

## COVID-19 vaccines and filler reactions: Should it be considered as a concern?

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**COVID-19 vaccines and filler reactions: Should it be considered as a concern?**

**Abstract:**

Any implant or external material used in the body tissues can potentially be followed by autoimmune or inflammatory reactions. With the global vaccination program against COVID-19, reports of tissue filler reactions would be increasingly demonstrated. Although the end of pandemic was announced, the necessity of continuing COVID vaccination in future mandates gathering data regarding safety of vaccines. Here in, we summarized the data regarding COVID vaccination and filler reactions and discussed its etiopathogenesis, management and importance.

**Key Words:** COVID-19 vaccines; filler reaction; Hyaluronic acid; Immunologic reactions

**Introduction:**

Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, abundant cases of dermatologic reactions have been reported in the settings of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection which many of them have been the result of exacerbation of previously recognized dermatoses, while the new-onset adverse events have not been uncommon(1-2).

With progresses made in cosmetic dermatology and surgery, a great majority of the world population are being interested in cosmetic and aesthetic procedures, particularly minimally invasive ones. Liposuction, dermal filler injection, platelet rich plasma treatment (PRP), mesotherapy, microdermabrasion, ablative resurfacing lasers, and botulinum toxin injection are among the related procedures. The COVID -19 pandemic has led to an increased rate of facial procedures as people spend hours watching their virtual images and evaluate themselves through video-conferencing. On the other hand, SARS-CoV-2 infection and its associated vaccine can be triggers for allergic and inflammatory reactions in previously-treated areas of the body, especially filler injected sites(3-6). With the global vaccination program against COVID-19, reports of tissue filler reactions would be increasingly demonstrated(7-8).

*Tissue filler reactions:*

Hyaluronic acid (HA) is a natural polysaccharide and the most commonly used dermal filler for tissue augmentation, due to its favorable safety profile and wide range of applications. In general, the more longer-lasting the HA fillers are, the higher would be the risk of dermal reactions(9-11).

In general, any implant or external material used in the body tissues can potentially be followed by autoimmune or inflammatory reactions. The early-onset or immediate-type reactions are actually type 1 hypersensitivity reactions mediated by immunoglobulin E (IgE) and usually take place within minutes or hours after filler injection. The underlying mechanism include histamine release from mast cells and is manifested as urticaria, angioedema or anaphylaxis. However, pain, and pruritus, ecchymosis, surface nodules, HSV reactivation, and thromboembolic events are also common. The delayed-type reactions (DTRs) are mainly type 4 hypersensitivity reactions, which occur later than 2–4 weeks, even years, after procedure and are mediated by macrophage and T-cell interactions. These reactions can present with local swelling, redness, dyspigmentation, scarring or granuloma formation. Systemic inflammatory responses of any cause, such as flu-like syndrome, facial trauma, consuming certain medications and chemotherapeutic agents or vaccination, can trigger LMW HA degradation and give rise to DTRs but they are usually triggered by dental procedures, inappropriate injection techniques, low-quality materials or mixing different fillers(12-17). Another possible mechanism might be the fact that tissue fillers might serve as adjuvants that increase antigen-specific responses; this can be associated with genetic predisposition(18).

HMW HA has anti-inflammatory effects while LMW HA has pro-inflammatory effects.

Therefore, the Vycross technology which is switched from the 100% HMW HA filler to a 10%

HMW and a 90% LMW HA filler has a higher probability to induce allergic reactions(19-20). It is interesting to know that HA fillers which are cross-linked with PEG, instead of BDDE, are associated with less allergic and anaphylactic AEs due to their less potent immunostimulatory effects(21).

### *Vaccine induced filler reactions*

COVID-19 vaccines have been associated with a wide range of allergic and anaphylactic reactions, some of which are serious and of medical significance (22). Nevertheless, facial filler reactions are being increasingly reported in this settings(23-25). Previously, dermal filler reactions had been reported after influenza and zoster vaccines(26-27).

As has previously been mentioned, vaccines can precipitate tardive adverse events in the filler injected tissues due to their immunostimulant effects. One possible mechanism for this phenomenon is related to autoimmune/inflammatory syndrome induced by adjuvants (ASIA), which explains most of the post-vaccination phenomena; it is believed that polyethylene glycol (PEG) is the responsible vaccine ingredient for these adverse events (AEs)(28-29). The interaction between the vaccine's spike protein and angiotensin converting enzyme (ACE) 2 receptors can trigger a CD8+ T-cell mediated response leading to DTRs(33). This is comparable to filler reactions following being infected with SARS-CoV-2, which is believed to be the result of reaction to the viral spike protein and immunogenic response(30-32).

The Advisory Committee on Immunization Practices (ACIP) and the Vaccine Adverse Event Reporting system (VAERS) have reported several local reactions in vaccinated ones who had undergone cosmetic filler injections(33). Most of the reactions took place within 10 days after

vaccination and were manifested as orofacial swelling, bilateral tear trough area swelling, progressive periorbital edema, and lip angioedema(30, 34-35). However, the causal relationship is still unclear. Some of them had a history of filler reaction after receiving routine vaccines like influenza or following an upper respiratory tract infection. Most of filler reactions have occurred following receiving m-RNA COVID-19 vaccines, that could be the result of hypersensitivity reaction to PEG or interaction with SARS-CoV-2 spike glycoprotein that are encoded by the vaccine(36-37). However, other vaccine platforms, including inactivated virus and vector-based ones, have also given rise to delayed dermal filler reactions(38-39).

#### *Dermal filler reactions management*

Most cases of filler reactions following COVID-19 vaccination are self-limiting and subside with no or minimal intervention(40). However, in prolonged or severe cases, we should think therapeutic measures to restrict the reactions. It is interesting to know that antihistamines are of no use in managing DTRs, although many of the aforementioned events had resolved by mere antihistamine use. Rather, corticosteroids, systemic or intralesional, are believed to be the main therapeutic solution for these phenomena. Other potential therapies include massaging, saline or water dilution, oral antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), ACE inhibitors such as Lisinopril, colchicine, 5-fluorouracil and methotrexate(26, 41-43). Rare cases have been reported that had not responded to medical therapy and necessitated surgical intervention like curettage, incision, and drainage, and granuloma or nodule removal(44, 45).

It should be kept in mind that since tissue fillers are foreign bodies, a biofilm-related infectious process should always be suspected in intractable cases. Hence, blood testing for

inflammatory biomarkers and taking cultures and sometimes biopsies should be considered if response to treatment is not demonstrated(46-47).

### *Vaccine-induced dermal filler reaction prevention*

As COVID-19 vaccination program is being held in large scale, the increasing rate of allergic and inflammatory reactions is inevitable; accordingly, since interest in cosmetic procedures are being increasingly demonstrated, measures should be thought out to prevent associated inflammatory and allergic reactions.

On the other hand, allergic and inflammatory reactions to facial fillers following COVID-19 vaccination can increase hesitancy to receive vaccines and this would be a challenge. In order to prevent vaccination hesitancy, patients should be counselled about the low risk of filler reactions following vaccination and it should be emphasized that these AEs, if ever occur, are usually short-lasting and treatable. Furthermore, it should be acknowledged that if filler reaction occurs following the first vaccine dose, they can receive the second dose with precautionary measures such as pretreating with antihistamines or corticosteroids. Moreover, protocols should be recommended for filler procedures in the field of aesthetic medicine in relationship with vaccination timing and dosing; since it takes up to 3 weeks for the peak immune response, some authorities advise not to undergo facial filler injection prior to SARS-CoV-2 vaccination up to at least 3-4 weeks after the last vaccine dose, in order to avoid AEs; however, there have been reports of vaccine-related filler reactions even in those who had undergone this cosmetic procedure 6 months to 1 year prior to vaccination(34, 43, 48-49). It is important to be more vigilant and give more space between vaccination and filler injection in individuals with a

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history of sensitivity to tissue fillers or those with autoimmune disorders or taking immunomodulatory/immunosuppressive agents. In addition, since PEG is probably the causative etiology of post-vaccination filler reactions, those individuals who have a history of allergy to PEG-containing products, such as penicillin and makeup, or are patch-test positive should be more cautiously cared after vaccination if undergone filler injections. Moreover, in those individuals tending to be vaccinated, dilution of tissue fillers with saline or lidocaine or utilizing non-HA fillers can lower the risk of vaccine-related filler reactions(14). In addition, in case of the presence of any infection or inflammation near the injection area, the cosmetic procedure should best be delayed(50)

### **Conclusion**

With the increasing rate of COVID-19 vaccination along with the high number of individuals undergoing aesthetic and cosmetic procedures, associated dermatologic reactions are inevitable and expectable. However, these complications should not lead to vaccine hesitancy; therefore, clinicians should first be aware of the potential vaccine-induced AEs and their management, reassure the population about the temporary nature of these reactions and encourage them to receive vaccines even they are intending to seek cosmetic procedures like tissue fillers.

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All the authors declare that there is no conflict of interest.

### **Data availability statement:**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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