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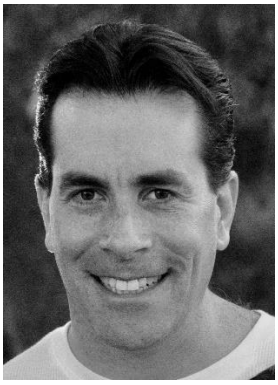

Anaphylaxis in Children

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Introduction

Anaphylaxis in children is one of the most feared acute systemic reactions that any pediatric physician, generalist or subspecialist, may ever come across. The fear stems from the cardiorespiratory compromise that can result in neurologic injury and even death in an otherwise normal, healthy child. However, with the recognition, anticipation of symptom progression, and prompt management of anaphylaxis, these devastating sequelae can be avoided.

Anaphylaxis is the term used for the most severe and, potentially, life-threatening manifestation of an allergic reaction incited by an allergen. The most common allergens that we associate with childhood allergic reactions are foods (37% - 85%), insect bites/stings (5% - 13%), and medications (5% - 12%).[1] For foods, milk products (19% - 29%), peanuts (9% - 36%) and tree nuts (9% - 19%), eggs (5% - 22%), shellfish (4% - 17%), and fruits/vegetables (9%) are the most common offenders.[1] But, allergic reactions can stem from almost anything. The severity of the allergic reaction can range from mild cutaneous urticaria to severe anaphylaxis.

Pathophysiology

Anaphylaxis is mediated by immunoglobulin E (IgE). An allergen induces IgE activation and binding to basophils in the blood and mast cells in the tissue, as well as various other cell types. However, it is the stimulation of mainly mast cells and basophils that causes the release of histamines, various proteases, and other inflammatory mediators, such as leukotrienes (i.e., cysteinyl leukotriene), platelet-activating factor, prostaglandins, and cytokines/chemokines, which cause the various clinical manifestations that we witness (Figure 1).[2] While the clinical signs and symptoms of anaphylaxis occur quite rapidly, a

minority of patients may exhibit a biphasic allergic reaction, where signs and symptoms of anaphylaxis recur hours after the initial reaction has subsided.[2] Blocking the effects of the histamines and various inflammatory mediators is the foundation of anaphylaxis therapy.

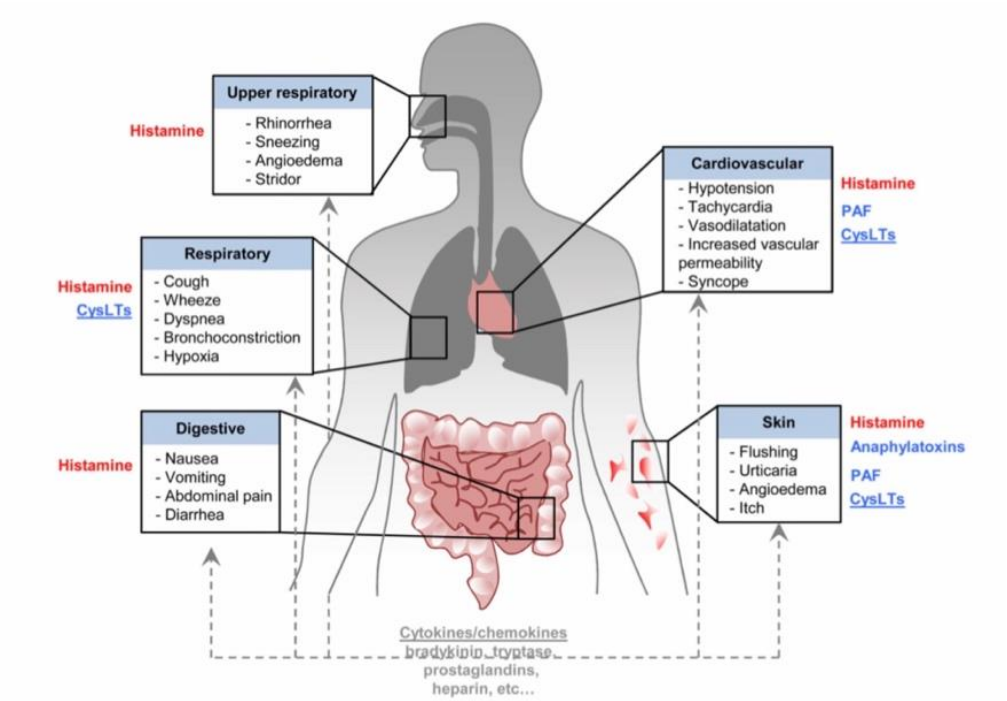

Figure 1. Clinical symptoms of anaphylaxis caused by various mediators.[2] *PAF = platelet-activating factor; CysLTs = cysteinyl leukotrienes.*

Clinical symptoms

Anaphylaxis may include a variety of cutaneous, cardiovascular, respiratory, and gastrointestinal symptoms. Nevertheless, absence of cutaneous symptoms does not exclude anaphylaxis from being present. Some of these symptoms include urticaria and angioedema, dyspnea, wheezing, upper airway obstruction from edema, nausea, vomiting, diarrhea, abdominal pain, dizziness, syncope, and hypotension (Figure 1).[2] Occasionally, headache, rhinitis, substernal chest pain, pruritus, and seizures can occur as well.[2,3] Ultimately, the most feared complications are respiratory distress and hypoxemia from airway compromise due to upper airway obstruction and bronchiolar narrowing due to bronchospasm, as well as cardiovascular collapse from hypotension due to vasodilation.

Management

The initial management is determined by the amount of cardiorespiratory compromise. Respiratory distress and hypotension require immediate attention. In severe cases of anaphylaxis with respiratory distress, immediate administration of an intramuscular injection of epinephrine and oxygen are critical.[1] If hypotension is also present,

intravenous isotonic fluids are required additionally. If the patient is being seen in the outpatient setting and the ability to manage and monitor the patient is limited, emergency medical services should be contacted simultaneously to have the patient transported to the nearest hospital for further care and evaluation. Anaphylaxis often occurs immediately, but can have a delayed reaction 3 to 6 hours after ingestion of an allergen as well. Anaphylaxis can be protracted, lasting for more than 24 hours, in some cases.[3] So, extended monitoring for recurrence or persistence of the anaphylactic reaction may be part of the management plan, depending on the severity of the reaction and the patient's medical history. Longer periods of observation of 4 to 8 hours after epinephrine administration or even admission to the hospital would be prudent in patients with risk factors such as asthma, previous biphasic or prolonged anaphylactic reactions, the requirement of repeated doses of epinephrine, wheezing, hypotension, or pharyngeal edema, whereas observation of no longer than 3 to 4 hours is recommended for low-risk patients after epinephrine administration with rapid resolution of symptoms.[4]

Epinephrine's effect is mediated by stimulation of alpha-1, beta-1, and beta-2 adrenergic receptors.[2] It stimulates alpha-1 adrenergic receptors to induce vasoconstriction to reduce tissue/airway edema and hypotension. Beta-1 adrenergic receptor stimulation increases the heart rate and contractility. Beta-2 adrenergic receptor stimulation relaxes smooth muscle in the airways and blocks further release of mediators from mast cells (i.e., histamine). The onset of action of epinephrine is almost immediate, but the effects may be transient and repeat doses of epinephrine may be required (every 5 to 15 minutes, as necessary). Other medications, used as adjuncts to epinephrine, require a bit more time to take effect, but last longer. They can be used to diminish the histamine and pro-inflammatory effects after the epinephrine effects become attenuated over time. Because histamines have 2 types of receptors, H1 and H2, histamine blockers for each receptor type should be used. Diphenhydramine blocks the H1 receptors and an H2 receptor antagonist, such as ranitidine, can block the H2 receptor effectively. H2 receptor-antagonists should be used in severe allergic reactions in conjunction with H1 receptor-antagonists, but should not replace them. Inhaled beta-2 adrenergic receptor agonists (such as albuterol) are useful treatments for the bronchospasm induced by the histamines and proinflammatory mediators. Finally, corticosteroids should be administered to attenuate the entire inflammatory response. While all of these adjuncts to epinephrine are useful to treat anaphylaxis, their use should only be initiated after epinephrine has been administered in the case of an anaphylactic reaction and not as a substitution for epinephrine.[1]

Prognosis

While anaphylaxis is a rare occurrence and the prognosis is relatively good, the number of visits for anaphylaxis from all sources appears to have increased from 5.7 to 11.7 per 10,000 visits to the ER from 2009 to 2013.[5] However, the mortality rate has been stable at 0.047 cases per 100,000 population.[5] It appears that a delay in epinephrine delivery is associated with a greater risk of fatal anaphylaxis.[5] With food-related anaphylaxis, approximately 50% of children presenting to the ER will be admitted to the hospital with almost 4% requiring admission to the intensive care unit.[4] Risk factors for hospitalization

for food related anaphylaxis include age < 1 year of age, reaction to tree nuts, and children with asthma or other complex chronic medical conditions.[4]

Conclusion

Anaphylaxis is one of the most feared acute systemic reactions that no pediatric physician, generalist or subspecialist, ever wants to witness. Nevertheless, even in the worst anaphylaxis episodes, prompt recognition and management will result in complete recovery and avoid the most severe complications. Preparation and education of families and medical personnel who care for children at risk for severe allergic reactions can make anaphylaxis a little less scary.

References

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