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Are Delayed Dermal Filler Granulomas More Common Since COVID-19?

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Purpose: Granuloma and delayed inflammatory reaction to hyaluronic acid facial esthetic fillers occurs rarely. More recently, these reactions have been reported with increasing frequency and have been associated with COVID-19 infection. The purpose of the study is to determine if delayed filler granulomas are more common after the start of the COVID-19 pandemic.

Materials and Methods: A retrospective cohort study including of all patients treated with dermal filler at 4 offices of a single cosmetic surgery practice between August 1, 2018 and October 31, 2021 was performed. The primary outcome variable was granuloma formation. The primary predictor variable was time period, either pre-COVID (8/1/18 to 2/29/20) or post-COVID (3/1/20 to 10/31/21). Other study variables recorded were age, amounts of dermal fillers used, and types of dermal filler used. Data were analyzed using chi-squared test, *t*-tests, and logistic regression.

Results: Over the study period, 3,255 patients receiving 8,067 syringes of filler over 6,800 sessions were reviewed. The average patient age was 46.8 ± 13.7 years and 2,583 sessions were performed in the pre-COVID time period and 4,217 sessions in the post-COVID time period. There were 11 granulomas in 9 subjects receiving filler in the post-COVID time period and 0 granulomas in the pre-COVID time period (0.3% vs 0.0%, respectively, $P = .009$). Juvederm Vollure was used in 64% of patients who developed granulomas but only accounted for 26% of filler administrations in the post-COVID time period and 28% in the cohort overall ($P = .02$).

Conclusions: Granuloma formation is a rare complication of hyaluronic acid filler injection that appears to be occurring with more frequency following the COVID-19 pandemic. Practitioners who administer dermal fillers should be aware of this complication and its apparent increased incidence.

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Dermal fillers are injected more than 2.7 million times each year in the United States of America.[1] In 2019, dermal fillers were a 1-billion-dollar industry with an average growth of 7.2%.[2] With the increasing popularity of dermal fillers, postinjection complications are becoming more common.[1-14]

In the United States of America, 78% of dermal filler injections are with hyaluronic acid (HA).[15] HA is extracted from a rooster's comb or produced by fermentation of *Streptococcus equi*. It then is modified by proprietary cross-linking to increase viscosity and prolonged resorption.[3,6,12] HA dermal filler cross-linking stabilizes the disaccharide every 2 to 500 units with a carbon bridge. Total size of HA is approximately 100,000 units and degree of cross-linking varies by filler.[12]

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Common early complications from filler injection include injection site redness, bruising, swelling, pain, and injection site tenderness.[6,12,14] Less common early complications include vascular infarction, allergy or hypersensitivity, bleeding, and inappropriate placement. Late complications include nodules, granulomas, dyspigmentation, and filler migration.[9,16] Granulomas and delayed inflammatory reactions to HA fillers occur in about 0.3% of patients and occur 2 weeks to 6 years after injection.[1,2,4-11,13,14] Granulomas are characterized by erythema, induration, and edema and can be caused by bacterial or fungal contamination and breakdown of proprietary ingredients or modified HA.[1,10,11,17] "Vycross" cross-linking technology by Allergan uses butanediol diglycidyl ether (BDDE) and small molecular weight HA in its proprietary formula. Both chemicals are proinflammatory and may be related to late granuloma formation.[18] Infectious granulomas are caused by *Staphylococcus aureus, Psuedomonas aeruginosa, mycobacterium abscessus,* and *Streptococcus spp.*[4,19] Noninfectious granulomas are T-lymphocyte cell–mediated and associated with human leukocyte antigen types B*08 and DRB*03.[4,5,10,20]

Histopathology of noninfectious granulomas show basophilic material with a honeycomb or amorphous appearance presumed to be HA which is then surrounded by multinucleated giant cells with peripheral infiltration of eosinophils and neutrophils. Peripheral vacuoles are commonly seen. HA molecules are nonbirefringent.[1,6,7,11,14,18,20]

Noninfectious granulomas have been associated with viral illnesses and vaccinations, including Sars-CoV-2 (COVID).[2,10,13,21-23] These granulomas usually present 3 to 5 days from the onset of illness. Management of postillness granulomas is treated with systemic steroids, antibiotics, antivirals, and hyaluronidase.[1,2,9,10,24]

COVID-related granulomas have been reported by several authors during the pandemic. Munavalli reported granuloma formation in 3 people after COVID infection or inoculation.[2] Two developed granulomas after vaccination with messenger ribonucleic acid (mRNA) vaccines while the other developed it after natural infection. Granulomas developed 2 to 14 days after the inciting event. Each person was treated with a different regimen including systemic steroids, intralesional steroids, hyaluronidase, lisinopril, antibiotics, and antihistamines. Two of the 3 patients had complete resolution after treatment while the third had recurrent flares of periorbital edema. Rice reported 4 cases of granuloma formation, all occurring after mRNA vaccination.[13] The onset of granuloma was 1 to 10 days after vaccine administration. All 4 patients were successfully treated with lisinopril. Beamish reported a single case of filler-related granuloma presenting to an emergency department 6 weeks after mRNA vaccination. The patient was treated in the emergency department with diphenhydramine and corticosteroids and discharged with an outpatient follow-up.[25] Calvisi reported 3 cases of granuloma after mRNA vaccination. Two of the 3 patients had complete resolution of their symptoms without intervention. The other patient required corticosteroids because the initial presentation was concerning for angioedema.[26] Ortigosa reported 5 patients who developed delayed filler granulomas, 3 after receiving an mRNA vaccine and the other 2 after receiving the AstraZeneca vaccine. All 5 cases were successfully treated with steroids.[27]

The purpose of the study is to determine whether delayed filler granulomas are more common after the start of the COVID pandemic. Our hypothesis is the frequency of delayed filler granulomas has not increased since the COVID pandemic. To test the hypothesis, we compared granuloma rates in a pre-COVID time period to a post-COVID time period.

Methods

STUDY DESIGN

A retrospective cohort study of all patients treated with dermal filler or hyaluronidase at 4 offices of a single cosmetic surgery practice was completed. Eligibility criteria included patients who received HA dermal filler at the practice between August 1, 2018 and October 31, 2021. An institutional review board approval (#2275) was obtained for this study.

STUDY VARIABLES

The primary outcome variable was granuloma formation (yes/no) which was determined by the use of hyaluronidase and confirmed by a manual chart review. The primary predictor variable was pre-COVID or post-COVID time period. The pre-COVID time period (pre-COVID) was defined as a dermal filler injection session occurring between 8/1/2018 and 2/29/2020 and the post-COVID time period (post-COVID) was defined as a dermal filler injection session occurring between 3/1/2020 and 10/31/2021. Other study variables recorded were age, syringes of dermal fillers used, and types of dermal filler used.

DATA COLLECTION

Electronic medical records (Nextech, Tampa, Florida) were queried for all HA filler billing items between 8/1/2018 and 10/31/2021. The fillers included were all HA fillers carried by the practice; Juvederm and Restylane. The Juvederm (Abbvie, Chicago, Illinois) fillers were Voluma, Vollure, Volbella, Ultra, and Ultra Plus. The Restylane (Galderma, Fort Worth, Texas)

Table 1. DESCRIPTIVE SUMMARY OF SUBJECTS AND DERMAL FILLERS

Variable	All Patients (m = 6,800)
Age at time of injection (yr)	46.8 ± 13.7
Average Syringes of Dermal Filler per Session	1.4 ± 0.8
Fillers Used (multiple fillers could be used in combination)	
Juvederm Ultra	2,362 (34.7%)
Juvederm Ultra Plus	694 (10.2%)
Juvederm Volbella	847 (12.5%)
Juvederm Vollure	1,934 (28.4%)
Juvederm Voluma	1,732 (25.5%)
Restylane	139 (2.0%)
Restylane Lyft	118 (1.7%)
Restylane Kysse	241 (3.5%)

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fillers were Restylane-L, Restylane Kysse, and Restylane Lyft. For each filler identified in the billing report, the patient's identifier, age, date of injection, and quantity of filler were also recorded.

A second search was completed for all instances of hyaluronidase administered during the study period. The charts of these patients were then reviewed to determine a reason for hyaluronidase administration. Granulomas were identified as tender nodules that developed more than 2 weeks after filler administration. Nodules attributed to poor filler placement or filler migration were excluded from this review.

DATA ANALYSIS

Categorical variables were summarized by reporting counts and percentages. Continuous variables were summarized by reporting means and standard deviations. Although independence was violated due to multiple fillers per patients, we performed chi-squared tests for categorical variables and *t*-tests for continuous covariates between granuloma and COVID-timing groups to determine nonadjusted differences.

Firth's correction was used in logistic regression to estimate the odds ratio of granuloma based on pre-COVID/post-COVID time period using the logistf package in R statistical software.[28] This approach was used due to the presence of separation because all granulomas took place during post-COVID time period. We attempted to adjust this regression for individual subjects, but this model did not converge, likely due to many patients having only 1 filler over the time period. We also did not adjust for other variables, as the granuloma event was rare—and we worried that this may further the issue of separation.

Table 2. COMPARISON OF COVID TIME PERIOD VERSUS STUDY VARIABLES

Variable	Pre-COVID (n = 2,583)	Post-COVID (n = 4,217)	*P* Values
# Syringes	1.4 ± 0.8	1.4 ± 0.7	.02
Age	48.4 ± 13.5	45.8 ± 13.8	<.001
Filler Used (multiple fillers could be used in combination)			<.001
Juvederm Ultra	944 (36.5%)	1,418 (33.6%)	.02
Juvederm Ultra Plus	294 (11.4%)	400 (9.5%)	.01
Volbella	330 (12.8%)	517 (12.3%)	.55
Vollure	848 (32.8%)	1,086 (25.8%)	<.001
Voluma	630 (24.4%)	1,102 (26.1%)	.12
Restylane	31 (1.2%)	108 (2.6%)	<.001
Restylane LYFT	49 (1.9%)	69 (1.6%)	.45
Restylane Kysse	0 (0.0%)	241 (5.7%)	<.001

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Results

There were 3,254 subjects who received HA filler over the study period in 6,800 different sessions, with many subjects receiving dermal fillers in both the pre-COVID and post-COVID time periods. The average age of the subjects was 46.8 years and a total of 8,067 syringes of filler were administered during the study period (Table 1).

Patients who had treatment sessions in the post-COVID period had a decreased number of syringes (1.39 vs 1.43, $P = .02$) and decreased age (45.8 vs 48.4, $P < .001$). Juvederm Ultra (33.6% vs 36.5%), Vollure (25.8% vs 32.8%), and Juvederm Ultra Plus (9.5% vs 11.4%) were less likely to be given during the post-COVID time period. Restylane Kysse (5.7% vs 0%) and Restylane (2.6% vs 1.2%) were more likely to be given during the post-COVID time period (Table 2).

Table 3 displays the outcome variable, granuloma formation, versus the study variables. There were 11 total granulomas that occurred in 9 patients (2 patients had 2 granulomas) (Figs 1-6). Seven/11 granulomas took place when Vollure was used and 4/11 took place when Voluma was used. The use of Vollure was associated with granuloma formation ($P = .02$).

There was a strong association between COVID time period and granuloma formation ($P = .009$), with 0.3% of patients with injection sessions in the post-COVID time period developing a granuloma, compared to 0% of the pre-COVID time period

Table 3. COMPARISON OF GRANULOMA FORMATION VERSUS STUDY VARIABLES

Variable	Granuloma (n = 11)	No Granuloma (n = 6,789)	*P* Values	Granuloma Rate
# Syringes	2.0 ± 1.4	1.4 ± 0.8	.19	
Age	51.2 ± 8.8	46.8 ± 13.7	.13	
Filler Used (multiple fillers could be used in combination)			.045	
Juvederm Ultra	2 (18.2%)	2,360 (34.8%)	.35	0.1%
Juvederm Ultra Plus	1 (9.1%)	693 (10.2%)	1	0.1%
Volbella	2 (18.2%)	845 (12.4%)	.64	0.2%
Vollure	7 (63.6%)	1,927 (28.4%)	.02	0.4%
Voluma	4 (36.4%)	1,728 (25.5%)	.49	0.2%
Restylane	1 (9.1%)	138 (2.0%)	.20	0.7%
Restylane LYFT	0 (0.0%)	118 (1.7%)	1	0
Restylane Kysse	0 (0.0%)	241 (3.5%)	1	0

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(Table 4). The granuloma formation outcome had evidence of separation, which is often a problem with rare binary events (11/6,800 sessions resulted in granuloma formation) and leads to infinite odds ratios. As a solution, we performed Firth's correction in logistic regression which resulted in an estimated odds ratio of 14.1 (95% confidence interval = 1.8 to 1,813, $P = .005$).[29] We attempted to adjust for subject dependence but the model would not converge due to the rarity of the event.

Discussion

The purpose of this article was to determine if the delayed filler granuloma formation rate increased since the COVID pandemic. We hypothesized that the granuloma rate would not change at a single cosmetic surgery practice cohort between a pre-COVID and post-COVID time period. However, our hypothesis was not supported. The post-COVID time periods had an increased rate of granuloma formation of

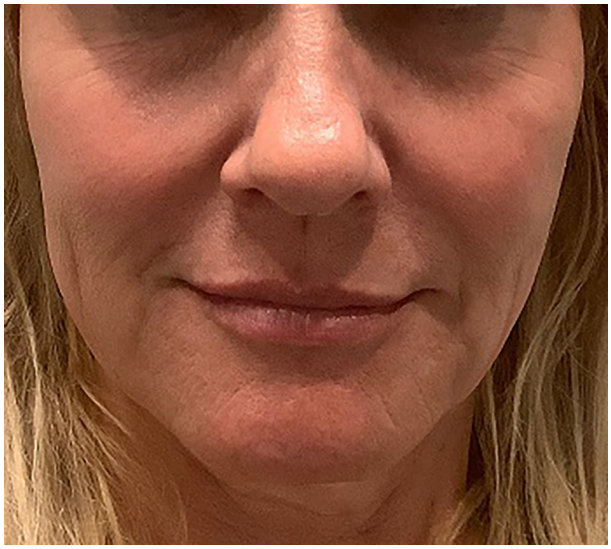

FIGURE 1. 52-year-old female with a history of ulcerative colitis on adalimumab after 4.8 cc of Voluma, Vollure, and Volbella to the mid and lower face. Prior to injections the patient had been fully vaccinated against COVID with an mRNA vaccine series.

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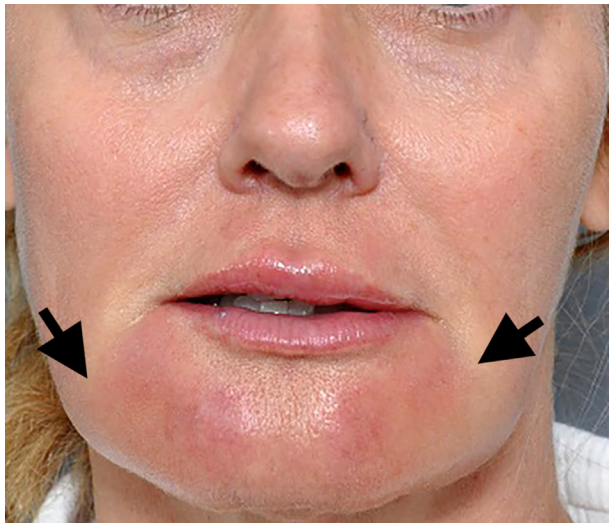

FIGURE 2. 3 months after filler injection and 3 days after developing a breakthrough COVID infection, the patient develops lower facial swellings that were erythematous and tender to palpation (*black arrows*). During her COVID infection the patient's rheumatologist discontinued her adalimumab. Differential diagnosis included granuloma and infection so the patient was treated with hyaluronidase (500 U) and antibiotics.

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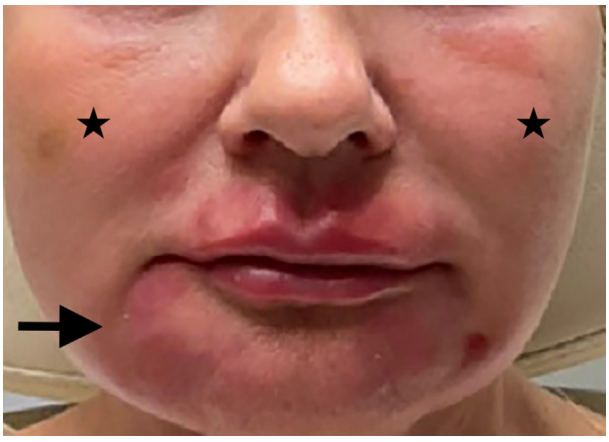

FIGURE 3. 5 days after initial granuloma presentation with worsening edema and erythema in the lower face (*black arrow*) and edema development in the midface (*black stars*). Antibiotics were broadened and hyaluronidase administered (900 U).

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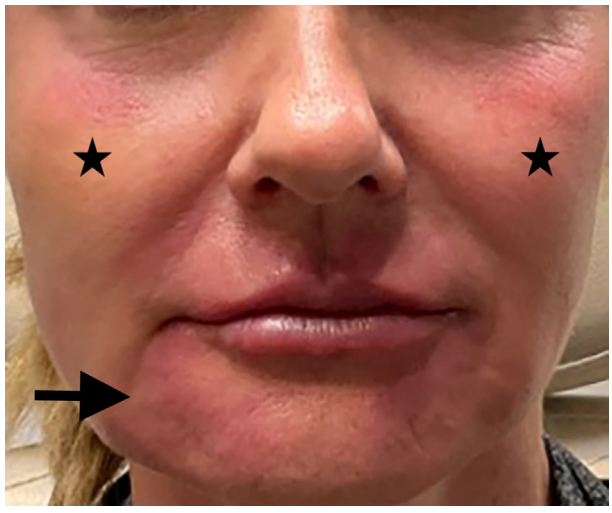

FIGURE 5. 13 days after initial granuloma formation and 4 days after beginning prednisone taper. Granulomas in the midface (*black stars*) and lower face (*black arrow*) still present but much improved. Lisinopril discontinued at patient's request and steroid taper extended. Hyaluronidase (2,300 U) administered to treat residual granulomas.

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0.3% compared to 0.0% in the pre-COVID formation ($P = .009$).

Vollure was correlated with granuloma formation ($P = .02$) and was responsible for 7 of 11 (77%) granulomas despite being 28.4% of the filler administered in the study period. Voluma, the filler used in the remaining granulomas, is also a member of the Vycross family. The Vycross filler family uses a BDDE crosslinker between HA chains to stabilize filler. Vycross fillers also contain high molecular weight and low molecular weight HA. Both BDDE and low molecular weight HA are proinflammatory.[17] It is hypothesized that normal breakdown of the product over time leads to release of low molecular weight HA precipitating delayed granuloma formation.[17]

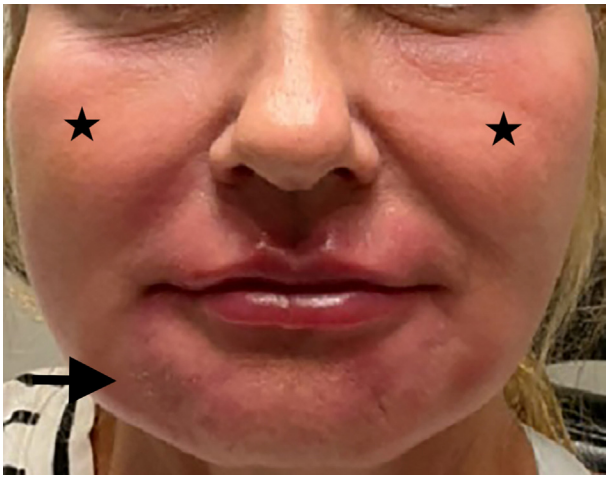

FIGURE 4. 9 days after initial granuloma formation with minimal improvement in the lower face and worsening midface edema, erythema, and tenderness (*black stars*). The lower facial granulomas had softened but were still painful (*black arrow*). Rheumatologist was consulted as clinical picture was consistent with granuloma, and not infection, so patient was restarted on adalimumab and antibiotics discontinued. Prednisone taper started at 60 mg, 5 mg lisinopril trialed, and hyaluronidase (1,000 U) administered.

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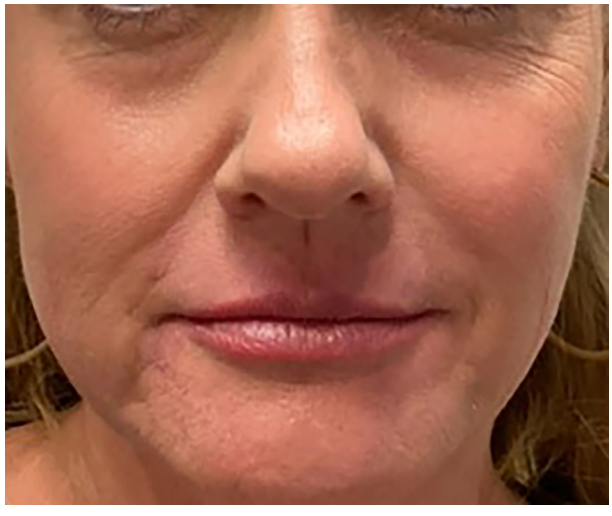

FIGURE 6. 36 days after granuloma formation. Patient required 6,725 U of hyaluronidase, prednisone, and triamcinolone injections to treat mid and lower facial granulomas. Patient had a minor flare of granuloma formation 2 months later after a radiofrequency microneedling treatment that was managed with 30 U of hyaluronidase and has not developed a granuloma since.

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Table 4. COMPARISON OF GRANULOMA FORMATION VERSUS COVID TIME PERIOD

Variable	All (n = 6,800)	Granuloma (n = 11)	No Granuloma (n = 6,789)	*P* Value	Relative Risk (95% CI)	Granuloma Rate
COVID Status				.009	4.72 (1.94-8.06)	
Pre-COVID	2,583 (38.0%)	0 (0.0%)	2,583 (38.0%)			0.0%
Post-COVID	4,217 (62.0%)	11 (100.0%)	4,206 (62.0%)			0.3%

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To our knowledge, this study is the first of its kind to address granuloma rates before and during the COVID pandemic. Prior case series have demonstrated anecdotal evidence of granuloma formation in patients who had received filler and recently been infected with COVID or inoculated against it (Figs 1-6).[2,13,25-27]

Limitations of this study include its retrospective nature. Granuloma formation is also a rare event and an absence of granuloma formation in the pre-COVID time period leads to perfect separation of the data by time period. Because of the rarity of this event, it is possible that the separation could be secondary to chance. To reduce the effect of this on the odds ratio formation, Firth's correction was used, otherwise statistical interpretation would have been nonsensical.[28] However, we should note that *P* values and confidence intervals from the analyses shown violated statistical independence assumptions. This is because there were repeated measurements from patients—and it can be argued that if a patient has (or does not have) a granuloma—they might be more (or less) likely to have a granuloma for a future filler. We attempted to adjust for this by including patient-specific fixed effects in the Firth-corrected logistic regression, but the resulting model did not converge. When we used a standard logistic regression model without Firth's correction, we were able to appropriately maintain independence assumptions; however, the resulting odds ratio was infinite due to the separation seen in the data. Therefore, we should note to the reader that the reported results do violate statistical assumptions of independence out of necessity. Despite these statistical limitations, our post-COVID granuloma formation rate of 0.3% aligns with published literature for delayed inflammatory granuloma formation rates.[1,2,4-6] In addition, it was not possible to determine COVID infection or record vaccination dates for the patient population. Because the COVID time period was used as a proxy for COVID infection or vaccination, there is a high likelihood that many patients were misclassified. In other words, patients may not have had COVID or the vaccine at the time their filler was administered in the post-COVID time period. They may also not have had a COVID infection or vaccination prior to the onset of their granuloma. This prevents the study from associating COVID infection or vaccines with granuloma formation directly as it is possible there is another factor that is increasing granuloma formation rates in the post-COVID time period. Heightened awareness of complications from medications and closer facial self-examination during video conferencing are trends that cooccurred with COVID-19 and could also explain this increase. However, while these explanations are plausible, they are unlikely. Granulomas are easily noticed by patients, especially on the face in patients who are already concerned enough about their appearance to seek out dermal filler injections. There is also the concern that some granuloma patients may have been lost to follow-up and had a granuloma treated at another practice. Despite these limitations, the sheer volume of patients included in this study is a strength that can somewhat mitigate these limitations. Further research in the form of a prospective cohort that recorded and monitored for any COVID infections or vaccinations would overcome limitations of this research.

Delayed HA granulomas have a variety of causes.[1-6,8-11,13-15,17-22,24] Anecdotal evidence brought a new concern with the COVID pandemic—the effect of COVID infection or vaccination on the development of granulomas. This retrospective cohort of the senior author's practice shows that there was a statistical increase in the development of HA granulomas during the COVID pandemic. However, our findings should be interpreted with caution given the rarity of this event. These results should not lead to a change in clinical practice at this time but clinicians who perform dermal filler injections should be aware of this potential complication and further research could help confirm these findings.

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References

1. Zhang FF, Xu ZX, Chen Y: Delayed Foreign body granulomas in the Orofacial region after hyaluronic acid injection. Chin J Dent Res 23:289, 2020
2. Munavalli GG, Knutsen-Larson S, Lupo MP, Geronemus RG: 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 II-induced cutaneous inflammation. JAAD Case Rep 10:63, 2021
3. Alcantara CEP, Noronha MS, Cunha JF, Flores IL, Mesquita RA: Granulomatous reaction to hyaluronic acid filler material in oral and perioral region: A case report and review of literature. J Cosmet Dermatol 17:578, 2018
4. Alijotas-Reig J, Miro-Mur F, Planells-Romeu I, Garcia-Aranda N, Garcia-Gimenez V, Vilardell-Tarres M: Are bacterial growth and/or chemotaxis increased by filler injections? Implications for the pathogenesis and treatment of filler-related granulomas. Dermatology 221:356, 2010
5. Decates TS, Velthuis PJ, Schelke LW, et al: Increased risk of late-onset, immune-mediated, adverse reactions related to dermal fillers in patients bearing HLA-B*08 and DRB1*03 haplotypes. Dermatol Ther 34:e14644, 2021
6. Ghislanzoni M, Bianchi F, Barbareschi M, Alessi E: Cutaneous granulomatous reaction to injectable hyaluronic acid gel. Br J Dermatol 154:755, 2006
7. Kaczorowski M, Nelke K, Luczak K, Halon A: Filler migration and florid granulomatous reaction to hyaluronic acid mimicking a buccal tumor. J Craniofac Surg 31:e78, 2020
8. Kim JH, Choi JS, Yun JH, et al: Foreign body reaction to injectable hyaluronic acid: Late granuloma formation. Ann Dermatol 27:224, 2015
9. Signorini M, Liew S, Sundaram H, et al: Global Aesthetics Consensus G. Global Aesthetics Consensus: Avoidance and management of complications from hyaluronic acid fillers-evidence- and opinion-based review and consensus recommendations. Plast Reconstr Surg 137:961e, 2016
10. Turkmani MG, De Boulle K, Philipp-Dormston WG: Delayed hypersensitivity reaction to hyaluronic acid dermal filler following influenza-like illness. Clin Cosmet Investig Dermatol 12:277, 2019
11. Yang JH, Lee SM, Won CH, et al: Foreign body granuloma caused by hyaluronic acid/dextranomer microsphere filler injection. Int J Dermatol 51:1517, 2012
12. Micheels P: Human anti-hyaluronic acid antibodies: Is it possible? Dermatol Surg 27:185, 2001
13. Rice SM, Ferree SD, Mesinkovska NA, Kourosh AS: The art of prevention: COVID-19 vaccine preparedness for the dermatologist. Int J Womens Dermatol 7:209, 2021
14. Tonin B, Colato C, Bruni M, Girolomoni G: Late granuloma formation secondary to hyaluronic acid injection. Dermatol Online J 26, 2020
15. Caldas Pozuelo C, Dominguez De Dios J, Mota Rojas X: Multiple oral granulomatous nodules to hyaluronic acid filler. J Cosmet Dermatol 19:3453, 2020
16. Kato K, Inoue E, Tanaka S, Kawamoto H: Increase in the incidence of acute inflammatory reactions to injectable fillers during COVID-19 era. J Cosmet Dermatol 21:1816, 2022
17. Liu J, Xin WQ, Liu LT, Chen CF, Wu L, Hu XP: Majocchi's granuloma caused by Trichophyton rubrum after facial injection with hyaluronic acid: A case report. World J Clin Cases 8:3853, 2020
18. Mu EW, Stokar E, Franks L, Meehan SA: Histopathologic reaction patterns to differentially cross-linked hyaluronic acid fillers: A retrospective case series. J Cutan Pathol 48:758, 2021
19. Alsaad SM, Fabi SG, Goldman MP: Granulomatous reaction to hyaluronic acid: A case series and review of the literature. Dermatol Surg 38:271, 2012
20. Cecchi R, Spota A, Frati P, Muciaccia B: Migrating granulomatous chronic reaction from hyaluronic acid skin filler (Restylane): Review and histopathological study with histochemical stainings. Dermatology 228:14, 2014
21. Heydenrych I, De Boulle K, Kapoor KM, Bertossi D: The 10-point plan 2021: Updated concepts for improved procedural safety during facial filler treatments. Clin Cosmet Investig Dermatol 14:779, 2021
22. Munavalli GG, Guthridge R, Knutsen-Larson S, Brodsky A, Matthew E, Landau M: "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". Arch Dermatol Res 314:1, 2022
23. Alijotas-Reig J, Garcia GV, Velthuis PJ, Niessen FB, Decates TS: Inflammatory immune-mediated adverse reactions induced by COVID-19 vaccines in previously injected patients with soft tissue fillers: A case series of 20 patients. J Cosmet Dermatol 21:3181, 2022
24. Saputra DI, Kapoor KM: Management of noninflammatory nodule in chin after a large volume bolus injection of hyaluronic acid filler. Dermatol Ther 33:e13424, 2020
25. Beamish IV, Bogoch II, Carr D: Delayed inflammatory reaction to dermal fillers after COVID-19 vaccination: A case report. CJEM 24:444, 2022
26. Calvisi L: Hyaluronic acid delayed inflammatory reaction after third dose of SARS-CoV-2 vaccine. J Cosmet Dermatol 21:2315, 2022
27. Ortigosa LCM, Lenzoni FC, Suarez MV, Duarte AA, Prestes-Carneiro LE: Hypersensitivity reaction to hyaluronic acid dermal filler after COVID-19 vaccination: A series of cases in Sao Paulo, Brazil. Int J Infect Dis 116:268, 2022
28. Firth D: Bias reduction of maximum likelihood estimates. Biometrika 80:27, 1993
29. Mansournia MA, Geroldinger A, Greenland S, Heinze G: Separation in logistic regression: Causes, consequences, and control. Am J Epidemiol 187:864, 2018