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Journal of Dermatology and Skin Care

CASE REPORT

Sudden-Onset Facial Puffiness with Myalgia in a Young Female: Diagnostic Overlap between Angioedema and Fibromyalgia

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Citation: Bhattacharya Shatanik (2026) Sudden-Onset Facial Puffiness with Myalgia in a Young Female: Diagnostic Overlap between Angioedema and Fibromyalgia, J Dermatol Skin Care 5: 102

Abstract

Facial swelling in young individuals presents a diagnostic challenge due to a wide spectrum of etiologies ranging from allergic reactions to systemic disorders. We report a case of a 19-year-old female who presented with acute-onset progressive facial puffiness associated with severe myalgia involving the neck, shoulders, and upper limbs. The initial clinical suspicion included angioedema, possibly drug-induced or allergic in origin. Despite corticosteroid and antihistamine therapy, symptoms showed only partial improvement with recurrence after tapering.

Extensive evaluation including autoimmune workup (antinuclear antibody by indirect immunofluorescence) and complement levels (C1 esterase inhibitor) were within normal limits, effectively excluding immunological causes such as connective tissue disease and hereditary angioedema [1]. Rheumatological assessment revealed benign joint hypermobility with fibromyalgia, explaining the persistent myalgia and functional limitation [2].

Interestingly, the episodic facial swelling demonstrated a waxing and waning course without a clear allergenic trigger, raising the possibility of non-classical angioedema or neurogenic inflammation associated with fibromyalgia [3]. Initiation of neuromodulators (duloxetine and pregabalin) along with physiotherapy resulted in significant symptomatic improvement [4].

Keywords: Facial Edema; Angioedema; Fibromyalgia; Joint Hypermobility; Neurogenic Inflammation; Young Female; Myalgia; Diagnostic Dilemma

Introduction

Acute facial swelling is a commonly encountered clinical presentation with etiologies ranging from allergic angioedema to infections, autoimmune disorders, and systemic conditions. Angioedema is characterized by transient, non-pitting swelling involving deeper dermal and submucosal tissues, mediated by histamine or bradykinin pathways [1].

Fibromyalgia is a chronic pain disorder characterized by widespread musculoskeletal pain, fatigue, and central sensitization [2]. Although swelling is not a classical feature, patients frequently report subjective swelling sensations, which may mimic inflammatory or allergic conditions [3].

Recent evidence suggests that patients with fibromyalgia frequently report subjective swelling, which may not correlate with true edema but rather reflects altered central pain processing and neurogenic inflammation. Dysregulation of autonomic function and peripheral nociceptive signaling has been proposed as a mechanism contributing to such atypical presentations, thereby mimicking inflammatory or allergic conditions.

Case Presentation

A 19-year-old female presented with sudden onset facial puffiness beginning on 1st January, initially involving the face, neck, and shoulders, associated with mild respiratory discomfort characterized by nasal obstruction, which improved with steam inhalation.

By the following morning, swelling progressed to involve bilateral cheeks, lips, and periorbital regions. The patient experienced dull aching pain over the cheeks, exacerbated by touch, along with difficulty in mouth opening and mastication. Concurrently, severe pain and tenderness developed in the shoulders and upper limbs, significantly impairing daily activities such as combing hair and dressing.

Initial investigations were within normal limits. Dermatological consultation suggested angioedema, and the patient was started on oral prednisolone and antihistamines, resulting in partial improvement [1].

Despite steroid tapering, symptoms recurred after approximately two weeks. ENT evaluation suggested allergic rhinitis, and treatment was initiated accordingly.

Past history included recent dental inflammation due to wisdom tooth eruption and recurrent upper respiratory infections.

Further evaluation revealed:

ANA (indirect immunofluorescence): Negative

C1 esterase inhibitor: Normal

Routine blood tests: Within normal limits

These findings effectively ruled out autoimmune disease and hereditary angioedema[1].

Rheumatological assessment revealed benign joint hypermobility with fibromyalgia, explaining the severity of pain and functional impairment [2].

Dermatological reassessment considered angioedema unlikely due to delayed recurrence and intermittent normalcy. A working diagnosis of fibromyalgia-associated episodic swelling with possible neurogenic inflammation was made [3].

Differential diagnoses considered included histamine-mediated angioedema, bradykinin-mediated angioedema, idiopathic angioedema, connective tissue disorders, hypothyroidism, and inflammatory myopathy. These were systematically excluded based on clinical features, normal complement levels, negative autoimmune workup, normal thyroid profile, and absence of muscle enzyme elevation.

The patient was treated with duloxetine and pregabalin along with physiotherapy, leading to significant clinical improvement [4].

Clinical Timeline of Events

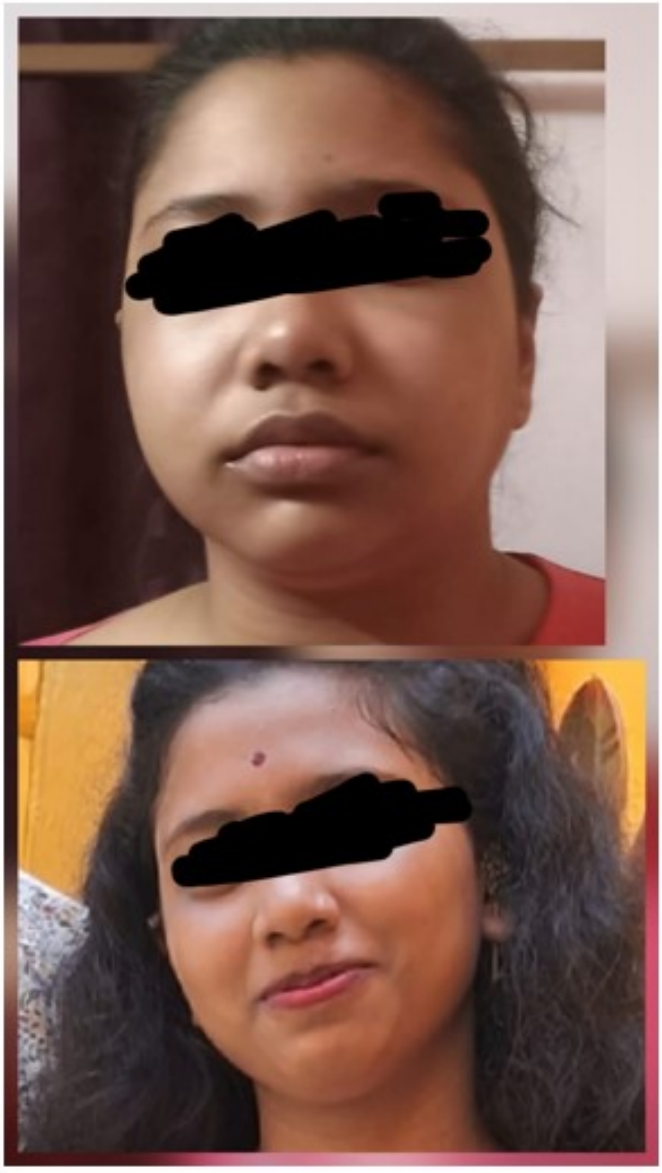

Figure 1A–B:

(A) Diffuse non-erythematous facial swelling involving cheeks, lips, and periorbital region during the acute episode.

(B) Marked reduction in swelling with return to near-normal facial appearance following treatment, demonstrating the waxing and waning course of the condition.

Day 1: Sudden onset facial swelling with nasal obstruction

Day 2: Progression to periorbital edema, lip swelling, severe myalgia

Day 3: Initial treatment started (no improvement)

Day 6: Prednisolone (30 mg) + antihistamines started → partial improvement

Day 10–15: Steroid taper → residual myalgia persists

Day 24–25: Recurrence of swelling and pain

Post evaluation: Rheumatological diagnosis of fibromyalgia

Final treatment: Duloxetine + pregabalin + physiotherapy → significant improvement

Investigations

Comprehensive laboratory evaluation revealed hemoglobin of 11.3 g/dL with a total RBC count of 3.89 million/cumm and packed cell volume of 32.9%, suggestive of mild anemia. Red cell indices were within normal limits. Total leukocyte count (5,400/cumm) and differential count were within normal range, with no significant eosinophilia. Platelet count was normal (2.15 lakh/cumm). Erythrocyte sedimentation rate was mildly elevated (23 mm/hour).

Renal function parameters were within normal limits, with serum creatinine of 0.60 mg/dL. Random blood glucose was 79 mg/dL. Thyroid profile showed free T4 of 1.0 ng/dL and TSH of 3.94 μIU/mL, both within reference range, thereby excluding thyroid dysfunction as a cause of facial swelling.

Serum vitamin D (25-hydroxy) level was 21.8 ng/mL, indicating insufficiency. Serum IgE level was within normal limits (31.3 IU/mL), reducing the likelihood of an active atopic or allergic etiology. C-reactive protein was 2.3 mg/L, within normal limits, suggesting absence of significant systemic inflammation.

Muscle enzyme levels were normal, with creatine kinase (CK) of 83 U/L, thereby excluding inflammatory myopathy as a cause of the patient's myalgia. Serum uric acid was within normal limits (3.2 mg/dL).

Urine routine examination revealed pale straw-colored, slightly hazy urine with normal pH (6.0) and specific gravity (1.020). There was no evidence of proteinuria, glycosuria, or ketonuria. Microscopy showed 2–3 pus cells/hpf with no red blood cells, casts, or crystals, which was within acceptable limits.

Autoimmune workup including antinuclear antibody (ANA) by indirect immunofluorescence was negative, and C1 esterase inhibitor levels were within normal limits, thereby excluding connective tissue disease and hereditary angioedema.

Overall, the investigations were largely unremarkable except for mild anemia, borderline elevated ESR, and vitamin D insufficiency, with no biochemical, immunological, or inflammatory evidence explaining the facial swelling and myalgia.

Angioedema typically presents with rapid onset swelling of the face and mucosal tissues and may be histamine-mediated or bradykinin-mediated [1]. Normal complement levels and lack of consistent triggers made classical angioedema unlikely in this case.

Fibromyalgia involves central sensitization with altered pain perception and frequently overlaps with benign joint hypermobility [2]. Patients often report subjective swelling, possibly due to altered neural signaling rather than true edema [3].

Emerging evidence suggests a role of neurogenic inflammation and dysregulated autonomic function in fibromyalgia, which may explain episodic swelling in such patients [3].

The patient's improvement with neuromodulators such as duloxetine and pregabalin further supports a central pain processing disorder rather than an immunological cause [4].

The absence of eosinophilia, normal IgE levels, and lack of response to antihistamines further argue against an allergic etiology, while normal C1 esterase inhibitor levels make hereditary angioedema unlikely.

Discussion

Although angioedema remains a key differential diagnosis in cases of acute facial swelling, the absence of urticaria, lack of consistent triggers, normal complement levels, and incomplete response to antihistamines and corticosteroids made classical angioedema less likely in this patient. Idiopathic angioedema was also considered; however, the associated severe myalgia and functional limitation were not consistent with typical presentations.

Fibromyalgia is increasingly recognized as a disorder of central sensitization, wherein patients may experience subjective swelling due to altered nociceptive signaling. Neurogenic inflammation mediated by substance P and other neuropeptides may contribute to vasodilation and perceived edema. Additionally, autonomic dysregulation in fibromyalgia may further exaggerate such symptoms.

The presence of benign joint hypermobility in this patient may have further contributed to pain amplification and symptom severity. The significant clinical improvement with neuromodulators such as duloxetine and pregabalin strongly supports a central pain processing mechanism rather than an immunological or allergic cause.

Diagnostic Approach (Flow-Style – Required)

Diagnostic Approach (Stepwise Reasoning)

Rule out allergic angioedema → No urticaria, normal IgE

Rule out hereditary angioedema → Normal C1 esterase inhibitor

Rule out autoimmune disease → ANA negative

Rule out endocrine causes → Thyroid function normal

Rule out inflammatory myopathy → CK normal

Consider rheumatological cause → Fibromyalgia with hypermobility confirmed

Conclusion

This case highlights the diagnostic overlap between angioedema and fibromyalgia. In patients with recurrent swelling and normal immunological workup, fibromyalgia should be considered as a differential diagnosis. Multidisciplinary evaluation is essential for appropriate diagnosis and management.

This case highlights the importance of considering fibromyalgia as a potential mimicker of angioedema in patients presenting with recurrent swelling and normal immunological workup. Recognition of this overlap is crucial to avoid misdiagnosis and unnecessary treatment. A structured, multidisciplinary diagnostic approach is essential for accurate diagnosis and optimal patient management.

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