

Nodules on the Anterior Neck Following Poly-L-lactic Acid Injection

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PRACTICE POINTS

- Injecting poly-L-lactic acid (PLLA) into the anterior neck is an off-label procedure and may cause a higher incidence of nodule formation.
- Most nodules from PLLA can be treated with injections of 5-fluorouracil, dexamethasone, triamcinolone, and hyaluronidase separated by 8-week intervals.
- Treatment-resistant nodules may require surgical excision.

Poly-L-lactic acid (PLLA) is a synthetic biologic polymer that is suspended in solution and can be injected for soft-tissue augmentation. The most common adverse events generally are transient in nature, such as swelling, tenderness, pain, bruising, and bleeding. Persistent adverse events of PLLA primarily are papule and nodule formation. Injecting PLLA into the anterior neck is an off-label procedure and may cause a higher incidence of nodule formation.

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Poly-L-lactic acid (PLLA) is a synthetic biologic polymer that is suspended in solution and can be injected for soft-tissue augmentation. The stimulatory molecule functions to increase collagen synthesis as a by-product of its degradation.¹ Poly-L-lactic acid measures 40 to 63 μm and is irregularly shaped, which inhibits product mobility and allows for precise tissue

augmentation.² Clinical trials of injectable PLLA have proven its safety with no reported cases of infection, allergies, or serious adverse reactions.³⁻⁵ The most common patient concerns generally are transient in nature, such as swelling, tenderness, pain, bruising, and bleeding. Persistent adverse events of PLLA primarily are papule and nodule formation.⁶ Clinical trials showed a variable incidence of papule/nodule formation between 6% and 44%.² Nodule formation remains a major challenge to achieving optimal results from injectable PLLA. We present a case in which a hyperdiluted formulation of PLLA produced a relatively acute (3-week) onset of multiple nodule formations dispersed on the anterior neck. The nodules were resistant to less-invasive treatment modalities and were further requested to be surgically excised.

Case Report

A 38-year-old woman presented for soft-tissue augmentation of the anterior neck using PLLA to achieve correction of skin laxity and static rhytides. She had a history of successful PLLA injections in the temples, knees, chest, and buttocks over a 5-year period. Forty-eight hours prior to injection, 1 PLLA vial was hydrated with 7 cc bacteriostatic water by using a continuous rotation suspension method over the 48 hours. On the day of injection, the PLLA was further hyperdiluted with 2 cc of 2% lidocaine and an additional 7 cc of bacteriostatic water, for a total of 16 cc diluent. The product was injected using a cannula in the anterior and lateral neck. According to the patient,

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Drs. Dunn and Long report no conflict of interest. Dr. Zarraga is a paid speaker for Galderma Laboratories and a consultant for Bioderma and Senté.

Dr. Aguilera has received honoraria for speaking engagements and training from Allergan, Cynosure, Galderma Laboratories, SkinCeuticals, Solta Medical, and Valeant Pharmaceuticals, and has served as a member of speaker bureaus for Allergan, Cynosure, Galderma Laboratories, Merz, SkinCeuticals, Solta Medical, and Valeant Pharmaceuticals.

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3 weeks after the procedure she noticed that some nodules began to form at the cannula insertion sites, while others formed distant from those sites; a total of 10 nodules had formed on the anterior neck (Figure 1).

The bacteriostatic water, lidocaine, and PLLA vial were all confirmed not to be expired. The manufacturer was contacted, and no other adverse reactions have been reported with this particular lot number of PLLA. The nodules initially were treated with injections of large boluses of bacteriostatic saline, which was ineffective. Treatment was then attempted using injections of a solution containing 1.0 mL of 5-fluorouracil (5-FU) 50 mg/mL, 0.4 mL of dexamethasone 4 mg/mL, 0.1 mL of triamcinolone 10 mg/mL, and 0.3 mL hyaluronidase. A series of 4 injections was performed in 2- to 4-week intervals. Two of the nodules resolved completely with this treatment. The remaining 8 nodules subjectively improved in size and softened to palpation but did not resolve completely. At 2 of the injection sites, treatment was complicated with steroid atrophy of the overlying skin. At the patient's request, the remaining nodules were surgically excised (Figure 2). Histopathology revealed exogenous foreign material consistent with dermal filler (Figure 3).

Comment

Causes of Nodule Formation—Two factors that could contribute to nodule formation are inadequate dispersion of molecules and an insufficient volume of dilution. One study demonstrated that hydration for at least 24 hours is required for adequate PLLA dispersion. Furthermore, sonification for 5 minutes after a 2-hour hydration disperses molecules similarly to the 48-hour hydration.⁷ The PLLA in the current case was hydrated for 48 hours using a continuous rotation suspension method. Therefore, this likely did not play a role in our patient's nodule formation. The volume of dilution has been shown to impact the incidence of nodule formation.⁸ At present, most injectors (60.4%) reconstitute each vial of PLLA with 9 to 10 mL of diluent.⁹ The PLLA in our patient was reconstituted with

16 mL; therefore, we believe that the anatomic location was the main contributor of nodule formation.

Fillers should be injected in the subcutaneous or deep dermal plane of tissue.¹⁰ The platysma is a superficial muscle that is intimately involved with the overlying skin of the anterior neck, and injections in this area could inadvertently be intramuscular. Intramuscular injections have a higher incidence of nodule formation.¹ Our patient had prior PLLA injections without adverse reactions in numerous other sites, supporting the claim that the anterior neck is prone to nodule formation from PLLA injections.

Management of Noninflammatory Nodules—Initial treatment of nodules with injections of saline was ineffective.



FIGURE 2. Surgical excision of a nodule was performed, with the nodule tightly embedded in the underlying tissue.



FIGURE 1. Multiple subcutaneous nodules developed on the neck 3 weeks after poly-L-lactic acid injection.

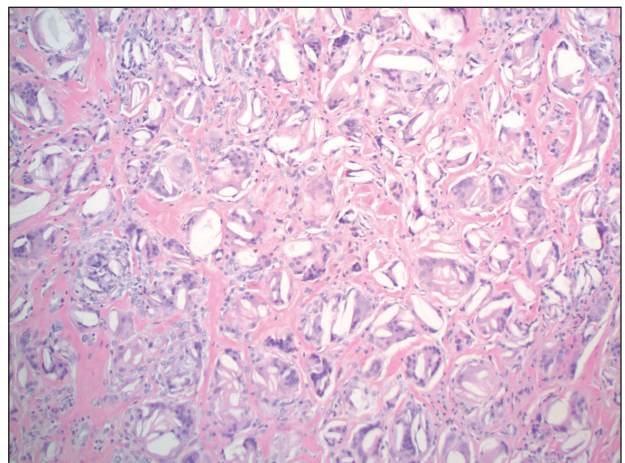


FIGURE 3. Histopathology revealed exogenous foreign material consistent with dermal filler (H&E, original magnification ×10).

This treatment can be used in an attempt to disperse the product. Treatment was then attempted with injections of a solution containing 5-FU, dexamethasone, triamcinolone, and hyaluronidase. Combination steroid therapy may be superior to monotherapy.¹¹ Dexamethasone may exhibit a cytoprotective effect on cells such as fibroblasts when used in combination with triamcinolone; monotherapy steroid use with triamcinolone alone induced fibroblast apoptosis at a much higher level.¹² Hyaluronidase works by breaking cross-links in hyaluronic acid, a glycosaminoglycan polysaccharide prevalent in the skin and connective tissue, which increases tissue permeability and aids in delivery of the other injected fluids.¹³ 5-Fluorouracil is an antimetabolite that may aid in treating nodules by discouraging additional fibroblast activity and fibrosis.¹⁴

The combination of 5-FU, dexamethasone, and triamcinolone has been shown to be successful in treating noninflammatory nodules in as few as 1 treatment.¹⁴ In our patient, hyaluronidase also was used in an attempt to aid delivery of the other injected fluids. If nodules do not resolve with 1 injection, it is recommended to wait at least 8 weeks before repeating the injection to prevent steroid atrophy of the overlying skin. In our patient, the intramuscular placement of the filler contributed to the nodules being resistant to this treatment. During excision, the nodules were tightly embedded in the underlying tissue, which may have prevented the solution from being delivered to the nodule (Figure 2).

Conclusion

Injectable PLLA is approved by the US Food and Drug Administration for soft-tissue augmentation of deep nasolabial folds and facial wrinkles. Off-label use of this product may cause higher incidence of nodule formation. Injectors should be cautious of injecting into the anterior neck. If nodules do form, treatment can be attempted with injections of saline. If that treatment fails, another treatment option is injection(s) of a mixture of 5-FU, dexamethasone, triamcinolone, and hyaluronidase

separated by 8-week intervals. Finally, surgical excision is a viable treatment option, as presented in our case.

REFERENCES

1. Bartus C, William HC, Daro-Kaftan E. A decade of experience with injectable poly-L-lactic acid: a focus on safety. *Dermatol Surg.* 2013;39:698-705.
2. Engelhard P, Humble G, Mest D. Safety of Sculptra: a review of clinical trial data. *J Cosmet Laser Ther.* 2005;7:201-205.
3. Mest DR, Humble G. Safety and efficacy of poly-L-lactic acid injections in persons with HIV-associated lipoatrophy: the US experience. *Dermatol Surg.* 2006;32:1336-1345.
4. Burgess CM, Quiroga RM. Assessment of the safety and efficacy of poly-L-lactic acid for the treatment of HIV associated facial lipoatrophy. *J Am Acad Dermatol.* 2005;52:233-239.
5. Cattelan AM, Bauer U, Trevenzoli M, et al. Use of poly(lactic acid) implants to correct facial lipoatrophy in human immunodeficiency virus 1-positive individuals receiving combination antiretroviral therapy. *Arch Dermatol.* 2006;142:329-334.
6. Sculptra. Package insert. sanofi-aventis U.S. LLC; 2009.
7. Li CN, Wang CC, Huang CC, et al. A novel, optimized method to accelerate the preparation of injectable poly-L-lactic acid by sonication. *J Drugs Dermatol.* 2018;17:894-898.
8. Rossner F, Rossner M, Hartmann V, et al. Decrease of reported adverse events to injectable poly(lactic acid) after recommending an increased dilution: 8-year results from the Injectable Filler Safety study. *J Cosmet Dermatol.* 2009;8:14-18.
9. Lin MJ, Dubin DP, Goldberg DJ, et al. Practices in the usage and reconstitution of poly-L-lactic acid. *J Drugs Dermatol.* 2019;18:880-886.
10. Sieber DA, Scheuer JF 3rd, Villanueva NL, et al. Review of 3-dimensional facial anatomy: injecting fillers and neuromodulators. *Plast Reconstr Surg Glob Open.* 2016;4(12 suppl Anatomy and Safety in Cosmetic Medicine: Cosmetic Bootcamp):E1166.
11. Syed F, Singh S, Bayat A. Superior effect of combination vs. single steroid therapy in keloid disease: a comparative in vitro analysis of glucocorticoids. *Wound Repair Regen.* 2013;21:88-102.
12. Brody HJ. Use of hyaluronidase in the treatment of granulomatous hyaluronic acid reactions or unwanted hyaluronic acid misplacement. *Dermatol Surg.* 2005;31:893-897.
13. Funt D, Pavicic T. Dermal fillers in aesthetics: an overview of adverse events and treatment approaches. *Clin Cosmet Invest Dermatol.* 2013;6:295-316.
14. Aguilera SB, Aristizabal M, Reed A. Successful treatment of calcium hydroxylapatite nodules with intralesional 5-fluorouracil, dexamethasone, and triamcinolone. *J Drugs Dermatol.* 2016; 15:1142-1143.