Histaminergic Angioedema

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KEYWORDS

• Angioedema • Histamine • Urticaria • Histaminergic • Inducible urticaria
• Spontaneous urticaria

KEY POINTS

- Angioedema, which involves the development of nonpitting edema affecting deep cutaneous layers and mucosal tissues, can be histamine or bradykinin mediated. Determining the subtype of angioedema is critical for the choice of therapy.
- Histamine-mediated angioedema is clinically distinguished by symptoms' duration (acute and chronic), the presence or absence of urticaria, and whether there are known factors inducing symptoms or not.
- Histaminergic angioedema is secondary to mast-cell and basophil activation, and therefore, the mainstay of treatment includes antihistamines, corticosteroids, and epinephrine (for emergency use).

INTRODUCTION

Angioedema is a result of increased vascular permeability with subsequent extravasation of intravascular fluid into the surrounding tissues, which include the skin, gastrointestinal (GI) tract, and upper airways.[1] Angioedema can be broadly classified into 3 categories based on the underlying mechanism and mediator producing symptoms:

1. Histaminergic angioedema
2. Bradykinin-mediated angioedema (eg, hereditary angioedema [HAE], ACE inhibitor–induced angioedema, and acquired C1 inhibitor deficiency, discussed in other articles in this issue)
3. Causes of unknown mechanisms.

There are certain key features of symptom onset and presentation that help evaluate whether angioedema is histamine or bradykinin mediated (**Table 1**). Determining

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Table 1
Differential features of histamine- versus bradykinin-mediated angioedema

Features	Histamine Mediated	Bradykinin Mediated
Rash	Urticaria	No urticaria, occasional erythema marginatum
Family history	Atopy	Recurrent angioedema in 75% of patients with HAE
Onset/duration of symptoms	Rapid; 24–48 h	Typically slower; 3–5 d
Pruritus	Present	None, may be painful
Response to antihistamines/CS/Epi	+	–

Abbreviations: CS, corticosteroids; Epi, epinephrine.

the category of angioedema is critical for its treatment. For example, histaminergic angioedema responds to antihistamines, corticosteroids, or epinephrine, whereas bradykinin-mediated angioedema requires medications targeting this peptide and/or its pathway. Histaminergic angioedema is the most common form of angioedema and is subdivided into acute and chronic forms based on its duration of symptoms (acute <6 weeks; chronic >6 weeks) (Fig. 1). Histaminergic angioedema is further classified as that occurring with or without urticaria (wheals). The organization of histaminergic angioedema in this review is derived from several sources: the 2014 Hereditary Angioedema International Working (HAWK) Group consensus report on angioedema,[2] the European Academy of Allergy and Clinical Immunology (EAACI), Global Allergy and Asthma European Network (GA^{2}LEN), European Dermatology Forum (EDF), World Allergy Organization (WAO) urticaria guideline (EAACI/GA^{2}LEN/EDF/WAO),[3] and the American Academy of Allergy, Asthma, and Immunology/American College of Allergy, Asthma, and Immunology Joint Task Force (JTF) guideline.[4] This article reviews the

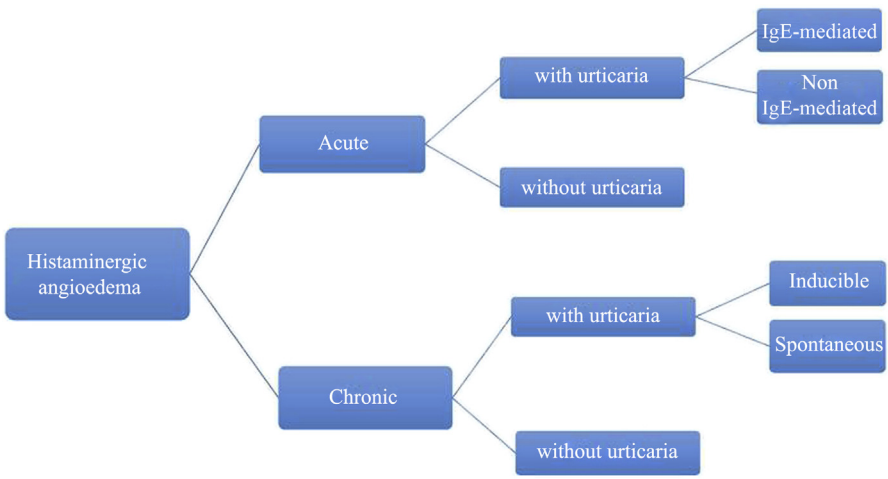

Fig. 1. Schematic of histaminergic angioedema.