CHAPTER 4

THE SKIN FINDINGS ASSOCIATED WITH COVID-19

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INTRODUCTION

Because of the rod-like protrusions on the surfaces of corona viruses, these viruses are named as crowned virus (corona virus) due to the meaning of “crown”, that is, “corona” in Latin. In December 2019 in Wuhan, China, the corona virus disease, which was defined as an unexplained viral pneumonia factor, was named Corona Virus Disease-2019 (COVID-19).

The virus can be transmitted from animal to human and from human to human. The most common form of transmission among humans is through the respiratory system via droplets. Other routes of transmission are fecal-oral and mother-to-child. The first entry point of the virus is the respiratory system, but it can also infect the urinary, digestive, hematological and neurological systems. The incubation period is five days on average and may vary between 2-14 days.

Typical symptoms of COVID-19 disease are respiratory system symptoms such as fever, cough, fatigue, myalgia, and shortness of breath. However, it is
known that COVID-19 has symptoms such as decrease in smell and taste, headache, vomiting, diarrhea and hemoptysis, and can cause multisystemic involvement that can result in organ failure or even death. COVID-19 disease remains at mild or moderate level in most patients and symptoms resolve within a week. It was reported that no symptoms were observed in some patients.

Some of the dermatological manifestations related to COVID-19 may start before other manifestations of the disease, some may start at the same time with other manifestations or after other manifestations. The most frequently reported areas for the dermatological manifestations of COVID-19 are hands and feet. Besides, lesions in one or more parts of the body have been reported.

Skin lesions in patients with COVID-19 infection have been reported in the literature with a rate of 0.2-20%. While the incidence was 0.2% in a case study of 1099 positive patients in China, it was reported as 20.4% in a case series of 88 patients in Italy.

PATHOGENESIS OF COVID-19 SKIN MANIFESTATIONS

The pathophysiology of skin lesions in COVID-19 is unclear. COVID-19 not only affects the respiratory system but also the erythrocytes. Damage to erythrocytes can cause vascular changes and damage all tissues and organs. This situation may explain the emergence of vascular changes seen in the skin.

In the case where the first COVID-19 skin manifestation was reported outside of China, the patient with petechial skin rash in Thailand was considered as dengue fever, which is common in this country. However, when respiratory symptoms began, COVID-19 was diagnosed by using polymerase chain reaction.

Case reports and studies on the skin manifestations of COVID-19 were reported from all over the world, and the data on the skin manifestations caused by the disease are increasing day by day. As per these data, we can divide the skin manifestations of COVID-19 into three groups. These findings are summarized in Table 1.
MUCOCUTANEOUS MANIFESTATIONS ASSOCIATED WITH COVID-19

Skin manifestation associated with COVID-19 are divided into seven subgroups according to the morphology of the lesions: They can be classified as maculopapular lesions, vesicular lesions, urticaria, pernio-like (acroischemic) lesions, livedoid/necrotic lesions, purpuric lesions and other lesions.

The most common lesions are maculopapular lesions. Pernio-like (acroischemic) lesions are generally observed in mildly severe cases, vesicular lesions in moderate cases, urticarial lesions and maculopapular lesions in severe cases, livedoid and purpuric lesions in the most severe cases.

a) Maculopapular lesions

Maculopapular lesions are nonspecific cutaneous manifestations in COVID-19 patients and are the most frequently reported skin lesions. It is similar to measles, often symmetrical erythematous macules and papules are observed. Maculopapular lesions usually start from the body and then spread to the extremities. As with other viral exanthems, involvement of the oral mucosa and palmoplantar areas has not been reported. The lesions are usually itchy and heal within 10 to 14 days. Symptoms usually occur at the same time as other symptoms of COVID-19, and can be seen in the early or later stages of the disease.

Perifollicular may appear as erythema multiforme-like, pityriasis rosea-like, erythema elevatum-like, purpuric, Dengue-like petechial eruption, itchy purpuric flexural eruption.

Treatment: Oral antihistamines and topical corticosteroids are used for symptomatic control of itching. Systemic corticosteroids may be given in more severe cases.

b) Vesicular lesions

These lesions initially begin as erythematous papules and then turn into vesicles. It can sometimes be seen as bullous or hemorrhagic. Lesions are not polymorphic like varicella but consist of monomorphic vesicles. It can be distributed as localized or generalized. Vesicular lesions generally start at the same time as systemic symptoms or after three days and heal without a trace within an average of 10 days. Lesions are usually located on the body, but can also be seen in the extremities. Those located in the feet are more severe and may show bulla, bruising and superficial necrosis. It is usually itchy and is more common in the middle age group. It was also been reported in asymptomatic children.
Treatment: Treatment is not necessary as it heals by itself. Wet dressing may be recommended to reduce itching.

c) **Urticaria**

Itchy, sharply demarcated, erythematous, edematous, pale papules and plaques are often seen. Urticaria lesions last less than 24 hours, but as the previous lesion heals, new lesions may appear in other areas. Urticaria is a nonspecific cutaneous manifestation in COVID-19 patients. It can be seen in any part of the body, but is usually reported on the body. It can rarely be seen in the palmar area. While urticaria usually occurs at the same time as the symptoms of COVID-19, it can sometimes be seen in the late period and rarely in the early period. It is generally more common in middle age. The clinical picture regresses within an average of one week. Fever with urticaria is more specific for COVID-19 than urticaria alone.

Treatment: It is treated with antihistamines as classic urticaria.

d) **Pernio-like lesions**

Pernio-like lesions (pseudo-pernio) are lesions characterized by pernio-like erythematous, violous patches or plaques that usually occur on the feet and rarely on the hands. These may also occur as erythematous edematous or bullous types. These lesions are called ‘COVID toes’. The lesions are usually painful and/or itchy and heal within two weeks on average without leaving a scar. It can be asymptomatic sometimes. It mostly shows an asymmetrical distribution. It was generally reported in children and adolescents. This usually occurs in the later stages of COVID-19 disease.

Treatment: Avoiding cold exposure, wearing socks, smoking cessation is recommended. Topical corticosteroids, pentoxifylline, hydroxychloroquine and calcium channel blockers can be used in severe cases.

e) **Livedoid/necrotic lesions**

The vascular reaction that presents as a mesh-like (reticular) red, purple discoloration in the body or lower extremities is called livedo. When this manifestation is symmetrical and continuous, it is called livedo reticularis, and when it is asymmetrical and dashed, it is called livedo racemosa. These manifestations may be a complication of the primary lesion of COVID-19 or the hypercoagulopathy associated with COVID-19 and vascular occlusion resulting from vascular damage. Livedoid and necrotic lesions are among the least common findings and are generally reported in older patients with more severe disease. These lesions often start at the same time as other symptoms of COVID-19, but rarely after systemic symptoms or in the early period.
Livedoid skin changes can be unilateral. In severe patients, bulla and necrosis may develop on the lesion and these lesions heal with atrophic, white scar tissue within an average of 10 days.

If livedoid and necrotic lesions are observed in COVID-19 patients, early clinical recognition of these lesions is extremely important, as this is an important clue for systemic thrombotic vasculopathy.

Treatment: Follow-up may be considered in mild cases and anticoagulant therapy in severe cases.

f) Purpuric lesions

Purpuric lesions in COVID-19 can resemble other viral rashes such as dengue fever. Purpuric lesions can be seen localized, acrally or generalized distributed in intertriginous areas. These lesions were not observed on the face, palmoplantar area, fold areas of the skin and mucous membranes. Purpuric lesions may turn into hemorrhagic bulla in severe cases. It was reported that purpuric lesions are generally seen in elderly patients with severe COVID-19 and may indicate a poor prognosis. In dermoscopy of purpuric lesions, a yellow colored central globule with a violous edge has been reported.

Treatment: Topical corticosteroids can be used in mild cases and systemic corticosteroids in severe cases.

g) Other skin lesions

Other skin manifestation mostly reported as case reports: perifollicular papules, erythema induratum bazin, erythema multiforme like lesions, pityriasis rosea like lesions, dyshidrotic eczema like lesions, Grover’s disease like lesions, SDRIFE (Symmetrical Drug Related Intertriginous and Flexural Exanthema) like lesions, miliaria like lesions, Sweet syndrome like lesions, erythema nodosum like lesions, perioral erythema, eyelid dermatitis, eosinophilic panniculitis, and androgenetic alopecia.

During the course of COVID-19 disease, the severity of pre-existing skin lesions such as acne, rosacea, seborrheic dermatitis, atopic dermatitis and neurodermatitis have been observed to increase.

Oral mucosal manifestation related to COVID-19 are co-infections such as nonspecific oral ulcers, desquamative gingivitis, petechiae, vesiculobullous lesions and candidiasis. The most commonly reported oral symptom in COVID-19 patients is taste disturbances.

In the early days of the COVID-19 pandemic, pediatric infections were rare, but over time, the frequency of COVID-19 in children has increased due to the transmission of the virus from the community and family. Cutaneous
symptoms such as erythematous rash, widespread urticaria, multiple erythematous-edematous macules and plaques resembling chilblain-like lesions on the dorsal faces of the fingers and varicella-like vesicles have been reported in COVID-19 positive pediatric patients.

Numerous erythematous-edematous macules and plaques resembling chilblain-like lesions on the dorsal faces of the fingers have also been described. Kawasaki-like hyperinflammatory syndrome and pernio-like bluish-red edematous lesions with borders on the dorsal surfaces of the toes have also been reported in children with possible COVID-19 infection.

Also, a syndrome with multiple organ involvement due to COVID-19 in children and adolescents has been defined and named as “Multisystem Inflammatory Syndrome”. Polymorphic mucocutaneous manifestations such as erythema of the hands and feet, induration, oral mucositis, and bilateral nonpurulent conjunctivitis have been reported in this syndrome.

SKIN MANIFESTATION DUE TO THE USE OF PERSONAL PROTECTIVE EQUIPMENT

Long-term use of personal protective equipment such as an N95 or FFP2 mask, protective goggles, face shield, gloves, and hand hygiene cleaners can cause various skin lesions. It can also cause exacerbation of pre-existing skin diseases. Skin lesions due to personal protective equipment can also be seen in healthcare workers, especially those who follow personal hygiene rules excessively.

Undesirable skin reactions that may occur due to long-term use of masks and protective glasses are mainly dry skin, pressure damage, contact dermatitis, urticaria and pigmentation on the bridge of the nose. Besides, exacerbation of an existing skin disease such as acne vulgaris, facial dermatitis, seborrheic dermatitis and rosacea has been reported.

Using odorless, mild moisturizers after every hand wash during the day and using odorless moisturizer before bedtime and wearing cotton gloves under latex gloves also reduce sweating and skin irritation.
DERMATOLOGICAL MANIFESTATIONS DUE TO DRUGS USED FOR THE TREATMENT OF COVID-19

Maculopapular lesions, acute hemorrhagic edema, petechiae, vesicles, livedoid lesions, urticaria, papules and plaques can be observed during the course of COVID-19 disease. It is necessary to understand whether such lesions are associated with infection or the drugs used in the treatment of COVID-19. Taking a detailed anamnesis on this subject is very important for this differential diagnosis. Atypical lymphocytosis, neutrophilia, eosinophilia, high blood drug level, edema on skin biopsy and an eosinophilic inflammation in whole blood examination are findings that indicate cutaneous drug reaction.

Reported side effects of drugs used in the treatment of COVID-19 disease: morbilliform drug eruption, urticaria / angioedema, pruritus, xerosis, mucocutaneous dyspigmentation, skin atrophy, acneiform eruption, telangiectasia, petechiae, ecchymosis, striae, hirsutism, acute generalized exanthematous pustulosis, psoriasis exacerbation, Stevens Johnson syndrome, erythematous syndrome rash, erythema annulare centrifigum, photosensitivity, DRESS (Drug Rash with Eoshinophilia and Systemic Symptoms) syndrome, vasculitis, fixed drug eruption, anaphylaxis, various skin manifestations such as erythroderma, leukocytoclastic vasculitis, papulopustular eruption, psoriasiform dermatitis.

CONCLUSION

Information about the skin manifestations of COVID-19 infection during the pandemic process is important for early diagnosis of the disease, appropriate management and evaluation of patients. Pernio-like acral lesions are usually seen in young adults infected with COVID-19 with an asymptomatic or mild course. Livedoid/necrotic lesions are seen in elderly people and as a manifestation of more severe COVID-19 disease. In terms of its prognostic value, it is extremely important to recognize such skin lesions early.
### Table 1: Classification of cutaneous findings associated with COVID-19

<table>
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<th>1. Mucocutaneous manifestations associated with COVID-19</th>
<th>2. Skin manifestation due to the use of personal protective equipment</th>
<th>3. Dermatological manifestations due to drugs used for the treatment of COVID-19</th>
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### REFERENCES


Jiang Q, Song S, Zhou J, et al. The prevalence, characteristics, and prevention status of skin injury caused by personal protective equipment among medical staff


