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*Case Report*

# Dermal Cosmetic Migration after Lip Augmentation Procedure: Clinical Management and Histological Analysis in a Case Report with Review of the Literature

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**Abstract:** Lip augmentation procedures have become gradually more popular and common due to cultural tendencies and an increasing association of the appearance of the lips with both beauty and youth. Different dermal fillers have been proposed for lip augmentation—such as collagen, calcium hydroxylapatite, hyaluronic acid, and polylactic acid—which are used as temporary fillers. The present case report describes the histopathologic and clinical management of one case of HA filler migrating into the intraoral cheek, which caused discomfort by intraoral swelling. There is also a review of the relevant literature. A female patient, V.A., 34 years old, smoker, no allergies to drug and food substances, came to our attention. The patient was referred to the Department of Innovative Technology in Medicine and Dentistry of the University "G. D'Annunzio" of Chieti-Pescara in Italy by her dentist for the removal of a mass present in the right cheek. The clinical examination of the patient revealed a single mobile mass mimicking a soft tissue tumor in the right anterior cheek. The mass was palpable and approximately 2 cm long and was causing pain and swelling. The mucosa appeared healthy without ulcers. The filler, which had migrated into the cheek, was removed by reaching it with a scalped blade. The material was stored immediately in 10% buffered formalin and processed for histological analysis. The literature search was carried out in accordance with the criteria of the PICO guidelines. Observed histologically, the filler was surrounded by fibroblasts and a few inflammatory cells and giant cells without granuloma formation. The clinical diagnosis was swelling and discomfort caused by chewing trauma, while the histological examination excluded discomfort due to a foreign body reaction caused by the HA used for a lip augmentation procedure. In conclusion, the high-pressure and high-volume filler injections probably caused a detachment of the tissues, with the orbicularis oris muscle concurrently acting as a pump and moving the HA implant, causing migration to the area with low-density tissue such as the cheek.

**Keywords:** injectable fillers; dermal fillers migration; complications; nodules; hyaluronic acid; aesthetic procedures



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## 1. Introduction

Over the years since fillers were introduced in aesthetic medicine, there has been a steady increase in the request for cosmetic treatments of facial fat atrophy and soft tissue augmentation. Lip augmentation procedures have become gradually more popular and common due to cultural tendencies and an increasing association of the appearance of

the lips with both beauty and youth [1]. Resorbable and permanent dermal fillers have been proposed for the treatment of wrinkles, for correction of the facial contour and facial atrophy. Collagen, calcium hydroxylapatite hyaluronic acid, and poly-L-lactic acid are used as temporary fillers, while polymethylmethacrylate (PMMA) is used as a permanent dermal filler [2]. Today, Hyaluronic acid (HA) gel alone or combined with glycine and proline is largely used for soft tissue augmentation [3–5]. It is a temporary soft-tissue filler, so the occurrence of complications is acute or delayed and temporary—for this reason, it continues to grow in popularity and acceptance [6]. The lips and perioral region play an important role in facial aesthetics and have an impact on the patient's self-confidence, their social and psychological spheres, and their quality of life [3]. However, in probabilistic terms, this greater use of dermal fillers also increases the incidence of complications [7]. The effects of HA are not permanent, and, after a relatively little time—3 or 4 months for lips—the aesthetic result could shrink. This happens because the tissues metabolize the HA filler [7]. In the present case report, we describe the histopathologic and clinical management of a case of HA filler migrating into the intraoral cheek which developed into discomfort caused by intraoral swelling, and we present a review of the relevant literature.

## 2. Materials and Methods

### *2.1. Case Report*

The present case report followed the CARE (CAse REport) Statement and Checklist guidelines [8]. A female patient, 34 years old, smoker, no allergies to drug and food substances, came to our attention. The patient was referred to the Department of Innovative Technology in Medicine and Dentistry of the University "G. d'Annunzio" of Chieti-Pescara in Italy by her dentist for the removal of a mass present in the right cheek (Figure 1). The patient was referred for swelling and pain in the lateral right cheek after a lip augmentation procedure performed 3 months previously. Data regarding the filler injections and their type were obtained from the submitting doctor and from the patient. All information was reported by the patient, who says she underwent lip augmentation with a horizontal technique and HA. The patient reported the packaging of the used HA: Skin-F 24 Italfarmacia srl (Rome, Italy). Immediately after the injection for the augmentation of the lips, she reported a swelling of the cheek (Figure 1); no nodules were observed in the perioral skin. The clinical examination of the patient revealed a single mass—mimicking a soft tissue tumor—in the right anterior cheek, which was palpable and approximately 2 cm long, and for a few days the patient had suffered pain and swelling in this area. The mucosa appeared healthy without ulcers. The mass was mobile on palpation. An ultrasound scan was performed to evaluate any clinical relevance and the size of the nodule, which showed subcutaneous cellular tissue that had fully integrated with the HA fillers, showing alternating hyperechoic and anechoic areas on the ultrasonography (Figure 2). The patient had a history of multiple dermal filler injections for lip augmentation, performed over many years by a dermatologist. The ultrasound showed a well-defined nodule with a size of 20 × 18 mm. The ultrasonography lesion appearance was characterized by alternating hyperechoic and anechoic evidence. After discussing the options with the patient, she agreed to the removal of the HA migrated into the cheek. The informed consent form was signed by the patient for the treatment of her case and for the documentation and publication of the case report. The surgery procedure was scheduled in an ambulatory setting and under local anesthesia. Prior to surgery, the patient's mouth was rinsed with a chlorhexidine 0.2% digluconate solution (Curaden Healthcare S.p.A., Saronno, Italy) for 2 min. Local anesthesia was provided by the administration of Articaine® (Ubistesin 4%—Espe Dental AG Seefeld, Seefeld, Germany) with epinephrine 1:100.000. The surgeon tried to remove the filler with a needle and by exerting pressure with his fingers on the cheek to push out the filler without results. As such, a scalpel blade was used to reach the filler mass (Figure 3).

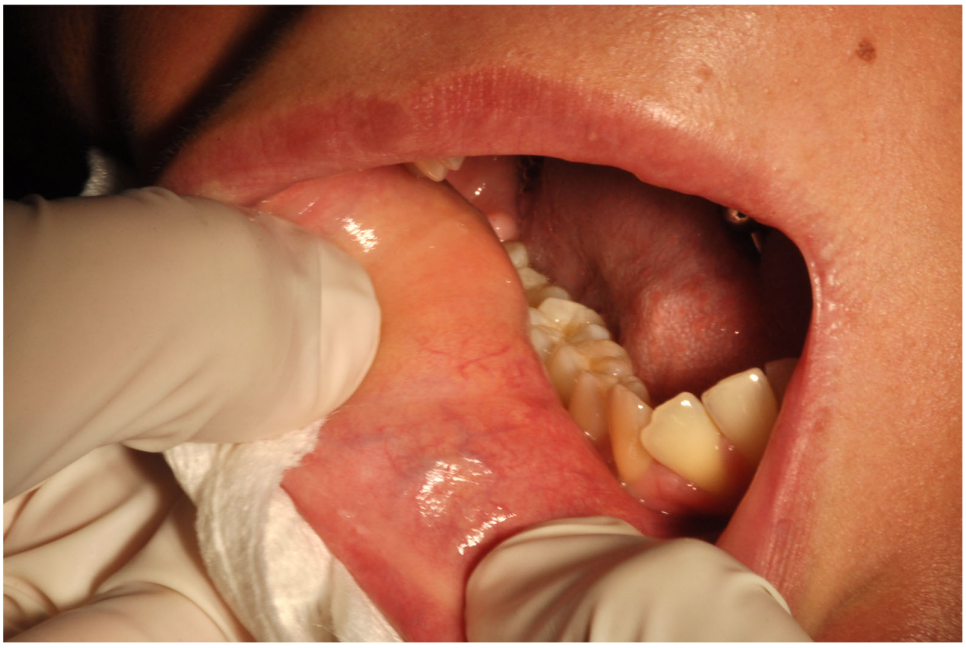

**Figure 1.** Clinical aspect of intraoral cheek. Evident presence of a swelling.

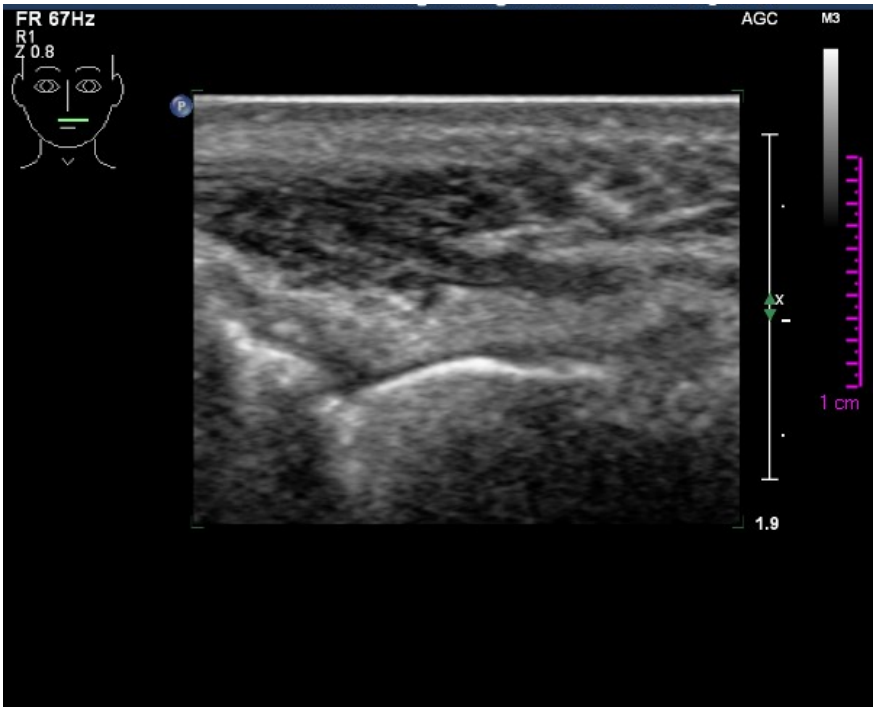


**Figure 2.** An ultrasound scan shows the size of the filler migrated into the cheek.

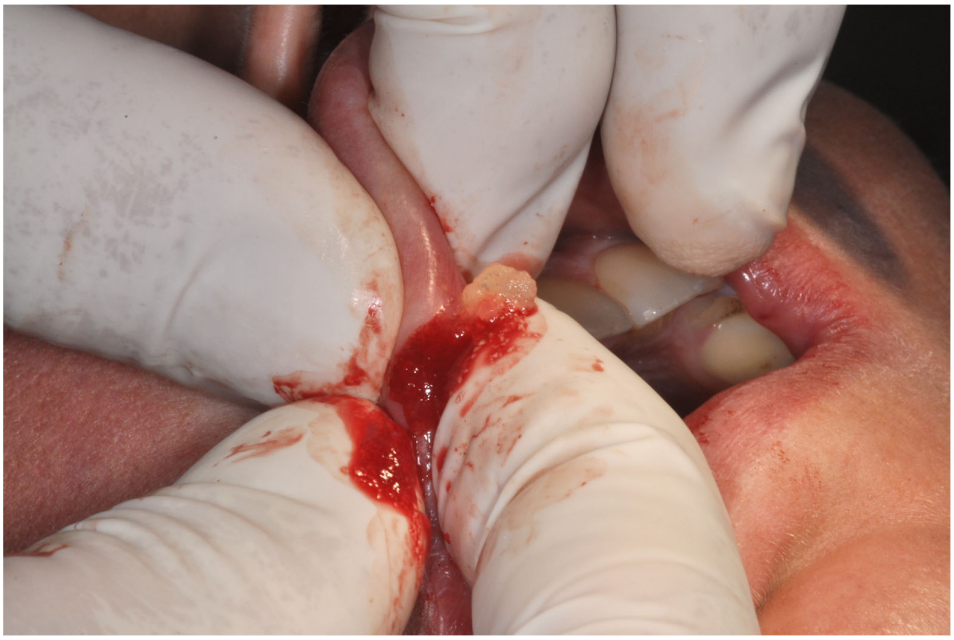

**Figure 3.** During surgical removal of the filler migrated into the cheek.

### *2.2. Histological Analysis*

On removal, the specimen was stored immediately in 10% buffered formalin and processed for histological analysis. The slides were stained with hematoxylin and eosin and observed in normal transmitted light under a Nikon microscope ECLIPSE (Nikon, Tokyo, Japan). The material was included in its entirety.

### *2.3. Systematic Literature Review Strategy*

#### 2.3.1. Articles Screening

The literature search was carried out in accordance with the criteria of the PICO guidelines (population, intervention, comparison, outcome) and is summarized in Table 1.

**Table 1.** Synthesis of the PICO study (population, intervention, comparison, outcome).

| Population\Patients | Intervention | Comparison | Outcomes |
|---|---|---|---|
| Subjects affected by facial dermal filler migration | Patients subjected to surgical removal | Patients subjected to alternative medical treatment | Efficacy and prognosis of surgical removal treatment for dermal filler migration |

The systematic search and data processing was carried out in accordance with the "Preferred Reporting Items for Systematic Reviews and Meta-Analyzes" (PRISMA) guidelines. The Boolean search was carried out according to the strategy described in Table 2 and conducted on the PubMed and EMBASE electronic databases.

**Table 2.** Boolean search strategy on electronic databases.

| | Search Strategies |
|---|---|
| Keywords: | Advanced keyword search: (Facial Dermal fillers AND migration) |
| Databases | PubMed/Medline, EMBASE |

#### 2.3.2. Inclusion and Exclusion Criteria

The following criteria were applied for the initial screening: human clinical studies, prospective and retrospective studies, case series, and case reports with no restrictions regarding the follow-up and dermal filler composition. The exclusion criteria consisted

of systematic reviews of the literature, editorial letters, and in vitro studies. Then, after eliminating duplicates, the articles were subjected to a full evaluation of the full-text manuscripts for inclusion in the eligibility analysis.

#### 2.3.3. Eligibility Process

The screening and selection of the articles was carried out independently and blindly by two expert reviewers (FL and IA) in order to evaluate the inclusion of the scientific products in the descriptive analysis process. The duplicates and the eliminated scientific articles were in any case classified by recording the reasons for exclusion in the review.

#### 2.3.4. Data Analysis

The study data of the included scientific products were recorded in a special database created using Excel software (Microsoft, Redmond, WA, USA) and classified according to the following characteristics: study design, population characteristics, number of patients treated/implants placed, analytical methodologies, inclusion/exclusion criteria, failed implants, follow-up, and outcome.

## 3. Results

### *3.1. Histological and Clinical Follow-Up*

Observed histologically, the filler was surrounded by fibroblasts and a few inflammatory cells and giant cells without granuloma formation. The microcystic-like spaces were empty of HA, and the presence of HA could be observed during the analysis of the histologic sections. Increased acid mucopolysaccharides in the mucosae were observed. Histological conclusions were an HA surrounded by fibroblasts without chronic inflammatory reactive tissue. The patient came back for follow-up at 7 and 15 days, demonstrating excellent compliance, and the trouble had completely disappeared. The discomfort had been caused by intraoral swelling and not by an inflammatory reaction (Figure 4).

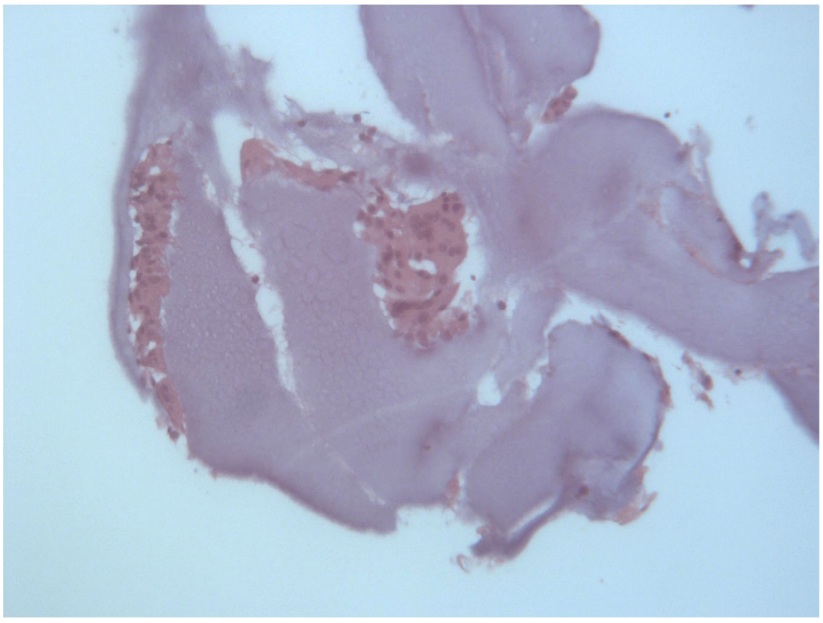

**Figure 4.** Histological image showed a soft tissue and amorphous substance and a few giant cells' infiltrate. Eosin staining X10.

### *3.2. Literature Review Findings*

#### 3.2.1. Selection Characteristic

The electronic database search phase (PubMed/Medline, EMBASE) produced a total of 58 articles and a publication identified by manual screening. A total of four duplicates and one article were removed from the preliminary evaluation phase. A total of 53 scientific

publications were submitted for eligibility assessment. A total of 38 articles were then excluded from the synthesis process, including 10 off-topic articles, three publications in non-compliant languages, eight scientific papers on animal models, 10 literature reviews, three in vitro studies, two cadaveric studies, one wrong drug, and one letter to the editor. A total of 15 scientific papers were included in the analysis and descriptive summary (Figure 5).

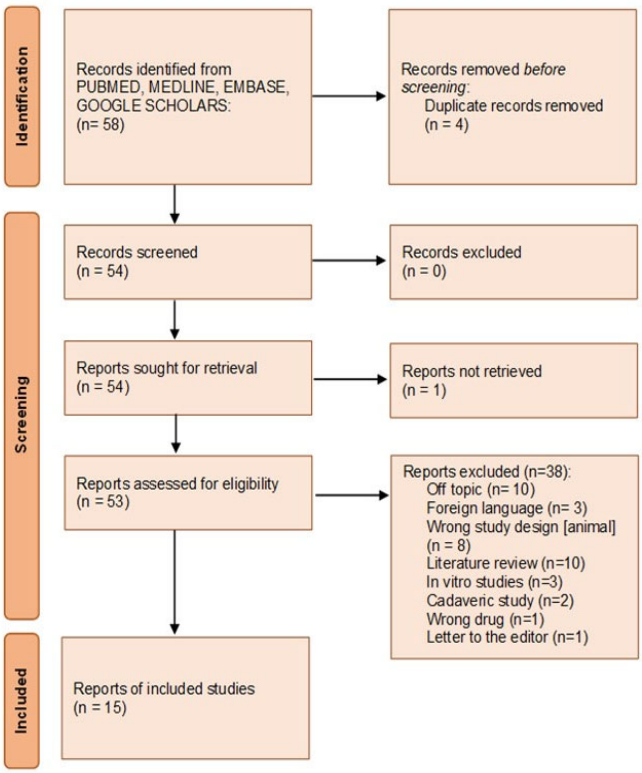


**Figure 5.** Summary of the article selection according to PRISMA guidelines.

### 3.2.2. Characteristic of the Included Studies

Therefore, the following articles were included in this systematic review of the literature: seven retrospective studies [9–15], seven case reports [16–22] and one case series [23]. The filling regions were: the nasolabial fold (NFL) [9,11–13], temples/lateral brow rim [9,13,23], cheeks [9,12,13,18–20,22], jawline [9], cheeks [9], lips [10,11,15–17], mental area [11], nasal tip and dorsum [12,14], glabellar [12,13], temple [12], nose, [12], forehead [13,14], tear troughs [13], perioral region [13], marionette lines [13], chin [13], lower eyelid [19,21,23], and periocular region [21].

The most frequent complications reported were orbital [9], lip enlargements and ulcers [10,16,20], intraoral nodule migration [11,17], allergic reactions [12], filler-material face migration [12,13,18,20,21,23], embolisms [12], foreign body granulomas [12,23], abscess formation [13,22], monocular blindness [14,19], necrosis [20], and swelling masses [21] (Table 3).

**Table 3.** Summary of the included studies.

| Authors | Journal | Year | Study Design | Population | Gender | Subject (s) Age | Filler Type |
|---|---|---|---|---|---|---|---|
| Hamed-Azzam et al. [9] | Aesthet Surg J | 2021 | Retrospective Study | 7 subjects | 6 female<br>1 male | Age range 42–67 years | NA |
| Grippaudo et al. [10] | J Cosmet Laser Ther | 2014 | Retrospective Study | 26 subjects | 26 female | Age range 28–74 years | 3 silicone (S); 1 S + AH, (Acrylic hydrogel particles (copolymer of 40% hydroxyl-ethyl-methacrylates); 7 polyacrylamide gel (PAAG); 1 AH + PAAG; 2 AH; 1 PMMA; 1 collagen; 1 hyaluronic Acid; (HA); 1 HA + S; 1 polyalkylimide gel (PAIG) |
| Abtahi-Naeini et al. [16] | J Cosmet Dermatol | 2018 | Case report | 1 subject | 1 female | 35 years old | Polydimethylsiloxane (PDMS) |
| Shahrabi-Farahani et al. [11] | Oral Surg Oral Med Oral Pathol Oral Radiol | 2014 | Retrospective Study | 25 subjects | 25 female | 35 to 78 years (median, 55 years) | 13 calcium hydroxylapatite (CHA);12 poly-L-lactic acid (PLA) |
| Kehily et al. [17] | J Ir Dent Assoc | 2015 | Case report | 1 subject | 1 male | 33 years old | Na |
| Lee et al. [12] | J Cosmet Laser Ther. | 2015 | Retrospective Study | 8 subjects | 6 female; 2 male | Mean 48.6 years (range, 30–74). | 1 (porcine atelocollagen1 2.5% cross-linked PAAG<br>2 Unknown<br>1 HA<br>1 HA)/NLF<br>1 Paraffin<br>1 Vaseline |
| Kadouch et al. [13] | Aesthet Surg J. | 2014 | Retrospective Study | 32 subjects (107 clinically assessed deposits) | 16 male, 16 female | 25 to 76 years (mean, 55.4 years) | Polyalkylimide gel and polyacrylamide gel; hydrogels 2.5% polyacrylamide gel and 4% polyalkylimide gel) |
| Kim et al. [23] | Dermatol Ther. | 2017 | Case series | 2 subjects | 2 female | 54 yo and 60 yo | Na |
| Wang et al. [14] | Aesthetic Plast Surg | 2021 | Retrospective study | 30 subjects | 1 male, 29 female | aged 18–35 years | Na |
| Lin et al. [18] | J Cosmet Laser Ther | 2017 | Case report | 1 subject | 1 female | 50 years old | Poly-L-lactic acid (PLLA), |
| Dryden et al. [19] | Cureus | 2021 | Case report | 1 subject | 1 female | 57 years old | Injectable hyaluronic acids |
| Choi et al. [20] | J Craniofac Surg. | 2004 | Case report | 1 subject | 1 female | 55 years old | Silicone injection |
| Kästner et al. [15] | Aesthetic Plast Surg | 2018 | Retrospective study | 11 subjects | 10 female, 1 male | 31 and 53 years old | Cross-linked polyacrylamide |
| Malik et al. [21] | Ophthalmic Plast Reconstr Surg. | 2013 | Case report | 1 subject | 1 female | 52 years old | Polyalkylimide |
| Zeltzer et al. [22] | Aesthetic Plast Surg | 2015 | Case report | 1 subject | 1 male | 42 years old | Polyalkylimide |

**Table 3.** *Cont.*

| Authors | Journal | Year | Filling Region | Complications | Time from the Treatment | Failed Intervention | Intervention | Follow-Up |
|---|---|---|---|---|---|---|---|---|
| Hamed-Azzam et al. [9] | Aesthet Surg J | 2021 | 3 nasolabial fold; (NFL); 1 temples/lateral brow rim; 1 NFL, cheeks; 1 jawline; 1 cheeks | (1) Orbital complitations (7): 3 inferior; 1 superolateral; 1 inferomedial;1 medial; 1 lacrimal sac | Post-operative complications (<1 month) | Steroid injection and hyalurodinase injections | 4 subjects: orbitotomy surgery 1 subject: lacrymal surgery 1 subject: strabismus surgery 1 subject: hyalurodinase injections | 11 months (range 2–15 months) |
| Grippaudo et al. [10] | J Cosmet Laser Ther | 2014 | Lip augmentation with injectable materials | Lip enlargement, asymmetry, edema, ulcers, lip hardening, Asymmetry, dyschromia, Lumps | 6 subj. Post operative complications (<1 month) 3 subj.at 1 year 17 subj. > 2 years | - | 9 patient surgeries, 10 medical treatments + drainage, 6 received both, 1 refused treatment. | 3 years |
| Abtahi-Naeini et al. [16] | J Cosmet Dermatol | 2018 | Lip augmentation with injectable materials | Lips extreme erythema, edema, fever and warmness; Periorbital area implant migration | 9 months | Local injection of triamcinolone | Gel implant surgical removal from the lip and periorbital area | 2 months |
| Shahrabi-Farahani et al. [11] | Oral Surg Oral Med Oral Pathol Oral Radiol | 2014 | Lips, nasolabial area, or mental area | Intraoral nodules (labial/buccal or vestibular mucosa) distant from the site of injections | 2–26 months | - | Surgical removal | 2–12 months |
| Kehily et al. [17] | J Ir Dent Assoc | 2015 | Lip augmentation with injectable materials; 'marionette lines' Nlfs | Lower labial sulcus migration (4.1, 4.2, 4.3 teeth) painless swelling | 12 days | - | No treatment/monitoring | 3 months |
| Lee et al. [12] | J Cosmet Laser Ther. | 2015 | Nasal tip and dorsum, Glabellar cheek & temple Nose | Allergic reaction (25%), filler material migration (12.5%), embolism (25%), foreign body granuloma (37.5%) | Immediately to 14 years | | Surgical removal | no follow up |
| Kadouch et al. [13] | Aesthet Surg J. | 2014 | Facial soft-tissue augmentation; (forehead, glabella, temporal region, tear troughs, cheeks/zygomatic arch, nasolabial area, perioral region, marionette lines, and chin. | Deposit/without inflammation deposit with inflammation abscess formation migration | 6 to 120 months (mean, 47.5 months). | - | Antibiotic treatment; surgical intervention (8%) | weeks |

**Table 3.** *Cont.*

| Authors | Journal | Year | Filling Region | Complications | Time from the Treatment | Failed Intervention | Intervention | Follow-Up |
|---|---|---|---|---|---|---|---|---|
| Kim et al. [23] | Dermatol Ther. | 2017 | Right lower eyelid; left temple | Subcutaneous nodule; multiple granulomas: filler migration with foreign body at | 7 years; | - | Surgical removal and histological analysis | 4 weeks |
| Wang et al. [14] | Aesthetic Plast Surg | 2021 | Forehead and nasal bridge | Monocular blindness | 20–120 h | - | Intra-arterial thrombolysis (hyaluronidase injection) (25) | 2 h |
| Lin et al. [18] | J Cosmet Laser Ther | 2017 | Cheeks | Temple subcutaneous nodule filler migration | 1 years | - | Surgical removal and histological analysis | 2 weeks |
| Dryden et al. [19] | Cureus | 2021 | Lower eyelid and lateral cheek junction | Occluded ophthalmic arteries | 6 months | Steroids and injected hyaluronidase (multiple periocular and perioral hard nodules) | Anterior orbitotomy through a transconjunctival incision t | 3 months |
| Choi et al. [20] | J Craniofac Surg. | 2004 | Multiple face liquid injection | Worsening edema and extensive necrosis of the face (malar;cheek, and preauricular region) palpable mass on her neck (palpable mass on her neck) | 2 years | Antibiotics were initiated, and multiple debridements of the face | Incision line on the neck | 5 days |
| Kästner et al. [15] | Aesthetic Plast Surg | 2018 | Eleven upper and six lower lips | Gel migration within the lips and into the surrounding perioral zone | 2–10 years | - | Surgical removal | 12 monhs |
| Malik et al. [21] | Ophthalmic Plast Reconstr Surg. | 2013 | Periocular filler | Mass and swelling left eyebrow, temple, and glabella. | 10 years | Sclerotherapy | Surgical removal | 2-weeks |
| Zeltzer et al. [22] | Aesthetic Plast Surg | 2015 | Facial lipodystrophy | Spontaneous abscess formation right cheek | 5 years | A high dose of oral ciprofloxacin; emergency percutaneous drainage of the multi-compartment abscess | Surgical removal | 3–4 weeks |

## 4. Discussion

In the present case report, the histological results demonstrate the absence of a granulomatous reaction to HA and the absence of tissue necrosis. As such, the discomfort reported by the patient was caused by intraoral swelling and not an inflammatory reaction due to a lip augmentation procedure with HA. As reported by the present literature review, the most common clinical presentation is characterized by filler migration associated with mild symptoms—swelling, fever [12,13,18,20,21,23], and abscesses [13,22]—that could be involved medium- to long-term following the treatment. Moreover, the time of presentation of complications is very heterogeneous and can be immediate, after a few hours following the filler injection [14], to a maximum of 14 years [12] from the treatment. On the other hand, the most common intervention for dermal filler migration was characterized by the surgical removal of the mass [9–13,15,16,18–21,23]. An embolism represents a critical and very insidious early complication that could take advantage of hyaluronidase thrombolysis injection in the case of HA dermal filler [12]. Augmentation procedures with HA have been on the rise over the past few decades and, for this reason, complications have also increased—such as edema, pain ulceration, scar itching, nodule formation, and migration of the injected material, described by different authors [24,25]. Although dermal fillers are usually non irritating and nonantigenic, acute short-term injection site events such as discomfort, bruising, erythema, swelling, pruritus, pain, or hematoma formation may occur [26]. Additionally, severe complications such as allergic hypersensitivity reactions, necrosis, and vascular occlusion scarring have been reported. Foreign body reactions may occur as intermediate or late-term unfavourable reactions occurring months or years after treatment. Granulomatous foreign body reactions have been reported—especially when using fillers based on calcium hydroxylapatite (CHA) [27] and poly-L-lactic acid (PLA) [28]. Dermal fillers based on crosslinked hyaluronic acid are often used in aesthetic medicine for correcting facial contour deficiencies, for reducing the appearance of wrinkles in the face, and for cosmetic rejuvenation [28]. It is popular because of its relatively low cost and minimal invasiveness compared with cosmetic surgery. Additionally, HA is most widely used for cosmetic rejuvenation because of its biocompatibility, non-immunogenicity, and biodegradability and it is completely resorbable by hydrolysis [29]. While these techniques are generally secure—with few immediate or delayed adverse events—the immediate complications can include blindness, vascular occlusion, and necrosis [30], while delayed adverse events include granulomas [31]. Another complication is filler migration from the original injection site; different mechanisms for this have been indicated, including excessive injection volume, bad injection technique, gravity, muscle activity, and lymphatic spread [31]. With time, natural ageing with atrophy and hollowing of facial tissues may increase the quantity of dermal filler injected for each site. Dermal filler migrations from the original anatomical injection area have been described in the literature.

In this case report, the migration of dermal filler material to the patient's cheek area suggests that the filler may have migrated immediately as a result of an overfilled injection, high pressure, high volume, and orbicular muscle activity, or due to an incorrect technique. This clinical case aims to increase awareness of the growing recognition of the risks of injectable dermal fillers. As the extensive use of dermal fillers grows, patients and doctors must be aware of complications that may require surgical intervention in some cases. The possibility of complications is lower with experienced providers, and risks generally arise when the implant is performed by doctors with less experience and inappropriate techniques. Low-pressure and low-volume filler injections are recommended, with more than one treatment per session to minimize dermal filler migration [7,32]. On the other hand, Goldman et al. reported that the use of permanent non-reabsorbable dermal filler nodules on the lips could be advantageous compared to intralesional neodymium:YAG lasers, associated with blunt suction cannulas and minor surgery [33]. Some authors recommended keeping the face at rest and limiting physical activity for the immediate time period after a dermal filler injection. For this reason, it should be recommended that a patient should avoid any excess orbicular muscle function for 24/48 h following the implant

of perioral dermal filler [7,32]. In this case report, no thyromegaly, lymphadenomegaly, or other relevant neck and head swelling were observed. Intraoral examination revealed a right cheek swelling and the absence of a hard nodule that was painful to palpation. The clinical diagnosis was swelling and discomfort caused by chewing trauma, while the histological examination excluded discomfort due to a foreign body reaction caused by the HA used for the lip augmentation procedure. Probably, the high-pressure and high-volume filler injections near the labial commissure caused a detachment of the tissues, with the orbicularis oris muscle acting as a pump concurrently and moving the HA implant, causing migration into an area with low-density tissue such as the cheek.

## 5. Conclusions

In conclusion, in some clinical circumstances, control of the extrusion pressure and volume of the filler are necessary to avoid a local tissue detachment with the orbicularis oris muscle. This event could be clinically associated with a pump effect, producing a considerable risk of HA filler migration into a low-density tissue.

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**Informed Consent Statement:** For this type of study, informed consent is not required.

**Data Availability Statement:** All experimental data to support the findings of this study are available upon request by contacting the corresponding author.

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