New-onset pemphigus after COVID-19

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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-19¹. 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 × 10^9/L; normal 3.5-9.5 × 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 bullae2,3,4. 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 reaction5. The onset time of the rash was similar to that in the cases of pemphigus previously reported by De Medeiros5 and Mohaghegh F6 (within 1.5 months). In our case, although direct immuno-fluorescence showed subepidermal 2/3 deposition, we still diagnosed pemphigus foliaceus in combination with the pathological presentation, indirect immuno-fluorescence, and good treatment outcome. We speculate that the reason why direct immuno-fluorescence 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 autoimmunity 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 autoantigens7. 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 pandemic8. 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


Figure 1: (A-D) Scattered superficial blisters on the trunk and upper limbs that devolved into crusted erosions on a erythematous base. (E-F) erythema and blisters almost disappeared.

Figure 2: (A) Hematoxylin–eosin, ×100, Subcorneal blister formation, acantholytic cell within the blister, and marked spongiotic edema in the spongiosa. (B) Direct immunofluorescence showed the deposition of IgG and C3 in subepidermal 2/3 interspinous cell with negative IgA and IgM.