Part VIII: Shock

Chapter 60: Anaphylaxis

M M Fisher

Anaphylaxis is the symptom complex accompanying the acute reaction to a foreign substance to which a patient has been previously sensitized (immediate hypersensitivity or Type 1 hypersensitivity). The term anaphylactoid reaction is used to describe reactions clinically indiscernible from anaphylaxis, in which the mechanism is non-immunological or has not been determined. Both conditions can be incorporated under the title "clinical anaphylaxis". The symptom complex may be produced by direct drug effects, physical factors, or exercise, and a causative agent cannot always be determined.

Aetiology and Pathophysiology

Clinical anaphylaxis commonly follows injection of drugs, blood products, plasma substitutes or contrast media; ingestion of foods or food additives; or insect stings.

In anaphylaxis, sensitization occurs following exposure to an allergenic substance, which either alone, or by combination with a hapten, stimulates the synthesis of immunoglobulin E (IgE) which binds to the surface of mast cells and basophils. Later, re-exposure to antigen produces an antigen-cell surface IgE antibody interaction, resulting in mast cell degranulation and the release of histamine and other mediators such as slow-reacting substance of anaphylaxis (SRS-A), eosinophil chemotactic factor (ECF-A) and platelet activating factor (PAF). The overall effects of the mediators are to produce vasodilation, smooth muscle contraction, increased glandular secretion and increased capillary permeability.

In an anaphylactoid reaction, the clinical picture is identical to anaphylaxis, but the mechanism of its initiation is uncertain. Intravenous hypnotic drugs and X-ray contrast media may activate complement C3. Plasma protein and human serum albumin reactions are thought to be induced by either albumin aggregates or stabilizing agent-modified albumin molecules. Other reactions, including those to dextrans and gelatin preparations, may be activated by antibody already present in the plasma.

The direct histamine releasing effects of some drugs may produce reactions due to the effect of histamine alone, and such reactions are related to volume, rate and amount of infusion. Anaphylactic reactions are largely seen in fit patients. It is likely that the adrenal response to stress "pretreats" sick patients and blocks the release and effects of anaphylactic mediators. The exception to this appears to be patients with asthma in whom reacions to additives in steroids and aminophylline may occur, and this may be related to the reduced catecholamine response reported in asthma.

Pathophysiology of Cardiovascular Changes

The traditional concept of the cardiovascular changes in anaphylaxis is that there is an initial vasodilation, followed by capillary leak of plasma which produces endogenous hypovolaemia, reduced venous return and lowered cardiac output. Whether or not cardiac

function is impaired has been a controversial issue. Although most anaphylactic mediators adversely affect myocardial function in vitro, most case reports of analphylaxis in which invasive cardiovascular monitoring was used, suggest a minimal impairment of cardiac function. Patients with premorbid normal cardiac function rarely showed evidence of cardiac failure or arrhythmias other than supraventricular tachycardia, but evidence of these cardiac complications increased in patients with pre-existing cardiac disease. Recently, prolonged global myocardial dysfunction was described in patients with no evidence of cardiac disease, and the use of a balloon counterpulsator was lifesaving.

Clinical Presentation

The latent period between exposure and development of symptoms is variable, but usually occurs within 30 min if the provoking agent is given parenterally. Reactions may be transient or protracted, lasting days, and may vary in severity from mild to fatal. Cutaneous, cardiovascular, respiratory or gastrointestinal manifestations may occur singly or in combination.

Cutaneous features include erythematous blush, generalized urticaria, angio-oedema, conjunctival injection, pallor and cyanosis.

Cardiovascular system involvement is evidenced by tachycardia, hypotension and the development of shock. It is the most common feature and may occur as a sole clinical manifestation.

Respiratory manifestations include rhinitis, bronchospasm and laryngeal obstruction.

Gastrointestinal symptoms of nausea, vomiting, abdominal cramps and diarrhoea may be present.

Other features include apprehension, metallic taste, choking sensation, coughing, paraesthesiae, arthralgia, convulsions, clotting abnormalities and loss of consciousness. In addition, pulmonary oedema is a common post-mortem finding, and rarely, a massive high protein pulmonary oedema may occur.

Management

1. *Oxygen* is given by facemask. Endotracheal intubation may be required to facilitate ventilation, especially if angio-oedema or laryngeal oedema is present. Mechanical ventilation may be indicated for bronchospasm, apnoea or cardiac arrest.

2. *Adrenaline* is the drug of choice for severe reactions. A dose of 0.3-1.0 mg is given intramuscularly (IM) and 0.5 mg is often sufficient. If muscle blood flow is thought to be compromised by shock, or as a chosen alternative, an intravenous infusion of 1-2 mg in 100 mL saline is started with electrocardiographic (ECG) monitoring. Adrenaline should be used with caution in patients who have received volatile anaesthetics and, in such patients, a trial of metaraminol may avoid ventricular arrhythmias. Adrenaline, by increasing intracellular levels of cyclic adenosine monophosphate (C-AMP) in leucocytes and mast cells, inhibits

further release of histamine and SRS-A. It has beneficial effects on myocardial contractility, peripheral vascular tone and bronchial smooth muscle.

3. *Cardiopulmonary resuscitation* should be instituted irrespective of rhythm, if the patient is pulseless. A common error in management is not to institute external cardiac massage (ECM) as the arrhythmia is benign.

4. *Plasma or plasma expanders* are given rapidly to correct the hypovolaemia consequent to acute vasodilatation and leakage of fluid from the intravascular space. Plasma protein solution, dextran 70, and gelatin preparations are favoured above crystalloids as they remain longer within the vascular compartment. Very large volumes of fluid may be required and central venous pressure (CVP) monitoring and measurement of haematocrit are helpful.

5. *Aminophylline* 5.6 mg/kg IV is given slowly over 30 min if bronchospasm is unresponsivew to adrenaline alone. Aminophylline increases intracellular C-AMP by phosphodiesterase inhibition, and its effect on inhibiting histamine and SRS-A release is theoretically additive to that of adrenaline. In patients with refractory hypotension despite adequate volume, noradrenaline may be lifesaving. If refractory bronchospasm occurs other bronchodilators are therapeutic agents and procedures should be tried.

6. *Steroids* have no proven benefit and should be reserved for refractory bronchospasm.

7. *Antihistamines* are only indicated in protracted cases or those with angio-oedema.

Ideally, patients are managed in an Intensive Care Unit. Continuous ECg monitoring enables detection of arrhythmial secondary to hypoxia, hypotension, or exogenous adrenaline. Close monitoring of arterial blood pressure, CVP, and arterial blood gases are mandatory during the acute phase. Blood for measurement of complement levels may be helpful in determining the nature of the reaction.

Follow Up

Following successful management of the anaphylactic reaction, the drug or agent responsible should be determined by in vitro or in vivo testing if possible. Hyposensitization should be considered for food, pollen and bee sting allergies. A "medic allert" bracelet should be worn and the patient given a note stating the nature of the reaction to the particular causative agent.

If re-exposure to the allergen is likely at home, patients or their relatives should be instructed in the use of adrenaline, salbutamol inhalation and antihistamines. Clinical anaphylaxis may be modified by pretreatment with disodium cromoglycate, corticosteroids, antihistamines, salbutamol and isprenaline.