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Type I Hereditary Angioedema Presenting with Recurrent Life-Threatening Facial and Laryngeal Edema: A Rare Case Report from India's Severely Underdiagnosed Population

Dr. Zaveri Yash Manishkumar[1], Dr. Shailja Swarnkar[2], Dr Patel Dev Manish[3], Dr. Ashutosh Farkya[4], Dr. Vivek Patidar[5], Prof. Dr. Bushra Khanam[6]

[1,2,3]2nd Year Postgraduate Resident, Index Medical College hospital and research center, Indore (MP)
[4,5]1st Year Postgraduate Resident, Index Medical College hospital and research center, Indore (MP)
[6]Prof. Index Medical College hospital and research center, Indore (MP)

Abstract

Background:
Hereditary angioedema (HAE) is a rare autosomal dominant disorder caused by C1 esterase inhibitor (C1-INH) deficiency or dysfunction, leading to bradykinin-mediated, non-pitting, non-pruritic edema. Type I HAE, the most common subtype, accounts for approximately 85% of cases. While the global prevalence is ~1 in 50,000, fewer than 500 confirmed cases have been reported from India, suggesting significant underdiagnosis.

Case Presentation: We report a biochemically confirmed case of Type I HAE in a male patient with recurrent, non-urticarial swelling involving the face, lips, eyelids, and neck, often progressing to laryngeal involvement requiring intubation. Complement studies revealed decreased serum C4 (<5.9 mg/dL) and reduced C1-INH function (65%), confirming the diagnosis. Imaging excluded infectious or allergic causes. The patient was stabilized and advised long-term HAE-specific prophylaxis.

Conclusion: This case underscores the diagnostic challenges of HAE in India and highlights the need for broader clinician awareness, early complement testing, and national registry initiatives to improve patient outcomes.

Keywords: Hereditary angioedema, Type I HAE, C1 esterase inhibitor deficiency, recurrent angioedema, airway obstruction, India, underdiagnosis.

Introduction

Hereditary angioedema (HAE) is a rare genetic disorder caused by a deficiency (Type I) or dysfunction (Type II) of C1 esterase inhibitor (C1-INH), leading to excessive bradykinin production and increased vascular permeability [1]. Clinically, it presents with recurrent episodes of non-pruritic, non-pitting edema

affecting the skin, gastrointestinal tract, and airway. Attacks can be spontaneous or triggered by trauma, stress, hormonal changes, or infections [2].

Type I HAE constitutes 85% of all cases and is diagnosed by low C4 and reduced quantitative or functional C1-INH levels. Globally, the estimated prevalence of HAE is ~1 in 50,000 individuals [3]. In India, despite a theoretical burden of over 27,000 cases, fewer than 500 patients have been reported, reflecting a significant diagnostic gap [4,5]. Misdiagnosis as allergic angioedema is common, delaying appropriate management and increasing morbidity and mortality risks.

Here, we present a rare, biochemically confirmed case of Type I HAE with recurrent facial and laryngeal angioedema, contributing valuable clinical and epidemiological data from India.

Case Presentation

A young male patient presented with multiple episodes of recurrent facial swelling over several years. The swellings were sudden in onset, non-pitting, and non-pruritic, involving the lips, cheeks, eyelids, and at times the neck. There was no history of urticaria, rash, fever, drug intake, or known allergies. Several episodes progressed to respiratory distress, requiring emergency intubation.

On physical examination during an acute episode, the patient had gross facial swelling with mild hoarseness of voice but stable hemodynamics. There were no signs of infection or anaphylaxis.

Investigations:

- **Serum C4:** <5.9 mg/dL (significantly decreased)
- **C1-INH functional assay:** 65% of normal (decreased)
- **C1q levels:** Within normal range
- **CBC, ESR, CRP:** Normal
- **ANA, IgE, eosinophil count:** Normal
- **CT Head and Neck:** Demonstrated diffuse soft tissue swelling without abscess or cellulitis
- **AFB stain, sputum GeneXpert:** Negative

Based on clinical history and laboratory findings, a diagnosis of **Type I Hereditary Angioedema** was established. The patient was treated supportively with IV fluids and oxygen, and **fresh frozen plasma (FFP)** was administered during acute attacks. He was counseled on the nature of his disease and educated regarding prophylactic therapy options, including attenuated androgens, antifibrinolytics, and newer agents like lanadelumab (where available).

Discussion

Hereditary angioedema is a bradykinin-mediated disorder, fundamentally distinct from histaminergic (allergic) angioedema. Its episodes are typically non-responsive to antihistamines, corticosteroids, or epinephrine, which can mislead clinicians and delay diagnosis [6]. Our patient had classical symptoms—recurrent swelling without urticaria, normal IgE and eosinophils, poor response to anti-allergic therapy, and life-threatening airway involvement.

The diagnostic hallmark of HAE includes **low C4**, **low C1-INH (functional or quantitative)**, and **normal C1q (to differentiate from acquired angioedema)** [2,7]. Imaging during acute episodes helps exclude differential diagnoses such as cellulitis, abscess, or trauma. Early identification is essential because untreated airway attacks have a reported mortality of up to 30% [8].

India lacks a centralized HAE registry, and awareness remains low. A 2023 multicenter study reported that fewer than 500 Indian patients have been formally diagnosed and reported in peer-reviewed literature, in contrast with a projected prevalence exceeding 27,000 cases [4]. Therefore, every confirmed case adds valuable insight and highlights the urgent need for:

- **Increased clinical suspicion in recurrent angioedema without urticaria**
- **Wider availability of C4/C1-INH testing**
- **National registry and treatment access programs**

Conclusion

This case represents a classic phenotype of **Type I Hereditary Angioedema**, confirmed biochemically, and complicated by life-threatening airway involvement. It reinforces the importance of early diagnosis through complement testing in patients with atypical or unexplained angioedema, especially in countries like India where underdiagnosis is widespread. Timely recognition and appropriate management can significantly reduce HAE-related morbidity and mortality.

References

1. Longhurst HJ, et al. Hereditary angioedema: impact of diagnosis and treatment on quality of life. *Clin Rev Allergy Immunol*. 2016;51(2):193–206. PubMed
2. Craig T, et al. WAO guideline for the management of hereditary angioedema. *World Allergy Organ J*. 2012;5(12):182–199. PMC
3. Bygum A, et al. International WAO/EAACI guidelines for HAE – 2021 update. *World Allergy Organ J*. 2021;14(12):100651. PMC
4. Katkar P, et al. Deciphering the landscape of hereditary angioedema in India. *Indian J Dermatol Venereol Leprol.* 2023;89(2):225–230. IJDVL
5. Aygören-Pürsün E, et al. Hereditary angioedema: diagnostic challenges and real-world management. *Front Med*. 2020;7:870. PMC
6. Nacmias B, et al. Hereditary angioedema: experience from a large tertiary center. *Allergy Asthma Proc.* 2018;39(6):472–478. PubMed
7. Cicardi M, et al. Classification, diagnosis, and approach to therapy in HAE. *Allergy Asthma Proc.* 2014;35(3):184–190.
8. Agostoni A, et al. Pathophysiology of angioedema. *Clin Exp Immunol*. 2005;139(3): 404–409.