

Oral foreign body reaction after migration of injected hydroxyapatite cosmetic filler: a case report

Reacción a cuerpo extraño en la cavidad oral tras la migración de hidroxiapatita infiltrada como sustancia de relleno tras un procedimiento estético: A propósito de un caso

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Abstract

Radiesse is a substance composed of calcium hydroxyapatite commonly administered as a facial filler. Numerous complications such as allergic reactions, edema, necrosis, arterial occlusion or facial paralysis have been described with its increasing use. The formation of nodules away from the injection site has rarely been described in the literature. This article describes the formation of a non-inflammatory nodule at the level of the oral mucosa years after injection of Radiesse in the nasolabial sulcus and discusses the possible causes and treatment options.

Keywords: Radiesse, Hydroxyapatite, Filler, nodule.

Resumen

Radiesse es una sustancia compuesta por hidroxiapatita cálcica que comúnmente se administra como producto de relleno facial. Se han descrito numerosas complicaciones, como reacciones alérgicas, edema, necrosis, oclusión arterial o parálisis facial, debido notablemente al aumento de su uso. La formación de nódulos que migran desde el sitio de inyección rara vez se ha descrito en la literatura. Este artículo describe la formación de un nódulo no inflamatorio a nivel de la mucosa oral años después de la inyección de Radiesse en el surco nasolabial y discute las posibles causas y opciones de tratamiento.

Palabras clave: Radiesse, Hidroxiapatita, sustancia de relleno, nódulo.

Introduction

Injectable fillers restore lost tissue volume beneath the skin and enhance facial contours; therefore, they are useful in preventing aesthetic changes associated with age. Since their use entails rapid recovery and a little discomfort, there has been an increase in the number of women who undergo these types of rejuvenation treatments, accompanied by a decrease in the age of treatment onset. Although there are multiple filler materials today, mostly affordable and associated with few complications, none of them ensure long-lasting results, which

is a cause for multiple applications. Moreover, many unapproved injectable substances continue to be used routinely¹.

The main classification of injectable substances divides them into absorbable materials (collagen, hyaluronic acid, calcium hydroxyapatite, L-lactic acid) and non-absorbable materials (polymethylmethacrylate, Silicone)². The areas most commonly infiltrated are the perioral and periorbital region, the nasolabial fold, the malar region, the glabella, the lips, and the marionette lines. It should be noted that the use of these substances is not only for aesthetic purposes; on many occasions,

they are used to correct post-surgical and post-traumatic deformities or to correct tissue loss in HIV-positive patients suffering from lipodystrophy³.

Complications described so far include allergic reactions, edema, skin necrosis, retinal artery occlusion, face paralysis, skin discoloration and filler migration^{4,5}. Filler migration is defined as the presence of the filler in other locations than where it was initially injected². Migration can lead to inflammation and foreign body reactions⁶. The diagnosis of masses secondary to migration can be challenging, especially when the patient does not know the filler name, the injection site or the exact product used^{6,7}. We describe a case where a patient had a compact mass in the lower gingival mucosa, which was later determined to be caused by the filler migration.

Clinical Case

A 45-year-old woman presented to our department with a palpable and asymptomatic mass in her lower gingival mucosa. She was currently healthy, did not associate the mass with anything in particular, and also denied undergoing any facial filler treatment. She had a history of submandibular pleomorphic adenoma surgically treated three years ago and endosseous dental implants placed five years ago in the upper molar arch, specifically on teeth 2 and 3. The physical examination revealed a painless, solid, regularly shaped mass of approximately half a centimeter at the level of the gingival mucosa below the left lateral incisor. The rest of the physical examination of the upper airway was normal. No other masses were identified.

In order to obtain more information about the nature of the lesion, a CT scan was performed. A hyperdense image was visualized adjacent to the anterior aspect of the left lateral incisor, where the mass was clinically localized (**Figure 1**). Images of a similar density were evidenced in the anterior maxillary region. Given the suspicion of a possible filler migration, the patient was asked again if she had gone through cosmetic filling procedures in the past. It was then that she admitted to having undergone nasolabial fold and cheek-

bone filling with calcium hydroxyapatite four years ago.

The patient was offered the possibility of performing an excision of the lesion under local anesthesia or maintaining active surveillance in time, and she decided to remove the mass. A white organized tissue was visualized (**Figure 2**) and removed.

Histopathologic examination evidenced a foreign body reaction in the deep dermis and hypodermis, which contained numerous



Figure 1. Axial CT: A hyperdense image was visualized adjacent to the anterior aspect of the left lateral incisor, where the mass was clinically localized.



Figure 2. Excision of the lesion under local anesthesia.

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histiocytes and giant cells (**Figure 3**). Within this foreign body reaction, a nonpolarizing exogenous material was identified, consisting of numerous round, uniformly-sized, gray and beige extracellular deposits, also seen in the cytoplasm of the giant cells (**Figure 4**). Although a foreign body reaction can also occur as a consequence of dental implants, the fact that these were in the upper right arch casts doubt on it being the underlying cause, as the lesion is located in the left inferior gingival mucosa, making it more likely as a result of the aesthetic infiltration procedure. The patient attended follow-up appointments at 3 and 5 months post-procedure and was found to be in good health without any complications.

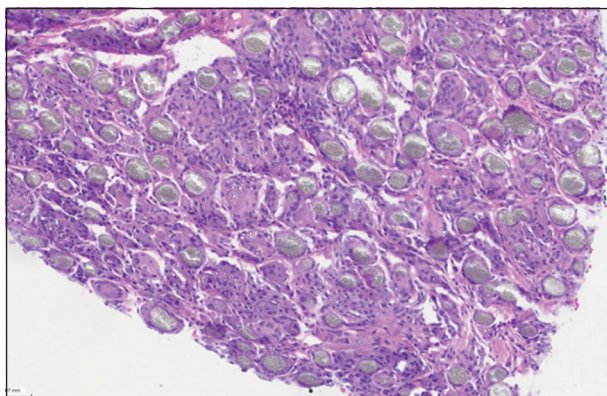


Figure 3. Histopathologic examination evidenced a foreign body reaction in the deep dermis and hypodermis, which contained numerous histiocytes and giant cells.

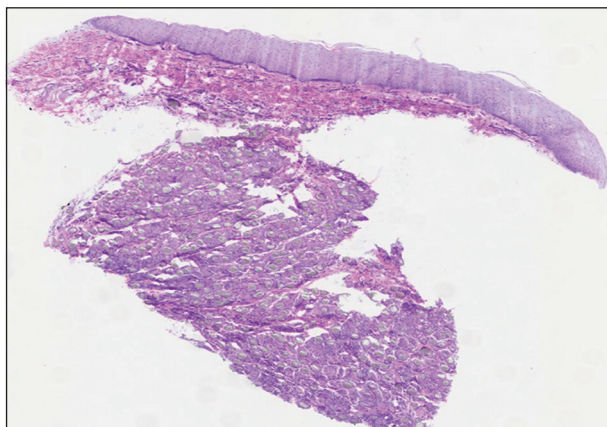


Figure 4. A nonpolarizing exogenous material was identified, consisting of numerous round, uniformly-sized, gray and beige extracellular deposits, which were also seen in the cytoplasm of the giant cells.

Discussion

Radiesse is a filling material composed of calcium hydroxyapatite, which works by stimulating collagen production and, therefore, recovering lost volume in specific areas. It is currently used in numerous aesthetic and reconstructive procedures, and its applicability is increasing⁸. Calcium hydroxyapatite is a substance composed of microspheres suspended in an aqueous gel of glycerin or carboxymethylcellulose that serves to carry them. After infiltration, the aqueous gel is resorbed over time, but the calcium hydroxyapatite microspheres serve as a matrix for collagen production^{4,9}.

Ideally, injected cosmetic materials should be biocompatible, safe, and stable at the injected site and should produce minimal foreign body reactions¹⁰. Generally, secondary effects produced by the use of Radiesse are mild and transitory. The most frequent ones include local bruise formation, pain, inflammation, edema, ecchymosis and itching¹¹. Nevertheless, more serious adverse events such as allergic reactions, vascular occlusion, necrosis or even blindness have also been described, although these are infrequent¹². Short-term complications are directly related to the infiltration technique and the patient's early immune response, while long-term complications are related to the infiltrated material and late immune responses⁷. Non-inflammatory nodules and granulomatous reactions in the presence of a foreign body, both examples of complications induced by filling materials, are different entities with specific radiological and histopathological findings¹. In the literature, several studies describe the great migratory capacity of Radiesse¹²⁻¹⁴. Shokoufeh states these substances can simulate soft tissue tumors and distant metastases by migrating through the lymphatic or hematogenous system. Therefore, when observing them, it is necessary to establish a differential diagnosis with other dermatological granulomatous disorders such as dermatomyositis, sarcoidosis or cutaneous lymphoma^{7,12}.

In a 2019 publication by Mosleh et al., the authors describe a case of an orbital mass secondary to a filler injection with hyaluronic acid in the forehead and the lateral eyebrow. The patient underwent anterior orbitotomy

for excisional biopsy as she did not recall having had the infiltration procedure, which was performed one year before symptoms onset⁶. In our case, the substance was injected at the nasolabial fold, and nodules appeared four years later at the lower gingival mucosa. It is known that some patients may be prone to the migration of injected material. Furthermore, Jordan. D and Stoica Bazil emphasize that filler injection is a blind procedure in which the injector cannot see precisely where the material is placed². Injection technique is important since poor technique, injection under pressure, or injection of too much material at the site are all relevant causes of filler migration. Excessive massage of the area after the procedure, recurrent movements of the facial muscles, gravity, subsequent injections and intravascular or lymphatic spread can also promote filler displacement². The motive for the occurrence of such intense inflammatory reactions to a biocompatible compound is not clear, but factors such as injecting excessive material, repeated or very superficial injections may favor this¹².

Magnetic resonance imaging (MRI) is the preferred technique to study the distribution of these substances due to the excellent discrimination capacity it provides and the anatomical, quantitative and functional information it offers, covering a wide field of visualization. Numerous studies have shown that MRI can detect facial fillers in 100% of patients. The MRI appearance of many of these fillers is similar due to their high-water content (hyaluronic acid, collagen). They are generally seen as hypointense in T1 sequences and hyperintense in T2. As distinctive characteristics, it should be noted that hyaluronic acid is visualized with well-defined serpiginous margins and that calcium hydroxyapatite appears hypo or isointense in both T1 and T2. In addition, it usually shows enhancement after contrast administration and on CT, it appears as lumpy or linear calcifications. The rest of the fillings do not show calcifications unless there is a reaction to a foreign body⁷. Finally, the radiological image associated to nodules differs from that shown by granulomatous reactions, as the latter characteristically presents post-contrast enhancement³. It should be noted that, in our case, the prompt

intervention with a biopsy upon suspicion of a possible malignancy based on the CT image, which pathology ultimately confirmed as a foreign body reaction, was the reason we avoided performing a MRI, even though it may have had higher sensitivity.

Histologically, foreign body granulomas are characterized by large spaces between the particles recognized as foreign bodies, numerous macrophages, fibroblasts and giant cells. They usually appear months or years after infiltration of the material and grow very slowly⁷. Their incidence is low and varies between 0.02%-1%¹². In contrast, the formation of nodules is much more frequent and has been reported in up to 12.4% of patients undergoing lip augmentation fillers. Another difference between both entities is that non-inflammatory nodules are masses that appear 1 or 2 months after superficial infiltration of the material. Histology shows an accumulation of foreign material, few macrophages, occasional giant cells, and a pseudofibrous capsule⁷. A study by Godin et al. revealed that they may temporarily appear in up to 33% of patients. The cause of these nodules may be due not only to tissue infiltration at the superficial level but also to injecting an excessive amount of product¹⁵.

Lemperle was among the first to describe how Radiesse is packed and surrounded by fibrin fibers at the histological level¹⁰. In 2007, the Vidya group described granulomatous reactions due to Radiesse at the level of the oral mucosa for the first time, showing that the distribution of this substance in oral cavity mucosa differs from the distribution described by Lemperle in forearm tissue⁸. Later, Daley et al. described eight other similar cases of granulomatous foreign body reactions at the level of the oral cavity¹³.

Regarding the treatment of this complication, it should be noted that foreign body granulomas are treated with local or systemic corticosteroid infiltration, and if no response is obtained, surgical removal is then performed. On the contrary, non-inflammatory nodules do not respond to intralesional or systemic corticosteroid therapy and require surgery directly⁷. In addition, in the early stages, these nodules may resolve by massaging the region.

Although this study sheds light on the potential complications of dermal filler injections,

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it is important to recognize its limitations. The lack of systemic evaluation for filler migration to distant body parts represents a significant limitation. Secondly, the low symptomatology of these processes, unless there is an associated compressive phenomenon, results in limited clinical experience and description. Therefore, future studies with larger sample sizes and longer follow-up periods are needed. Lastly, a more detailed characterization of these complications in terms of temporality is also necessary, as the literature and our experience diverge in this regard. Foreign body reactions can be observed a few days after injection with these substances or even years later, as seen in the attached case.

Conclusion

Injectable substances can produce foreign body granulomatous reactions with histological and radiological characteristics specific to each substance. These materials also have a great migratory capacity and can mimic soft tissue tumors in other distant locations. Physicians should be aware of the potential for dermal filler migration, as our case demonstrates that migrated filler can penetrate unusual and problematic areas, leading to compressive phenomena and associated symptoms. With the increasing number of patients undergoing filler treatments, in those presenting with new masses after the procedure, a history of injections should be considered in the differential diagnosis. Clinical history is of great importance since, in many cases, the patient does not remember undergoing infiltration procedures, and many practitioners do not inquire about the history of aesthetic procedures in the anamnesis.

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