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Self-limiting pernio-like 'Covid-Toe' reaction following oxford-astrazeneca vaccination in a renal transplant patient

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Abstract

The Covid-19 pandemic has resulted in the rapid development and deployment of vaccination programs globally. While most adverse reactions are well-documented, rarer manifestations continue to be reported. Here, we present a detailed case of self-limiting pernio-like 'Covid-Toe' reaction in a 40-year-old female with a history of kidney/pancreas transplant who received the Oxford-AstraZeneca Covid-19 vaccine. The patient experienced bilateral digital skin inflammation, erythematous papules, blistering, and ulceration in the proximal interphalangeal joints, which spontaneously resolved. Extensive investigations ruled out other causes, and subsequent doses of the vaccine and an episode of SARS-Cov-2 infection did not trigger a similar reaction. The underlying mechanism of Covid-Toe remains uncertain, but it may involve immune activation by the virus or vaccine.

Introduction

The Covid-19 pandemic has led to the development of several successful vaccination programs globally. While vaccination has been essential in curbing the spread of the virus, monitoring and understanding adverse reactions remain crucial to maintaining public trust in vaccination efforts.

The incidence of dermatologic signs in SARS-CoV-2 infection is reported to be as low as 0.2% and as high as 20% [1,2]. One rare adverse reaction reported is Chilblain/Perniosis, more commonly known as 'Covid-Toe' [3], however it is rarer still as a consequence of mRNA vaccination. Herein, we present a case of self-limiting Covid-Toe in a patient who received the Oxford-AstraZeneca vaccine.

Case presentation

A 40-year-old female with a medical history of Type 1 Diabetes Mellitus and diabetic nephropathy underwent a simultaneous kidney/pancreas transplant in December 2020. Her immunosuppressive regimen consisted of Mycophenolate and Tacrolimus. In February 2021, she received her first dose of AZD1222, an adenovirus vector Covid-19 vaccine. Approximately five weeks later, she noticed bilateral proximal interphalangeal joint swelling and digital skin inflammation, accompanied by progressive pain and a painful right wrist. The condition worsened, leading to pruritic, erythematous digital papules that later blistered and ruptured, leaving areas of ulceration (Figures 1 and 2). The patient also reported reduced grip function due to skin pain rather than muscle weakness.

Investigations

Extensive investigations were performed to ascertain the cause of the pernio-like reaction. Infectious agents such as tuberculosis, fungal, and yeast growth were ruled out. Additionally, the patient's autoimmune profile and Covid-19 PCR test were both negative. X-rays and an ultrasound of the hands with Doppler revealed no evidence of underlying inflammatory arthritis, venous thrombosis, or arterial thrombosis (Figures 3 and 4).

Figures 1,2: Hand presentation post blister rupture.

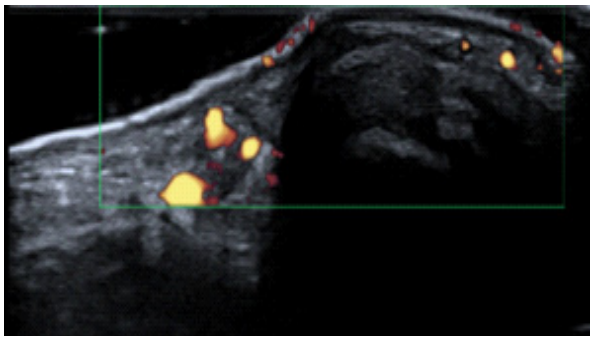

Figure 3: Ultrasound with Doppler of patient's left hand (both hands were scanned) showing no evidence of synovitis.

Figure 4: X-Ray of patient's hands showing no features of either inflammatory or degenerative arthropathy.

Management and outcome

Given the temporal proximity to Covid-19 vaccination, no other plausible cause for the observed pernio-like reaction was identified other than exposure to AZD1222. The lesions gradually improved and spontaneously resolved in April 2021 without any specific intervention. Notably, the patient did not experience a recurrence of the reaction following subsequent doses of AZD1222, a Moderna mRNA-1273 booster, or during an episode of acute symptomatic SARS-Cov-2 infection in January 2022.

Discussion

Covid-Toe, a condition characterized by pernio-like lesions on the toes following Covid-19 mRNA vaccination. Despite case reports and exploratory research, the exact cause of this reaction is not fully understood. However, several theories have been proposed to explain its development [4-8].

Vaccine-induced type I interferonopathy

Type I interferons play a crucial role in the body's immune response to viral infections. SARS-CoV-2 infection may lead to abnormal or excessive production of interferon, leading to immune system dysfunction [4,5]. According to this theory, the Covid-19 vaccine might also trigger an abnormal interferon response in some individuals, which could contribute to the development of Covid-Toe. Our patient's lack of reaction during a subsequent SARS-CoV-2 infection may support this theory. Additionally, there has been documented exacerbation of the reaction following Rituximab infusions which suggests an immune-mediated process [9].

Circulating vaccine-induced spike glycoprotein

The spike glycoprotein is a part of the SARS-CoV-2 virus responsible for facilitating viral entry into human cells. The Covid-19 vaccines typically contain the genetic information (mRNA) to produce this spike glycoprotein, which then triggers an immune response to prepare the body to fight the actual virus [6]. The theory suggests that in some cases, the circulating spike glycoprotein produced after vaccination might interact with the immune system in a way that leads to the manifestation of Covid-Toe. However, our patient's lack of reaction to the second AZD1222 dose, despite low anti-SARS-CoV-2 spike antibody levels, challenges this hypothesis.

Both theories suggest that Covid-Toe is likely a consequence of patient immune activation by either the virus or its vaccine, rather than a direct result of active infection.

Conclusion

This detailed case report presents a self-limiting pernio-like 'Covid-Toe' reaction in a renal transplant patient following the Oxford-AstraZeneca Covid-19 vaccine. The underlying mechanism of this reaction remains uncertain and requires further investigation to better understand its pathophysiology.

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