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EXPERT'S CORNER: A PERSONAL APPROACH

Anaphylaxis: Practical aspects of diagnosis and treatment

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Introduction

Anaphylaxis is a severe systemic allergic reaction that is rapid in onset and is potentially fatal. Its severity varies in relation to the affected organs and the intensity of the damage to these. The more severe forms are associated with airway obstruction (laryngeal edema, severe bronchoconstriction) and/or vascular collapse (anaphylactic shock).[1,2]

The frequency of anaphylaxis ranges from 0.03% to 0.95%. Its lifetime can be of up to 2.6%. Although anaphylaxis occurs more frequently in children and adolescents, fatal cases are more common in adults. Even though mortality rates are sub-reported, it is estimated to occur in 0.65–2% of severe anaphylaxis cases. Laryngeal edema and cardiovascular complications are the main cause of death.[2–6]

Anaphylaxis can occur as a consequence of immunological and non-immunological mechanisms. In general, the most frequent form of anaphylaxis is associated with IgE-mediated hypersensitivity reactions. Nevertheless, aside from the mechanism involved in the onset of response, a common pathophysiological characteristic of anaphylaxis is the degranulation of basophils and mast cells, with the consequent liberation of mediators of inflammation, including histamine, leukotrienes and prostaglandins. The action of these mediators in the skin, mucous membranes, airways, gastrointestinal tract, cardiovascular system, and other target organs, originates the signs and symptoms of anaphylaxis.[2,4] The most common causes of anaphylaxis are medications, drugs and hymenoptera venoms. Other causes of anaphylaxis mediated by immunological mechanisms include allergen immunotherapy, latex, occupational allergens, seminal fluid, aeroallergens and monoclonal antibodies. Exercise, some physical factors (cold, heat and radiation), ethanol, opioid medications and contrast media, may cause non-immunological anaphylaxis. Idiopathic anaphylaxis, where it is not possible to identify the cause, represents over 20% of all anaphylaxis cases.[2–7]

Anaphylaxis is characterized by a varied clinical presentation and its manifestations include skin, respiratory, ocular, cardiovascular and gastrointestinal symptoms. Vital functions are compromised in the most severe forms, and if this occurs during the first minutes after the onset of the reaction, the risk of death is greater.[1,2,8,9]

Over 90% of the patients display skin symptoms. Most episodes begin with pruritus and flushing and continue with the progressive development of hives and/or angioedema. Eyes and mucous membranes can acquire a congestive-like aspect, changes generally associated with intense itching, epiphora and rhinorrhea. Gastrointestinal symptoms include abdominal pain, nausea, vomiting, and diarrhea. At a respiratory level, the symptoms can include tightness in the throat, dysphagia, dysphonia, inspiratory stridor

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and even signs of asphyxia, which is caused by the generation of laryngeal edema. On the other hand, cough, dyspnea, wheezing, a feeling of tightness in the chest may onset as a consequence of bronchoconstriction, which can also cause hypoxemia and cyanosis. Cardiovascular manifestations may onset with tachycardia and a feeling of dizziness or instability, and progress until the loss of consciousness. Peripheral vasodilatation and the increase in vascular permeability, characteristics of anaphylaxis, lead to hypotension and shock, which increase heart rate and reduce coronary perfusion. These cardiovascular changes, in addition to hypoxemia related to the obstruction of the airways, reduce cardiac oxygenation and may lead to arrhythmias and myocardium necrosis, which are causes of cardiac arrest. In some cases, anaphylaxis onset can be abrupt, like syncope, or even cause sudden death. Other manifestations that may occur during anaphylaxis are; disorientation, anxiety, seizures and profuse sweating.[1,2,8–11]

Approximately 20% of patients presenting anaphylaxis may suffer biphasic reactions. In these cases, the late phase begins between 1 and 72 h after the initial phase, usually with similar clinical manifestations. No clinical data has been identified which allows the prediction of risk of late reactions in a trustworthy manner. However, the patients who present severe initial reactions may have a greater risk of suffering biphasic reactions.[1,8,9]

Diagnosis

The diagnosis of anaphylaxis is fundamentally clinical. Clinical history constitutes the most important tool in the identification of a patient who is suffering from anaphylaxis and it is also of great help to identify its cause. In addition to the detailed description of signs and symptoms present in the patient, it is important to obtain information about the moment of onset of the reaction, medication used to treat it, the duration of the episode and exposure to allergens or potential triggers. Whenever possible, we ought to question the people who witnessed the event.[9–13]

Useful clinical criteria have been established for the diagnosis of anaphylaxis, which are listed in Table 1. With the proper use of these criteria, it is possible to identify over 95% of anaphylaxis cases.[1]

During the clinical evaluation of the patient, we should always consider other conditions which may occur with similar signs and symptoms to those of anaphylaxis. Differential diagnoses include: vasovagal reactions, anxiety, myocardial dysfunction, pulmonary embolism, foreign body aspiration, poisoning, hypoglycemia, convulsive disorders, urticaria and angioedema, hereditary angioedema and asthma. Although urticaria and angioedema may occur up to 90% of anaphylaxis episodes, when it occurs without affecting other organs or systems, it does not correspond to anaphylaxis cases.[9–13]

Serum tryptase, plasmatic histamine and histamine metabolites in urine (methyl-histamine) may be useful to confirm an anaphylaxis diagnosis. The best time for its measurement after the onset of the anaphylaxis episode is between 1 and 6 h for serum tryptase, from 10 min to 1 h for histamine and during the first 24 h for methyl-histamine. Nevertheless, these studies are not always available and the administration of the treatment should not be delayed.[1,10–14]

On the other hand, as a part of the attention in the emergency service, in moderate to severe anaphylaxis, it is convenient to perform a complete blood count, metabolic panel, arterial blood gas, and chest x-rays in order to assess the patient's general condition as well as rule out other diagnoses.[9,11–13,15]

Treatment

Timely treatment considerably reduces the risk of mortality in patients with anaphylaxis. Management ought to begin

Table 1 Clinical criteria for anaphylaxis diagnosis.

The probability of anaphylaxis in a patient is high when at least one of the following three criteria are met:
1. Acute onset (from a few minutes to a few hours) of a condition characterized by affectation of the skin and/or mucous (ex. hives, itching or generalized flushing/edema of the lips, tongue and/or uvula)
AND AT LEAST ONE OF THE FOLLOWING
a. Compromised breathing (ex. dyspnea, wheezing [bronchospasm], stridor, reduced PEF, hypoxemia)
b. Arterial hypotension or symptoms associated with circulatory compromise (e.g. hypotonia [collapse], syncope, incontinence)
2. Two or more of the following situations which occur rapidly after exposure to a *probable* allergen (a few minutes to a few hours):
a. Affectation of the skin and/or mucous (ex. hives, itching or generalized flushing/edema of the lips, tongue and/or uvula)
b. Compromised breathing (ex. dyspnea, wheezing [bronchospasm], stridor, reduced PEF, hypoxemia)
c. Arterial hypotension or symptoms associated with circulatory compromise (e.g. hypotonia [collapse], syncope, incontinence)
d. Persistent gastrointestinal symptoms (ex. crampy abdominal pain, vomiting)
3. Hypotension after exposure to a known allergen for this patient (a few minutes to a few hours)
a. Children: low systolic BP (according to age) or a reduction greater than 30% in the systolic BP
b. Adults: systolic BP less than 90 mm Hg or a decrease greater than 30% in the systolic BP

Source: Adapted from Sampson H.A., et al. J Allergy Clin Immunol 2006;117: 391-7.
PEF, peak expiratory flow; BP, blood pressure.
*Low systolic blood pressure in children is defined as less than 70 mm Hg in children from 1 month to 1 year old; less than 70 mm. Hg + 2× years of age, in children from 1 to 10 years old, and less than 90 mm Hg in patients from 11 to 17 years old.