Lipofilling after Laser-Assisted Treatment for Facial Filler Complication: Volumetric and Regenerative Effect

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Background: Nonresorbable substances are still injected to enhance soft-tissue volumes and fill subcutaneous defects. The minimally invasive intralesional laser treatment can remove foreign substances and the inflammatory reaction, eventually leaving depression and scar tissue in the treated area. Fat grafting can restore volume loss and improve scar tissue.
Methods: From March of 2010 to February of 2017, 33 patients were studied. All of them had suffered from inflammatory reactions to permanent facial fillers and had been treated with the 808-nm diode laser at the authors' institution. The evacuation of material had left facial asymmetry and visible depression. To restore facial aesthetic units, fat grafting was performed. The minimum follow-up was 6 months.
Results: Volume restoration was recognized (according to the Global Aesthetic Improvement Scale) as significantly improved in 22 patients, moderately improved in eight patients, and slightly improved in three patients. Improvement in atrophic and scarred tissues (with an apparent thickening of the skin or even elimination of scars) was also assessed with the following results: 25 patients were very much improved and eight were moderately improved.
Conclusions: This is the first study on filler-induced complications of the face treated by intralesional laser treatment followed by lipofilling. A systematic approach to volume restoration is proposed to patients who had filler removal of the face. There was a high degree of patient satisfaction with this technique. (*Plast. Reconstr. Surg.* 147: 585, 2021.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

Botulinum toxin and injectable filler substances are the two most popular nonsurgical aesthetic products in the world.[1] Although injectable fillers are considered to be safe, significant adverse reactions have been described, especially for permanent fillers.[2–5] Nonresorbable fillers last for years in soft tissues and can cause inflammation at any time.[6] These adverse events are frequent because illegal fillers are frequently used in many parts of the world.

Long-lasting inflammatory reactions of different severity are responsible for complications,[7,8] such as granulomas, infections, inflammatory or noninflammatory nodules, ulceration, cellulitis, and migration, that may take months to years to occur. Foreign body granuloma can occur as a culture-negative mass or nodule and frequently causes pain and induration. It is a foreign body reaction with activation of the inflammatory response, secretion of cytokines, and macrophage transformation in multinucleated giant cells.[9–12]

Delayed infections are thought to be caused by biofilm formation, consisting of bacteria, protozoa, or fungi encapsulated in a polymeric matrix.[13]

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These lesions are difficult to treat. Systemic antibiotics, antiinflammatory drugs, intralesional corticosteroid and 5-fluorouracil injection, needle aspiration, surgical drainage, and excision are the most described therapeutic approaches.[14] Surgical excision is possible only in case of small nodules, whereas large sheets of hard subcutaneous tissue or rock-like lesions are difficult to cut through, and a large defect is left after removal.[15] Consequently, there has been interest in laser techniques, which are minimally invasive and can be considered an effective and safe alternative treatment.

Cassuto et al. reported their experience (2006 to 2013)[16] at the University Hospital of Modena (regional referral center for the treatment of filler complications in the face) based on laser treatment of 219 consecutive patients affected by inflammatory reactions to permanent facial fillers, with complete disappearance of lesions (lumps and inflammation) in 62 percent of cases and partial improvement (with >50 percent reduction) in 30 percent of cases. The authors described a treatment algorithm based on ultrasound soft-tissue examination. Lesions can be classified as either cystic or infiltrating.

Infiltrating patterns are treated with an intralesional laser treatment procedure consisting of several small holes drilled directly into the material, which is heat-liquefied and removed by squeezing. Eventual further treatment may be required and is performed after 6 months.

In case of cystic implant, the same procedure is performed and a stab incision (no. 11 blade) has to be added and left open for drainage. Nevertheless, this technique has shown satisfying results; patients ask for their previous aspect to be restored.

If the removed material has a cystic distribution, eliminating the polymer can leave a visible depression, whereas facial asymmetry results in cases of infiltrating pattern. Furthermore, smallpox-like scarring at the laser entry and fibrosis of the surrounding tissue caused by excessive heating are rare but occur in some cases. In this article, we report our experience in the treatment of these sequelae using fat grafting for aesthetic and functional refinements.

PATIENTS AND METHODS

Thirty-three patients referred from March of 2010 to February of 2017 for inflammatory reaction to permanent fillers and treated with the 808-nm diode laser (LASEmaR 800; Eufoton, Trieste, Italy) and fat grafting at our institution were included in the study. The minimum follow-up was 12 months.

Exclusion criteria were as follows: (1) patients with cancer or collagen disorders; (2) patients with other acute or chronic dermatologic disorders; (3) patients with coagulation defects and platelet count less than 150,000/mm^3; (4) pregnant or lactating patients; (5) patients who underwent further subsequent facial rejuvenating procedures during the study period; and (6) patients with evidence of infection at the time of the treatment. The mean age of the patients was 45 years (range, 29 to 63 years). Thirty-one were women and two were men. All patients showed facial lesions (specific locations are listed in Fig. 1). Most patients were referred to our center after being treated elsewhere with local or systemic corticosteroids and antibiotics with limited and temporary improvement, if any.

Medical records included sex, age, medical history, ongoing medication, and concomitant medical conditions. According to the ultrasound soft-tissue examination (cystic or infiltrative pattern) and clinical evaluation, on the basis of the treatment algorithm suggested by Cassuto et al., 23 patients (infiltrating pattern) were treated with intralesional laser treatment alone, whereas 10 patients (cystic pattern) were also drained through stab wound incisions The laser used was an 808-nm diode laser (LASEmaR 800).

Different materials have been removed (e.g., Bio-Alcamid, Aquamid, Dermalive, Silicon oil, Artecoll) according to different information (e.g., ultrasound distribution pattern, appearance of the evacuated material, filler material behavior during the laser procedure, patient anamnesis). The average number of treatment sessions per lesion was 1.94, with a minimum of 2.5 months from the first session to the next one.

Complete disappearance of lesions (lumps and inflammation) was obtained in all cases without recurrence of symptoms and with the cessation of the steroid therapy. Patients were referred to us because facial asymmetry and visible depression occurred after the evacuation of material. Furthermore, skin and soft tissue showed scarring (because of laser entry and excessive heating) and atrophy (because of a chronic inflammatory process and repeated steroid injections usually administered before laser). Fat grafting was performed to restore facial aesthetic units starting at least 3 months after the last treatment.

Study Procedures

Fat grafting is performed according to the Coleman technique.[17,18] Fat harvesting areas are selected by patient preference, by the volume of fat required, and by easy access in the supine position. Medial thighs, flanks, and abdomen were our most suitable areas as a donor site.

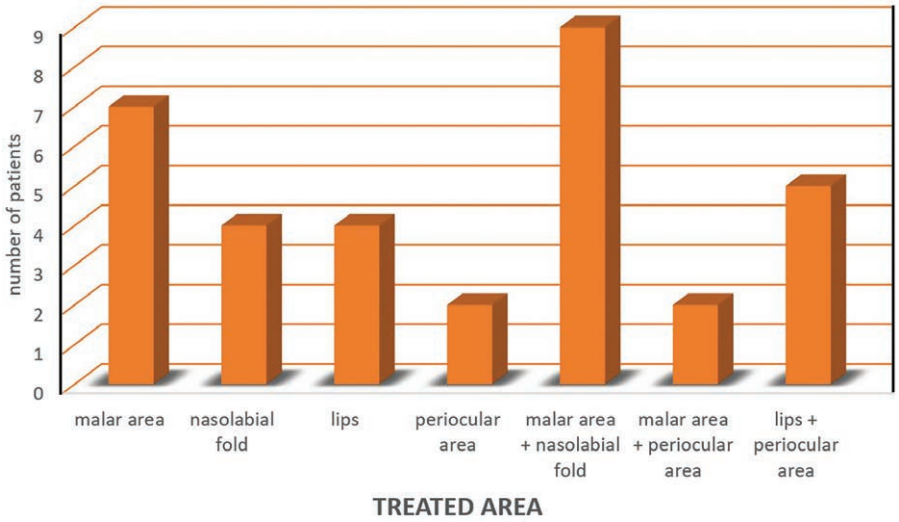

Fig. 1. Graph showing the different location of the facial lesions: malar area, seven patients; nasolabial fold, four patients; lips, four patients; periocular area, two patients; malar area and nasolabial fold, nine patients; and malar area and periocular area, two patients; lips and periocular area, five patients.

Fat is harvested under local anesthesia using a tumescent solution containing 0.5% lidocaine with 1:200,000 epinephrine (with a ratio of aspirated fat to tumescent solution of approximately 1:1) infused with a blunt infiltration cannula. The harvesting cannula (2-mm diameter with 1-mm holes) is connected with a 10-ml Luer-Lok (Becton, Dickinson & Co., Franklin Lakes, N.J.) syringe. Fat graft is processed through centrifugation at 3000 rpm (approximately 1200 *g*) for 3 minutes.

The oil of the upper layer is removed, the aqueous layer is easy drained out, and the remnant concentrated fat is transferred from 10-ml to 1-ml injection syringes. A solution of 0.5% lidocaine with 1:200,000 epinephrine is infused into the recipient site.

If necessary, release of firm attachment of the skin over the proposed injected areas (adhesions, fibrotic tissue, scar, ligament attachments) is performed with a sharp 20-gauge needle. Small blunt cannulas (from 20- to 12-gauge in diameter and from 5 to 9 cm in length, and in selected superficial areas, a 21-gauge needle) are used for fat injection in small volume (no more than 0.1 ml in each pass) through multiple passes at different depths and with various directions to obtain the maximal amount of contact with the native tissue with its blood supply.

Compressive dressings and ice packing are applied to the donor site to prevent hematoma. Massage, compression, or ice packs to the face are not allowed, because these may compromise fat graft survival. A period of up to 4 months is usually necessary to fully realize the eventual reabsorption of fat in addition to the healing from mechanical trauma. The need for further treatment is evaluated at 6 months. Patients were photographed at first consultation, before each treatment session, and at 12 months.

Outcome Measures

At 12 months after the last treatment, aesthetic correction, patient satisfaction, and adverse events were evaluated. Aesthetic correction (both volume replacement and scarring and atrophy) was scored using the patient-graded Global Aesthetic Improvement Scale,[19] which uses the following scale: 1, very much improved; 2, much improved; 3, improved; 4, no change; and 5, worse. This was conducted by two independent board-certified plastic surgeons. Overall patient satisfaction was evaluated using a questionnaire with a five-point scale, ranging from very satisfied (score of 0) to very dissatisfied (score of 4) (Table 1), submitted to every single patient. Adverse events including pain, edema, bruising, infection, nodule formation, oily cyst, calcification, and persistent asymmetry were recorded.

RESULTS

Of the 33 patients that met inclusion criteria and were enrolled in the study, all started and finished the treatment; none of them discontinued the treatment because of a lack of patient satisfaction. All patients were Caucasian.

Table 1. Patient Satisfaction Evaluation Scale

Level of Satisfaction	Score
Very satisfied	0
Satisfied	1
Neither satisfied nor dissatisfied	2
Dissatisfied	3
Very dissatisfied	4

The average number of lipofilling sessions per patient was 4.4. The average quantity of injected fat per area per session was 2 ml in the nasolabial fold, 1 ml in the periocular area, 6 ml in the malar area, and 2 ml in the lip area.

Aesthetic outcome was satisfactory for almost all patients. Volume restoration was recognized (according to the Global Aesthetic Improvement Scale) as very much improved in 22 patients, as moderately improved in eight patients, and as improved in three patients (Fig. 2). Improvement in atrophic and scarred tissues (with an apparent thickening of the skin or even elimination of scars) was also assessed, with the following results: 25 patients were very much improved and eight were moderately improved (Fig. 3). Patients reported high levels of satisfaction; 30 defined themselves as score 0 (very satisfied) and three as score 1 (satisfied) (Fig. 4).

The high overall patient satisfaction is evident in patient willingness to undergo the procedure again. No patient reported appearing worse than at baseline. Three cases are presented in Figures 5 through 7.

The vast majority of complications were transient and caused by the inflammatory response to the lipofilling procedure in the treated area. There were no reported infections. We report the occurrence of an oily cyst in only one patient, which was treated with drainage of the lesion. No complications were detected in the donor site.

DISCUSSION

Inflammatory reactions, together with steroid injections and, to a lesser extent, the laser treatment itself can be responsible for scar skin processes. Furthermore, removal of material causes a loss of volume in the treated area.

In our opinion, the use of commercial fillers for this purpose is not recommended. Even though most filler materials are generally regarded as safe, there is the risk of adverse reactions.[2–4] In our patients, this risk is increased because, after laser treatment, even a nano quantity of the permanent filler previously injected can remain in the treated area, resulting in a combination of different types of filler in a single area.

It has in fact been recommended not to inject a filler in an area previously injected with another type of filler, especially if that filler is a permanent filler.[8] Case reports on adverse reactions after consecutive filler injections are constantly disclosed.[20,21] Several theories have tried to explain the increased risk of adverse reactions after the combination of different fillers in limited space, including activation of the immune system caused by repetitive injection[8–21] and biofilm theory.[9,22,23] Furthermore, different factors might also play a role in foreign body reactions such as implant size and volume, implant morphology, surface area, chemical composition, electrical charge, and implantation site.[8–24]

On the basis of previous considerations, we selected only fat because it represents an ideal

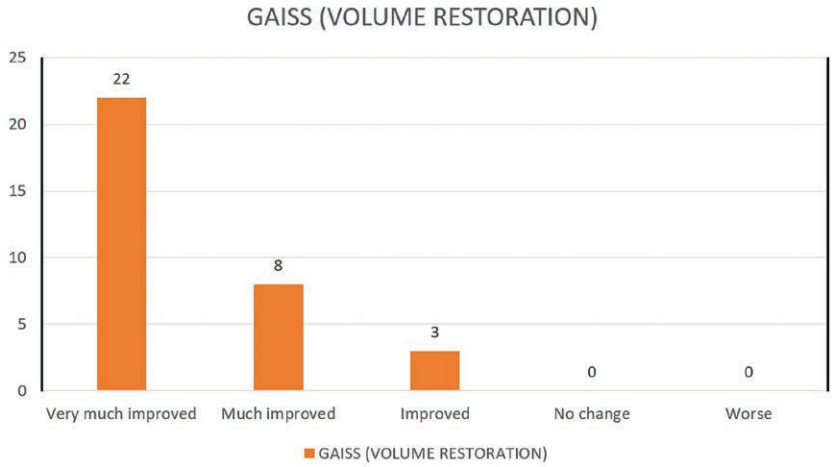

Fig. 2. Volume restoration was recognized as very much improved in 22 patients, as much improved in eight patients, and as improved in three patients. *GAISS*, Global Aesthetic Improvement Scale score.

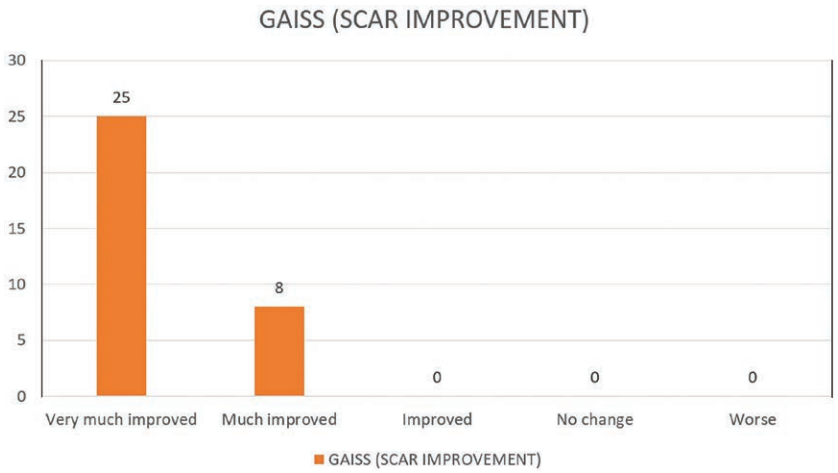

Fig. 3. Scar improvement was recognized as very much improved in 25 patients and as much improved in eight patients. *GAISS*, Global Aesthetic Improvement Scale score.

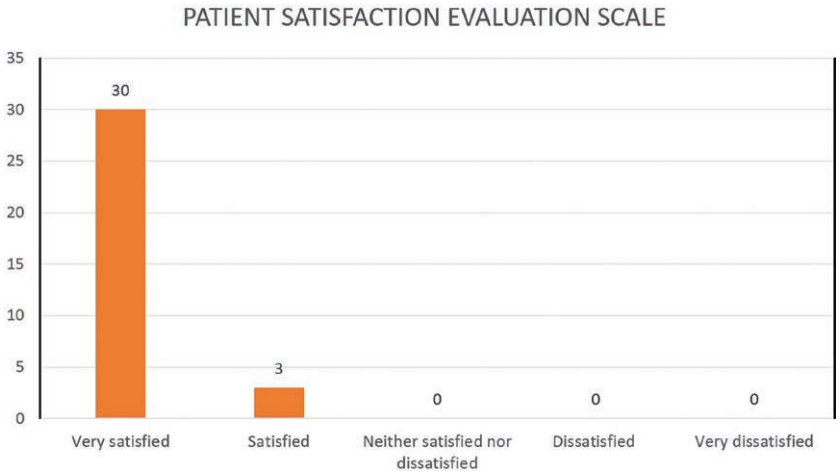

Fig. 4. Thirty patients defined themselves as score 0 (very satisfied) and three as score 1 (satisfied).

filler because of its availability, ease of harvest, low donor-site morbidity, low cost, permanence, versatility, and exceptional biocompatibility. It is suitable for both aesthetic[25,26,27] and reconstructive[28–31] purposes. In fact, fat grafting in our patients aims to not only restore the facial volume loss and contour deformities but also improve the quality of the scar tissue and the overlying skin, which is usually atrophic because of the previous chronic inflammatory process and repeated steroid injections.

Adipose-derived stem cells have also been shown to play a role in antiaging and skin regeneration by forming tissue consisting of hypodermis, dermis, and epidermis.[32–34] The inflammatory nodule basically replaced the dermis as a support to the epidermis, and the removal of the polymer left a visible skin depression.

Fat was placed in the intradermal or subdermal layer to improve skin quality and to correct superficial irregularities and in a deeper plane to restore volume and facial proportions. Thus, fat placement at different depths is necessary, and multiple lipofilling sessions are required to avoid fat necrosis and reabsorption eventually caused by large-bolus grafting.

According to the authors' experience, the total amount injected and the number of treatment sessions when we compare the same area were higher in patients who underwent permanent filler removal than in patients who simply wanted facial rejuvenation. The average number of sessions after filler removal of a malar or nasolabial area is 4.4 (range, three to six); for rejuvenation purpose, it is less than half that. Despite our limited experience, in our opinion, the indication of volume replacement after intralesional laser treatment for filler granulomas is with fat grafting.

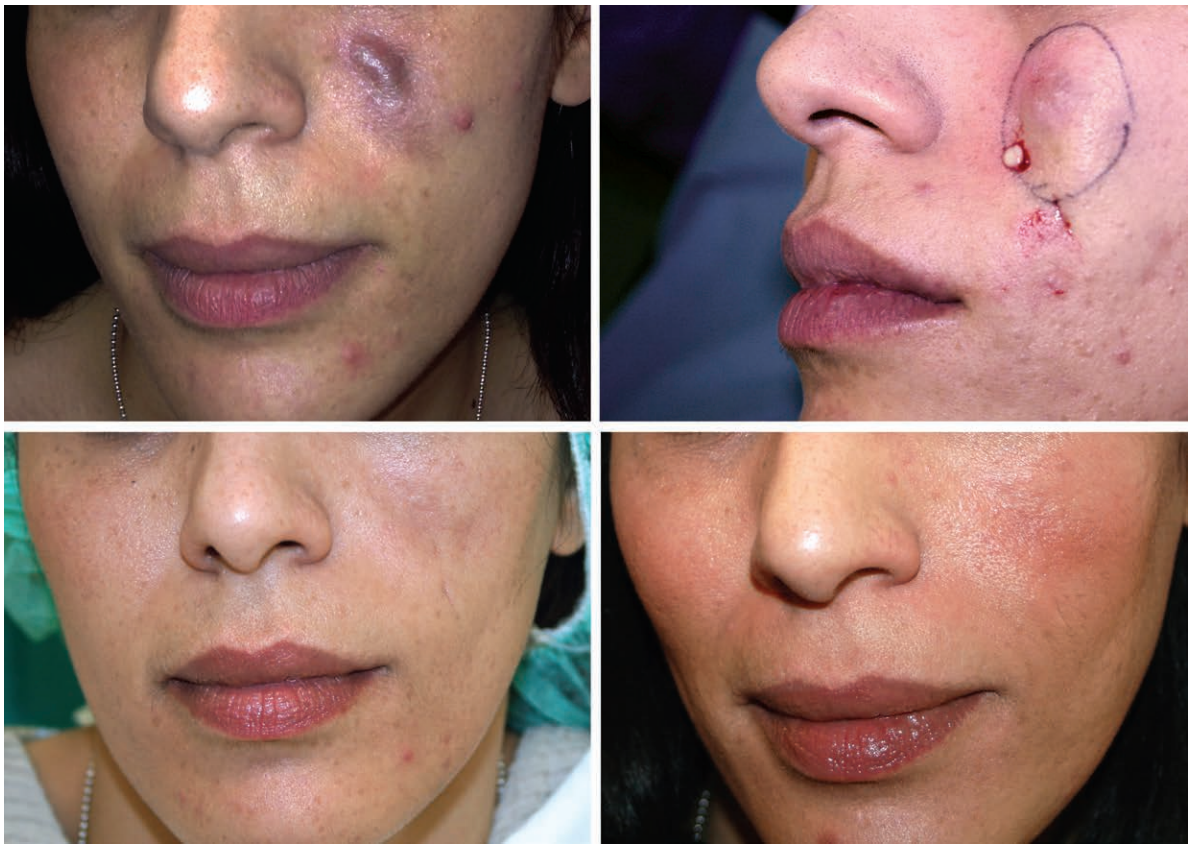

Fig. 5. Patient 1. (*Above*, *left*) Granuloma of the left malar region. (*Above*, *right*) Filler outflow during laser treatment and stab incision. (*Below*, *left*) Volumetric defect 3 months after removal of the filler. (*Below*, *right*) Final result after three lipofilling treatments.

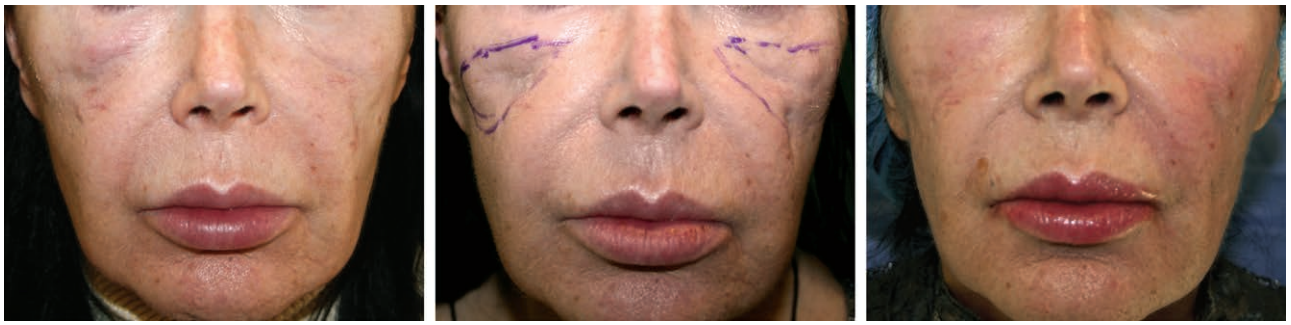

Fig. 6. Patient 2. (*Left*) Granuloma of bilateral malar areas. (*Center*) Volumetric defect 3 months after removal of the filler. (*Right*) Final result after four lipofilling treatments.

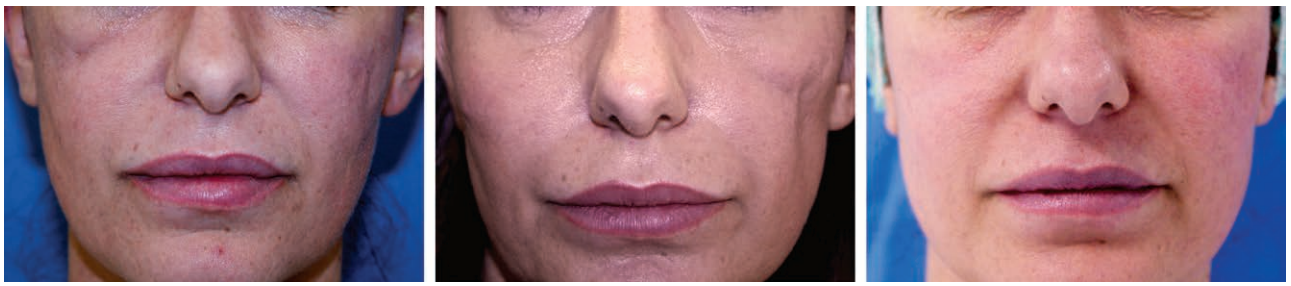

Fig. 7. Patient 3. (*Left*) Granuloma of the malar areas. (*Center*) Volumetric defect 3 months after removal of the filler. (*Right*) Final result after five lipofilling treatments.

CONCLUSIONS

In the literature, there are no reports of fat grafting after laser treatment for filler granulomas. Based on our experience, we suggest autologous fat grafting for volume restoration and scar improvement because of its biocompatibility, availability, and antiinflammatory properties. The overall satisfaction of both surgeons and patients allows us to continue performing such procedures.

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PATIENT CONSENT

Patients provided written consent for the use of their images.

REFERENCES

1. Carruthers JDA, Glogau RG, Blitzer A, et al. Advances in facial rejuvenation: Botulinum toxin type A, hyaluronic acid dermal fillers, and combination therapies. Consensus recommendations. *Plast Reconstr Surg.* 2008;121(Suppl 5):5S–30S; quiz 31S–36S.
2. Broder KW, Cohen SR. An overview of permanent and semipermanent fillers. *Plast Reconstr Surg.* 2006;118(Suppl):7S–14S.
3. Eppley BL, Dadvand B. Injectable soft-tissue fillers: Clinical overview. *Plast Reconstr Surg.* 2006;118:98e–106e .
4. Wiest LG. Historie und anwendung der filler zur faltenbehandlung. *Hautarzt* 2007;58:224–231.
5. Zielke H, Wölber L, Wiest L, Rzany B. Risk profiles of different injectable fillers: Results from the Injectable Filler Safety Study (IFS Study). *Dermatol Surg.* 2008;34:326–335; discussion 335.
6. Rohrich RJ, Monheit G, Nguyen AT, Brown SA, Fagien S. Soft-tissue filler complications: The important role of biofilms. *Plast Reconstr Surg.* 2010;125:1250–1256.
7. Requena L, Requena C, Christensen L, Zimmermann US, Kutzner H, Cerroni L. Adverse reactions to injectable soft tissue fillers. *J Am Acad Dermatol.* 2011;64:1–34.
8. Nicolau PJ. Long-lasting and permanent fillers: Biomaterial influence over host tissue response. *Plast Reconstr Surg.* 2007;119:2271–2286.
9. Christensen L, Breiting V, Janssen M, Vuust J, Hogdall E. Adverse reactions to injectable soft tissue permanent fillers. *Aesthetic Plast Surg.* 2005;29:34–48.
10. Rapinini R, Bolognia J, Jorizzo J. *Dermatology.* St. Louis: Mosby; 2007.
11. Ratner B, Hoffman A, Schoen F. *Biomaterial Science: An Introduction to Materials in Medicine.* 2nd ed. Philadelphia: Elsevier Science; 2004.
12. Funt D, Pavicic T. Dermal fillers in aesthetics: An overview of adverse events and treatment approaches. *Clin Cosmet Investig Dermatol.* 2013;6:295–316.
13. Sadashivaiah AB, Mysore V. Biofilms: Their role in dermal fillers. *J Cutan Aesthet Surg.* 2010;3:20–22.
14. Carruthers A, Carruthers J. (Discussion) Adverse granulomatous reaction to Artecoll treated by intralesional 5-fluorouracil and triamcinolone injections. *Dermatol Surg.* 2006;32:1082.
15. Woodward J, Khan T, Martin J. Facial filler complications. *Facial Plast Surg Clin North Am.* 2015;23:447–458.
16. Cassuto D, Pignatti M, Pacchioni L, Boscaini G, Spaggiari A, De Santis G. Management of complications caused by permanent fillers in the face: A treatment algorithm. *Plast Reconstr Surg.* 2016;138:215e–227e.
17. Coleman SR. Long-term survival of fat transplants: Controlled demonstrations. *Aesthetic Plast Surg.* 1995;19:421–425.
18. Coleman SR. Facial recountouring with lipostructure. *Clin Plast Surg.* 1997;24:347–367.
19. Narins RS, Brandt F, Leyden J, Lorenc ZP, Rubin M, Smith S. A randomized, double-blind, multicenter comparison of the efficacy and tolerability of Restylane versus Zyplast for the correction of nasolabial folds. *Dermatol Surg.* 2003;29:588–595.
20. Rossner M, Rossner F, Bachmann F, Wiest L, Rzany B. Risk of severe adverse reactions to an injectable filler based on a fixed combination of hydroxyethylmethacrylate and ethylmethacrylate with hyaluronic acid. *Dermatol Surg.* 2009;35(Suppl 1):367–374.
21. Bentkover SH. The biology of facial fillers. *Facial Plast Surg.* 2009;25:73–85.
22. Christensen L. Normal and pathologic tissue reactions to soft tissue gel fillers. *Dermatol Surg.* 2007;33:S168–S175.
23. Christensen LH. Host tissue interaction, fate, and risks of degradable and nondegradable gel fillers. *Dermatol Surg.* 2009;35:1612–1619.
24. Laeschke K. Biocompatibility of microparticles into soft tissue fillers. *Semin Cutan Med Surg.* 2004;23:214–217.
25. Endara MR, Allred LJ, Han KD, Baker SB. Applications of fat grafting in facial aesthetic skeletal surgery. *Aesthetic Surg J.* 2014;34:363–373.
26. Ellenbogen R, Youn A, Yamini D, Svehlak S. The volumetric face lift. *Aesthetic Surg J.* 2004;24:514–522.
27. Gamboa GM, Ross WA. Autologous fat transfer in aesthetic facial recontouring. *Ann Plast Surg.* 2013;70:513–516.
28. Coleman S, Saboeiro A, Sengelmann R. A comparison of lipoatrophy and aging: Volume deficits in the face. *Aesthetic Plast Surg.* 2009;33:14–21.
29. Moratalla Jareño T, González Alonso V, López Blanco E, Domenèch Tárrega A, Carazo Palacios E, Gutiérrez Ontalvillas P. Use of lipofilling in pediatric patients (in Spanish). *Cir Pediatr.* 2013;26:189–194.
30. Balaji S. Subdermal fat grafting for Parry-Romberg syndrome. *Ann Maxillofac Surg.* 2014;4:55–59.
31. Hunstad JP, Shifrin DA, Kortesis BG. Successful treatment of Parry-Romberg syndrome with autologous fat grafting: 14-year follow-up and review. *Ann Plast Surg.* 2011;67:423–425.
32. Salinas HM, Broelsch GF, Fernandes JR, et al. Comparative analysis of processing methods in fat grafting. *Plast Reconstr Surg.* 2014;134:675–683.
33. Starnoni M, De Santis G, Pinelli M. Dermal matrix fixation: A good adhesion to wound edges without vascularization impairment. *Plast Reconstr Surg Glob Open* 2019;7:e2327.
34. Foppiani EM, Candini O, Mastrolia I, et al. Impact of HOXB7 overexpression on human adipose-derived mesenchymal progenitors. *Stem Cell Res Ther.* 2019;10:101.