

COVID-19 Vaccine Reactions in Dermatology: “Filling” in the Gaps

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As we marked the 1-year anniversary of the COVID-19 pandemic, nearly 100 million Americans had received their first dose of the COVID-19 vaccine, heralding some sense of relief and enabling us to envision a return to something resembling life before lockdown.¹ Amid these breakthroughs and vaccination campaigns forging ahead worldwide, we saw new questions and problems arise. Vaccine hesitancy was already an issue in many segments of society where misinformation and mistrust of the medical establishment have served as barriers to the progress of public health. Once reports of adverse reactions following COVID-19 vaccination—such as those linked to use of facial fillers—made news headlines, many in the dermatology community began facing inquiries from patients questioning if they should wait to receive the vaccine or skip it entirely. As dermatologists, we must be informed and prepared to address these situations, to manage adverse reactions when they arise, and to encourage and promote vaccination during this critical time for public health in our society.

Cutaneous Vaccine Reactions and Facial Fillers

As public COVID-19 vaccinations move forward, dermatologic side effects, which were first noted during clinical trials, have received amplified attention, despite the fact that these cutaneous reactions—including localized injection-site redness and swelling, generalized urticarial and morbilliform eruptions, and even facial filler reactions—have been reported as relatively minor and self-limited.² The excipient polyethylene glycol has been suspected as a possible etiology of vaccine-related allergic and hypersensitivity reactions, suggesting care be taken in those who are patch-test positive or have a history of allergy

to polyethylene glycol-containing products (eg, penicillin, laxatives, makeup, certain dermal fillers).^{2,3} Although rare, facial and lip swelling reactions in those with a prior history of facial fillers in COVID-19 vaccine trials have drawn particular public concern and potential vaccine hesitancy given that more than 2.7 million Americans seek treatment with dermal fillers annually. There has been continued demand for these treatments during the pandemic, particularly due to aesthetic sensitivity surrounding video conferencing.⁴

Release of trial data from the Moderna COVID-19 vaccine prompted a discourse around safety and recommended protocols for filler procedures in the community of aesthetic medicine, as 3 participants in the experimental arm—all of whom had a history of treatment with facial filler injections—were reported to have facial or lip swelling shortly following vaccination. Two of these cases were considered to be serious adverse events due to extensive facial swelling, with the participants having received filler injections 6 months and 2 weeks prior to vaccination, respectively.⁵ A third participant experienced lip swelling only, which according to the US Food and Drug Administration briefing document was considered “medically significant” but not a serious adverse event, with unknown timing of the most recent filler injection. In all cases, symptom onset began 1 or 2 days following vaccination, and all resolved with either no or minimal intervention.⁶ The US Food and Drug Administration briefing document does not detail which type of fillers each participant had received, but subsequent reports indicated hyaluronic acid (HA) fillers. Of note, one patient in the placebo arm of the trial also developed progressive periorbital and facial

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edema in the setting of known filler injections performed 5 weeks prior, requiring treatment with corticosteroids and barring her from receiving a second injection in the trial.⁷

After public vaccination started, additional reports have emerged of facial edema occurring following administration of both the Pfizer and Moderna COVID-19 vaccines.^{2,8,9} In one series, 4 cases of facial swelling were reported in patients who had HA filler placed more than 1 year prior to vaccination.⁹ The first patient, who had a history of HA fillers in the temples and cheeks, developed moderate periorbital swelling 2 days following her second dose of the Pfizer vaccine. Another patient who had received a series of filler injections over the last 3 years experienced facial swelling 24 hours after her second dose of the Moderna vaccine and also reported a similar reaction in the past following an upper respiratory tract infection. The third patient developed perioral and infra-orbital edema 18 hours after her first dose of the Moderna vaccine. The fourth patient developed inflammation in filler-treated areas 10 days after the first dose of the Pfizer vaccine and notably had a history of filler reaction to an unknown trigger in 2019 that was treated with hyaluronidase, intralesional steroids, and 5-fluorouracil. All cases of facial edema reportedly resolved.⁹

The observed adverse events have been proposed as delayed-type hypersensitivity reactions (DTRs) to facial fillers and are suspected to be triggered by the COVID-19 spike protein and subsequent immunogenic response. This reaction is not unique to the COVID-19 vaccines; in fact, many inflammatory stimuli such as sinus infections, flulike illnesses, facial injury, dental procedures, and exposure to certain medications and chemotherapeutics have triggered DTRs in filler patients, especially in those with genetic or immunologic risk factors including certain human leukocyte antigen subtypes or autoimmune disorders.³

Counseling Patients and Reducing Risks

As reports of DTRs to facial fillers after COVID-19 vaccination continue to emerge, it is not surprising that patients may become confused by potential side effects and postpone vaccination as a result. This evolving situation has called upon aesthetic physicians to adapt our practice and prepare our patients. Most importantly, we must continue to follow the data and integrate evidence-based COVID-19 vaccine-related counseling into our office visits. It is paramount to encourage vaccination and inform patients that these rare adverse events are both temporary and treatable. Given the currently available data, patients with a history of treatment with dermal fillers should not be discouraged from receiving the vaccine; however, we may provide suggestions to lessen the likelihood of adverse reactions and ease patient concerns. For example, it may be helpful to consider a time frame between vaccination and filler procedures that is longer than 2 weeks, just as would be advised for those having

dental procedures or with recent infections, and potentially longer windows for those with risk factors such as prior sensitivity to dermal fillers, autoimmune disorders, or those on immunomodulatory medications. Dilution of fillers with saline or lidocaine or use of non-HA fillers also may be suggested around the time of vaccination to mitigate the risk of DTRs.³

Managing Vaccine Reactions

If facial swelling does occur despite these precautions and lasts longer than 48 hours, treatment with antihistamines, steroids, and/or hyaluronidase has been successful in vaccine trial and posttrial patients, both alone or in combination, and are likely to resolve edema promptly without altering the effectiveness of the vaccine.^{3,5,9} Angiotensin-converting enzyme inhibitors such as lisinopril more recently have been recommended for treatment of facial edema following COVID-19 vaccination,⁹ but questions remain regarding the true efficacy in this scenario given that the majority of swelling reactions resolve without this treatment. Additionally, there were no controls to indicate treatment with the angiotensin-converting enzyme inhibitor demonstrated an actual impact. Dermatologists generally are wary of adding medications of questionable utility that are associated with potential side effects and drug reactions, given that we often are tasked with managing the consequences of such mistakes. Thus, to avoid additional harm in the setting of insufficient evidence, as was seen following widespread use of hydroxychloroquine at the outset of the COVID-19 pandemic, well-structured studies are required before such interventions can be recommended.

If symptoms arise following the first vaccine injection, they can be managed if needed while patients are reassured and advised to obtain their second dose, with pretreatment considerations including antihistamines and instruction to present to the emergency department if a more severe reaction is suspected.² In a larger sense, we also can contribute to the collective knowledge, growth, and preparedness of the medical community by reporting cases of adverse events to vaccine reporting systems and registries, such as the US Department of Health and Human Services' Vaccine Adverse Event Reporting System, the Centers for Disease Control and Prevention's V-Safe After Vaccination Health Checker, and the American Academy of Dermatology's COVID-19 Dermatology Registry.

Final Thoughts

As dermatologists, we now find ourselves in the familiar role of balancing the aesthetic goals of our patients with our primary mission of public health and safety at a time when their health and well-being is particularly vulnerable. Adverse reactions will continue to occur as larger segments of the world's population become vaccinated. Meanwhile, we must continue to manage symptoms, dispel myths, emphasize that any dermatologic risk posed by

the COVID-19 vaccines is far outweighed by the benefits of immunization, and promote health and education, looking ahead to life beyond the pandemic.

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