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Title: COVID-19 vaccines and the skin: The landscape of cutaneous vaccine reactions worldwide

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Introduction

As mass vaccinations for COVID-19 are underway and more vaccines are approved, it is increasingly important for dermatologists to recognize potential cutaneous adverse reactions of COVID vaccination. As of April 15, 2021, there are 11 approved COVID-19 vaccines with published clinical trial data. The most common cutaneous reactions reported in clinical trials involve local injection site reactions. Up to 88% of subjects experienced mild to moderate injection site pain that typically resolved within 24-48 hours after onset. Erythema, swelling, induration and itch were less common and reported in up to 20%, 15%, 25% and 35% of subjects, respectively. The trial data, however, is limited. There is frequently a lack of details on other types of skin reactions, which were often categorized as "unspecified rash". We aim to understand the landscape of dermatological side effects from COVID-19 vaccines in real-world settings.

Material and Methods

We reviewed published case reports, cross-sectional studies, cohort studies, and other observational studies reporting cutaneous reactions after COVID-19 vaccination, published between October 15, 2020 to March 24, 2021. We extracted the type of skin reaction, timing of onset, and demographics of affected individuals.

Results

We identified 20 observational studies, including two large studies of local and international registries of vaccine-related skin manifestations, eight case series and 10 case reports. While the most common adverse cutaneous reactions in clinical trials were local injection site reactions, in real world observational studies, delayed large local reactions were the most commonly reported skin side effect. Across six observational studies of 1307 cases, 350 patients (27%) experienced at least one episode of these delayed reactions, with a typical onset of eight days or more after vaccination. Of these 350 patients, 33.4% received the BNT162b2 vaccine and 66.6% received the mRNA-1273 vaccine. Women younger than 65 years of age composed the majority of these reactions. The morphology of delayed large local reactions ranged from erythematous targetoid patches to large plaques ranging from 5 cm to 19.5 cm in diameter. Most were mild and transient and did not necessitate treatment. In a study of 414 COVID-19 dermatology registry cases, local injection site reactions were the second most common. Other cutaneous reactions in the non-trial literature included morbilliform rashes (49% from the BNT162b2 vaccine, 51% from the mRNA-1273 vaccine), urticaria (55% from the BNT162b2 vaccine, 45% from the mRNA-1273 vaccine), delayed inflammatory reactions to dermal hyaluronic acid fillers (27% from the BNT162b2 vaccine, 73% from mRNA-1273 vaccine), pernio/chilblains (60% from BNT162b2 vaccine, 40% from mRNA-1273 vaccine) and varicella zoster (50% from BNT162b2 vaccine, 50% from mRNA-1273 vaccine). Herpes simplex reactivations, erythema multiforme, erythromelalgia and pityriasis rosea were also reported.

Discussion

Over 1 billion COVID-19 vaccine doses have been administered worldwide as of May 2021. As vaccinations scale up, dermatologists must remain aware of the various cutaneous reactions in real-world settings, as clinical trial data are limited with regards to the characterization of cutaneous reactions to COVID-19 vaccines. Given that the COVID-19 vaccine frontier is evolving rapidly, understanding the landscape of cutaneous manifestations to these vaccines is key to patient counseling.

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