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Case report

Oral granuloma formation after injection of cosmetic filler

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ABSTRACT

The increased use of orofacial fillers in cosmetic procedures has led to new diagnostic challenges for dentists and oral pathologists. Here, we describe a case with multiple oral foreign body granulomas, which were formed after a polymethylmetacrylate injection for cosmetic purposes.

1. Introduction

In recent years the demand for cosmetic fillers to augment lips and to correct wrinkles, deep sulcus, and acne scars has increased markedly (Sanchis-Bielsa et al., 2009; Mandel et al., 2010). In this context, the ideal filler is described as easily applied, non-immunogenic, and biocompatible. It should cause no skin protrusions, evoke minimal foreign-body reactions (Lemperle et al., 2004), allow fast healing, and give long-term results. Easy removal is desirable, and toxicity is unacceptable.

In spite of their wide use all over the world, the medical literature is full of reports and discussions of complications after the use of cosmetic fillers (Lemperle et al., 2004; Christensen et al., 2005; Lemperle et al., 2006; Anastassov et al., 2008; Alijotas-Reig and Garcia-Gimenez, 2008; Lemperle et al., 2009; Alijotas-Reig et al., 2010; Lemperle et al., 2010). More recently, dental journals have carried such reports in order to help surgeons, general dentists and oral pathologists to come to a correct diagnosis (Lombardi et al., 2004; Da Costa Miguel et al., 2009; Jham et al., 2009; Sanchis-Bielsa et al., 2009; Mandel et al., 2010). Regarding this, the most reported complications in oral or facial injections are granuloma formation, asymmetry, migration, extrusion and, more rarely, allergic reactions, infection, and haematomas (Christensen et al., 2005; Lemperle et al., 2006). The literature does not support that the combination of different fillers injected in the same region can increase the risk of adverse reactions, especially in cases of biodegradable fillers (Alijotas-Reig and Garcia-Gimenez, 2011; Bachmann et al., 2011).

Non-permanent fillers, such as collagen, hyaluronic acid, dextran and polylactic acid, are metabolized enzymatically or phagocytozed. Depending on the amount of filler used, they lead to minimal histological reactions after 3–24 months. Permanent fillers, such as liquid silicon and polymethylmetacrylate (PMMA), are composed of particles with irregular surfaces that are often larger than 15 μm. They cannot be phagocytozed, and instead, they become surrounded by fibrous tissue. Permanent fillers, such as Artecoll® and ArteFill®, are made of solid microspheres (40–60 nm in diameter) of PMMA suspended in collagen (Lemperle et al., 2010).

The popularization of the use of cosmetic orofacial fillers has brought new diagnostic challenges for dentists and oral pathologists. Clinically diagnosing oral foreign body granulomas can sometimes be complex, especially when patients are unaware of the relationship between their cosmetic fillings and symptoms, or when patients deliberately withhold information related to cosmetic injections in their history (Lombardi et al., 2004). We report a case of multiple oral and perioral foreign body granulomas after PMMA injection, highlighting the difficulties in the diagnostic process.

2. Case report

The publication of the following case was approved by the Committee of Ethics in Research at the University of Taubaté.

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A 54 year old female was referred to the outpatient oral diagnostic clinic in the Department of Dentistry at the University of Taubaté, complaining of "small balls" on her face, which had appeared 1 month before the first appointment. According to the patient, the lesions were hard and mobile. Although the patient reported that the lesions were painless and did not interfere with mastication, she was annoyed by the round appearance her face had acquired (Fig. 1).

During the history the patient reported that she used paroxetine, clonazepam, and simvastatin, and that she suffered from nervous gastritis. When asked, she denied undergoing any facial aesthetic procedures. The extraoral examination revealed periorbicular and cheek swellings that were barely noticeable. On palpation, four nodules ranging from 2 to 3 cm (Fig. 2) were noticed. Intraoral examination revealed that each quadrant had one nodule covered by healthy mucosa, with an irregular surface and fibrous consistency. The differential diagnosis was difficult to establish. Based on the consistency of the lesions, neurofibromas or salivary gland neoplasms were suspected. Imaging examinations including panoramic radiograph, ultrasonic and magnetic resonance exams were performed.

The panoramic X-ray exam showed that six dental implants were present in the four quadrants. According to the patient, the implants were placed 2 years previously. Magnetic resonance imaging revealed that there were multiple well-limited, bilateral, perioral areas in the upper and lower lips. The ultrasonic examination showed hypoechoic nodules, which suggested lymphadenopathy. For further information, we performed an incisional biopsy of the left superior lip. Prior to the procedure, routine, preoperative blood tests were performed, and no abnormalities were noted. During surgery, the lesion was observed to adhere to the surrounding tissue. When cut, the lesion had a whitish surface comparable to cartilage.

Histopathological examination of the biopsy sample showed multiple round spaces with similar sizes that were near to or within multinucleate giant cells. These giant cells were distributed among connective fibrous tissue with intense lymphocytic infiltrate and epithelioid macrophages (Fig. 3). Upon lowering the condenser, round, sharply circumscribed, translucent, non-birefringent, foreign bodies were vaguely visible within the round spaces.

Based on the morphological findings, the patient was diagnosed with foreign body granulomas. The patient was asked again whether she had undergone any aesthetic facial procedures. Only at this time did she report that she had undergone facial cosmetic filling, but she did not know which product had been used. We contacted her dermatologist, who had filled the patient's nasolabial folds with 1 mL of PPMA (Artecoll, Artes Medical Inc, San Diego, CA, USA) 4 years previously.

The patient was treated with intralesional injections of triamcinolone acetonide (40 mg). After three sessions, the upper left nodule disappeared, and the other nodules were reduced in size by 50–75%. The patient discontinued the treatments, being satisfied with the results. The patient has been monitored for 20 months, and the result was stable for this period.

3. Discussion

Granulomas represent an unfortunate complication following the injection of cosmetic fillers. In literature reviews, less than 60 cases of oral and perioral granulomas have been reported after the injection of cosmetic substances (Da Costa Miguel et al., 2009; Jham et al., 2009). The pathogenesis of granuloma formation remains unknown and may be related to infections, traumatic or pharmacologic stimuli (Lemperle et al., 2009). In our case, we could not identify any triggering cause. Although the patient underwent dental implant treatments, this occurred 2 years before the nodules appeared and the authors judge that it does not represent a traumatic event that could be associated with the granulomatous reaction which presented.

Clinically, foreign body granulomas develop many months or years after implantation. At approximately the same time, all of the injected areas show mild inflammation, and nodules become visible (Lemperle et al., 2009). In the absence of information on whether a patient received cosmetic filler injections, the differential diagnosis can vary due to the nonspecific appearance of the granuloma lesions. The differential diagnoses can include cheilitis glandularis, orofacial granulomatosis, sarcoidosis, Melkersson–Rosenthal syndrome (Jham et al., 2009), salivary gland mucocele or soft tissue neoplasm (Da Costa Miguel et al., 2009). The lesions in our case had a consistency similar to neurofibromas or salivary gland pathology, which, in the absence of information on the use of cosmetic filler, brought an extra challenge for diagnosis. This was only confirmed after histopathological examination.

In our case, the adverse reaction was caused by the injection of Artecoll®. This filler is a second-generation of polymeric microsphere-based filler, which started to be used as a predecessor of ArteFill®, the third-generation and the first and only permanent filler to receive FDA approval. It consists of PMMA microspheres (40 μm in diameter), suspended in a 3.5% bovine collagen solution (Lemperle et al., 2010). The microspheres remain in the tissue after the absorption of the collagen, becoming encapsulated by connective tissue, which partly contributes to the material's bulking effect (Christensen et al., 2005). In this case report, histological examination of PMMA granulomas revealed multiple, small, round, and apparently empty structures either in the cytoplasm of multinucleate giant cells or surrounded by collagen fibres, fibroblasts, giant cells, and macrophages, as previously reported (Lombardi et al., 2004; Lemperle et al., 2009). Histopathological diagnosis of granulomas can be difficult because of the morphologic similarity of PMMA implants to fat cells. Additionally, the formation of foreign body granulomas following cosmetic filler injection is rarely mentioned in oral pathology textbooks (Lemperle et al., 2009).

The treatment of choice for this complication should be initiated as soon as possible after presentation using intralesional injections of corticoid crystals (triamcinolone, betamethasone or prednisolone). The injections can be repeated in monthly cycles until the correct dose is achieved, focussing on stopping the invasion of cells and the increased secretion of interstitial substances without leaving a scar (Lemperle and Gauthier-Hazan, 2009). Systemic

Fig. 1. Extraoral appearance of the patient. The indurations were barely perceptible. The skin's yellow hue is due to iodine antisepsis, which was performed prior to the incisional biopsy.

Fig. 2. Intraoral appearance of the patient. The nodules were located by palpation. They were covered by healthy mucosa and had a fibrous consistency.

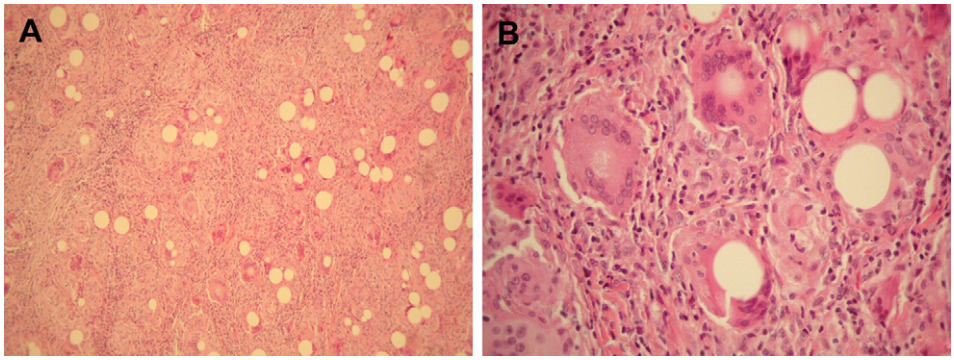

Fig. 3. Histopathological features of the incisional biopsy specimen. Multiple small round structures are observable near or within the cytoplasm of multinucleate giant cells. Additionally, epithelioid macrophages and lymphocytic infiltrate can be observed. Haematoxylin and eosin staining. A. Original magnification 100×. B. Original magnification 400×.

corticosteroids can be also used due to their ability to control granulomatous reactions (Sanchis-Bielsa et al., 2009). Based on the association of late reactions to cosmetic fillers with infections, suggesting that bacteria and viruses might be involved in this process, some authors had suggested the use of antibiotic therapy (Christensen et al., 2005), but this does not represent a consensus and should not be a mandatory treatment (Alijotas-Reig and Garcia-Gimenez, 2008; Alijotas-Reig et al., 2010; Alijotas-Reig and Garcia-Gimenez, 2011). Surgical excision should be the last option, since foreign body granulomas extend in finger-shaped growth within the surrounding tissues (Lemperle and Gauthier-Hazan, 2009).

4. Conclusion

Surgeons, dental practitioners and oral pathologists should be aware of the increased possibilities of intraoral manifestations following the use of cosmetic fillers which may become more common due to the popularity of new cosmetic procedures, as well as of the related diagnostic difficulties, especially when appropriate medical information is lacking. In order to achieve an accurate diagnosis, practitioners should ask the patient about previous cosmetic treatments.

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