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Original Article

Different clinical features of anaphylaxis according to cause and risk factors for severe reactions

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Abbreviations:
ED, emergency department; NOS, Not otherwise specified; KCD, Korean standard classification of disease; MAST, multiple allergosorbent test; WBC, white blood cell; ECP, eosinophil cationic protein; AST, aspartate transaminase; ALT, alanine transaminase; NSAIDs, nonsteroidal anti-inflammatory drugs; CT, computed tomography

ABSTRACT

Background: Anaphylaxis is a life-threatening allergic reaction. Several studies reported different anaphylactic reactions according to the causative substances. However, a comparison of anaphylaxis for each cause has not been done. This study was conducted to identify common causes of anaphylaxis, characteristics of anaphylactic reaction for each cause and to analyze the factors related to the severity of the reaction.

Methods: Medical records of patients who visited the emergency room of Ewha Womans University Mokdong Hospital from March 2003 to April 2016 and diagnosed with anaphylactic shock were retrospectively reviewed. We compared the clinical features of anaphylaxis according to the cause. In addition, the severity of anaphylaxis was analyzed and contributing factors for severe anaphylaxis were reviewed.

Results: A total of 199 patients with anaphylaxis were analyzed. Food was the most common cause (49.7%), followed by drug reaction (36.2%), bee venom (10.1%), and unknown cause (4.0%). Cardiovascular symptoms of syncope and hypotension were more common in drug-induced anaphylaxis. The incidence of severe anaphylaxis was the highest in anaphylaxis due to drugs (54.2%). Urticaria and other skin symptoms were significantly more common in food-induced anaphylaxis. Risk factors for severe anaphylaxis included older age, male, and drug-induced one. Epinephrine treatment of anaphylaxis was done for 69.7% and 56.9% of patients with food-induced and drug-induced anaphylaxis, respectively.

Conclusions: More severe anaphylaxis developed with drug treatment and in males. Low rate of epinephrine prescription was also observed. Male patients with drug induced anaphylaxis should be paid more attention.

Introduction

Anaphylaxis is a severe systemic allergic reaction in which typical symptoms that include systemic urticaria, angioedema, dyspnea, abdominal pain, and hypotension, develop immediately or within minutes upon exposure to the allergen.[1,2] Timely and appropriate treatment is crucial, as the reaction progresses rapidly and affects several organs. It can be fatal in some cases.[3] The prevalence of anaphylaxis in the general population in the United States reportedly exceeds 1.6%.[4] In Europe, the frequency is 1.5–7.9 cases per 100,000 people.[5] In South Korea, the precise prevalence has not been reported, but data suggest that 7.2 patients per 10,000 patients visited the emergency department (ED) because of anaphylaxis.[6]

Anaphylaxis is multifactorial, and its etiology varies according to region and race.[4,5,7] Moreover, clinical symptoms may vary from patient to patient, even when the same allergen is involved. These variations have complicated research on anaphylaxis.

It is important to identify the causes and risk factors for severe and potentially fatal anaphylaxis, to prevent allergen re-exposure and to manage subsequent anaphylactic episodes.[8,9] Accordingly, this study aimed to investigate the clinical manifestations among anaphylactic patients. Particularly, this study sought to identify different clinical features of anaphylaxis according to causes and risk factors for severe anaphylaxis.

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Methods

Patients

We searched the electronic medical records of patients who visited the ED at Ewha Womans University Mokdong Hospital, a tertiary hospital in Seoul, South Korea, between March 2003 and April 2016, and who were diagnosed with anaphylactic shock, unspecified (T782), anaphylactic reaction Not Otherwise Specified (NOS) (T78202), anaphylaxis NOS (T78203), anaphylactic shock due to adverse effect of a correctly prescribed drug or medication that was properly administered (T886) according to Korean standard classification of disease (KCD). Electronic medical records were reviewed by an allergist, and cases meeting the definition of anaphylaxis were selected.[10,11] The study was approved by the Institutional Review Board at Ewha Womans University Mokdong Hospital and it met the ethical principles of the Declaration of Helsinki. IRB waived informed consents of patients because this was a retrospective chart review study and patient anonymity was preserved using methods approved by the Ethics Committee (Ewha Womans University Mokdong Hospital IRB number: 2017-02-020-001).

Anaphylaxis

As previously described, anaphylaxis was diagnosed when any one of the following three criteria were fulfilled.[10,11] First, symptoms occurred suddenly (within a few hours) in the skin and mucous membranes (systemic urticaria, itching, flushing, lip-tongue-uvula edema) plus either respiratory symptoms (dyspnea, wheezing, stridor, hypoxemia) or cardiovascular symptoms (syncope, hypotension, urinary incontinence, chest discomfort). Second, two or more of the following occurred rapidly (within a few hours) after exposure to a suspected allergen: (i) involvement of skin-mucosal tissues, (ii) respiratory symptoms, (iii) reduced blood pressure or associated symptoms, and (iv) persistent gastrointestinal symptoms (crampy abdominal pain, vomiting, diarrhea). Third, blood pressure reduction occurred suddenly (within a few hours) after exposure to known allergen for the patient. Severity of anaphylaxis was classified as mild, moderate, or severe.[12] Mild anaphylaxis was defined as cases those had limited skin or mucosal symptoms, involving urticaria, erythema, and edema near the eyes or angioedema and combined mild symptoms of other organs. Moderate anaphylaxis was defined as reactions involving respiratory, cardiovascular, and gastrointestinal symptoms (such as dyspnea, wheezing, vertigo, nausea, vomiting, and abdominal pain); the patient also had to be conscious with systolic blood pressure >90 mmHg. Severe anaphylaxis was defined as reactions involving cyanosis, hypotension, and neurological symptoms with oxygen saturation <92% or systolic blood pressure <90 mmHg. With regard to clinical course, cases involving one episode of symptoms were classified as monophasic and cases involving a second episode of symptoms 1–72 h after resolution of the initial symptoms were classified as biphasic.[13,14]

Skin prick and laboratory tests

The electronic medical records were reviewed and obtained demographic information including age, sex, history of underlying disease, allergic diseases, suspected causes and clinical features of the anaphylaxis, and laboratory tests. Skin prick test and serum allergen specific IgE tests (multiple allergosorbent test, MAST) were also performed. In some cases, MAST were performed at emergency department at the time of patient's visit, or skin prick tests or MAST were performed in Allergy outpatient clinic when the patients were referred to the Allergy department after emergent treatment. The skin prick test was performed using 55 common inhalant and food allergens at least 2 weeks after the anaphylaxis for those patients who agreed to undergo skin testing. Histamine and normal saline were used as positive and negative control, respectively. After 15 min application of the allergens, a positive reaction was a wheal diameter >3 mm. In the case of MAST, class 1 or more was defined as positive. The presence of atopy in the patient was defined as a positive skin prick test or when at least one allergen-specific IgE test for common food and inhalation allergens was positive. The probable causative agent was estimated based on clinical history. Peripheral blood laboratory tests included white blood cell (WBC), eosinophil counts, total IgE level, eosinophil cationic protein (ECP), aspartate transaminase (AST), alanine transaminase (ALT), and creatinine.

Statistical analyses

Variables with normal distribution were expressed as the mean ± standard deviation or percentage (%). Variables with non-normal distribution were expressed by median value. Continuous variables were analyzed by *t*-test or Mann–Whitney test. Categorical data were analyzed using the chi-square or Fisher's exact test. To identify the risk factors related with severe anaphylaxis, multiple logistic regression analysis was used. Variables that are clinically important and those P value < 0.1 in the univariate analysis were adjusted in the multiple variate analysis. Statistical analyses were performed using SPSS version 20.0 (IBM, Armonk, NY, USA). Statistical significance was considered for P-values < 0.05.

Results

General characteristics of anaphylactic patients

During the study period, 199 patients visited the ED for treatment of anaphylaxis. Of these, 103 were male (51.8%). The overall mean age was 41.1 ± 23.4 years, and 45 patients were under 18 years (22.6%). Atopy was present in 58 (29.1%) patients and 55 (27.6%) had a history of allergic disease including asthma, allergic dermatitis, allergic rhinitis, food allergies, and drug allergies. Fifty five (27.6%) patients had a history of chronic disease including hypertension (16.1%), malignant disease (4.5%), ischemic heart disease (4.0%), diabetic mellitus (4.0%), neurologic disease (2.5%), and renal disease (1.0%). Average values of laboratory tests were: WBC 9287.9 ± 4131.2/uL, eosinophil count 154.2 ± 178.4/uL, total IgE 430.1 ± 762.6 IU/mL, ECP 18.1 ± 16.3 ug/L, AST 44.6 ± 152.0 IU/L, ALT 29.5 ± 74.0 IU/L, and creatinine 1.03 ± 1.09 mg/dL (Table 1).

Causes of anaphylaxis

Food-induced anaphylaxis was the most frequent (n = 99, 49.7%), followed by drug-induced (n = 72, 36.2%), bee venom-induced (n = 20, 10.1%), and cause unknown anaphylaxis (n = 8, 4.0%). The causes of food-induced anaphylaxis included seafood (n = 28, 28.3%), meat (n = 18, 18.1%), grain/wheat flour (n = 18, 18.1%), fruit (n = 11, 11.1%), egg (n = 7, 7.1%), milk/dairy product (n = 6, 6.1%), nuts (n = 6, 6.1%), and pupa (n = 3, 3.0%). Of the 72 patients with drug-induced anaphylaxis, antibiotics were the most common culprit drugs (n = 29, 40.2%), followed by nonsteroidal anti-inflammatory drugs (NSAIDs; n = 24, 33.3%), computed tomography (CT) radiocontrast agents (n = 8, 11.1%), amino acids solutions (n = 6, 8.3%), lidocaine (n = 3, 4.1%), ranitidine (n = 1, 1.4%), and midazolam (n = 1, 1.4%) (Table 2).

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