Etiology, Prevention, and Management of Infectious Complications of Dermal Fillers

Ryan D. Wagner, BS[1] Abdulla Fakhro, MD[1] Joshua A. Cox, MD[1] Shayan A. Izaddoost, MD, PhD[1]

[1] Division of Plastic and Reconstructive Surgery, Baylor College of Medicine, Houston, Texas

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Address for correspondence Shayan A. Izaddoost, MD, PhD, Department of Surgery, Baylor College of Medicine, 1977 Butler Blvd., Suite E6.100, Houston, TX 77030 (e-mail: shayani@bcm.edu).

Abstract

The demand for aesthetic augmentation with soft tissue fillers has greatly increased in recent years and has led to an expansion in the number of products available. Unfortunately, an increase in adverse events has followed. These can be categorized into early, late, and delayed. Early infectious complications generally present as a localized skin infection, cellulitis, or abscess. Fillers can also serve as a focus for chronic infection, which is associated with the development of foreign body granulomas, a late complication. Bacterial colonization and indolent infections of the filler site can lead to biofilms that are extremely difficult to treat. Therefore, it is important to focus on prevention through eliciting a thorough patient history including an injection history, practicing sterile technique, and minimizing tissue trauma. Looking forward, much can be done to curtail complication rates. Early teaching and training, a central recording registry for complications, and a standardized filler passport for patients are suggested.

Keywords
- fillers
- infectious complications
- foreign body granuloma
- biofilm

The field of aesthetic surgery has experienced an immense expansion in the products available and the demand for soft tissue fillers. Their use has increased among aesthetic surgeons based on their rejuvenating and aesthetically enhancing properties previously only achievable by surgery.[1,2] Compared with conventional surgery, dermal fillers are more affordable and require limited-to-no recovery time after injection. According to the American Society for Aesthetic Plastic Surgery (ASAPS) Cosmetic National Data Bank, approximately 1.7 million dermal filler treatments were performed in 2014. This was second only to botulinum toxin injections in terms of the number of nonsurgical aesthetic procedures.[3]

Soft tissue fillers are indicated for the restoration of youthful semblance through the replacement of lost tissue volume and the filling and effacement of coarse wrinkles. They vary widely in their specific properties, associated risks, and injection requirements. A thorough patient history paired with a comprehensive understanding by the practitioner is essential in the avoidance of technical errors and adverse events. With increased advertising and subsequent rise in public awareness, there has been a steady increase in the use as well as the complications associated with dermal fillers.[4] In this article, we outline the range of adverse events related to dermal fillers, review preventative measures, and suggest a management approach with a special focus on late complications.

Filler Classification

Today, there are a variety of injectable soft tissue fillers available for clinical use with over 160 products belonging to $>$ 50 companies on the market. Factors such as defect type and location, preferred duration of effect, and clinician expertise with specific agents determine the most appropriate choice of agent. These fillers can be categorized into resorbable (biodegradeable), nonresorbable (permanent), and viable autologous fat.[5,6] Resorbable fillers include hyaluronic acid (HA), collagen, calcium hydroxylapatite, and poly-L-lactic acid with HA-based fillers being the most common injectable agents used today.[6,7] Common permanent fillers include polymethylmethacrylate (PMMA) microspheres, hydrogel polymers, and silicone injections. Because most patients are satisfied with temporary filler use, the decision to pursue permanent fillers must be considered carefully.

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Adverse Events

Patients should always be counseled prior to treatment on the risks, alternatives, and necessary postprocedural care. Adverse events are often categorized based on time of onset following injection. Rohrich et al described complications as early (< 14 days), late (14 days–1 year), and delayed (> 1 year).[2,8] Of note, it is important to distinguish adverse events from poor aesthetic outcomes due to technical error. Common early complications include injection-associated discomfort, bruising, edema, itching, and erythema. There is a tendency for more discomfort when the injectant is highly viscous or a thicker needle is used.[9] Bruising may develop at the time of injection; however, it is usually self-limiting and resolves within a week.[10] Posttraumatic edema frequently occurs after injection; edema can more rarely result from an antibody-mediated immune response to the foreign material.[11] Severe early complications are related to nerve damage or vascular occlusion. Nerve damage from direct trauma or compression can lead to paresthesias or dysesthesias with most injuries being reversible. Vascular occlusion from filler injection directly into a vessel or local edema can quickly cause visual impairment if the retinal artery is involved, or necrosis in tissues supplied largely by a single artery.

The most common late complication of all dermal fillers is foreign body granuloma formation. They present clinically as erythematous nodules or papules 6 to 24 months after a prior filler injection.[8,10] It is important to distinguish granulomas from the noninflammatory lumps and bumps that form soon after injection due to poor technique or overcorrection.[8,11] Granulomas represent a confined chronic inflammatory response and function to isolate the foreign filler material. The origin of the inflammatory response has in the past been attributed to an immune hypersensitivity reaction; however, increasing evidence is showing that many of these granulomas are associated with chronic infection and biofilm formation.[2,12–14] Other notable late complications include persistent discoloration, hypertrophic scarring, and delayed hypersensitivity reactions causing erythema and edema.[11,15]

Infections can occur at any time after the procedure. Infectious agents can be introduced through direct inoculation during the initial injection or through the hematologic spread of a systemic infection. Infection can present as a localized skin infection, a deeper cellulitis, or an abscess. The filler can also serve as a focus for bacterial colonization and later contribute to the formation of granulomas.[11,12,16] It is these colonization events and indolent infections that are thought to function as the source for biofilm formation. Biofilms are composed of heterogeneous and sessile bacterial colonies supported by a glycocalyx. They can become activated through a variety of avenues. Once active, biofilms can cause acute purulent infections and sepsis or chronic inflammation with a subsequent granulomatous response. Biofilms are less susceptible to the host's immune system, and display antibiotic resistance.[2,8,12,17] They are very difficult to treat and can require antibiotic concentration over 32 times that necessary for free-floating bacteria. Efforts need to be directed toward prevention.[12,18]

Prevention

Although the risk of complications with the injection of fillers can never be eliminated, there are steps that practicing surgeons should take to minimize their occurrence. A thorough patient history is the first step in the evaluation of any patient for a filler procedure. A tendency toward keloid or hypertrophic scaring should be documented, as there is a potential correlation with granuloma formation.[10] A history of infection, bleeding diathesis, and immunocompromised conditions should also be elicited.[8] Most importantly, the patient's previous injection history should also be recorded in detail.

In the presence of a foreign body such as filler, the bacterial load sufficient to cause clinical infection is drastically reduced.[16,19] Therefore, when preparing for filler injections, special care should be taken to follow sterile techniques. All make-up should be removed and the area should be thoroughly cleaned before and after the procedure. Chlorhexidine gluconate has been recommended as a cleansing agent in the literature.[8,20] Patients with a history of oral herpes simplex should be pretreated with acyclovir or valacyclovir as filler injection, especially in the area in the lips or nose, can reactivate the viral infection.[10,11] Injection into an active acne lesion or area of skin infection should be avoided.[8]

Surgeons should also aim to optimize their injection technique to reduce contamination and poor aesthetic outcomes from inappropriate use. Smaller gauge needles reduce trauma and the potential introduction of bacteria.[8] Alternatively, a cannula could be used to minimize the number of individual skin punctures.[20] The stacking of fillers should be avoided when possible to avoid contamination of the previous filler site. Filler stacking and large volume filler injection has also been associated with an increased inflammatory response.[8,21] Injection of fillers into the correct dermal–subdermal plane is essential to avoid technical errors such as superficial granules, ridges in the dermis, and persistent redness. The gray of the needle should not be visible under the skin as this indicates an inappropriately superficial injection plane. An exception would be in the treatment of acne scars.[10] Meticulous attention to anatomy is required for correct filler placement and to avoid vascular occlusion. The depth and course of the named facial arteries should be considered before injection, with particular attention paid to those areas supplied by a single artery.[16]

Management

In this section we focus mainly on the treatment of late and delayed complications of fillers. The initial step in management is determining the type of filler used and if the nodule or foreign body granuloma is of infectious origin. Ultrasonic imaging can be used to detect unreported materials, the location of fillers, and the surrounding anatomy.[20] If HA was used, then hyaluronidase can be used as a form of antidote. If the mass is fluctuant, then it should be treated as an abscess. Recommended treatment includes needle drainage, cultures, and antibiotic therapy. Both aerobic and anaerobic cultures should be properly obtained and

monitored for 2 to 3 weeks. Extended monitoring is necessary, as atypical organisms may take longer to culture. Antibiotic therapy should be initiated with two drugs such as a macrolide and a quinolone until culture susceptibility results return.[8,20] Of note, care should be taken not to use hyaluronidase in the setting of cellulitis as it can extend the boundaries of the infection.[16]

Although there is not a consensus on the underlying cause of foreign-body granuloma formation after filler injection, substantial evidence has pointed toward an infectious cause. A trial of empiric antibiotics similar to those outlined above is therefore warranted with the development of late filler nodules. If antibiotics fail to demonstrate improvement, then a noninfectious etiology or biofilm should be considered. High-dose steroids injected directly into the nodule should then be utilized. Because a high dose is required to reduce recurrence, patients should be informed about the risk for steroid atrophy. 5-Fluorouracil can be used in combination with intralesional steroids to enhance the anti-inflammatory and immunomodulatory effects.[11,16] Excision of the nodule should be reserved as the last management option.

Looking Forward

Dermal filler injections are the second most frequently performed nonsurgical aesthetic procedure; the numbers should continue to grow as public awareness increases and more fillers are introduced to the market.[3] However, much can be done to decrease poor aesthetic outcomes from technical error and to better understand the causes of and optimal treatments for complications. Inappropriate use can largely be curtailed through early teaching and training with injection classes. Continued learning in anatomy through coursework and cadaveric dissections is also important.[16]

Evidence regarding filler complications is largely anecdotal or retrospective based on smaller case series. Case series and reports can identify complications associated with specific products or patient characteristics, but do not provide enough information to accurately estimate the size of the risk.[16] Compounding this lack of data is a reluctance to report from some physicians.[8,16] However, when complications are published, rates often differ from those published by manufacturers for the same product.[10]

It is clear that there is a need for standardized recoding of complications. A centralized government-enforced registry should be created to track filler complications. This would not only help to identify and discourage inappropriately trained professionals, but also help to fill the gap in data on late complications.[8,10] In addition, a standardized filler passport should be mandated for manufacturers and patients. This passport would help surgeons to plan procedures on patients with previous injections and provide valuable information for the treatment of complications.[8]

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