

Cutaneous Manifestation in COVID-19 Hospitalized Patients: New Report from Secondary Hospital in Jakarta, Indonesia

Firyal Maulia, Muthia Kamal Putri, Ruri D Pamela*

Department of Dermatology, Suyoto Hospital Centre of Rehabilitation, Ministry of Defense, South Jakarta, Indonesia

ABSTRACT

From December 2019, the world has been in appalling condition since pneumonia of unknown cause was detected in Wuhan, China. The outbreak was declared a Public Health Emergency of International Concern on January 30, 2020, and on February 11, the World Health Association defined the new coronavirus disease as COVID-19. From the March 11, 2020 declaration of coronavirus 2019 disease (COVID-19) as a pandemic.

Keywords: Cutaneous manifestation; Jakarta; COVID-19

INTRODUCTION

From December 2019, the world has been in appalling condition since pneumonia of unknown cause was detected in Wuhan, China [1]. The outbreak was declared a Public Health Emergency of International Concern on January 30, 2020, and on February 11, the World Health Association defined the new coronavirus disease as COVID-19 [2]. From the March 11, 2020 declaration of coronavirus 2019 disease (COVID-19) as a pandemic [3].

As of 31 January 2021, 103.066.730 cases of COVID-19 have been reported world-wide, with 2.226.548 deaths [4]. The virus enters the body through mucosal surfaces via droplets, aerosols or hand contact. Disease presentation can range from no symptoms to acute respiratory distress syndrome (ARDS), multiple organ failure and death [5]. As a new emerging virus infection, the skin involvement in patients with COVID-19 was not noticed at the early stages of this pandemic, but it has received much more attention recently [6]. The most important skin manifestations in people with COVID-19 are red spots on the hands, blisters on the trunk, and itchy hives [7]. Although actual worldwide prevalence is still far from being clearly defined, it has been estimated to approach 1%-2% of the world's population [3]. According to Indonesian National Task Force against COVID-19, there are 1.078.314 confirmed positive cases and 29.998 deaths reported per 31 January 2021 [8]. Ongoing studies are being conducted to comprehend this virus behavior. Skin manifestations were also found in COVID-19 positive patients in Indonesia. Firmansyah, et al. reported a 24-year-old woman on day seven symptoms of skin lesions appear in the upper and lower extremities, symmetrical distribution, erythema color, lenticular

size, multiple numbers of discrete maculopapular rashes, and itching [9]. In Tangerang, Indonesia, Widysanto, et al. reported a 69-years-old male patient on day 25 of hospitalization, the patient suddenly developed non-palpable and painless ecchymosis involving the back and flank [10].

In Europe, most commonly reported symptoms are chilblain-like (40.1%), maculopapular (23.1%) and vesicular lesions (10.1%), urticaria (21.8%), livedoid/necrotic lesions (2.3%), and other non-classified skin lesions (19.8%) [11]. The polymorphic nature of COVID-19-associated cutaneous manifestations led Genovese and colleagues summarized COVID-19-associated cutaneous manifestations into six main clinical patterns. (i) urticarial rash, (ii) confluent erythematous/maculopapular/morbilliform rash, (iii) papulovesicular exanthem, (iv) chilblain-like acral pattern, (v) livedo reticularis/racemosa-like pattern, (vi) purpuric "vasculitic" pattern [12-14].

This article made as a report from our observation to find out the potential relationship between COVID-19 and skin manifestations that hopefully will bring us closer to better understanding in pathogenesis of the disease and adoption of better infection control policies. This case report is also part of Indonesia contribution in attempt to fully comprehend skin manifestations of COVID-19 cases that occur worldwide.

CASE STUDY

The observation for this report took place from July 2020 until November 2020. All the patients gave their informed consents to participate in this case report and explicit consents to use their

Correspondence to: Ruri D Pamela, Department of Dermatology, Suyoto Hospital Centre of Rehabilitation, Ministry of Defense, South Jakarta, Indonesia, E-mail: ruripamela@gmail.com

Received: February 26, 2021; **Accepted:** March 12, 2021; **Published:** March 19, 2021

Citation: Maulia F, Putri MK, Pamela RD (2021) Cutaneous Manifestation in COVID-19 Hospitalized Patients: New Report from Secondary Hospital in Jakarta, Indonesia. J Clin Exp Dermatol Res. 12:555.

Copyright: © 2021 Maulia F, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

pictures in publications.

We collected data on 45 cases for 5 months (from July until November 2020). From all subjects, 29 were male and 16 were female. All cases were included for being compatible with COVID-19 diagnosis of skin manifestations and confirmed by positive testing for SARS-CoV-2 by reverse transcription polymerase chain reaction. No skin biopsies were performed.

RESULTS

Of the 45 patients, the most common skin lesions observed were urticaria in 19 patients (42.2%), followed by erythematous/maculopapular rash in 16 patients (35.5%), pustular/papulovesicular exanthem in 7 patients (15.5%), purpuric/"vasculitis" pattern in 3 patients (6.6%). No chillblain-like acral pattern and livedo reticularis-like pattern were detected during the observation.

DISCUSSION

Recalcati published first case reports of skin manifestations in COVID-19 patients on March 2020 based on his patients in the Lecco Hospital, Lombardy. From 88 patients, 18 patients (20.4%) developed cutaneous manifestations. Eight patients developed cutaneous involvement at the onset, 10 patients after the hospitalization. Cutaneous manifestations were erythematous rash (14 patients), widespread urticaria (3 patients) and chickenpox-like vesicles (1 patient). He and his colleagues speculated that skin manifestations are similar to cutaneous involvement occurring during common viral infections [15]. Reports on COVID-19 skin manifestation are increasing afterward. Dermatologists around the world are conducting researches to get full comprehension on how this virus affects the skin [16,17].

The result of this study is similar with previous study performed by Rerknimitr, et al. at King Chulalongkorn Memorial Hospital, Bangkok, Thailand. Urticaria lesions were most common skin manifestations detected in that report, five patients (21.7%), followed by maculopapules in four patients (17.4%) from 23 patients with skin complains related to COVID-19 [18].

The pathogenesis of skin manifestations in COVID-19 patients are not yet fully understood [19]. Urticaria and acute urticarial rashes go along with up to 50% of all cases with infections of the upper respiratory tract [75] and are most often mediated by complement activation and serum sickness induced by viral antigens or secondary mechanisms, due to the interaction of the immune system with viral antigens. This could be also the case in part of the SARS-CoV-2-positive patients with urticarial eruptions (Figure 1) [20]. Aerosolized uptake of SARS-CoV-2 leads to infection of the functional receptor angiotensin-converting enzyme (ACE) type II (ACE2)-expressing target cells such as alveolar type 2 or other unknown target cells. ACE2 is present in the skin in the basal layer of the epidermis, in endothelial cells of dermal blood vessels and in eccrine adnexal tissue. A direct pathogenic effect of the virus in the epidermis via ACE2, leading to acantholysis and dyskeratosis, has been proposed [21,22].

It should be noted that immune-pathogenesis is associated with an out-of-control immune response, which may result in pulmonary tissue damage, functional impairment, and reduced lung capacity. Chemotactic factors are essential to the immune responses against the virus infections, given their regulatory effect on dilations and positions of leukocytes in the host lungs. Therefore, spectral changes

in chemotactic factors may lead to severely maladjusted immune responses. Immune insufficiency or misdirection may increase viral replication and cause tissue damages. In a subset of patients, by the end of the first week, the disease can progress to pneumonia, respiratory failure, and death. This progression is related to an extreme rise in inflammatory cytokines including interleukin (IL)2, IL7, IL10, GCSF, IP10, MCP1, MIPI A, and TNF α . The increase in the pro-inflammatory cytokines, in particular, IL6 is associated with severe pneumonia and it can have deleterious effects on the adaptive immune system. In these subsets of patients, overactive immune responses may induce immune-pathological conditions, named as "cytokine storm" and in some individuals leads to macrophage activation syndrome (MAS)-like, often causing a fatal outcome. Cytokines could reach the skin and stimulate dermal dendritic cells, macrophages, mast cells and lymphocytes, in addition to polymorphonuclear cells and promote eruptions such as erythema, urticarial lesions, vesicles and others [21-23].



Figure 1: Cutaneous manifestation in COVID-19 patients presented clinically in the form of urticaria lesion, erythematous/maculopapular rash, pustular/papulovesicular exanthema, and purpuric lesion.

According to study conducted by Tezza et al. the association between urticaria and general viral infections is common either in children and adults but the real role of viruses in the pathogenesis of skin lesions still needs to be clarified. The skin manifestations during SARS-CoV-2 infection might become evident during the "symptoms-storm" phase. These skin manifestations are unrelated to COVID-19 drugs treatment, they do not require any specific drug treatment. They will disappear very late even after swab test became negative [16,24].

CONCLUSION

COVID-19 can have various cutaneous manifestations. Clinicians should be aware of these manifestations that may help in diagnosing, treating COVID-19, and preventing further transmission. Further research is required to comprehend more about COVID-19 pathogenesis and how it can develop cutaneous manifestation. This case report hopefully contributes in completing series of case reports related COVID-19 cutaneous manifestations which are found around the world.

REFERENCES

1. Andina D, Belloni-Fortina A, Bodemer C, Bonifazi E, Chiriac A, Colmenero I, et al. Skin manifestations of COVID-19 in children: Part 3. *Clin Exp Dermatol*. 2020;1-16.
2. Burlando M, Russo R, Cozzani E, Parodi A. Six months into the pandemic: A review of skin manifestations in SARS-CoV-2 infection. *Dermatol Ther*. 2020;e14641.
3. Atzori L, Recalcati S, Ferrel C, Hoenig L, Rongioletti F. COVID-19-related skin manifestations: Update on therapy. *Clin Dermatol*. 2020; 1-16.

4. World Health Organization (WHO). Coronavirus disease (COVID-19) weekly epidemiological update and weekly operational update.
5. Gisondi P, Plaseric S, Bordin C, Alaibac M, Girolomoni G, Naldi L. Cutaneous manifestations of SARS-Cov-2 infection: A clinical update. *J Eur Acad Dermatol Venereol.* 2020;34:2499-2504.
6. Darlenski R, Tsankov N. COVID-19 pandemic and the skin: What should dermatologists know? *Clin Dermatol.* 2020;38:785-787.
7. Sameni F, Hajikhani B, Yaslianifard S, Goudarzi M, Owlia P, Nasiri MJ, et al. COVID-19 and skin manifestations: An overview of case reports/Case series and meta-analysis of prevalence studies. *Front Med.* 2020;7.
8. Indonesian National Task Force Against COVID-19 (SATGAS Penanganan COVID-19 Indonesia). Data Distribution of COVID-19 of COVID in Indonesia.
9. Firmansyah Y, Elizabeth J, Tan ST. Skin manifestation in COVID-19 infection: A thousand appearances (immune response perspective). *Int J Res Dermatol.* 2020;6:776.
10. Widysanto A, Wahyuni TD, Simanjuntak LH, Sunarso S, Siahaan SS, Haryanto H, et al. Ecchymosis in critical coronavirus disease 2019 (COVID-19) patient in Tangerang, Indonesia: A case report. *J Thromb Thrombolysis.* 2020;1-5.
11. Kubanov A, Deryabin D. Skin manifestations in COVID-19 provide a clue for disease's pathophysiology understanding. *J Eur Acad Dermatol Venereol.* 2020;35.
12. Casas GC, Català A, Carretero Hernández G, Rodríguez-Jiménez P, Fernández-Nieto D, Rodríguez-Villa Lario A, et al. Classification of the cutaneous manifestations of COVID-19: A rapid prospective nationwide consensus study in Spain with 375 cases. *Br J Dermatol.* 2020;183:71-77.
13. Estébanez A, Pérez-Santiago L, Silva E, Guillen-Climent S, García-Vázquez A, Ramón M. Cutaneous manifestations in COVID-19: A new contribution. *J Eur Acad Dermatol Venereol.* 2020;34.
14. Genovese G, Moltrasio C, Berti E, Marzano A. Skin manifestations associated with COVID-19: Current knowledge and future perspectives. *Dermatology.* 2020;1-12.
15. Recalcati S. Cutaneous manifestations in COVID-19: A first perspective. *J Eur Acad Dermatol Venereol.* 2020;34.
16. Tang K, Wang Y, Zhang H, Zheng Q, Fang R, Sun Q. Cutaneous manifestations of the coronavirus disease 2019 (COVID-19): A brief review. *Dermatol Ther.* 2020;33.
17. Wollina U. Challenges of COVID-19 pandemic for dermatology. *Dermatol Ther.* 2020;33.
18. Rerknimitr P, Theerawattanawit C, Lertpichitkul P, Jantarabjenjakul W, Putharoen O, Puthanakit T, et al. Skin manifestations in COVID-19: The tropics experience. *J Dermatol.* 2020; 47.
19. Tatu A, Nadasdy T, Bujoreanu F. Familial clustering of COVID-19 skin manifestations. *Dermatol Ther.* 2020;33.
20. Novak N, Peng W, Naegeli MC, Galvan C, Kolm-Djamei I, Bruggen C, et al. SARS-CoV-2, COVID-19, skin and immunology – What do we know so far? *J Eur Acad Dermatol Venereol.* 2020;1-6.
21. Criado P, Abdalla B, de Assis I, van Blaricum de Graaff Mello C, Caputo G, Vieira I. Are the cutaneous manifestations during or due to SARS-CoV-2 infection/COVID-19 frequent or not? Revision of possible pathophysiologic mechanisms. *Inflamm Res.* 2020;69:745-756.
22. Kaya G, Kaya A, Saurat J. Clinical and histopathological features and potential pathological mechanisms of skin lesions in COVID-19: Review of the literature. *Dermatopathology.* 2020;7:3-16.
23. Kolivras A, Dehavay F, Delplace D, Feoli F, Meiers I, Milone L, et al. Coronavirus (COVID-19) infection-induced chilblains: A case report with histopathologic findings. *JAAD Case Rep.* 2020;6:489-492.
24. Tezza F, Silvestro GD, Gerosa G. Skin manifestations and SARS-Cov-2 infection: First the Egg or the Chicken? *Med Read J Dermatol.* 2020;1:1002.