Annals of Clinical and Medical Case Reports[R] ISSN 2639-8109 Volume 17

Case Report Open Access

# Disproportionate Inflammatory Reaction After Lip Filler as A Revealing Event of Possible Mast Cell Disease: A Case Report

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Received: 05 Sep 2026
Accepted: 14 Sep 2026
Published: 17 Sep 2026
J Short Name: ACMCR

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**Keywords**:

Inflammatory; Hyaluronic Acid; Mastocytosis

**Citation:**

Sandra Rocio Inofuente Pacha, Disproportionate Inflammatory Reaction After Lip Filler as A Revealing Event of Possible Mast Cell Disease: A Case Report. Ann Clin Med Case Rep® 2026; V17(1): 1-3

## 1. Abstract

### 1.1. Background

Dermal fillers are generally safe, but adverse events can occur. We report a rare case of an exuberant inflammatory response to hyaluronic acid (HA) filler, which served as a sentinel event for the diagnosis of systemic mastocytosis.

### 1.2. Case Presentation

A 37-year-old woman presented with a 1-month history of recurrent urticarial lesions. Following HA lip filler injection, she developed severe, disproportionate edema and nodules. Histopathology and immunohistochemistry (CD117+, CD25+) confirmed mastocytosis.

### 1.3. Conclusion

This case highlights the importance of considering mast cell disorders in patients with hypersensitivity-like reactions to aesthetic procedures.

## 2. Introduction

We report an unusual and disproportionate inflammatory reaction after hyaluronic acid lip filler injection that served as a sentinel event for the recognition of an underlying mast cell disorder. The procedural lesson is that severe, painful, or persistent edema after filler injection, particularly in patients with recurrent urticarial lesions or a positive Darier sign, should prompt consideration of mast cell activation rather than being attributed solely to a local procedure-related complication.

The use of hyaluronic acid (HA)-based dermal fillers has established itself as a minimally invasive procedure with high aesthetic demand and a well-established safety profile [1]. However, despite its biocompatibility, inflammatory and immune-mediated adverse events, may occur and can present with clinical features that overlap with infection, delayed hypersensitivity, vascular complications, or excessive tissue trauma, representing significant diagnostic and therapeutic challenges [2]. We report an unusual and disproportionate inflammatory reaction after hyaluronic acid lip filler injection that served as a sentinel event for the recognition of an underlying mast cell disorder. The procedural lesson is that severe, painful, or persistent edema after filler injection, particularly in patients with recurrent urticarial lesions or a positive Darier sign,should prompt consideration of mast cell activation rather than being attributed solely to a local procedure-related complication.

## 3. Case Report

### 3.1. Medical History

A 37-year-old previously healthy woman presented with monomorphic, oval, well-demarcated, reddish-brown macules and papules distributed multifocally, predominantly on the trunk and proximal portions of the limbs. The lesions exhibited whealing and erythema upon friction, consistent with a positive Darier sign Figure 1. The patient denied any known history of atopy or previous severe adverse drug reactions.

**Figure 1.** Clinical presentation of cutaneous mastocytosis.

Monomorphic, oval, well-demarcated, reddish-brown macules and papules distributed multifocally over the trunk and proximal portions of the limbs. The lesions exhibited whealing and erythema following friction, consistent with a positive Darier sign.

### 3.2. Procedure

The patient underwent lip augmentation with the injection of 1 mL of hyaluronic acid (Rennova Lips®), which does not contain lidocaine in its formulation. The procedure was performed using a 22-gauge cannula following infiltrative anesthesia of the buccal mucosa. It was completed under sterile conditions without immediate complications, including signs of vascular occlusion, tissue trauma, or other adverse events.

### 3.3. Adverse Event

Approximately 24 hours after the procedure, the patient developed marked, progressive, and painful edema, predominantly in the perioral region, associated with the appearance of granular and nodular formations on the labial mucosa. The symptoms persisted for more than 48 hours, suggesting an active and exacerbated cellular immune response. The changes were photographically documented throughout the clinical course Figure 2.

Management: Systemic corticosteroid therapy was promptly initiated with prednisone at 40 mg/day for five days, followed by 20 mg/day for three days, in combination with levocetirizine 10 mg twice daily for seven days. The patient showed a favorable clinical course, with progressive regression of the edema and nodular changes until complete resolution Figure 3.

**Figure 2.** Disproportionate inflammatory reaction after hyaluronic acid lip filler injection.

Marked, painful perioral edema associated with granular and nodular lesions of the labial mucosa, developing approximately 24 hours after injection of 1 mL of hyaluronic acid filler.

**Figure 3.** Clinical resolution after treatment.

Progressive regression of the perioral edema and labial nodules following treatment with prednisone and levocetirizine, with complete clinical resolution and no evident residual inflammatory changes

### 3.4. Diagnosis

A biopsy of the perilesional mucosa/skin revealed a perivascular and interstitial infiltrate of lymphocytes and mast cells. Immunohistochemistry demonstrated mast-cell infiltration with CD117 and aberrant CD25 expression.

The diagnosis of systemic mastocytosis was established based on the 2016 World Health Organization (WHO) classification criteria, which require the presence of one major criterion (multifocal dense mast cell infiltrates in the bone marrow or extracutaneous organs) and at least one minor criterion-or at least three minor criteria-including aberrant CD25/CD2 expression on mast cells, presence of KIT D816V mutation, and elevated serum tryptase levels [3,4]. In this case, the combination of clinical cutaneous findings (positive Darier sign), histopathological evidence (CD117+), and the immunophenotypic profile (aberrant CD25+) confirmed the diagnosis of systemic mastocytosis.

## 4. Discussion

Although HA is considered an inert polysaccharide, it may act as an unsuspected trigger in patients with pre-existing mast cell disorders. Recent literature has documented cases in which HA fillers precipitated episodes of systemic mast cell activation, mimicking local hypersensitivity reactions [5]. The pathophysiological mechanism may involve a reduced threshold for mast cell activation in these patients; the mechanical stress caused by injection (shear pressure) and the tissue response to the product may trigger local degranulation of hypersensitive mast cells [5,6].

In the present case, the diagnosis was confirmed based on WHO criteria. Although CD117 positivity confirms mast cell lineage, aberrant CD25 expression is a decisive diagnostic criterion for systemic mastocytosis, enabling differentiation between an isolated allergic reaction and an underlying clonal disorder [4]. This case underscores the importance of viewing disproportionate post-filler edema not merely as a technical complication, but also as a possible “revealing event” indicating an underlying systemic disease and warranting thorough investigation.

## 5. Ethical Statement

This study was conducted in accordance with the Declaration of Helsinki and written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

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