Cutaneous manifestations associated with coronavirus disease-19: a review

Sultan Alshammari1*, Sultan Alanazi1, Khalid Alanazi1, Ammar Khalifa2, Yara Alfehaid3, Khalid Alabdulwahab4

ABSTRACT

Coronavirus disease-19 (COVID-19) is a universal pandemic caused by the severe acute respiratory syndrome coronavirus-2; its first appearance was recorded in December 2019 in Wuhan (China). Although pulmonary validity is the principal center of examinations through the beginning of COVID-19 infection, cutaneous signs have been described in connection with the COVID-19 pandemic. Notwithstanding an expansion in correlation, many vaguely persist about the description, frequency, and pathogenesis of those dermatological indications. Our review discusses the cutaneous signs correlated with COVID-19, including types of lesions and classifications of rashes. A web-based search utilizing the advanced characteristics of different databases like PubMed, Google Scholar, Embase, Scopus, and Cochrane electronic databases was carried out.

Keywords: Coronavirus disease-19, cutaneous, manifestations, classification, rashes.

Introduction

In December 2019, scientists in Wuhan, China, separated a new RNA virus called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) within pneumonia cases. The infection induced by this virus is named coronavirus disease-19 (COVID-19) [1].

The high infection and mortality rates and asymptomatic transmission between the aged and the immune-compromised connected with this condition influenced the World Health Organization to report COVID-19 as a pandemic disease in March 2020 [2]. In August 2020, more than 20 million cases of COVID-19 were approved universally, with an excess of 750,000 deaths recorded in more than 200 nations and regions [3].

After an incubation time of 1-14 days, fever, cough, sputum production, fatigue, sore throat, breathing shortness, and headache begin to appear [3]. Additionally, these general symptoms, and uncommon ones such as various cutaneous signs, have been reported globally [4].

Case series worldwide have identified a range of potential dermatological manifestations of COVID-19 [5-8]. The frequency (ranging from 0.2% to 20.4% of cases) and timing of COVID-19 cutaneous signs are difficult to ascertain [4,9,10]. Also unclear is the relationship of certain skin signs with the severity of the disease [11]. Moreover, it cannot be excluded that in some patients, the observed skin findings may represent cutaneous reactions to the numerous treatments used for COVID-19 [11,12].

Cutaneous signs of COVID-19 have been grouped into the accompanying six primary examples: maculopapular rash, vesicular lesions, urticarial, chilblain-like acral design, and livedo reticularis and livedo racemosa-like pattern [5,13,14]. This review aimed to discuss the cutaneous signs correlated with COVID-19, including types of lesions and classifications of rashes.

Methods of literature search

Web-based literature researches applying the advanced features of several databases like Scopus, PubMed, Google Scholar, Cochrane electronic databases, and Embase were carried out. The keywords like cutaneous manifestations associated with COVID-19, cutaneous symptoms related to COVID-19, classification of cutaneous manifestation related to COVID-19, etc., were used to explore the databases. The search included the latest articles issued and published in the English language.

Pathophysiology

The mechanisms of COVID-19 cutaneous changes are not yet well understood, but some well-known assumptions

Correspondence to: Sultan Alshammari
*AlMaarefa University, Riyadh, Saudi Arabia.
Email: su.ltan86@hotmail.com
Full list of author information is available at the end of the article.
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are accepted. It can be supposed that viral particles existing in the cutaneous veins in cases with COVID-19 contamination could cause lymphocytic vasculitis like those distinguished in thrombophilic arteritis impacted by blood immune complexes animating cytokines. Keratinocytes might be an auxiliary objective after the stimulation of Langerhans cells, enhancing a range of various clinical indications [15]. It is assumed that the virus does not target the keratinocyte. Furthermore, the virus’ first immune response stimulates Langerhans cells, causing spongiosis and vasodilation [15]. Additional hypotheses recommend livedo reticularis-resembling signs can occur due to the micro-thromboses cumulation originating in different organs, thus decreasing the flow of blood to the cutaneous microvasculature system [16]. Likewise, low-grade spread of intravascular clotting and hypoxia-associated cumulation of deoxygenated blood in venous plexes may additionally describe such signs [16].

Also, pauci-provocative thrombogenic vasculopathy with precipitation of C5b-9 and C4d and co-confinement of these with COVID-19 spike glycoproteins was accounted for by Magro et al. [17]. It is uncertain whether cutaneous manifestations are auxiliary results of respiratory-related sickness or essential contamination of the actual skin. A mix of such components is liable for cutaneous signs found in sure COVID-19 people.

Classification of rashes associated with COVID-19

After reviewing the present research on case reports by clinicians across the world on cutaneous signs of COVID-19, various types of rashes in patients of COVID-19 have been reported. Few classifications of rashes have been explained [18,19].

Urticarial rash

Urticaria and angioedema can be set off by bacterial and viral specialists, like cytomegalovirus, herpesvirus, Epstein-Barr infection, and mycoplasma. In any case, setting up a reason impact relationship might be troublesome in single cases [20,21]. Urticarial emissions associated with COVID-19 have been first declared by Recalcati [4] among his population of hospitalized cases, representing 16.7% of complete skin indications. Urticaria-like emissions have been subsequently characterized in other studies. Galván Casas et al. [5] stated that urticarial rash happened in 19% of their populations, would, in general, appear simultaneously with fundamental manifestations, endured around multi-week, and was related with medium-to-high seriousness of COVID-19 (Figure 1). Besides, the itch was practically often found [5]. Freeman et al. [14] recognized a similar incidence of urticaria (16%) among their series of 716 patients, in which urticarial injuries included the limbs and trunk, almost saving the acral positions.

Treatment of urticaria in patients with COVID-19 can be trying as the primary and delayed nature of as far as possible remedial choices, and patients may start prescriptions for COVID-19 that can conceivably trigger or deteriorate urticaria19. However, urticarial rashes in many patients with COVID-19 vanished or clinically improved within 7 days. Patients were
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Dealt fundamentally with oral antihistamines [22-26]. Oral steroids were additionally alone [27] or related to antihistamines [23,25,26].

**Maculopapular rash**

A maculopapular rash is accounted for alongside COVID-19 symptoms and is considered a marker of serious infection. The trunk is the most well-known site for maculopapular rash. Face, palms, and soles are typically spared [28]. It is related to itching in 56% of the cases, and the injuries generally recovered in 10 days [18]; for 47% of all cutaneous indications in the study of Galván Casas et al. [5], for 44% of the skin appearances remembered by the investigation by Freeman et al. [14]. Histopathological ends for those sores are dependent on the hour of beginning [29]. Early-start rashes are found with average epidermal spongiosis and perivascular lymphocytic infiltrate with eosinophils in the dermal area [29].

Conversely, the histology of late-beginning sores showed perivascular lymphocytic penetration and histiocytes between collagen strands. These late-beginning injuries are deficient with regard to mucin stores [29]. Extra assessment by Reymundo et al. [30] announced gentle shallow perivascular lymphocytic invasion in the skin biopsies.

Effective corticosteroids can be sufficient as a rule; foundational corticosteroids having the right to be directed simply in more extreme and far and broad presentations [31].

**Chilblain-like lesions (COVID toes)**

Chilblain lesions, also referred to as pernio, are characterized as a localized flaming skin condition, believed to be influenced by susceptibility to low temperatures or wet, humid conditions causing discoloration limbs and swelling (Figure 3) [32]. The raised occurrence of pernio/acral-like or chilblain-like lesions joined with the temporal relationship with viral symptoms causing “COVID toes”. The word originates from the cutaneous classification in which the skin, including their toes, works as erythematous or violaceous injuries. However, some cases are idiopathic; prior research supports chilblain’s connection with autoimmune diseases such as lupus [33].

In detail, two different patterns were detected from histopathology [34]. In the original one (chilblain-like pattern), variable superficial to profound lymphocytic infiltrate neighboring vessels were observed. The infiltrate was peri-eccrine in some patients, and changes of eccrine glands were largely detectable. The epidermal basal lamina showed vacuolar alteration in most cases. Lichenoid dermatitis interface was infrequently seen. The thrombotic vasculopathy is the second pattern was distinguished by no or small infiltrates of inflammatory cells and multiple intraluminal fibrin thrombi compared with ischemic necrosis of dermis.

Furthermore, dermoscopic examinations were carried out. The standard erythematous-edematous lesions of toes often revealed a widespread coppery-red background simultaneously with dotted vessels and hemorrhagic dots. At the same time, blistering chronic lymphocytic leukemia dermoscopy revealed a similarly coppery-red background, commonly with hemorrhagic dots and deposits. These conclusions are not new because they overlap with those we usually discover in pigmented purpuric dermatoses, particularly the coppery-red background combined with hemorrhagic dots [35].

With the lack of effective therapeutic choices for chilblain-like acral lesions correlated with COVID-19 and presenting their aim to heal immediately, a “wait-and-see” approach may be recommended [28].

**Livedo reticularis and racemosa**

Livedo reticularis or racemosa is characterized by a dotty, lace- or net-like vascular model of erythematous to violaceous splotch correlated with cutaneous capillaries ischemia (Figure 4) [5,13]. By comparing with other cutaneous symptoms in COVID-19, livedo reticularis seems limited frequently (2.3%) but correlated with the extra critical condition and probably higher death [36]. Livedo eruptions are reported in many cases, probably as a result of inflammation induced by SARS-CoV-2 coupling to vascular endothelium [36-39]. The cases may be a hazard for large systemic thromboembolic situations and multi-organ involvement [36]. It is shown that in the thrombotic retiform purpura of cases with severe COVID-19, the vascular thrombosis is correlated with a minimum interferon response allowing enhanced viral replication with the liberation of viral proteins.

**Figure 3.** Cases of chilblain-like rash observed through the COVID-19 infection [32].
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that localize to the endothelium, influencing general complement stimulation [17], which is prevalent in COVID-19 cases and included in the pathophysiology of its clinical complexities [40].

**Vesicular lesions**

Vesicular is a representative name related to distinguished injuries that are obvious liquid-filled cysts below the epidermal layer and tend to be fewer than 1 cm in diameter [41]. The vesicular lesions predominance between COVID-19 cases with cutaneous signs is not very obvious when correlated to the lesions discussed earlier (Figure 5). Several researches have recorded rates varying from 3.77% to 15% [5,13,40,42]. The trunk was the most common are for these rashes, although, a moderate amount of these lesions were also identified on the extremities [5,13,42,43]. Fernandez-Nieto et al. [43] further characterized vesicular rash. Among the 22 vesicular lesions cases, 75% of them had a scattered pattern of polymorphic lesions, and 25% had a localized pattern of trunk monomorphic lesions [14]. Other cases have additionally recognized monomorphic trunk vesicles [5].

**Figure 4.** Cases of livedoid rash were observed through the COVID-19 [5,13].

**Figure 5.** Cases of vesicular lesions observed through the COVID-19 [5,13,41].

**Additional COVID-19-associated cutaneous manifestations**

Other uncommon COVID-19-related cutaneous manifestations that cannot be categorized in the classification suggested by our group [13] include, among others, purpuric “vasculitic” pattern [14], the erythema multiforme-like eruption [44], pityriasis rosea-like rash [45], a multi-system inflammatory syndrome in infants [46], anagen effluvium [23], and a pseudoherpetic variant of Grover disease [47]. Nevertheless, the spectrum of possible COVID-19-associated skin manifestations seems to be incomplete, and it is believed that new items correlated with this disease will be explained in the future.

**Conclusion**

We were concerned with the cutaneous manifestations that correlated with COVID-19; those may assist physicians in approaching cases with the disease and identify patients with few symptoms. The use of these guides for diagnosis should be established in clinical use. We recommend that additional studies could be enhanced
by having more tests to validate COVID-19 and eliminate other diseases and by explaining the clinicopathological association and some of the models that have been classified in our study.

**List of Abbreviations**

COVID-19  Corona virus disease-19  
CLL  Chronic lymphocytic leukemia

**Conflict of interest**
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