Late-onset granuloma formation after poly-L-lactic acid injection

Molly Storer, MS, Rebecca Euwer, MD, Antoanella Calame, MD, and Arianne Shadi Kourosh, MD
Boston and Worcester, Massachusetts; Dallas, Texas; and San Diego, California

Key words: foreign body granuloma; late-onset granuloma; poly-L-lactic acid.

INTRODUCTION

Poly-L-lactic acid (Sculptra, Sanofi Aventis, Bridgewater, NJ) is a gel polymer made of poly-L-lactic acid microspheres and water suspended in a mannitol and carboxymethyl cellulose suspension. This injectable tissue filler has been used for correction of lipoatrophy in HIV patients as well as for cosmetic purposes since its US Food and Drug Administration approval in 2004. The mechanism of action involves induction of a subclinical inflammatory response that stimulates fibroblast proliferation and collagen formation, ultimately leading to a progressive increase in volume of the dermis and subcutaneous tissues. Late-onset immune-mediated adverse effects associated with the use of poly-L-lactic acid can appear years after the initial injection with reported range of 6 to 60 months. These effects include inflammatory nodules, papules, and edema. Previous reports of adverse effects associated with poly-L-lactic acid identify a maximum of 60 months before development of a subcutaneous nodule. These adverse effects can cause significant distress for patients, as the erythema, edema or nodules that can result may cause cosmetic disfigurement and mimic an infectious process, necessitating, at times, extensive workup including biopsy. Here, we present a case of granuloma formation that appeared more than 70 months after treatment, surpassing the previously reported maximum latency of 60 months for poly-L-lactic acid and long surpassing the 2-year duration that the product is purported to last in the tissues. To our knowledge, this is the longest reported latency period for development of a subcutaneous nodule with foreign body reaction observed with poly-L-lactic acid. Practitioners should be aware of the extent of adverse events associated with procedural complications to adequately inform their patients, provide the highest standard of care, and maintain awareness of this etiology in their differential diagnosis for patients presenting with facial nodules of unknown etiology, even if poly-L-lactic acid exposure was several years prior.

CASE

A 48-year-old immunocompetent woman presented with a solitary visible noninflammatory nodule on her right temple, which at the time of presentation had been present for 2 months. The nodule was firm and indurated, without erythema, tenderness, fluctuance, edema, or ulceration. The patient was afebrile, and review of systems was otherwise negative. Her medical history was unremarkable, and her only known allergy was to penicillin. The patient had received a series of injections of poly-L-lactic acid bilaterally in the temporal and cheek regions for the indication of lipoatrophy secondary to aging. Her history of poly-L-lactic acid exposure began 7 years prior with injection in the temporal and cheek areas, with 3 injections of 2.5 mL of poly-L-lactic acid in 6 mL dilution to each side spaced monthly. She also received an additional 2.15 mL of injections bilaterally to the same regions 70 months (approximately 5.8 years) before nodule formation. The dilution of this round of poly-L-lactic acid injection was 5 mL.

From the Departments of Dermatology at Massachusetts General Hospital, Boston; University of Massachusetts Medical School, Worcester; University of Texas Southwestern, Dallas, Texas; and Compass Dermatopathology and University of California, San Diego.

Funding sources: None.

Conflicts of interest: Dr Euwer is a peer-to-peer trainer contracted with Galderma. The remaining authors have no conflicts of interest to declare.
She received injections of botulinum toxin A and hyaluronic acid after her last poly-L-lactic acid treatment and before the development of the temporal nodule. However, none of these other treatments were on or near the temporal regions.

Ultimately, the time from last transdermal poly-L-lactic acid injection to the time the nodule was first noted by the patient was 2,113 days (70.4 months). Notably, the same amount of product was administered to both sides of the face, and the patient did not recall any other external factors that would cause a difference in the sides of her face (eg, unequal pressure, massage, or history of trauma to one side).

Histopathologic analysis of the lesion on the temple, including analysis under polarized light (Fig 1), showed a subcutaneous foreign body granuloma compatible with foreign body reaction to poly-L-lactic acid. Results of periodic acid–Schiff stain, Gram stain, and fungal and bacterial cultures for the presence of organisms were negative. At her follow-up visit, the patient reported that another physician treated the nodule once with intralesional kenalog, and the patient was uncertain of what dosage was used. The nodule resolved over a period of months, and it was unclear as to whether or to what extent the intralesional kenalog played a role in this resolution versus time alone. Since the initial temporal granuloma formation, she has had 2 additional nodules form in the cheek areas in locations of previous injection sites of poly-L-lactic acid (also in the same period over 70 months), which also resolved over a period of months without further intervention.

DISCUSSION

Late-onset granulomatous reactions to poly-L-lactic acid have been reported since the approval of poly-L-lactic acid for lipoatrophy secondary to aging and antiretroviral treatment for HIV. Suggested mechanisms for the development of these granulomas include local clustering of poly-L-lactic acid most commonly because of inadequate massage of the area after injection and incorrect depth of injection. The reason these lesions develop years after injection remains unclear. Cases of late-onset granuloma formation are reported primarily in hypermobile areas such as the nasolabial folds, glabella, and lips. The temporal region, where a late-onset granuloma developed in this case, is not classically considered hypermobile. However, this region does move during chewing and talking and perhaps the qualities and behavior of this region as a cosmetic focus warrant further study. The dilution of the product in 5 mL of bacteriostatic water and lidocaine was adequate to prevent granuloma formation as outlined by safety and efficacy reviews of poly-L-lactic acid. Histopathology confirmed that the depth of injection was indeed in the correct, subcutaneous plane. Suture granulomas occurring after abdominal surgery have appeared as long as 12 years after surgery. Because of the similarity in chemical composition of poly-L-lactic acid and surgical sutures, a longer extent of granuloma latency may theoretically be considered for cosmetic dermatologic procedures. This patient experienced clinical resolution of the granulomas. Although she was treated with an intralesional steroid, it was unclear whether or to what extent this actually provided clinical benefit in terms of resolution, especially given that she also had other granulomas that later resolved without any treatment. This case of the longest yet reported latency period for development of subcutaneous nodules with foreign body reaction observed with poly-L-lactic acid serves to raise awareness of a broader expected time course for complications associated with poly-L-lactic acid injection procedures. With increased awareness,
practitioners can better inform patients of the range of possible complications and can broaden their differential diagnosis for patients presenting for facial nodules of unknown etiology, even if poly-L-lactic acid exposure was several years prior.

The authors thank Southwest Dermatopathology (Carrollton, TX) for initial pathology analysis and shipment of slides.

REFERENCES
1. Sculptra Aesthetic [package insert] Bridgewater, NJ: sanofi-aventis. 2009. Available from: URL: http://products.sanofi-aventis.us/sculptra/sculptra.html.
2. Hanke CW, Rohrich RJ, Busso M, et al. Facial Soft-Tissue Fillers conference: Assessing the State of the Science. J Am Acad Dermatol. 2011;64:566.
3. Alijotas-Reig J, Garcia-Gimenez V, Vilardell-Tarres M. Late-onset immune-mediated adverse effects after poly-L-lactic acid injection in non-HIV patients: clinical findings and long-term follow-up. Dermatology. 2009; 219:303-308.
4. Dijkema J, van der Lei B, Kibbelaar R. New-Fill Injections May Induce Late-Onset Foreign Body Granulomatous Reaction. Plast Reconstr Surg. 2005;115(5):76e-78e.
5. Lam SM, Azizzadeh B, Graivier M. Injectable poly-L-lactic acid (Sculptra): technical considerations in soft-tissue contouring. Plast Reconstr Surg. 2006;118(3 Suppl):S55-S63S.
6. Narins RS. Minimizing adverse events associated with Poly-L-lactic Acid injection. Dermatol Surg. 2008;34: S100-S104.
7. Eunyoung J, Woo-Hyun P, Soon-Ok C. Mesenteric suture granuloma caused by retained fragments of suture material in a girl who had a laparotomy 12 years previously. J Pediatr Surg. 2013;48(1):e25-e27.