

Potential Mechanisms Driving the Development of Psoriasis after COVID-19 Vaccine

Xiangyue Lei^{1,a}, Xiaoning Yan^{2,b,*}

¹Department of Traditional Chinese Medicine, First Clinical Medical College, Shaanxi University of Chinese Medicine, Xianyang, 712046, China

²Department of Dermatology, Shaanxi Provincial Hospital of Traditional Chinese Medicine, Xi'an, 710000, China

^a15353988928@163.com, ^b641335348@qq.com

*Corresponding author

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Abstract: This paper conducts a systematic review of the pathogenesis of psoriasis with the COVID-19 vaccine, using skin inflammation as a key point and delayed inflammatory response and cytokines as potential mechanisms driving psoriasis after COVID-19 vaccination. Reports from the global Centers for Disease Control (CDC) Vaccine Adverse Event Reporting System (VAERS) data reveal that psoriasis can be newly developed or exacerbated following vaccination against novel coronavirus pneumonia (COVID-19) despite global vaccination.

1. Introduction

The COVID-19 pandemic of 2019 has had a significant impact on the health and economy of people worldwide. To combat this, vaccines have been developed to protect against SARS-CoV-2 infection, and high vaccination rates are necessary to achieve herd immunity. As of January 2022, the COVID-19 vaccine has been widely distributed, with 60.8% of the global population having received at least one dose[1-2].

Vaccines have immunogenic effects that cause changes in the levels of chemokines and cytokines. These changes activate various components of the innate and acquired immune system, such as different T and B cell subsets, histiocytes/macrophages, dendritic cells, and eosinophils. As a result, the skin and mucous membranes, which serve as the boundary surfaces of the environment, are significantly impacted by the general activation of the immune system that is triggered by vaccines. Cutaneous adverse events (CAEs) associated with COVID-19 vaccination have been reported globally and are believed to be new cases or episodes of pre-existing skin disease associated with the vaccine[1,3-5]. These events have caused concern, particularly in cases where new or exacerbated psoriasis has been reported following vaccination[6]. The study on this matter was conducted by the global Center for Disease Control (CDC). This systematic review analyzed data from the global Centre for Disease Control (CDC) Vaccine Adverse Event Reporting System (VAERS) to investigate the relationship between COVID-19 vaccination and new or exacerbated

psoriasis. The study aims to identify potential mechanisms driving the development of psoriasis after vaccination and provide a theoretical basis for the rational administration of COVID-19 vaccines to prevent or minimize the occurrence and progression of psoriasis. Overall, this study offers valuable insights into the impact of COVID-19 vaccination on psoriasis and highlights the need for careful consideration when administering vaccines to individuals with psoriasis.

2. The Relationship between COVID-19 Vaccine and Psoriasis

2.1 Can Drive New or Exacerbated Psoriasis after COVID-19 Vaccination

The literature suggests that certain vaccinations, such as influenza, BCG, tetanus, and diphtheria vaccines, may have the potential to cause psoriasis[7-11]. However, studies have shown that the COVID-19 vaccine is safe and effective for patients with psoriasis who are on systemic therapy[12-15]. Guidelines have been established to determine the optimal timing of vaccination for individuals on immunomodulatory drugs to ensure a proper vaccine response[16]. Despite this, there have been reports of new or worsening psoriasis with an increase in the number of vaccinations received[17]. According to recent studies, COVID-19 vaccination may trigger psoriasis, especially when there are no other underlying factors. The short interval between vaccination and psoriasis onset indicates a potential correlation. Skin biopsy findings in cases of cutaneous adverse reactions associated with COVID-19 vaccine suggest that the immune response generated in the body after vaccination may be responsible[18]. Psoriasis is a complex immune-mediated inflammatory disease that involves various immune cells and cytokines, such as tumour necrosis factor, interleukin (IL)-17, IL-22 and IL-23[19]. Patients who experience new or aggravated psoriasis after vaccination, regardless of their prior diagnosis or treatment history, may exhibit different clinical manifestations[20-22]. There have been reported cases from abroad suggesting that the COVID-19 vaccination could trigger various types of psoriasis, including pustular, palmoplantar, erythrodermic, and plaque psoriasis (among others) [6].

2.2 Types, Doses and Morbidity Characteristics of Vaccines That Commonly Trigger or Exacerbate Psoriasis

There are currently several COVID-19 vaccines approved worldwide, including mRNA vaccines like Comirnaty® (Pfizer BioNTech/ Pfizer; BNT162b2) and Spikevax® (Moderna Moderna; mRNA1273), which are composed of a lipid-nanoparticle-encapsulated structure. Additionally, there are viral vector vaccines like Covishield® (AstraZeneca; AZD1222/ChAdOx1) that contain DNA from novel coronavirus spiked proteins in viruses other than coronaviruses, most commonly adenoviruses. Inactivated coronavirus vaccines, such as CoronaVac (Coxin Sinovac), contain a variety of novel coronavirus antigens and are not restricted to the spike protein. Currently, the majority of administered vaccines against the neo-coronavirus pneumonia have been adenovirus vector or mRNA vaccines. Phase III clinical trials have reported that mRNA vaccines have displayed an efficacy rate of 90-95% in preventing the disease[23,24]. Adverse skin reactions have been reported more frequently following mRNA vaccination, specifically Pfizer (BNT162B2) and Moderna (mRNA1273) vaccines, and are often associated with subsequent psoriasis flares[25]. The inherent immunostimulatory properties of RNA in mRNA vaccines can act as both an immunogen (encoding viral proteins) and an adjuvant, leading to over-stimulation of innate immunity and inducing systemic inflammation. This can trigger serious side effects such as psoriatic skin lesions, as mentioned in a study. The onset of psoriasis can occur during any of the three doses of the vaccine, with most attacks occurring after the second dose, possibly associated with a secondary boost in the inflammatory response[26].

3. Potential Mechanisms of COVID-19 Vaccine and Psoriasis Development

The relationship between psoriasis and COVID-19 vaccination is complex, and researchers have identified the inflammatory response as a key factor. Specifically, delayed inflammatory response and cytokines are being studied to better understand how the COVID-19 vaccine may trigger new onset or exacerbation of psoriasis. Ongoing research is focused on gaining a deeper understanding of this relationship.

3.1 Delayed Inflammatory Response and Psoriasis

COVID-19 vaccination elicits both humoral and cellular immune responses, effectively inducing antiviral immunity in the body. However, it may also cause various cutaneous adverse reactions. These reactions can be categorized into 11 common categories[25], including local injection site reactions such as redness, swelling, and pain, delayed local reactions, urticaria, angioedema, measles-like rash, herpes zoster, maculopapular rash, filler reactions, frostbite, pityriasis rosea, and severe adverse skin reactions such as scarring.

This article discusses delayed inflammatory reactions (DIRs) as the most common cutaneous adverse reactions (CAEs) following vaccination against Neocoronas pneumonia. It also notes that these reactions may be involved in the pathogenesis of psoriasis and are mostly observed after mRNA vaccination. The article further highlights that DIRs to hyaluronic acid-based fillers (HA) manifest as multiple erythema, painful nodules, hard nodules, and eyelid edema. However, the exact mechanism of action for the delayed inflammatory response is still unclear and may be immune-mediated and multifactorial. Some observational studies suggest that T cell-mediated hypersensitivity may be the mechanism for delaying the injection site response based on skin biopsy results[27]. The skin can experience a Delayed Inflammatory Response (DIR) at various injection sites, primarily in the dermal and subcutaneous regions, with the adipose tissue being the most commonly affected area[28]. This is due to the high expression of ACE2 in these regions. A recent study has suggested that blocking or binding ACE2 could potentially be a mechanism to alleviate DIR[29]. ACE2 is an immunomodulatory factor that plays a crucial role in converting angiotensin I to the pre-inflammatory metabolite angiotensin II-VII. Local blockade of ACE2 can trigger a pre-inflammatory cascade that leads to inflammation in adipose tissue at the site of vaccination[30]. ACE2 is expressed in various cell types in the skin, including fibroblasts and keratinocytes[31], which are known to be causative cells of psoriasis. Reduction of ACE2 levels in keratinocytes can activate inflammatory vesicles and lead to IL-1 secretion, ultimately resulting in the development of a psoriatic inflammatory response[32].

In addition to the COVID-19 vaccination, individuals who contract COVID-19 may also experience psoriasis[33]. Researchers have suggested that this is due to the virus's spike-in protein binding irreversibly to ACE2, a target protein, which can lead to downregulation of ACE2 and a decrease in the ability to control AngII. Accumulation of AngII, in turn, can upregulate the expression of various proteins, including those that activate neutrophils and are associated with psoriasis-like symptoms[34]. Elevated levels of AngII can induce inflammation in the pericapillary environment and activate CD8+ T-cell and Th1 immune responses[35]. This interaction promotes an inflammatory response and triggers a local Th1 cascade, ultimately leading to the development of DIR and contributing to the pathogenesis of psoriasis.

3.2 Cytokines and Psoriasis

3.2.1 Tumour Necrosis Factor Alpha (TNF- α)

Upon administration of the COVID-19 vaccine, various components of the innate and acquired immune system are activated, including different subsets of T and B cells, histiocytes/macrophages, dendritic cells, and eosinophils. This activation leads to the secretion of large amounts of interferon- γ (IFN- γ) and tumour necrosis factor- α (TNF- α) by CD4+ T cells, as well as other key cytokines such as interleukins IL-2 and IL-6. This inflammatory skin response pattern is characterized by the aforementioned cytokines[1].

Psoriasis is a chronic skin disease characterized by the infiltration of inflammatory cells, hyperproliferation of keratin-forming cells, and abnormal differentiation[36]. IFN- γ is considered a pathogenic cytokine that triggers the inflammatory cascade in psoriasis and may serve as a marker of severity[37]. Currently, TNF- α is the most commonly targeted cytokine in psoriasis treatment. It is suggested that an increase in TNF- α may be an immune factor in triggering psoriasis after COVID-19 vaccination[38,39].

3.2.2 Type I Interferon (IFN-I)

According to Elamin, a researcher found that a 66-year-old woman developed GPP shortly after receiving the AstraZeneca adenoviral vector vaccine. The researcher suggested that PDCs and their secretion of IFN-I may be involved in the development of GPP after vaccination for neocrown pneumonia. The study concluded that the IL36/IFN-I axis plays a significant role in the development of psoriatic inflammation[40]. Upon COVID-19 vaccination, plasmacytoid dendritic cells (PDCs) play a crucial role in initiating the innate antiviral immune response by activating Toll-like receptors (TLR), specifically TLR-9 and TLR-7, which detect nucleic acids in the endosome[41]. This activation leads to the production of IFN-I, which triggers the adaptive immune response against the virus. However, it is important to note that overstimulation of nucleic acid sensing can result in IFN-driven inflammatory or autoimmune skin conditions. The over-activation of the innate immune system can activate skin memory T cells in susceptible individuals, leading to their differentiation towards Th17/Th22[42,43]. This differentiation process may reactivate memory Th17 cells, contributing to the chronic course of psoriasis by causing inflammation, activating keratinocytes, damaging cells, and disrupting the skin barrier, ultimately resulting in psoriasis-like lesions[44]. The COVID-19 vaccine has a central regulatory role in the pathogenesis of psoriasis. COVID-19 vaccination activates IFN-I-mediated immune responses, which can trigger IFN-driven inflammatory diseases like psoriasis in individuals with a genetic susceptibility[45].

4. Conclusion

It is important to note that serious cutaneous adverse reactions are rare, and most cutaneous reactions are self-limiting and require minimal or no treatment. However, new onset or worsening of psoriasis is a potential skin adverse reaction following vaccination against Neocoronavirus. Studies have shown that the most commonly used COVID-19 vaccines rely on adenoviral vectors, mRNA, or virus-associated proteins that can trigger Th1 and Th17 responses. Recent studies have suggested that the activation of psoriasis may be linked to the increased production of tumour necrosis factor alpha and type I interferon by CD4+ T cells and plasmacytoid dendritic cells. It has also been found that COVID-19 infection may cause psoriasis. While there have been limited reports of cases linking the COVID-19 vaccine to psoriasis, further investigations are required to establish any potential link and the underlying mechanisms driving the development of psoriasis

following vaccination, both nationally and internationally.

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