# New-onset pemphigus after COVID-19

Yihang Xie[1], Mei Yang[1], Peimei Zhou[1], Jiaming Fan[1], and Sijie Zhou[1]

[1]Chengdu Second People's Hospital Department of Dermatology

March 11, 2023

New-onset pemphigus after COVID-19

Yihang Xie[1] Mei Yang[1] Peimei Zhou[1]* Jiaming Fan[1] Sijie Zhou[1]

1.Department of Dermatovenereology, Chengdu Second People's Hospital, Chengdu, China

* Corresponding Author: 46551704@qq.com

**running head:** pemphigus after COVID-19

**The category of the article:** Letter

**Keywords:** COVID-19, pemphigus

**Manuscript word count:** 690 words

**The number of figures:** 2

**The number of tables:** 0

**The number of references:** 8

**Correspondence to:** Peimei Zhou, M.D, Ph.D., Department of Dermatovenereology, Chengdu Second People's Hospital, Qingyun Street, Chengdu, 610041, China.

Tel: +86 18908176315; E-mail:*46551704@qq.com*

**Full conflict of interest statement:** Y. Xie, and my co-authors have no conflict of interest to declare.

**Ethics statement:** The patient has consented to publish this information.

**Data availability statement:** Data sharing does not apply to this article as no new data were created or analyzed in this study.

**Funding sources:** none

Dear Editor,

Cutaneous manifestations of coronavirus disease (COVID-19), the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; family *Coronaviridae,* genus *Betacoronavirus,* subgenus*Sarbecovirus* ), have been increasingly reported. SARS-CoV-2 infection is multisystemic and leads to potentially detrimental effects on various organs. Maculopapular, urticarial, vesicular, livedoid, and Chilblain-like lesions (CBLL) have been commonly reported to be associated with COVID-19[1]. Here, we encountered an intriguing case of pemphigus that developed after COVID-19 infection.

A 73-year-old male presented with a 42-day history of pruritic flaccid blisters that arose on the trunk and both upper limbs on normal and erythematous skin. Cutaneous lesions started 3 days after the positive reverse transcription polymerase chain reaction (RT-PCR) test diagnostic for SARS-CoV-2. He denied any

history of systemic diseases, medication, and medicine or food allergies, and had not used any medication before symptom onset. The patient had first been diagnosed with allergic dermatitis caused by COVID-19 at another hospital and was prescribed oral prednisone (8 mg once daily for 4 days). The patient reported no new blisters, but the erythema did not fade; therefore, he visited our hospital. Physical examination revealed cutaneous lesions on the trunk and both upper limbs without mucosal involvement and scattered superficial blisters that developed into crusted erosions on an erythematous base(Figure1 A-D). Laboratory examination revealed normal white cell count (8.63 Ã–$10^9$/L; normal 3.5-9.5 Ã–$10^9$/L) with eosinophilia (6%; normal 0.5%-5.0%). Desmoglein (Dsg) 1 antibody levels were $>$ 150 U/mL (positive: $>$ 20), while Dsg3, BP(bullous pemphigoid)180, and BP230 antibody levels were within normal ranges. Other laboratory tests including RT-PCR targeting SARS-CoV-2, immunoglobulin, erythrocyte sedimentation rate, the spectrum of antinuclear antibodies, and T-spot were negative or normal. Chest and abdominal computed tomography revealed chronic inflammatory changes but no obvious tumors. Histological analysis of an incisional cutaneous biopsy taken from the patient's abdomen showed subcorneal blister formation, acantholytic cells within the blister, and marked spongiotic edema in the spongiosa layer that had mixed inflammatory infiltrate with eosinophils, leukomonocytes, and neutrophils(Figure2A). Direct immunofluorescence (DIF) showed deposition of intracellular IgG and C3 in subepidermal 2/3 interspinous cells, though was negative for IgA and IgM, confirming pemphigus(Figure2B,C). Considering the good response to hormone treatment, the patient continued oral prednisone at 8 mg once daily along with the use of topical corticosteroids. Symptoms were completely absent after 3 weeks(Figure1 E-F).

An increasing number of studies on cutaneous manifestations of COVID-19 have been reported; however, knowledge is still lacking on the common skin manifestations of this disease. Nonspecific cutaneous manifestations due to SARS-CoV-2 infection have also been reported, such as immune thrombocytopenic purpura (ITP), dengue-like exanthem, pityriasis rosea-like eruptions, acral ischemia, mucositis, dusky lesions, and bullae[2.3.4]. We searched all relevant articles and found only two cases of pemphigus vulgaris induced by COVID-19. In the case presented here, we realized that COVID-19 may be responsible for the rash eruption, possibly due to an inflammatory reaction[5]. The onset time of the rash was similar to that in the cases of pemphigus previously reported by De Medeiros[5] and Mohaghegh F[6] (within 1.5 months). In our case, although direct immunofluorescence showed subepidermal 2/3 deposition, we still diagnosed pemphigus foliaceus in combination with the pathological presentation, indirect immunofluorescence, and good treatment outcome. We speculate that the reason why direct immunofluorescence showed subepidermal 2/3 deposition may be the marked sponge edema of the epidermis, which may lead to a discontinuity of acantholysis, resulting in leakage of Dsg1 into the deeper epidermis.

Pemphigus is defined as a group of rare mucocutaneous autoimmune diseases. Its etiology is unknown, though there are studies on autoimmune etiology which is believed to be related to stimulation by certain drugs, ultraviolet radiation, and malignant tumors; these induce autoimmune reactions by making the adhesive substances between the spiny cell layers become autoantigens[7]. It is rarely considered, however, that viral infections might cause pemphigus. The ability of SARS-CoV-2 to induce a hyper-stimulated immune state was discovered at the beginning of the pandemic[8]. As an instrumental trigger of autoimmunity, SARS-CoV-2 infection could be a trigger for autoimmune reactions, possibly through more than one mechanism. Because of this, all factors should be considered in any patient presenting with new-onset or exacerbating cutaneous reactions.

## REFERENCES

1. Huynh T, Sanchez-Flores X, Yau J, Huang JT. Cutaneous Manifestations of SARS-CoV-2 Infection. Am J Clin Dermatol 2022;23:277-286.
2. Bhattacharjee S, Banerjee M. Immune Thrombocytopenia Secondary to COVID-19: a Systematic Review. SN Compr Clin Med 2020;2:2048-2058.
3. J Joob B, Wiwanitkit V. COVID-19 can present with a rash and be mistaken for dengue. J Am Acad Dermatol 2020;82:e177.
4. Ehsani AH, Nasimi M, Bigdelo Z. Pityriasis rosea as a cutaneous manifestation of COVID-19 infection.

J Eur Acad Dermatol Venereol 2020;34:e436-e437.
5. De Medeiros VLS, Monteiro-Neto AU, França DDT, Castelo Branco R, de Miranda Coelho ÉO, Takano DM. Pemphigus Vulgaris After COVID-19: a Case of Induced Autoimmunity. SN Compr Clin Med 2021;3:1768-1772.
6. Mohaghegh F, Hatami P, Refaghat A, et al. New-onset pemphigus foliaceus following SARS-CoV-2 infection and unmasking multiple sclerosis: A case report. Clin Case Rep 2022;10:e05910.
7. Korman N. Pemphigus. J Am Acad Dermatol 1988;18:1219-1238.
8. Dotan A, Muller S, Kanduc D, David P, Halpert G, Shoenfeld Y. The SARS-CoV-2 as an instrumental trigger of autoimmunity. Autoimmun Rev 2021;20:102792.

Figure 1: (A-D) Scattered superficial blisters on the trunk and upper limbs that devolved into crusted erosions on a erythe

Figure 2: (A) Hematoxylin–eosin, ×100, Subcorneal blister formation, acantholytic cell within the blister, and marked spon