



Delayed inflammatory reaction to dermal fillers after COVID-19 vaccination: a case report

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Introduction

New yet infrequent side effects of COVID-19 vaccination continue to appear in the literature and remain a diagnostic challenge to emergency physicians [1]. One such clinical entity is the purported association of delayed inflammatory reactions to dermal fillers in response to mRNA COVID-19 vaccination [2]. Indeed, case reports suggest these reactions may present dramatically and initially raise concern for possible angioedema or infection [2, 3].

Delayed inflammatory reactions to fillers include induration, edema, painful nodules and discolouration at sites of dermal filler injection [4, 5]. They may spontaneously appear days to months post-procedure and their pathophysiology remains poorly understood [4, 6]. Interestingly, delayed inflammatory reactions have been linked to viral infections, dental procedures and vaccinations, leading to the proposal that immunogenic triggers may play a role in the development of local inflammatory responses at sites of filler injection [4–7].

In recent years, the injection of hyaluronic acid dermal fillers for cosmetic enhancement has exploded in popularity and now represents the second most prevalent non-surgical cosmetic procedure [8]. Estimates for the overall incidence of delayed inflammatory reactions to dermal fillers vary from as low as 0.02% up to 4.25% [4, 5]. However, further research is needed to determine the incidence of delayed

inflammatory reactions that may potentially be associated to mRNA COVID-19 vaccines as only a handful of case reports have been published so far [2, 3]. Herein, we report a case of a delayed inflammatory reaction to dermal fillers presenting to the emergency department 6 weeks post-vaccination against COVID-19.

Case report

A previously healthy 23-year-old female patient without significant past medical history and no known allergies presented the emergency department complaining of painful asymmetric swelling over her maxilla, lips and lower jaw. The patient was triaged as a Canadian Triage and Acuity Scale (CTAS) 2 for angioedema/allergic reaction. The symptoms started acutely 1 day prior. The patient denied difficulty breathing or gastrointestinal symptoms. She reported no fever or constitutional symptoms, nor use of an angiotensin-converting enzyme inhibitor or other medications, no exposure to plants or insects and no change in cosmetic products or soaps. Further questioning revealed the patient had received dermal filler injections to her malar eminences, lips, jaw and chin 1 year prior. She had received her second dose of the Pfizer-BioNTech mRNA COVID-19 vaccine 6 weeks before presentation and at that time suffered a mild, self-resolving systemic reaction including fatigue, malaise, and fever.

Her triage vitals included a heart rate 92 beats/minute, respiratory rate 14 breaths/minute, blood pressure 112/76 mmHg, oxygen saturation 99% on room air, and oral temperature of 36.8 °C (98.2 °F). She had no evidence of tongue swelling, drooling or difficulty speaking and her oropharynx was unremarkable. There was tender induration

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and edema at the right malar eminence and lower mandible. Additionally, there was significant edema of her upper lips (more prominent on the right), lower lips, and chin (Fig. 1). She had no palpable nodules or areas of fluctuance. A detailed physical exam revealed no other rashes or other signs of allergic reaction or infection.

A single intravenous dose of antihistamine (diphenhydramine 50 mg) was administered out of precaution and for the possibility of symptom control. Given the relation of her symptoms to the underlying dermal fillers and recent reports of delayed reactions to fillers following COVID-19 vaccination, a consultation was arranged with plastic surgery. The plastic surgeon suspected that the presentation was consistent with a delayed inflammatory reaction that may be related to COVID-19 vaccination and recommended a single dose of intravenous steroid (dexamethasone 10 mg). Follow-up was arranged in an outpatient plastic surgery clinic.

Discussion

A growing number of case reports suggest that delayed inflammatory reactions to dermal fillers may occur following vaccination with mRNA COVID-19 vaccines [2, 3]. While a definitive link remains to be established, the overall risk of delayed inflammatory reactions in response to mRNA vaccines is likely very low. However, delayed inflammatory reactions may none-the-less be quite dramatic and result in significant anxiety on behalf of the patient. Immediate concern for airway-compromising angioedema and infection must be quickly ruled out. A careful and detailed cosmetic history is then required to elicit the relation to sites of soft tissue filler injections. Identification of a possible



Fig. 1 Tender induration and edema at sites of dermal filler injection most pronounced at right malar eminence, right lower mandible, right upper lip, lower lips bilaterally and chin

immunogenic trigger may then guide collaborative care and patient education.

The exact mechanism of delayed inflammatory reactions to dermal fillers is not well understood. While often thought to represent a type IV hypersensitivity reaction mediated by T-cells, a recent panel of experts have removed the term *hypersensitivity* in describing delayed reactions to dermal fillers and proposed the more general term *inflammatory* to highlight the likely multifactorial nature of these varied adverse reactions [5]. Indeed, many causes for delayed inflammatory reactions have been proposed. These include biofilms, infections, vaccinations and protein impurities acting as immunogenic triggers to produce an inflammatory reaction [4–7].

While most delayed inflammatory reactions are self-limiting, appropriate medical management may hasten resolution of symptoms [4–6]. Unfortunately, there is no clear consensus on the management of these varied reactions and evidence to guide therapy is lacking. As delayed inflammatory reactions are widely thought to be immunological in nature, the use of either intralesional or systemic corticosteroids is a reasonable first-line approach [4, 6]. Intralesional hyaluronidase to dissolve the fillers may also be considered [5]. Emergency department care should be patient-centred which may include analgesia for pain and clinical judgement weighing the risks and benefits of systemic steroid administration. Collaborative care with consultants in plastic surgery, dermatology or ophthalmology may provide the broad perspective necessary to manage this rare condition.

In this case, symptoms appeared suddenly 6 weeks after receiving the second dose of the Pfizer vaccine. This could represent a potential delayed inflammatory reaction to vaccination, but alternative immunogenic triggers cannot be ruled out. It is interesting to speculate, however, that this may represent the peak of antibody response to the COVID-19 vaccine in a subset of the population, although there are no data available to confirm this. Certainly, the temporal relationship between the timing of vaccination against COVID-19 and subsequent onset of delayed inflammatory reactions to dermal fillers will only become clear as more cases are reported and the pathophysiology of delayed inflammatory reactions is better understood. As such, only additional research may yet establish whether delayed inflammatory reactions to dermal fillers in response to mRNA COVID-19 vaccines fulfill the Bradford-Hill criteria for causality and a clear link becomes evident [9].

Conclusion

Given emergency departments are often the first point of contact for patients with acute dermatologic reactions, it is important for emergency providers to be aware of apparent

rare side-effects to the novel COVID-19 vaccines, including delayed inflammatory reactions at sites of dermal filler injection. This requires the clinician to take a cosmetic history about the possibility of prior injectable use. Maintaining a broad differential diagnosis and ruling out serious illness remain the key focus while ensuring thorough patient care.

Learning points

1. Dermal fillers are associated with delayed inflammatory reactions in response to inoculation via infection or vaccination.
2. Vaccination against SARS-CoV-2 with mRNA vaccines may lead to rare instances of inflammatory reactions to dermal fillers days to weeks after initial vaccination.
3. Emergency physicians should be aware of this rare side effect of COVID-19 vaccines in patients with dermal fillers which may mimic serious illness such as angioedema or infection.
4. Routine integration of a detailed cosmetic history in the emergency department is paramount to establish a diagnosis of a delayed inflammatory reaction to dermal fillers when faced with diagnostic uncertainty.

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Declarations

Conflict of interest IVB and DC declare no competing interests. IIB reports consultation to BlueDot, a social benefit corporation that tracks emerging infectious diseases, and to the NHL Players' Association.

Ethical approval Written informed consent for publication of clinical details and images were obtained from the patient.

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