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CASE REPORT

New-Onset of Diffuse Systemic Sclerosis Following COVID-19 Vaccination: 3rd Case Described

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ABSTRACT

Systemic sclerosis (SSc) has been reported in rare cases following COVID-19 vaccination, raising concerns about potential autoimmune triggers. Herein, we describe the third documented case of diffuse SSc post-vaccination in a 22-year-old woman with no prior autoimmune history. Symptoms, including Raynaud's phenomenon, polyarthritis, and sclerodactyly, emerged within a month after the first dose of the Pfizer-BioNTech vaccine. Laboratory and clinical evaluations confirmed the diagnosis, with no evidence of interstitial lung disease or internal organ involvement. Previous reports and the temporal association suggest a potential role of vaccination in SSc onset, emphasizing the need for further research into autoimmune risks linked to immunization.

Introduction

The Coronavirus Disease 2019 (COVID-19) emerged as a pandemic viral infection originating in Wuhan, China, in December 2019, and rapidly disseminated globally. Notably, it resulted in approximately 771,291,203 confirmed cases and around 7 million fatalities, with a total of 13,513,324,853 vaccine doses administered worldwide.[1] The swift global spread of the virus and its severe impact on public health prompted unprecedented efforts in the development and deployment of vaccines. In this context, the role of vaccination in mitigating the disease burden has been critical, but concerns have emerged regarding potential adverse effects.

Two prior case reports have documented instances of systemic sclerosis (SSc) potentially induced by COVID-19 vaccination.[2,3] These reports raise important questions about the interaction between the immune response triggered by the vaccine and autoimmune diseases. In this report, we present the third documented case of the diffuse form of SSc following COVID-19 vaccination, contributing further evidence to this rare but significant phenomenon.

Although the development of vaccines for COVID-19 has been pivotal in controlling the pandemic, the immune activation induced by vaccination may, in certain genetically predisposed individuals, trigger autoimmune diseases. Systemic sclerosis, a chronic autoimmune disorder characterized by skin fibrosis and vascular abnormalities,[4] has been rarely reported in association with vaccination, including other viral vaccines. The mechanisms underlying vaccine-induced autoimmunity are not yet fully understood but may involve molecular mimicry, epitope spreading, or the polyclonal activation of B cells. These immune responses could lead to the emergence of autoimmune diseases, particularly in individuals with an underlying predisposition or subtle genetic risk factors. This report aims to further investigate the connection between COVID-19 vaccination and the onset of systemic sclerosis, adding valuable insight to the ongoing discussion about the safety of immunization in individuals with certain risk factors.[3]

This study aims to highlight a rare but significant potential complication of COVID-19 vaccination, focusing on its role in triggering autoimmune diseases like SSc, and to encourage vigilance in identifying and managing such cases. Furthermore, it seeks to advance understanding of the mechanisms through which vaccines may influence autoimmune responses and to underline the importance of timely diagnosis and appropriate management strategies in affected individuals.

Case report

A 22-year-old previously healthy woman received her first dose of the COVID-19 vaccine (Comirnaty, Pfizer-BioNTech, US) in October 2021. Five days post-vaccination, she experienced fever and polyarthralgia, prompting a visit to the emergency department. On the day of vaccination, she had also been prescribed a non-steroidal anti-inflammatory drug to manage nausea, vomiting, and cephalalgia. One month later, she developed bilateral polyarthritis affecting her knees, metacarpophalangeal, wrist, and proximal interphalangeal joints, accompanied by Raynaud's phenomenon and noticeable changes in the skin on her hands and fingers.

The patient was treated with dexamethasone, which resulted in a marked improvement in joint inflammation; however, Raynaud's phenomenon and skin symptoms worsened. She continued taking dexamethasone at 4 mg/day for 18 months. In April 2023, she presented to our private clinic, where we observed sclerodactyly, skin thickening above the knees and elbows, microstomia, telangiectasias, and persistent Raynaud's phenomenon. There was no personal or familial history of autoimmune disease. Laboratory tests revealed a positive antinuclear antibody (1:80 speckled pattern) with negative anti-Scl-70 and anti-centromere antibodies. Complement levels were within normal range: CH50 at 150 U/mL (normal range: 60-350 U/mL), C3 at 99 mg/dL (normal range: 90-180 mg/dL), and C4 at 20 mg/dL (normal range: 16-38 mg/dL). Additional autoimmune markers, including antibodies to dsDNA, Ro/SS-A, La/SS-B, RNP, Sm, and histone, were negative. Cardiac echocardiography revealed normal pulmonary arterial pressure, and a thoracic computed tomography scan showed no signs of interstitial lung disease. A diagnosis of diffuse systemic sclerosis (SSc) was established based on 2013 classification criteria for SSc [5]. However, the patient relocated to another city, and we subsequently lost her to follow-up.

Discussion

The development of systemic sclerosis (SSc) following COVID-19 vaccination, though rare, has raised concerns about the potential role of vaccines in triggering autoimmune diseases. As more individuals are vaccinated globally, rare adverse events, such as autoimmune diseases, have been documented, prompting further investigation into the relationship between vaccines and autoimmune responses. The close temporal association between the onset of SSc and vaccination, as seen in previous cases and the patient described in this report, suggests that the immune system's response to the vaccine may act as a trigger for these diseases.

In reviewing the two previously reported cases, one involved a 70-year-old man who developed diffuse systemic sclerosis (SSc) two weeks after receiving the COVID-19 vaccine, with a positive antinuclear antibody (ANA) but no specific SSc-related antibodies.[2] The second case described a patient who developed diffuse SSc without internal organ involvement and required treatment with cyclophosphamide [3]. The close temporal proximity of SSc onset to vaccination, coupled with the absence of other identifiable triggering factors, suggests a potential role of the COVID-19 vaccine in initiating SSc in our patient.

There have been reports of systemic sclerosis (SSc) induced by various vaccines, including those for hepatitis A and B, influenza, rubella, poliomyelitis, tetanus, diphtheria, mumps, measles, anthrax, and typhoid, among others.[6,7]

The pathogenesis of autoimmune disease triggered by vaccines is multifaceted and may involve several immune

mechanisms. One widely proposed explanation is molecular mimicry, wherein the immune system mistakenly attacks self-antigens that resemble foreign antigens present in the vaccine. In the case of COVID-19 vaccination, the spike protein of SARS-CoV-2 could share structural similarities with host proteins, leading to the activation of autoreactive immune cells. This activation could result in the development of autoimmune diseases such as systemic sclerosis, particularly in individuals with an underlying predisposition. Another potential mechanism is epitope spreading, where an initial immune response against a specific target expands to affect other tissues, resulting in the broadening of the autoimmune response.[6,7]

In addition to molecular mimicry and epitope spreading, other immune mechanisms may contribute to the development of autoimmune diseases post-vaccination. Polyclonal activation of B cells, for example, could lead to the production of autoantibodies that target self-tissues, a hallmark of many autoimmune disorders, including systemic sclerosis.[7] Furthermore, vaccine adjuvants, which are included to enhance immune response, could potentially trigger inflammatory pathways that result in autoimmunity. While these mechanisms are not fully understood, the combination of these immune responses with genetic predispositions is thought to increase the risk of autoimmune disease development. This underscores the need for continued monitoring of vaccine recipients and further research into the long-term effects of vaccination, particularly in individuals with genetic risk factors for autoimmune disorders.[7]

Conclusion

The temporal association between the onset of diffuse systemic sclerosis (SSc) and COVID-19 vaccination in this case, alongside similar reports, suggests a potential, albeit rare, link between immunization and autoimmune disease activation. While vaccines, including those for SARS-CoV-2, are overwhelmingly safe and crucial in combating infectious diseases, these findings underscore the importance of monitoring for autoimmune manifestations in susceptible individuals. Further studies are needed to elucidate the underlying mechanisms, such as molecular mimicry or epitope spreading, and to identify potential genetic or environmental predispositions, ensuring a comprehensive understanding of these rare adverse events.

Acknowledgments

ETHICAL STATEMENT
An informed consent was obtained from the patient's relatives.

CONFLICTS OF INTEREST:
None

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