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Case Report **Medicine**

When Cosmetic Fillers Disguises Facial Angioedema: A Case Report

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Abstract

Background: Facial angioedema is a challenging for the medical profession, particularly in patients received cosmetic dermal fillers. ***Case presentation:*** A 43 years old fmale presented with one-year history of recurrent facial swelling after receiving unlabeled dermal fillers given by unlicensed esthetician. Her symptom improved with systemic steroid prescribed at private clinic. Dermatologic examination revealed nodular lesions on both cheeks measured 1-3 cm in diameter. Foreign body reaction to injectable filler was highlighted by plastic surgeon and surgical biopsy was advised. Upon allergy review, she reported associated symptoms of mild throat discomfort and occasional difficulty of swallowing. A diagnosis of idiopathic angioedema was raised. However, patient strongly believed that her facial swellings were related to her dermal fillers and reluctant to start antihistamines. Immunologic work up for idiopathic and congenital angioedema was unremarkable. She was labeled allergic to Chlorpheniramine in the past. This however, was excluded by supervised oral graded challenge performed in the allergy clinic. The patient was shortly admitted for of an episode of angioedema, upper gastrointestinal (GI) endoscopy was performed for other complaints of heart burn and mild difficulty of swallowing. Not surprisingly, laryngeal edema was pictured during the procedure, rapid urease test for (H. pylori) was positive. These finding have further supported the diagnosis of idiopathic angioedema. Patient has completed (H. Pylori) eradication therapy. Afterward, she was commenced on a combination H1 and H2 antihistamines, this has resulted in significant improvement of her facial angioedema and throat discomfort. ***Conclusion****:* Facial angioedema in patients received injectable dermal fillers may not necessarily be due to local adverse reaction, in certain clinical setting a diagnosis of idiopathic angioedema should be suggested. Therefore, consulting allergy specialist is essential in evaluating such patients.

Keywords: Cosmetic, dermal, fillers, facial angioedema.

INTRODUCTION

After injection of permanent cosmetic dermal fillers, delayed adverse effects including chronic edema, inflammatory nodules, foreign body granulomas, fibrosis, tissue hardening, migration of filler material, facial asymmetry, and delayed immune-mediated reactions may develop after months or even years. [1] These effects also known as type IV hypersensitivity reaction, which is a T-cell–mediated immune response. [2]

Permanent cosmetic fillers represent a unique trigger for delayed hypersensitivity because the injected material may persist indefinitely within soft tissues.[3] Histologically, these reactions are commonly characterized by lymphocytic infiltrates, activated macrophages, multinucleated giant cells, granulomatous inflammation, collagen deposition, and fibrosis surrounding filler particles. [4] Chronic inflammatory stimulation may eventually produce painful nodules, facial hardening, contractures, tissue distortion, and functional impairment.[5]

Chronic idiopathic angioedema is a recurrent disorder characterized by transient, non-pitting swelling involving the deeper layers of the skin and submucosal tissues that persists or recurs for more than six weeks without an identifiable external cause. [6] The condition most commonly affects the face, lips, eyelids, tongue, extremities, and upper airway, and may occasionally involve gastrointestinal mucosa. Episodes may occur spontaneously and unpredictably, with variable duration and severity. [7]

Chronic angioedema can be classified as histaminergic and non-histaminergic forms based on the dominant inflammatory mediator involved. Histaminergic angioedema is mediated predominantly through mast cell and basophil activation with subsequent release of histamine, leukotrienes, prostaglandins, tryptase, and other vasoactive mediators while non-histaminergic angioedema involves alternative pathways, particularly bradykinin-mediated vascular permeability, which is a potent vasoactive peptide that produces endothelial relaxation and vascular leakage independent of mast cell degranulation. [8]

As both of chronic idiopathic angioedema and permanent dermal fillers conditions may present with recurrent facial swelling and upper airway symptoms, their differentiation is a complex issue. [9] Thus, distinguishing between both conditions is essential because of considerable variation in their management. Delayed granulomatous reactions need immunomodulatory therapy, corticosteroids, surgical excision, or reconstructive intervention, whereas chronic idiopathic angioedema needs antihistamines, biologic therapies, or targeted anti-inflammatory treatment depending on the underlying mediator pathways. [10]

CASE PRESENTATION

A 43 years old female known patient of iron deficiency anemia and uterine fibroids patient was initially presented with recurrent painful swelling of the face and hands, recurrent throat discomfort, inability to open the mouth completely, facial disfigurement and asymmetry as well as hand swelling with nodules and mild dysfunction. History revealed that these symptoms began approximately 2 months after receiving permanent dermal filler injections in the face and hands by an unlicensed beautician around 2010–2012. The patient had multiple hospital admissions and emergency visits due to recurrent swelling episodes. On one admission the patient came with Left mandibular sialoadenitis presenting with left submandibular swelling, dysphagia, and sore throat.

She was previously diagnosed as hypersensitivity to filler material and received repeated courses of oral prednisolone, intravenous hydrocortisone, intramuscular dexamethasone, antibiotics and analgesics. Symptoms improved temporarily with steroids but recurred after discontinuation. Additionally, prolonged use of steroids caused the patient to manifest complications in the form of gastritis, weight gain and recurrent oral thrush.

Past history included iron deficiency anemia secondary to menorrhagia from uterine fibroids treated surgically, and idiopathic chronic angioedema diagnosed in 2012.

Physical examination revealed bilateral cheek swelling and induration, hardened cheek tissues, multiple mandibular and cervical nodules measuring 2–4 cm, tender inflammatory masses in both cheeks, Jaw contracture with limited mouth opening, multiple nodules and diffuse swelling over the dorsum of both hands, as well as minor hand dysfunction. During further admission for an episode of angioedema, left submandibular swelling approximately 4 × 3 cm was observed. Upper gastrointestinal endoscopy was performed for other complaints of heartburn and mild difficulty of swallowing. and laryngeal edema was illustrated. Rapid urease test for H-pylori was positive. These pictures have supported the diagnosis of idiopathic angioedema. Afterward, she was commenced on a combination H1 and H2 antihistamines, with significant improvement in and facial angioedema and throat discomfort.

Blood investigations were within normal limits. Histopathology and clinical evaluation suggested foreign body granulomatous reaction, and extensive fibrosis secondary to permanent silicone dermal fillers. Multidisciplinary consultation involved plastic surgery, maxillofacial surgery and clinical immunology.

Final diagnosis of the case was severe delayed foreign body granulomatous reaction secondary to permanent dermal filler injections (likely silicone), extensive facial and hand fibrosis, hypersensitivity reaction to filler materials, idiopathic chronic angioedema and left mandibular sialoadenitis (during separate admission). The patient received intravenous clindamycin, intravenous dexamethasone (Decadron), oral steroids, analgesics (Brufen), and antibiotics (Keflex). Conservative treatment produced only temporary improvement. Patient underwent surgical excision and removal of foreign material, plastic reconstructive surgery and referral to a higher specialized center with plastic surgery, hand surgery, and neurosurgery support with potential use of Minocyclin. Imiquimod as anti-inflammatory therapy was discussed but considered late in disease progression. Patient improved symptomatically during admissions and was discharged stable. However, recurrent swelling persisted, and significant facial and hand deformity remained

DISCUSSION

There are two types of cosmetic dermal fillers; permanent and temporary and both types are injectable biomaterials used for soft tissue augmentation of soft tissue, facial contouring, removal of wrinkles, and cosmetic reconstruction. Permanent fillers are characterized by their persistence within host tissues because they resist physiologic enzymatic degradation. [2]

Despite the fact that these fillers gained popularity because of their prolonged aesthetic impacts and decrease need for repeated procedures, their permanent persistence within tissues may predispose

consumers to delayed immune-mediated as well as inflammatory adverse effects as the retained filler material might trigger innate and adaptive immune pathways leading to delayed hypersensitivity reactions together with fibrosis, granulomatous inflammation, tissue hardening, recurrent edema, as well as progressive facial disfigurement. [11]

Complications associated with permanent fillers may happen months or even years after the initial exposure. In severe reactions, histopathologic examination commonly shows multinucleated giant cells, macrophage infiltration, chronic lymphocytic inflammation, collagen deposition, and granulomatous foreign body responses surrounding retained filler material. In addition, permanent fillers are commonly accompanied with higher risk of chronic inflammatory complications that may continue to induce immune activation over prolonged periods. [12]

Management of complications of permanent filler is usually challenging and may necessitate prolonged therapy with corticosteroid, immunomodulatory treatment, surgical intervention, and multidisciplinary evaluation involving allergy/immunology, dermatology, pathology, plastic surgery, and maxillofacial surgery. Furthermore, severe cases may progress toward chronic fibrosis, painful nodularity, jaw restriction, dysphagia, as well as airway-related symptoms with permanent impairment. [13]

Delayed hypersensitivity reaction, also known as type IV hypersensitivity reaction, is a cell-mediated immune response involving activation of T lymphocytes, macrophages, dendritic cells, and cytokine-mediated inflammatory pathways that typically develops several hours to days after exposure to an antigen. [14]

Chronic idiopathic angioedema is a recurrent inflammatory disorder, commonly affecting the face, lips, eyelids, tongue, extremities, and upper airway and being characterized by episodic swelling (non-pitting), lasting several hours to days before spontaneous resolution, of deeper dermal, subcutaneous, and submucosal tissues in the absence of an identifiable underlying etiology. [15]

Trigger for reactivation of previously asymptomatic delayed hypersensitivity reactions associated with cosmetic fillers include viral infections, vaccinations, trauma, bacterial biofilms, chronic inflammatory disorders, and systemic immune dysregulation through cytokine-mediated activation of filler sites. [16]

The overlap between delayed hypersensitivity reaction and chronic foreign body granulomatous inflammation remains particularly important clinically because both processes frequently coexist in patients with permanent filler complications, creating significant diagnostic complexity and potentially delaying accurate diagnosis and appropriate multidisciplinary management. [17]

Histaminergic mast cell activation is considered the most common mechanism in chronic idiopathic angioedema, although non-histaminergic and bradykinin-mediated pathways may also contribute in selected cases. [18]

In patients with previous cosmetic dermal filler exposure, recurrent facial swelling may initially be attributed solely to local filler-related inflammatory reactions. However, concomitant chronic idiopathic angioedema may coexist and significantly complicate clinical assessment because both conditions may present with recurrent edema, facial swelling, dysphagia, airway symptoms, and inflammatory soft tissue changes. Consequently, comprehensive allergy/immunology evaluation remains critically important in patients presenting with recurrent swelling after cosmetic filler procedures.

As both of chronic idiopathic angioedema and cosmetic filler-associated inflammatory disease often present with recurrent facial swelling, edema, throat discomfort, dysphagia, as well as airway-related symptoms, it is challenging in the diagnosis of both conditions. [19]

This case indicates the diagnostic difficulty as a result of coexistence of these two conditions in a patient who had chronic painful nodules, fibrosis, facial hardening, jaw contracture, and persistent swelling after receiving unknown permanent dermal fillers. However, findings strongly suggestive of severe delayed granulomatous foreign body reaction. At the same time, the patient had recurrent throat discomfort, dysphagia, laryngeal edema, and episodic swelling with unremarkable immunologic evaluation for hereditary and acquired angioedema, which are suggestive of chronic idiopathic angioedema. Clinical improvement after treatment of Helicobacter pylori and intake of H1/H2 antihistamine treatment supported coexistence of histaminergic angioedema.

CONCLUSION

This case focuses on the importance of early diagnosis and management of cases presented with delayed inflammatory complications of permanent cosmetic dermal fillers. The present case emphasizes that recurrent facial edema in patients with cosmetic filler exposure should not attributed only, by fast impression to local filler-related complications as the coexistence of delayed hypersensitivity reaction and chronic idiopathic angioedema created substantial clinical overlap, making the diagnosis and management more challenging because both conditions may have the same presentation in the form of recurrent swelling, dysphagia, throat discomfort, and laryngeal involvement. Thus, these

complex inflammatory conditions need comprehensive multidisciplinary evaluation including allergy/immunology specialists for proper diagnosis, prompt management, and decrease of long-term complications

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