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Foreign body granulomas to polymethylmethacrylate soft tissue filler following COVID-19 infection



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INTRODUCTION

An increasing number of patients are seeking minimally invasive aesthetic procedures, particularly soft tissue fillers, for facial rejuvenation. Although most hyaluronic acid (HA) fillers last between 6 and 24 months, some patients seek longer lasting results with permanent fillers, such as polymethylmethacrylate (PMMA). Because of its irreversible nature, complications with PMMA may be more durable than those associated with HA soft tissue fillers. A specific subtype of complications, recently termed “delayed inflammatory reactions” (DIRs) occur weeks to months after injection.¹ Common features include erythema, pain, induration, or solid edema. DIRs may occur following an infectious trigger but have also been reported from the use of substandard product or poor injection technique.¹ To this end, there are several reports of DIR triggered by COVID-19 infection among temporary fillers; however, similar reports among permanent fillers are lacking.

CASE REPORT

A 57-year-old woman presented to a dermatology clinic with chief complaint of several week history of numerous subcutaneous, painful nodules of the bilateral temples, cheeks, and marionettes (Fig 1). Patient noted history of PMMA filler injected to her forehead, temples, and cheeks with a nurse injector 2 years prior; in addition to PMMA filler, patient also had HA filler to bilateral malar cheeks. Two weeks after HA filler injections, she described hyperosmia,

Abbreviations used:

DIR:	delayed inflammatory reaction
HA:	hyaluronic acid
PMMA:	polymethylmethacrylate

rhinorrhea, and fatigue. She tested positive for COVID-19. Over the next 1 to 2 months, swelling, erythema, and painful, subcutaneous nodules developed in areas treated with PMMA filler alone as well as areas treated with both PMMA and HA filler. Our patient had been otherwise previously healthy and had received COVID-19 vaccinations and booster shots 7 months prior to presentation. She was treated by an outside provider with intralesional steroid mixed with 5'-fluorouracil to treat presumed granulomas, with noted mild improvement. Two months after initial presentation, patient presented to our clinic for second opinion, given the uncertainty of her diagnosis. Punch biopsies of left and right cheek were performed for hematoxylin and eosin and tissue culture to rule out atypical infection. Tissue cultures for aerobic/anaerobic bacteria, fungi, and mycobacteria were negative. On histology, there were numerous histiocytes surrounding punched-out spaces within the subcutaneous fat, consistent with foreign body reaction to PMMA (Fig 2).

Treatment options were reviewed including oral antibiotics, prednisone taper, and intralesional

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Fig 1. Firm, painful subcutaneous nodules involving temple and cheek (*arrows*) with associated swelling and erythema of the face. Punch biopsies were performed from site A for hematoxylin and eosin.

steroid + 5'-fluorouracil injection; hyaluronidase injections were also offered to dissolve any residual HA filler in the malar cheeks. Our patient elected to proceed with intralesional steroid + 5'-fluorouracil injections, mixed in a 1:2:2 ratio of triamcinolone (10 mg/mL), 5'-fluorouracil (50 mg/mL), and 1% lidocaine, to the subcutaneous nodules. This was then followed by a high dose prednisone taper, prednisone 50 mg (approximately 1 mg/kg), decreased by 10 mg every 4 days, until completion. She had noticeable improvement of nodularity after 3 treatments.

DISCUSSION

Granulomatous DIRs are a feared complication among all injectable soft tissue fillers, including PMMA filler. Usually in cases of PMMA, DIRs occur without warning, presenting with sudden onset swelling, erythema, and tenderness.¹⁻³

The frequency of granuloma development among patients receiving PMMA filler has been estimated to be approximately 1.9%.⁴ Although the exact pathogenesis remains unknown, granuloma formation has been observed following infections or surgery.² Although reports of COVID-19 causing DIR in PMMA filler are lacking, there have been numerous reports of both COVID-19 infection and vaccination triggering DIR in patients with HA filler.⁵

Diagnosing granulomatous DIR is challenging. Some experts define DIR as a clinical diagnosis, established with visualization of firm nodules that appear months or years after PMMA injection.² Others emphasize the importance of ruling out infection with incision and drainage followed by culture before establishing diagnosis and initiating treatment; if diagnosis remains equivocal, further biopsy, tissue culture, and ultrasound may be required.¹

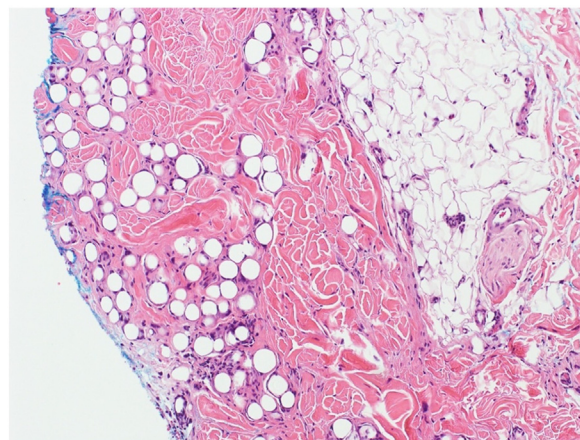


Fig 2. Punch biopsy of subcutaneous nodule of cheek with numerous histiocytes surrounding punched-out spaces adjacent to the subcutaneous fat, consistent with foreign body reaction to polymethylmethacrylate.

There is no consensus regarding best management of DIRs. Some experts hypothesize that granulomas may resolve on their own and no treatment is necessary.² Others have developed algorithms to manage these complications. Algorithms for both HA and PMMA filler share features including dual antibiotic treatment followed by intralesional therapies (eg, intralesional steroid and 5'-fluorouracil) and oral prednisone.^{1,3} Some therapeutics such as allopurinol, tacrolimus, and surgical excision have also demonstrated success.²

Our patient had been injected with 2 types of filler, HA and PMMA, with history of sudden, but delayed, nodule development after COVID infection. HA filler DIRs triggered by COVID-19 have also been reported to rapidly occur days to months after infection and was not a helpful distinguishing feature.⁵ Punch biopsy was therefore performed, implicating PMMA, as demonstrated by the presence of uniform spaces typical of PMMA microspheres, as opposed to the amorphous, heterogenous shape characteristic of HA filler. Negative concomitant tissue culture ruled out bacterial, fungal, or mycobacterial etiology. With confirmation of the originally presumed diagnosis, we were able to more confidently treat our patient with a series of 3 rounds of intralesional steroid + 5'-fluorouracil injections, each separated by 1 week. She had significant decrease in size and nodularity of granulomas. Further swelling and pain was treated with a high dose prednisone taper thereafter.

Although our patient is significantly improved, it is difficult to counsel her about prognosis, as it is somewhat undetermined. With PMMA filler product still in place, she could experience development of

another DIR to future immunogenic triggers (ie, reinfection with COVID-19 versus booster vaccination in the future). This case represents an unusual report of PMMA DIR after COVID-19 infection with suggestions for treatment.

Conflicts of interest

None disclosed.

REFERENCES

1. Artzi O, Cohen JL, Dover JS, et al. Delayed inflammatory reactions to hyaluronic acid fillers: a literature review and proposed treatment algorithm. *Clin Cosmet Investig Dermatol*. 2020;13:371-378.
2. Gelfer A, Carruthers A, Carruthers J, Jang F, Bernstein SC. The natural history of polymethylmethacrylate microspheres granulomas. *Dermatol Surg*. 2007;33(5):614-620.
3. Park TH, Sang WS, June-Kyu K, Choong HC. Clinical experience with polymethylmethacrylate microsphere filler complications. *Aesthet Plast Surg*. 2012;36(2):421-426.
4. Paulucci BP. PMMA safety for facial filling: review of rates of granuloma occurrence and treatment methods. *Aesthet Plast Surg*. 2020;44(1):148-159.
5. Shome D, Komal D, Sapna V, Rinky K. Delayed hypersensitivity reaction to hyaluronic acid dermal filler post-COVID-19 viral infection. *J Cosmet Dermatol*. 2021;20(5):1549-1550.