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Systematic Review Article

# A Review of Dermatological Manifestation of COVID-19 Infection and Vaccination

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Conflict of interest: Nil

### Abstract

**Background:** The outbreak of COVID-19, caused by the novel coronavirus SARS-CoV-2, has swiftly become a global health crisis. As the number of cases escalates worldwide, medical professionals are gaining a clearer understanding of the disease's clinical presentation, including its impact on the skin. Various studies have reported diverse skin manifestations in individuals diagnosed with COVID-19.

**Objectives:** This study aims to offer a concise overview of the cutaneous manifestations associated with COVID-19.

**Methodology:** A comprehensive search of literature databases including PubMed, Scopus, and Web of Science was conducted up to April 30, 2022. This narrative review synthesizes the available information regarding the clinical and histological characteristics of skin manifestations linked to COVID-19.

**Results:** The literature review revealed a broad spectrum of cutaneous manifestations associated with COVID-19, exhibiting variability in presentation and timing alongside extracutaneous symptoms. While the exact mechanisms remain unclear, hypotheses point to an overactive immune response, complement activation, and microvascular damage. Histopathological examination of skin lesions in COVID-19 patients reveals various patterns depending on the specific manifestation. For instance, histopathological features of maculopapular eruptions often include superficial perivascular lymphocytic infiltrates with mild spongiosis, while urticarial lesions typically exhibit perivascular edema and a sparse inflammatory infiltrate.

**Keywords:** COVID-19, SARS-CoV-2, Dermatopathology, Skin Manifestations, Vaccination, Histopathology. This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

### Introduction

The coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has emerged as a global health crisis, affecting millions worldwide. While primarily characterized by respiratory symptoms, COVID-19 has been associated with a spectrum of extrapulmonary manifestations, including dermatological manifestations. [1] Concurrently, the rapid development and deployment of COVID-19 vaccines have raised awareness of potential dermatological reactions following vaccination. [2,3] Dermatopathological examination plays a crucial role in elucidating the underlying pathophysiology of cutaneous manifestations COVID-19 associated with infection and vaccination. [4,5] In this review, we aim to summarize the dermatopathological findings observed in COVID-19 patients and those

associated with COVID-19 vaccination, providing insights into the diagnostic and therapeutic implications of these dermatological reactions.

### Methodology

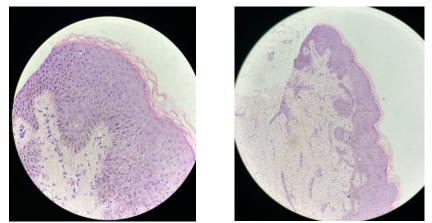
For our methodology, we conducted a thorough literature search using electronic databases such as PubMed, Scopus, and Web of Science until April 30, 2022. We employed various search terms including 'COVID-19' along with terms like 'skin', 'cutaneous 'exanthem'. manifestations', 'eruption', 'rash', 'urticarial', 'chilblain', 'livedo', and 'purpura' to gather reports of skin manifestations in COVID-19 patients. Due to the limited number of available papers on this recent topic, we included all relevant clinical reports, which predominantly consisted of individual cases or small case series. Articles were initially screened based on title and abstract, and full

texts were meticulously reviewed to assess their content. Additionally, we manually searched the references cited in the retrieved papers to ensure comprehensive coverage of relevant literature.

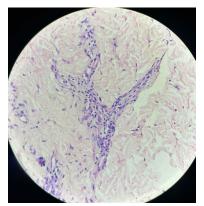
## Results

## **Dermatopathology of COVID-19 Infection:** COVID-19- associated dermatological manifestations encompass a diverse range of clinical presentations, including but not limited to maculopapular eruptions, urticaria, chilblain-like lesions (COVID toes), and livedo reticularis. Histopathological examination of skin lesions in COVID-19 patients reveals various patterns depending on the specific manifestation. For instance, histopathological features of

maculopapular eruptions often include superficial perivascular lymphocytic infiltrates with mild spongiosis, while urticarial lesions typically exhibit perivascular edema and a sparse inflammatory Chilblain-like lesions demonstrate infiltrate. features of perniosis with a lymphocytic infiltrate in the dermis and occasional fibrin thrombi in dermal vessels. Livedo reticularis may show features suggestive of a thrombotic vasculopathy, including microthrombi and endothelial cell damage. [6,7,8,9] The exact pathogenesis of these dermatological manifestations remains incompletely understood but is thought to involve immune dysregulation, vascular injury, and prothrombotic states triggered by SARS-CoV-2 infection.



Photograph showing Spogiosis like lesion in COVID19 skin lesion



Photograph showing perivascular lyphocytic near COVID vaccination site

Dermatopathology of COVID-19 Vaccination: In addition to dermatological manifestations COVID-19 associated with infection, dermatopathological reactions following COVID-19 vaccination have been reported. These reactions include local injection site reactions, urticaria, and eruptions. morbilliform Histopathological examination of vaccine-related dermatological reactions often reveals nonspecific findings, such as perivascular lymphocytic infiltrates and mild spongiosis, consistent with an inflammatory reaction. Rarely, more pronounced histopathological changes, such as interface dermatitis or vasculitis, may be observed. [10] The mechanisms underlying vaccine-related dermatological reactions are multifactorial and may involve hypersensitivity reactions, immune complex deposition, or direct inflammatory responses to vaccine components. [11]

#### Conclusion

The dermatopathological evaluation of COVID-19associated skin manifestations and vaccine-related dermatological reactions provides valuable insights

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into the pathophysiology and clinical management of these conditions. By correlating clinical findings with histopathological features, dermatologists, pathologists, and clinicians can accurately diagnose and manage cutaneous manifestations in COVID-19 patients and vaccine recipients. Continued vigilance and further research are warranted to elucidate the complex interplay between SARS-CoV-2 infection, COVID-19 vaccination, and dermatological pathology, ultimately enhancing our understanding of COVID-19 immunopathogenesis and guiding therapeutic interventions.

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