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A Vascular Filler Complication

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Abstract

Facial filler injections represent an increasing procedure in nonsurgical facial rejuvenation field. In the United States, in 2014, soft tissue fillers comprised 2.3 million procedures performed, with a 4.5% increase from the previous year.

Of these 2.3 million total dermal filler injections, about 78% (1.8 million) was represented by Hyaluronic Acid (HA) fillers. The widespread use of this material may be caused by the reversibility of the HA fillers, with time and with hyaluronidase, which allows both the doctor and the patient a greater serenity by being able to reduce any exaggerated fillings.

Despite of the over increasingly use of this material the complication could be severe depending on the type of damage and the affected area. The aim of this paper is to present a particular complication occurred during facial filler injection.

Introduction

Hyaluronic Acid (HA) fillers are the most commonly used injectable fillers, followed by autologous fat. According to the American Society for Aesthetic Plastic Surgery, nearly 900,000 soft tissue augmentation procedures were performed in 2004 where hyaluronic acid was used as filler [1-3].

Other substances commonly used for "filling and bulking" include bovine and human collagen (active for 1 to 3 months before degradation); poly-L-lactic acid, which causes endogenous collagen stimulation for up to 15 months; and calcium hydroxyapatite, whose duration is around 2 years [4].

These fillers are commonly used both to restore volumes and to improve and give greater definition to areas of the face. They can therefore be used, depending on the concentration of hyaluronic acid and the strength of the bonds between the molecules, as volumizers for areas such as cheeks and chin and lips; to redefine in areas such as the lacrimal groove or at the level of the nose in the so-called non-surgical rhinoplasty [5].

In literature the first injection of autologous fat in *viz.* is reported in 1893 [6]. And at the beginning of the 20th century, the first injections of liquid paraffin were performed in Vienna [7]. It was in this period, precisely in 1914, that the term "paraffinoma" was coined for the first time to describe the delayed complications of paraffin injections causing a decline in its use in the Western world.

Despite all this, we went in search of substances that could be injected and have a "filling" effect, so silicone oil infiltration became popular in the 1960s, with the description of the injection technique of micro-droplets [8,9].

A big step in the advancement of injectable fillers occurred in 1981, when bovine collagen (Zyderm, Zyplast; Inamed Corp., Santa Barbara, CA) became the first FDA-approved injectable filler for cosmetic use. The modern era of injection with synthetic selective bioactive materials began in December of 2003 with the FDA's approval of Restylane (Q-Med, Uppsala, Sweden), a Hyaluronic Acid (HA) product.

The growing use of dermal fillers in medical practice, in particular the use of Hyaluronic Acid (HA), can be explained based on the efficacy, naturalness, versatility of the products but also and above all by the real safety profiles of these materials.

Although the incidence of complications is low and the majority of adverse events are mild, the increase in the number of procedures has produced the concurrent increase in the number of complications [10-12].

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Material and Method

In this case report, the author analyzed a rare complication of intravascular injection that involved all the hemiface of the patient.

The patient was submitted to both nasolabial folds treatment. The injection was carried out with needle following the fold course. After the second injection the patient referred an iced feeling in all the hemiface. The operator then stopped the procedure and the patient face start to become marbled. The affected area included the spraying territories of the facial artery but also probably those of the vein due to both the antegrade and retrograde trend of the marbling. The area in fact extended from the skin over and laterals of the nose, to the upper lip, to the Malarone to the cheek.

The complications occurred in the Saturday evening. For the first hours the operator recommended the patient to apply a warm medication to increase the vascularization reducing the vascular ischemia (Figure 1).

After 10 h, the doctor organized a visit in the office to check the face condition. The occlusion area was then delimiting involving more clearly the upper lip and the nasolabial fold reducing in the sub-palpebral and cheek zone (Figure 2). Then the doctor started to administer to the patient cardio aspirin once a day, 4,000 UI Seleparin once a day, and did several local injections of lidocaine and hyaluronidase. The rationale that led to combine lidocaine with hyaluronidase was to exploit the vasodilatory action of lidocaine in order to increase the penetration of hyaluronidase into the tissues. The dose of hyaluronidase was 30 U divided into four sub-ministration administrated into several points in the right upper lip, right nasojugal fold and right cheek skin. Cause the important vascular damage, 4 mg/g nitroglycerin ointment was used too. Unfortunately, the use of this ointment caused an excessive lowering of patient blood pressure due probably to the mucosal absorption causing the interruption of use (Figure 3).

The patient was then checked once a day.

The third day, the upper lip was highly dolent and the vascular damage, even if it was limited in extension, was confining itself to an arch with a posterior convexity that had the upper lip as its center (Figure 3).

The day after the nose was free from vascular damage, but the upper lip became violet, and the mobility was highly reduced cause the important edema. The patient continued the drugs sub-ministration (Figure 4).

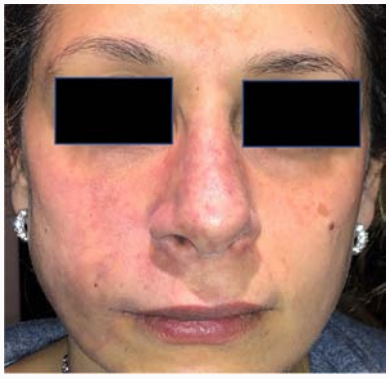

Figure 1: Immediate vascular damage.

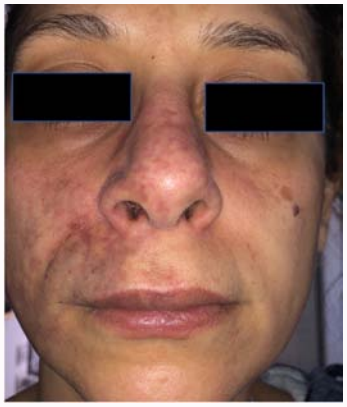

Figure 2: Skin compromise after 10 hours.

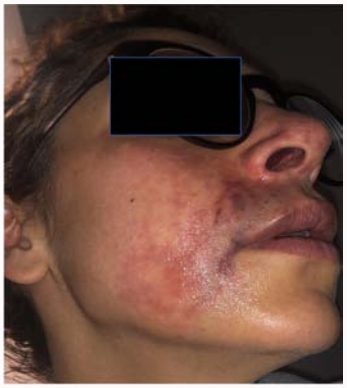

Figure 3: Third day skin damage.

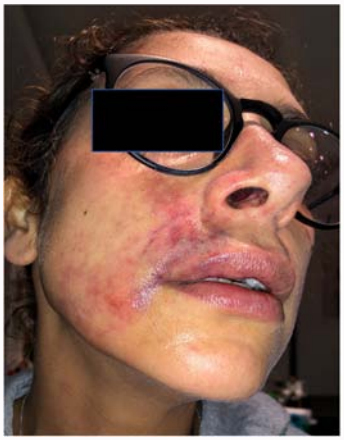

Figure 4: Fourth day vascular compromise.

On the fifth day, small painful and bleeding ulcers began to appear on the lip then an antibiotic ointment was suggested (Figure 5).

Results

After 10 days the vascular damage started to solve and in fifteen days the ulcers healed.

The complete *restitutio ad integrum* occurs in 40 days but a darker area remains for more than six months over the upper lip.

Discussion

Dermal fillers are increasingly used in clinical practice as a

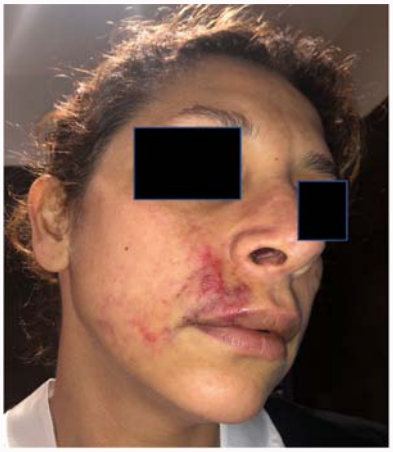

Figure 5: Fifth day skin damage.

volumetric and restorative treatment of the soft tissues of the face, décolleté and hands. Obviously, the exponential increase in the use of these substances, although safe, has led to an increase in reports of associated complications. Although most complications are mild and transient, serious, and long-lasting complications have been observed [12].

Among the various options of choice, we can differentiate the fillers made up of biodegradable particles that stimulate the body to produce its own collagen such as calcium hydroxyapatite (CaHA; Radiesse®; Merz Pharmaceuticals GmbH) and poly-L acid -lactic (PLLA; Sculptra®; Valeant, West Laval, QC, Canada). Compared to the others these have a longer duration. The first consists of synthetic CaHA microspheres suspended in a carrier gel. Infiltration results in both immediate visual improvement and long-term stimulation of deposition which contributes to an average duration of effect of approximately 15 months [13]. PLLA is a synthetic polymer that determines a volumetric increase in tissues through the stimulation of an inflammatory response with subsequent deposition of collagen.

On the other hand, the mechanism of action of non-biodegradable fillers is different, which instead cause a foreign body reaction with consequent fibroblastic deposition of collagen around the non-absorbable microspheres [14]. Products in this category include Polymethyl Methacrylate (PMMA; Artecoll®; Rofil Medical International BV, Breda, The Netherlands), Aquamid® polyacrylamide hydrogel (Contura International, Soeborg, Denmark) and Silikon® 1000 (Alcon Laboratories, Inc., Fort Worth, TX, USA), a pure form of medical grade silicone [15].

Hyaluronic acid is a Glycosaminoglycan (GAG), the main component of the extracellular matrix which has the function of binding proteins, filaments, collagen fibers and connective tissue cells [16].

It consists of a disaccharide polymer composed of D-glucuronic acid and D-N-acetylglucosamine, linked with β-1,4 and β-1,3 glycosidic bonds. The enzyme involved in the degradation of hyaluronic acid is hyaluronidase, an endoglycosidase that depolymerizes HA with multiple effects in the tissues. This in fact decreases the normal viscosity of the HA by decreasing its lubricating quality. The enzyme also acts as a "diffusion factor" facilitating the diffusion of various substances injected subcutaneously, such as dyes and antiviral vaccines [17]. Knowledge of the mechanisms involved in hyaluronidase pharmacokinetics is limited. Serum clearance occurs with a half-life of 2.1 ± 0.2 min by inactivation in the kidneys and liver. The most common interactions occur with furosemide, benzodiazepines, phenytoin, dopamine and α-adrenergic agonists. Hyaluronidase antagonists include anti-inflammatory agents (e.g.: indomethacin, dexamethasone, and salicylates), numerous plant-based drugs (e.g.: flavonoids and antioxidants), antihistamines, mast cell stabilizers, heparin, vitamin C, and dicumarene [18,19].

According to Szepfalusi et al. [20], hyaluronidase may represent a potent antigen when co-administered with chemotherapeutic agents and dexamethasone, triggering IgE synthesis. The indications for which it is approved for use by the European Union are: (1) adjuvant therapy in the subcutaneous administration of drugs, (2) increased penetration of a local anesthetic, (3) to promote resorption of the contrast medium in urology and (4) to promote resorption of subcutaneous hematomas.

The importance of hyaluronidase in clinical practice is related to the management of a variety of facial filler complications. In fact, hyaluronidase has the ability to dissolve HA, which is the most injected molecule in the United States. Its activity was first described in 1929 by Duran-Reynals [21]. It is approved by the FDA as a dispersing agent, usually for local anesthetics, having the ability to temporarily modify the permeability of connective tissue through the hydrolysis of HA, a polysaccharide present in the intracellular ground substance of connective tissue [22]. In clinical practice, approximately 30 U of hyaluronidase are commonly used to dissolve 0.1 mL of hyaluronic acid.

Facial aesthetic procedures, being medical-surgical procedures, are not without complications. The risk, although low, nevertheless exists. The so-called "local" adverse events are those involving the injection site (e.g.: swelling, tenderness, pain, bruising). These include edema, erythema, and scarring, granuloma formation, hyper- and hypopigmentation, infection, abscess formation, paraesthesia (if the nerve structure was involved during the infiltration procedure. Although these adverse reactions are generally transient, the use of three-dimensional facial volume restoration techniques, in which the filling material can be injected at any depth, has led to the onset of more serious complications. Among these, vascular, rare but serious and often irreversible, are caused by infiltration of the material into the vessel lumen with consequent occlusion of the same.

The classification of filler complications can be based on the severity of the lesions (mild, moderate or severe); on the triggering cause of the complication itself (ischemic and non-ischemic complications); or the time elapsed between infiltration and onset (early or late) [23]. Rohrich et al. [24] proposed in his work a classification based on the time elapsed between the infiltrative event and the time of onset of symptoms since these time intervals correlate well with the potential underlying etiology, therefore going to divide the complications into early, late and delayed, depending on whether approximately less than 14 have elapsed, from 14 days to 1 year and more than 1 year respectively. In general, it is possible to highlight the complications with immediate onset, represented by bruising/bruising; swelling and edema; erythema; infections; herpetic outbreak; lumps and bumps; dysesthesia, paraesthesia and anesthesia; and late/late onset complications, represented by bruising; edema; skin discoloration; infection; nodules and tissue necrosis [25].

Knowledge of facial anatomy and its many variables is of paramount importance and serves as a basis for avoiding disastrous

complications [26].

The position of the needle tip or cannula determines the precise location of the product inoculum. This volume of infiltrated product can, if placed in the wrong area, be responsible for a vascular occlusion. It is therefore of fundamental importance to clearly and carefully understand the depths of the various vascular-nerve structures in order to highlight potential areas of danger [25]. Aesthetic doctors must therefore have full knowledge and mastery of the different facial districts and the different treatment sites [27].

Facial injection anatomy training is specific to non-surgical syringe therapy and is highly recommended for optimal results and avoids complications.

Knowledge of optimal placement and depth of injection is critical to the aesthetic success of dermal fillers. An improperly superficial placement can lead to negative effects such as surface irregularities and the Tyndall effect [28].

The hallmarks of the sage injection technique include a slow injection rate with the release of small boluses of material with minimal pressure. Still controversial is the usefulness of aspirating before injecting in order to evaluate the possible intravasal position (especially in high-risk areas), compared to the constant movement of the needle tip. In any case, it is preferable to inject small quantities of product, 0.1 to 0.2 cc, continuously monitoring the color of the overlying and surrounding skin [29]. The rapid injection rate, large deposits of high-density products or techniques such as the aggressive fan, induces greater contusion and the occurrence of delayed inflammatory reactions [3].

The most dangerous complication is the vascular damage that could be a venous or an arterial one. The intra-venous infiltration present itself with livido, lack of significant pain and the treatment is represented by heat, massage, oral prednisone, and injection of hyaluronidase if HA. The operator has to be aware of anatomy danger zones, consider injection with cannulas, aspiration before injection, slow retrograde injections, and avoid bolus injections greater than 0.1 mL.

Arterial embolization is most commonly anterograde resulting in occlusion of an artery resulting in a zone of ischemia localized distal to the injection site.

In case of arterial damage, it could be anterograde in which the patient refers pain, blanching distal to site of injection and which treatment is heat, massage, aspirin, hyaluronidase, oxygen infusion cream, hyperbaric oxygen. To prevent this complication is important to be aware of anatomy danger zones, consider injection with cannulas, aspiration before injection, slow retrograde injections, and avoid bolus injections greater than 0.1 mL. Retrograde vascular damage is caused by a flow of the filler against the direction of arterial pressure, and then retrogrades, towards an arterial bifurcation followed by an antegrade flow through the branch artery. In these cases, Freudenthal-Nicolau syndrome or embolism cutis medicamentosa occurs.

The retrograde injury, that normally follows the anterograde one, presents with dizziness, blindness, cerebrovascular accident, pain. In this case the treatment is heat, massage, acetylsalicylic acid (aspirin), hyaluronidase, and hyperbaric oxygen. To prevent this disadvantage the measures are the same of the other complications.

In-depth knowledge of vascular anatomy is essential to prevent vascular complications. In addition to a good knowledge of anatomy, it becomes of fundamental importance to consider and therefore know that there can be numerous congenital or iatrogenic anatomical variants. In patients after surgery, for example, the onset of altered anatomical connections is frequent; it is possible that there are anatomical variants correlated with the development of some blood vessels or in case of malformations; evaluate and know the anastomotic flows with particular attention to the nasal, perioral and periorbital region, which could spread the filler from one area to another [30].

The most fearful vascular complications are persistent skin necrosis, ophthalmoplegia, permanent unilateral or bilateral vision loss and stroke.

The skin necrosis symptoms are pain, redness of the skin, swelling, blisters, fluid collection, skin discoloration and numbness. It is caused by a sudden and important reduction in the blood supply to the cells resulting in their death. Ocular and cerebral embolism occurs when the injected material causes occlusion of the distal and proximal retinal and ophthalmic arteries. Symptoms are characteristic and are characterized by sudden and excruciating pain, persistent blindness and further tissue necrosis. In addition to damage from intravascular infiltration, vascular occlusion can occur due to compression by the bolus of material on the vessel wall.

In most cases, blindness is the main consequence of the vascular complication, but blindness and skin necrosis can occur simultaneously.

In this paper we describe a particular vascular complication that occurs after nasojugal fold infiltration. Analyzing the course of vascular damage, both retrograde and antegrade damage is appreciated, probably as a result of the involvement of the facial vessels.

Fortunately, the timely treatment of the vascular damage avoided the onset of necrosis of the involved regions with particular attention to the right upper lip and the tip of the nose.

Conclusion

Dermal fillers are increasingly used in clinical practice as a volumetric and restorative treatment of the soft tissues of the face, décolleté and hands. Obviously, the exponential increase in the use of these substances, although safe, has led to an increase in reports of associated complications. Although most complications are mild and transient, serious and long-lasting complications have been observed [12]. Knowledge of facial anatomy and its many variables is of paramount importance and serves as a basis for avoiding disastrous complications [26].

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Compliance with Ethical Standards

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.

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