

# Delayed inflammatory reaction 12 years after PAAG injection

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## INTRODUCTION

Soft tissue augmentation has evolved dramatically since 1893, when autologous fat transplant was first used to correct facial defects. Since then, numerous materials and techniques have been employed. Dermal fillers were first used in the 1980s and there are now more than 200 products used all over the world <sup>1</sup>. In recent years, injectable tissue fillers have gained significant popularity for soft tissue augmentation with rejuvenative as well as aesthetic purposes, mostly due to their relatively simple application and rapid outcomes <sup>2</sup>. Dermal fillers are classified as biodegradable versus non-degradable. Non-degradable fillers usually

Polyacrylamide hydrogel (PAAG) was initially considered to be a compatible, non-toxic, non-biodegradable material. However, recent studies have shown that numerous adverse events occur after using this permanent filler. The incidence of complications following PAAG injection has been reported to be about 6.7%.

Herein, we report a 32-year-old female who developed an inflammatory reaction 12 years after PAAG injection for zygomatic facial augmentation. Microscopic evaluation of the lesion showed giant cells and granuloma formation. The patient was successfully treated with prednisolone. PAAG is associated with inflammatory reactions which may present even years after injection.

**Keywords:** fillers, polyacrylamide gel, inflammatory reaction

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consist of particles suspended in a resorbable matrix. Examples of non-degradable fillers are silicone, polyacrylamide hydrogel (PAAG), and poly(methyl methacrylate) <sup>3</sup>. Permanent fillers provoke a foreign body reaction resulting in the formation of a fibrous tissue around the material which holds the injected material in place. PAAG is a hydrophilic gel composed of 97.5% sterile water bound to 2.5% cross-linked acrylamide polymer. Water and bioactive molecules readily exchange between the hydrogel and the surrounding tissues, a process which allows gradual integration of PAAG into the host tissue <sup>2,4</sup>.

Despite the simplicity of the application and wide acceptability of the filler use, several short-term

and long-term complications have been reported which limit their application. These complications include erythema, ecchymosis, infection, pain, swelling, localized permanent indurations, purulent secretion or cysts, migration of the gel, asymmetry, and scarring<sup>3,5-10</sup>.

Here, we report a 32-year-old female with bilateral erythematous and indurated facial plaques with a history of polyacrylamide gel injections 12 years ago. To our knowledge, there is no report for such an interval between the filler injection and an inflammatory reaction.

### CASE REPORT

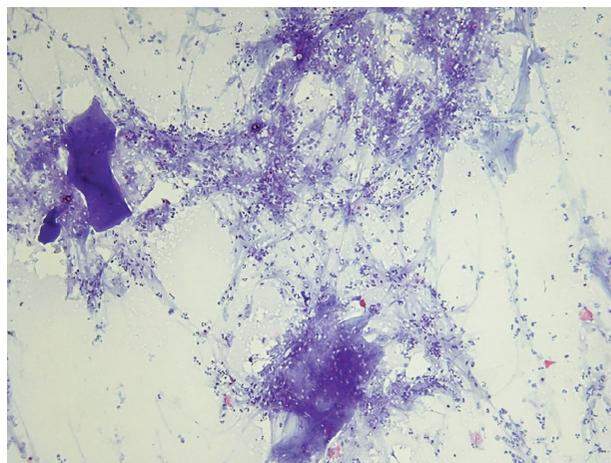
A 32-year-old female presented to the dermatology clinic with bilateral periorbital swelling and erythematous facial plaques since 8 days ago (Figure 1). The involved skin was indurated, tender, and warm. The initial lesion was a nodule on the left zygoma which progressed to bilateral facial inflammation. Tenderness was most severe on the left cheek bone, where an abscess-like fluctuating mass was palpated. Eye movements were painless. Vital signs were normal and the patient was afebrile.

The patient did not mention trauma, insect bite, or upper respiratory tract infection prior to her problem and the only positive finding was a history of PAAG injection for zygomatic facial augmentation 12 years ago. Laboratory tests (CBC, LFT, renal function tests, ESR, CRP) were within normal limits. No abnormality was detected on chest X-ray and cranial or orbital CT-scan.

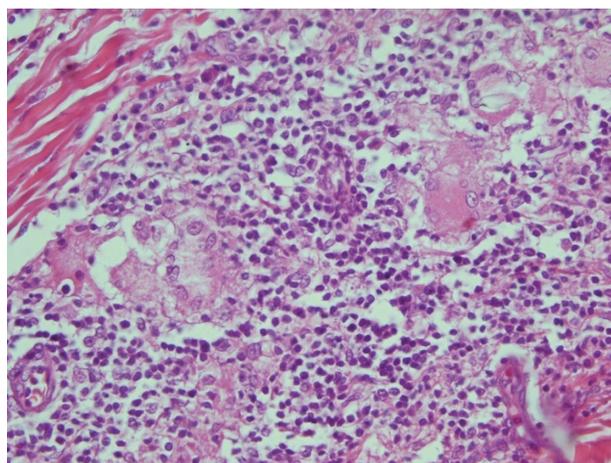


**Figure 1.** Bilateral periorbital swelling and erythematous plaques.

After consultation with infectious diseases specialist and taking blood samples, antibiotic therapy with ceftriaxone and metronidazole was initiated with an impression of facial cellulitis. We performed neurologic and ophthalmologic consultations but no neurologic or ophthalmologic abnormalities were detected. Blood culture was negative and cerebrospinal fluid analysis and culture were normal. The abscess-like lesion on the left cheek was aspirated and studied. Microscopic evaluation of the aspirated specimen showed injected gel material with giant cell inflammation (Figure 2). Biopsy of the erythematous facial plaque on the left cheek was performed and histologic study showed granulomatous inflammation with multi-nucleated giant cells (Figure 3). Ziehl-Neelsen stained smears and mycobacterial culture of the biopsy material were negative.



**Figure 2.** Giant cell inflammation within the injected gel material.



**Figure 3.** Granulomatous reaction with giant cell inflammation (H & E, ×100).



**Figure 4.** Improvement of symptoms after four days of treatment with prednisolone.

After 72 hours of antibiotic therapy, the symptoms did not change. Considering the evidence of the inflammatory reaction and foreign body granuloma formation, prednisolone (30mg/day) was initiated. Four days after steroid therapy, the swelling and other symptoms improved markedly (Figure 4). Then, prednisolone was tapered and the patient was discharged.

## DISCUSSION

Here we reported a 32-year-old female with a 12-year history of PAAG injection in the zygomatic area, complaining of facial swelling and redness since 8 days ago. Ruling out the infectious events, aspiration/biopsy and microscopic evaluation of the lesions revealed injected gel material with foreign body granulomatous reaction. Symptoms subsided after 4 days of steroid treatment.

PAAG is permanent filler composed of 97.5% sterile water bound to 2.5% cross-linked acrylamide polymer that is used for the correction of wrinkles and facial volumization. This product is not biodegradable and thus exerts long-lasting effects. After injection, macrophages enter the gel and following vascularization, collagen-producing fibroblasts replace macrophages. Since PAAG is a homogenous hydrophilic gel devoid of microparticles, the inflammatory response elicited by the gel is usually minimal<sup>11-13</sup>. Christensen *et al.* studied biopsies from non-reactive tissue and inflammatory nodules after PAAG injection. They concluded that the structural characteristics of PAAG, which prevent biofilm formation, may

explain the absence of late inflammatory nodules in this permanent filler<sup>13</sup>.

Although the long-lasting effect has increased the popularity of PAAG, several studies have reported serious complications after its use. These complications may present early after injection or years later and include hematoma, inflammation, infection and abscess formation, nodule formation, asymmetry, irregularity, and migration. Histologic findings consist of granuloma formation, fat necrosis, and fibrosis<sup>8-10,14</sup>.

In 2004, Amin *et al.* reported a patient with zygomatic augmentation using PAAG who presented with erythematous nodules on the injection sites 2 months after the injection. The symptoms did not change with oral antibiotic and further evaluation revealed a negative wound culture and Gram stain. She was finally treated with local injection of corticosteroid<sup>15</sup>. In the same year, De Bree *et al.* reported a 40-year-old female who underwent bilateral cheek augmentation using polyacrylamide hydrogel injection. She presented with desensitization of her cheeks six months after the injection. Histological evaluation showed a severe granulomatous reaction. She was treated with repeated local injections of corticosteroid<sup>16</sup>. These are the first case reports of delayed reaction to polyacrylamide gel injected into the face for soft tissue augmentation.

A 2-year prospective study by von Buelow *et al.* on 228 patients who underwent facial augmentation with polyacrylamide hydrogel showed that complications such as swelling, hematoma, redness, pain, and itching might occur in 7% of the cases<sup>5</sup>.

Wolters *et al.* followed 81 patients with PAAG injection for 36 to 48 months and found that this permanent filler was well tolerated without any significant adverse effects. However, they reported a patient with persistent itching after 1 year<sup>17</sup>.

In 2010, Liu *et al.* reported 2 patients with PAAG facial augmentation who presented with severe complications. One of the patients complained about nodularity and swelling over the injection site 6 years after the injection. She was finally diagnosed with and treated for osteomyelitis despite the negative culture results of the excised tissue. The second patient presented with an ulcer and nodule formation on her left cheek 3 years after the injection of PAAG at the site. Debridement was performed and microscopic evaluation of the tissue

revealed infiltration of the inflammatory cells into the dermis and subcutaneous fat<sup>18</sup>.

Studies have shown inflammatory and granulomatous reactions after breast augmentation with PAAG<sup>19,20</sup>. Histologic specimens have shown macrophages and granulomatous reaction. Wang *et al.* studied 96 patients with PAAG breast augmentation who presented with infection. The time interval between gel injection and the presentation of infection ranged from 3 to 108 months. Microscopic study of the involved tissue showed PAAG granules that were surrounded by giant cells in some cases<sup>21</sup>.

Xu *et al.* reported a case of nasal dorsum augmentation with PAAG who presented with gel migration and nodule formation 3 years after the injection<sup>22</sup>.

Kadouch *et al.* studied 85 patients with delayed-onset complications after facial injection with permanent fillers and concluded that the intrinsic characteristics of the injected filler as well as the immune status of the patient were important factors in the determination of the timing of the complications and the type of the event. They noted that invasive oral or facial procedures, such as dental procedures or additional filler injection, could trigger the onset of complications<sup>23</sup>.

Polyacrylamide hydrogel injection may have additional long-term effects on the human body. One of the long-term complications of PAAG injection is the formation of foreign body granulomas. The host response to PAAG injection may lead to cellular reactions and granuloma formation. We reported delayed foreign body granuloma, which is one of the relatively rare adverse events of PAAG injection in the facial area with positive response to oral prednisolone.

Christensen *et al.* recommend that infectious nodules related to polyacrylamide hydrogel should be treated with antibiotics, whereas granulomas should be treated with a combination of both steroids and antibiotics or excision<sup>24,25</sup>. Our patient showed no signs of infection and did not respond to broad-spectrum antibiotics. Initially, we tried to aspirate the injected polyacrylamide hydrogel using a needle. However, it was difficult to remove all of the injected material and the patient was ultimately treated with corticosteroid.

PAAG is a non-toxic non-biodegradable gel that is used as a permanent filler for soft tissue

augmentation. Although it was initially known as a relatively safe material, there are several case reports and studies that show adverse effects associated with PAAG use. Thus, it seems that before using PAAG confidently for aesthetic purposes, more studies should be performed. Regarding the fact that PAAG is a permanent filler, special attention should be paid to its interaction with host tissue and long-term effects. Besides, accurate diagnosis of adverse events due to PAAG is essential for proper treatment.

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