

Case report

Successful treatment of recalcitrant pemphigus vulgaris with cold argon plasmaDanijela Milčić,^{1,2} Marko Demenj,¹ Maja Vilotijević,¹ Mirjana Milinković Srećković^{1,2}✉¹Dermatology and Venereology Clinic, University Clinical Center of Serbia, Belgrade, Serbia²Department of Dermatology and Venereology, University of Belgrade School of Medicine, Belgrade, Serbia**Abstract**

Pemphigus vulgaris is a severe autoimmune blistering disease that occasionally develops lesions refractory to conventional systemic immunosuppressive therapy. We report the first documented case of successful treatment of therapy-resistant pemphigus vulgaris using cold atmospheric plasma. A 34-year-old woman presented with extensive oral and genital erosions that dramatically improved after initiating therapy with pulse corticosteroids in combination with cyclophosphamide. In the following weeks, she developed treatment-resistant facial erosions that persisted for 6 months despite aggressive systemic therapy consisting of intravenous immunoglobulin, azathioprine, and plasmapheresis. After 3 weekly cold atmospheric plasma treatments at 33 to 37 °C with a 2 cm torch gap for 3 min per treatment zone, the patient had remarkable clinical improvement, with an estimated > 80% epithelialization of facial erosions within 4 weeks, progressing to complete epithelialization by week 6. Disease activity assessment using the Pemphigus Disease Activity Index confirmed rapid improvement from a baseline of 14 to 0 within 6 weeks. Indirect immunofluorescence was negative throughout treatment. Sustained disease remission was achieved for 24 months. This novel application of cold atmospheric plasma is a promising therapeutic approach for recalcitrant lesions of pemphigus vulgaris.

Keywords: pemphigus vulgaris, recalcitrant lesions, cold atmospheric plasma (CAP), argon plasma therapy, wound healing

Received: 18 January 2026 | **Returned for modification:** 29 May 2026 | **Accepted:** 3 June 2026

Introduction

Pemphigus vulgaris (PV) is a chronic autoimmune life-threatening disease characterized by the formation of blisters and erosions on the skin and mucous membranes. The modern approach to treatment involves systemic corticosteroids and immunosuppressive agents, intravenous immunoglobulins, plasmapheresis, and monoclonal antibodies directed against CD20 (rituximab) (1–4). In most cases, single or combined therapeutic approaches lead to complete resolution of lesions. However, there are cases of recalcitrant lesions, which represent a unique challenge for treatment (4, 5). In the current literature, managing localized recalcitrant lesions has been attempted by using new approaches, such as intralesional rituximab and CO₂ laser (6, 7). Here, to our knowledge, we present the first case of treatment-resistant PV lesions successfully treated with cold argon plasma (CAP).

Case report

We present a 34-year-old Caucasian woman with oral and genital blisters and erosions, initially involving 5% of the body surface area (BSA) with Pemphigus Disease Activity Index (PDAI) 15. The disease started after a family tragedy (the suicide of the patient's sister). In the same period, our patient also developed severe

✉ mirjana.milinkovicsreckovic@yahoo.com

mental and psychological disorders. The diagnosis of pemphigus vulgaris was established using standard diagnostic tests.

The patient was initially treated with combined pulse therapy using dexamethasone and cyclophosphamide (C) in high doses, oral prednisolone, and low-dose C between pulses. After the first pulse cycle, the patient had a COVID-19 infection, and pemphigus progressed rapidly, eventually involving more than 30% of the BSA with PDAI 64.

Subsequently, intravenous immunoglobulin (IVIg) was combined with pulse doses of dexamethasone and oral azathioprine (150 mg daily), and C was discontinued due to hepatotoxicity. Plasmapheresis was performed twice but was discontinued due to severe hypofibrinogenemia. The serious complications that necessitated the patient's 4-month hospitalization included skin infections, sepsis, pathological fractures of nine vertebrae, pulmonary embolism, and severe depression and anxiety, all requiring multidisciplinary management.

With appropriate multidisciplinary therapy, the patient's condition improved. Epithelialization ensued in all lesions except for the erosions on the face, which persisted for 6 months (Fig. 1). These lesions posed a significant clinical challenge. The patient exhibited high levels of anxiety, and it was suspected that behavioral factors might be contributing to lesion aggravation. Occlusive bandaging and silicone dressings for burn wound healing were applied, but no significant improvement was observed. It is worth noting that rituximab, although available in Serbia at that time, was not approved as a government-funded therapy option.

Due to resistance of the facial lesions, we initiated treatment with argon plasma, using the AdTech SteriPlas device (Adtec Healthcare Limited, London, UK). This device features a six-electrode plasma torch that produces plasma via microwave-induced discharges, with argon serving as the medium for transporting the gas stream to the treated area. An important technical consideration is that the temperature of the applied plasma at the target site is approximately 33 to 37 °C, as stated by the manufacturer, thereby minimizing thermal damage concerns. The plasma torch's aperture is suitable for a surface area of 4 to 5 cm².

Because the patient had extensive erosions involving the forehead and cheeks, the area was divided into nine zones to ensure complete coverage. In accordance with the manufacturer's recommendations, a 2 cm distance was maintained between the plasma torch and lesions. Treatment consisted of 3 minutes of plasma application per zone, administered three times a week for 4 weeks.

We achieved dramatic clinical improvement following CAP treatment. The procedure was tolerated well, and local adverse reactions were not observed. Clinically, epithelialization progressed from approximately 20% at baseline to 80% of the extensive facial erosions within 4 weeks (Fig. 2). The remaining lesions achieved complete epithelialization by week 6. PDAI improved rapidly: it decreased from 14 to 6 after 4 weeks of treatment and reached 0 at week 6. Serologically, indirect immunofluorescence (IIF) remained negative throughout the treatment period and at follow-up, indicating no exacerbation of the autoimmune response.

Following CAP treatment, systemic therapy was continued with low-dose prednisolone and azathioprine. The patient has been in complete remission for the following 2 years (Figs. 3, 4). A graphical timeline of the disease course and CAP treatment sessions is presented in Figure 5.

Discussion

CAP is an innovative therapeutic technology with broad applications in various medical fields, including dermatology. CAP utilizes a partially ionized gas, most often argon, that operates at room temperature, making it convenient for medical applications (8–10). CAP exerts its therapeutic effects in tissue through the formation of ultraviolet (UV) radiation and the generation of various reactive oxygen species (ROS) and reactive nitrogen species (RNS), which activate multiple cellular pathways and initiate various biological mechanisms. The therapeutic properties of CAP include suppressive effects on microbial skin infections (bacterial, fungal, and viral), promotion of wound healing, and inhibition of tumor cell growth and migration. (9, 11–13). Furthermore, CAP accelerates wound healing by reducing bacterial load, stimulating cell proliferation, and inducing gene expression, and it can serve as a promising therapy for persistent chronic wounds (14, 15).

In our patient, the persistence of the erosions from September 2022 to April 2023 met the criterion for a chronic wound, which, by definition, is a wound that exhibits delayed healing. As found in previous studies reporting bacterial colonization of PV lesions, microbiological analysis during our patient's hospitalization revealed various microbial pathogens, most commonly *Staphylococcus aureus* and *Acinetobacter* species. These pathogens were treated with appropriate local and systemic antibiotic therapy, combined with local antiseptics and various silicone and antiseptic dressings.

However, these conventional measures resulted in minimal to inadequate improvement of the patient's recalcitrant lesions, even when erosion swab cultures were sterile. Notably, at baseline, the patient had colonization with *S. aureus* and *Klebsiella-Enterobacter* species. After completing 4 weeks of CAP treatment combined with concomitant intravenous and local antibiotic therapy, *S. aureus* was unexpectedly detected again in control cutaneous erosion swabs from the remaining eroded areas. This finding suggests that, although CAP possesses documented antimicrobial properties, its primary mechanism of action in this case may not have been simple sterilization (14, 16).

In addition, objective disease activity assessment using the PDAI demonstrated rapid improvement: baseline PDAI 14 decreased to PDAI 0 within 6 weeks of CAP initiation, with sustained remission at 24-month follow-up. The negative IIF throughout the treatment course indicates no exacerbation of autoimmune response and argues for mechanisms underlying the therapeutic benefit of CAP other than, or complementary to, systemic immunosuppression.

In PV, the direct pathogenic role of anti-Dsg1 and anti-Dsg3 Abs was established because they interfere with intracellular pathways, inducing cell acantholysis and/or cell death. Recent studies have identified additional autoantibodies in the sera of PV patients, suggesting either a synergistic action in blister formation or, alternatively, epitope spreading. Moreover, animal model studies have proposed a possible role of matrix metalloproteinases as effectors of antibody-activated pathways in PV (17, 18).

Therefore, because the exact pathological mechanism in PV remains incompletely elucidated, other known or yet unknown CAP-induced mechanisms could have contributed, providing beneficial therapeutic effects. To our knowledge, this is the first case of recalcitrant PV lesions successfully treated with CAP.

As a single case report, this work lacks comparative control and cannot definitively determine CAP's independent contribution given concurrent systemic therapy. However, this is the first documented application of CAP in pemphigus vulgaris and warrants further investigation through prospective studies and clinical trials.

Conclusions

This case report demonstrates the potential of CAP as a novel, effective, and safe therapeutic modality for recalcitrant PV lesions refractory to conventional systemic therapy. Although the precise molecular mechanisms in this patient were not investigated, it can be hypothesized that the positive effects of CAP on wound healing in our PV case may be influenced by several factors: long-term reduction in bacterial colonization, direct pro-epithelialization properties, and potential synergistic effects with corticosteroid and immunosuppressive treatment.

This report opens new possibilities in plasma medicine, including recalcitrant lesions in autoimmune bullous dermatoses as an emerging indication. Future studies should focus on elucidating the molecular mechanisms underlying the complex interaction between CAP and PV pathogenesis.

References

1. Lim YL, Bohelay G, Hanakawa S, Musette P, Janela B. Autoimmune pemphigus: latest advances and emerging therapies. *Front Mol Biosci.* 2022;8:808536.
2. Hertl M, Jedlickova H, Karpati S, Marinovic B, Uzun S, Yayli S, et al. Pemphigus. S2 guideline for diagnosis and treatment—guided by the European Dermatology Forum (EDF) in cooperation with the

- European Academy of Dermatology and Venereology (EADV). *J Eur Acad Dermatol Venereol.* 2015;29:405–14.
3. Marzano AV, Fanoni D, Venegoni L, Berti E, Caputo R. Treatment of refractory pemphigus with the anti-CD20 monoclonal antibody rituximab. *Dermatology.* 2007;214:10–8.
 4. Harman KE, Brown D, Exton LS, Groves RW, Hampton PJ, Mohd Mustapa MF, et al. British Association of Dermatologists' guidelines for the management of pemphigus vulgaris 2017. *Br J Dermatol.* 2017;177:1170–201.
 5. Rajkumar K, Samuel J, Poornima, Ramesh A. A case series of recalcitrant pemphigus. *J Clin Diagn Res.* 2022;16:WR01–5.
 6. Lima PB, Formentini MS, Jorge S, Abbade LPF, Marques SA. Pemphigus vulgaris aggravated by obsessive-compulsive behavior: the importance of adjuvant topical occlusive dressing. *An Bras Dermatol.* 2021;96:523–5.
 7. Vinay K, Kanwar AJ, Mittal A, Dogra S, Minz RW, Hashimoto T. Intralesional rituximab in the treatment of refractory oral pemphigus vulgaris. *JAMA Dermatol.* 2015;151:878–82.
 8. Gan L, Jiang J, Duan JW, Wu X, Zhang S, Duan XR et al. Cold atmospheric plasma applications in dermatology: a systematic review. *J Biophotonics.* 2021;14:e202000415.
 9. Khalaf AT, Abdalla AN, Ren K, Liu X. Cold atmospheric plasma (CAP): a revolutionary approach in dermatology and skincare. *Eur J Med Res.* 2024;29:487.
 10. Laroussi M. Cold plasma in medicine and healthcare: the new frontier in low-temperature plasma applications. *Front Phys.* 2020;8:74.
 11. Tan F, Wang Y, Zhang S, Shui R, Chen J. Plasma dermatology: skin therapy using cold atmospheric plasma. *Front Oncol.* 2022;12:918484.
 12. Yan D, Sherman JH, Keidar M. Cold atmospheric plasma, a novel promising anti-cancer treatment modality. *Oncotarget.* 2017;8:15977–95.
 13. Bekeschus S, von Woedtke T, Emmert S, Schmidt A. Medical gas plasma-stimulated wound healing: evidence and mechanisms. *Redox Biol.* 2021;46:102116.
 14. von Woedtke T, Emmert S, Metelmann HR, Rupf S, Weltmann KD. Perspectives on cold atmospheric plasma (CAP) applications in medicine. *Phys Plasmas.* 2020;27:070601.
 15. Matthes R, Lührmann A, Holtfreter S, Kolata J, Radke D, Hübner NO, et al. Antibacterial activity of cold atmospheric pressure argon plasma against 78 genetically different *mecA*, *luk-PV*, *agr* or capsular polysaccharide type *Staphylococcus aureus* strains. *Skin Pharmacol Physiol.* 2016;29:83–91.
 16. Amber KT, Valdebran M, Grando SA. Non-desmoglein antibodies in patients with pemphigus vulgaris. *Front Immunol.* 2018;9:1190.
 17. Cirillo N, Lanza M, Rossiello L, Gombos F, Lanza A. Defining the involvement of proteinases in pemphigus vulgaris: evidence of matrix metalloproteinase-9 overexpression in experimental models of disease. *J Cell Physiol.* 2007;212:36–41.
 18. Cirillo N, Prime SS. A scoping review of the role of metalloproteinases in the pathogenesis of autoimmune pemphigus and pemphigoid. *Biomolecules.* 2021;11:1506.



Figure 1. Persistent treatment-resistant facial erosions at the beginning of the treatment protocol. Pemphigus disease area index (PDAI) 14.



Figure 2. Considerable epithelialization of cheek and forehead erosions after the 4-week mark. Pemphigus disease area index (PDAI) 6.



Figure 3. Complete clinical remission at follow-up, 6 months after treatment completion.



Figure 4. Sustained clinical remission at 24 months.

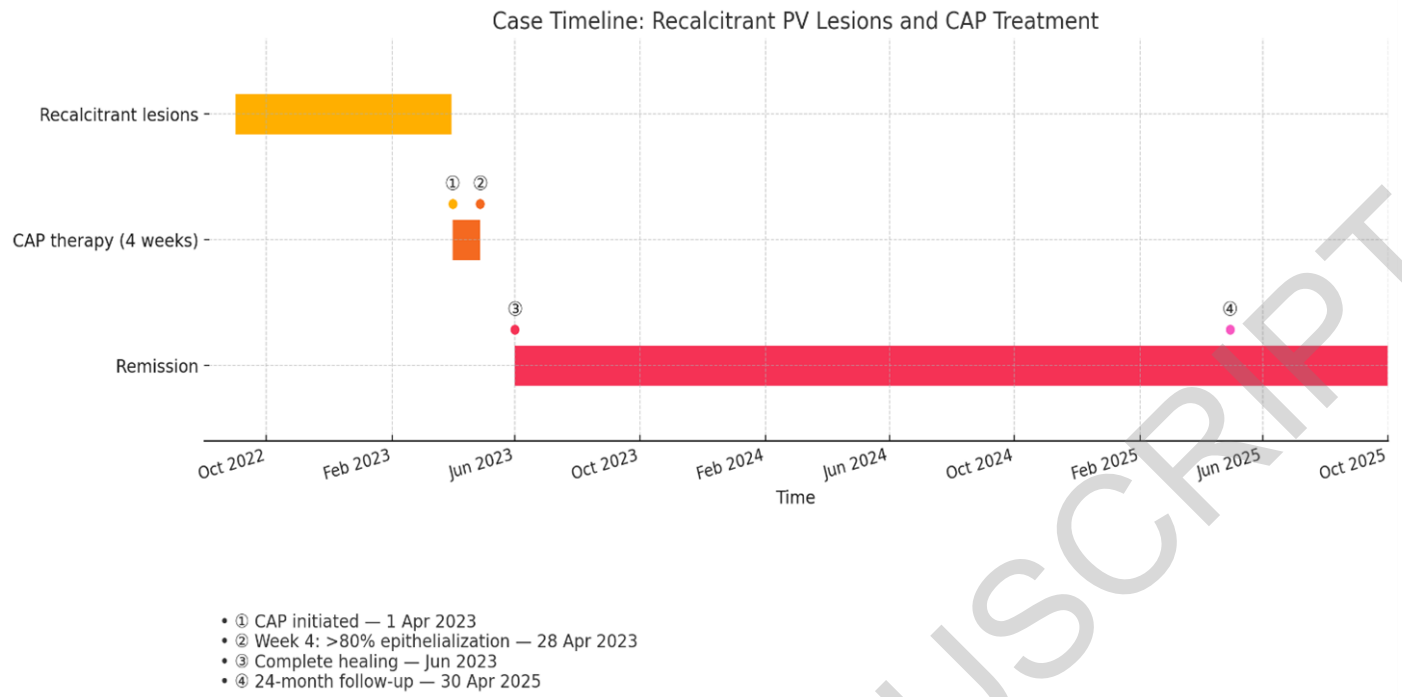


Figure 5. Case timeline of disease course and cold atmospheric plasma (CAP) treatment of pemphigus vulgaris (PV); numeric markers correspond to the legend.