

Dermal Filler Induced Granulomatous Reaction Post Covid 19 Vaccination – A Case Report

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ABSTRACT

Introduction: Adverse reactions after having permanent dermal fillers is not uncommon. This could vary from immediate to delayed inflammatory reactions (DIR). There are cases reported on patients who had dermal fillers, developed DIR following infection with SARS-CoV-2 or after having the vaccination.

Case presentation: We present a case on a patient who developed delayed hypersensitivity reaction confirmed by histopathology, on the left cheek where she had dermal fillers injected in the past.

Management and prognosis: On review following the procedure after 4 weeks, the lesion had completely resolved.

Conclusion: Once the dental infection is excluded, DIR is to be considered in the differential diagnosis on patients presenting with facial swelling developed following COVID-19 infection or vaccination and with the history of Dermal filler application.

Keywords: delayed inflammatory reaction (DIR), Dermal fillers, covid-19 vaccination.

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INTRODUCTION

Dermal fillers are now widely used as an aesthetic treatment and popular among the middle aged female population. Rawland-Warman et al have mentioned that the properties of an ideal filler are to be effective, predictable, non-carcinogenic, non-migratory, cost-effective and stable¹. Although Majority of these fillers in the market are safe, there are cases reported with various adverse reactions to dermal fillers. Delayed or late inflammatory reaction (DIR) is the most common complication following the use of dermal fillers². Delayed type hypersensitivity reaction (DTH) is one of the delayed inflammatory reactions and several studies and case reports are published on DTH following dermal filler application³. Hyaluronic acid is the most commonly used dermal filler. Granulomatous type of DTH to Hyaluronic acid (HA) is rare⁴ but can develop weeks or even months after having HA^{1,2}. The factors that could trigger DTH are infection trauma and vaccination^{4,5}. T-lymphocyte mediated response is thought to be the cause for the DTH⁵.

Our case report is of a patient who had a dermal filler approximately 20 years ago presented with a subcutaneous semisolid left infraorbital lesion following the booster dose of mRNA Pfizer-BioNTech COVID 19 vaccine. The lesion was biopsied to exclude metastasis of the breast cancer and the histopathology was subsequently reported as a granulomatous reaction to the hyaluronic acid dermal filler.

To date there are no case reports in the English literature, with the histopathology on DTH to HA facial dermal fillers following mRNA Pfizer-BioNTech COVID 19 vaccine been reported.

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CASE REPORT

82 year female patient with a history of breast cancer was referred by her General practitioner for an unusual area in the left infra orbital region.

She recently commenced treatment with Latrazole. A sub dermal area of fluctuant swelling which measured 2cm by 1cm was evident in the left infra orbital region. There was no associated punctum or ulceration. Clinically there were no palpable neck nodes. There was no history of dental infection, trauma or viral infection.

Metastatic Breast carcinoma was on top our differential diagnosis.

Fine needle aspiration of the lesion was done and the cytology revealed cohesive macrophages, cohesive groups of epithelioid cells and pauci-inflammatory coagulum and fibrinous material. It was advised biopsy under local anaesthesia to obtain tissue for a more definitive diagnosis.

The histopathological report was highly suggestive of dermal filler material with an associated granulomatous reaction with Fragments of tissue comprising unremarkable hair bearing skin; the dermal fragments feature what appeared to be exogenous foreign material at least focally resembling hyaluronic acid with an associated mildly palisaded, epithelioid histiocytic granulomatous reaction with occasional multinucleate giant cells. The special stains for fungal organisms were negative. Definite refractile or non-refractile particulate material were not identified.

The immunostains showed the histiocytes to be positive for CD68 and were negative for pancytokeratins, S100 and GATA3. (Figure 1) (Figure 2)

Patient was informed regarding the diagnosis and she confirmed that she had dermal fillers injected 20 years ago for pocketing under her eyes. The exact dose and the type filler couldn't be identified at the time of presentation.

On review following the procedure after 4 weeks, the lesion has completely subsided and the patient was happy with surgical site healing with minimal scarring.

DISCUSSION

COVID-19 is the disease caused by a new corona virus called SARS-CoV-2. WHO first learned of this new virus on 31 December 2019, following a report of a cluster of cases of 'viral pneumonia' in Wuhan, People's Republic of China. To the best of our knowledge 19 cases has been reported so far on DTH reaction to dermal fillers following SARS-CoV-2 (COVID-19) infection or following vaccination for COVID-19 as reported in systemic review by Yara Bachouretal² in 2022. Three patients developed DTH reaction after being contracted by SARS-CoV-2 virus and 16 had the reaction following Vaccination for COVID 19. A registry based study conducted on 414 cases by Deven Mc Mahonet al showed that 6 of them had DTH reaction on arms.³ Patients with previous history of dermal filler placement

developed DTH reaction along with facial swelling after vaccination with both Moderna and Pfizer.

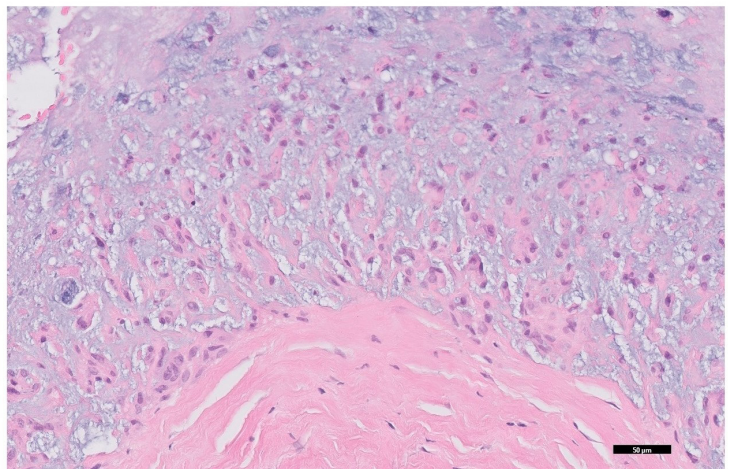
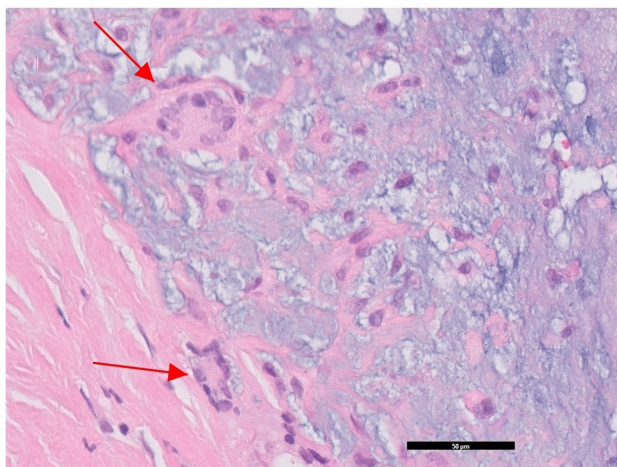
Bhojani lynch et al reported that the patients presented with varying symptoms ranging from tender erythematous swelling to facial odema Girish Gilly munavalli et al reported that all 4 cases who developed DTH location to dermal fillers were either due to SARS-COV-2 infection or followed vaccination and the presenting symptoms were erythema, tenderness and facial oedema.

DIR is mostly self-limiting and usually doesn't require a diagnostic biopsy. In our case the diagnostic tissue biopsy was carried out to rule out metastasis of the breast cancer that the patient has recently been diagnosed with.

The mechanism of DIR in these patients is not clear and various theories have been proposed. In most of the published cases the authors favoured the mechanism of T-cell mediated DTH reaction^{1,2,8}. This is due to increased local concentration of Angiotensin II (AngII) which promotes the CD8 + T-cell mediated reaction to form granuloma⁸. Spike protein of the SARS-CoV-2 virus binds to the Angiotensin converting enzyme 2(ACE2) receptors and down regulates the ACE2 expression⁹. ACE 2 receptors are found in dermal and subdermal tissues¹⁰. Hypothesis that is widely believed is that down regulation of ACE2 receptors when the spike protein of SARS-CoV-2 virus binds to it increases the local concentration of (AngII). This favours the pro-inflammatory cascade by the up regulation of AngII / Angiotensin II receptor type1 (ATR1) that not only provokes the T-cell mediated DTH reaction to dermal fillers and induces fibrosis leading to agranulomatous reaction, but also influences the activation of the macrophages to produce pro-inflammatory cytokines¹¹.

Girish Gilly Munavalli et al have recommended the administration of Angiotensin converting enzyme inhibitor (ACE-I) OR Angiotensin receptor blocker (ARB) in the acute phase or pre-treatment with ACE-I to prevent DIR before giving the first dose of the vaccine on patients has have history of filler placement. They have also suggested pre-treatment with ACE-I prior to the booster on patients who developed DIR following the first dose of vaccination⁸.

Girish Gilly Munavalli et al in their second publication have concluded that there isn't a definite treatment for DIR



Figs. 1 and 2: Histiocytes to be positive for CD68 and were negative for pancytokeratins, S100 and GATA3 (IHC)

as most of them will self resolve. However further studies are recommended for a better understanding¹².

Intralesional hyaluronidase, steroid in the form of intralesional injection or systemic administration have also been recommended to prevent the progression of the reaction^{4,5}.

However review by Raoro Raffaele highlights the fact that large numbers of people who had dermal fillers among the huge population who received Moderna and Pfizer vaccination. Among these were people who reacted to vaccines were considerably very low¹³.

Yasamin Kalantari et al highlights the importance of reporting these cases to establish a better understanding of these process and to define a definite management plan¹³.

CONCLUSION

Further studies are required to confirm the mechanism behind the DIR following COVID-19 infection or vaccination. Once the dental infection is excluded DIR is to be considered in the differential diagnosis on patients presenting with facial swelling developed following COVID-19 infection or vaccination and with the history of Dermal filler application. Informed consent, educating the patient with regards to DIR and timing of the vaccination or filler applications are some of the things to be considered. Due to the impact on health with post COVID-19 infection, patients should be educated not to discontinue the vaccination programme.

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