IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 1, September 2025
Impact Factor: 7.67

Relapse of Pemphigus Vulgaris Following Rituximab Therapy: A Case Report Highlighting the Role of Alcohol Use and Poor Glycemic Control

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Abstract: *Pemphigus vulgaris (PV) is an autoimmune blistering disorder characterized by intraepithelial acantholysis due to autoantibodies against desmogleins. Rituximab, a CD20-directed monoclonal antibody, is increasingly recognized as a first-line treatment for moderate-to-severe PV. Despite its efficacy, relapses may occur, especially in the presence of modifiable risk factors. We present the case of a 60-year-old man with a known diagnosis of PV who experienced a relapse following multiple cycles of rituximab administered according to the rheumatoid arthritis protocol. The patient's history revealed poor glycaemic control, nutritional deficiencies, and recent resumption of chronic alcohol use. Clinically, he presented with widespread mucocutaneous erosions and vesiculobullous lesions, with positive Marginal Nikolsky and Asboe-Hansen signs. Laboratory results showed leucocytosis, hypoalbuminemia, microcytic hypochromic anaemia, and slightly abnormal liver function tests. The patient was managed with high-dose corticosteroids, azathioprine, and supportive topical and systemic therapies. While no direct causal relationship has been established between alcohol use and PV relapse, this case underscores the potential impact of lifestyle factors and metabolic instability on treatment outcomes. To our knowledge, there are limited case reports describing alcohol-induced PV relapse. This case emphasizes the significance of lifestyle changes and thorough patient education are to the long-term treatment of autoimmune skin conditions.*

Keywords: Pemphigus vulgaris, Rituximab, Alcohol use, Immunosuppressive therapy, Glycaemic control

I. INTRODUCTION

Clinically, pemphigus is an autoimmune bullous illness marked by blistering and erosion of the skin and/or mucous membranes due to autoantibodies against desmogleins (Dsgs) (1, 2, 3) Pemphigus vulgaris (PV) and Pemphigus foliaceus (PF) are two prevalent subtypes of pemphigus that have been identified with significant clinical and immunopathological characteristics (2, 3, 4) In comparison to Western literature, the epidemiology of pemphigus in India has demonstrated distinct trends on several counts. The incidence of pemphigus among dermatological outpatients has ranged from 0.09 to 1.8% (3). PV manifests clinically as a series of flaccid blisters that are restricted to the suprabasal layer of the mucosal membrane or epidermis, while the keratinocytes in the upper layers of the epidermis retain their cell cohesiveness. The collapse of the epidermal barrier, which results in fluid loss, electrolyte imbalances, and the acquisition of an opportunistic infection, makes PV lethal if treatment is not received. There is currently no specific treatment for these conditions, and the most popular treatment approach is the use of immunosuppressive drugs and oral steroids (4). In this case, we detail how alcohol use and inadequate glycaemic control led to Rituximab therapy's failure.

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www.ijarsct.co.in
DOI: 10.48175/IJARSCT-28930

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II. CASE PRESENTATION

An easy way to comply with the conference paper formatting requirements is to use this document as a template and simply type your text into it.

Patient information - A 60-year-old male patient who was known case of Pemphigus vulgaris since past 3 years with history of painful lesions in the oral cavity and oral candidiasis with genital warts. The patient appeared to be normal for 15 days before he developed fluid-filled lesions on his scalp. These lesions started abruptly and spread gradually affecting both upper and lower limbs. The lesions showed no signs of healing and left behind raw regions. For ten days, the patient complained of painful, fluid-filled ulcers in the oral cavity. These lesions begun suddenly, grew quickly in size and quantity, spread over the entire oral cavity, and were associated with pain consuming solid and semi-solid food. They also showed little sign of healing. The patient denies having ever used a topical irritant before lesions, photosensitivity, or an insect bite.

Medical History - The patient has an inguinal hernia and a known small vessel disease. The patient has had type 2 diabetes mellitus for four years and has not taken any medication in the last week. The patient reports having a decreased appetite because of their widespread pain. The patient had a positive social history of drinking alcohol (90–180 ml per day) and smoking tobacco (10 beedis per day) for ten years until quitting in February 2025. The patient has resumed using it for the past month.

Treatment History - In accordance with the Rheumatoid Arthritis protocol, the patient got intravenous infusions of Rituximab 1g in July 2024 (18/07/2024), August 2024 (02/08/2024), and February 2025 (03/02/2025 and 18/02/2025). Dexamethasone and other glucocorticoids were also provided to the patient to manage the condition and stop fresh blisters. Dexamethasone 2cc was administered for 10 days after rituximab, and then Dexamethasone 1cc was administered for 4 days. Following the conclusion of treatment, the patient was discharged. Later, the patient experienced a relapse because of drinking alcohol, which caused the Rituximab treatment to fail.

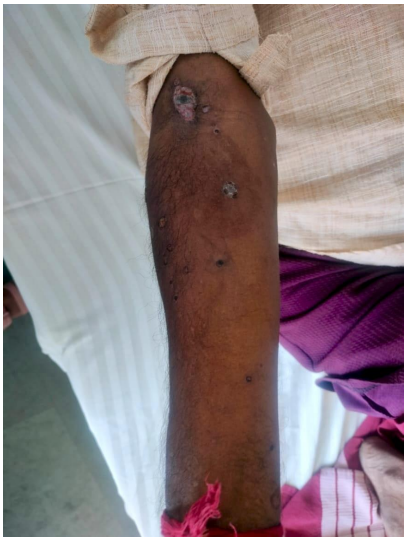

Figure 1

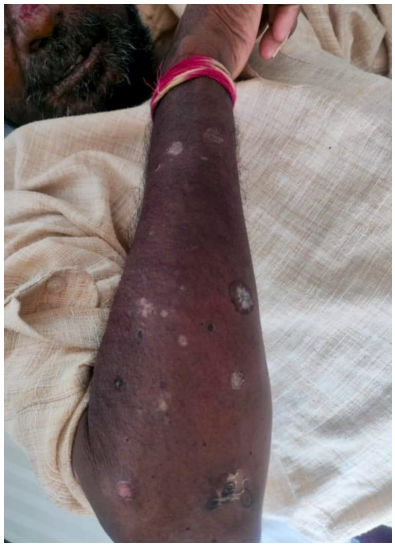

Figure 2

Clinical Findings and Investigations - The patient is pallor positive, moderately built and fed, and well-oriented to time, place, and people. Upon cutaneous inspection, multiple vesicles are observed over the trunk, gluteal area, and bilateral upper limbs. Numerous crusted plaques were observed on the forehead, chest, scalp, back, and both upper and lower limbs. Numerous erosions were seen on both the upper and lower limbs, as well as the scalp, back, and chest. The patient has oral cavity involvement. There are several erosions on the tongue, mouth angle, and bilateral buccal mucosa, along with haemorrhagic crusts on the lip and a white coating on the tongue. The patient's palms and soles were normal, but they exhibited subungual hyperkeratosis over the nails, onychoschizia, onychorrhexis, and dystrophy. The anal and

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genital mucosa were not affected. The pemphigus exhibits a negative Direct Nikolsky sign and a positive Marginal Nikolsky sign, and positive Asboe Hansen's sign.

Figure 1 and Figure 2. Multiple crusted erosions, hyperpigmented macules, and healing ulcers over the extensor aspect of the forearm, showing post-bullous lesions in a patient with pemphigus vulgaris. The lesions are at various stages of healing, indicative of the chronic relapsing course of the disease.

Histopathological report of punch biopsy taken from right side of the back shows that epidermis is lined by stratified squamous epithelium and shows suprabasal bulla. Bulla is composed of neutrophils and acantholytic cells. Floor of the bulla is lined by intact keratinocytes showing row of tombstones pattern.

The full blood panel shows Microcytic Hypochromic Anaemia with Leucocytosis. The other abnormal test results are as shown in the following tables:

Table 1 - Complete Blood Count

Test Parameters	Result	Units	Biological Reference Interval	Remarks
Haemoglobin	11.2	g/dL	13 – 16.5	**Low**
Total WBC count	11.850	10^3 µL	4.0 – 11.0	**High**
Neutrophil	65.0	%	40.0 – 80.0	Normal
Lymphocytes	29.0	%	20.0 – 40.0	Normal
Eosinophil	2.0	%	1.0 – 6.0	Normal
Monocytes	4.0	%	2.0 – 10.0	Normal
Basophils	0.0	%	0.0 – 2.0	Normal
Platelet Count	191	10^3 µL	150 – 410	Normal
Red Blood Cells	5.14	10^6 µL	4.5 – 5.5	Normal
PCV	36.8	%	40 – 54	Normal
MCV	71.6	fL	83.0 – 101.0	**Low**
MCV	21.9	Pg	27.0 – 32.0	**Low**
MCHC	30.4	%	31.5 – 34.5	**Low**

Table 2 - Liver Function Tests

Test Parameters	Result	Units	Biological Reference Interval	Remarks
Blood Urea	24	mg/dL	10 – 50	Normal
Serum Creatinine	0.7	mg/dL	0.7 – 1.3	Normal
Serum Uric Acid	7.5	mg/dL	3.5 – 7.2	**High**
Total Bilirubin	1.2	mg/dL	0.3 – 1.2	Normal
Direct Bilirubin	0.6	mg/dL	0.1 – 0.4	**High**
Indirect Bilirubin	0.6	mg/dL	0 – 0.9	Normal
SGOT	9	U/L	8.0 – 46	Normal
SGPT	10	U/L	7.0 – 49	Normal
ALP	63	U/L	40 – 129	Normal
Serum Total Protein	5.3	g/dL	6.3 – 8.3	**Low**
Serum Albumin	3.1	g/dL	3.5 – 5.2	**Low**
Serum Sodium	134	mEq/L	136 – 145	**Low**
Serum Potassium	3.6	mEq/L	3.5 – 5.2	Normal

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Table 3 - Blood Glucose Tests				
Test Parameters	**Result**	**Units**	**Biological Reference Interval**	**Remarks**
HbA1c	5.1	%	Normal: <5.7 Pre-diabetic: 5.7 – 6.4 Diabetic: >6.5	Normal
FBS	123.7	mg/dL	70 – 100	**High**
PPBS	149.9	mg/dL	70 – 140	**High**

Treatment: Patient was treated with Injection Dexamethasone, a Glucocorticoid 8mg/day given intravenously for 9 days and then tapered to 6mg/day. Further, patient was prescribed with Tablet Prednisolone 40mg/day for 20 days. Patient was also started on Tablet Azathioprine 50mg/day for first 2 days, 100mg/day for next 15 days, 50 mg/day for next 4 days followed by 100 mg/day for next 15 days. Patient was started on Injection Pheniramine maleate and then changed to Tablet Levocetirizine for treating allergic reactions. To treat lesions in the mouth patient was prescribed with Injection Triamcinolone given intralesional, topical treatment with clotrimazole mouth paint, Triamcinolone Acetonide buccal paste, and betadine mouth gargle. Framycetin skin cream was applied topically to prevent secondary bacterial infections. Skin lesions were topically treated with clobetasol cream for lesions over the scalp and Fusidic acid and Beclomethasone dipropionate cream for lesions over the body. Supportive therapy was provided with multivitamins, calcium supplements, and antibiotics. Later patient was started on oral hypoglycaemic agent after completion of immunosuppressant therapy.

III. DISCUSSION

Each patient faces a varied set of drawbacks since PV presents differently. Patients with refractory disease or numerous remissions are managed very differently from those who are treated at the beginning of the disease; the latter group frequently has lower health-related quality of life and treatment compliance (5).

PV can be effectively treated with RTX, a monoclonal antibody that targets the CD20 antigen on B-lymphocytes. After one cycle of RTX, a 76% full remission rate was found by a meta-analysis of 30 studies involving 578 pemphigus patients. The median duration of response was 14.5 months, and the mean time to remission was 5.8 months (6, 7). In 90 patients with newly diagnosed PV, a randomized controlled trial comparing RTX to standard therapy (prednisolone alone) revealed that RTX caused remission in a significantly larger percentage of patients (89% vs. 34%) (8).

In this instance, a 60-year-old man with a known history of PV underwent several rounds of Rituximab treatment before experiencing a disease relapse. Rituximab, an anti-CD20 monoclonal antibody, is being used more and more in PV because it targets the B cells that produce autoantibodies. The patient received corticosteroid cover with dexamethasone and received Rituximab infusions in July, August, and February 2025 in accordance with the rheumatoid arthritis protocol.

The patient had a major relapse despite receiving the proper immunosuppressive treatment. Poor glycaemic control, inadequate nutrition, and the return to alcohol use—which might have disrupted liver and immune function—are probably contributing factors. Alcohol is known to have detrimental effects on liver metabolism and immune responses, which can reduce medication effectiveness and patient compliance.

Widespread mucocutaneous involvement and positive Asboe-Hansen and Marginal Nikolsky signs, which indicate active disease, were found during the clinical examination. Microcytic hypochromic anaemia, hypoalbuminemia, and mild hyponatremia were observed in laboratory tests. These conditions are common in chronic inflammatory states and may reflect disease burden and nutritional compromise. The slightly elevated WBC count indicated a potential secondary infection or continued inflammation.

The patient was put on high-dose intravenous dexamethasone after relapsing, and then switched to oral prednisolone along with azathioprine, a steroid-sparing medication. The goals of supportive and topical treatments were to reduce symptoms and stop secondary infections. Clinical stabilization was probably aided by the combination of local therapies and systemic immunosuppression.

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No case reports that explicitly link alcohol use to relapses in pemphigus vulgaris have been published. There is insufficient evidence that drinking alcohol by itself triggers a relapse in pemphigus vulgaris. A 39-year-old male PV patient with a history of excessive alcohol and tobacco use is the subject of another case report from India; however, this study concentrated on the results of rituximab treatment without mentioning that alcohol caused relapse (9).

According to Omar Jimenez-Zarazu et al. A comprehensive case report describes multiple relapses in a patient with a long history of alcohol use, but these are only associated with continued cocaine use and not with alcohol (10).

IV. CONCLUSION

In summary, although rituximab is still a mainstay in the treatment of refractory PV, patient outcomes are greatly influenced by lifestyle choices, metabolic regulation, and nutritional status. Long-term disease control and quality of life enhancement depend on ongoing patient education, careful observation, and customized treatment plan.

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