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Abscess Formation as a Complication of Injectable Fillers

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Abstract

Importance: Dermal filler use in aesthetic clinics, are now widespread and although complications are rare, the formation of granulomas or abscesses and subsequent defects can be devastating to the patient. Design: Retrospective chart review of 4 cases over the period of 10 years, from 2002-2012 were examined from The Nasal and Facial Plastic Cosmetic Surgery Institute. Results: Four female patients experienced delayed onset reactions (>2 weeks) with sterile abscess formation and eventual resolution with serial drainage and macrolide antibiotics were observed over a prolonged period until resolution occurred. Only 1 case identified an organism (streptococci) on culture after 8 months, however, the initial culture still showed only sterile abscess. All 4 had a history of previous injectable fillers, 2 patients had evidence of pre existing autoimmune disorders. Conclusions and Relevance: Since the treatment of all of these patients, there is new evidence that infections may present as delayed onset sterile abscesses due to biofilm formation. Fluorescent *in situ* hybridization (FISH) test has shown to be as specific in identifying responsible organisms in biofilm infections as simple culture but is more sensitive; thus preventing misdiagnosis of sterile abscess. Counter intuitively steroid injection may promote abscesses, while hyaluronidase may be useful.

Keywords

Injectable Filler, Abscess, Biofilm, FISH Test, Hyaluronidase

1. Introduction

Over a period of 28 years using injectable fillers, at the "The Nasal and Facial Plastic Cosmetic Surgery Institute", it was noted that despite the majority of patients achieving good to excellent results, during the last 10

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years, 4 patients underwent a long and protracted course of abscess formation which was difficult to treat. Of note many patients had received other injectable fillers prior to attending the clinic including Hyaluronic acid, Polyacrylamide and others. This case study therefore sought to obtain any pattern in these cases which may flag up at risk individuals and also to review current literature to identify optimal management of such complications when they occur.

2. Patients and Methods

Retrospective chart review of all cases performed from 2002-2012 (total of 1559) flagged four cases (0.3%) affected by abscess formation. These charts were reviewed for analysis, with regard to predisposing medical conditions, filler history, treatment given and response.

Case 1: A 52-year-old female was injected on February 2011 with Hyaluronic acid gel filler to the lower lip. An inflammatory reaction ensued. After 5 days hyaluronidase enzyme was injected to break down the filler. After 7 days a lower lip abscess had formed and was incised and drained. Over the next 6 months, incision and drainage of the same perioral site was required a further four times, as well as the use of the antibiotic clindamycin. Initial cultures were sterile but 8 months later, streptococci were cultured although the abscess had nearly settled. There was no recurrence at 12 month review. Of note this patient was taking long term low dose steroid orally for Systemic Lupus Erythrematosis and had previous fillers injected in the perioral area, with Hyaluronic acid in 2008 and Polyacrylamide in 2009 and 2010. (Patient did not consent to the use of pictures. See **Figure 1** for artist rendition).

Case 2: A 56-year-old female was injected in 2009 with Hyaluronic acid gel to the nasolabial fold. Shortly afterwards the nasolabial fold became inflamed requiring the antibiotic Clindamycin. The next month an abscess had formed at the left angle of the mouth and required incision and drainage with injection of steroid and intravenous Clindamycin for 7 days. All cultures were sterile. No further recurrence was noted. Of note the patient was a smoker with pre-existing contact and solar dermatitis and was injected with Artecoll (Polymethyl methacrylate suspended in collagen) to the nasolabial fold, corner of the mouth and lateral mental groove in September 2002. 4 years later the same substance was injected in the same area without event (see **Figure 2**).

Case 3: A 39 year old female was injected with Hyaluronic acid gel to the upper and lower lips in January 2011. One month later she developed upper and lower lip abscesses, which were incised and drained. Two months

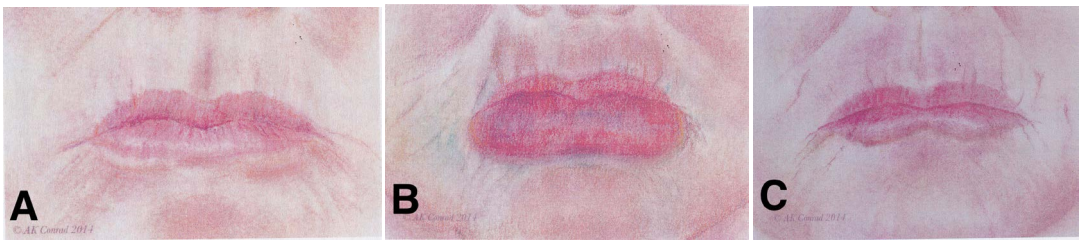

Figure 1. Hyaluronic acid gel injection to lower lip. (A) Pre injection; (B) Abscess formation; (C) Resolution (post multiple Incision & Drainages and antibiotics).

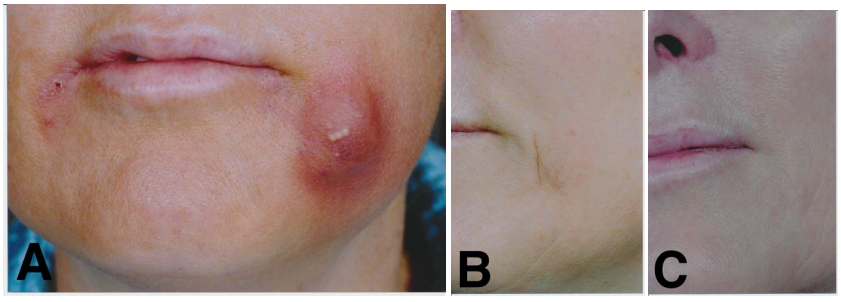

Figure 2. Hyaluronic acid gel injection to nasolabial fold. (A) Abscess formation; (B) Resolution of abscess following IV Clindamycin and Incision & Drainage; (C) Re-injection after 4 years.

later these abscesses recurred and were again incised and drained, with no further treatment required. All blood tests were normal and all cultures were sterile. She had a history of scleroderma and Reynaud's phenomenon, later confirmed as part of the CREST syndrome (Calcinosis, Reynauds, Esophageal dysmotility, Sclerodactyly and Telangectasia). She also had prior injection with polyacrylamide gel in 2009 to the nasolabial folds (See **Figure 3**).

Case 4: A 58-year-old female injected with Hyaluronic acid gel to the pre-jowl sulcus and nasolabial fold in April 2009. After 8 months, abscesses formed in the same two areas. Pus aspirated was sterile. The areas drained pus intermittently over the next month. The areas were injected with steroid three times over the next 6 months. Four months later the inflammation had settled and therefore the patient underwent geometric broken line scar revision to the healed areas. The scars were then resurfaced with CO_2 LASER 6 weeks later. CT scanning showed a ruptured cyst wall which was removed using a separate incision, well camouflaged under the rim of the mandible. A week later the depression resulting from the subcutaneous necrosis was reconstructed with a Gortex implant with a further Gortex implant added 9 months later with subsequent further CO_2 LASER resurfacing of the scars. The patient had no medical history of note other than injection of Artecoll to the nasolabial fold in December 2002 (See **Figure 4**).

3. Discussion

This series brings up three main problems in the treatment and prediction of abscess formation as a complication of dermal fillers:-

The first is identification of the causative pathogen, within the so called sterile abscess.

The second is, the appropriate treatment of delayed onset abscess formation.

The final issue is that of risk identification within the population of patients receiving dermal filler injections.

The first dilemma is that biofilms which appear to be present in these filler abscesses seem to demonstrate a dormant state and this may allow the bacteria to temporarily cease replication in foreign environments such as culture media [1]. This may be potentially addressed by PNA FISH test, which has been used to identify bacteria in biofilms as the need for replication in culture media is bypassed. PNA FISH test stands for Peptide Nucleic Acid Fluorescent In Situ Hybridization, which is a cytogenetic technique. It is more commonly used to identify genetic anomalies in syndromes and cancers, it can also be used to identify pathogenic organisms. This is done by introducing fluorescent probes that bind to DNA or RNA sequences. Artificial chromosome sequences of about 1000 oligonucleotide pairs are introduced to multiplying clonal populations of bacteria and are then stored in laboratories to allow probe manufacture. These probes undergo hybridization where they are tagged with a

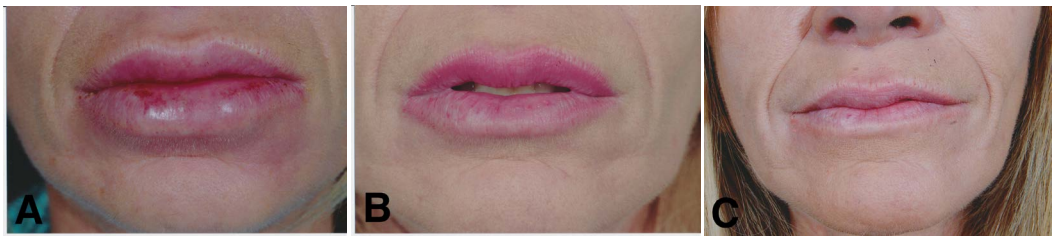

Figure 3. Hyaluronic acid gel injection to upper and lower lips. (A) Abscess formation; (B) Following incision & drainage; (C) 1 year follow-up.

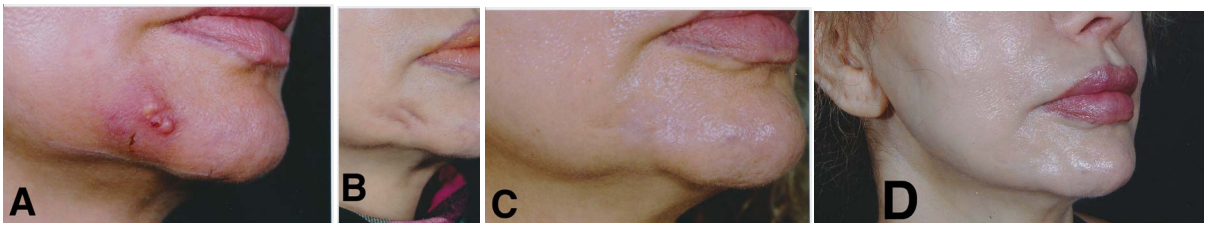

Figure 4. Hyaluronic acid gel injection to pre-jowl sulcus. (A) Abscess formation; (B) Following incision & drainage and subsequent steroid injections; (C) Following scar revision and CO_2 laser resurfacing; (D) Following 2 Gortex implants and CO_2 laser resurfacing.

fluorophore, which acts as a dye to identify their presence under fluorescent microscopy. This technique allows the use of multiple genetic probes with more than one fluorescent dye, which in turn allows identification of multiple bacteria simultaneously; useful in identifying the mixed colonies of bacteria often found in biofilms. However before the assay can take place, and the probe is bound to its target, the specimen must be permeable to allow target accessibility [2]. This test has been shown to be highly sensitive and specific [3]. To aid in this process we suggest that all target lesions are treated with hyaluronidase prior to obtaining a sample, to break up the protective hyaluronic acid matrix in the biofilm manufactured by the bacteria. The same method of breaking up the hyaluronic acid matrix with hyaluronidase is used to facilitate antibiotic therapy. Fish test has the advantage that in addition to being as highly specific as ordinary culture, it is much more sensitive with respect to identifying bacteria in biofilms; with one study of 44 cases showing FISH test identifying 58% of cases compared to none identified with two different culture methods [4]. Another study also showed FISH test to be up to 3 days faster in producing results [5]. Given that all biofilms demonstrate this matrix; detection of it may help to decide which samples obtained require further analysis with PNA FISH testing [6]. In addition application of the new slippery liquid-infused porous surfaces (SLIPS) technology to syringes may be potentially preventative of biofilm formation, by preventing adherence to the syringe surface for the assembly of a biofilm [7]-[9]. Proposal of the use of such a SLIPS surface to coat the inner surface of the filler syringes supposes that the combination of the untreated syringe surface with its hyaluronic acid gel contents creates the ideal conditions for biofilm formation if contamination occurred. Further research would be required to establish this hypothesis.

Secondly the treatment of, these presumed sterile abscesses, is particularly difficult and often follows a protracted and remitting course. It appears though that the initial presentation is similar to a hypersensitivity reaction, because the hydrogel fillers that may have become contaminated with bacteria can cause a foreign body response mimicking an allergic reaction. The remitting course is now thought to be due to the nature of biofilms contained within the abscesses. The biofilm exhibits a sub population of “persister cells” during the mid exponential growth phase which were initially thought to be due to quorum sensing signaling molecules (a paracrine messaging system).The tolerance of these cells to antibiotics is thought to be due to chaperone molecules, produced by the biofilm, which bind simultaneously with the antibiotic preventing them from attacking the bacteria. These cells remain dormant within the biofilm and begin to replicate after the antibiotic course has finished [10]. In addition the biofilm secretes an extracellular matrix which may act as an initial barrier to antibiotic penetration [1]. For this reason an algorithm was proposed by Dayan *et al*. which included initial injection of the area with hyaluronidase to break up the biofilm thus making it susceptible to broad spectrum antibiotics, such as fluoroquinolones or macrolides, which are then given in high doses intravenously followed by a prolonged course of oral administration. The use of anti-inflammatory agents, especially steroids which mask symptoms and favor bacterial assembly into a biofilm, is contraindicated. If the abscess reforms despite drainage, then intra-lesion injection with 5 fluoro-uracil (to retard DNA synthesis and RNA activity in both gram positive and negative bacteria), have been shown to be useful in the treatment of biofilms. This can be repeated in 4 weeks and if that fails intra-lesion LASER lysis prior to consideration of incision and drainage with antibiotic washout or final excision of the granuloma or abscess wall should be considered [11].

Our final consideration is that of risk factors which may increase the likelihood of this rare complication. First of all 3 of these patients had a predisposition to inflammation which may have aided abscess formation. These conditions were Lupus, Reynauds phenomenon with co-existing scleroderma now identified as part of CREST syndrome and another patient had solar and contact dermatitis. The relevance of these inflammatory disorders is that they may facilitate infective processes, by allowing bacteria to become deep seated within the interstitial tissue. Notably, two patients had previously received polyacrylamide prior to hyaluronic acid injection. Within the manufacturers literature it is commented that the acrylic hydrogel is biodegradable over a 2 to 5 year period and that its effect on indigenous collagen is by way of its positive charge{procytechcom:tu}. The first statement regarding how long the filler is present, would explain why the reaction could be so late (as in case 3), if the bacteria in the filler is effectively temporarily mummified. The second comment that the filler is positively charged, is of significance as two separate studies showed that positive charge attracts giant cells and may promote granuloma formation [12]. Indeed the second issue is that negatively charged bacteria would be attracted to this positive charge associated with the acrylic hydrogel [13].

4. Conclusion

Delayed onset abscess formation is most likely due to infection associated with the formation of a biofilm. Cul-

ture is best carried out by PNA FISH test. We postulate that the use of hyaluronidase prior to obtaining samples for culture by any method may increase the sensitivity of the said test. The treatment algorithm described, by Dayan *et al*. appears to be helpful once this complication has occurred. Finally previous use of polyacrylamide gel (in the same anatomical site) or pre-existing inflammatory disorders are relative contraindications to the use of Hyaluronic acid fillers. In the future, there may be a role for analysis of the exopolysaccharide matrix to determine the presence of a biofilm and possibly identify the offending organism within it.

Conflict of Interests

None declared.

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