Battling Blistering: A Case Report on Pemphigus Vulgaris

Dr. Krishnaveni K[1], Dr. Ravikiran S[2*]

[1]Professor and Head, Department of Pharmacy Practice, Vivekanandha Pharmacy College for Women, Sankari, Tamil Nadu.
[2*]Assistant Professor, Assam Downtown University, Guwahati, Assam.

***Corresponding author:** Dr. Ravikiran S
*Assistant Professor, Assam Downtown University, Guwahati, Assam, Email: drravikiran22@gmail.com

Abstract:
Introduction: Pemphigus is a rare group of autoimmune disorders that cause blistering of the skin and mucous membranes. It affects various parts of the body, including the eyes, genitalia, mouth, nose, and throat. The most common type of pemphigus is known as pemphigus vulgaris. It is characterized by the loss of adhesion between keratinocytes, a condition called acantholysis.
Case Report: A 52-year-old male patient was admitted to the hospital with complaints of dizziness and blisters on the skin, lips, and inner layer of the mouth. Initially, he experienced difficulty in swallowing solid foods, which progressed to difficulty in swallowing liquid foods. The patient was diagnosed with pemphigus vulgaris and was treated with Methotrexate as a first-line therapy.
Conclusion: According to the guidelines provided by the British Association of Dermatologists (BAD), the first-line treatment for pemphigus vulgaris involves the use of corticosteroids, typically in the form of oral prednisolone. If treatment failure occurs, defined as the lack of disease control after 12 weeks, second-line treatments such as azathioprine, MMF, methotrexate, cyclosporine, dapsone, and cyclophosphamide may be initiated. It is crucial to select the appropriate drug therapy to prevent delays in the healing of blisters and ulcers. Although there is no permanent cure for pemphigus vulgaris, medications can help reduce the severity of symptoms. Therefore, the selection of drugs plays a significant role in treating the clinical condition.

Keywords: Autoimmune disorders, Pemphigus vulgaris, acantholysis, corticosteroids, Blisters

Introduction:

Pemphigus is an uncommon class of autoimmune disorders that affects the mucous membranes and skin, leading to the formation of blisters. It can impact various parts of the body, including the eyes, genitalia, mouth, nose, and throat. The most prevalent type of pemphigus is known as pemphigus vulgaris [1]. While pemphigus vulgaris can occur in people of all ages, genders, and races, there is a higher likelihood of occurrence among Jews and Indians aged 30 to 60, possibly due to unknown hereditary factors [2]. The oral cavity and throat are commonly affected, leading to discomfort while swallowing. In many cases, skin blisters develop several months after oral symptoms appear. While the condition can be highly dangerous, proper medication can help prevent the worsening of symptoms [3].

Pemphigus vulgaris occurs when the immune system mistakenly targets cells in the mucous membranes and epidermis of the skin. Antibodies are developed against desmogleins, which are proteins responsible for connecting skin cells. When these connections are disrupted, the skin becomes fragile, and the accumulation of fluid between its layers results in blister formation [4]. Researchers have found that specific variations in the HLA gene family, part of the immune system, are associated with an increased risk of pemphigus vulgaris. Additionally, medications containing the thiol chemical group have been linked to the development of pemphigus [1,4].

Case Report:

A 52-year-old male patient was admitted to the hospital with complaints of giddiness, blisters on the skin, lips, and inner layer of the mouth, and difficulty swallowing solid foods. Over the past 25 days, the condition had deteriorated, resulting in difficulty swallowing liquid foods. The patient had a previous history of Type 2 diabetes mellitus and hypertension. There was no significant family history related to the current clinical condition. The patient's social history revealed poor oral hygiene and chronic alcoholism spanning 15 years.

Upon examination, the patient appeared to have average build and displayed symptoms of anemia. Swollen, palpable, and painful submandibular lymph nodes were observed bilaterally. Intra-oral examination revealed bilateral buccal mucosal ulcerative lesions along the occlusion line, extending posteriorly to the retromolar trigone from the retrocommissural tissues. The lesions appeared erythematous, had uneven shapes, and extended superiorly from the occlusion line. Erosive lesions were also observed in the oropharynx, soft palate, tongue, and posterior hard palate. The patient was advised to

undergo biopsy and enzyme-linked immunosorbent assay (ELISA) tests, which led to the diagnosis of pemphigus vulgaris.
The recommended treatment course included T.Metformin 500mg, T.Atenolol 50mg, T.Amlodipine 2.5mg, Silver Sulfadiazine Ointment, Doxycycline 100mg, Inj. Chlorpheniramine 4 mg, Inj. Ranitidine 50 mg, oral Methotrexate 15 mg/week, as well as analgesics and multivitamins for 30 days. Additionally, the patient received mouthwash and silver sulfadiazine ointment. During the first follow-up, the patient's symptoms had decreased by 20%, the lesions had partially healed, and there was reduced erythema and ulcer-related inflammation. As a result, the methotrexate dosage was tapered to 7.5 mg/week. By the third follow-up, 60% of the symptoms had disappeared, and the lesions had almost completely healed.

Discussion:
Pemphigus is a group of potentially life-threatening disorders that cause blistering of the skin and mucous membranes, characterized by acantholysis (loss of adhesion between keratinocytes) [5]. Pemphigus vulgaris, specifically, is caused by autoantibodies targeting keratinocyte proteins called desmogleins. Acantholysis occurs when circulating immunoglobulin G (IgG) autoantibodies bind to intercellular adhesion molecules, leading to the loss of keratinocyte-to-keratinocyte adhesion [6,7]. Keratinocytes are the primary cells that make up the epidermis, producing a protein called keratin that helps hold the skin cells and layers together [8]. The distribution of DSG1 and DSG3, the desmogleins involved in pemphigus vulgaris, is distinct throughout the skin and oral mucosa. When both DSG1 and DSG3 are present, the inactivation of one by autoantibodies can be compensated by the other, maintaining adhesion and preventing acantholysis [9,10].

Pemphigus vulgaris can be triggered by exposure to certain drugs such as captopril and penicillamine. These drugs can interfere with cell adhesion molecules, enzymes that control keratinocyte aggregation, and promote the formation of neoantigens [11]. Other medications like penicillin, cephalosporins, and nonsteroidal anti-inflammatory drugs have also been associated with drug-induced pemphigus vulgaris [11,12]. There have been some controversial case reports suggesting a link between pemphigus vulgaris and certain foods like red wine, garlic, leeks, and peppers, but the evidence supporting these claims is limited [13].

To diagnose pemphigus vulgaris, clinical manifestations, direct immunofluorescence microscopy (DIF), histopathology of perilesional skin, and serologic detection of serum autoantibodies against epithelial cell surface antigens using indirect immunofluorescence (IIF) microscopy and/or enzyme-linked immunosorbent assay (ELISA) are required. A positive DIF microscopy result or the identification of autoantibodies against epithelial cell surface antigens in the serum, along with compatible clinical presentation and histology, confirm the diagnosis of pemphigus [14].

The goal of pharmacologic therapy for pemphigus vulgaris is to reduce autoantibody production and the inflammatory response. The first-line therapy typically involves systemic corticosteroids, initially with prednisolone at a dose of 0.5 mg-1.5 mg/kg/day. If there is no improvement within 14 days, a higher prednisolone dose (up to 2 mg/kg) may be administered. When glucocorticoids are contraindicated or long-term use is anticipated, immunosuppressants such as azathioprine, mycophenolate mofetil (MMF), methotrexate, cyclosporine, dapsone, and cyclophosphamide can be used as second-line therapy alone or in combination. In refractory cases, biologics such as rituximab and infliximab, especially, have shown promising results [15]. Monoclonal antibodies, particularly those targeting CD20, such as obinutuzumab, ofatumumab, and veltuzumab, could be potential alternatives to rituximab [16]. Future research in pemphigus should focus on better understanding the individual pathogenic factors and cytokines to develop more effective therapeutic strategies [17].

In the presented case, methotrexate was prescribed as a first-line therapy instead of corticosteroids, which is not in line with the treatment guidelines. The selection of inappropriate drug therapy can result in delayed healing of blisters and ulcers. It is important to note that there is no permanent cure for pemphigus vulgaris, but medications can help reduce the severity of symptoms. Therefore, the selection of the appropriate drugs is crucial in effectively treating the clinical condition.

Conclusion:
According to the guidelines provided by the British Association of Dermatologists (BAD), the first-line treatment for pemphigus vulgaris involves corticosteroids, typically in the form of oral prednisolone. The recommended dosage varies, with limited evidence to support specific doses. However, a common practice is to start with 1 mg/kg/day or 0.5-1 mg/kg/day for milder cases. If blistering persists, the oral prednisolone dosage can be increased by 50-100% every 5-7 days. Second-line treatments, such as azathioprine, mycophenolate mofetil, cyclophosphamide, or methotrexate, are initiated if there is a lack of disease control after 12 weeks, in addition to corticosteroids.

In the presented case, methotrexate was prescribed as a first-line therapy instead of following the treatment guidelines that recommend corticosteroids. The selection of inappropriate drug therapy can result in delayed healing of blisters and ulcers. It is important to note that pemphigus vulgaris does not have a permanent cure, but medications can help reduce the severity of symptoms. Therefore, the selection of drugs plays a crucial role in effectively treating the clinical condition.

Conflicts of Interest:
All the authors shows no conflict of interest

Ethics approval:
The patient identity was not revealed either directly or indirectly anywhere in the manuscripts. So no ethical approval is warranted.

Contributions:
All the authors contributed equally in the preparation of the manuscript.

References:

1. Johns Hopkins Medicine. Pemphigus Vulgaris. Available from: https://www.hopkinsmedicine.org/health/ conditions-and-diseases/pemphigus-vulgaris. Accessed November 11, 2022.
2. DermNet NZ. Pemphigus Vulgaris. Available from: https://dermnetnz.org/topics/pemphigus-vulgaris. Accessed November 11, 2022.
3. NHS. Pemphigus Vulgaris. Available from: https://www.nhs.uk/conditions/pemphigus-vulgaris/. Accessed November 11, 2022.
4. National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). Pemphigus. Available from: https://www.niams.nih.gov/health-topics/pemphigus. Accessed November 11, 2022.
5. Abarna Lakshmi Ravi, Rajganesh Ravichandran, Nikhil Cherian Sam, Jaya Shree Dilibatcha, et al. Phemphigus vulgaris an autoimmune acantholysis: a case report. Vol. 6 No. 6 (2020): November-December.
6. Mihai S, Sitaru C. Immunopathology and molecular diagnosis of autoimmune bullous diseases. J Cell Mol Med. 2007 May-Jun;11(3):462-81.
7. Hertl M, Eming R, Veldman C. T cell control in autoimmune bullous skin disorders. J Clin Invest. 2006 May;116(5):1159-66.
8. Bragulla HH, Homberger DG. Structure and functions of keratin proteins in simple, stratified, keratinized and cornified epithelia. J Anat. 2009;214(4):516-559.
9. Amagai M., Tsunoda K., Zillikens D., Nagai T., Nishikawa T. The clinical phenotype of pemphigus is defined by the anti-desmoglein autoantibody profile. J. Am. Acad. Dermatol. 1999;40:167–170. doi: 10.1016/S0190-9622(99)70183-0.
10. Sitaru C, Zillikens D. Mechanisms of blister induction by autoantibodies. Exp Dermatol. 2005 Dec;14(12):861-75.
11. Brenner S, Goldberg I. Drug-induced pemphigus. Clin Dermatol. 2011 Jul-Aug;29(4):455-7. [PubMed]
12. Feng S, Zhou W, Zhang J, Jin P. Analysis of 6 cases of drug-induced pemphigus. Eur J Dermatol. 2011 Sep-Oct;21(5):696-9. [PubMed]
13. Ruocco V, Ruocco E, Lo Schiavo A, Brunetti G, Guerrera LP, Wolf R. Pemphigus: etiology, pathogenesis, and inducing or triggering factors: facts and controversies. Clin Dermatol. 2013 Jul-Aug;31(4):374-381.
14. Murrell, D. F., Peña, S., Joly, P., Marinovic, B., Hashimoto, T., Diaz, L. A., Sinha, A. A., Payne, A. S., Daneshpazhooh, M., Eming, R., Jonkman, M. F., Mimouni, D., Borradori, L., Kim, S. C., Yamagami, J., Lehman, J. S., Saleh, M. A., Culton, D. A., Czernik, A., Zone, J. J., Werth, V. P. (2020). Diagnosis and management of pemphigus: Recommendations of an international panel of experts. Journal of the American Academy of Dermatology, 82(3), 575–585.e1.
15. Gregoriou, S., Efthymiou, O., Stefanaki, C., & Rigopoulos, D. (2015). Management of pemphigus vulgaris: challenges and solutions. Clinical, cosmetic and investigational dermatology, 8, 521–527. https://doi.org/10.2147/CCID.S75908
16. Didona D, Maglie R, Eming R, Hertl M. Pemphigus: Current and Future Therapeutic Strategies. Front Immunol. 2019;10:1418.
17. Bilgic A, Murrell DF. What is novel in the clinical management of pemphigus. Expert Rev Clin Pharmacol. 2019 Oct;12(10):973-980.