SKIN

BRIEF ARTICLE

Extensive Foreign Body Granulomas induced by Calcium Hydroxyapatite Filler

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ABSTRACT

Background: Calcium hydroxylapatite (CaHA) is a biocompatible dermal filler used for soft tissue augmentation and collagen stimulation. While generally well-tolerated, rare cases of delayed onset inflammatory nodules, including foreign body granulomas, have been reported. The mechanism for these reactions remains unclear, with potential contributing factors including large particle size, injection technique, and pathogenic contamination leading to biofilm formation.
Case presentation: A 69-year-old female presented with multiple firm, erythematous nodules on the face and neck six months after receiving CaHA filler injections at her esthetician's house. Histopathologic analysis revealed granulomatous inflammation with foreign body giant cells surrounding birefringent material, consistent with a foreign body reaction to CaHA. Although no biofilm was identified, concerns were raised regarding potential contamination due to the non-sterile injection environment. The patient was treated with oral corticosteroids and weekly intralesional triamcinolone injections, leading to gradual improvement over ten months, though residual nodules remained.
Conclusion: This case underscores the potential for granulomatous reactions following CaHA filler injections, especially in non-sterile environments. Given the increasing popularity of soft-tissue fillers, dermatologists should maintain a high index of suspicion for inflammatory reactions and emphasize the importance of sterile injection practices.

INTRODUCTION

Soft tissue filler has been a commonplace procedure in dermatology offices since 1981, steadily increasing in both types and safety. One of the biocompatible options includes calcium hydroxylapatite (CaHA), a particulate gel widely used in regenerative medicine for volume replacement and collagen biostimulation.[1] Besides transient edema, erythema, ecchymosis, and pruritus, filler can cause rarer side effects such as nodule formation, specifically inflammatory nodules. Due to CaHA's natural occurrence in the human body as components of bone and teeth, inflammatory nodules were theorized to be an almost negligible risk of occurrence

and initially seen in 0% of patients.[2] However, since its emergence in 2006, sporadic case reports have reported foreign body reactions to CaHA with no clear trigger for their formation.[3-5] Here we describe a case of extensive foreign body granulomas of the face and neck secondary to treatment with CaHA filler.

CASE REPORT

A 69-year-old female with a past medical history of asthma presented our dermatology office with multiple dark, enlarging, and tender growths on her bilateral cheeks, jaw line, and neck.(**Figure 1**) She denied all other symptoms related to the growths including itching, drainage, fever or chills. The only abnormal activity the patient could recall completing prior to the eruption was filler treatment with CaHA. This was done at an esthetician's house about six months prior to the dermatology appointment. Her cheeks, temples, jawline, nasolabial folds and neck underwent augmentation. A physical exam showed multiple large, firm, erythematous nodules and violaceous patches over the anterior neck, jawline and bilateral malar region. Labs revealed monocytosis and elevated inflammatory markers, such as erythrocyte sedimentation rate.

Two biopsies were obtained for histologic analysis. The left superior buccal cheek showed granulomatous inflammation in the dermis while the left inferior lateral neck resulted in well-formed granulomas with surrounding lymphocytes, plasma cells and rare neutrophils within the dermis and subcutis.Within the granulomas from both biopsy locations, small round spherules of polarizing blueish-gray foreign material were seen at the center.(**Figure 2**) Correlating these findings with the patient's history, she was diagnosed with foreign body granulomas secondary to CaHA filler injections. Oral steroids were prescribed and both kenalog and sodium thiosulfate were injected in the office. Kenolog was injected on a weekly basis starting with a concentration of 5mg/cc and increasing to 10mg/cc at the third weekly appointment. The patient reported a better response to intralesional Kenalog than sodium thiosulfate–which was only injected once–and saw improvement after the 3rd injection. At her most recent follow up, approximately 10 months since her presentation, the nodules were much improved but not completely resolved.

DISCUSSION

CaHA injectable filler is a semi-permanent, synthetic, biodegradable soft tissue filler composed of uniform microspheres suspended in an aqueous gel carrier of glycerin and sodium carboxymethylcellulose.[1] A potential side effect of all fillers is nodule formation, further subdivided into non-inflammatory and inflammatory groups. The non-inflammatory category consists of smaller nodules that form shortly after injection due to poor technique and improper placement within the epithelial layers. Foreign body granulomas are a type of inflammatory nodule that occurs months after injection with their incidence based on the type of filler utilized. Hyaluronic acid has the highest incidence at 0.4%, while CaHA rate is 0.001%.[6]

Due to its natural presence in the body as part of teeth and bones, CaHA filler is more biocompatible than most other types. With its nontoxic, nonantigenic, and minimal inflammatory stimulation, CaHA was initially theorized to not lead to granuloma formation.[5] However, our case report and several others from the literature were confirmed histopathologically as foreign body

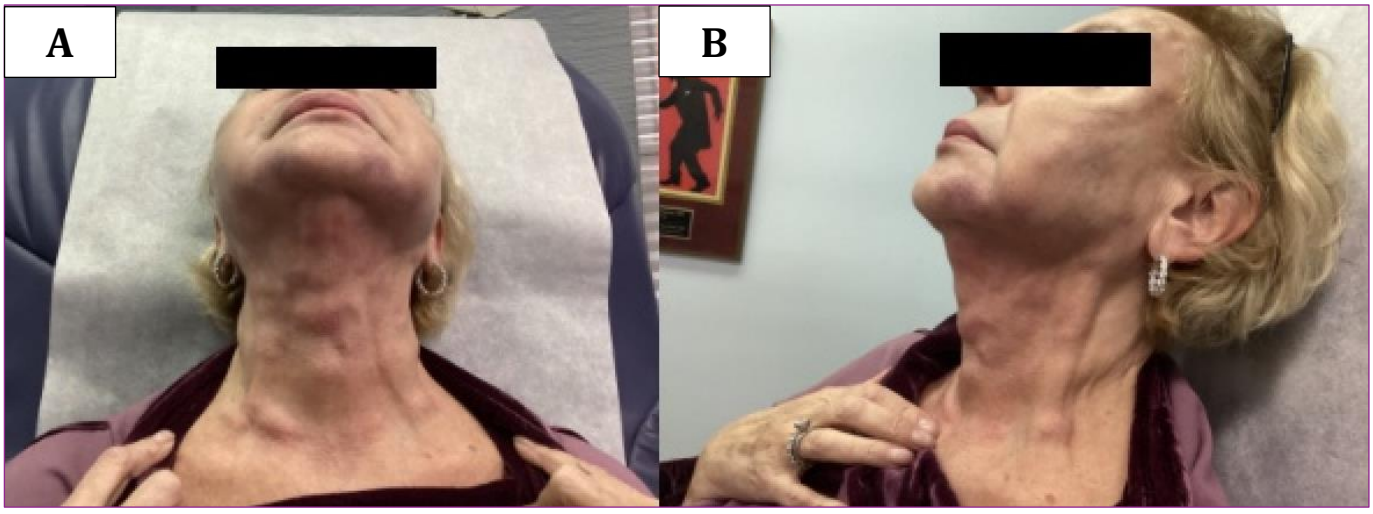

Figure 1. Multiple large, firm, erythematous nodules and violaceous patches over the anterior neck **(A)**, jawline and bilateral malar region **(B)**.

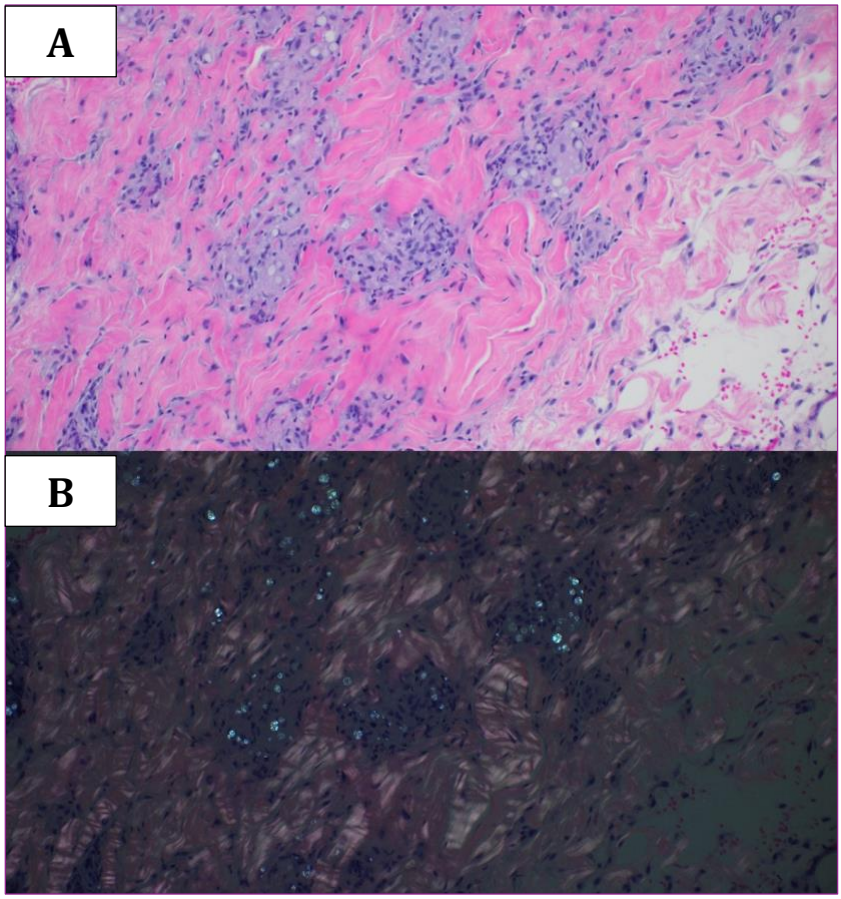

Figure 2 Punch biopsy of a representative lesion (H&E, 200x) demonstrates nodular aggregates of histiocytes surrounding small spherules of foreign material with bluish-grey hue and admixed black particulate dust. **(A)** Polarized light highlights the foreign material. **(B)**

reactions with numerous giant cells and histiocytes surrounding foreign material.[3-5] There is currently no consensus of why CaHA filler causes such an inflammatory response. One postulation is that their large particle size (25-45µm) cannot be efficiently broken down by the body's macrophage response, leading to aggregation, creation of foreign body giant cells and release of proinflammatory cytokines that propagate a granulomatous response. Other possible contributors include injected volume, repetition of injection, impurities, particle smoothness and surface charge, and hydrophilicity.[5] Another possible culprit is bacterial infection of the aqueous gel during injection that eventually forms a biofilm. Biofilms are aggregates of microorganisms that adhere to both each other and a surface, creating a self-protective matrix. They have been seen for years in chronic skin ulcers, various types of implants from orthopedic to dental, and indwelling catheters.[8] Contamination of filler is thought to be from both direct inoculation from the skin and contiguous spread from adnexal structures that have a varied clinical presentation from asymptomatic to erythematous and tender nodules.[8] Biofilms are historically difficult to diagnose based off hematoxylin and eosin staining (H&E) and culture alone. Advanced techniques such as fluorescence in situ hybridization (FISH) analysis and IS-pro novel PCR technique have been shown to detection of bacteria in filler-associated nodules after negative H&E and gram stain and in late onset nodules, respectively.[9-10]

While our patient was of similar age and had a similar time frame from date of injection to nodule appearance (2-36 months, median of 6.5) as its literary companions, a notable difference was the setting in which she received her treatment.[3-5] Originally stating the injections were completed at a medispa, the patient later revealed they were done at the home of a licensed injector. Outside of a controlled and sterile environment, there exists more for potential contamination of both the patient's skin and injection needles. While this factor raised concerns for biofilm formation as a potential cause for our patient's nodule formation, no evidence of biofilm formation was noted on histopathology slides, and besides staining with Grocott's, acid-fast, and Fite, no advanced analyses were conducted. As noted above, it is possible for biofilms to have been missed via H&E, however, we cannot definitively attribute this eruption of nodules to their formation. Regardless of the origin of our patient's granuloma trigger, these cases emphasize the importance of increasing and maintaining consistent sterile injection practices no matter the setting.

Conflict of Interest Disclosures: None

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