

Is COVID-19 Expanding its Symptom List? The Case of Acute Acro-ischemia and Skin Rash

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ABSTRACT

As the spread of SARS-CoV2 continues to increase globally, newer information gets reported every day. We are learning more and more about the presentation, symptoms and treatment of this infection. Earlier cardinal symptoms of COVID-19 had been fever, cough, and shortness of breath. New findings in its symptoms are now being reported some of which includes neurological symptoms, dizziness and diarrhoea. Of recent skin manifestations due to COVID-19 have drawn the attention of medical experts. The presence of a livedoid pattern (red mottled-net like coloration) rash and a rare skin lesion at the extremities also known as acro-ischemia in patients diagnosed with COVID-19 or patients presenting with symptoms of COVID-19 is now on a surge. Though the correlation between acute acro-ischemia, skin rash and COVID-19 is yet to be fully documented these dermatological and clinical observations in patients might just be another possible key indicator for the presence of the COVID-19 disease.

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INTRODUCTION

Months after COVID-19 appeared on the world stage the number of COVID-19 positive cases keep increasing globally and newer reports about its symptoms are reported on a regular basis. The most cardinal symptom of COVID -19 has been dry cough, sore throat muscle pain, fever, rhinorrhoea and fatigue. Other symptoms such as production of sputum and difficulty in breathing manifest with progression of the disease [1]. It is now becoming apparent that while the COVID-19 disease is primarily respiratory, other organs can also be affected. Other symptoms are now seen outside the respiratory tract including the skin. It is not uncommon to find dermatological manifestation caused by viruses in humans. Unfortunately, a prominent feature appearing amongst COVID-19 cases or patients presenting with symptoms of COVID-19 is the development of a foot lesions and skin rashes. This now poses a challenge to dermatologists due to limited literature about these manifestations. Foot lesions have been termed 'COVID toes' and have been noticed to also be present in

patients with the other symptoms of COVID-19. Could these skin manifestations offer clues to corona virus? The foot lesions developed appear as red to purplish fluid filled blisters on one or more toes, measures about a few millimetres (**Figure 1a**) and are often painful though often resolved within a period of about 2 weeks [2]. These fluids filled blisters often proceed to dry gangrene. In some cases, the lesions appear on the hands typically the fingers (**Figure 1b**) and have been referred by other researchers as 'COVID fingers' [3]. Such presentations might just be confused with frostbite, chickenpox and measles symptoms. These lesions are typically a presentation of acute acro-ischemia though the clinical implications and etiopathogenesis of the lesions are yet to be uncovered.

Acro-ischemic lesions are lesions formed at the tip of extremities such as the limbs or digits a result of disruption of tissues or death usually due to interference or shortage of the supply of blood in that area.

Apart from these lesions other patients present with nonspecific rash or viral

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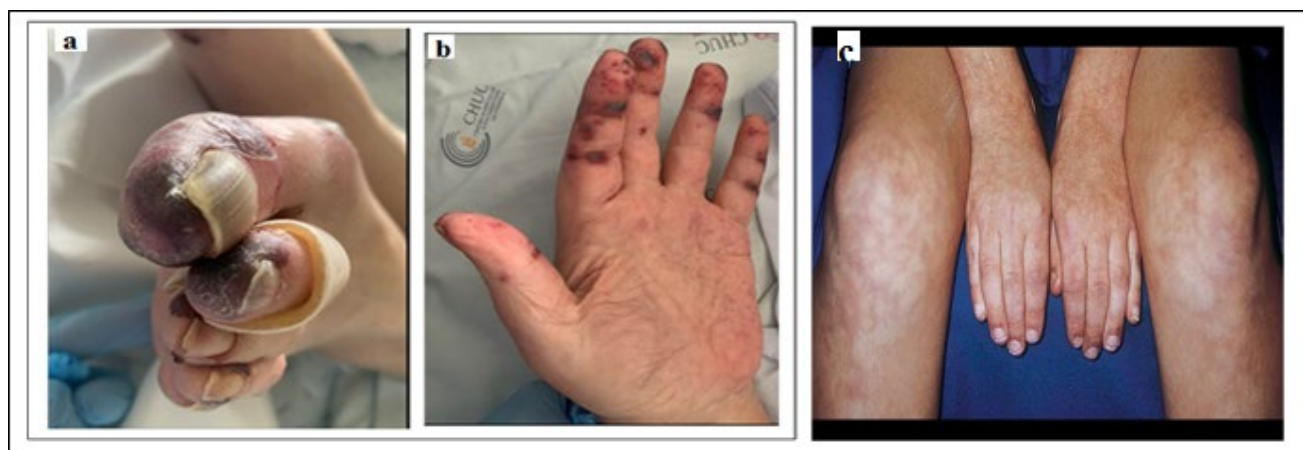


Figure 1. Acro-ischaeamic lesions in patients infected with COVID-19

- a) Red to purplish Lesions on toes of patients
- b) Red to purplish lesions on fingers of patients
- c) Livedoid pattern rash

(Source; Calvão J et al., 2020. Acro-ischemia and COVID-19 infection)
 (Source; <https://www.medicinenet.com /livedo reticularis>)

exanthema lesions. A typical example of this skin rash is a livedoid (a red or purple-colored, mottled) pattern rash (Figure 1c). These rashes are not contagious but simply reflects inflammation in the body which heals in a few days.

Other literature suggests that some of these skin manifestations can be presented prior to the development of the other COVID- 19 symptoms such as fever, headache, muscle pain and any other kind of respiratory symptom. Such manifestations could also serve as a warning sign to individuals not showing the other COVID-19 symptoms. It is particularly important for people who are asymptomatic and presenting these skin manifestations to go for early diagnosis so as to prevent further spread of the disease.

REVIEW CASE STUDY REPORTS OF ACRO-ISCHEMIA AND SKIN RASH IN COVID-19 PATIENTS

Earlier studies from Central China showed a low occurrence of skin disease in COVID-19 patients with only 0.2 % of these patients presenting with dermatological symptoms [4]. With the recent involvement of dermatologist in this pandemic, the interest on cutaneous signs associated to the SARS-CoV-2 infection increased. Since then, subsequent case reports and case series have described COVID-19 associated skin lesions in patients with confirmed COVID-19 including clinical features. A few results obtained from case reports based on similar reviewed literature are summarised below.

In a community based study carried out at King’s College London between the month of March and April 2020 it was revealed that 8.8 % of people that were tested positive for SARS-COV-2 presented with a skin rash [5]. Still in the same study 8.2 % of people who had not been tested but showed a symptom of COVID-19 also presented with skin rash.

Another preprint report also revealed a cluster between skin rash and COVID-19 symptoms [6]. Earlier case report of acro-ischemic lesion was first observed on the 29th of March 2020 in Italy in a 13-year -old boy [7]. This case report was confirmed as linked to COVID-19 when a few dozen cases presented with the same acro-ischemic lesion over a week. The lesions though not only limited to the fingers and toes have also been shown to affect the plantar region. Other of such cases have been reported in Madrid- Spain with the patients testing positive for nasopharyngeal swab for severe SARS-CoV-2 [7]. These presentations have particularly been noted in children and adolescents linked to other symptoms of COVID-19.

Similar dermatological manifestations were also reported in a 47-year-old woman and a 67-year-old male from Atlanta, GA, USA [8].

DISCUSSION

COVID-19 that originated in Wuhan, China in December 2019 with a high fatality rate has caused a great impact to the world. Its high transmissibility and variation in time and nature of presentation poses an insufferable challenge. With its recent manifestation of ‘mystery’ symptoms it is feared that there might be a surge in the number of infection as time progresses. One typical manifestation that has drawn the attention to most medical committee is the development of acro-ischemia now referred to as ‘COVID toes’. Two types of ‘COVID toes’ have been described of late; the first type has been shown to occur in young asymptomatic patients where these patients present with burning, itchy and blue toes containing vesicles. The second type occurs typically in severe cases of COVID-19 patients especially those in the ICU. Though the main cause of the ‘COVID toe’ symptom has not been documented recent theories have linked the symptoms to under recognised vascular component to the disease [9]. In the ICU

patients vasospasm could bring about 'COVID toes'. It could be that in these patients the COVID-19 is resulting in toe specific vasoconstriction. Other studies have associated these new dermatological manifestations to angiotensin converting enzyme 2 (ACE2) which is a membrane protein that has an enzyme domain situated on the external surface of cells in humans which also is the primary target and receptor for the SARS-CoV-2 virus that causes COVID-19. SARS-CoV-2 is known to attack and attach to the transmembrane homologue- ACE2 protein thereby gaining access to cells in the body. This enzyme performs an anti-inflammatory role by mitigation of the pathological effects of angiotensin II. The attachment of the receptors of ACE2 by the SARS-CoV2 leads to a reduction in the number of ACE2 and typically interferes with its function thus resulting in susceptibility of cells to inflammation, cell death and organ failure [10].

Dermatologists are now working to investigate the relationship and causal factor between the 'COVID toe' manifestation and COVID-19 though other medical reports have shown the presence of hyper coagulation components in COVID-19 infected individuals [11]. These elevated levels of coagulation components suggest that as the virus infects the cells it definitely could cause ischemia.

Jimenez [12] also reported the presence of erythematous rash in the lower extremities of 18 patients in Italy diagnosed of COVID-19. It should however be noted that not all patients with COVID -19 will present with rashes or lesions at the lower extremities. Some COVID-19 patients might present with rashes in their trunk. However, though other viral infections are known to cause rashes the co-occurrence of rashes, lesions and respiratory symptoms might be a significant indicator in the confirmation of COVID-19.

Dermatologists however recommend that patients keep a symptom diary containing photograph of rashes if present so as to contact their doctors.

CONCLUSION

This new dermatological manifestation in the time of COVID-19 underscores the need for more testing to see who has been affected or who could possibly be developing antibodies to COVID-19. If further investigations and clinical findings are carried out we might just discover that these dermatological presentations could also serve as a useful indicator for the identification and confirmation of COVID-19. It is therefore of great necessity that more research be done so as to bring about a correlation between the 'COVID toe', skin manifestations and COVID-19 infection.

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