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Beauty is only mucosa deep- A retrospective analysis of oral lumps and bumps caused by cosmetic fillers

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ABSTRACT

Introduction-Injection of dermal fillers into orofacial tissues is becoming increasingly popular for cosmetic purposes, in particular for lip augmentation. Both natural and synthetic filler materials are available, producing a spectrum of clinical and histological appearances.

Aims-The aim of this study was to review the clinicopathological characteristics of dermal filler cases from 2006-2016 reported at a specialist Oral Pathology unit.

Methods-An archival search of the Pathology database was performed to retrieve cases reported as being consistent with cosmetic fillers.

Results- 10 cases of orofacial cosmetic fillers were retrieved. 100% of these cases were from female patients and the mean age of presentation was 47.6 years (range 24-68 years). The lips were the most frequently involved site (80%, n=8). The majority of provisional diagnoses were related to salivary gland disease including neoplasms (30%, n=3), cysts (20%, n=2) or inflammatory disease (10%, n=1). Only two cases (20%) were clinically thought to be related to previous cosmetic injections. A variety of filler materials were seen, including collagen, hydroxyapatite and silicone, however hyaluronic acid-based materials were the most common (50%, n=5).

Conclusions- Complications of cosmetic dermal fillers are becoming frequently more common and should be considered within a differential diagnosis for unusual orofacial swellings.

In brief points:

- Cosmetic fillers can migrate away from the original site of injection and cause unusual and varied clinical presentations resembling other oral lesions
- All filler material types, including natural material, were associated with host inflammatory responses
- Cosmetic fillers should be included in a differential diagnosis of peri-oral swellings

Introduction

Injection of dermal fillers into orofacial tissues is becoming increasingly popular, in particular for lip augmentation (1, 2). Fillers are injected into the dermis to increase the bulk of soft tissue to improve the cosmetic appearance. Filler materials can be natural or synthetic, with the latter producing lasting results. More frequently, many dentists are providing this service or are seeing patients with cosmetic filler related oral lesions highlighting that they should be able to recognize such lesions and be aware of the adverse effects of fillers to avoid this diagnostic pitfall. The management of filler related lesions is often difficult and protracted (3-5) especially for permanent fillers such as silicones which may never resolve (6).

A wide range of cosmetic filler related oral adverse effects can be seen including short term and reversible changes, such as oedema and erythema, or long term complications, such as nodules or granulomas. In some instances these effects can be life changing i.e. blindness (4, 6-8). Material migration is quite common, resulting in nodularity of the soft tissues away from the site of injection therefore the association is not always clear in the first instance (1). Moreover, the reaction may occur months to years after filler injection even for the temporary fillers such as hyaluronic acid (HA) making it difficult to establish this relationship (9, 10).

The frequency of cosmetic filler related adverse effects is difficult to establish as there is variable reporting of the use of fillers and related complications (4). Also, dermal fillers can be administered by a wide range of clinical and non-clinical individuals in the UK; the latter being unregulated and with limited training.

Whilst the majority of materials are considered inert, inflammation and foreign body giant cell reactions can occur for all currently used filler materials producing a spectrum of clinical and histological appearances. One of the most common long term adverse effects is development of a nodule or granuloma, (11) with an estimated incidence of 0.02-2.8% (4). Here, we present a case series of cosmetic filler related lesions reported within a specialist Oral and Maxillofacial Pathology department over a 10-year period in a tertiary care setting. Interestingly, almost all of these patients were referred to the hospital with an unrelated clinical diagnosis and no suspicion of a filler induced response.

Materials and Methods

A search of the pathology database, School of Clinical Dentistry, Sheffield, was conducted to identify cases with cosmetic filler materials over a 10-year period between January 2006 to December 2016.

For each case identified, the patient's gender and age were recorded. Clinical presentation and provisional diagnosis was documented and, if available, clinical photographs were reviewed. Additionally, histological features, including the type of filler material and the presence of a host response was assessed. Clinicopathological correlation of clinical appearance, filler type and the presence of an inflammatory reaction was carried out.

Results

A total of 10 cases involving cosmetic filler materials were identified (Table 1). All patients were female, and ranged over an age range of 24 to 68 years (Table 1.). The mean age was 48 years (range 24-68 years). 80% (n=8) of cases affected the lips, with the upper and lower lips equally affected (Figure 1). Other sites affected included the buccal mucosa and pre-auricular/parotid region of the face.

The clinical appearance was extremely variable with both discrete masses and generalised swelling being reported. A well-demarcated nodule was seen in the half of cases (50%, n=5, Figure 1A) and multiple nodules were described in two cases (20%). 30% of lesions presented as diffuse labial swelling (Figure 1B). Where assessed, the lesions were described as mobile, slow-growing and yellow coloured.

60% of pathology forms contained multiple provisional diagnoses, spanning reactive and immune reactions as well as both benign and malignant neoplasms (Figure 4). The majority of diagnoses were related to salivary gland lesions (41%, n=7). In just three cases (30%), the presence of dermal filler was included in the clinical history or provisional diagnosis.

In keeping with the variable clinical appearances, a variety of different cosmetic filler including natural, synthetic and combination-type materials were seen during histopathological examination (Figure 2). The most frequent finding was of filler material containing hyaluronic acid based products (50%, n=5). In six cases (60%), a host reaction was seen, including foreign-body type giant cell reaction (50%, n=5) and non-specific chronic inflammation (10%, n=1). 40% of cases showed no host response to the injected material.

All types of cosmetic filler materials were found to cause a host response, however, this was greatest in combination i.e. hyaluronic acid with acrylic (100%) and synthetic i.e. Poly-L lactate, silicone (67%) type materials (Table 2).

Discussion

Increasing use of a variety of natural and synthetic cosmetic fillers, particularly at perioral and maxillofacial sites, can lead to unusual clinical and histological presentation, particularly if a history of dermal filler use is not known. Salivary gland pathology is most frequently considered, including neoplastic disease, which can lead to undue patient concern.

There is a wide variety of adverse effects ranging from self-limiting immediate manifestations such as erythema, oedema, ecchymosis or more serious immediate complications such as occlusion of vessels potentially leading to skin necrosis or blindness (4, 8, 11). It is likely that most of these post-filler manifestation will not undergo a biopsy as the clinical course might be obvious. However, there are many delayed effects such as nodules, granuloma formation, low grade infections and migration of filler material (4, 7, 8). These often present late, may mimic other diagnoses (including neoplasms) and often the patient will not consider them related to fillers injected weeks, months or years ago.

The overwhelming majority of cases occur in women as was found in this case series and others (10, 12). One review reported two cases in males compared to 104 in females (12). The mean age is generally in the 5^{th} or 6^{th} decade. Our cohort had a mean age of 48 years, which is slightly younger than other studies that have reported a mean age of 53 years (12) and 58 years (10).

There is significant variance in the clinical appearance of such reactions predominantly dictated by the type of the complication. Early adverse effects such as oedema and erythema that present immediately are usually self-limiting and are of little concern (4). More concerning immediate features include blanching or red/bluish discoloration of the skin and pain following injection. This may indicate vascular occlusion or compromise which may lead to necrosis of skin or blindness (for peri-orbital injections) requires immediate clinical attention (4).

The most common late complications are that of nodules or foreign body granulomas (11). Clinical presentations tend to be of multiple or singular nodules, oedema, generalised swellings or local indurations (2, 6, 9, 10, 12). They may be either at the injection site or somewhat distant having migrated (2). Our cases showed a similar variety of presentations as previously described in the literature. It is worthwhile considering infections and abscesses in the differential diagnosis however bilateral nodules at multiple sites (with a clinical history of a filler injection) are likely to be indicative of a foreign body response (3, 4). Infections may present either early or late, potentially months after the filler was used which further complicates diagnosis (4).

There are many factors which determine the likelihood of dermal filler complications. The first is the experience, training and techniques of the individual administering the filler. Awareness and understanding of the facial anatomy, planes and structures and a safe, steady and aseptic technique can significantly reduce the likelihood of complications. The type of the filler used is also important. Temporary filler materials such as hyaluronic acid gels have a minimal foreign body response (3, 13) with a lower chance of significant adverse effects and can be managed more easily with hyaluronidase (11). Permanent fillers, such as PMMA and especially silicones, are much more likely to elicit a long lasting and strong foreign body reaction (3, 13, 14). Silicone gels may also leave permanent scars and disfigurement which are often resistant to treatment (4, 6). Using a combination of filler types does not appear to increases the risk of an adverse reaction although there is a greater likelihood of a stronger immune reaction (14).

There is some evidence to suggest that some reactions may be due to bacterial biofilms around the gel particles (13). It is therefore important to ensure sterile, aseptic technique, avoid injections during active infections and thorough cleaning of the skin before injection (3, 4).

As mentioned earlier, a detailed knowledge of the anatomy of the sites to be injected is incredibly important. Areas such as the nose, nasolabial folds and glabella are much more likely to encounter serious adverse effects such as tissue necrosis (11). Knowledge of the local vasculature can also reduce the risk of these complications. Moreover, ensuring appropriate depth of injection and avoiding large bolus injections from fine needles can help reduce the risk of vascular occlusion (4). Due to the high mobility of the lips, fillers injected here are particularly prone to migration. It is therefore recommended to avoid using large amounts of filler (4, 11) or those considered permanent or semi-permanent (11).

As would be expected, an appropriate injection technique is vital to prevent adverse effects. Techniques which tend to increase dissection of subdermal planes such as fan-like injections, rapid injection, rapid injections or injection of high volumes increase the risk of complications (14) including bruising (15). Moreover, use of a blunt canula and appropriate speed of injection can also reduce oedema, erythema and bruising (4).

Patch testing before the use dermal fillers especially with the collagen containing formulas can prevent hypersensitivity reactions (3, 4). Reactions may occur in 2-4% of cases with collagen, 0.15% for hyaluronic acid and 0.2% for PMMA (3).

The management of early adverse effects is generally straight forward. To reduce and prevent oedema and erythema, ice packs can be applied immediately after injection (4, 15). In case of persistent adverse effects, use of hyaluronidases for HA fillers and intralesional or oral steroids tends to help (4, 18). Infections can be treated with antibiotics (if systemically indicated) whereas hypersensitivity reactions usually require antihistamines or if persistent intralesional or oral steroids. If vascular occlusion is suspected, injection should be discontinued immediately followed by injection of hyaluronidase, vigorous massaging, topical nitro-glycerine paste, warm compress application, oral aspirin administration and daily monitoring of the patient. Referral for specialist input should be organised as soon as possible and if there are changes to vision an immediate referral to an ophthalmologist should be made (4, 15).

The management of late onset adverse effects such as nodules and granulomas can often be difficult and varies with the filler used. The first line of recommended treatment is local injection of corticosteroids such as betamethasone or triamcinolone acetonide sometimes with 5-fluoroucracil (3, 5, 14, 15). Depending on the fillers used, hyaluronidases or collagenases may also be used (3, 5, 15). The mechanical breakup of nodules during injection is also recommended (3, 15). Failing this, systemic treatment may be required by immunomodulatory medication or drugs used to manage other granulomatous disorders. These include; allopurinol (3), antimalarials, some antibiotics or high dose histamines (14). As a last resort other medications such as azathioprine, tacrolimus or biologic drugs like the TNF-alpha blockers may be required in a specialist setting (3, 14).

Generally, surgical options are not recommended due to the risk of potentiating complications such as infection, further migration of filler particles, new or persistent granulomas and scarring (13) however, this may be necessary if other treatment strategies fail (5). It has been recommended that both high frequency ultrasound and magnetic resonance imaging (MRI) can be used to aid diagnosis and surgical planning for filler induced complications of the lips (16, 17).

Conclusions

Complications of cosmetic dermal fillers are becoming increasingly common and should be considered within a differential diagnosis for unusual orofacial and maxillofacial swellings. Clinical presentation can be variable ranging from firm submucosal masses to diffuse swellings, therefore consideration to any perioral soft tissue mass should warrant a full clinical history, with documentation of any previous cosmetic procedures. These adverse effects can often be difficult to manage hence prevention of complications is paramount.

Declaration of interests

The authors confirm no conflict of interest.

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Table 1. List of cases with cosmetic fillers including age, gender, site, presentation and provisional diagnosis.

Case	Gender	Age	Site	Presentation	Provisional diagnosis
1	F	67	Lower lip	Multiple nodules	Plasma cell reaction
2	F	62	Upper lip	Discrete mass	Mucocele
3	F	44	Lower lip	Labial swelling	Lichen planus
4	F	68	Buccal mucosa	Multiple nodules	Sialadenitis
5	F	36	Lower lip	Slow growing lump	Salivary gland neoplasm
6	F	48	Parotid region	Discrete mass	Cosmetic filler
7	F	24	Upper lip	Labial swelling	Mucocele
8	F	43	Upper lip	Discrete mass	Benign salivary gland neoplasm
9	F	48	Lower lip	Mobile lump	Benign salivary gland neoplasm
10	F	36	Upper lip	Labial swelling	Cosmetic filler

Table 2: Summary of Histological features of cosmetic filler cases.

Case	Histological appearance	Filler material	Host reaction
1	Non-birefringent irregular particles	Hyaluronic acid and acrylic	Foreign body type
2	Non-birefringent irregular particles	Hyaluronic acid and acrylic	Foreign body type
3	Multiple small clear round spaces	Silicone	No
4	Clefts of birefringent material	Poly-L lactate	Foreign body type
5	Non-birefringent spheroids	Hydroxyapatite	Foreign body type
6	Homogenous basophilic material	Hyaluronic acid	No
7	Homogenous basophilic material	Hyaluronic acid	No
8	Homogenous basophilic material	Hyaluronic acid	No
9	Homogenous eosinophilic material	Collagen	Foreign body type
10	Multiple small clear round spaces	Silicone	Chronic inflammation