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REVIEW ARTICLE

A systematic review on COVID-19 vaccination and cosmetic filler reactions: A focus on case studies and original articles

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Abstract

Background: Tissue fillers are among the most popular cosmetic procedures performed and notably, cases of filler reactions after COVID-19 vaccination have been reported.

Objective: The objective was to determine the characteristics of patients with filler reaction after COVID-19 vaccination and address several considerations that have to be taken into practice.

Methods: A PRISMA compliant systematic search was conducted in Scopus, Web of Science, and PubMed/MEDLINE databases for articles published from inception up to October 21, 2021.

Results: Out of 106 initially retrieved articles, four of them were included in our study, and a total number of 13 cases were analyzed. In this study, we found that all of the patients who developed delayed-type reaction (DTR) following COVID-19 vaccination were middle-aged women without any known history of allergy to foods or drugs. All patients had a history of hyaluronic acid (HA) filler injection in their head and neck and demonstrated symptoms particularly swelling, from <1 day up to 10 days after the first or second doses of vaccines. Lisinopril, hyaluronidase, and corticosteroids seemed to have good results in management.

Conclusion: Although rare, DTR to fillers after COVID-19 vaccination can happen. Physicians should be aware of the pathogenesis and management of this phenomenon.

KEYWORDS
augmentation, cosmetic, delayed-type reaction, Hyaluronic Acid fillers, Non-Hyaluronic Acid fillers

Abbreviations: DTR, developed delayed-type reaction; HA, hyaluronic acid; CaHA, calcium hydroxyapatite; PMMA, Polymethylmethacrylate; PLLA, Poly-L-lactic acid; IgE, immunoglobulin E; LNP, lipid nanoparticle; PEG, polyethylene glycol.

Both Yasamin Kalantari and Zeinab Aryanian contributed equally preparing this article.

1 | INTRODUCTION

Tissue fillers are among the most popular non-surgical aesthetic procedures worldwide and are currently being used for facial and non-facial areas.[1,2] There exist different types of tissue fillers such as hyaluronic acid (HA), calcium hydroxyapatite (CaHA), polymethylmethacrylate (PMMA), Poly-L-lactic acid (PLLA), and collagen-based products. It is believed that an ideal dermal filler should be safe, non-allergenic, non-immunogenic, non-carcinogenic, non-migratory, cost-effective, and stable for the desired time within the target tissue. However, various adverse reactions associated with dermal fillers have been reported.[3]

Immediate hypersensitivity reactions also known as type 1 hypersensitivity reactions, with an incidence rate of 0.8% for HA fillers, are immunoglobulin E (IgE)-mediated and can happen rapidly after the filler injection within minutes or hours. These types of reactions result from the histamine release from mast cells and can present with urticaria, angioedema, and dangerously, anaphylaxis. Delayed-type hypersensitivity reactions (DTR) also known as type 4 hypersensitivity reactions, with an incidence rate of 0.42%, can occur 24 h, weeks, or even years after the injection. DTRs result from macrophage and T-cell interactions and can manifest as swelling, erythema, or granuloma formations at the site of injection.[3,4] While the exact mechanisms for DTRs following the filler injection still remain unclear, various factors such as infections, filler properties, trauma, vaccinations, and injection technique are reported to be responsible.[5]

With the emergence of the coronavirus pandemic in 2019 caused by the SARS-CoV-2 virus (COVID-19 virus), numerous vaccines came available for individuals globally and the number of people who are getting vaccinated against COVID-19 is increasing each day.[6] However, various adverse effects associated with different COVID-19 vaccines have been reported and notably, cases of tissue filler reactions after COVID-19 vaccination have been observed in practice.

Herein, we aimed to give a comprehensive systematic review of the reported cases of cosmetic filler reactions following COVID-19 vaccination in order to address several considerations that have to be taken into practice and also, to give better guidance for people who are seeking both COVID-19 vaccines and cosmetic fillers.

2 | MATERIAL AND METHOD

2.1 | Protocol and registration

This study was done according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.

2.2 | Information databases

By using the related keywords, a systematic search was done in PubMed/MEDLINE http://ncbi.nlm.nih.gov/pubmed), Scopus (http://www.scopus.com), and Web of Science (http://webofknowledge.com) for articles published from the inception until October 21, 2021.

2.3 | Search strategy

In order to conduct a systematic search, we used the following search keywords in our selected databases:

((((((Post) OR (After)) OR (Following)) AND (((COVID-19) OR (coronavirus)) OR (SARS-CoV-2 virus))) AND (((vaccination) OR (immunization)) OR (inoculation))) AND (((cosmetic filler) OR (Hyaluronic acid)) OR (Dermal filler))) AND ((reaction) OR (hypersensitivity)).

2.4 | Inclusion criteria

Inclusion criteria comprised all original studies presenting cases who manifested filler reactions after getting COVID-19 vaccines. We only included original human studies that were written in the English language. Exclusion criteria were non-English studies, review articles, and articles that did not present a case of post-COVID-19 vaccine filler reaction.

2.5 | Study selection

A total of 106 articles obtained from our systematic search were imported to Endnote X8 (Clarivate Analytics, Philadelphia). After removing the duplicates, we screened the articles based on their titles and abstracts and selected eligible articles for the full-text screening phase. Afterward, we read the full texts of the selected articles that met our inclusion criteria and we extracted data.

3 | RESULTS

One case series and three case reports were enrolled in our study.[7–10] Furthermore, we found three additional cases of DTR to filler injected sites which were reported in the Moderna FDA Briefing document.[11] Eventually, a total of 13 fully described reported cases of filler reaction following COVID-19 vaccination were found.

Also, we found a registry-based study of 414 cases regarding cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination.[12] In this article, nine reports of swelling at the site of cosmetic fillers were mentioned. Three out of these nine patients demonstrated symptoms after the first dose of the Moderna vaccine, and five of them had their symptoms after the second dose of the Moderna vaccine. Moreover, one of these nine patients showed a filler reaction after getting the second dose of the Pfizer vaccine, and notably, no cases of filler reaction after the first dose of the Pfizer vaccine were observed. These nine patients were not described in detail and hence, no more data could be extracted.

The mean age of the reviewed cases was 44.61 ± 12.38 (range 29–76) years and all of the patients were female. Six (46.15%) patients developed symptoms after injecting the Pfizer vaccine and 7 (53.86%) of them demonstrated DTR after the Moderna vaccine injection. The mean time interval of filler injection in patients that reacted to the vaccine was 433.33 ± 323.11 (range 13–1095) days. Of all the cases that had reported the type of the filler injected, all of them had a history of HA filler injection. The mean time interval between vaccine injection and the reaction to fillers was 2.67 ± 2.76 days.

In Table 1, we have summarized all data associated with these patients in detail (Table 1).

4 | DISCUSSION

With the emergence of the COVID-19 pandemic and the subsequent global vaccination against this virus, many adverse effects associated with COVID-19 vaccines were reported. Tissue fillers are among the most popular cosmetic procedures performed globally and of note, cases of filler reactions after COVID-19 vaccination have been observed in practice.

In our study, all patients experiencing filler reactions following COVID-19 vaccination had a history of HA fillers injections. The global incidence of DTR reaction after HA injection is reported to be 0.8%.[4] HA is a natural polysaccharide that is found in high amounts in connective tissues forming an essential part of the extracellular matrix. HA fillers are the most frequently used fillers for soft-tissue augmentation which might be due to their biocompatibility and ease of reversibility by hyaluronidase.[13] HA-based fillers are temporary and they can last in the tissue from 3 to 12 months or even more which can vary in different patients.[9] Interestingly, in a study by Master et al. using magnetic resonance imaging, it was found that HA fillers can be detected as long as 12 years.[14] Also, it is believed that longer lasting HA fillers might increase the risk of inflammation and delayed-type inflammatory response (DIR).[9]

Complications associated with tissue fillers injection can be divided into two groups: early-onset and delayed onset adverse effects. Early-onset complications which occur up to several days post treatment, contain injection site reactions such as edema, pain, erythema, itching, and ecchymosis, hypersensitivity reactions, infections such as herpes simplex virus infections, abscess or cellulitis, and mycobacterial infections, Tyndall effect, surface irregularities and nodules, vascular occlusions such as local tissue necrosis, and embolization of blood vessels. Delayed onset adverse effects that occur days to years post procedure contain biofilms and infections, foreign body granuloma, dyspigmentations, scarring, migration of the implants, erythema, edema, pain, nodules, and induration.[15,16]

The exact pathogenesis of DIR following filler injection remains unclear but is believed that some triggering factors such as infection, active sinusitis, using products with low quality, combining different fillers, using inappropriate techniques, and dental procedures can be associated with DIR development. Moreover, DIR following filler injection is thought to be related to the amount of filler injected as well as the filler technique (bullous versus non-bullous).[7] Generally, HA fillers begin to degrade in 3–5 months post injection. It is also postulated that DIR is caused by catabolism of filler which forms short-chain and low-molecular-weight (LMW) HA molecules and these new unknown antigens can trigger the immune response activating CD44 probably when accompanied by other triggering factors, such as biofilms.[7] Moreover, HA fillers containing low-molecular weight-degraded products are generally associated with higher pro-inflammatory activities.[8] Another theory is that fillers might enhance the antigen-specific immune response as adjuvants without triggering one on their own rather than activating T cells directly.[4] In this regard, Decates et al. suggest that patients with human leukocyte antigen subtypes B*08 or DRB1*03 have an increased risk of DIR s and adverse reactions associated with dermal fillers.[17]

Several cases of DTR to fillers have been reported after vaccinations against influenza, shingles, and of our interest COVID-19.[8,18] In this vein, in a study done by Munavalli et al., it was proposed that COVID-19 spike protein acts as a triggering factor in forming DIRs following COVID-19 vaccination. Spike protein interaction with angiotensin-converting enzyme (ACE2) receptors causes a pro-inflammatory TH1 response and promotes a CD8+ T-cell-mediated reaction resulting in DIR formation.[8]

While DIR does not involve extensive soft tissue, it can easily be misdiagnosed as edema, facial edema, or angioedema due to the presence of acute-onset swelling on the skin and lips.[8] In this regard, Munavalli et. al presented a case of infraorbital swelling and perioral angioedema after receiving the COVID-19 vaccine.[8] As well, the Moderna FDA Briefing document reported a case of lip swelling in a 29-year-old woman with a history of lip filler placement after Moderna vaccine injection. The reaction was classified as medically significant angioedema.[11]

Regarding the presented symptoms, none of the reported cases demonstrated urticarial lesions. Moreover, none of them developed cutaneous lesions on other parts of their bodies including their limbs or trunks.

In our study, no case had a known history of allergy to drugs or foods. In terms of past medical histories, two of our reviewed cases had a prior history of reactions to dermal fillers. One of these patients had manifested edema after an upper respiratory tract infection in filler-treated areas which had lasted for 1 week and had been successfully treated with antihistamines in addition to oral prednisone. The other case had a history of dermal filler reaction in her cheeks 1 year after the filler injection which was controlled with hyaluronidase and intralesional corticosteroid with 5-fluorouracil. [7] Furthermore, one case had a past medical history of idiopathic urticaria which was well-tolerated with daily cetirizine. It is worth noting that this patient did not develop urticarial lesions in response to the COVID-19 vaccine injection.[7]

TABLE 1 Characteristics of the reviewed cases

First author	Title and year of publication	Type of study	Age	Gender	Past medical or allergic history	Symptom
Muna valli et al.	Oral angiotensin-converting enzyme inhibitors for treatment of delayed inflammatory reaction to dermal hyaluronic acid fillers following COVID-19 vaccination-a model for inhibition of angiotensin IIeinduced cutaneous inflammation (2021)	Case series	43	Woman	Idiopathic urticarial which was well controlled by daily cetirizine (10 mg)	Moderate swelling in the periorbital area, which extended to involve the medial and lateral cheeks
Muna valli et al.	Oral angiotensin-converting enzyme inhibitors for treatment of delayed inflammatory reaction to dermal hyaluronic acid fillers following COVID-19 vaccination-a model for inhibition of angiotensin IIeinduced cutaneous inflammation (2021)	Case series	31	Woman	History of reaction to filler with mild prolong edema in the filler treatment areas lasting more than a week following an upper respiratory tract infection, which was treated with antihistamines and oral prednisone	Swelling of the upper mucosal lip, which progressed to involve the left earlobe and bilateral zygomas
Muna valli et al.	Oral angiotensin-converting enzyme inhibitors for treatment of delayed inflammatory reaction to dermal hyaluronic acid fillers following COVID-19 vaccination-a model for inhibition of angiotensin IIeinduced cutaneous inflammation (2021)	Case series	36	Woman	None	Worsening bilateral infraorbital and perioral edema beginning 18 hours after vaccination. By 48 hours after vaccination, the right infraorbital edema worsened, making it difficult to open the right eye. Subsequently, edema worsened in the upper lip and swelling and inflammation expanded to include the mid-cheeks

Cosmetic filler	Filler area	Interval between filler injection and first dose vaccine injection	Vaccine name	First or second dose of vaccine responsible for reaction	Interval between the vaccine injection and symptoms	Management	Time to complete recover
Hyaluronic acid	Temples	Approximately 2 years	Pfizer	Second	2 days	5 mg of lisinopril	Less than one day
Hyaluronic acid	lateral parts of the cheeks						
Hyaluronic acid	Lips	Almost 3 years	Moderna	Second	24 hours	5 mg of lisinopril, 48 hours after the vaccine dose, which had minimal effect on the swelling. The lisinopril dose was increased to 10 mg daily, and after 72 hours on the 10 mg daily dose, she returned back to baseline	72 hours
Hyaluronic acid	earlobes	26 months					
Hyaluronic acid	nasolabial folds	18 months					
Hyaluronic acid	bilateral malar cheeks	18 months					
Hyaluronic acid	nasolabial folds	6 months					
Hyaluronic acid	Bilateral tear troughs	13 months	Moderna	First	18 hours	Cetirizine (20 mg) did not provide relief. At this time, Cetirizine was stopped, all other drugs were stopped, and oral lisinopril 5 mg once daily was initiated.	24 hours
Hyaluronic acid	in the upper and lower part of the lips						

TABLE 1 (Continued)

First author	Title and year of publication	Type of study	Age	Gender	Past medical or allergic history	Symptom
Munavalli et al.	Oral angiotensin-converting enzyme inhibitors for the treatment of delayed inflammatory reaction to dermal hyaluronic acid fillers following COVID-19 vaccination-a model for inhibition of angiotensin IIeinduced cutaneous inflammation (2021)	Case series	76	Woman	She had a prior history of a filler reaction consisting of mild firmness and tenderness occurring 12 months after injection with hyaluronic acid in the cheeks in 2019, which responded to hyaluronidase and intralesional corticosteroid combined with 5-fluorouracil.	Filler-treated areas became inflamed, along with panfacial and periorbital swelling.
Munavalli et. al	"COVID-19/SARS-CoV-2 virus spike protein-related delayed inflammatory reaction to hyaluronic acid dermal fillers: a challenging clinical conundrum in diagnosis and treatment" (2021)	Case report	51	Woman	Pseudo membranous colitis	Facial edema, erythema and tenderness of the periorbital area and malar cheek, formation of painful indurated plaques and nodules
Munavalli et. al	"COVID-19/SARS-CoV-2 virus spike protein-related delayed inflammatory reaction to hyaluronic acid dermal fillers: a challenging clinical conundrum in diagnosis and treatment" (2021)	Case report	36	Woman	None	Increased tenderness in the right tear trough, unilateral infraorbital edema and perioral edema and angioedema which progressed to facial swelling

Cosmetic filler	Filler area	Interval between filler injection and first dose vaccine injection	Vaccine name	First or second dose of vaccine responsible for reaction	Interval between the vaccine injection and symptoms	Management	Time to complete recover
Hyaluronic acid	Cheeks	Not mentioned	Pfizer	First	10 days	Lisinopril (5 mg)	7 days
Hyaluronic acid	Earlobes, nasolabial folds, tear troughs, malar and mid cheeks, and upper/lower lips over the course of 18 months	5 weeks after the last filler injection to cheeks and lips	Moderna Phase III pivotal clinical trial (after the trial she was notified that she had received the placebo)	First	8 days	Recombinant and Bovine hyaluronidase, 60 mg Prednisone taper over 12 days, Doxycycline capsules 100 mg BID × 7 days Nitrofurantoin 100 mg BID × 7 days, Intralesional 5-fluorouracil, 10 mg hydroxyzine, sulfa methoxazole and trimethoprim	Six-weeks
Hyaluronic acid Hyaluronic acid	Bilateral tear troughs the upper and lower lip	18 months	Moderna	First	Less than 1 day	Certirizine, 5 mg of lisinopril	24 hours

TABLE 1 (Continued)

First author	Title and year of publication	Type of study	Age	Gender	Past medical or allergic history	Symptom
Munavalli et. al	"COVID-19/SARS-CoV-2 virus spike protein-related delayed inflammatory reaction to hyaluronic acid dermal fillers: a challenging clinical conundrum in diagnosis and treatment" (2021)	Case report	43	Woman	None	Mild tenderness underneath the right eye, followed hours later by swelling under the left eye
Michon	Hyaluronic acid soft-tissue filler delayed inflammatory reaction following COVID-19 vaccination – A case report (2021)	Case report	39	Woman	None	Tender, erythematous swelling at her left tear trough area
Michon	Hyaluronic acid soft-tissue filler delayed inflammatory reaction following COVID-19 vaccination – A case report (2021)	Case report	61	Woman	Intermittent benign vertigo	Intermittent facial swelling, left undereye swelling
Savva et al.	Hypersensitivity reaction to hyaluronic acid dermal filler after the Pfizer vaccination against SARS-CoV-2 virus	Case report	38	Woman	None	Small erythematous nodules on both upper and lower lips with mild pain mild tenderness on her upper lip and 2 days later a painful erythematous edema was developed on both the upper and lower lip
FDA	The Moderna FDA Briefing document	Brief Ing Docu ment	46	Woman	Not mentioned	Bilateral cheek swelling
FDA	The Moderna FDA Briefing document	Brief Ing Docu ment	51	Woman	Not mentioned	Bilateral facial swelling with the left side being more pronounced
FDA	The Moderna FDA Briefing document	Brief Ing Docu ment	29	Woman	Lip angioedema after receipt of an influenza vaccine in the past	Lip swelling, angioedema

All of the reviewed cases in our study developed symptoms after Pfizer or Moderna vaccine injections. In our study, we found a case of DTR in the filler injected areas after participating in Moderna Phase III pivotal clinical trial. This was a double-blinded, placebo-controlled trial, and saline was injected as the placebo since it usually does not trigger a biological response. Interestingly, after the trial, the revealed data showed that she had received the placebo vaccine. However, the exact cause of this DTR that she experienced was not defined.[8]

Cosmetic filler	Filler area	Interval between filler injection and first dose vaccine injection	Vaccine name	First or second dose of vaccine responsible for reaction	Interval between the vaccine injection and symptoms	Management	Time to complete recover
Not mentioned	Tear trough	2.5 years	Pfizer	Second	24 hours	Medrol dose pack	24 hours
Hyaluronic acid	Tear trough	6 months	Pfizer	First	2 days	Wait and watch	5 days
Hyaluronic acid	zygomatic arch	9 months	Pfizer	First	A few days later	hyaluronidase	1 day
Hyaluronic acid	the chin and jawline						
Hyaluronic acid	palpe-bromalar groove						
Hyaluronic acid	tear trough						
Hyaluronic acid	lips	1 month	Pfizer	First second	2 days 2 days	Wait and watch Methyl-prednisolone tab	7 days 5 days
Hyaluronic acid	Cheeks	5 months	Moderna Trial	Second	1 to 5 days	Diphenhydramine and methylprednisolone	Not mentioned
Hyaluronic acid	Cheeks	13 days	Moderna trial	Second	2 days	Prednisolone	Not mentioned
Not mentioned	lips	Unknown	Moderna trial	Not mentioned	2 days	Not mentioned	Not mentioned

All patients had a history of filler injection in the head and neck area and the interval time between the filler injection and the first dose of vaccine ranged between 1 month and 3 years. Patients developed symptoms after either the first or second dose of vaccines except for two cases that developed a filler reaction after both the first and the second doses of vaccines. In one case, the first reaction resolved spontaneously in 1 week without any medical intervention, which did not keep them away from injecting the

second dose of vaccine, but the latter reaction was treated with methylprednisolone.[10]

Data regarding the second dose of vaccine injection were not clearly mentioned in all cases who had developed reaction following the first dose of vaccine. As a result, a definite judgment cannot be made. In this regard, Munavalli et al reported a case of filler reaction following the first dose of the COVID vaccine. In that study, after 1 month, the second Moderna vaccine dose was administered. Two days before vaccination, lisinopril at a dose of 10 mg daily was started. Mild perioral and periorbital edema occurred but was noticeably less involved in comparison to that after the first dose. Residual swelling resolved completely 3 days after vaccination.[7]

The interval time between the vaccine injection and symptoms manifestations ranged from <1 day to up to 10 days.

Regarding the management of patients in our study, we found two cases that were cured without any intervention or medications. Notably, antihistamines are not beneficial in the management of DTR.[3,19,20] Steroids seem to be good options in the management of these patients with the recommended dose between 30 and 60 mg daily and tapering down over 5 days based on the patient's symptoms. Also, in some cases, hyaluronidase was used in order to dissolve the filler in the target tissue. In our study, we found cases of filler reactions following COVID-19 vaccination which were successfully treated with angiotensin-converting enzyme inhibitors (ACE-I). In this regard, Munavalli et al. postulated that COVID-19 mRNA vaccines have the ability to decrease the conversion of the pro-inflammatory angiotensin-II (ANGII) in the skin. As a result, the accumulation of ANGII provokes an inflammatory and immune response by activating CD8+ and TH1, respectively. Hence, ACE-Is such as lisinopril 10 mg for 3–5 days seem to be promising treatments for DIRs associated with COVID-19 vaccines, but more studies are needed in order to confirm the efficacy and safety of this treatment modality. All of the cases were resolved, and no cases of death were reported. In the reviewed cases, biopsies and histological analysis were not performed, but they can be conducted for further evaluation in cases with no response to treatment.

In our study, all cases developed reactions after injection of m-RNA COVID-19 vaccines (Pfizer and Moderna). M-RNA COVID-19 vaccines are synthetic molecules of the RNA sequence that encodes the viral spike (S) glycoprotein of SARS-CoV-2.[21] Both mRNA vaccines BNT162b2 and mRNA-1273 contain lipid nanoparticle (LNP) and polyethylene glycol-2000 (PEG-2000).[22] Previous studies have suggested that hypersensitivity and allergic reactions to m-RNA vaccines might be related to a hypersensitivity response to PEG.[23] Meanwhile, adenovirus vector vaccines such as AstraZeneca ChAdOx1 contain the gene that encodes the glycoprotein spike (S) antigen of SARS-CoV-2 and contain polysorbate-80.[22] However, polysorbate-80 might principally be responsible for hypersensitivity reactions, but so far, there have been no reports of allergic reactions, other than a case of anaphylaxis in a single study.[22] Until the time of our systematic search, only cases of filler reaction following m-RNA vaccines were reported. However, due to the small sample size, a comprehensive and definite judgment cannot be made based on our results. More cases of such reaction should be reported, so more reliable judgment can be made.

In a global survey done by Gotkin et al., the information of 106 survey participants from 18 different countries was evaluated. The authors of that study concluded that there is not an increased risk of developing adverse reactions following soft-tissue filler injections associated with the COVID-19 vaccines in comparison to other previously described triggers or the default risk following soft-tissue filler injections.[24]

To the best of our knowledge, this is the first systematic review regarding cases of filler reaction following COVID-19 vaccinations. Due to the small number of reported cases, a comprehensive and reliable judgment cannot be made. In our study, we found that all of the patients who developed DTR following COVID-19 vaccination were middle-aged women and all of them developed reactions to HA fillers. This finding might be due to fact that HA fillers are the most commonly used fillers, but it should be in mind to use these fillers more cautiously in those who are seeking both cosmetic fillers and COVID-19 vaccines. Also, longer lasting fillers have a higher risk of DTR, and it is better to choose other fillers to avoid reactions. Since all of our cases developed a reaction after Pfizer or Moderna vaccine injections, these vaccines should be used more cautiously in patients with cosmetic fillers. Additionally, two of our reviewed cases had a previous history of reaction to dermal fillers and hence, more caution should be exercised in this group of patients. It is worth mentioning that the authors of this manuscript have broadly worked in COVID-19 and dermatologic fields. [25–33]

Practitioners should be aware of the side effects associated with different COVID-19 vaccines and they should be able to manage them. It is pivotal to inform patients seeking tissue fillers and those who have already injected fillers about the possible risk of DIRs following COVID-19 vaccinations. Furthermore, we recommend that in future vaccine trials, a complete history of tissue filler injection to be taken. Additionally, we recommend more studies with a large number of patients in order to better understand the exact pathogenesis, mechanisms, treatment, and prevention of this phenomenon.

AUTHORS' CONTRIBUTIONS

YK. performed the research. AG, ZA. designed the research study. SMSM, SA contributed essential reagents or tools. YK, PH. analyzed the data. YK, AG, ZA, SMSM, SA. wrote the paper. All authors have read and approved the final manuscript.

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CONFLICT OF INTERESTS

None to declare.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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