Recognition and Management of Anaphylactic Shock

Leon-Yum Phoon, MD; Chee-Fah Chong, MD; Tzong-Luen Wang, MD, PhD

Abstract

Anaphylactic shock is medical emergency characterized by circulatory collapse resulted from severe acute allergic reactions, namely anaphylaxis and anaphylactoid reaction. Anaphylaxis is an acute, systemic, IgE-mediated, immediate hypersensitivity reaction caused by the release of mediators by mast cells and basophils after exposure to antigens. A diversity of antigens could trigger anaphylaxis and the most common causes are medications, insect stings and foods. Whereas anaphylactoid reaction is IgE-independent and contrast media is the widely known triggering agent. Anaphylaxis is a clinical diagnosis with a combinations of symptoms and signs that include weakness, dizziness, flushing, angioedema, urticaria of the skin, congestion, and sneezing. More severe symptoms include upper respiratory tract obstruction, hypotension, vascular collapse associated with angioedema and urticaria, gastrointestinal distress, cardiovascular arrhythmias, and arrest. Prompt administration of epinephrine is critical for the success in the treatment of acute anaphylaxis. H1 and H2 antihistamines, corticosteroids and appropriate fluid supplement should be given. Infusion of inotropic agents may be required. When the symptoms subside, observation in the emergency department before discharge is prudent.*(Ann Disaster Med. 2004;2 Suppl 2:S61-S68)*

Key words: Anaphylactic Shock; Anaphylaxis; Severe Allergic Reaction

Introduction

Anaphylaxis is the clinical syndrome that represents the most severe systemic allergic reaction that occurs in previously sensitized persons. It is an acute, systemic, IgE-mediated, immediate hypersensitivity reaction caused by a release of mediators from mast cell and basophils. [1] Previous studies suggested that the incidence of anaphylaxis occurred at the rate of 21 per 100000 patient-years.[2] Among those who suffered from anaphylaxis, 1/12 patients will experience recurrence, and 1/50 will require hospital treatment.[3] Anaphylaxis is a medical emergency that requires immediate attention as respiratory distress and, in case of anaphylactic shock, vascular collapse may occur within minutes after exposure to the allergic substances. Fatality from anaphylactic shock, though uncommon, may occur most commonly from cardiovascular collapse and airway obstruction if medical attention is delayed. Potentially any substance is able to cause anaphylaxis, however the most common causes of IgE-mediated anaphylaxis are insect stings, medications, latex,

From Department of Emergency Medicine, Shin-Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan
Address for reprints:Dr. Tzong-Luen Wang, Department of Emergency Medicine, Shin Kong Wu Ho-Su Memorial Hospital, No 95, Wen Chang Road, Taipei, Taiwan
Received: Feb 5 2004. Revised: Feb 20 2004. Accepted: Mar 5 2004.
TEL: 886-2-28389425 FAX: 886-2-28353547 E-mail: M002183@ms.skh.org.tw

peanuts and tree nuts, shellfish and fish, milk, eggs and wheat.[4,5,6] Shock could also arise in severe anaphylactoid reaction which is clinically indistinguishable from anaphylaxis, but are not IgE-mediated and is seen in response to opiates, nonsteroidal anti-inflammatory drugs and radiocontrast agents.

Etiology

In a retrospective study the causative agents was recognized in 75% of the cases of anaphylaxis presented to the emergency department.[7] Drugs are the most commonly documented causative agents of anaphylaxis in emergency department visit, ranges from 28% to 49%. Insect sting is the second most commonly reported agent in the same series, ranging from 17.5% to 29% of the cases with known etiology.[7,8] Nonsteroidal anti-inflammatory drugs and antibiotics, are the most common drugs involved in anaphylaxis. Within the later subcategory cephalosporins, penicillin and trimethoprim are the drugs most commonly associated with anaphylaxis. Other medications reported to provoke anaphylaxis include acetaminophen, angiotensin-converting enzyme inhibitors, and intravenous contrast. Among insects associated with anaphylaxis, hornet, bee and wasp in the order of Hymenoptera are the most commonly recognized agents. The prevalence of Hymenoptera sting systemic reactions in the general population ranges from 0.155 to 3.3%.[9] In the general population, adult age, male sex (male: female ratio, 2:1) and the type of stinging insect (honeybee stings are more dangerous than vespid stings) are well known risk factors for both the occurrence of the first systemic reaction and the recurrence of the systemic reactions.[9,10] Food allergy represented one of the most common cause for the documented anaphylaxis with known etiology. Various foods included fish, seafood, nut, mango, kiwi, soy, and mustard have been reported to be the provoking agents. Exercised induced-anaphylaxis is characterized by a spectrum of symptoms occurring during physical activity that ranges from mild cutaneous signs to severe systemic manifestations such as hypotension, syncope and even death. Certain foods or medications may be the predisposing factors for exercised-induced anaphylaxis. In susceptible persons, ingestion of NSAIDs, aspirin, seafood, celery, wheat and cheese before physical activity may induce the anaphylaxis. Other less frequent provoking anaphylaxis includes are latex, allergen immunotherapy, foreign proteins (insulin, antitoxins), and blood transfusion. Table 1 shows some causes of anaphylaxis.

Clinical Features (Table 1)

Anaphylaxis and anaphylactic shock are mainly clinical diagnoses. When there is an obvious history of exposure such as wasp sting, or the symptoms occurred immediately after drugs or foods known to be anaphylactic to the patient the diagnosis could be straight forward. But very often the causative agent could only be identified later after the patient is stabilized. Accurate diagnosis and prompt intervention relied on the treating physician's capability to differentiate anaphylaxis from other disease entities. When appropriate treatment is delayed such potentially reversible medical crisis could be fatal. Therefore, physicians should be familiar with the clinical features of anaphylaxis. Because anaphylaxis is a systemic allergic reaction, a wide variety of clinical signs and symptoms may

be observed. The reaction usually has an acute and sudden onset, usually within minutes but occasionally occurs as late as 1 hour after exposure to the offending antigen. These symptoms generally last less than 24 hours.[11,12] Patients with anaphylaxis will often note an impending sense of death (*angor animi*). Common symptoms usually include weakness, dizziness, flushing, angioedema, urticaria of the skin, congestion, and sneezing. More severe symptoms include upper respiratory tract obstruction, hypotension, vascular collapse associated with angioedema and urticaria, gastrointestinal distress, cardiovascular arrhythmias, and/or arrest.[13] In the emergency department setting, up to 94% of the presented cases have cutaneous features. Generalized erythema, pruritus, urticaria and angioedema are the most common cutaneous features of anaphylaxis.[7] The second common system is the respiratory (55-78%) followed by cardiovascular (30%) and gastrointestinal (14%).[8] Respiratory features are results of swelling and edema of the respiratory mucosa and bronchospasm. Dyspnea, wheeze, stridor, chest tightness, cough, and tachypnea may occur. Laryngeal edema may occur immediately after exposure to anaphylactic stimulus and result in upper airway obstruction and death if untreated. Shock due to profound peripheral vasodilatation may occur with or without respiratory symptoms. Any combinations of the above symptoms (common vs. severe) have been observed among patients who have suffered an anaphylactic reaction. Common symptoms do not always precede the more severe symptoms as a warning or indicator of a possible oncoming anaphylactic reaction. However, generally, the time to onset of symptoms is a good indicator of the severity of the reaction, ie, the faster the onset, the more severe the reaction. In a retrospective review of anaphylaxis presented to emergency department, respiratory arrest was the major cause (80%) of the food-related anaphylaxis. Shock was more common in iatrogenic and insect sting reactions. The median time to respiratory or cardiac arrest was 30 min for foods, 15 min for venom and 5 min for iatrogenic reactions.[14] Table 1 summarizes the clinical features of anaphylaxis.

Laboratory studies are of no benefit in diagnosis and treatment of anaphylaxis. However the diagnosis may be confirmed by the elevated serum level of mast cell tryptase and the causative agent may be demonstrated by certain agent specific serum IgE antibodies. Nev-

Table 1. Signs and Symptoms of Anaphylaxis

Dermatologic	Angioedema, urticaria, pruritus, general erythema
Respiratory	Dyspnea, chest tightness, wheeze, cough
Otorhinolaryngologic	Stridor, hoarseness, sneeze, nasal congestion/itching, dysphagia
Gastrointestinal	Vomiting, nausea, abdominal pain, fecal incontinence
Cardiovascular	Tachycardia, hypotension, syncope
Neurologic	Headache, mental status change
General	Anxiety, sense of impending doom, pallor

ertheless these tests are not available in the emergency setting and are not used routinely. Ancillary tests are helpful for alternating diagnoses.

Differential Diagnosis (Table 2)

It is not practical to differentiate between anaphylactic and anaphylactoid reactions, because both respond to the same treatment in the acute stage. However if anaphylactic shock is present, it must be differentiated from other causes of cardiovascular collapse. As in anaphylactic shock, hypotension, pallor, bradycardia, weakness, nausea, vomiting and diaphoresis also present in vasovagal reactions, making it the most common condition that mimic anaphylaxis. However urticaria, pruritus, angioedema, tachycardia and bronchospasm are not present in vasovagal reactions. Besides warm phase of septic shock may also mimic anaphylactic shock as hypotension resulted from peripheral vasodilation. However the progressive onset, fever and other signs of infection may be present.

Acute respiratory decompensation seen in severe asthma attacks, foreign body, foreign body aspiration and pulmonary embolism can mimic the respiratory symptoms suggestive of anaphylaxis but other dermatologic features are absent. Other conditions such as seizure disorders, myocardial infarction and arrhythmias may infrequently present initially with similarities to anaphylaxis, but are readily distinguished clinically. A list of differential diagnosis is summarized in Table 2.

Treatment

Anaphylaxis is a medical emergency and may

Table 2. Differential Diagnosis of Anaphylaxis

Pulmonary Asthma, foreign body, aspiration, pulmonary embolus, epiglottitis
Cardiac Myocardial infarction, cardiac arrest, arrhythmias
Shock Cardiogenic, septic, hemorrhagic
Neurologic Autonomic epilepsy, cerebrovascular accident
Flushing syndromes Red man syndrome (vancomycin), carcinoid
Mast cell disorder Cold-induced urticaria, Cholinergic urticaria, systemic mastocytosi, urticaria pigmentosa
Psychogenic Panic attack, hyperventilation
Miscellaneous Vasovagal reaction, hereditary angioedema

progress to shock and death if not treat immediately. Airway patency and circulatory restoration are pivotal. Parenteral epinephrine is critical in the management of acute anaphylaxis. For the adult patient, 0.3-0.5mL epinephrine of a 1:1000 dilution given subcutaneously or intramuscularly may be effective. Recent study found that intramuscular route superior to subcutaneous route. The former had shorter time (8 min after intramuscular route vs. 34 min after subcutaneous route) to peak plasma epinephrine concentration, accompanied by prompt physiologic effect, though the total amount of epinephrine eventually absorbed did not differ significantly.[15] Peak plasma epinephrine concentrations were significantly higher after epinephrine injection in the vastus lateralis muscle.[16]

The dosage for children is 0.01mL/kg, up to a maximum 0.3mL of a 1:1000 dilution of epinephrine.[17] Repeated dose of epinephrine could be administered every 5-15 minutes until the anaphylaxis is controlled or signs of palpitations, tremor, uncomfortable apprehension occur. Intravenous epinephrine in 1:10000 dilution should only be reserved to patients with severe hypotensive shock in the fear of its potential effects of tachyarrhythmia and ischemia. For patients with conscious disturbance due to severe hypotensive shock, oxygen supplement with adequate airway must be given and maintained. When signs of laryngeal edema and upper airway obstruction are suspected, early intubation could be life-saving. The patient should be placed supine or in Trendelenburg's position.

Other medications for acute anaphylaxis include the administration of H1 and H2 antihistamines. Diphenhydramine 25-50mg intravenously may be administered after initial use of epinephrine. Ranitidine, an H2 antihistamine, 50mg intravenously or 150mg orally could be given to enhanced the effects. Inhalation of β_2-agonists (e.g. salbutamol and terbutaline) is effective for bronchospasm. Though corticosteroids do not reverse the acute symptoms, they may help prevent or minimize second-phase reaction. Despite the controversy of corticosteroids in anaphylaxis, methlprednisolone, 125mg intravenously, or prednisolone 50mg orally are widely acceptable as part of the initial management regimen. The intravenous route is usually reserved to patient with more severe reactions.

When anaphylactic shock fails to respond to the initial epinephrine, persisted hypotension patient should receive intravenous fluid challenge. Caution should made to avoid overzealous fluid administration as pulmonary edema may develop. In severe case, continuous infusion of vasopressor like dopamine and epinephrine may be required.

For patients who use β-blockers or ACE inhibitors, epinephrine may not be effective in reversing the hypotensive shock. Then glucagon in the dose of 5-15 μg/min should be administered intravenously. Glucagon has direct chronotropic, inotropic and vasoactive effects that are independent of catecholamine receptors. Additionally, glucagon also promotes endogenous release of catecholamines. For patients with bradycardia refractory to initial treatment, intramuscular or intravenous administration of atropine 0.5mg (up to 2mg) may be warranted. The hemodynamic status should be assessed frequently for response to treatment.

Additional measures may be individualized.[1,18] To slow absorption of in-

jected antigens (e.g., insect stings), a tourniquet may be placed proximal to the injection site. It should be released every five minutes for at least three minutes, and the total duration of tourniquet application should not exceed 30 minutes. The tourniquet pressure should ideally occlude venous return without compromising arterial flow. Alternatively, 0.15 to 0.3 mL of 1:1,000 aqueous epinephrine (0.1 to 0.2 mL in children) may be injected into the site.

Patient with anaphylactic shock not completely respond to initial treatment should be admitted to an intensive unit for further care. For those responds initially, post-treatment observation in the emergency department for a period of time is necessary because of the potential for a second phase of reaction. Most of these reactions occur within 1-8 hours, but second phase reactions may occur 38 hours later. [19] Prolonged observation in a monitored setting period is ideal but not practical. So it may be appropriate to discharge asymptomatic patient after 4-8 hours of observation for those with less severe reactions. These patients must be told returning to emergency department immediately if any symptom recurs and their family should also be informed of the discharge precautions. Outpatient follow up to primary care physicians or an allergist should also be made. Upon discharged, some experts advocate a short course of antihistamines with oral corticosteroids (e.g., 30 to 60 mg of prednisone).[1]

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過敏性休克

潘麟鑫 張志華 王宗倫

摘要

過敏性休克是因為全身過敏性反應和類全身型過敏反應所造成的循環衰竭。 全身過敏性反應是一種由於再次接觸同種過敏原後，由IgE刺激肥胖細胞及嗜鹼性白血球，造成有可能會致命的全身過敏性反應. 許多抗原可以引起全身過敏性反應，又以藥物，昆蟲螫刺和食物最常見。類全身型過敏反應則不須通過IgE刺激就可引起全身過敏性反應，顯影劑是較常見的誘發因子。全身過敏性反應是臨床診斷，其症狀可包括全身無力，暈眩、潮紅、血管性水腫、蕁麻疹，鼻塞。較嚴重的症狀包括上呼吸道阻塞、低血壓、腸胃道不適、心律不整和心臟停止。及時給予腎上腺素是在急性期治療全身過敏性反應成功的關鍵。同時也應給予 H1 及 H2 抗組織胺、類固醇和適當的輸液治療。偶爾也需使用昇壓劑。當症狀緩和後，病人應在急診留觀數小時後才能出院。
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財團法人新光吳火獅紀念醫院急診科
抽印本索取：王宗倫　台北市士林區文昌路95號　財團法人新光吳火獅紀念醫院急診科
收件：93年2月5日　修正：93年2月20日　接受刊載：93年3月5日
電話：(02)28389425　傳真：(02)28353547　E-mail：M002183@ms.skh.org.tw