Aesth Plast Surg (2019) 43:115–122
https://doi.org/10.1007/s00266-018-1250-7

ORIGINAL ARTICLE OCULOPLASTIC

Managing Periocular Filler-Related Syndrome Prior to Lower Blepharoplasty

Christopher I. Zoumalan[1]

Received: 14 July 2018 / Accepted: 22 September 2018 / Published online: 8 October 2018

Abstract

Background Hyaluronic acid (HA) fillers are extensively used in periocular volume augmentation. Although they have an excellent safety profile, filler-related issues such as visibility/palpability, contour abnormalities, malar edema, and blue-gray dyschromia can occur. Recognition and management of filler-related issues are critical prior to subsequent procedures. The clinical course of patients who had periocular HA filler-related issues and subsequently underwent lower eyelid blepharoplasty is described.

Methods HA filler was dissolved with hyaluronidase (15–30 U/cm^2) treatment. Visible lower eyelid fat prolapse after filler removal was corrected with transconjunctival blepharoplasty with fat repositioning and skin resurfacing. Complications and outcome were assessed and recorded.

Results Twenty-three patients (46 eyelids) were treated. All presented with contour abnormalities, 19 with contour abnormalities and malar edema, and seven with blue-gray dyschromia. In 15 patients, one session of hyaluronidase completely dissolved the filler, and in eight patients, two sessions were required. Of these eight patients, edema resolved after the second hyaluronidase injection in four; in the remaining four, mild edema persisted despite absence of visible/palpable filler. Postblepharoplasty, 19 patients had an acceptable outcome with no complications (82.6%). Four patients had prolonged edema postoperatively; three had a resolution by 6 months. In 23 patients who had skin resurfacing procedures, there was no incidence of postinflammatory hyperpigmentation.

Conclusions HA filler-related issues need to be identified and managed prior to further intervention. Hyaluronidase treatment effectively dissolves the filler, but mild malar edema can persist. Outcomes are acceptable after subsequent blepharoplasty, but adequate patient counseling is necessary about expectations and limitations.

Level of Evidence IV This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Hyaluronic acid · Under eye fillers · Infraorbital rim hollowing · Tear trough deformity · Hyaluronidase · Blepharoplasty

Introduction

Hyaluronic acid fillers are extensively used in periocular rejuvenation procedures to treat lower eyelid hollowness and mask lower eyelid fat prolapse [1–3]. With proven safety and efficacy (albeit temporary), coupled with greater longevity and high patient satisfaction, hyaluronic acid fillers are currently regarded as the gold standard for soft tissue fillers [4]. Despite their track record and popularity, hyaluronic acid fillers are not without undesirable consequences. Filler persistence, blue-gray dyschromia, filler migration, skin expansion from overfilling, contour abnormalities, and persistent edema are notable short- and long-term filler-related issues for patients in the periocular area [5–10].

✉ Christopher I. Zoumalan
drchris@zoumalanmd.com

[1] Keck School of Medicine, University of Southern California, 9401 Wilshire Blvd, Suite 1105, Beverly Hills, CA 90212, USA

Filler-related issues may arise from improper selection of patients for injectable fillers below the infraorbital rim. Generally speaking, patients with infraorbital rim hollowing with little to no orbital fat prolapse are potential candidates for injectable filler treatment, while those with orbital fat prominence are likely better candidates for lower eyelid blepharoplasty. Injectable filler treatments to "mask" the prolapsed orbital fat can result in undesirable filler-related issues [11].

Patients who have received hyaluronic acid injections often require repeat injections or additional treatments such as lower eyelid blepharoplasty and presence of filler-related issues can adversely affect the subsequent procedure and may lead to suboptimal outcomes. Furthermore, those particular patients that have prominent prolapsed lower eyelid fat in the setting of hyaluronic acid fillers may ultimately require a lower eyelid blepharoplasty surgery, and the prompt recognition and management of hyaluronic acid filler-related issues is critical prior to additional procedures.

Taban recently published a case series describing the management and excellent surgical outcomes in 15 patients that underwent lower eyelid blepharoplasty given a history of prior injectable fillers [12], but this is the first study to describe the management of periocular filler-related issues and clinical course of patients who subsequently underwent lower eyelid blepharoplasty.

Methods

This is a retrospective study of patients who had previously received hyaluronic acid gel injections for lower eyelid periocular rejuvenation and presented to the author's practice between January 2015 and January 2018 desiring further improvements in their appearance. Previous hyaluronic acid gel injections were performed elsewhere and not at the author's practice. On examination, all patients had contour abnormalities, malar edema, and/or blue-gray dyschromia along their lower eyelid and surrounding periocular area. Treatment with hyaluronidase was undertaken to dissolve the filler material prior to any further intervention.

Generic, bovine-based hyaluronidase (150 U/mL; O'Brien Pharmacy, Mission, Kansas, USA), which has been found to be equally effective as the discontinued product Wydase® (Wyeth, Marietta, PA), was mixed 1:10 with lidocaine 1% and used to dissolve hyaluronic acid [13]. Hyaluronidase intradermal forearm skin testing (10 U) was performed in patients prior to hyaluronidase treatments. Patients proceeded with treatment if they had no allergic reaction. Fifteen to 30 U/cm^2 was used per treatment setting, based on the amount of product that was visible or palpable and/or on the chronicity of the filler-related issue. Larger U/cm^2 of hyaluronidase was used in patients that had chronic fillers (> 6 months), visible, and/or significantly palpable product. Following removal of the hyaluronic acid filler, patients were re-examined 10–14 days later to determine whether they required further hyaluronidase treatments. Patients that had visible lower eyelid fat prolapse following removal of the hyaluronic acid were candidates for lower eyelid blepharoplasty and were included in the study. Patients who had prior lower eyelid blepharoplasty or additional eyelid or facial plastic procedures at the same setting were excluded from the study. All patients underwent a transconjunctival lower eyelid blepharoplasty with fat repositioning and skin resurfacing as described in a prior article [11]. Depending on the severity of fat prolapse and the infraorbital rim hollowing, varying amounts of prolapsed fat were surgically debulked, and a varying amount of orbital fat was repositioned. Patients were photographed before and after each treatment. Complications and outcomes were assessed and recorded, and compared to a control group with no previous history of periocular HA filler. The control group underwent transconjunctival blepharoplasty with fat repositioning and skin resurfacing during the same time period (January 2015 to January 2018). In this control group, all patients presented preoperatively with herniated lower lid fat prominence, with variable degree of lower lid rhytids or skin excess.

Written consent was obtained from all patients prior to hyaluronidase treatment and lower eyelid blepharoplasty. Photographic and publication consent was also obtained. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

Results

Periocular Filler-Related Issues and Blepharoplasty Group

Twenty-three patients, seven men and 16 women, with an average age of 48 ± 12 years, were included in the study (Table 1). A total of 46 eyelids were treated. All patients presented with evidence of contour abnormalities, and 19 patients (38 eyelids; 82.6%) presented with both contour abnormalities and malar edema. Blue-gray dyschromia was seen in seven of the patients (14 eyelids), (30.4%). There was no statistically significant difference in the incidence of blue-gray dyschromia with specific hyaluronic acid gel

Table 1 Patient baseline data—filler-related issues group

Characteristic	Value
Patients, no.	23
Gender, no.	
Male	7
Female	16
Mean age ± SD, years	48 ± 12
Eyelids with filler-related issues, no.	46
Filler-related issues, no. of patients	
Contour abnormalities	23
Contour abnormalities and malar edema	19
Blue-gray dyschromia	7

SD standard deviation

brands. In 14 patients, the filler material was known: JUVÉDERM® Ultra Plus XC [Allergan, Irvine, CA] in six patients, Restylane® [Galderma Laboratories, L.P.; Fort Worth, TX] in seven patients, and Belotero® [Merz Pharmaceuticals LLC; Raleigh, NC] in one patient. As patients were from outside referral sources, the volume of filler material injected, the number of injections that they had received, or the time from last injection was unknown and could not be reliably estimated.

Patients underwent their first hyaluronidase injections at 26 ± 7 days prior to blepharoplasty. An average of 61 ± 20 U of hyaluronidase was injected per eyelid. In 15 patients, 30 eyelids (65.2%), one hyaluronidase injection was sufficient to dissolve the filler (Fig. 1). The remaining eight patients, 16 eyelids (34.8%), required a second hyaluronidase injection at 13 ± 4 days prior to surgery to dissolve residual filler. Repeat injections consisted of 41 ± 7 U of hyaluronidase per eyelid. Of the 19 patients who presented with malar edema, 15 had complete resolution of their edema prior to surgery. In four patients (eight eyelids), there was an improvement in malar edema but mild edema persisted. These patients elected to proceed with lower eyelid blepharoplasty since there was no visible or palpable product or any contour abnormalities. None of the patients had allergic or inflammatory reactions around the eyelid area from hyaluronidase treatments.

Following removal of filler and resolution or near resolution of edema, prominent lower eyelid fat pockets were noted in all 23 patients (46 eyelids), and lower eyelid transconjunctival blepharoplasty with fat repositioning was performed. No transcutaneous incisions or skin pinches were performed. In patients with mild to moderate rhytids, resurfacing of the skin was performed at the same setting. Those with Fitzpatrick Type 3 or lower skin type underwent fractionated CO_2 laser resurfacing, (13 patients; 26 eyelids), while those with Fitzpatrick Type 4 underwent 30% trichloroacetic acid (TCA) chemical peel (seven patients; 14 eyelids), and those with Fitzpatrick Type 5 or above (three patients; six eyelids) underwent a series of microneedling treatments (needle depth of 0.5–1.5 mm) that included one intraoperative and two postoperative

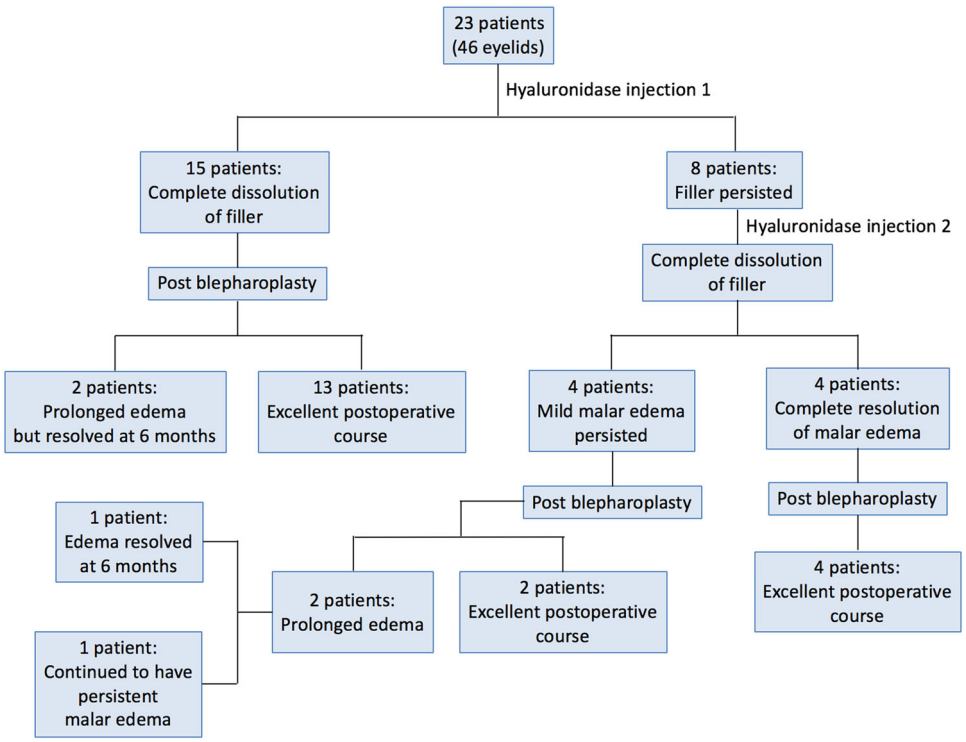

Fig. 1 Outcome of hyaluronidase treatment

treatments spaced 6–8 weeks apart. All patients that underwent a resurfacing procedure were pretreated with a 3-week course of topical hydroquinone (4%) and retinoic acid (0.05%) applied nightly, starting 1 month prior to surgery.

The immediate postoperative course was uneventful in all patients. At an average follow-up of 10.4 ± 7 months, 22 patients (95.6%) had an acceptable outcome with no complications such as contour abnormalities, blue-gray dyschromia, delayed chemosis, or eyelid retraction (Figs. 2, 3). There was no reported incidence of postinflammatory hyperpigmentation (PIH) following skin resurfacing procedures that were performed in 23 patients (46 eyelids).

Postoperatively, four patients (eight eyelids) had prolonged postoperative edema. Edema resolved by 6 months after blepharoplasty in three patients (six eyelids). One patient continued to have persistent mild malar edema (similar to what was seen preoperatively) and was last seen 12 months postsurgery. This patient also had persistent edema prior to surgery. Of particular interest, two of the patients that had prolonged edema postoperatively had complete resolution of their edema prior to surgery.

Six patients (12 eyelids) required postoperative hyaluronic acid filler injections to the lower eyelid, cheek, and midface area to address residual periorbital hollowing. There were no adverse reactions or prolonged edema in these patients. Filler was injected at 18 ± 6 weeks postsurgery. A total of 0.54 ± 0.26 mL of filler (Restylane® 0.43 ± 0.03 mL in five patients and JUVEDERM® Voluma XC [Allergan, Irvine, CA] 1 mL in one patient) was injected in each lower eyelid/midface/cheek area. A 1.5-inch, 25-gauge micro-cannula was used for filler delivery at a deep, near periosteal level. Of particular note, two of the six patients that received postoperative filler injections were those that had a prolonged course of edema. In both patients, edema had resolved prior to postsurgical filler treatments.

Control Group

A total of 160 patients (320 eyelids) (55 men, 105 women; average age 54 ± 16 years) were included in the control group. All patients presented with lower eyelid fat prominence and underwent lower eyelid transconjunctival blepharoplasty with fat repositioning. No transcutaneous incisions or skin pinches were performed. In patients with mild to moderate rhytids, resurfacing of the skin was performed at the same setting. Those with Fitzpatrick Type 3 or lower skin type underwent fractionated CO_2 laser resurfacing, (68 patients; 136 eyelids), while those with Fitzpatrick Type 4 underwent 30% trichloroacetic acid (TCA) chemical peel (54 patients; 108 eyelids), and those with Fitzpatrick Type 5 or above (25 patients; 50 eyelids) underwent a series of microneedling treatments (needle depth of 0.5–1.5 mm) that included one intraoperative and two postoperative treatments spaced 6–8 weeks apart. All patients that underwent a resurfacing procedure were

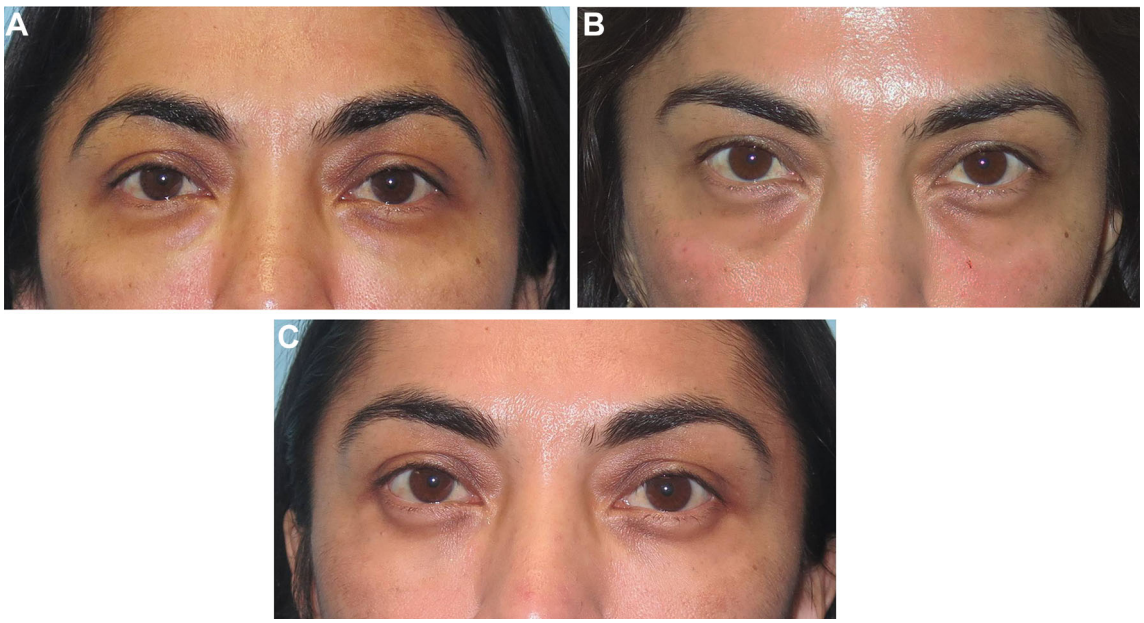

Fig. 2 A 35-year-old female, Fitzpatrick Type 4, with previous injections of hyaluronic acid fillers for periocular rejuvenation. **a** At presentation with visible product, edema, and blue-gray dyschromia. **b** After removal of filler with hyaluronidase treatment, showing prominent lower eyelid fat prolapse and infraorbital rim hollowing. **c** Nine months after blepharoplasty, lower eyelid repositioning, and application of TCA 30%. The patient has healed well with no residual postoperative edema

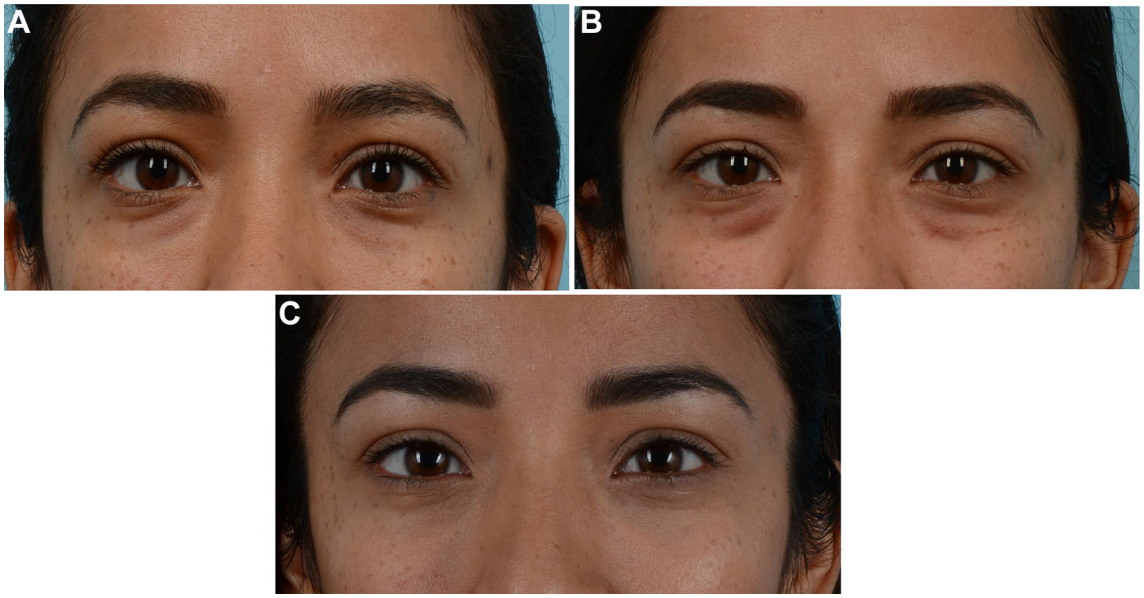

Fig. 3 A 32-year-old female, Fitzpatrick Type 4, with previous injections of hyaluronic acid fillers for periocular rejuvenation. **a** At presentation with visible product, edema, and blue-gray dyschromia. **b** After removal of filler with hyaluronidase treatment, showing prominent lower eyelid fat prolapse and infraorbital rim hollowing. **c** Six months after blepharoplasty, lower eyelid repositioning, and application of TCA 30%. The patient has healed well with no residual postoperative edema

pretreated with a 3-week course of topical hydroquinone (4%) and retinoic acid (0.05%) applied nightly, starting 1 month prior to surgery.

The immediate postoperative course was uneventful in all patients. At an average follow-up of 6.9 ± 3 months, 154 patients (308 eyelids, 96.2%) had an acceptable outcome with no complications delayed chemosis, or eyelid retraction. There was no reported incidence of PIH following skin resurfacing procedures that were performed in 147 patients (294 eyelids).

Postoperatively, six patients (12 eyelids) had prolonged postoperative edema. Edema continued to persist in one patient due to an idiopathic autoimmune condition. In the other five patients, edema resolved by 6 months.

Twenty-four patients (48 eyelids) required postoperative hyaluronic acid filler injections to the lower eyelid, cheek, and midface area to address residual periorbital hollowing. There were no adverse reactions or prolonged edema in these patients. Filler was injected at 16 ± 4 weeks post-surgery. A total of 0.76 ± 0.32 mL of filler was injected in each lower eyelid/midface/cheek area. A combination of fillers was used—Restylane® in the lower eyelid and JUVEDERM® Voluma XC in six patients in the midface/cheek area. A 1.5-inch, 25-gauge micro-cannula was used for filler delivery at a deep, near periosteal level.

Discussion

Hyaluronic acid is a naturally occurring glycosaminoglycan disaccharide that is present in human and animal tissues, including joints, cartilage, skin, and eyes [1]. Hyaluronic acid used in fillers is a cross-linked version that is more resistant to breakdown. A number of hyaluronic acid fillers are available in the market and are distinguished by their particle size, degree and method of cross-linking, ratio of cross-linked versus free hyaluronic acid, G prime, degree of elasticity and viscosity, and resistance to deformation [14–16].

Initially approved for treating facial rhytids, hyaluronic acid fillers are now extensively used in periocular volume augmentation, although their use in the periocular space is considered off label. Their popularity is not surprising given that results are immediate and complications rare when administered by experienced professionals. Nonetheless, their use can be associated with undesirable consequences, including filler visibility or palpability and/or edema that may prompt patients to seek additional procedures to improve their appearance. Filler-related issues can obscure decision making for subsequent procedures and or compromise the outcome of subsequent procedures. Thus, it is important to recognize and manage filler-related issues before embarking on further procedures. The purpose of this study was to document the author's clinical experience with hyaluronic acid filler-related issues in patients who subsequently underwent lower

eyelid blepharoplasty and highlight best practices in patient management (Fig. 4).

As patients may present from outside referrals, proper work-up is important to identify filler-related issues. Ability to identify filler-related issues is crucial to preventing lengthy, unnecessary work-ups. The work-up should focus on diligent history taking coupled with careful evaluation for signs/symptoms of filler presence. Presence of malar edema, visible/palpable filler, or blue-gray dyschromia should prompt a high suspicion of injectable fillers, as highlighted in the present study. Typically, fillers last from about 6 months to up to 2 years after injection [1]. However, there are reports of the filler persisting even after 6–8 years or more after injection [17, 18]. In these unusual cases, filler persistence was manifested by persistent edema, which resolved after hyaluronidase injection. As hyaluronic acid is hydrophilic, early edema may occur, but late or persistent edema can also be seen. Clinicians should be cognizant of the possibility that filler-related edema can persist years after filler placement.

Once filler-related issues are identified, hyaluronidase treatment should be considered to dissolve and remove the filler. The amount of hyaluronidase needed to completely dissolve the filler depends on the hyaluronic acid filler that was injected, the amount that was injected, and the duration of filler persistence [19, 20]. Higher doses of hyaluronidase are required in patients that have received treatment with a highly cross-linked injectable filler, large or repeated amounts of injectable filler over the course of many treatment periods, and/or increased length of filler persistence [21–25].

There is no current standardized protocol for the timing and dosage of hyaluronidase in the setting of periorbital filler-related edema prior to lower eyelid blepharoplasty, and also the optimal timing between hyaluronidase injections and proceeding with surgery. It has been shown that there is a wide variation in enzyme activity among different hyaluronidase products, and the treating physician must take that into consideration when attempting to dissolve hyaluronic acid filler [26].

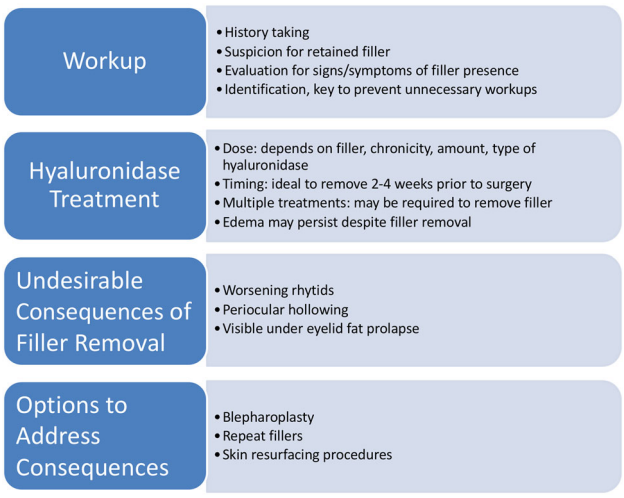

Fig. 4 Hyaluronic acid filler-related issues: patient management considerations

The author typically uses an initial dose of 15–30 U/cm^2 of surface area of a generic bovine-based hyaluronidase. It is important to note that this dose could vary depending on the type of hyaluronidase used. Similar to hyaluronic acid fillers, there is difference in enzymatic activity among various hyaluronidase products depending on source (ovine versus bovine versus human recombinant) and concentration [26]. Given that most edema from hyaluronidase resolved in the author's experience by approximately 10–14 days, the author would proceed with surgery at that time as long as (1) the periorbital filler-related issues were largely resolved and (2) the edema from the hyaluronidase injection treatments was resolved.

Clinicians should be aware that one round of hyaluronidase treatment may not completely dissolve the filler and additional treatments may be required. In the present study, a third of the patients required subsequent injection of hyaluronidase. For subsequent treatments, a lower dose of hyaluronidase is generally used, about half of the initial dose. It should be noted that even after complete filler removal, edema may persist. Nearly 35% of patients (eight patients, 16 eyelids) required a second round of hyaluronidase injections in the present study, and yet although significantly improved, four patients (17.4%) still had some mild edema present despite complete removal of hyaluronic acid filler. These patients opted to proceed with lower eyelid blepharoplasty surgery and with careful intraoperative and postoperative management, two had an excellent postoperative course, while the other two had prolonged edema (50%). One of the four continued to have persistent malar edema at their last follow-up period of 12 months (25%).

Filler removal may produce undesirable consequences such as worsening rhytids, periocular hollowing, and/or visible under eyelid fat prolapse. Options to address these issues may include lower eyelid blepharoplasty with or without fat repositioning to address the lower eyelid hollowing, repeat hyaluronic acid injections, and/or skin resurfacing procedures. In cases of under eyelid fat prolapse, aging changes need to be evaluated to determine the degree of fat prolapse versus volume depletion. For prominent fat prolapse, lower eyelid blepharoplasty may be a better option than hyaluronic acid fillers as the former provides a more appropriate solution. In the present study, all patients had prominent fat prolapse and were offered lower eyelid blepharoplasty.

Careful planning and meticulous intraoperative techniques are important for successful outcomes with lower eyelid blepharoplasty. As the technical details of lower eyelid blepharoplasty are beyond the scope of this study, readers may refer to a prior publication on this topic that describes a similar technique [11]. A few items that are of relevance to the present study are discussed here.

The quality of the entire lower eyelid esthetic unit skin is often affected from periorbital filler-related edema, and resurfacing treatments should be considered for collagen induction to help the overall integrity and texture of the skin postoperatively. Ablative fractionated CO_2 laser provides the optimal improvement in lower eyelid rhytids with minimal downtime and reduced risk of PIH when compared to traditional ablative CO_2 lasers [27]. TCA 30% chemical peels can also provide a satisfactory result in rhytids [28]. Given the author's experience, transcutaneous removal of skin (i.e., skin pinch) can help remove excess skin, but it will not address excess rhytids, loss of elasticity, and the attenuated texture of the skin in cases of prolonged edema within the entire lower eyelid esthetic unit. The skin is often stretched out from the expansive filler material, and an ablative procedure can ultimately help improve the collagen structure and texture of the skin postoperatively. Patients with rhytids and Fitzpatrick Type 5 and above skin type underwent microneedling. Microneedling provides percutaneous collagen induction therapy to the skin and is well established to improve rhytids with minimal downtime and decreased risk of PIH [29]. In contrast to fractionated CO_2 laser and TCA 30% chemical peel treatments, there are limitations with microneedling such that the degree of improvement in rhytids is limited and multiple treatments need to be performed. The author prefers fractionated CO_2 laser in those with Fitzpatrick Type 3 or below skin types. In patients with Fitzpatrick Type 4 skin types, the author prefers TCA 30% chemical peel to help minimize the risk of PIH. The author also recommends a postoperative routine topical regimen consisting of retinol 0.05% nightly. It is well established that topical retinol increases collagen synthesis and visible improvement in fine wrinkles [30, 31].

Patients that undergo lower eyelid blepharoplasty surgery or other facial plastic procedures may undergo hyaluronic acid filler injections around the surgical site for issues pertaining to volume loss, folds, and wrinkles which the initial surgery did not directly address or not fully improve. Patients in both groups tolerated periocular injectable fillers post blepharoplasty. There are no current data to support the safety and efficacy of injectable fillers postblepharoplasty. The author's current practice patterns recommend postoperative periocular filler injections to be performed approximately 12 weeks status post blepharoplasty and in those with no active lower eyelid or malar edema. With these guidelines, the author found no postoperative filler-related complications in either group that was evaluated.

In our retrospective study, nearly 18% of our patients in the "filler-related issues group" had prolonged edema that persisted up to 6 months. In contrast, prolonged edema was seen in nearly 4% of the patients in the control group, which is significantly lower ($p = 0.024$). This is a significant finding, and patients that present with periocular filler-related issues need to be adequately counseled on their higher likelihood of having a prolonged healing course postoperatively. Although rare, there is a possibility that edema can persist indefinitely as seen in one of our patients.

Following the best practices described above, acceptable outcomes were obtained in 19 of the 23 patients included in the periocular filler-related issues and blepharoplasty group. One patient continues to have mild malar edema, despite hyaluronidase treatment followed by lower eyelid blepharoplasty. The nature or cause of this edema is unknown.

This study is limited by its retrospective nature, small sample size in the filler-related issues group, as well as potential bias in patient selection.

Conclusion

Care must be taken to properly select patients for injectable fillers to the infraorbital rim. Patients with infraorbital rim hollowing in the setting of mild to no orbital fat prolapse are potential candidates for injectable fillers, while those with predominant orbital fat prominence are better candidates for lower eyelid blepharoplasty. Proper injection techniques, proper selection of hyaluronic acid filler, and adequate knowledge of eyelid anatomy are important to help reduce potential complications that may occur with hyaluronic acid fillers. In patients presenting for additional rejuvenation procedures after hyaluronic acid filler treatment, filler-related issues need to be identified and managed prior to further intervention. Hyaluronidase treatment effectively dissolves and removes the filler, but mild malar edema can persist. Outcomes are acceptable after subsequent lower eyelid blepharoplasty. Patients need to be adequately counseled about their treatments, and they need to be aware of the higher likelihood of prolonged edema that can persist postoperatively despite removal of hyaluronic acid filler.

Compliance with Ethical Standards

Conflict of interest Christopher I. Zoumalan, MD, FACS, is a consultant for Allergan, Irvine, CA, and owns stock and is the scientific advisor for MD Medical Designs, Inc., Los Angeles, CA.

References

1. Lee S, Yen MT (2017) Nonsurgical rejuvenation of the eyelids with hyaluronic acid gel injections. Semin Plast Surg 31:17–21
2. Goldberg RA, Fiaschetti D (2006) Filling the periorbital hollows with hyaluronic acid gel: initial experience with 244 injections. Ophthalmic Plast Reconstr Surg 22:335–341
3. Mustak H, Fiaschetti D, Goldberg RA (2017) Filling the periorbital hollows with hyaluronic acid gel: long-term review of outcomes and complications. J Cosmet Dermatol. https://doi.org/10.1111/jocd.12452
4. American Society of Plastic Surgeons (2017) Plastic surgery statistics report. https://www.plasticsurgery.org/documents/News/Statistics/2017/plastic-surgery-statistics-report-2017.pdf Accessed May 2018
5. Weinberg MJ, Solish N (2009) Complications of hyaluronic acid fillers. Facial Plast Surg 25:324–328
6. Park TH, Seo SW, Kim JK, Chang CH (2011) Clinical experience with hyaluronic acid-filler complications. J Plast Reconstr Aesthet Surg 64:892–896
7. Dayan SH, Arkins JP, Somenek M (2012) Restylane persisting in lower eyelids for 5 years. J Cosmet Dermatol 11:237–238
8. Jordan DR, Stoica B (2015) Filler migration: a number of mechanisms to consider. Ophthal Plast Reconstr Surg 31:257–262
9. Teo AA, Mokhtarzadeh A, Cameron JD, Harrison AR (2017) Late presentation of enlarging lower eyelid mass and muscle degeneration secondary to hyaluronic acid filler. Ophthal Plast Reconstr Surg 33:S9–S11
10. Khan TT, Woodward JA (2015) Retained dermal filler in the upper eyelid masquerading as periorbital edema. Dermatol Surg 41:1182–1184
11. Zoumalan CI, Roostaeian J (2016) Simplifying blepharoplasty. Plast Reconstr Surg 137:196e–213e
12. Taban MR (2017) Lower eyelid blepharoplasty in eyelids previously injected with hyaluronic acid gel filler. Am J Cosmetic Surg 34:103–106
13. Hagan JC 3rd, Hill WE (2001) Use of a compounding pharmacy hyaluronidase for ophthalmic injection anesthesia. J Cataract Refract Surg 27:1712–1714
14. Micheels P, Sarazin D, Tran C, Salomon D (2016) Effect of different crosslinking technologies on hyaluronic acid behavior: a visual and microscopic study of seven hyaluronic acid gels. J Drugs Dermatol 15:600–606
15. Sundaram H, Cassuto D (2013) Biophysical characteristics of hyaluronic acid soft-tissue fillers and their relevance to aesthetic applications. Plast Reconstr Surg 132:5S–21S
16. Sundaram H, Rohrich RJ, Liew S et al (2015) Cohesivity of hyaluronic acid fillers: development and clinical implications of a novel assay, pilot validation with a five-point grading scale, and evaluation of six U.S. Food and Drug Administration-approved fillers. Plast Reconstr Surg 136:678–686
17. Yu JTS, Peng L, Ataullah S (2017) Chronic eyelid edema following periocular hyaluronic acid filler treatment. Ophthal Plast Reconstr Surg 33:e139–e140
18. Iverson SM, Patel RM (2017) Dermal filler-associated malar edema: treatment of a persistent adverse effect. Orbit 36:473–475
19. Cavallini M, Gazzola R, Metalla M, Vaienti L (2013) The role of hyaluronidase in the treatment of complications from hyaluronic acid dermal fillers. Aesthet Surg J 33:1167–1174
20. Hilton S, Schrumpf H, Buhren BA et al (2014) Hyaluronidase injection for the treatment of eyelid edema: a retrospective analysis of 20 patients. Eur J Med Res 19:30
21. Menon H, Thomas M, D silva J (2010) Low dose of Hyaluronidase to treat over correction by HA filler–a case report. J Plast Reconstr Aesthet Surg 63:e416–e417
22. Pierre A, Levy PM (2007) Hyaluronidase offers an efficacious treatment for inaesthetic hyaluronic acid overcorrection. J Cosmet Dermatol 6:159–162
23. Lambros V (2004) The use of hyaluronidase to reverse the effects of hyaluronic acid filler. Plast Reconstr Surg 114:277
24. DeLorenzi C (2013) Complications of injectable fillers, part I. Aesthet Surg J 33:561–575
25. Juhász MLW, Levin MK, Marmur ES (2017) The kinetics of reversible hyaluronic acid filler injection treated with hyaluronidase. Dermatol Surg 43:841–847
26. Casabona G, Marchese PB, Montes JR, Hornfeldt CS (2018) Durability, behavior, and tolerability of 5 hyaluronidase products. Dermatol Surg. https://doi.org/10.1097/DSS.0000000000001562
27. Brightman LA, Brauer JA, Anolik R et al (2009) Ablative and fractional ablative lasers. Dermatol Clin 27:479–489
28. Han SH, Kim HJ, Kim SY et al (2011) Skin rejuvenating effects of chemical peeling: a study in photoaged hairless mice. Int J Dermatol 50:1075–1082
29. Alster TS, Graham PM (2018) Microneedling: a review and practical guide. Dermatol Surg 44:397–404
30. Kitano Y, Yoshimura K, Uchida G et al (2001) Pretreatment with topical all-trans-retinoic acid is beneficial for wound healing in genetically diabetic mice. Arch Dermatol Res 293:515–521
31. de Campos Peseto D, Carmona EV, Silva KC et al (2016) Effects of tretinoin on wound healing in aged skin. Wound Repair Regen 24:411–417