

Delayed Type Hypersensitivity Towards Cosmetic Hyaluronic Acid Dermal Filler: A Case Report

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Abstract

At the present time, the most common nonsurgical procedure in the aesthetic field are hyaluronic acid (HA) dermal fillers. It is appealing to many injectors as they are reversible with hyaluronidase and are generally well tolerated. However, there are several case studies which report hypersensitive reactions weeks after HA filler injections. The exact pathophysiology is inconclusive, but many agree that patients' biological factors, injection technique and variations in the properties of the fillers could potentially play a role. In this case report, we discuss our encounter with a 60-year-old Chinese lady who presented to us two weeks after lower face hyaluronic acid filler injections with generalised pruritic facial rash and oedema. A clinical diagnosis of atopic dermatitis was made and the symptoms resolved with systemic corticosteroids.

Keywords: Delayed hypersensitivity, Hyaluronic acid dermal fillers, Dermal filler injections

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In the aesthetic field, the most common nonsurgical procedure is dermal filler injections [1]. Dermal fillers, especially hyaluronic acid dermal fillers, are popular due to their ease of administration and ability to deliver the desired aesthetic benefit. There are four categories of dermal fillers according to FDA based on composition:

1. Hyaluronic acid which usually lasts between 6-12 months.
2. Calcium Hydroxylapatite – is a mineral found in bones. This material lasts up to 18 months.
3. Poly-L-lactic acid is a biodegradable synthetic material. These fillers may last up to two years.
4. Polymethylmethacrylate beads (PMMA) are the only filler that can't be absorbed by the body. They're only used around the mouth and the results are permanent.

Besides that, they can also be classified as temporary, semi-permanent, or permanent depending on the duration of time the filler remains in the tissue [2].

There are risks involved with the use of dermal fillers, most side effects reported in clinical trials and post-market surveillance occur shortly after injection and subside within a few weeks. In some cases, side effects may emerge weeks, months, or years later. Common risk includes, bruising, redness, swelling, pain, tenderness and itching and rashes. Serious problems are rare but can include:

- Infection
- A lumpy appearance under the skin, which might need to be treated with surgery or medicine.
- The filler moving away from the intended treatment area, which may need to be removed using surgery.
- Scarring
- Blocked blood vessels in the face, which can cause tissue death and permanent blindness.

Based on a study in the United States, hyaluronic acid (HA) fillers made up 78.3% of all injectable dermal fillers [1]. The compatibility of HA with the human body and the reversibility of injected HA via intralesional hyaluronidase enzyme make HA-based dermal fillers appealing to a large number of injectors. They are generally well tolerated, but as dermal filler demand increases, more problems are anticipated. Even in the hands of a skilled injector, complications may arise.

Most reported cases on delayed hypersensitivity are thought to be immunological in etiology, as all injected sites were concurrently affected [3]. It is impossible to predict, and it can occur in both people who have been injected before and those who have not [3]. The primary objective is to prevent them; however, it might not always be feasible. Adverse effects often linger as long as the filler remains in the skin, meaning that temporary fillers have short-term adverse effects while permanent fillers may generate lifelong adverse effects. Otherwise, infections must be prevented with the utmost care, and the injection technique must be precise to prevent further complications from occurring [4]. This report's purpose is to examine late-onset inflammatory reactions by discussing a case observed in an aesthetic clinic.

Case Presentation

Madam FSW, a 60-year-old Chinese lady presented with itchy, red and dry patches all over her face two weeks after injection of hyaluronic acid filler. Apart from underlying hypertension and dyslipidemia on medications, she has no known allergies towards any foods or drugs. At the encounter, she was comfortable and did not have any difficulty breathing. She was a subject during a lower face hyaluronic acid filler training in an aesthetic clinic two weeks prior to the skin eruption and that was her first time undergoing an invasive aesthetic procedure. She received a total of 3 ml of monophasic hyaluronic acid fillers during the

said procedure with 0.5 ml on each canine fossa, 0.5 ml on each side superficially over the wrinkles at the nasolabial folds, and 1.0 ml on her upper lip. The procedure was done under aseptic technique and was uneventful during as well as immediately post procedure for two weeks. Madam FSW did not recall eating anything out of the norm, and her skincare routine was not changed. There was also no change in household detergents and environment.

On examination, there were multiple erythematous, scaly, and pruritic polymorphic patches and macules scattered all over her face, most prominently over her forehead and bilateral cheeks. The lesions were not raised, and the borders were not defined. The largest patch measured 1.5 cm x 1.2 cm. The eruptions were only confined to the face and were not seen anywhere else on her body. Her face was notably oedematous as well. Her vital signs were normal and systemic review revealed no abnormalities. She was seen once at first encounter and was given one more appointment one week later to reassess her condition.

Management and Outcome

A clinical diagnosis of atopic dermatitis was made. Madam FSW was prescribed Topical Clobetasone Butyrate 0.05% Cream twice daily, Tablet Levocetirizine Dihydrochloride 20 mg BD and Tablet Prednisolone 10 mg BD for five days. Her symptoms resolved on day 2 of treatment and she has been well since the completion of treatment.

It is rather clear that the only thing she has been newly exposed to for the past few weeks was the monophasic hyaluronic acid filler injection. Thus, it is likely that it is a delayed hypersensitivity reaction from the product. This is further supported by her signs and symptoms resolving shortly after commencing treatment for atopic dermatitis. Figure 1, Figure 2, Figure 3 and Figure 4 show the picture of the patient before the hyaluronic acid filler injection, during presentation, close

up pictures of the generalised facial rash and oedema and on day 2 of treatment with systemic and topical corticosteroids respectively.



Figure 1 Picture taken before the hyaluronic acid filler injection 2 weeks prior to presentation



Figure 2 Pictures taken at presentation showing facial oedema and erythematous patches and macules all over the face, more pronounced over the forehead and bilateral cheeks at the nasolabial folds.

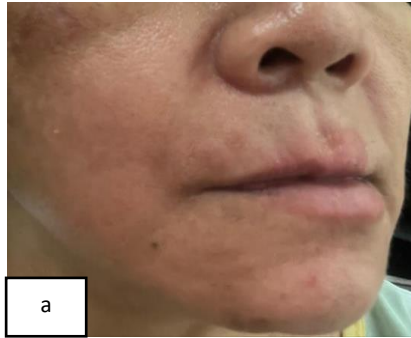


Figure 3: Close up pictures of the abovementioned generalised facial rash and oedema.



Figure 4: Pictures taken on day 2 of treatment with systemic and topical corticosteroids.

Discussion

Hypersensitivity can be broken down into four distinct subtypes; however, for the purposes of

this discussion, we will focus on the fourth type which is the delayed type of hypersensitivity. Delayed type hypersensitivity (DTH) originates from a skin test for tuberculosis diagnosis, referring to the cellular infiltrates that cause induration and erythema at the skin test site within 24 to 72 hours. DTH initially explains the response to the tuberculosis skin test and to distinguish between antibody-mediated immediate and delayed cellular skin test results [5]. The definition of the term has now been broadened to cover skin reactions to chemicals and plants as well as cell-mediated responses to bacterial or fungal respiratory infections [5].

It is uncertain when delayed hypersensitivity may occur after an HA filler injection, as it can manifest from weeks to months later. Therefore, predicting the likelihood of its occurrence is not possible [6]. Multiple reports have been published in an attempt to understand the cause of delayed hypersensitivity amongst use of hyaluronic acid fillers [7, 8]. Several factors have been proposed as potential causes of the development of adverse reactions to HA fillers, including biological or patient-related factors (such as previous skin or systemic conditions like infections or trauma), injection technique (including filler volume, repeat treatments, and intramuscular injection), and variations in the properties of the fillers themselves [6].

Hyaluronic acid, a type of glycosaminoglycan, are generally non-immunogenic, as polysaccharide molecules that are found in them are identical to those that make up a significant portion of our skin. However, it is important to note that the presence of trace protein contamination or other constituents in the filler (such as cross linkers and conservatives) may potentially trigger an immune response [9]. This is further compounded by the rise of counterfeit and non-FDA approved products in the market in which more adversities are observed with the use of those products [10].

Commercially available fillers made with hyaluronic acid possess diverse properties, such as the extent of cross-linking and gel concentration, significantly influencing their clinical results. To comprehend the reasons behind delayed hypersensitivity reactions, it is crucial to understand these attributes. It should be emphasized that the factors causing such reactions are not solely determined by the properties of the hyaluronic acid fillers, but also by the reaction of the biological host.

The pathophysiology of delayed hypersensitivity towards hyaluronic acid fillers is not well understood, but is often observed in patients following a flu-like illness [3, 6, 11, 12]. It is believed that a systemic inflammatory response could speed up the breakdown of the filler, causing fragments of low molecular weight of hyaluronic acid to be immunogenic [8], especially since in vitro studies have shown that CD44 is a receptor through which hyaluronic acid activates T-lymphocytes [13]. When an allergen comes into contact with the skin, the pathophysiology of allergic contact dermatitis begins. Langerhans cells absorb this allergen when it reaches the stratum corneum of the skin [14, 15]. These cells then digest the antigens, which are then exhibited on their surfaces. Langerhans cells then proceed towards nearby lymph nodes. The T-lymphocytes nearby are exposed to the antigens that these cells have taken up. Thus, antigen-specific T cells are generated through the processes of clonal expansion and cytokine-induced proliferation. These lymphocytes may then enter the epidermis via the blood. The sensitization phase of allergic contact dermatitis is the aggregate name for this process. After a second exposure to the antigen, the elicitation phase starts. The interaction between the antigen-containing Langerhans cells and the T lymphocytes specific to that antigen causes cytokine-induced proliferation. In turn, this proliferation causes a focused inflammatory reaction.

In this report, we present a rare case of hypersensitivity reaction to hyaluronic acid dermal fillers that occurred after a 2-week period. This particular case was unique in that the skin eruptions were not limited only to the treated area but over her face generally, however, a flu-like prodrome is not observed in our patient in this case study, which raises more questions regarding the pathophysiology of the disease process.

The mechanism behind this delayed hypersensitivity reaction is not yet fully understood, however, its association is hypothesized due to the resolution of symptoms with systemic corticosteroids. One notable drawback of this article is the lack of histological analysis, which was not conducted as the patient preferred minimally invasive treatments for her symptoms with a speedy resolution. Consequently, biopsy was not performed. A similar Type 4 reaction to cosmetic filler following COVID-19 vaccination was observed as well in Canada [16].

Physicians can take certain preventive measures to minimize the risk of allergy. A detailed allergy history should always be included in every consultation. Identical hyaluronic acid filler that will be administered to the patient can be utilised to conduct an allergy work-up such as a skin allergy test. However, due to costing and limited sensitivity of these tests, even if the findings are negative, a hypersensitive reaction cannot be completely ruled out, making it difficult to draw firm conclusions from this test.

In conclusion, as the demand for and use of hyaluronic acid dermal fillers continues to rise across the country, it is imperative that medical professionals be vigilant regarding the possibility of complications when counselling patients and carrying out the treatment itself. Physicians should take the initiative to stay up-to-date with the latest research and guidelines

in this field and should always prioritize patient safety and well-being.

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