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An update of dermatologic problems in adults suffering from Covid-19

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RESEARCH

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ABSTRACT

The novel coronavirus (SARS-CoV-2), the cause of coronavirus 2019 disease (COVID-19) pandemic, is associated with some cutaneous manifestations. This novel disease is associated mostly with significant morbidity and mortality. While the cutaneous presentations of COVID-19 are infrequent, it is of great importance for all clinicians to be aware of these manifestations, as it may contribute to sooner and better diagnosis and management of the disease, even in asymptomatic or paucisymptomatic patients. Although known to primarily cause interstitial pneumonia and respiratory failure, there are several important dermatologic components in adults that clinicians must be aware of. The reported cutaneous manifestations of COVID-19 are various, dispersed, and sometimes confusing. The aim of this review was to collate and categorize the dermatologic findings reported in adult patients with COVID-19 and identify specific lesions that may facilitate diagnosis and prognostication.

Key Words
COVID-19, Adults, Dermatologic, Skin, Lesion

Background

The symptoms of COVID-19 viral disease, generally ranging from mild to moderate flu-like conditions to critical situation connected with acute respiratory distress syndrome and cytokine storm with decreased adaptive immune response, portending high morbidity and mortality. On 31 December 2019, a newly emerged pneumonia caused by a novel coronavirus, named SARS-CoV-2, was announced by China[1]. It spread out so rapidly until WHO announced coronavirus 2019 disease (COVID-19) as a pandemic condition on 11 March 2020. The firstly reported presentations of COVID-19 were like other viral respiratory infections, including high fever and dry cough. However, it might lead to acute respiratory distress syndrome and the mortality rate was quite high[2]. Since then, a wide spectrum of clinical manifestations has been described, ranging from the absence of any symptoms to fever, cough, dyspnea, diarrhea, ageusia, anosmia, and even cutaneous lesions[3,4]. Although the cutaneous manifestations of COVID-19 are infrequent and much of the focus has been on the cardiac and pulmonary complications, it is of great importance for all clinicians to be aware of these presentations, as they may contribute to sooner and better diagnosis and management of the disease, even in asymptomatic or paucisymptomatic patients. This could be a valuable help for epidemiological control of the disease, especially in regions where diagnostic kits are limited[5]. Therefore, cutaneous lesions are likely to have been underestimated for obvious reasons, including the paucity of dermatology consultations in this group of patients[6]. On the other hand, the reported cutaneous manifestations of COVID-19 are various, dispersed, and sometimes confusing. Moreover, the difficulty in determining the actual prevalence of COVID-19-associated skin manifestations has also been linked to the fact that in some countries only patients with respiratory illness or requiring hospitalization are screened[7]. While the majority of patients will experience respiratory complaints with congestion, cough, and shortness of breath, some patients may present without any pulmonary symptoms[8-10]. Recently, there has been increasing recognition of the

dermatologic complications of COVID-19. Thus, we aimed to review and summarize the different skin lesions in adults, which have been reported in adult patients association with COVID-19 to date, in this article. Recent reports from around the world have indicated that this novel coronavirus may be associated with specific cutaneous manifestations. These dermatologic symptoms may be useful in identifying otherwise asymptomatic COVID-19 carriers, which may help slow the transmission of this highly infectious and dangerous virus. As such, an evidence-based review of peer-reviewed scientific literature was conducted to collect clinically relevant information on the cutaneous signs and symptoms of patients with COVID-19.

Main dermatological signs in adult subjects with COVID-19 include: (1) urticaria, (2) maculopapular exanthem, (3) papulovesicular exanthem, (4) chilblain-like acral lesions, (5) livedo reticularis or racemosa, (6) purpuric vasculitis. Mostly every dermatological problem may noticeable at phases of the prodromal, active, or convalescent of COVID-19 disease[11]. SARS-CoV-2 can specifically be responsible for various cutaneous manifestations via direct viral binding or secondarily through various allergic-immunologic mediated processes[12]. Normally SARS-CoV-2 binding to the angiotensin-converting enzyme 2 (ACE2) receptor facilitates viral entry into epithelial cells, primarily in the upper respiratory mucosa. Again, the ACE2 receptor is expressed in the cutaneous or subcutaneous and vascular tissues and thus may contribute to dermatologic problems in SARS-CoV-2 infection[13]. The dermatological signs of COVID-19 can be classified to: (1) the viral exanthems, which is immune response to viral nucleotides or (2) the systemic immunologic consequences of SARS-CoV-2 such as vasculopathy or micro-thrombotic skin lesions[6]. The Viral exanthems include urticaria or angioedema, maculopapular or morbilliform rashes, vesicular eruptions, and erythema multiforme. The Vasculitic-type lesions includes: acral lesions, sacral ulcerations, purpuric lesions, and vasculitis. Moreover, evidence directs that cytokine release, coagulation pathway disturbance, and complement-mediated microvascular injury play a role in the pathology of this latter group. Medication-caused hypersensitivity exanthems and petechiae in case of acquired thrombocytopenia represents other cutaneous problems.

Method

This review outlines the underlying pathophysiology and dermatologic manifestations specifically of adult patients having COVID-19. A literature review of the Scifinder, PubMed and Google Scholar databases was performed from the beginning to 07 February 2021, for articles using the keywords COVID-19, SARS-CoV-2, dermatologic, adult patients and skin for generation of this review article. In this case, authors included case reports and series, retrospective and prospective studies, systematic reviews and meta-analyses, clinical guidelines, narrative reviews, commentaries, and letters.

Discussion

Pathophysiology and clinical presentations

SARS-CoV-2 is an RNA virus that may enter cells through the angiotensin-converting enzyme 2 (ACE2) receptor found on lung alveolar epithelial cells, small intestine enterocytes, and vasculature, as well as neurologic, endocrine, and cardiac systems[14,15]. ACE2 plays several key roles in normal physiology, including breakdown of angiotensin II[15]. SARS-CoV-2 may cause direct lung injury and systemic inflammation, as well as increased coagulation[16-18]. These factors can result in multiorgan dysfunction. Recent literature suggests ACE2 is also located in the skin, which may explain some of the dermatologic manifestations in the setting of COVID-19 infection[13].

Dermatological manifestations in adults

Although the most common symptoms of COVID-19 include congestion, cough, dyspnea, and fever, skin symptoms can occur in up to 21 per cent of patients[19]. One early study found that only 2 of 1099 patients had a “rash”, but investigators may have missed several patients[8]. A more recent study found rash occurred in 20 of 91 patients, with 8 of these patients having rash at onset, while another study found that rash occurred in 6 out of 108 patients[7]. A rash associated with COVID-19 can involve various body regions, most commonly the trunk, but extremity involvement may also occur. Pruritus is often minimal but depends on the type of rash, and lesions typically heal quickly, appearing within 3 days and disappearing within 8 days.

Urticaria and Angioedema

Urticaria exhibits a histamine-caused reaction due to cutaneous mast cell degranulation, which is characterized by circumscribed wheals with surrounding erythema, localized, scattered, or generalized in distribution. Again, angioedema with histamine-caused may accompany urticaria or occur in isolation, representing deeper dermal edema. Urticaria with or without angioedema in the setting of confirmed or highly suspected COVID-19 infection has been observed in several reports and case series[19,7]. Most likely other viral infections, urticarial rash may occur concurrently with COVID-19 systemic signs (fever, cough) and last for several days[20,21]. Broad scale studies suggest that urticaria is highly connected with severe COVID-19 disease, although case reports recount otherwise.

Moreover, acute urticaria may occur in asymptomatic or subclinical SARS-CoV-2 infection.

Maculopapular rash

There are multiple reports of patients presenting with a maculopapular rash, characterized by erythematous macules covered with small papules, or with large plaques (Figure 1)[22,23]. The rash may also be perifollicular and associated with scaling and confluence, which may cause it to be mistaken for pityriasis rosea[24]. This type of rash has been suggested to have a mean duration of approximately 9 days[24]. One study of 88 patients in Italy found that a maculopapular rash was present in 14 patients (16 per cent)[19].

Vesicular eruption

Vesicular eruptions or rashes usually expressed as small and fluid-filled lesions. Vesicular eruptions with distinct monomorphic lesions occur mainly on the trunk or limbs; those were observed in 9 per cent of cases[24]. Most lesions were pruritic, appeared before the onset of other COVID-19 symptoms in 15 per cent of cases, and usually lasted for a mean of about 10 days. A case series on 22 patients with varicella-like papular-vesicular lesions and confirmed SARS-CoV-2 infection[25]. The majority were middle-aged adult men with non-pruritic to mildly pruritic scattered lesions presented on the trunk that showed a median of 3 days after onset of systemic COVID-19 symptoms; the mortality rate was 13.6 percent[25].

Chilblains

Chilblains (also known as pernio or perniosis) is an abnormal response to cold, wherein distal arteries and veins constrict, which can lead to pruritic and tender wounds on the extremities. Patients can present with erythematous or violaceous papules and macules, bullae, or digital swelling[26]. This has been increasingly recognized in association with COVID-19. There have been nearly 100 cases of chilblains associated with COVID-19 already described in the literature[23,27]. Still the pathogenesis of acral chilblain-like lesions remains unclear. But various proposed mechanisms include: cutaneous microthrombi, acquired coagulopathy, or CD8+ T lymphocyte endothelial cell cytotoxicity.

Livedo racemosa

Normally, Livedo reticularis or racemose (LR) is known by a mottled, lace- or net-like vascular pattern of erythematous which is associated with mild to moderate ischemia of the cutaneous capillaries. By comparing with other cutaneous findings in COVID-19, livedo reticularis is less common (2.3 per cent) but associated with more severe disease and possibly has greater mortality[28]. The livedo eruptions are described in multiple case reports prominently due to inflammation caused by SARS-CoV-2 binding to vascular endothelium. Patients may be at risk for massive systemic thromboembolic cases and multi-organ connection[29]. One series of 21 cases found that the rash had a mean duration of 9.4 days[29]. LR was more common in older patients, with a mean age of 63 years[29]. LR was also associated with more severe disease (10 per cent mortality rate)[24].

Vasculitis

Vesicular rashes include small, fluid-filled blisters, often on an erythematous base. Numerous case reports have documented vesicular rashes in patients with COVID-19, with the study by Recalcati et al. finding vesicles in 1.1 per cent of patients[19]. Vesicles are more commonly scattered, rather than diffuse in appearance, with one series finding scattered lesions in 16 of 22 patients and diffuse lesions in the remaining 06 patients[25]. Other case reports have described the appearance of vesicles[23], with one discussing diffuse involvement of the face and limbs in an 8-year-old[30]. A separate case series found that the vesicular rash occurred for a mean duration of 10.4 days, with vesicles appearing mostly on the trunk and extremities.

Sacral Ulcer

"Sacral ulcer" shows a peculiar finding in adult patients with COVID-19. Several risk factors for the development of sacral decubitus ulcer include: immobility and prolonged bed rest, incontinence, malnutrition, diabetes, and vascular disease. Sacral ulcer may represent with purpuric lesions, violaceous induration, livedoid plaques, and eschars. The pathogenesis is assumed to be multifactorial including a combination of systemic coagulopathy, cutaneous ischemia, and pressure-induced deep tissue injury. The cases of sacral ulcers in old patients with critically ill, multi-organ system COVID-19 disease[31].

Distal ischemia and necrosis

For adult patients having COVID-19, one of the most severe complications includes distal ischemia resulting in tissue necrosis. One case study described seven patients with acro-ischemia including finger and toe cyanosis, skin bullae, and dry gangrene[32]. Another report of two patients described the appearance of red and purple papules on the distal fingers due to distal ischemia, which occurred before the appearance of other symptoms[33]. Other case reports describe a 13-year-old with distal toe ischemia presenting with blistering and necrosis[34], as well as one patient with necrotic purpura[23]. Given the coagulopathic impact of SARS-CoV-2, these findings necessitate discussion with vascular surgery specialists and consideration of intravenous thrombolytics.

Conclusion

Adult Patients with COVID-19 most commonly present with respiratory symptoms, but multiorgan involvement can occur, with multiple skin manifestations. In conclusion, we

can say that SARS-CoV-2 has been connected with several different dermatological manifestations, likely of varying pathophysiology, some preceding COVID-19 symptomatology and others occurring during active involvement of disease or later in the progression. Adult subjects having COVID-19 cutaneous presentations may demonstrate a range of illness. These dermatological rashes should trigger consideration of COVID-19, and understanding these manifestations is important to help identify potential COVID-19 patients and properly treat complications. We believe modern handful research and updated reporting will more precisely determine the incidence, underlying pathophysiology, potential prognostication, and best treatment options of dermatological manifestations in COVID-19 disease.

Declaration of competing interest

The authors declare no conflicts of interest relevant to this manuscript.

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Figure

Figure 1: Flow Chart of the sample