Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
COVID-19: Important Updates and Developments
Edited by Franco Rongioletti, MD, and Leonard J. Hoenig, MD

COVID-19 (SARS-CoV-2) infection presenting as acute urticaria
Mariam Farhan, MDa,⁎, Bilori Bilori, MDa, Steven Aronin, MDb

aDepartment of Internal Medicine, Griffin Hospital, Derby, Connecticut, USA
bIterum Therapeutics, Old Saybrook, Connecticut, USA

Abstract In addition to typical respiratory clinical manifestations,1 patients with SARS-CoV-2 infection may also exhibit extrapulmonary clinical manifestations. As we continue to discover more about SARS-CoV-2, it is becoming evident that its presentation, course of disease, and clinical manifestations differ from person to person. Not only that, it is presenting with a wide range of findings, skin manifestations might be one of the rare signs of the disease.2 We encountered a unique case in our outpatient setting via telemedicine. Our patient presented with usual signs and clinical manifestations of the disease and developed a total body urticarial eruption with red margins and raised skin-colored center 4 days after our initial encounter. Later, she tested positive for COVID-19. She did not require hospitalization and was managed with supportive care and antihistamines.

© 2020 Elsevier Inc. All rights reserved.

Case report

A 57-year-old woman working in an assisted care facility consulted us with a 2-day history of fever (Tmax 100.6°F), chills, dry cough, joint pain, body aches, headache, and fatigue. She reported loss of appetite but denied nausea, vomiting, diarrhea, or change in taste or smell. Notably, 12 residents at the facility where she worked had tested positive for SARS-CoV-2. Her medical history is significant for myxomatous mitral valve with mitral valve prolapse and mild mitral regurgitation. A nasopharyngeal swab for SARS-CoV-2 polymerase chain reaction was ordered, and she was to self-isolate for 14 days while avoiding nonsteroidal anti-inflammatory drugs. Over the next 4 days, her signs and clinical manifestations worsened with chest tightness, syncope, and a full-body eruption, which she described as raised and pale in the center with surrounding red edges consistent with hives (Figure 1). She denied use of new medications, detergents, soaps, lotions, or cosmetics. Her eruption was severe enough to prompt a visit to the emergency room, where she was prescribed diphenhydramine.

SARS-CoV-2 polymerase chain reaction results were still pending at this time. Two days after her visit to the emergency department, she had a follow-up video visit, at which time she reported the recurrence the eruption. The antihistamine therapy had only been transiently effective. Treatment was started with hydroxyzine and triamcinolone acetonide 0.1% cream. Upon a follow-up video call, there had been another mild episode of urticaria involving her left knee and thigh (Figure 2), which again promptly responded to antihistamine therapy. Twenty-eight days after the initial presentation, her eruption and all other COVID-19 clinical manifestations had completely disappeared except for fatigue, which resolved after 50 days of the initial presentation.

⁎ Corresponding author.
E-mail address: mabid141@gmail.com (M. Farhan).

https://doi.org/10.1016/j.clindermatol.2020.09.004
0738-081X/© 2020 Elsevier Inc. All rights reserved.
Discussion

Skin manifestations are common for viral infections. Urticaria, specifically, has been associated with a number of viral infectious agents.\(^3\) COVID-19 is associated with skin manifestations, including widespread urticaria, a morbilliform eruption, chicken pox–like vesicles, purpuric eruptions, dusky acrocyanosis, dry gangrene, petechiae, transient livedo reticularis, and red papules on the fingers resembling chilblains.

There is a report of a 20.4% (18 of 88 patients) incidence of cutaneous manifestations for patients with COVID-19. Eight patients developed skin manifestations at onset, 10 after hospitalization, and 3 patients had urticaria.\(^4\) In the most recent Spanish prospective study,\(^5\) urticarial lesions made up 19% of the skin manifestations in patients with COVID-19. The urticarial signs appeared concurrently with the other findings and lasted for a mean of 6.8 days. Our patient developed an eruption on day 6 of her illness, lagging slightly behind the rest of her signs. The Spanish group also reported an association between urticaria and more severe COVID-19 disease (2% mortality in the sample).

The significance of these findings is not known, however, there are also reports of complete recovery in patients with similar dermatologic clinical manifestations.\(^5\) The pathophysiology of urticaria in COVID-19 remains unclear and is likely multifactorial. It is already known that viral infections can present as urticaria secondary to complement activation and resulting in mast cell activation. A cytokine storm might also play a role in this manifestation, especially given the robust response to antihistamines.\(^6\) It is also possible that an excess of angiotensin II might be contributing to vasoconstriction and vascular permeability. Angiotensin-converting enzyme 2 is a cellular receptor for COVID-19, and this mode of entry leads to angiotensin II accumulation.\(^7\)

Conclusions

Clinical manifestations of COVID-19 may include urticaria early or late in the disease process. As the COVID-19 pandemic unfolds, clinicians should become aware of the atypical manifestations of the disease, including urticaria.

Declaration ofCompeting Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. \textit{N Engl J Med} 2020;382:1708-1720.
2. Joob B, Wiwanitkit V. COVID-19 can present with a rash and be mistaken for dengue. \textit{J Am Acad Dermatol} 2020;82, e177.
3. Wedi B, Raap U, Wieczorek D, et al. Urticaria and infections. \textit{Allergy Asthma Clin Immunol} 2009;5:10.
4. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. \textit{J Eur Acad Dermatol Venereol} 2020;34:e212-e213.
5. Galván Casas C, Català A, Carretero Hernández G, et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. \textit{Br J Dermatol} 2020;183:71-77.
6. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the ‘Cytokine Storm’ in COVID-19. \textit{J Infect} 2020;80:607-613.
7. Vaduganathan M, Vardeny O, Michel T, et al. Renin-angiotensin-aldosterone system inhibitors in patients with Covid-19. \textit{N Engl J Med} 2020;382:1653-1659.