulating autoantibodies that target **desmogleins** , which are key components of desmosomes structures responsible for maintaining epithelial integrity . [(1) (2)] PV is the most prevalent form of pemphigus, comprising over 80% of cases within the broader pemphigus group. [(3)]

Epidemiology

Pemphigus vulgaris is a rare autoimmune disorder, with an annual incidence estimated at **0.1 to 5 cases per million** people. It is more commonly observed in middle-aged and elderly individuals, with a peak occurrence between the fourth and sixth decades of life. Women are affected slightly more frequently than men, with a reported male-to-female ratio of **1:2**. [(1)]Certain populations, such as **Ashkenazi Jews** and individuals of **Mediterranean descent**, have a higher genetic predisposition to PV due to associations with specific **HLA class II alleles**. [(3) (4)]

Etiology

The development of pemphigus vulgaris is influenced by both inherited genetic factors and external environmental triggers. It is often associated with genetic predisposition, particularly **the HLA-DR4 and HLA-DR14 alleles**. External factors like infections, stress, or certain **drugs** such as **penicillamine, captopril, and rifampicin** can initiate the autoimmune response in susceptible individuals. [(5)]

Pathophysiology

Pemphigus vulgaris is caused by circulating IgG autoantibodies targeting desmoglein 3 and, in some cases, desmoglein 1, which are key components of desmosomes responsible for keratinocyte adhesion. [(1) (6)] These autoantibodies impair desmosomal function by disrupting intercellular junctions, leading to loss of cohesion between epidermal cells (acantholysis) and subsequent formation of fragile intraepidermal blisters. [(7)]

Clinical Significance

PV is a potentially life-threatening condition if left untreated. It often begins with oral lesions, which can precede skin involvement by

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months. These oral lesions present as painful erosions that impair basic functions such as eating and speaking. [2] [7] **Diagnosis** relies on histopathological examination and immunofluorescence testing to detect the characteristic suprabasilar acantholysis and autoantibody deposits [6] [7]. Before the advent of corticosteroid therapy, PV had a high mortality rate, mainly due to dehydration and secondary infections. Modern treatments, including systemic corticosteroids and immunosuppressants, have significantly improved patient outcomes, but long-term management remains a challenge. [8]

Treatment Options

The primary approach to treating pemphigus vulgaris involves the use of systemic corticosteroids, with **oral prednisolone,** treatment usually begins at a dose of approximately 1 mg/kg/day, with adjustments made based on disease severity.[9]These corticosteroids are effective in managing disease activity and minimizing the development of blisters. However, long-term steroid use can lead to significant adverse effects, necessitating the inclusion **of immunosuppressive agents** such as **azathioprine** or **mycophenolate mofetil**, which help lower the required steroid dose and act as steroid-sparing options.[10] In patients who do not respond adequately to standard therapy or who experience frequent relapses**, biologic agents** like **rituximab**, a monoclonal antibody targeting CD20 on B cells, have shown promising efficacy and are increasingly being adopted as first-line therapy in moderate to severe cases. [11]Additionally, **intravenous immunoglobulin**(IVIG) and **plasmapheresis** may be considered for refractory cases, particularly when rapid disease control is necessary or when other treatments are contraindicated [10]

II. CASE PRESENTATION

A **45-year-old female** with a past medical history of hypothyroidism for the last five years presented to the hospital on 2nd February 2025 with complaints of painful, fluid-filled blisters on the chest, back, and oral mucosa. The patient reported associated difficulty in swallowing and eating, along with a low-grade fever persisting for two days. She also had a long-standing history of recurrent oral ulcers, which had worsened in recent days.

On general examination, the patient appeared pale and mildly dehydrated. Her **vital signs** were stablethroughout admission**. Dermatological examination** revealed multiple flaccid bullae and erosions distributed over the chest, back, and upper limbs. The bullae ruptured easily with minimal trauma, leaving behind raw erosions. **Oral examination** showed erosive lesions on the buccal mucosa, tongue, and palate, which contributed to odynophagia and reduced oral intake. A positive**Nikolsky sign** was elicited, suggestive of intraepidermal acantholysis and supporting the clinical suspicion of pemphigus vulgaris.**Initial laboratory investigations** were significant for iron deficiency anemia and suboptimal thyroid control**: hemoglobin** was 9.4 g/dL, **serum iron** was 4 µmol/L (low),**total iron-binding capacity** (TIBC) was 420 µg/dL (elevated), and **serum ferritin** was 9 ng/mL (low**). Thyroid-stimulating hormone** (TSH) was elevated at 8.3 µIU/ml. Other routine haematological and biochemical parameters were within normal limits. Autoimmune work-up, including ANA and connective tissue disease screening, was negative.

A **skin biopsy** was performed, and **histopathology** showed suprabasal acantholysis with a "row of tombstones" appearance. **Direct immunofluorescence** (DIF) confirmed the diagnosis by demonstrating intercellular IgG deposits on keratinocytes within the epidermis, characteristic of pemphigus vulgaris.

The patient was started on **high-dose intravenous prednisolone 60 mg once daily**, planned for gradual tapering based on clinical response. **Azathioprine 50 mg twice daily** was initiated as a steroid-sparing immunosuppressant. She was also continued on her thyroid medication, **levothyroxine 75 mcg once daily**. Supportive management included oral iron therapy (OROFER XT), calcium with vitamin D3 supplementation, topical **Triamcinolone acetonide oral paste** (Kenacort) for symptomatic relief of mucosal lesions, along with antihistamines and analgesics (BENADRYL, DOLO) as needed.

The patient responded well to treatment. Over the course of hospitalization, new lesion formation ceased, existing erosions began to heal, and oral discomfort reduced significantly, allowing better food intake. Her vitals remained stable throughout her stay.

She was discharged on 10th February 2025 with a tapering dose of oral steroids and was advised regular follow-up for monitoring of complete blood count (CBC), thyroid profile, and disease activity. She was counselled on the importance of strict oral hygiene, sun protection, and avoiding over-the-

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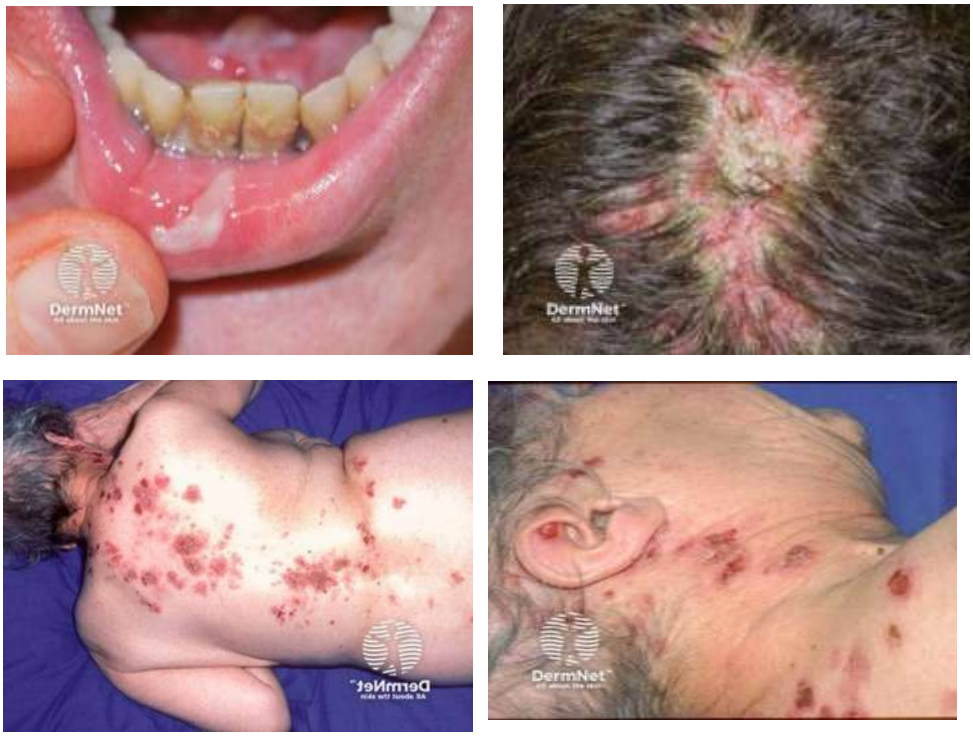
counter use of NSAIDs and antibiotics, which are known to trigger disease flares in pemphigus patients.



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III. DISCUSSION

Pathophysiology

A comprehensive knowledge of the immunopathologicalmechanisms underlying pemphigus vulgaris (PV) is crucial for accurate diagnosis and optimum treatment.

The disease is characterized by the presence of IgG autoantibodies, primarily target desmoglein 3 (Dsg3) a key adhesion molecule in epidermal desmosomes. In mucocutaneous cases, autoantibodies may also recognize desmoglein 1 (Dsg1), both of which are critical components of desmosomal adhesion in the epidermis. The disruption of these desmosomes leads to intraepidermal acantholysis and blister formation. (12).

CD4+ T-helper cells, especially those belonging to the Th2 and Th17 subsets, play a pivotal role in activating B cells and facilitating the production of pathogenic autoantibodies. (12) Cytokines such as IL-4, IL-17, and IL-21 are critically involved in maintaining and amplifying the autoimmune response. (13)

The Desmoglein Compensation Theory further explains the clinical spectrum observed in PV. In cases where only Dsg3 is affected, mucosal lesions dominate due to compensation by Dsg1 in the skin. However, when both Dsg1 and Dsg3 are targeted, patients present with both mucosal and cutaneous involvement. (15)

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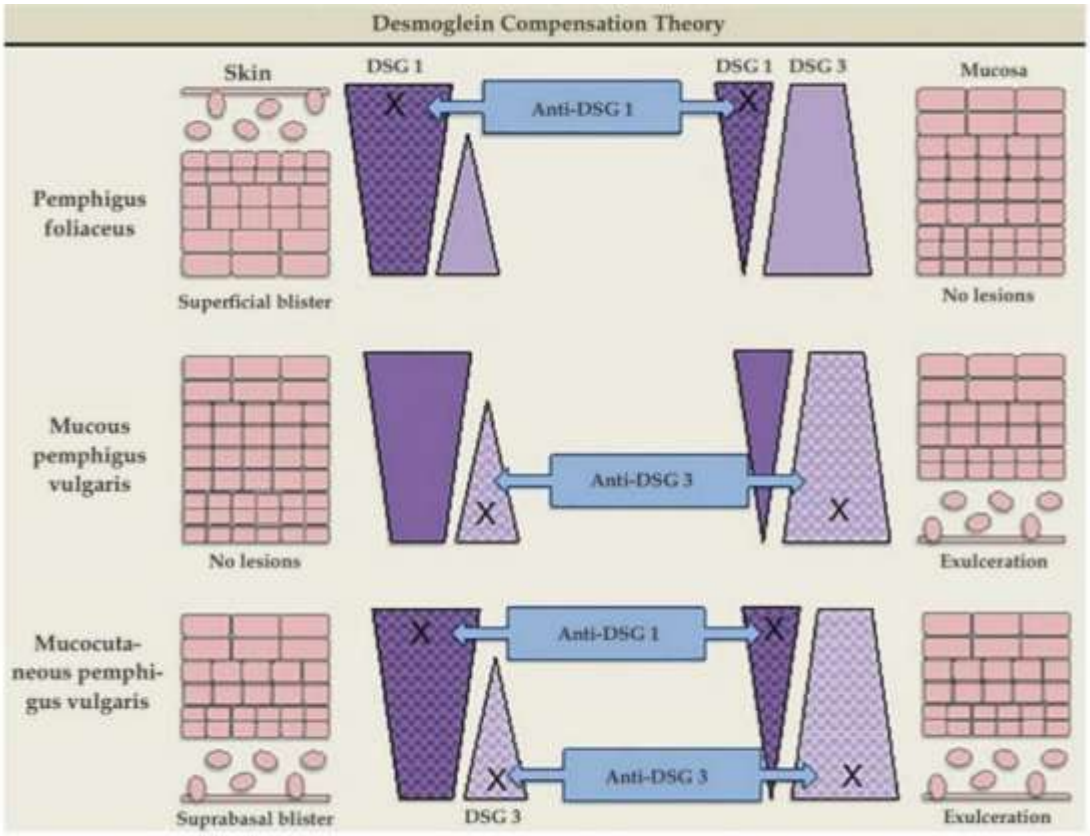

Adapted from: Porro AM, Seque CA, Ferreira MCC, Enokihara MMSS. Pemphigus vulgaris. An Bras Dermatol. 2019;94(3):264–78. doi:10.1590/abd1806-4841.20199011. [14]

Figure 1: The Desmoglein Compensation Theory explains the lesion pattern in pemphigus based on Dsg1 and Dsg3 distribution. In pemphigus foliaceus, anti-Dsg1 antibodies cause superficial skin blisters, but no mucosal lesions due to Dsg3 compensation. In mucosal pemphigus vulgaris, anti-Dsg3 antibodies lead to mucosal damage, while skin is spared as Dsg1 compensates. In mucocutaneous pemphigus vulgaris, both Dsg1 and Dsg3 are targeted, resulting in lesions on both skin and mucosa.

Treatment and Management

Treatment is centered around halting disease progression, promoting healing, and minimizing treatment-associated adverse effects.

Systemic corticosteroids, such as prednisone (1–1.5 mg/kg/day), remain the cornerstone of initial therapy due to their rapid anti-inflammatory effect. [16] For fulminant presentations, high-doseintravenous methylprednisolone pulses (500–1000 mg/day for 3 days) may be used. However, prolonged corticosteroid therapy is associated with adverse effects such as impaired glucose metabolism, decreased bone mineral density, and increased susceptibility to infections. [17]

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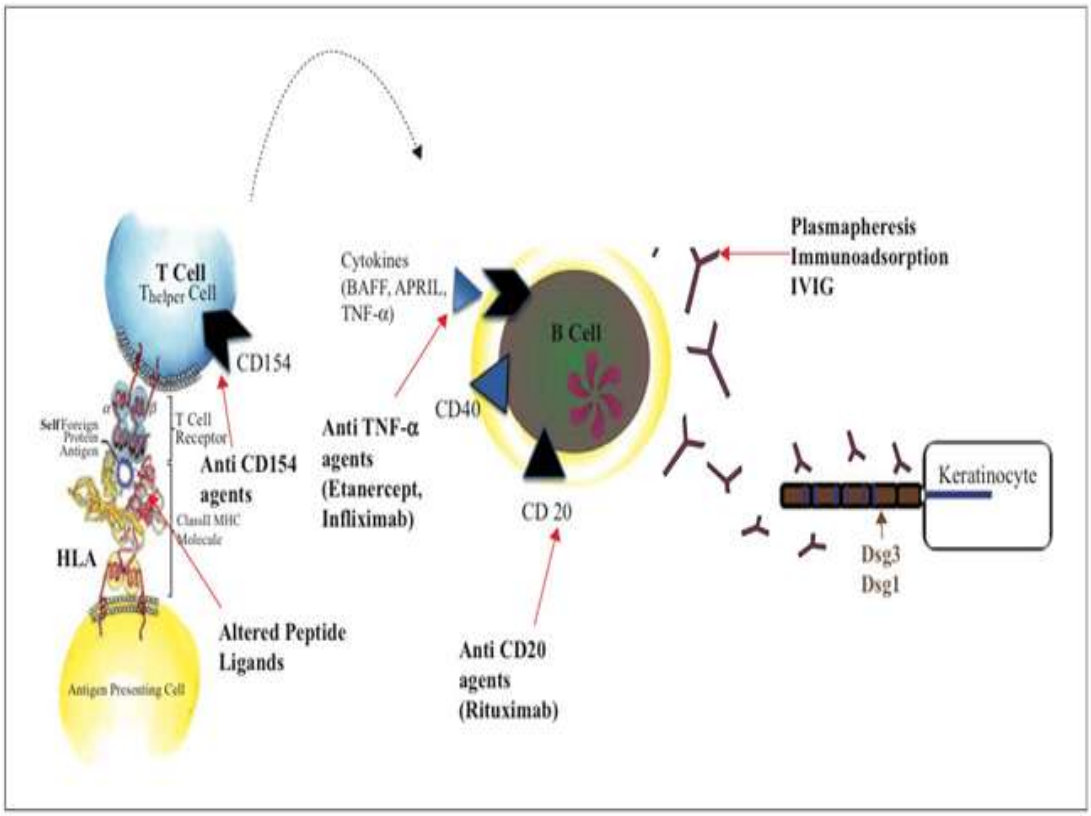

Figure 2: Pemphigus vulgaris pathogenesis and emerging immune-targeted treatment options. T-helper cell interaction with antigen-presenting cells, activation of B cells, and autoantibody production contribute to acantholysis. Immune therapies including anti-CD20, anti-CD154, anti-TNF agents, and IVIG/plasmapheresis target various stages of this autoimmune cascade. (13)

To reduce steroid dependence, **steroid-sparing agents** such as azathioprine (1–3 mg/kg/day)and **mycophenolate mofetil** (2–3 g/day) are frequently used. Azathioprine inhibits DNA synthesis in lymphocytes and requires TPMT testing to avoid myelotoxicity [18] Mycophenolate, which inhibits inosine monophosphate dehydrogenase, is generally better tolerated. For refractory or severe disease, cyclophosphamide (1–2 mg/kg/day)may be introduced, although its use is limited due to risks like hemorrhagic cystitis and infertility. [19]

Rituximab, a **monoclonal antibody targeting CD20** on B cells, has emerged as a highly effective therapy and is now approved as **a first-line treatment** in moderate-to-severe PV by the FDA and EMA. [19] Two regimens are commonly used:

• RA protocol: 1000 mg IV on days 1 and 15

• Lymphoma protocol: 375 mg/m² IV weekly × 4 weeks. [20], [21]

In cases unresponsive to conventional therapy or requiring rapid disease control, **intravenous immunoglobulin (IVIG)**(2 g/kg over 3–5 days) and **plasmapheresis** can be beneficial. IVIG modulates immune activity and neutralizes circulating antibodies, while plasmapheresis physically removes them. These are typically used in conjunction with corticosteroids or immunosuppressants to avoid rebound flares. [22]

Supportive management includes the use of **topical corticosteroids** (**e.g., clobetasol gel, triamcinolone acetonide oral paste**), analgesics, antiseptic rinses, nutritional support, and supplementation with calcium and vitamin D. [23] Long-term follow-up with regular clinical assessment and blood monitoring is essential. A multidisciplinary approach is crucial for sustained remission and improved patient quality of life. [24]

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Table 1: Common Systemic Therapies for Pemphigus Vulgaris

Drug	Mechanism of Action	Dose	Common Side Effects	Monitoring Parameters	Reference
Prednisone	Anti-inflammatory, immunosuppressive	1–1.5 mg/kg/day	Hyperglycaemia, osteoporosis, infections	Blood glucose, bone density	(16)
Azathioprine	Inhibits purine synthesis	1–3 mg/kg/day	Myelosuppression, hepatotoxicity	CBC, LFTs, TPMT activity	(18)
Mycophenolate mofetil	acts by inhibiting inosine monophosphate dehydrogenase.	2–3 g/day	gastrointestinal disturbances and leukopenia.	CBC, renal function	(18)
Cyclophosphamide	DNA alkylation, immunosuppressant	1–2 mg/kg/day	Haemorrhagic cystitis, infertility	CBC, urinalysis	(19)
Rituximab	Anti-CD20 monoclonal antibody	1000 mg ×2 or 375 mg/m² ×4	Infusion reactions, infections	CBC, viral serologies	(20) (21)
IVIG	Immune modulation, neutralizes antibodies	2 g/kg per cycle	Headache, renal dysfunction	Renal function, IgG levels	(22)

Table 2: Suggested Treatment Algorithm for Pemphigus Vulgaris

Disease Severity	First-Line Therapy	Second-Line/Add-On	Notes	Reference
Mild mucosal	Topical corticosteroids	Low-dose systemic steroids	Dental/oral hygiene important	(17)
Moderate mucocutaneous	Systemic corticosteroids + AZA or MMF	Switch immunosuppressant if needed	Regular monitoring of CBC/LFT	(17) (18)
Severe/Extensive	Systemic corticosteroids + Rituximab	Add IVIG or plasmapheresis if no response	Consider early biologics	(20) (21)
Refractory	Rituximab + IVIG or plasmapheresis	Cyclophosphamide	Hospitalization often needed	(22)

Treatment algorithm for mild pemphigus vulgaris: Applies to patients with less than 5% of body surface area involvement and/or limited oral lesions that do not interfere with eating or require pain relief, and/or a PDAI score of 15 or less. (23)

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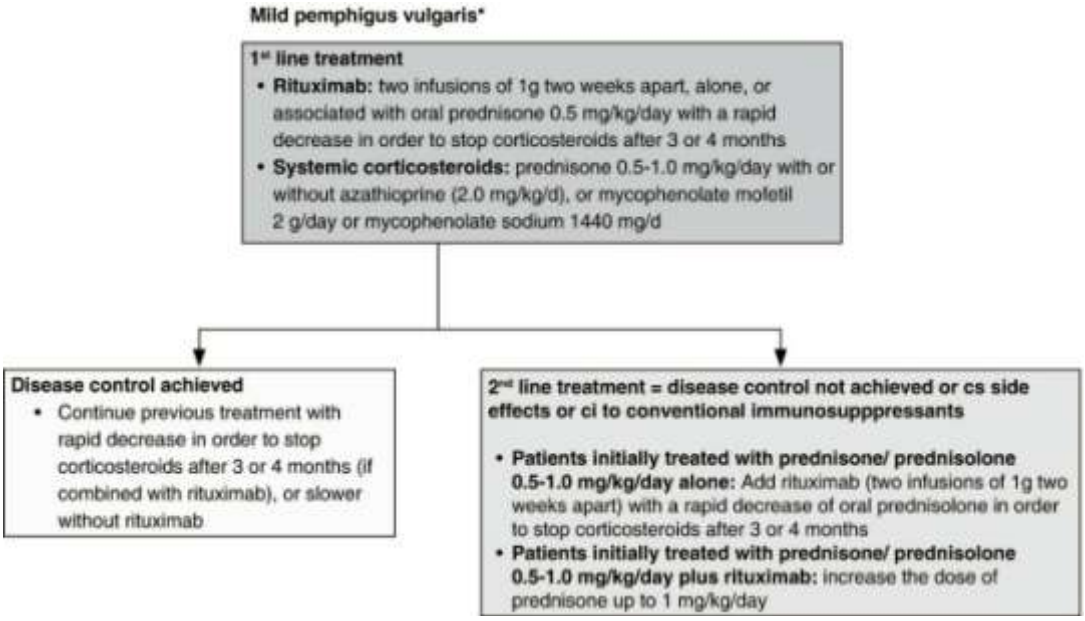
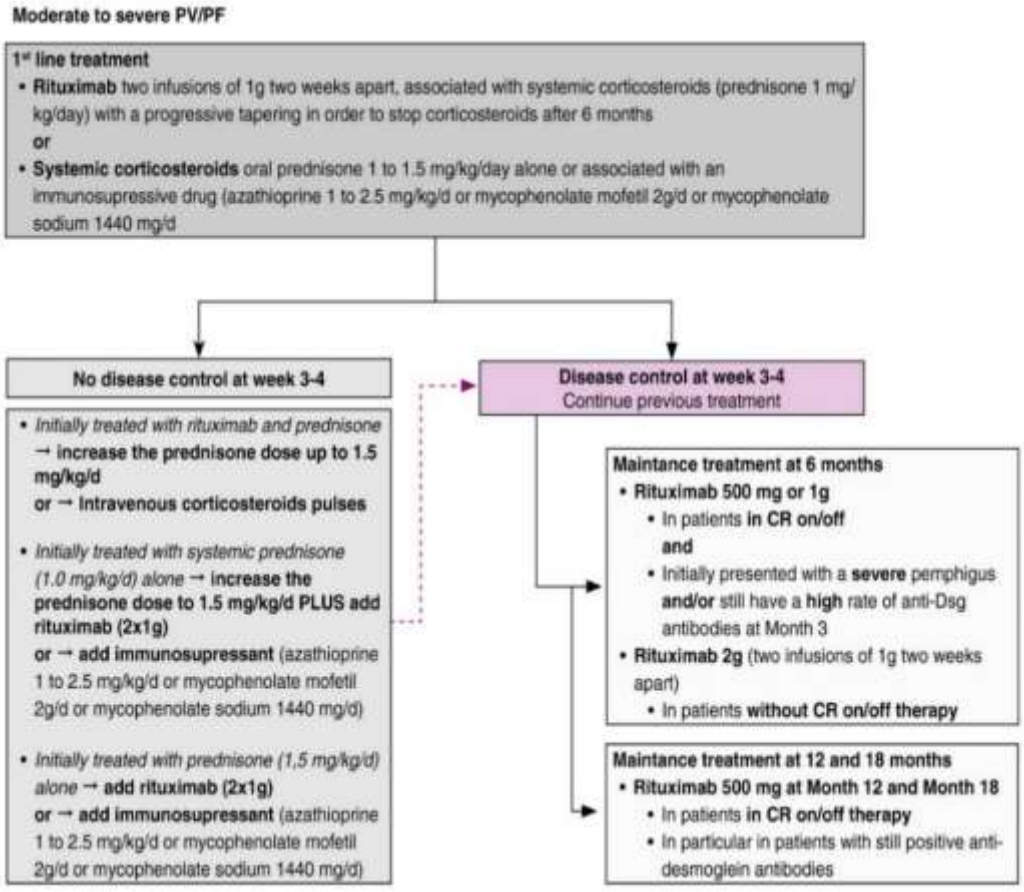


Treatment algorithm for moderate to severe pemphigus vulgaris and pemphigus foliaceus: Designed for cases with more extensive disease activity; "CR" denotes complete remission.[23]



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❖ **Learning Points**

1. Pemphigus vulgaris often begins with painful oral erosions before skin involvement. (13) (14)
2. A positive Nikolsky sign is a classic clinical clue and should prompt histopathological and immunofluorescence confirmation. (12) (15)
3. Early initiation of systemic corticosteroids and immunosuppressants is essential to avoid complications and disease progression. (15) (17)
4. Rituximab is now considered a first-line agent in moderate-to-severe or refractory cases, offering sustained disease control. (19) (21)
5. A multidisciplinary team—including dermatologists, internists, and pharmacists—optimizes long-term management and improves patient outcomes. (8) (23)

IV. CONCLUSION

This case not only illustrates the classical clinical and pathological features of pemphigus vulgaris but also emphasizes the transformative impact of early diagnosis and appropriate therapeutic intervention. Recognizing oral erosions as an initial sign of an underlying autoimmune process can lead to prompt management, thereby reducing morbidity and preventing severe complications.

While systemic corticosteroids remain the foundation of treatment, the incorporation of immunosuppressive agents like azathioprine and the introduction of biologic therapies such as rituximab have significantly expanded the therapeutic landscape. These advancements have improved the potential for sustained remission and reduced dependence on long-term steroid use.

Ultimately, this case reinforces the importance of a multidisciplinary, patient-centered approach—where clinical suspicion, timely diagnosis, and tailored immunotherapy work in synergy to alter the course of disease and enhance patient quality of life.

REFERENCES

[1]. Popescu IA, Statescu L, Vata D, Porumb-Andrese E, Patrascu AI, Grajdeanu IA, et al. Pemphigus vulgaris – approach and management (Review). Exp Ther Med. 2019;18(6):5056-5060. doi:10.3892/etm.2019.7964.

[2]. Tamgadge S, Tamgadge A, Bhatt DM, Bhalerao S, Pereira T. Pemphigus vulgaris. Contemp Clin Dent. 2011;2(2):134–7.

[3]. Scully C, Challacombe SJ. Pemphigus vulgaris: update on etiopathogenesis, oral manifestations and management. Crit Rev Oral Biol Med. 2002;13(5):397-408. doi:10.1177/154411130201300506.

[4]. Rai A, Arora M, Naikmasur V, Sattur A, Malhotra V. Oral Pemphigus Vulgaris: Case Report. Ethiop J Health Sci. 2015;25(4):367–70.

[5]. Moghadamnia AA, Hossaini SM, Dinarvand R. Pemphigus vulgaris: etiology, pathogenesis, and therapeutic options. Acta Med Iran. 2012;50(5):340-346.

[6]. Ahmed AR, Spigelman Z, Cavacini LA, Posner MR. Treatment of pemphigus vulgaris with rituximab and intravenous immune globulin. N Engl J Med. 2006;355(17):1772–9.

[7]. Yeo JF, Aw DCW, Loh FC, Yeo JG. Oral pemphigus vulgaris: a case report and literature update. Ann Acad Med Singap. 2004;33(4 Suppl):63S–8S.

[8]. Cholera M, Chainani-Wu N. Management of Pemphigus Vulgaris. Adv Ther. 2016;33(6):910–58.

[9]. Baigrie D, Nookala V. Pemphigus Vulgaris. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. [Accessed 2025 Apr 7]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459208/.

[10]. Didona D, Maglie R, Eming R, Hertl M. Management of pemphigus vulgaris: challenges and solutions. Clin Cosmet Investig Dermatol. 2019;12:757–765. doi:10.2147/CCID.S187287.

[11]. Pilla M, Vora R. Management of pemphigus vulgaris. Indian J Dermatol. 2020;65(2):85–91.

[12]. Sinha, A. A., et al. (2000). Pathogenic and molecular mechanisms in PV. J Clin Invest.

[13]. Sinha AA, Hoffman MB, Janicke EC. Pemphigus vulgaris: approach to treatment. Eur J Dermatol. 2015;25(2):103–13. doi:10.1684/ejd.2014.2483.

[14]. Carson, P. J., et al. (1996). Oral lesions and early signs of PV. Oral Surg Oral Med Oral Pathol Oral Radiol Endod.

[15]. Porro AM, Seque CA, Ferreira MCC, Enokihara MMSS. Pemphigus vulgaris.

An Bras Dermatol. 2019;94(3):264–78. doi:10.1590/abd1806-4841.20199011.

[16]. Ahmed, A. R., & Moy, R. (1982). Systemic corticosteroids in pemphigus. Arch Dermatol.

[17]. Bystryn, J. C., & Rudolph, J. L. (2005). Pemphigus treatment update. Dermatol Clin.

[18]. Ahmed, A. R., & Dahl, M. V. (1990). Azathioprine and mycophenolate use in PV. Arch Dermatol.

[19]. Chams-Davatchi, C., et al. (2007). Cyclophosphamide in PV: A randomized study. Arch Dermatol.

[20]. Joly, P., et al. (2017). First-line rituximab vs prednisone in PV. N Engl J Med.

[21]. FDA (2018). Approval of Rituximab for PV. www.fda.gov.

[22]. Hertl, M., et al. (2015). Consensus on management of PV. Br J Dermatol.

[23]. Joly P, Horvath B, Patsatsi A, Uzun S, Bech R, Beissert S, et al. Updated S2K guidelines on the management of pemphigus vulgaris and foliaceus. J Eur Acad Dermatol Venereol. 2020;34(9):1900–1913. doi:10.1111/jdv.16752.

[24]. Daniel, B. S., & Murrell, D. F. (2013). Pemphigus: a review of management. Clin Dermatol.