

Cutaneous Manifestations in Patients with SARS-CoV-2 Infections

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ABSTRACT While SARS-CoV-2 is known to cause pneumonia and acute respiratory distress syndrome (ARDS), many extrapulmonary manifestations of COVID-19 have also been observed. Cutaneous manifestations including erythematous rash, urticaria, and chickenpox-like vesicles have been described in patients with SARS-CoV-2. Six patients, two men and four women, in the age group of 50 to 60 years old, hospitalized with SARS-CoV-2 infection confirmed with real-time polymerase chain reaction (real-time PCR) presented cutaneous manifestations. The rash was confluent, spotty, centrifugal, and non-itchy on the head and torso. It was not hemorrhagic, and no crust or blisters were observed. The results of laboratory tests were normal, and the rash disappeared on its own. Several cases of cutaneous manifestations have been reported in patients with SARS-CoV-2 infection. Further studies are needed in order to assess the skin lesions and determine their association with COVID-19.

KEY WORDS: COVID-19, SARS-CoV-2, skin lesions, cutaneous manifestations

INTRODUCTION

In December 2019, several cases of pneumonia of unknown etiology were observed in Wuhan City in Hubei Province in central China. The majority of cases were people who worked at or live around the local Huanan Seafood Wholesale Market (1). A novel coronavirus was identified from the throat swab samples of patients (2). The coronavirus was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the Coronavirus Study Group, and the coronavirus disease 2019 (COVID-19) by the WHO (3). Within a few months, COVID-19 spread rapidly, and was declared to be a pandemic by the WHO on March 12 (4). COVID-19 has caused a global health and economic crisis as a result of closed borders, travel bans, closed schools and businesses, quarantines, and other strict measures (5).

While SARS-CoV-2 is known to cause pneumonia and acute respiratory distress syndrome (ARDS), many extrapulmonary manifestations of COVID-19 have been also observed, such as cardiovascular, gastrointestinal, neurologic, and dermatologic symptoms (6). Cutaneous manifestations including erythematous rash, urticaria, and chickenpox-like vesicles have been described in patients with SARS-CoV-2 infection (7). The mechanisms of these disturbances are not yet well known (8). Cutaneous manifestations are crucial in the diagnosis of various infectious diseases, such as toxic shock syndrome, meningococemia, and rickettsial diseases (9). They may be an indicator of infection in asymptomatic cases of COVID-19, leading to timely diagnosis (8).

The purpose of the present article is to report cases and provide a literature review of cutaneous manifestations in patients with COVID-19 pneumonia.

CASE PRESENTATION

Six patients, two men and four women, in the age group of 50 to 60 years old, hospitalized with SARS-CoV-2 infection confirmed with real-time polymerase chain reaction (real-time PCR) presented cutaneous manifestations. The rash was confluent, spotty, centrifugal, and non-itchy, localized on the head, torso, and limbs, with different expiration time. There was no rash on the palms and soles. The rash was not hemorrhagic, and no crust or blisters were observed (Figure 1). The patients had radiological findings of COVID-19 pneumonia with bilateral infiltrations, but they had already completed 8 to 10 days of hospital-

ization and had experienced significant clinical improvement. During hospitalization, they received antiviral therapy with lopinavir/ritonavir and hydroxychloroquine and empiric antibiotic therapy with third generation cephalosporin (ceftriaxone). Other drugs administered included paracetamol, esomeprazole, and subcutaneous low molecular weight heparin. During the occurrence of dermatological symptoms, no systematic symptoms were observed. Laboratory tests revealed a normal white blood cells and platelet count without increased levels of eosinophils, normal liver and kidney function, and normal values of C-reactive protein. Blood cultures were negative. IgM antibodies for measles, varicella-zoster virus and parvovirus B19 was negative, and IgG antibodies were positive. In the subsequent 4-5 days, the patients recovered and the rash disappeared.



Figure 1. The rash was confluent, spotty, centrifugal, and non-itchy, localized on the head, torso, and limbs with different expiration times. No rash on the palms and soles. Non hemorrhagic. Without crust or blisters.



DISCUSSION

Other than common clinical features including fever, dry cough, shortness of breath, myalgia, and fatigue, dermatological manifestations have been also documented in patients with COVID-19 pneumonia. A dermatologist nationwide case collection survey was conducted in Spain in order to describe the cutaneous manifestations of COVID-19 disease and to relate them to other clinical findings (10). The skin manifestations were classified into five categories: acral areas of erythema-edema with some vesicles or pustules (pseudo-chilblain) (19%), other vesicular eruptions (9%), urticarial lesions (19%), other maculopapules (47%), and toledo or necrosis (6%) (10).

In Italy, in a series of 88 cases, Recalcati reported that 20.5% of patients developed skin manifestations (11). Eight of the 18 (44%) had skin eruptions with symptoms at presentation, while the rest of the patients presented with these symptoms after hospitalization (11). Erythematous maculopapular lesions on the face and frostbite-like lesions were reported in French patients with very probable or confirmed COVID-19 infection (12). Four clinical patterns were described in a Spanish study including 20 children and adolescents with acral lesions: acral erythema (30%) (Figure 1), dactylitis (20%), purpuric maculopapules (35%), and mixed pattern (15%) (13). The most common cutaneous presentations documented in a study in Lombardy were erythematous rash (77.8% or 14/18), urticaria (16.7% or 3/18) and vesicle formation (5.6% or 1/18) (11). Some reported cases were intensely pruritic, in the form of a petechial rash or an urticarial eruption (14), with distinctive skin rash (15), with herpetiform lesions, or with immune thrombocytopenic purpura (16).

Skin lesions might constitute a late manifestation of COVID-19 due to immunological reactions, especially in young healthy individuals (17). However, there have been cases in which dermatological manifestations occurred before other characteristic symptoms (18). Most skin lesions were self-resolving (19).

The mechanisms cutaneous disturbances caused by COVID-19 are not yet well known. Potential mechanisms include an immune hypersensitivity response to SARS-CoV-2, cytokine-release syndrome, deposition of microthrombi, and vasculitis (19). The viral particles present in the cutaneous blood vessels in patients with COVID-19 infection may cause a lymphocytic vasculitis similar to those observed in thrombophilic arteritis leading to cytokine activation (20). Immune response to infection leads to Langerhans cells activation, resulting in a state of vasodilation and spongiosis (21). Superficial perivascular

dermatitis, dyskeratotic keratinocytes, diffuse and dense lymphoid infiltrates, and signs of endothelial inflammation have been described in histopathological examinations (22).

Drug exposure and temporal association with hydroxychloroquine, remdesivir, tocilizumab, and other experimental drugs should always be evaluated before any skin lesion is attributed to the viral infection. In a study by Sharma *et al.*, a total of 21 unique dermatologic reactions were reported in 3578 patients treated with hydroxychloroquine (23). Azithromycin is another drug used in combination with hydroxychloroquine in COVID-19 treatment regimens. It has been associated with skin reactions such as generalized red or purple skin rashes, angioedema, blisters, skin peeling, or painful skin (24).

In conclusion, several cases of cutaneous manifestations have been reported in patients with SARS-CoV-2 infection. Further studies are needed in order to assess the skin lesions and determine their association with COVID-19. Skin lesions could be an indicator of infection in asymptomatic patients or of clinical progress in patients with COVID-19 pneumonia.

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