Anaphylaxis

Neil H Young

Graham R Nimmo

Abstract

Acute anaphylaxis has been described as 'a serious allergic reaction that is rapid in onset and may cause death'. It is becoming more common and is underdiagnosed. Even when anaphylaxis is recognized, it tends to be undertreated. All clinical staff should maintain a high level of awareness of anaphylaxis in order to recognize, assess and manage it optimally. In this article, we have concentrated equally on treatment and on recognition with assessment. The patient who exhibits the full range of manifestations of anaphylaxis may be readily diagnosed, but many present with only one or two of the features, thereby increasing diagnostic uncertainty and leading to delays in definitive treatment with adrenaline (epinephrine).

Keywords Adrenaline; anaphylaxis; critical care; hypersensitivity

Key points

- The diagnosis of anaphylaxis is not always obvious
- Anaphylaxis should therefore be considered in any patient with rapid-onset deterioration in respiratory function, or hypotension or an acute airway problem
- Both the presentation and the causative factor can vary depending on the clinical situation
- Adrenaline (epinephrine) is the treatment of choice and should be given without delay if any life-threatening problems are present
- All patients need appropriate immediate and long-term follow-up

Acute anaphylaxis is a medical emergency that presents in many guises and can occur anywhere from the community to the variety of in-hospital clinical settings. It has been described as 'a serious allergic reaction that is rapid in onset and may cause death',[1] and is becoming more common. Because of the variability in presentation, it can be difficult to recognize and diagnose.

Recognition and assessment

Making the diagnosis

There are a few important questions to ask when considering the diagnosis (Table 1):

- Is there a trigger/cause? (this may not always be apparent).
- Is there significant past history? (e.g. atopy, previous reactions).
- Is there multisystem involvement (respiratory/cardiovascular/skin/gastrointestinal)?
- Is the patient taking a β-adrenoceptor blocker? (these can prevent the innate adrenergic response to an allergic reaction, resulting in an increased severity of reaction, and can cause catecholamine resistance, making treatment more difficult).

A diagnosis of anaphylaxis should be considered in any illness of acute onset involving otherwise unexplained respiratory or cardiovascular compromise.

Neil H Young *MB ChB MRCP(UK) FRCA DICM FFICM is a Consultant in Intensive Care Medicine and Anaesthesia at the Royal Infirmary of Edinburgh, Edinburgh, UK. Competing interests: none declared.*

Graham R Nimmo *MB ChB MD (Edin) EdD (Stirling) FRCP(Edin) FFARCSI FFICM is a Consultant in Intensive Care Medicine and Clinical Education at the Western General Hospital, Edinburgh, UK. Competing interests: none declared.*

Assessing severity-initial resuscitation

An early assessment of severity is essential to decide whether adrenaline (epinephrine) is necessary and whether the support of a doctor skilled in advanced airway management and circulatory is needed (Table 2).

Patients with any of the major manifestations (airway, breathing or circulatory problems) should immediately be given adrenaline. In addition to adrenaline, the mainstays of initial resuscitation in anaphylaxis include administration of a high inspired concentration of oxygen and a rapid fluid bolus. The Resuscitation Council (UK) guideline for the management of anaphylaxis[2] is reproduced in Figure 1.

Patient positioning

A number of guidelines recommend lying the patient flat and raising their legs. In the presence of upper airway swelling, bronchospasm or pulmonary oedema, this is potentially dangerous and can cause severe respiratory distress and respiratory arrest. We strongly counsel against this practice if airway or respiratory compromise is a prominent feature of the presentation. Our applied clinical practice is to keep the patient in a semi-recumbent position to optimize airway management, even in the presence of significant hypotension.

Features

Stridor is an inspiratory, high-pitched sound caused by partial obstruction of the laryngeal inlet. The condition is potentially lethal, even in the absence of bronchospasm, pulmonary oedema or shock. Tachypnoea is usual, often accompanied by a paradoxical (see-saw) breathing pattern. High-concentration humidified oxygen and systemic adrenaline should be given, and an emergency call for advanced airway expertise made. It may be impossible to secure the airway by conventional endotracheal intubation, and emergency front of neck airway access may be necessary and life-saving. Early administration of adrenaline can reverse the upper airway oedema causing the stridor. Adrenaline acts at α_1-adrenergic receptors to cause vasoconstriction, thus increasing blood pressure and decreasing mucosal oedema. It

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Differential diagnosis of anaphylaxis

- Stridor: infection (epiglottitis, croup, abscess), tumour, foreign body, smoke or toxin inhalation
- Wheeze: asthma; chronic obstructive pulmonary disease, pulmonary oedema, smoke or toxin inhalation
- Pulmonary oedema: left ventricular failure, acute respiratory distress syndrome, smoke or toxin inhalation
- Rash (acute generalized urticaria)
- Gastrointestinal symptoms: scombroid poisoning (decayed fish), monosodium glutamate
- Hereditary angioedema: classic symptom triad of abdominal pain, peripheral oedema and laryngeal oedema in the absence of urticaria
- Angioedema caused by an ACE inhibitor: this can occur because ACE inhibitors alter the degradation of bradykinin

ACE, angiotensin-converting enzyme.

Table 1

also acts at β_1-adrenergic receptors to increase force and rate of cardiac contraction, and β_2-adrenergic receptors to cause bronchodilatation and a decrease in mediator release.

The initial recommended adult dose of adrenaline/epinephrine in anaphylaxis is 500 micrograms (0.5 ml of 1:1000 solution) intramuscularly. In some cases, a doctor experienced in the use of intravenous adrenaline for circulatory support may titrate adrenaline intravenously in boluses of up to 50 micrograms. There is some evidence that a delay in the administration of adrenaline increases mortality.

Major and minor manifestations of anaphylaxis

Major manifestations

- Orofacial swelling with airway compromise
- Laryngeal swelling, manifesting as stridor
- Bronchospasm, manifesting as wheeze
- Pulmonary oedema
- Shock
- Cardiovascular collapse with faintness, palpitations, loss of consciousness
- Cardiac arrest

Treatment

- Stabilization and reversal of the process
- Stop or remove any cause: stop intravenous infusions of drugs, plasma expanders and blood products
- Give immediate oxygen and adrenaline (epinephrine)

Minor manifestations – the importance of these relates to their role in pointing to the diagnosis

- Upper respiratory tract features: rhinitis, conjunctivitis
- Skin rashes/colour changes: angioedema, urticaria, erythema, pallor, itch
- Gastrointestinal symptoms: abdominal pain, nausea and vomiting

Table 2

Bronchospasm is caused by the effects of histamine, leukotrienes and cytokines on bronchial smooth muscle, and may be profound. Tachypnoea and accessory respiratory muscle activity are common; paradoxical breathing, bradypnoea and bradycardia signify a life-threatening situation, heralding imminent respiratory arrest.

Immediate administration of high-concentration humidified oxygen and intramuscular adrenaline plus high-dose corticosteroids intravenously and nebulized salbutamol (in that order) is often beneficial. Second-line bronchodilators such as aminophylline can be effective but should be administered carefully under expert supervision. Early access to advanced airway expertise is important, remembering that intubation of the trachea (and the drugs used to facilitate it) can worsen bronchospasm and cause circulatory collapse. Slow rates of mechanical ventilation with prolonged expiratory times are employed, and side-to-side manual compression of the chest to encourage exhalation has been described as a useful rescue therapy. Repeated doses of adrenaline or an intravenous adrenaline infusion may be required.

Pulmonary oedema is generated by capillary leak in the pulmonary microcirculation. In addition to oxygen and adrenaline, continuous positive airways pressure or mechanical ventilation may be essential to maintain adequate oxygenation. Both bronchospasm and pulmonary oedema can take many hours to improve.

Hypotension, shock and circulatory collapse result from a combination of vasodilatation and capillary leak. The onset can be impressively fast, even over a couple of minutes, especially in reactions secondary to intravenous drug administration. Vasodilatation is caused by histamine, bradykinin and cytokines, and mediated through nitric oxide production. This causes hypotension through relative hypovolaemia in which the circulating blood volume is inadequate to fill the increased vascular 'space'. Capillary leakage then results in absolute hypovolaemia with plasma loss into the tissues, which compounds the hypotension.

Both tachycardia and bradycardia have been described clinically, but the latter often signifies imminent cardiac arrest. High-concentration oxygen should be given with adrenaline as described above. Rapid intravenous fluid administration is required so large-bore vascular access is necessary; this can be difficult because of tissue oedema. Intraosseous access to the circulation is a potential alternative. A fluid bolus of 500 ml to 1 litre should be administered as quickly as possible. Given the increasing evidence that colloids have no benefits over crystalloids in critically ill patients, we recommend crystalloid as the initial fluid resuscitation of choice. Repeated doses of adrenaline or an adrenaline infusion may be required, but should be given in a critical care setting and guided by invasive haemodynamic monitoring.

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