

# Angioedema and urticaria as early presentations of a COVID-19 patient: a case report

Iran J Dermatol 2022; 25: 86-88

DOI: 10.22034/ijd.2022.293267.1402

**Dear Editor,**

Coronavirus disease 2019 (COVID-19) usually presents with fever, sore throat, myalgia, cough, and respiratory symptoms <sup>1</sup>, but sometimes features unusual cutaneous manifestations <sup>2</sup>. Dermatological manifestations might be due to direct viral invasion or immunological response <sup>3</sup>. Here, we describe a COVID-19 case with prodromal manifestations of angioedema and urticaria.

In August 2020, a 46 year-old-woman was admitted to the Emergency Department with a five-day history of a widespread, red, raised, blanching, itchy rash, which started from the lower extremities and gradually extended to the trunk and upper extremities. She had no fever, myalgia, or cough and had no allergy to drugs or food, except for a possible allergy to peanuts. Also, she had no previous airway diseases or asthma. She had not taken any NSAIDs or ACE inhibitors in the preceding two weeks. On the admission day, the rash extended, with swelling of the lips and eyelids. After 24 hours, a non-productive cough was added to the skin lesions. Her temperature was 36.2° C, pulse rate was 98 beats/min, oxygen saturation was 98% in room air, and respiratory rate was 16 times/min. On physical examination,

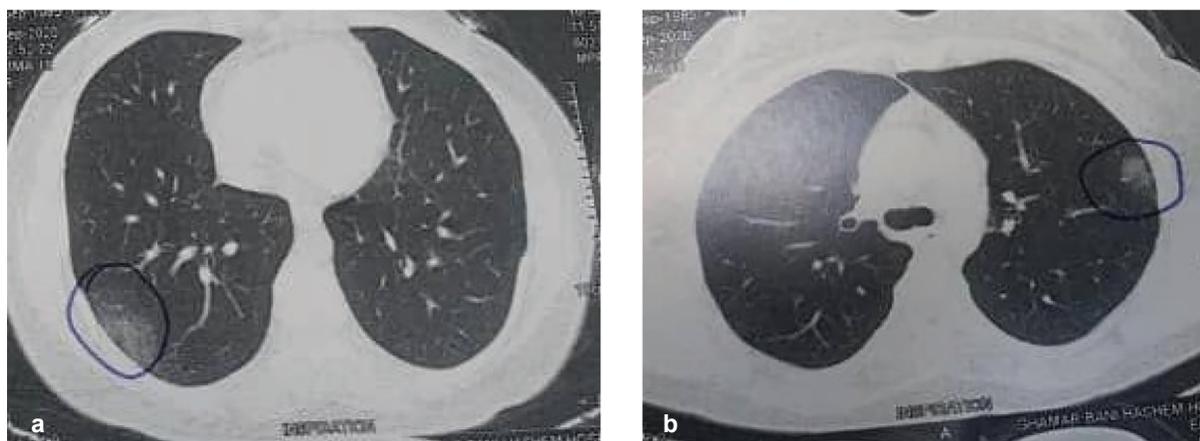
she was conscious without any respiratory distress. Her face, lips, and periorbital area were edematous, without erythema. On the extremities and trunk, red, raised, blanching wheals were seen (Figure 1a, b). She had no tongue or throat swelling and no wheezing on the chest examination. The laboratory findings included 8300/μL white blood cells (lymphocytes: 17%) and an elevated C-reactive protein (CRP) level of 98 mg/dl (Table 1). The RT-PCR for SARS-CoV-2 was positive. Computed tomography of the chest showed patchy ground-glass opacities with a subpleural distribution (Figure 2a, b). The patient received intravenous hydrocortisone (100 mg TID), atazanavir-ritonavir (300 mg daily), famotidine (20 mg BID), and

**Table 1.** Patient's laboratory results.

|                                 | Day 0  | Day 3  |
|---------------------------------|--------|--------|
| WBC ×10 <sup>9</sup> per L      | 8300   | 4400   |
| Neutrophils %                   | 80     | 57     |
| Lymphocytes %                   | 17     | 37     |
| Platelet ×10 <sup>9</sup> per L | 173000 | 160000 |
| C-reactive protein (mg/dl)      | 98     | 52     |
| Lactate dehydrogenase (U/liter) | 455    | 281    |
| Ferritin, ng/mL                 | 60.4   |        |
| Alanine transaminase, U/L       | 52     | 14     |
| Aspartate transaminase, U/L     | 48     | 17     |



**Figure 1.** (a) Urticarial erythematous eruptions on the neck on day 0. (b) Mild angioedema of the upper and lower lips on day 0. (c) Lip angioedema disappeared five days later.



**Figure 2.** Chest CT images revealing the peripheral ground-glass appearance of (a) the left and (b) right lungs on day.

diphenhydramine (10 mg TID). The patient's swelling significantly improved two days later and disappeared on day 4 (Figure 1c). She was discharged in a stable condition on day 5, and prednisolone was continued for five more days.

Common presentations of COVID-19 include fever, cough, dyspnea, myalgia, and sometimes gastrointestinal symptoms<sup>1</sup>. In one study, urticaria was seen as a dermatological manifestation in 9.7% (7/72) of patients, and in 12.5% of patients, skin manifestations occurred before diagnosis or onset of respiratory symptoms<sup>2</sup>. Knowing the unusual presentations of COVID-19 helps us achieve an earlier diagnosis and prevent the further spread of this highly infectious disease.

Some viral infections such as HSV, CMV, and EBV can cause skin lesions such as urticaria and angioedema<sup>3</sup>. Lymphocytic vasculitis, microthrombosis due to immune complex molecules, and low-grade Disseminated Intravascular Coagulopathy (DIC) may explain the dermatologic features of COVID-19<sup>4</sup>. Angioedema is due to fluid extravasation to subcutaneous tissue; this self-limited swelling is caused by mast cells (histamine) or bradykinin mediators<sup>5</sup>. In mast cell-related angioedema, respiratory symptoms and skin lesions appear several minutes after allergen exposure and last for 24-48 hours. Bradykinin-mediated urticaria remains more than 36 hours; it might be associated with drugs such as ACE inhibitors<sup>5</sup>. Urticaria in this patient lasted more than 48 hours and did not resolve with antihistamines, so mast cell-related angioedema was not its cause. On the other hand, our patient

had no recent history of drug use.

Allergic reaction, idiopathic angioedema, ACE inhibitor-induced angioedema, and hereditary and acquired angioedema are the most common causes of angioedema<sup>6</sup>. In allergic angioedema, there is a history of exposure to allergens such as anesthetics, neuromuscular blocking agents, antibiotics, and NSAIDs<sup>6</sup>. Our patient had no consumption of these drugs in previous weeks.

Physical and emotional stress (such as surgery) can trigger the idiopathic angioedema that appears immediately after stress<sup>7</sup>. The present case had none of these previous triggers, so idiopathic angioedema was ruled out for our patient. In C1 esterase inhibitor deficiency, there is usually a positive family history of angioedema. It is triggered by surgery, trauma, stress, exercise, infection, alcohol consumption, menstruation, and some drugs (ACE inhibitors, estrogens, etc.)<sup>8</sup>. In the present case, none of these agents were involved. Our patient had no significant pain or burning of the skin, and there was no peeling in the resolution period, so contact dermatitis was ruled out.

Facial lymphedema lasts a long time and is created by the accumulation of lymph fluid in the face, and warmth is an important sign of this diagnosis<sup>9</sup>; these factors were not evident in our case. Myxedema and superior vena cava syndrome are sometimes mistaken with angioedema but were not compatible with our case as the patient's edema was localized. In our case, similar to the cases of the Shahidi Dadras *et al.* study<sup>10</sup>, the skin manifestations were benign and improved with no permanent side effects.

Neda Faraji, MD <sup>1</sup>

Hadiseh Hosamirudsari, MD <sup>2\*</sup>

Narjes Zarei Jalalabadi, MD <sup>3</sup>

Forough Goudarzi, BSc <sup>4</sup>

1. *Department of Internal Medicine, Baharloo Hospital, Railway Square, Tehran University of Medical Sciences, Tehran, Iran*
2. *Department of Infectious Diseases, Baharloo Hospital, Railway Square, Tehran University of Medical Sciences, Tehran, Iran*
3. *Department of Internal Medicine, Imam Khomeini Hospital Complex, Tohid Square, Tehran, Iran*
4. *Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*

*\*Corresponding author:*

*Hadiseh Hosamirudsari, MD*

*Department of Infectious Diseases, Baharloo Hospital, Railway Square, Tehran University of Medical Sciences, Tehran, Iran*

*Email: h-hosami@sina.tums.ac.ir*

*Received: 02 July 2021*

*Accepted: 05 January 2022*

## REFERENCES

1. Lu L, Zhong W, Bian Z, et al. A comparison of mortality-related risk factors of COVID-19, SARS, and MERS: a systematic review and meta-analysis. *J Infect.* 2020;81:e18-e25.
2. Sachdeva M, Gianotti R, Shah M, et al. Cutaneous manifestations of COVID-19: report of three cases and a review of literature. *J Dermatol Sci.* 2020;98:75-81.
3. Imbalzano E, Casciaro M, Quartuccio S, et al. Association between urticaria and virus infections: a systematic review. *Allergy Asthma Proc.* 2016;37:18-22.
4. Henry D, Ackerman M, Sancelme E, et al. Urticarial eruption in COVID-19 infection. *J Eur Acad Dermatol Venereol.* 2020;34:e244-5.
5. Zuraw B. An overview of angioedema: clinical features, diagnosis, and management. In: *Up To Date*, Saini S (Ed). (Accessed on October, 2020). Available from: [www.uptodate.com](http://www.uptodate.com).2020.
6. Hoyer C, Hill MR, Kaminski ER. Angio-oedema: an overview of differential diagnosis and clinical management. *Continuing Education in Anaesthesia, Critical Care & Pain.* 2012;12:307-11.
7. Cicardi M, Zanichelli A. Acquired angioedema. *Allergy Asthma Clin Immunol.* 2010;6:14.
8. Kaplan AP. Angioedema. *World Allergy Organ J.* 2008;1:103-13.
9. Sleigh BC, Manna B. Lymphedema. *StatPearls. Treasure Island (FL): StatPearls Publishing LLC.; 2020.*
10. Shahidi Dadras M, Dadkhahfar S, Bahmanjahromi A, et al. Skin manifestations in three cases of COVID-19 infection from Iran and a narrative literature review. *Iran J Dermatol.* 2020; 23:60-6.