Translations

Cosmetic Medicine

Review Article

Update on Blindness From Filler: Review of Prognostic Factors, Management Approaches, and a Century of Published Cases

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Abstract

Vision loss secondary to aesthetic filler treatment is a rare but disastrous complication. The aim of this review was to update the published cases of blindness after filler injection that have occurred since our group published reviews of 98 cases in 2015 and an additional 48 cases in 2019. A literature review was performed to identify all cases of visual complications caused by filler injection published between September 2018 and March 2023. The cases were analyzed independently and in combination with previously reviewed cases. Analyses were based on the number of cases with data available. A total of 365 new cases of partial or complete vision loss after filler injection were identified. The sites that were highest risk were the nose (40.6%), forehead (27.7%), and glabella (19.0%). The filler injected was hyaluronic acid in 79.6% of cases. The most common associated signs were ptosis (56.2%), ophthalmoplegia (44.1%), pain (31.2%), and skin changes (73.2%). Strokelike features were seen in 19.2% of cases. Of the cases reporting visual outcomes (318), 6.0% experienced complete vision recovery, 25.8% had partial improvement in visual acuity, and 68.2% had no vision recovery. Partially preserved visual acuity at onset was a significant predictor of visual improvement ($P < .001$). The 3 most common treatments were subcutaneous hyaluronidase at or near the filler site (70.1%), systemic steroids (57.3%), and intraarterial thrombolytic therapy (56.0%). No treatments were significantly associated with visual improvement ($P > .05$). Although blindness and stroke from fillers is a rare complication, practitioners who inject filler should have a thorough knowledge of prevention and management strategies.

초록

미용 필러 시술로 인한 시력 손실은 드물지만 치명적인 합병증입니다. 이 검토는 2015년 98건의 사례와 2019년에 추가로 48건의 사례에 대한 검토를 발표한 이후 발생한 필러 주입 후 실명 사례를 업데이트하기 위해 수행되었습니다. 2018년 9월부터 2023년 3월 사이에 발표된, 필러 주입으로 인한 시각적 합병증 사례를 모두 확인하기 위해 문헌 검토를 수행했습니다. 사례는 독립적으로, 그리고 이전에 검토한 사례와 함께 분석되었습니다. 분석은 사용 가능한 데이터가

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있는 사례 수를 기준으로 이루어졌습니다. 필러 주입 후 부분적 또는 완전한 시력 상실의 새로운 사례가 총 365건 확인되었습니다. 가장 위험도가 높은 부위는 코(40.6%), 이마(27.7%), 미간(19.0%)이었습니다. 주입된 필러는 79.6%의 사례에서 히알루론산이었습니다. 가장 흔한 관련 증상은 안검하수(56.2%), 안근 마비(44.1%), 통증(31.2%), 피부 변화(73.2%)였습니다. 19.2%의 사례에서 뇌졸중과 유사한 특징이 나타났습니다. 시력 관련 결과를 보고한 사례(318건) 중 6.0%는 완전한 시력 회복을 보였고, 25.8%는 부분적인 시력 개선이 있었으며, 68.2%는 시력 회복이 나타나지 않았습니다. 발병 시점에 부분적으로 보존된 시력은 시력 개선의 유의미한 예측 인자였습니다($P < .001$). 가장 흔한 3가지 치료법은 필러 부위 또는 그 부근의 피하 히알루로니다제 주사(70.1%), 전신 스테로이드 투여(57.3%), 동맥 내 혈전 용해 요법(56.0%)이었습니다. 어떤 치료법도 시력 개선과 유의미한 연관성을 보이지 않았습니다($P > .05$). 필러로 인한 실명 및 뇌졸중은 드문 합병증이지만, 필러를 주입하는 의사는 예방 및 관리 전략에 대한 완전한 지식을 갖추고 있어야 합니다.

Level of Evidence: 3

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The use of soft tissue fillers for noninvasive facial rejuvenation has surged in the last decade. The global market for dermal fillers was valued at $5.08 billion USD in 2023 and is projected to grow to $10.16 billion by 2032.[1] However, the rise in popularity of these procedures has been accompanied by an increase in reported complications. The most serious complications are vascular in nature, and although rare, may lead to blindness and stroke. The current hypothesis for the mechanism is inadvertent injection of filler into a blood vessel and retrograde flow of the filler embolism to the arteries supplying the retina or the brain (Figure 1).

In our group's initial 2015 publication, we identified 98 case reports of visual compromise from filler in the world literature, spanning from 1906 and 2015.[2] Our follow-up paper encompassed an additional 48 published cases from January 2015 through September 2018.[3] At that time, the number of cases with complete recovery had increased from 2.0% to 20.8%, which we hypothesized may have been attributable to a greater proportion secondary to hyaluronic acid filler. It was important to substantiate this trend with updated data.

Additionally, an exponential number of treatments have been attempted in recent years, namely intraarterial thrombolytic therapy and retrobulbar hyaluronidase. The latter has remained controversial since first proposed. Now that numerous injections have been documented, a critical review of the impact of these advanced techniques was warranted. Most of the literature on the topic are single-center case series or small literature reviews focusing on a particular filler material, highlighting the value of a global, comprehensive review of recent cases.

Here, the authors reviewed 365 new cases of ocular complications secondary to fillers published between October 2018 and March 2023. With this larger data set, we assessed prognostic factors, risk factors for concurrent stroke, and evolution of visual acuity over time. We presented the data from this most recent review, but also summarized the injection locations and filler material data collectively between 1906 and 2023. By trending the injection locations and filler material data since the first case report over 100 years ago, we have provided a comprehensive review of the published cases of filler-induced blindness, deepening our understanding of this rare complication. To the best of our knowledge, with a cumulative total of 511 cases, this is the largest review to date of ocular complications secondary to fillers in the literature.

METHODS

Search Strategy

Three databases (MEDLINE, National Institutes of Health, Bethesda, MD; EMBASE, Elsevier, Amsterdam, the Netherlands; and Web of Science, Clarivate, Philadelphia, PA) were searched from September 2018 to March 2023, with search strings related to blindness and filler (detailed search strategy in Appendix A in Supplementary Material located online at www.aestheticsurgeryjournal.com). The search was conducted by C.L. in March 2023, with assistance from an experienced librarian. Articles that cited our team's 2 previous reviews on blindness from fillers were screened. Additionally, other review articles on the topic that were identified in the search results were examined and their reference lists were cross-verified for additional studies.

A total of 766 posts on the Injectables & Threads discussion forum of the International Master Course on Aging Science (IMCAS) Academy were also searched with keywords, including "eye," "ophthalmic," "blind," "vision," "ophthalmoplegia," and "retinal artery."[4] One case was reported of "blurry vision" but was not included because the post did not provide sufficient details and was not published in peer-reviewed literature.

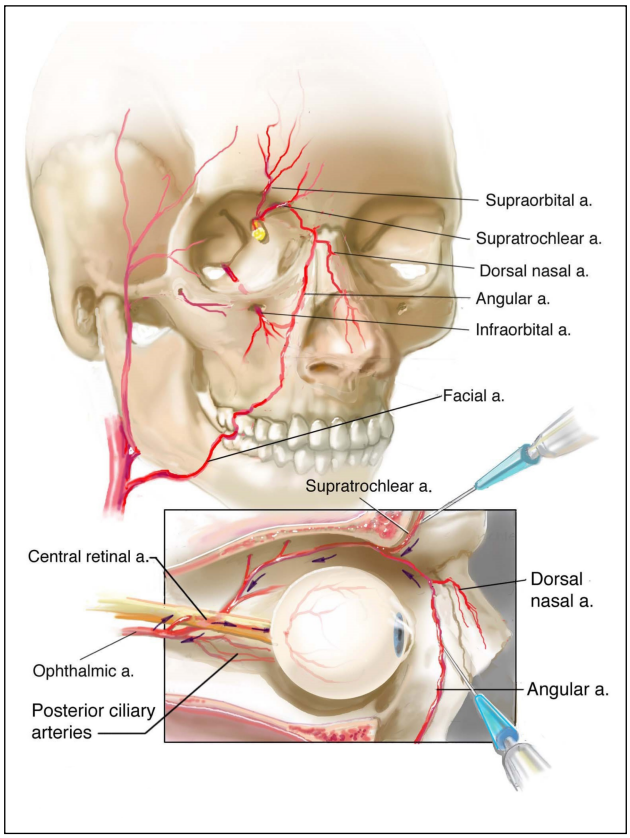

Figure 1. Vascular anatomy of the face. A selection of facial vessels are highlighted here. This is one depiction of the blood vessels of the face; there is individual anatomic variability. Inset demonstrates the mechanism of filler-induced blindness. In this diagram, filler is shown being injected directly into the supratrochlear artery or into the angular artery, which anastomoses with the supratrochlear artery. From here filler can travel retrograde, as shown by the arrows, into the ophthalmic artery and its branches, blocking blood supply to the retina and causing visual complications. Permission was granted from authors and the *Aesthetic Surgery Journal* for reprinting of this illustration, originally published in Beleznay et al.[3]

Inclusion and Exclusion Criteria

The titles and abstracts of articles identified in the literature search were screened by 2 authors (V.D. and C.L.) with predefined inclusion and exclusion criteria. The full text of each relevant study was reviewed to include any reported cases of blindness or visual impairment from filler injection (Figure 2). Non-English and animal studies were excluded. Disagreements were resolved through discussion and third-party vote (K.B.). A standardized data extraction form was utilized to record patient demographics, filler type, injection site, cannula use, presenting signs and symptoms, management, diagnosis, and outcome.

Outcome of Interest and Measures

Partial visual improvement was defined liberally as any increase in visual acuity between the initial evaluation and the final best corrected visual acuity (BCVA). Complete visual improvement was a return to normal vision. Chi-square tests were performed only if at least 80% of the cells had an expected frequency of 5 or greater, and no cell had an expected frequency smaller than 1. A *P* value of less than .05 was considered significant. Odds ratios were calculated with 95% confidence intervals.

RESULTS

Dealing With Missing Data

Nineteen corresponding authors were contacted via email for missing data. Upon clarification of case details, 1 response led to exclusion from the study. Additional data provided by 4 authors was included. Missing data were assumed to be random, and only the available data were included in each factor subanalysis.

Study Characteristics

Sixty-three studies were included, providing a total of 365 cases for analysis. The cases originated from 21 different countries, with most stemming from China ($n = 226$, 61.9%) and Korea ($n = 93$, 25.5%) (Figure 3). The average age was 27.5 years, based on the 293 cases that reported age-related data. The type of injector was mentioned in 35 cases. Of these, 14 (40.0%) were nonphysicians, with the majority of these being unlicensed or nonmedical. One incident occurred at a "Botox and filler party."[5] Needle vs cannula use was only mentioned in 38 cases. A needle was employed in 22 cases (57.9%) and a cannula in 16 cases (42.1%). Cannula size was reported in 10 cases, ranging from 23 to 27 gauge.

In total, 363 cases reported the type of filler injected. Hyaluronic acid (HA) was administered the most frequently (289 cases, 79.6%) followed by autologous fat (49 cases, 13.5%), collagen (7 cases, 1.9%), and calcium hydroxyapatite (CaHA; 6 cases, 1.6%). Other injectables included platelet-rich plasma (PRP) in 5 cases (1.4%), poly-L-lactic acid (PLLA) in 4 cases (1.1%), sodium thiosulfate (1 case, 0.3%), petroleum jelly (1 case, 0.3%), and 2% lidocaine with epinephrine (1 case, 0.3%). Tallying the 502 cases that reported the filler type across all published studies (1906-2023), the causative filler was HA in 351 cases (69.9%), autologous fat in 95 cases (18.9%), collagen in 15 cases (3.0%), CaHA in 13 cases (2.6%), and PLLA in 7 cases (1.4%) (Figure 4).

Among the 365 cases between 2018 and 2023, 9 (2.4%) did not report the specific injection location. In total, 401

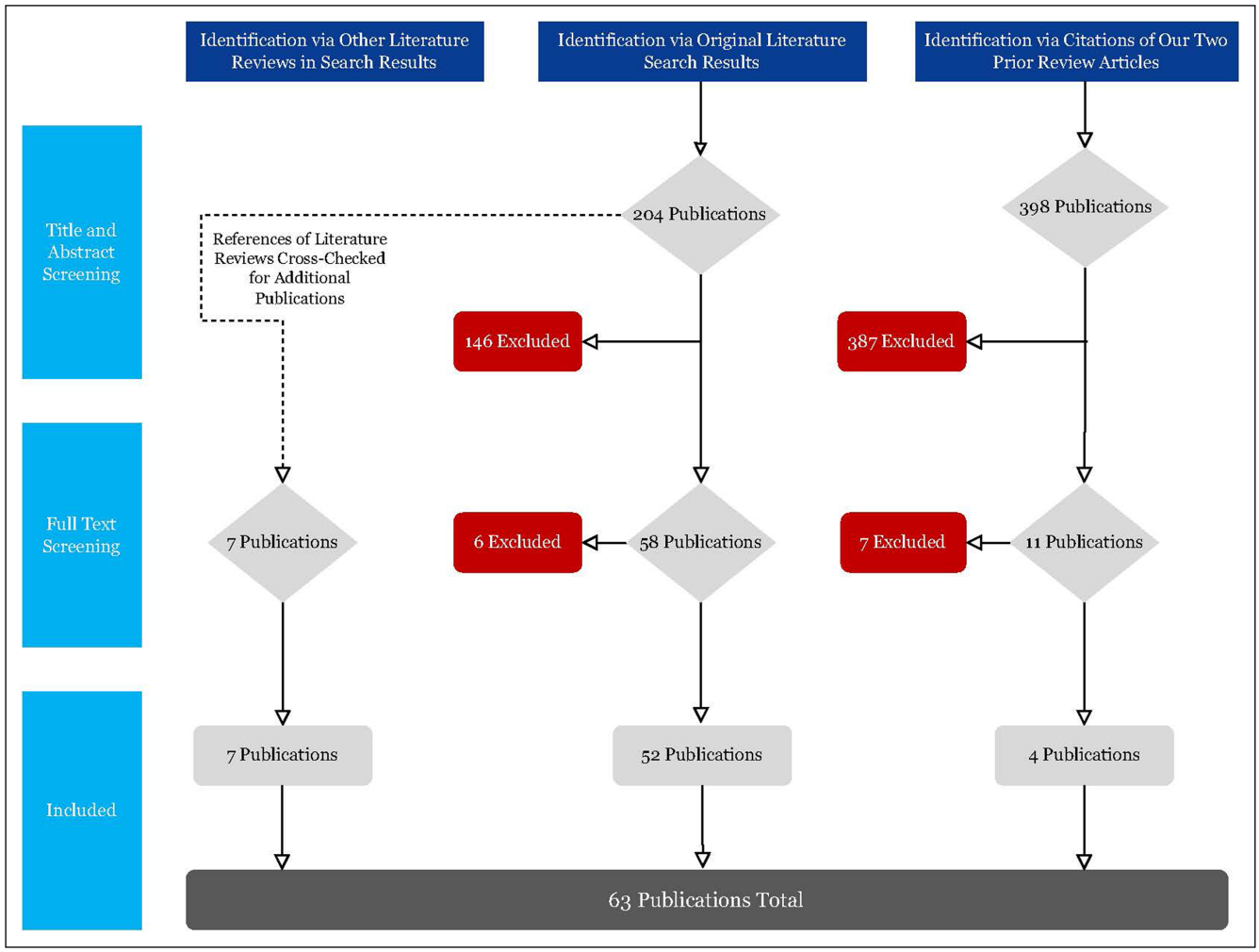

Figure 2. Flowchart illustrating the identification and screening of articles found in the world literature. Articles were identified through 3 sources: the literature search results (center column), reference lists of literature reviews found in the search results (left column), and citations of our group's 2 preceding review articles published in 2015 and 2019 (right column). After preliminary abstract screening by a librarian, the authors screened the titles and abstracts of all identified articles. Next, the full texts were screened. Articles were eliminated at each step. Included articles contained 1 or more case reports of visual impairment or blindness secondary to filler injection. Exclusion criteria included non-English language, animal data, lack of visual complications, and duplicate articles already captured from a different search source.

anatomic locations were injected, because some had multiple areas treated during the same visit. The most common locations for filler injections that caused visual changes were the nose ($n = 163$, 40.6%), forehead ($n = 111$, 27.7%), and glabella ($n = 76$, 19.0%) (Figure 5). Among the nasal injections that specified the exact anatomical location ($n = 89$), there were 34 listed as in the nasion, 29 in the nasal bridge, 20 in the nasal dorsum, 2 radix nasi, and 1 in each of the following locations: nasal tip, crease, ala, and apex nasi. Because terminology can differ between authors, locations were reported verbatim. Other reported locations included the temple ($n = 14$, 3.5%), periorbital region ($n = 8$, 2.0%), cheek ($n = 6$, 1.5%), eyebrow ($n = 3$, 0.7%), and lip ($n = 3$, 0.7%).

Between 1906 and 2023 (577 injection locations reported), the nose was the most common location at 216 injections (37.4%), followed by the forehead ($n = 133$, 23.1%) and glabella ($n = 127$, 22.0%) (Figures 6, 7). Less common sites were the nasolabial fold ($n = 37$, 6.0%), temple ($n = 21$, 3.6%), periorbital region ($n = 19$, 3.3%), cheek ($n = 12$, 2.1%), lip ($n = 6$, 1.0%), eyebrow ($n = 4$, 0.7%), and chin ($n = 2$, 0.3%). However, some sites such as the chin were never injected in isolation.

Clinical Features

At initial presentation, no light perception (NLP) was reported in the majority of cases ($n = 229$, 62.7%). The remaining

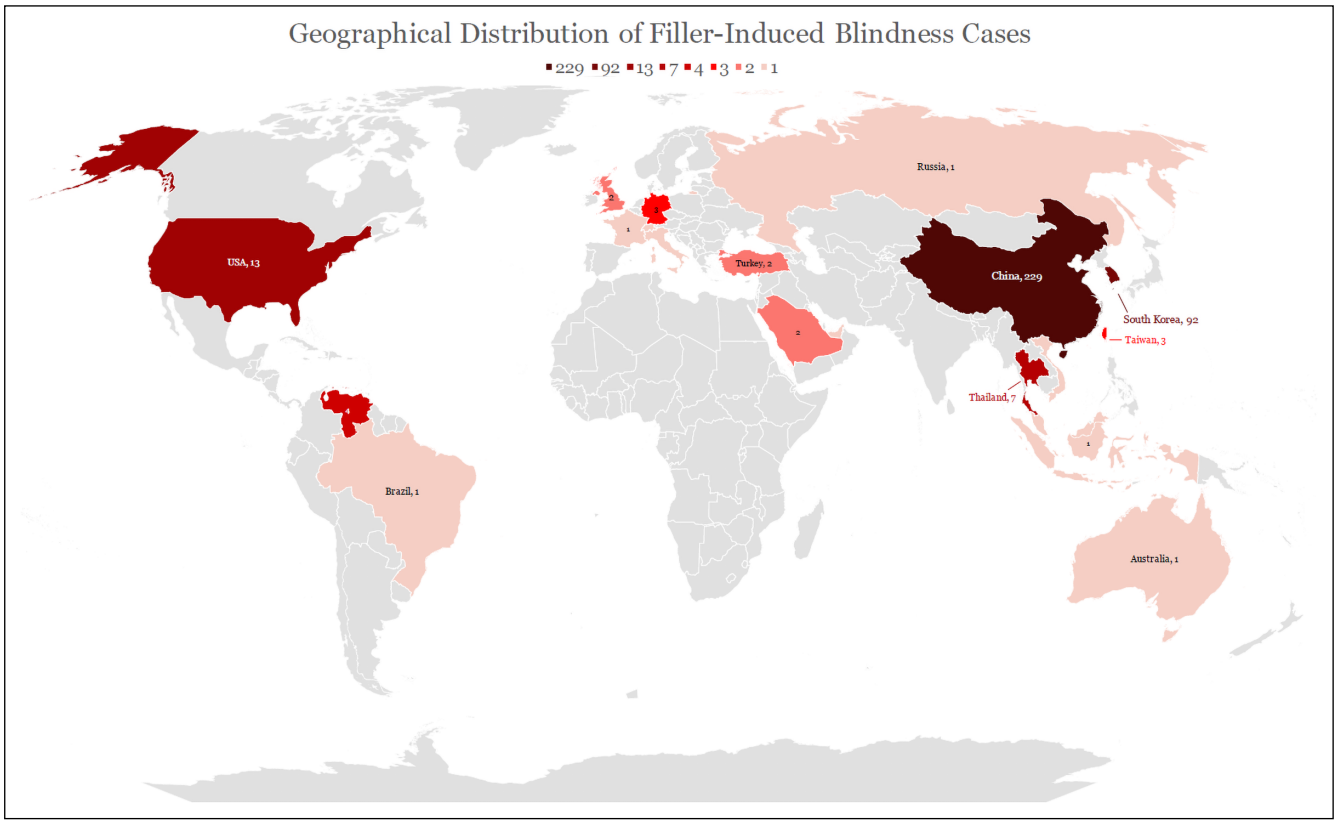

Figure 3. Geographic distribution of cases of visual complications from filler between 2018 and 2023. The darkness of the shade of each country represents the number of cases. Data are not scaled per capita. Microsoft Excel screen capture reprinted with permission from Microsoft Corporation (Redmond, WA). Map created with Bing software (Microsoft).

cases had partial vision loss, visual field defects, and other vision-related symptoms. Two cases had binocular visual impairment; therefore, data were tabulated per count of eyes affected when applicable. Typically, vision loss occurred immediately, or within 10 minutes after filler injection, based on the reported data.[6-11] Two cases had delayed presentations, albeit both showed immediate warning signs during injection treatment. One had nausea, vomiting, and headache suddenly after glabella and nasal dorsum filler, then developed vision loss 1 hour after leaving the office.[12] The second was an individual who felt immediate ocular pain during self-injection with microwaved petroleum jelly, but only noticed unilateral blurry vision (Snellen 20/40) upon waking the following day.[13]

Ptosis was the most common associated sign overall (205 cases, 56.2%), followed by ophthalmoplegia (161 cases, 44.1%). Pain was reported in 114 cases (31.2%), including ophthalmodynia, periocular pain, nasal pain, headache, burning, and a stinging sensation. Twenty-six cases (7.1%) reported nausea or vomiting. Relative afferent pupillary defect (RAPD) was reported in 18 cases (4.9%). Across studies, an array of other ocular signs and examination findings were reported (see Appendix B in supplemental material, located online at www.aestheticsurgeryjournal.com, for case details).

The presence or absence of cutaneous changes was reported in 246 cases. In sum, 180 (73.2%) had cutaneous changes and 66 (26.8%) had none. Any reported cutaneous changes were included, such as pallor, bruising, petechia, and blistering; only a small proportion led to scarring. A total of 124 cases (34.0%) presented with central nervous system (CNS) complications. Of these, 54 cases (14.8%) had mild or nonfocalizing neurologic symptoms such as nausea, vomiting, dizziness, tinnitus, chest tightness, urinary urgency, or behavioral changes. The rest (70 cases, 19.2%) had strokelike features, including unilateral limb weakness, coma, imaging evidence of infarction, or were otherwise diagnosed with stroke. Nearly all strokelike symptoms manifested within an hour post filler, except for 1 case of delayed upper limb weakness on day 6 and another case that developed cerebral venous sinus thrombosis on the second day.[10,14]

Of 33 strokes with filler information reported, 15 (45.4%) were caused by autologous fat, 17 (51.5%) by HA, and 1 case by collagen. The odds of concurrent stroke from

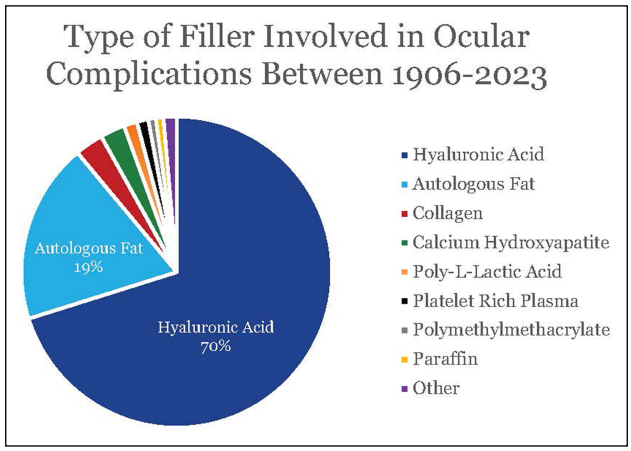

Figure 4. Number of cases of visual complications from each filler material. Cases published between 1906 and 2023. Cases that did not report filler material type were excluded. Note: One case of poly-D,L-lactic acid was included in the poly-L-lactic acid category.

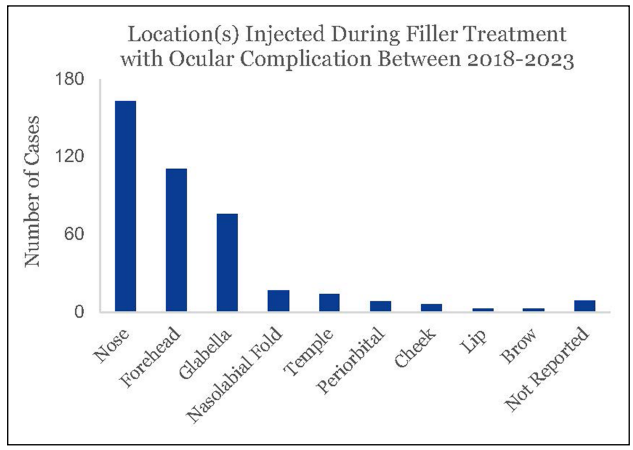

Figure 5. Anatomic sites of filler treatment in case reports of filler-induced ocular complications published between 2018 and 2023. Case counts are nonexclusive. Often, multiple facial locations were injected at the same visit. Anatomical areas reported infrequently such as the lip were often injected in conjunction with other high-risk areas.

autologous fat were 7 times greater than with HA (odds ratio [OR] = 7.06; CI [3.23, 15.4]). Stroke complications were most common with glabellar injections ($n = 15$, 42.9%), followed by nose ($n = 7$, 20.0%), forehead ($n = 7$, 20.0%), temple, periorbital, and nasolabial folds ($n = 2$, 5.7% each). Compared to the nose and forehead, glabellar injections had 5.48 and 3.65 greater odds of concurrent stroke, respectively (OR = 5.48, CI [2.13, 14.1]; OR = 3.65, CI [1.41, 9.46]).

A total of 3 cases of venous sinus thromboses induced by hyaluronic acid filler were documented. Three of the cerebral infarction cases were found to have bilateral lesions, although these cases had only unilateral symptoms clinically.[7,15] In 3 cases, strokes were completely asymptomatic and only diagnosed incidentally on imaging.

Diagnosis

Diagnoses were described inconsistently, at times by the artery occluded, other times by the resulting ischemic area ("anterior segment ischemia," "choroidal infarction"), or generally by clinical syndrome ("ocular ischemic syndrome"). A total of 346 cases were assigned a specific diagnosis. Ophthalmic artery occlusion (OAO) and central retinal artery occlusion (CRAO) were most frequent, occurring in 114 (32.9%) and 112 (32.4%) cases, respectively. There were 20 branch retinal artery occlusions (BRAO) and 12 posterior ciliary artery occlusions (PCAO). Often, multiple vessels were occluded at once. Seven nerve palsies were diagnosed, with 3 occurring concurrently with ocular emboli. Rarely, nonischemic cases were reported, such as optic perineuritis and a case of subconjunctival fat infiltration from autologous fat embolism.[16,17]

Treatment

A total of 302 cases reported data on treatment, with most cases receiving subcutaneous injections of hyaluronidase (HYAL) at the filler injection site (214 cases, 70.1%). The second most common treatment was systemic steroids, given in 173 cases (57.3%), followed by intraarterial thrombolytic therapy (IATT; 169 cases, 56.0%). Thrombus-dissolving agents consisted of urokinase, HYAL, papaverine, and alteplase. A combination of thrombolytics was frequently administered. Time to IATT was typically 24 to 48 hours. From a technical standpoint, IATT interventions were often successful in achieving at least partial recanalization, if not complete recanalization, of the occluded arteries. However, fewer cases saw clinical benefit in reversing vision loss. Based on 161 cases that reported on the impact of IATT, this procedure improved vision in 55 cases (34.2%). Most did not improve to a significant degree clinically. For instance, 10 cases only regained light perception (LP). At best, 12 cases successfully regained visual acuity of 20/70 or better.

Retrobulbar HYAL was the next most common procedure, attempted in 38 cases (12.6%). The median time to retrobulbar HYAL was 9 hours and ranged from 15 minutes to 6 days post injection. Retrobulbar HYAL improved vision in 2 cases (5.3%).[18,19] One case received a retrobulbar injection 12 hours post filler and had gradually restored normal vision over 1 month, but they also received 14 two-hour sessions of hyperbaric oxygen.[20] The second case underwent retrobulbar HYAL injections on the fourth and fifth day post filler and began regaining vision 4 hours after the procedure on day 5.[11] The patient was also treated with aspirin and multiple rounds of subcutaneous HYAL injections, eventually recovering normal vision over 3 months.

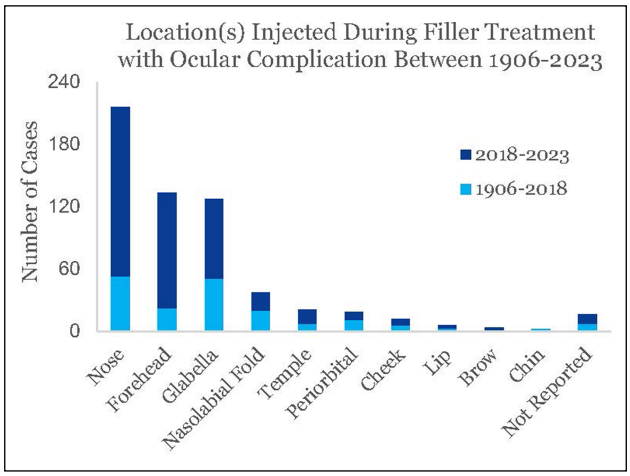

Figure 6. Total tally of filler treatment anatomic sites in cases of filler-induced ocular complications published between 1906 and 2023. The cases are separated by publication period: 1906 to 2018 in light blue and 2018 to 2023 in dark navy. Anatomical areas reported infrequently such as the chin were often injected in conjunction with other high-risk areas.

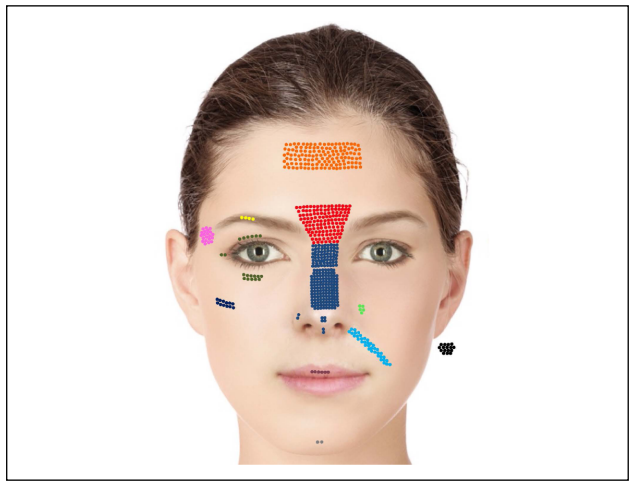

Figure 7. Location of filler injection resulting in visual complication. Cases published between 1906 and 2023. The 16 dots below the ear represent cases in which the location was not specified or listed as "face."

Other techniques aimed at delivering HYAL near ocular vessels were attempted in 7 cases. There was a total of 3 peribulbar injections, 2 injections aiming for the supratrochlear artery, 2 injections aiming for the supraorbital artery, and 3 subtenon injections. The latter entailed the insertion of a cannula in the potential space between the sclera and the Tenon capsule, which courses along the contour of the globe. These techniques were administered sooner than retrobulbar HYAL, averaging around 2 to 2.5 hours post filler. Of the 7 cases, only the 2 that received injections targeting the supratrochlear or supraorbital arteries had visual recovery. The first was immediately administered supratrochlear HYAL after noting blurry vision during filler treatment, resulting in rapid improvement in vision.[18] HYAL was injected inside and surrounding the supratrochlear notch. After ocular massage and hyperbaric oxygen later that day, they recovered full vision. The second case immediately underwent HYAL rescue targeting the supratrochlear and supraorbital arteries after going blind during nose filler treatment.[21] Vision improved to counting fingers at 4 hours post filler. Next, a repeat supraorbital injection and 2 peribulbar injections led to visual gains recorded at 16 hours, followed by full recovery over a month. Both of these blindness reversal cases had also initially received subcutaneous injections of HYAL at the area of the original filler bolus, without immediate effect.

Twenty-nine cases underwent hyperbaric oxygen therapy. Twelve cases (41.4%) experienced improvements in vision, including 5 that recovered normal vision. It should be noted that hyperbaric oxygen was co-administered with other treatments, such as IATT and advanced HYAL rescue techniques (eg, retrobulbar or supratrochlear injections). A total of 20 cases (6.6%) had anterior chamber puncture or paracentesis. Across studies, dozens of other management strategies were attempted, including ocular massage, aspirin, anticoagulants, acetazolamide, eye drops, nitroglycerin, antibiotics, mannitol, and prostaglandins.

Outcomes

Of the 367 affected eyes, 357 had decreased visual acuity after the incident, while 10 suffered other visual disturbances, such as visual field defects. Eighty cases of decreased visual acuity did not document the specific final outcomes, leaving 271 cases for complete analysis. A total of 58.3% (158/271) were permanently blind, consisting of 151 with NLP and 7 reported as "blindness" not otherwise specified. BCVA was reported with various visual acuity scales across studies, including light perception (17 cases), seeing hand motion (9 cases), counting fingers (3 cases), and 1 reported as "blurry vision." The remaining cases (83 cases) had a wide range of final visual acuities. In total, only 19 cases (20 eyes) regained normal vision. Although not all authors specified the final visual acuity, the relative change in vision at follow-up was more frequently reported (318/357). Vision remained unchanged from presentation in 217 cases. Over time, 101 cases (31.8%) had visual improvement after the event. Of these, 19 cases (6.0%) made full recovery to normal vision. The other 82 cases partially regained their vision, including 20 cases that recovered to 20/70 vision or better. However, visual gains were generally modest, such as 16 cases only improving from NLP to LP. In regression analysis with logMAR-converted visual acuity values, initial visual acuity predicted final visual acuity at nearly a 1:1 ratio, indicating that, on average, visual outcomes only

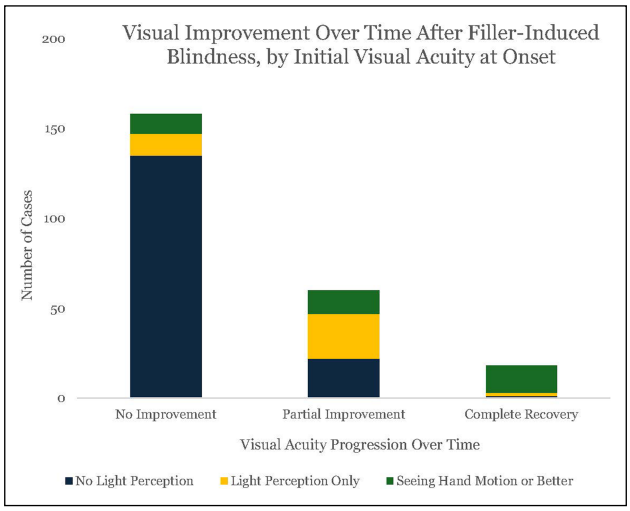

Figure 8. Visual improvement over time following filler-induced blindness, by initial visual acuity at onset. Initial visual acuity was significantly associated with final outcome after treatment/time: X2 (2, $n = 236$) = 115.64, $P < .001$. Blue, yellow, and green colors segregate cases by initial severity of visual impairment after the incident. Complete improvement is defined as achieving return to normal vision (Snellen 20/20). Cases with partial improvement had some degree of visual gain but without achieving normal vision. Cases without visual acuity impairment or without specific visual acuity measurements were excluded.

minimally improved with time (β = .8752; CI [0.818, 0.933]; $P < .001$). See Supplemental Figure 1, located online at www.aestheticsurgeryjournal.com.

Some of the cases with complete visual recovery had atypical initial presentations, for instance 3 had nonischemic processes (keratitis, optic perineuritis, and superior ophthalmic vein occlusion). Others had only partial vision loss, with initial visual acuities of 20/50, 20/30, and 0.3 on the decimal scale.[14,22,23] Patients in 4 cases complained of subjective "blurred vision" that was hard to confirm without objective measurements. These may have been due to a different etiology such as a vasovagal episode, ocular migraine, extraocular movement limitation, or a visual field defect.

Factors associated with regaining visual acuity were assessed. Initial visual acuity (NLP, LP, or better) at onset was a significant predictor of whether there would be visual improvement over time [X^2 (2, $n = 236$) = 115.64; $P < .001$]. These data are visualized in Figure 8. Additionally, 90.3% of the variation observed in final visual acuities was determined by the initial acuity at time of injury [$R^2 = 0.903$; F(1277) = 2573.79; $P < .001$]. See Supplemental Figure 1, located online at www.aestheticsurgeryjournal.com. Regarding injection material, of 101 cases that recovered some degree of visual acuity, 90 were injected with HA (89.1%), 3 with autologous fat (3%), 3 with CaHA (3.0%), and 2 with polylactic acid (2.0%). The odds of having visual improvement were significantly greater in cases due to HA compared to autologous fat (OR = 6.93; CI [2.10, 22.9]).

Compared to their distribution in the overall data set, all injection locations had similar rates of visual improvement, except the forehead injections, which were underrepresented, with only 12.3% having visual improvement. Cases secondary to forehead injections had 2.5 times lower odds of visual improvement than those injected in other areas (OR = 2.51; 95% CI [1.07, 5.91]). Regarding treatments, subcutaneous HYAL, retrobulbar HYAL, systemic steroids, IATT, and hyperbaric oxygen were not statistically significant predictors of visual improvement ($X^2 = 0.276$, 0.113, 0.078, 0.029, and 0.146, respectively).

Two strokes led to coma and death (0.55%). There were at least 16 documented cases with scarring of the skin. Ophthalmoplegia and extraocular movement disorders nearly always resolved completely.

DISCUSSION

Background

This update article presents a rapid rise in filler-induced blindness publications over the last 5 years. Case reports have jumped from a total of 146 cases reported up to October 2018, to 511 cases by March 2023. The rise in case reports likely stems from the growing popularity of filler injections, a greater awareness of this complication, and collective efforts to share innovative approaches with the hope of discovering effective treatments. Last, the cosmetic injectables industry faces a lack of regulation in many countries worldwide. Given that aesthetic procedures are typically elective and self-funded, governmental and insurance agencies exert minimal control over the qualifications of those administering such treatments. As a result, individuals without formal training are injecting filler, and multiple authors noted that the injector was unlicensed, a nonmedical practitioner, or a nurse without physician oversight.[5,9,16,20,24-29] To mitigate these risks, stringent measures must be implemented. It is important to establish standardized training pathways and regulate the scope of practice depending on the backgrounds of practitioners (eg, aesthetician, nurses, physicians, etc.). New or existing professional bodies should play a pivotal role in upholding standards of care, ensuring the competency of injectors. Greater public awareness of the potential risks from cosmetic procedures can serve to steer consumers toward reputable clinicians, further bolstering safety standards. However, practitioners should be aware that this complication has happened in well-trained and experienced hands. All potential risks should be included on informed consent forms, including blindness, cerebral infarction, and death.

Mechanism of Action

The current hypothesis for blindness following filler injection is retrograde embolization of filler against arterial flow, into the ocular circulation. Although the majority of cases present with total blindness within minutes of the filler injection, some are delayed for hours or even days, some present with partial vision or field cut, and some with blindness and stroke. Newer anatomic insights relevant to our understanding of these atypical presentations have recently been published by reconstructive surgeons who have been studying flap and graft viability for decades.[30-33]

Multiple new pathways leading to ophthalmic artery embolism have been proposed. Left-to-right true anastomoses at remote sites such as the lip can potentially explain bilateral presentations observed in a minority of our cases.[32] Venous involvement is increasingly recognized in the pathogenesis of filler-induced blindness, with 3 cases of associated venous sinus thromboses documented in our review. There are large-caliber avalvular veins in the glabella that connect to both orbits and permit flow in any direction.[33] After injection in a vein, a filler embolus could migrate slowly through an avalvular venous path and eventually cross into the ophthalmic artery through 1 of many arteriovenous connections, such as an anastomosis identified in the inner canthus.[33] Other hypotheses for delayed blindness are a filler embolus in the ophthalmic vein or ciliary arteries. The above anastomoses and venous pathways are highly concentrated in the glabella and inner canthal (nose) area, which has been likened to a vascular "bag of worms," with easy targets for filler injection. This offers insight into why the glabella and nose have consistently been identified in the top 3 highest-risk locations. Additional pathways for filler to reach the orbital or cerebral circulation are depicted in Figure 9.

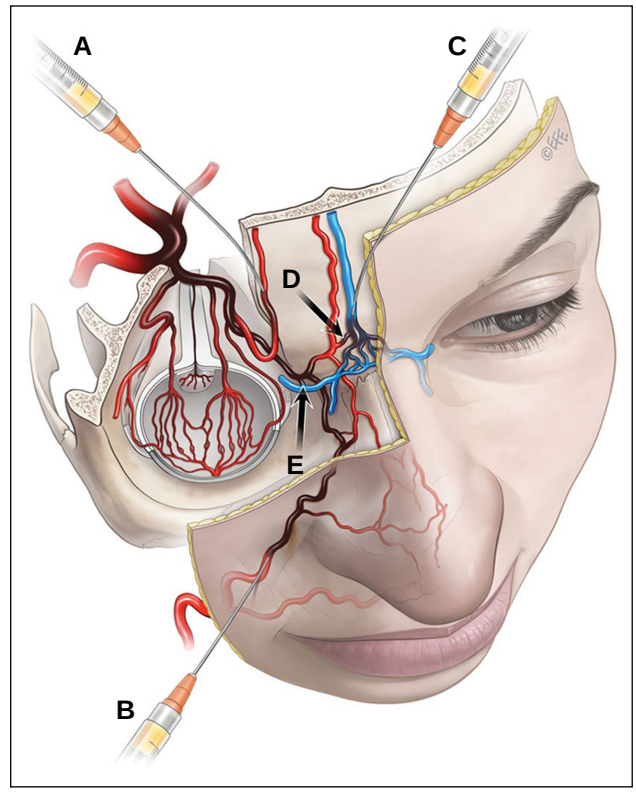

Figure 9. Diagram depicting potential pathways for the filler embolus (shaded black) to reach the ophthalmic artery, eyeball, and cerebral circulation through (A) 1 of its cutaneous branches, in this case the supraorbital; (B) a remote site connected by true anastomoses, shown here through the facial artery and the connection between its angular branch and the external nasal branch of the ophthalmic artery; and (C) possibly through an arteriovenous shunt in the glabella region, or (D, E) in the orbit between the ophthalmic artery and vein. Source: Taylor GI, Shoukath S, Gascoigne A, Corlett RJ, Ashton MW. The functional anatomy of the ophthalmic angiosome and its implications in blindness as a complication of cosmetic facial filler procedures. *Plast Reconstr Surg*. 2020;146(4):745. Permission was granted for republication.

Clinical Presentation

In our review, most cases of filler-induced blindness presented immediately or in the first 10 minutes. Involving 79.6% of cases, hyaluronic acid filler remains the primary cause of this devastating complication. The filler-type distribution in our cases has remained steady since our previous review and closely mirrors filler trends worldwide, with HA holding 77.5% of the global market share in 2023.[1] Congruent with previous studies, autologous fat cases, compared to HA, were less likely to recover vision and had a 7-fold greater rate of concomitant stroke.[34,35] This may be due to fat having a bigger particle size and occluding larger vessels such as the proximal end of the ophthalmic artery, causing diffuse ischemia. Blindness was also a reported complication from PRP and PLLA, neither of which are conventional fillers. This speaks to the problematic nature of the term "filler" and may have impacted the yield of our search.

The anatomical area where the filler is injected remains the most significant risk factor in the development of blindness. This review confirmed the nose as the anatomical area associated with the most ocular complications, followed by the forehead and glabella. A 2020 expert consensus paper highlighted the same 3 locations as "very high risk" areas.[36] Since 2018, there has been a 509% increase in blindness cases from forehead filler, which has a significantly worse prognosis with regard to vision recovery. Forehead augmentation is a frequently requested procedure in East Asia.[37] With 87.5% of the cases stemming from China and South Korea, our results could be biased by Asian beauty objectives such as greater medial and central face projection, which commonly involves injections in the nose, glabella, forehead, and nasolabial fold: high-risk anatomic locations.

The sites of previous trauma or surgery are particularly dangerous due to the high concentration and unpredictability of vascular anastomoses.[38] Considering the existence of multiple anatomical variations, filler-induced blindness can ultimately occur after injection in any location with connections to the ophthalmic artery. Indeed, risk locations have now expanded to ear filler injections.[39,40]

Blindness can present in isolation without any other symptoms. In OAO, ocular pain tended to be reported immediately and even before visual changes. Other than 2 cases with delayed presentations, the onset of blindness occurred within a few minutes after the filler had been injected. Our findings are contrary to those of 92 cases reported to the FDA in the 2015-2020 MAUDE database analysis, in which 18 (19.6%) patients developed visual impairment 1 to 24 hours after injection and 8 (8.7%) developed vision loss over 24 hours after injection.[41] In the FDA's current protocol for filler safety studies, vision assessment preinjection and 30 minutes post injection are required, including visual acuity, confrontational visual fields, and ocular motility.[41]

Outside of visual sequelae, other complications, such as anterior segment ischemia, strabismus, ptosis, and scarring of the skin, were associated with filler injection. Our review also included cases with stroke, and 2 deaths. A greater number of neurological complications were documented in the last 5 years. The percentage of all CNS complications was 34.0%, compared to 23.5% in 2015 and 18.8% in 2018. However, 34.0% encompasses mild or nonfocalizing CNS symptoms; specific strokelike symptoms such as hemiplegia or evidence of infarction on imaging was only present in 19.2%, which may be a more accurate number to compare.

In subgroup analyses, glabellar injections were associated with significantly more strokes ($P < .001$). While the glabella was only the third most common treatment area, there were more glabellar injections ($n = 15$) causing stroke than the nose ($n = 7$) and forehead ($n = 7$) combined. Filler complications were not isolated to the arterial vasculature; 3 cases of venous sinus thromboses were documented secondary to HA filler. Cutaneous changes were documented in 73.2% of cases but only a small proportion led to necrosis or scarring. The majority resolved over a few days following subcutaneous injections of HYAL, but some patients needed to undergo laser treatment or even skin grafting.

Prognosis

Cases with partially preserved vision at onset had significantly better prognoses than those with complete blindness, similar to the results of another review.[42] Indeed, the initial visual acuity at onset predicted 90.3% of the variability in final outcomes. OAOs and CRAOs presented as either LP or NLP and rarely regained vision. Forehead injections were associated with significantly lower rates of visual improvement. Compared to HA, cases secondary to autologous fat had significantly worse outcomes.

Pain relief was a frequent early signal of thrombus dissolution and may serve as a useful monitoring tool, similarly to the way chest pain is a disease marker in myocardial infarction. Our results validate that most muscular disorders such as ophthalmoplegia and ptosis recover over time, likely because of the extraocular muscles' abundant blood supply and anastomoses. A long-term study of filler-induced blindness cases showed that ophthalmoplegia spontaneously recovers in nearly all patients.[43]

Initial Bedside Management

Filler-related blindness is an ophthalmologic emergency. The goal of treatment is to recanalize the vessel and reperfuse tissue. The most cited time window for reperfusion is 90 minutes.[44] However, newer literature suggests it may be as little as 10 to 15 minutes, emphasizing the need for immediate recognition and management.[45] A streamlined guide is depicted in Figure 10 and detailed as follows:

1. Establish a filler-induced blindness protocol, review it with team members, and always have an abundant supply of nonexpired hyaluronidase on hand.[46]
2. Stop injecting at the first suspicion of visual complication. Blanching and other skin changes, ocular pain, nausea, headache, ophthalmoplegia, and ptosis may also occur.
3. If there is any concern about CNS involvement, the patient should be promptly transferred to the nearest emergency department for stroke assessment.
4. Even if there is no suspicion of CNS involvement, cerebral imaging should be performed to rule out a subclinical stroke after initial management of the ocular event.
5. Immediately contact an ophthalmologic expert who is familiar with filler-induced blindness and its management. Injectors should have a preestablished relationship with an ophthalmologist or oculoplastic surgeon to facilitate rapid consultation and care transfer during an event.
6. Before starting treatment, briefly examine each eye separately and document the following: (1) pupillary response to light; (2) extraocular muscle function; and (3) visual acuity, eg, the ability to read letters (Snellen chart or magazine print), count fingers, or perceive light.
7. If the filler material was hyaluronic acid, inject high-dose hyaluronidase immediately into the original filler treatment site, anywhere with skin ischemia, and along the arterial pathways leading to the eye. Recent literature indicates that increased ocular venous pressure (seen with supine position, holding one's breath, or digital pressure around the nose and inner canthi) may open arteriovenous shunts in the periorbital area, which may be advantageous when flooding this area with hyaluronidase.[33]

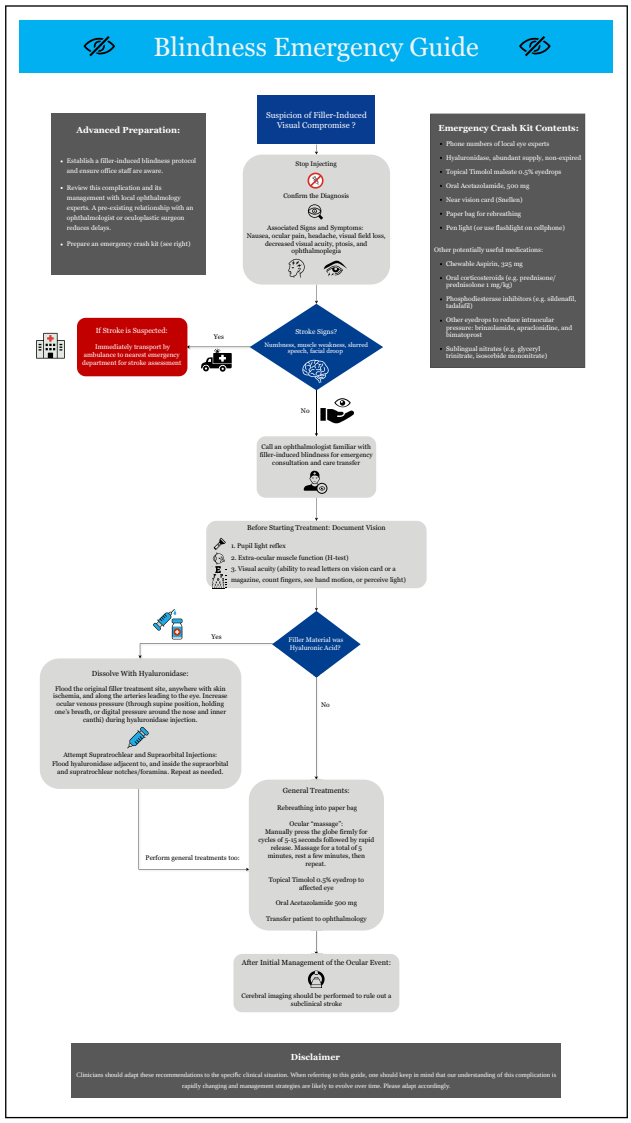

Figure 10. Initial bedside emergency management guide for filler-induced blindness. Designed for nonophthalmologist clinicians while awaiting transfer to a higher level of care.

8. Injectors are encouraged to attempt supratrochlear and supraorbital injections, with which hyaluronidase is injected adjacent to and inside the supraorbital and supratrochlear notches. Repeat in quick succession as needed. These are relatively simple and safe.
9. Conservative measures that can be done simultaneously include rebreathing into a paper bag and ocular "massage."[46-49] Manually press the globe firmly for cycles of 5 to 15 seconds followed by rapid release. Massage for a total of 5 minutes, rest a few minutes, then repeat. This may be continued over hours.
10. Intraocular pressure reduction with agents such as topical timolol drops and 500 mg of oral/intravenous acetazolamide may benefit cases with CRAO.[46-49]
11. Clinicians should keep in mind that management strategies are likely to evolve over time, and that this guide should be adapted to the specific clinical situation.

Treatment

The most commonly reported treatments are discussed here. There has been a large increase in use of HYAL in the last 5 years, from 41% of cases in the 2018 review to a total of 70.1% in our current review. Unfortunately, the increased utilization of both HA fillers and HYAL in our latest review has not led to a greater rate of vision recovery. The success of HYAL is contingent upon the dose, timing, and route of administration. Subcutaneous injections of HYAL at the original injection site, along the path of the vessels, and around the supratrochlear and supraorbital artery notches or foramina are noninvasive and easy to carry out immediately at the bedside.

In the latest review, 2 cases that received supratrochlear and supraorbital HYAL injections had their vision successfully restored, but these results are confounded by other concurrent treatments. Previously, other publications in 2016 and 2018 employed these techniques, among others, and reported successful outcomes.[50,51] However, neither of them had visual acuity or pupillary function evaluations at presentation, raising speculation that the symptoms could have represented a transient visual loss from migraine or a vasovagal response. Retrobulbar injections only demonstrated success in 5.3% of attempts, although this may be influenced by the timing and dose of HYAL. Its use remains controversial. Recent papers suggest this technique is unlikely to be helpful and should only be attempted by physicians familiar with this treatment.[36,48,52,53]

Overall, IATT improved vision in a total of 55 cases (34.2%), but the degree of recovery was modest. Only 7.4% of IATT procedures led to significant vision recovery of at least 20/70 BCVA. Hyperbaric oxygen therapy was associated with favorable outcomes, with 41.4% of patients who received hyperbaric oxygen having some degree of visual improvement. Because it is almost always administered in combination with a host of other treatments, it is difficult to conclude whether hyperbaric oxygen plays a major role in long-term recovery.

Proposed future treatments include intravenous HYAL, dual-pipe syringes with HA and HYAL, and HYAL nanoparticles incorporated in filler with externally-controlled triggered release.[52,54] A more detailed discussion of treatment strategies is beyond the scope of this review, however several are referenced here.[36,47,48]

Prevention

Because there is no gold standard of treatment, strategies to prevent this complication are paramount. Knowledge of

facial vascular anatomy is crucial, but not failsafe, because there is variation in the branching and depth of the vessels. Key prevention strategies aim to avoid penetrating a vessel, or to minimize the amount of product injected if the vessel is inadvertently compromised.

These include awareness of the areas at highest risk for serious complications (including any area where there has been a previous surgery or trauma), avoiding supraperiosteal injections around the foramina or antegonial notch, injecting slowly with low plunger pressure, in small volumes with each pass, and keeping the cannula or needle moving. Aspiration and employing a cannula to reduce risk of intravascular injection remains controversial. Extra caution should be applied with nondissolvable fillers such as autologous fat. Prevention strategies have been discussed in detail in our previous review paper and a recent review.[3,36] Importantly, since our previous update, duplex ultrasound has proved to be an increasingly promising tool due to its ability to visualize vasculature and filler. There is now a growing body of literature providing evidence for its role in the prevention and management of vascular occlusions.[55,56] However, ultrasound is user-dependent and has a steep learning curve. The cost and length of training and the additional time required for ultrasound visualization during procedures form barriers to its uptake in daily practice.

Limitations

Given that filler-induced blindness is a rarely described phenomenon, this research area faces the challenge of incomplete and inconsistent data. During this review, the BCVA was not always objectively assessed and sometimes only reported as subjective blurriness. Visual "recovery" was often not clearly defined, and patients may have had imperfect baseline BCVA before injury.

There may be duplicate or missing cases not captured in our literature review. Often case series did not provide data at an individual patient level. Drawing conclusions from a collection of case reports is inherently flawed by selection bias, and may not be an accurate representation of the spectrum of visual complications from filler in reality. Acknowledging these limitations, one must understand that the true prevalence of ocular complications from filler is much more extensive than currently documented.

Future case reports should aim to provide as many details as possible surrounding presentation, management, and evolution. We recommend that authors of filler-induced blindness case studies consult Martel and colleagues' checklist of important data to include when publishing new cases.[48]

CONCLUSIONS

Visual impairment is a rare but life-changing adverse event that can result from cosmetic filler treatments. Iatrogenic blindness cases may continue to rise with the rapid growth of the aesthetic industry. Given the existence of anatomical variations and numerous anastomoses between the internal and external carotid artery systems, filler-induced blindness can ultimately occur after injection in any location of the face. Blindness may be accompanied by severe complications outside of the eye, namely stroke. It is imperative for vascular occlusion to be identified and managed on an emergent basis. All injectors should be prepared to face this catastrophic complication. Prompt in-office management with emergency kits and written protocols are warranted. Current patient outcomes are poor and prevention remains the best strategy.

Supplemental Material

This article contains supplemental material located online at www.aestheticsurgeryjournal.com.

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Disclosures

Dr Rebecca Fitzgerald is a consultant, speaker, and advisory board member for Allergan (Irvine, CA) and Galderma (Lausanne, Switzerland). Dr Derek Jones is a consultant and investigator for Allergan and an investigator for Galderma and Symatese (Bornel, France). Dr Shannon Humphrey is a speaker, consultant, and/or investigator for Allergan, Evolus (Newport Beach, CA), Galderma, Merz (Frankfurt, Germany), and Revance (Nashville, TN). Dr Jean Carruthers is a consultant and investigator for Allergan, Merz, and Revance Biopharma. Dr Katie Beleznay is a speaker, consultant, and investigator for Abbvie Inc., Galderma, and L'Oreal (Paris, France).

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