Case Report

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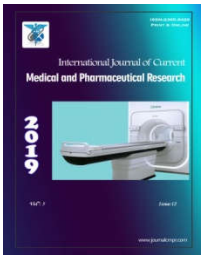

RECURRENT HEREDITARY ANGIOEDEMA IN CHILDREN: CASE REPORT

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ABSTRACT

Hereditary angioedema (HAE) is a condition characterized by recurrent episodes of angioedema affecting the upper airway, bowel wall, or skin, which typically last two to four days. The angioedema of HAE is mediated by bradykinin and does not respond to epinephrine, antihistamines, or glucocorticoids. Instead, first-line therapies for HAE act by replacing the C1 inhibitor (C1INH) that is deficient or dysfunctional in this disease or by inhibiting the production or function of bradykinin. HAE affects men and women equally. There are no known racial predilections. Although symptoms often begin in childhood, the disease is commonly diagnosed during puberty or early adulthood, when attacks become more frequent. An attack of HAE usually involves one site at a time (skin, viscera, or larynx). A prodrome of fatigue or erythematous rash is noticed by some patients. Attacks build in severity for 24 hours and then subside over the next 24 to 72 hours. Once attacks have begun, they generally continue throughout the patient's life, although the frequency of attacks can be dramatically reduced by therapy. The mortality rate for patients with HAE, despite effective therapies, has been estimated to be as high as 13 percent.

INTRODUCTION

Hereditary angioedema (HAE) is a disease characterized by recurrent episodes of angioedema, without urticaria or pruritus, which most often affect the skin or mucosal tissues of the upper respiratory and gastrointestinal tracts. Although the swelling is self-limited, laryngeal involvement may cause fatal asphyxiation. Prior to the availability of effective therapy, this disorder was associated with a mortality rate of approximately 30 percent due to asphyxiation from laryngeal swelling. [1]

The prevalence of hereditary angioedema (HAE) is estimated at 1 individual per 50,000, with reported ranges from 1:10,000 to 1:150,000 [1]. Males and females are affected equally, and there are no known differences in prevalence among ethnic groups [2,3,4].

The age at which attacks begin is variable, with rare reports of initial episodes of angioedema in the perinatal period. Approximately 40 percent of patients experience their first attack before age 5, and 75 percent, by age 15, although repeated attacks in preadolescent children are uncommon. Thus, for the majority of patients, the disease first presents in childhood or adolescence. Attack frequency usually increases after puberty. In most cases, the diagnosis is eventually made in the second or third decade of life and can be further delayed if there is no family history.[6]

An attack of HAE usually involves one site at a time (skin, viscera, or larynx). A prodrome of fatigue or erythematous rash is noticed by some patients. Attacks build in severity for 24 hours and then subside over the next 24 to 72 hours. The most life-threatening type of attack involves the upper airway, and any swelling in this area should be regarded as an emergency. Laryngeal attacks usually develop over hours, but there are reports of precipitous airway closure. Laryngeal edema occurs in approximately one-half of all patients over their lifetimes, although only a few percent experience recurrent episodes. [6]

There are several types of HAE

Types I and II result from deficiency or dysfunction of C1 inhibitor (C1INH), respectively, and are collectively called HAE with C1INH deficiency (C1INH-HAE). C1INH plays a role in regulating bradykinin production. However, the precise mechanisms by which these defects predispose to episodic angioedema are not understood. Complement studies are abnormal in C1INH-HAE. In at least 90 percent of patients with C1INH-HAE, plasma levels of complement component 4 (C4) are always low, even during asymptomatic periods, and

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thus, C4 is a good screening test. The inheritance pattern of C1INH-HAE is autosomal dominant, although 25 percent of cases result from de novo mutations, and occasional affected individuals may be asymptomatic.

The other types of HAE are characterized by normal complement studies. At least four disorders have been defined: HAE associated with variants in the genes for factor XII (FXII-HAE), angiopoietin-1 (***ANGPT1***), or plasminogen and HAE of unknown etiology (U-HAE). [7,8,9]

Case Report

Child of six years, male and born in Manaus (AM). She has a facial edema (especially in the eyelid and labial mucosa) since 4 months of age, also accompanying itching and non-painful hands and feet, without other signs and symptoms. The signs and symptoms recorded after therapeutic management with antihistamines and corticosteroids, or recorded spontaneously. Sheshowed a progressive increase in the number of seizures since the age of four, with great demand for medical attention in the emergency room. Due to the clinical picture, the child had as a diagnostic hypothesis of hereditary angioedema (HAE), confirmed by the detection of low C4 levels (below 8 mg / dL - RV: 19 to 52 mg / dL). The values of fractions C1q and C3 were normal. In September 2019, at 6 years and 4 months of age, seek care at the emergency department showed bilateral eyelid and labial edema, difficult in the left jaw region after dental treatment. She underwent fresh frozen plasma therapy for three days and was discharged after five days, asymptomatic.

COMPLEMENTO C4		Valor de referência
Resultado:	Inferior a 8 mg/dL	19 a 52 mg/dL

Método..: TURBIDIMETRIA
Material: SORO

Resultado conferido e liberado

Figure 1 Low C4 level

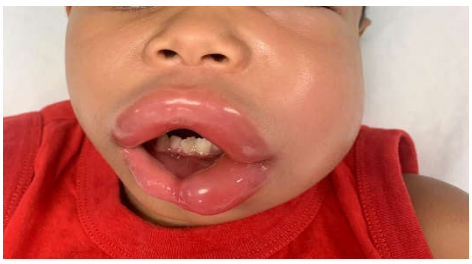

Figure 2 Bilateral eyelidand labial edema

DISCUSSION

Hereditary angioedema (abbreviated HAE throughout this review) is a rare autosomal dominant disorder characterized by recurrent episodes of well-demarcated angioedema without urticaria, which most often affects the skin or mucosal tissues of the upper respiratory and gastrointestinal tracts. Although swelling resolves spontaneously in two to four days in the absence of treatment, laryngeal edema may cause fatal asphyxiation, and the pain of gastrointestinal attacks may be incapacitating or lead to unnecessary abdominal surgery. The most common forms of HAE (types I and II) are caused by deficiency or dysfunction in C1 inhibitor (C1INH-HAE) [1].

Attacks of HAE are commonly categorized as laryngeal, gastrointestinal, or cutaneous. Laryngeal attacks are the least common but most dangerous type of attack because airway obstruction can progress to asphyxiation and death. More than one-half of all HAE patients experience a laryngeal attack at some point [2]. Therefore, all patients should be educated about the early signs and symptom of laryngeal attacks, even if the individual has never experienced one.

Gastrointestinal attacks can range from mild to severe but usually resolve without serious complications, unless the patient undergoes unnecessary surgical interventions because the disorder is not recognized as HAE . Cutaneous attacks are not associated with significant risk of serious complications or death but often cause substantial morbidity, as patients' lives can be significantly disrupted by repeated episodes [3].

First-line therapies for HAE are:

- Human plasma-derived C1INH concentrate;
- Recombinant human C1INH (rhC1INH);
- Icatibant, a bradykinin B_2-receptor antagonist;
- Ecallantide, a kallikrein inhibitor (available only in the United States)
- If none of the first-line agents are available, then the approach to treatment depends upon the type and severity of attack:
- For patients with any laryngeal edema or moderate-to-severe gastrointestinal attacks, we suggest solvent-detergent-treated plasma or if not available, fresh frozen plasma;
- For patients with mild gastrointestinal attacks, we suggest supportive therapy (rehydration and symptomatic therapy);
- For patients with cutaneous attacks not involving skin adjacent to the airway, we suggest no treatment. [10,11]

CONCLUSION

Hereditary angioedema (HAE) is a rare condition characterized by recurrent episodes of angioedema, without urticaria or pruritus, which most often affect the skin or mucosal tissues of the upper respiratory and gastrointestinal tracts. It is predominantly mediated by bradykinin, a potent vasodilatory peptide, although other mediators may be involved [1]. Patients with HAE (of any type) do not respond to antihistamine therapy. Most patients with HAE have been given antihistamines and glucocorticoids multiple times in the past without benefit, like in this case. Our approach to evaluation and testing depends upon whether the clinical suspicion is low or high because this determines how extensive complement testing should be. The complemente C4 alone is an adequate screening test [7]. In this case complemente C4 is low.

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