

Review Article

Cutaneous Manifestations in Patients with COVID-19: A Review

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Abstract

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global pandemic after its emergence in Wuhan, China. COVID-19 causes a wide range of clinical manifestations involving multiple organ systems. After the first report of cutaneous manifestation by Dr. Recalcati, the role of dermatologists in the management of COVID-19 has increased, skin involvement in COVID-19 have been higher than expected. In this article, we have reviewed

the skin presentations in COVID-19 by analyzing the published literature in PubMed and Google scholar, using the search terms “COVID-19” and “dermatological presentation”. Petechial rash, livedo reticularis, vesicular eruptions, morbilliform rash, and erythema multiforme-like rash have been observed in many patients. Newly reported eruptions like vascular lesions and peculiar (perniosis-like) skin lesions could be of concern. There is also a need to differentiate these lesions from drug reactions. Given the high mortality

rate of the infection, timely and accurate identification of relevant cutaneous manifestations could help physicians in the early diagnosis and management, triage of patients, and risk stratification. Associated symptoms, latency time, treatment, and prognosis are also summarized in this manuscript.

Keywords: Maculopapular Rash; Vesicular Rash; Urticarial Lesions; COVID-19; SARS-CoV-2

1. Introduction

The coronavirus disease 2019 (COVID-19) global pandemic and its rapid spread throughout the globe are of major concern. With the first documented case in Wuhan, China [1], the peculiar nature of the virus, high infectivity, and the myriad of different types of presentations, it has crossed borders manifesting itself as a global pandemic. The World Health Organization has declared it a global emergency and it has been challenging for health care providers and systems throughout the globe [2]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an enveloped positive sensed single-stranded virus belonging to the family of coronaviruses. It enters via angiotensin-converting enzyme 2 and presents with a range of symptoms from mild flu-like to fulminant pneumonia and respiratory distress. With many peculiar manifestations ranging from neurological, cardiovascular, hematologic, and psychological, new ones other than these remain much of a concern. In this review, we have enumerated the variable cutaneous spectrum of COVID-19 by highlighting the various case reports, reviews, and data obtained to date.

2. Discussion

Guan et al. initially reported that 2 out of 1,099 patients with COVID-19 presented with rashes in China, [3]

whereas Recalcati [4] found that 18 patients (20.4%) developed erythematous rash, widespread urticaria, or chickenpox-like vesicles, which were similar to cutaneous involvement that occurred during common viral infections in Italy. Professionals have paid more attention to the cutaneous manifestations in patients with COVID-19. Based on the evidence from retrospective nationwide study from Spain, there were a variety of cutaneous manifestations in patients with COVID-19, including acral areas of erythema with vesicles, urticarial lesions, maculopapular eruptions, and livedo [5].

2.1 Vascular complications

Since seven patients with COVID-19 and acro-ischemia presentations were first reported in March 2020 in China, COVID-19 associated vascular complications have attracted attention [6]. This might be due to higher levels of D-dimer, fibrin degradation products and fibrinogen in patients with COVID-19 than in the healthy controls [7], and also in patients with severe COVID-19 [8]. Galván Casas et al. [5] found that 6% of patients with COVID-19 presented with livedo or necrosis. Alramthan et al. [9] reported a case of COVID-19 that presented with chilblain-like edematous and erythematous eruptions. Similarly, Garcia-Lara et al. have highlighted acro-ischemic lesions, also called chilblain-like lesions, in children and adolescents without typical symptoms of COVID-19 [10]. These lesions fully recovered within 2 weeks without any treatment. Landa et al. [11] also reported six patients with COVID-19 who manifested with chilblain-like lesions with the hypothesis that these lesions could be a late manifestation of COVID-19. In Italy, Recalcati et al. [12] reported that 14 cases presented with acral eruption of erythematous-violaceous papules and macules without the development of obvious systemic

symptoms. In addition, a patient with COVID-19 initially presented with a skin rash with petechiae, which was misdiagnosed as dengue and eventually confirmed to be COVID-19 [13]. Diaz-Guimaraens et al. [14] reported a similar case: a 48-year-old man presented with erythematous macules, papules, and petechiae affecting the popliteal fossae, abdomen, and buttocks with biopsy revealing a perivascular lymphocytic infiltrate with abundant red cell extravasation. A generalized pruritic morbilliform rash developed in a 32-year-old female professional 6 days after the onset of COVID-19. Thus, cutaneous vascular complications could be an early presentation, late presentation, or clinical predictor for severe COVID-19.

2.2 Vesicular eruptions

As reported, patients with COVID-19 may present with vesicle, bullous eruption, or chickenpox-like rash. Galván Casas et al. [5] reported that 9% of patients with COVID-19 presented with a chickenpox-like rash on the trunk. Recalcati also found that 1 out of 88 patients with COVID-19 developed chickenpox-like vesicles. Jimenez-Cauhe et al. [15] observed that in all patients with cutaneous manifestations, skin lesions began as erythematous papules that progressively turned into a pseudo-vesicle. Lagziel et al. [16] reported that a confirmed COVID-19 case presented with bullous. A dermatopathological biopsy revealed a bullous drug reaction with an erythema multiform-like reaction pattern.

2.3 Maculopapular eruption

Maculopapular eruption in patients with COVID-19 has been reported recently and more common in patients with a severe condition. From the study in Spain [5], maculopapular rash was found in 47% of Spanish COVID-19 patients with complaints of pruritus. The

first digitate papulosquamous eruption case with COVID-19, confirmed by skin biopsy with the presence of mild diffuse spongiosis in the epidermis and rounded spongiotic vesicles containing lymphocytes and Langerhans cells, was reported by Sanchez et al. [17]. Ehsani et al. [18] reported that a 27-year-old man presented with pityriasis rosea 3 days after the onset of COVID-19 in Iran. Ahouach et al. [19] reported that a 57-year-old woman with COVID-19 presented with diffuse fixed erythematous blanching maculopapular lesions with negative skin PCR for SARS-CoV-2. A 67-year-old Italian woman [20] and a 58-year-old Hispanic man [21] also presented with erythematous maculopapular lesions.

2.4 Urticarial rash

Urticarial rash was reported to present before, associated with, or after the onset of other COVID-19 symptoms. Henry et al. [22] reported that a 27-year-old woman presented with pruritic disseminated erythematous plaque eruptions, which were diagnosed as urticaria. After 48h, this patient developed chills, fever, and eventually was diagnosed with COVID-19. In Belgium, two patients who presented with urticarial rash and pyrexia were diagnosed with COVID-19, as reported by Damme et al. [23]. The frequency of urticarial rash was 19% in Spain as reported by Galván Casas et al. [5] but only 2% from a study in Italy [4]. The youngest patient with COVID-19 associated urticarial rash was a 2-month-old child in Spain, who fully recovered from the rash 9 days after the onset [24]. Thus, an urticarial rash is suggestive of early SARS-CoV-2 infection or is associated with COVID-19.

2.5 Other cutaneous manifestations

Erythema multiforme-like rash has been reported in 2 children among 27 patients with mild COVID-19

without infection of herpes simplex [5]. Similarly, two children from Italy also developed targetoid lesions after the onset of COVID-19 [4]. Goren et al. [25] conducted a preliminary observational study on the prevalence of androgenic alopecia among hospitalized COVID-19 patients in Spain and found that 71% of them were visually diagnosed with clinically significant androgenic alopecia. The controlled study determined the correlation between androgens and COVID-19 disease severity, and a potential anti-androgenic treatment will be administered in the near future.

3. Conclusions

There were a variety of cutaneous manifestations in patients with COVID-19, including vascular complications, vesicular eruptions, maculopapular eruption, urticarial rash, erythema multiforme-like rash, androgenic alopecia. These manifestations could occur before, during, or after the onset of other COVID-19 associated non-cutaneous symptoms. During the COVID-19 pandemic, we need to keep COVID-19 in the differential diagnosis in patients with presentations of cutaneous symptoms because patients may be misdiagnosed with other diseases. It is still debatable whether cutaneous manifestations are correlated with disease severity in patients with COVID-19. All COVID-19 patients with cutaneous manifestations were mild in intensity and resolved within a few days. Therefore, there is no correlation between cutaneous manifestations and disease severity.

In addition, it is also important to determine whether these cutaneous manifestations are caused directly by SARS-CoV-2 infection, or they are secondary to some drugs during the treatment of COVID-19. Additionally, it is important to determine whether these cutaneous manifestations result from exacerbations of previous

dermatological diseases, they result from emotional stress, or from permanent use of personal protective equipment. The physicians and healthcare workers should be aware of such cutaneous manifestations because patients may be misdiagnosed with other diseases.

Conflict of Interest

The authors declare that there are no conflicts of interest.

Authors Contributions

All authors contributed equally in the preparation of this manuscript.

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