Similarity between cutaneous reactions due to SARS-CoV-2 and its vaccinations

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“There are certain similar skin disorders that are both associated with the new coronavirus and its vaccines”

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COVID-19, caused by SARS-CoV-2, continues to spread at full speed with its new variants including Omicron, while SARS-CoV-2 vaccination also continues at full speed. Currently, the most powerful tool in combating the COVID-19 pandemic is vaccination along with personal measures against SARS-CoV-2. During the 2 year pandemic period, it was observed that SARS-CoV-2 is associated with multiple system involvements, including the skin, apart from lung involvement. There are certain similar skin disorders that are both associated with the new coronavirus and its vaccines [1,2]. Fortunately, these reactions are commonly short, benign and self-limited. Herein, we have discussed the common cutaneous manifestations that are both associated with the new coronavirus and its vaccines.

Chilblain-like lesions

Chilblain-like lesions (CLL) are mostly asymmetrical acral distributed in patients with COVID-19. It is a sign of mild-course COVID-19 and is predominant in younger patients. The localized acral skin damage may be the result of a strong immune-mediated reaction triggered by SARS-CoV-2. Therefore, patients with CLL have mild or no symptoms, negative RT-PCR and localized endothelial injury to the acral sites. The average occurrence time of lesions is about 10–14 days and lasts about 2 weeks, with spontaneous improvement [3,4]. There are numerous reports that revealed both virus related protein based weakened inactivated SARS-CoV-2 virus and mRNA vaccines including BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) can lead to CLL. The CLL may occur after the first and second doses of the vaccines. The onset of the lesions has been reported as 2–21 days [5,6]. Considering the characteristic formation and disappearance times of CLL lesions, no significant difference was found between the lesions that occurred after the COVID-19 and SARS-CoV-2 vaccination [7].

Vasculitis

Vasculitis is another common cutaneous manifestation of the new coronavirus and its vaccines. As it is known, leukocytoclastic vasculitis can be associated with infections, drugs and vaccines. Similarly, there are numerous reports that revealed leukocytoclastic vasculitis is related to COVID-19 and its vaccines. The other reported vasculitic patterns that occurred after COVID-19 were small-vessel vasculitis, IgA vasculitis, granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis, purpura fulminans, urticarial vasculitis, lymphocytic and anti-neutrophil cytoplasmic antibody-associated vasculitis. The SARS-CoV-2 and its vaccines can imitate the self antigens of the body that resulted in immune dysregulation that resulted in vasculitis [1,2]. Most cases of COVID-19-related vasculitis run a mild to moderate course. The cornerstone of the medical treatment is systemic corticosteroids. Complete remission could be achieved in most patients [1].
Morbiliform eruptions
Maculopapular rash, which also includes morbilliform eruptions, is the most common cutaneous side effect of the COVID-19 followed by CLL. The morbilliform eruption is also one of the common side effects of the COVID-19 vaccines and usually has a mild course [1,2]. Considering the characteristic formation and disappearance times of CLL lesions, there is also no significant difference between the lesions that occurred after the COVID-19 and SARS-CoV-2 vaccination.

Pityriasis rosea & urticaria
We previously reported that there is an increased number of urticaria and pityriasis rosea (PR) during the COVID-19 pandemic when compared with the corresponding previous year of the current pandemic. Subsequent reports suggested that patients with COVID-19 who have PR-like dermatosis and urticarial rash include SARS-CoV-2 particles in their skin lesions [8]. Similarly, numerous cases contain reports that PR-like dermatitis and urticaria can be developed after COVID-19 vaccines. Of note, in our daily routine practice, we also encountered numerous cases of new urticarial eruptions after both inactivated and mRNA-based COVID-19 vaccines. As per our observations PR cases that developed after SARS-CoV-2 vaccinations were not demographically distinct from the ordinary and general PR. Interestingly, there is a higher incidence of PR cases among inactivated SARS-CoV-2 vaccines in the literature [1]. The exact effect of the differences should be illuminated with further studies.

Herpes zoster
Herpes zoster can be triggered by COVID-19 vaccines. The occurrence of herpes zoster after the COVID-19 vaccine is mostly within 7–10 days. Interestingly, there is a report that even though a patient who has been vaccinated against the herpes zoster virus developed herpes zoster after COVID-19 vaccination. Similarly, to date, there are over 30 reports which suggested the possible relationship between COVID-19 and herpes zoster. The majority of cases of herpes zoster in patients with COVID-19 have a typical clinical presentation [9]. Considering the characteristic formation and disappearance times of herpes zoster lesions reveals similarity between cutaneous reactions due to SARS-CoV-2 and its vaccinations.

Erythema multiforme
Many types of drug reactions including erythema multiforme, which developed after COVID-19, have been reported. Similarly, four cases of mRNA vaccine-related erythema multiforme have been recently documented [1,2]. Increased vaccine-mediated immune boosting may lead to delayed hypersensitivity reaction which is responsible for erythema multiforme like reactions.

Other cutaneous manifestations
Apart from relatively common similar cutaneous manifestations of COVID-19 and its vaccine aforementioned above, there are certain rare skin disorders that can be seen as a result of both COVID-19 and its vaccine. These disorders can be listed as vesiculobullous eruptions, lichen planus, granuloma annulare, erythema annulare centrifugum, flare of herpes simplex, Rowell’s syndrome, DRESS syndrome, and recurrence of alopecia areata. Of note, to date, there are still no reports on the relationship between livedo reticularis-like eruption, one of the main serious cutaneous manifestations of the COVID-19 and COVID-19 vaccines.

In the early stages of the pandemic, cutaneous side effects of SARS-CoV-2 were described, while in the current stages of the pandemic, cutaneous side effects of the COVID-19 vaccine were described. In general, these cutaneous side effects are commonly temporary, benign, self-limited and generally not a contraindication to further doses of the vaccine. In this article, we would like researchers to pay attention to the similarity between cutaneous reactions due to SARS-CoV-2 and its vaccinations.

Future perspective
The immune-based skin reactions due to both conditions may show that SARS-CoV-2 has a more immunological effect rather than infectious effect on the skin as in toxic shock syndrome. In addition, mRNA containing lipid nanoparticles found in COVID-19 vaccines can trigger autoimmunity by increasing the production of proinflammatory cytokines and chemokines. Furthermore, we know that the vaccines have mostly been developed against the antigenic Spike protein of the SARS-CoV-2 virus. Therefore, we would like to emphasize that the
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Editorial

Similarity of the skin reactions both after the COVID-19 and SARS-CoV-2 vaccinations may suggest the focus of Spike proteins of the virus in the pathogenesis of the skin-related diseases.

Skin manifestations associated with COVID-19 apart from livedo reticularis-like eruption are usually associated with milder disease, while it is not yet known whether the presence of post-vaccination skin findings is a strong or weak indicator of vaccine immunity. This condition is another gap that should be filled. As a result, further novel studies are required in order to find the exact pathogenesis of the cutaneous manifestations of SARS-CoV-2. In this context, addressing COVID-19 and its vaccine together may lead to new discoveries on the disease.

In the meantime, air pollution may increase the risk of getting coronavirus. Recent research from Rachel Nethery, Xiauo Wu, Francesca Dominici and other colleagues at Harvard showed that people who live in places with poor air quality are more likely to die from COVID-19 despite other factors such as pre-existing medical conditions, socioeconomic status and access to healthcare [10]. The comparison of cutaneous manifestations of vaccinations between the different air pollution areas may give certain indirect clues regarding the effects of COVID-19 and vaccines. In the next future, the effect of the different environmental conditions on the virus and vaccines may be important fields to deal with.

Author contributions

O Kutlu did the manuscript conception. O Kutlu and SA Temiz fulfilled the following contributions to the article: substantial contributions to the conception or design; or the acquisition, analysis or interpretation of data; drafting or revising critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects, ensuring that questions related to the accuracy or integrity of any part are appropriately investigated and resolved.

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Papers of special note have been highlighted as: ● of interest

1. Temiz SA, Abdelmaksoud A, Wollina U et al. Cutaneous and allergic reactions due to COVID-19 vaccinations: a review. J. Cosmet. Dermatol. 21(1), 4–12 (2021).

● This review article was written on the cutaneous reactions due to COVID-19 vaccines including mRNA, vector and inactive SARS-CoV-2 based vaccines. The comprehensive article contains searching the PubMed, EMBASE and Web of Science databases using the keywords ‘coronavirus’, ‘COVID-19’, ‘vaccine’, ‘cutaneous reactions’, ‘allergic reactions’ and ‘SARS-CoV-2’. Chilblain-like lesions (CLL), vasculitis, pityriasis rosea, maculopapular rash, erythema multiforme, herpes zoster, urticarial lesion, etc., have been reported as cutaneous reactions after the COVID-19 vaccine.

2. Seque CA, Enokihiara M M S E S, Porro AM, Tomimori J. Skin manifestations associated with COVID-19. An. Bras. Dermatol. 97(1), 75–88 (2021).

● Addresses the main aspects of skin manifestations associated with COVID-19. The article gathers a report of prospective studies and systematic reviews. The authors stated that there are more than 1500 articles regarding COVID-19-related cutaneous reactions at the time of this review. In this review, the main skin manifestation of COVID-19 has been reported as maculopapular eruption, pernio-like eruption, herpes zoster, urticarial lesion, etc.

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● The authors reports two cases of COVID-19 presenting with cutaneous lesions, specifically, CLL, which have been stated for the first time.

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● The authors reports the characteristics of six cases of CLL after COVID-19. These characteristics contain location, symptoms and time in weeks during/prior/after COVID-19. The author’s hypothesis is that these lesions could be a late manifestation of COVID-19.

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Authors claim that this is the first case report which shows COVID toes-like syndrome linked to COVID-19’s vaccine. The case consisted of COVID toes during the French campaign of vaccination that occurred 4 days after the vaccination with the Pfizer-BioNTech mRNA vaccine against COVID-19.

6. Lopez S, Vakharia P, Vandergriff T, Freeman E, Vasquez R. Pernio after COVID-19 vaccination. *Br. J. Dermatol.* 185(2), 445–447 (2021).

Author stated that The American Academy of Dermatology/International League of Dermatological Societies COVID-19 registry has noted eight of these pernio-like reactions after vaccination, but at present no cases of patients with biopsy confirmation have been reported. This is the first report a patient with pernio that appeared after the Pfizer BNT162b1 COVID-19 vaccine, in an asymptomatic individual with negative PCR testing.

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Authors highlights that they report the first case of CLL following inactivated SARS-CoV-2 vaccination, although previous reports on the skin manifestations of COVID-19 vaccine was mostly regarding the effect of mRNA based vaccines.

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Authors investigated the total number and diagnosis of patients, who attended a tertiary care hospital for the dermatology outpatient clinic between 2020 and 2021. These data were compared with the corresponding period of the previous year. The percentage of certain skin conditions including pityriasis rosea and urticaria were statistically significantly increased a month after the occurrence of the COVID-19 pandemic. Authors hypothesized that an increase in the number of certain diseases such as urticaria and pityriasis rosea may indicate the risk of asymptomatic COVID-19 carriage in these patients. Therefore, they claimed PCR and/or antibody-based further studies should be performed to explore whether certain dermatologic diseases are related to asymptomatic COVID-19 cases.

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