CASE REPORT

Anaphylaxis: A life threatening but treatable condition

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ABSTRACT

We present a case of perioperative anaphylaxis associated with the administration of intraoperative antibiotics. Perioperative anaphylaxis remains an important preventable cause of morbidity and mortality during anesthesia particularly if diagnosed early. Diagnosis can be challenging because multiple drugs are administered simultaneously during anaesthesia and surgery and any of these agents can potentially cause anaphylaxis. Early suspicion, immediate diagnosis and prompt management are vital as early specific management of anaphylaxis improves the outcome.

Key words: Anaphylaxis**;** Morbidity**;** Systemic hypersensitivity reaction

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INTRODUCTION

Anaphylaxis is a severe, life-threatening, systemic hypersensitivity reaction that involves multiple organ systems. Anaphylaxis may be divided into allergic and non-allergic anaphylaxis. The clinical features of allergic anaphylaxis and non-allergic anaphylaxis are often indistinguishable.

Allergic anaphylaxis, also known as anaphylactic reaction, is mediated by IgE antibodies after exposure to a foreign protein antigen. On further exposure, the antigen binds with IgE antibodies and leads to release of inflammatory mediators.[1] Non-allergic anaphylaxis also known as anaphylactoid reactions are not mediated by IgE. It results from a direct release of histamine and other inflammatory products from mast cells after exposure to a particular drug or substance.

CASE REPORT

A forty-five year-old male patient presented to the hospital for elective laparoscopic cholecystectomy. He had a past medical history of diabetes mellitus and was allergic (erythema and itching) to ibuprofen. After a standard general anaesthesia induction with propofol 200 mg, Fentanyl 100 μg and atracurium 50 mg, tracheal intubation was performed uneventfully. General anaesthesia was maintained with sevoflurane 2% in an oxygen and air mixture.

Amoxicillin/clavulanate 1.2 g was given about six minutes after induction for surgical site infection prophylaxis. Two minutes later the patient developed a tachycardia of 160 beats per minute, hypotension of 50/20 mmHg, severe bronchospasm with high peak airway pressure of 40 cmH_2O.Oxygen saturation was not recordable due to poor perfusion. End-tidal CO_2 decreased to 12 mmHg. Examination of the chest revealed no chest movement and no air entry on auscultation. A diagnosis of acute anaphylaxis was made. No skin changes were observed.

The FiO_2 was increased to 1 and anesthetic agents were discontinued. Adrenaline 200 μg was given as a bolus intravenously and repeated twice, followed by infusion at a rate of 0.15 μg/kg/min. Chlorpheniramine 4 mg and hydrocortisone 200 mg, atropine 0.5 mg and midazolam 2 mg were administered intravenously. Two puffs of salbutamol were repeated twice, via the endotracheal route. A central venous catheter and an arterial line were inserted and serial arterial blood gases samples were drawn. The patient's blood pressure improved reaching 130/78 mmHg, and the bronchospasm improved significantly allowing normal ventilation to be recommenced.Tryptase levels were sent within 30 minutes of the event. The incident occurred prior to the incision, and the operation was postponed. The patient was transferred to ICU while intubated and mechanically ventilated in a stable condition.

The patient's course in ICU was uneventful. Tryptase levels were sent on transfer to ICU and at six hours post event. Diagnosis was confirmed by measuring serum tryptase level which rose to 68.7μg/l. Ventilation and adrenaline infusion was continued for 24 hours along with remifentanil sedation. The patient was extubated the following day without any sequel.

DISCUSSION

Peri-operative anaphylaxis is rare, but can rapidly evolve into life-threatening situations if not recognized and managed promptly. The operating theatre is a unique clinical environment where patients are exposed to numerous medications over a relatively short period of time, particularly during the induction of anaesthesia. During general anaesthesia, several drugs are administered in rapid succession while patients are also exposed to numerous other substances, such as antiseptic skin preparations, latex and intravenous colloids. As a consequence, anesthetists may witness and manage more allergic reactions as compared to other physicians.

The reported incidence of peri-operative anaphylaxis varies from 1 in 6000 to 1 in 20,000 anaesthetics,[2] but it is very difficult to know the exact frequency and its associated morbidity and mortality. Females are more prone to suffer from these reactions as compared to males. It is estimated that mortality from anaphylaxis related to anaesthesia could be as high as 6%.[3]

The multiple physiologic changes occurring before and during general anaesthesia pose a challenge in recognition of anaphylaxis, as some features may not be appreciated in anaesthetized patients. Signs of anaphylaxis include hypotension 17.8%, bradycardia 2.1%, cardiovascular collapse 53.7%, cardiac arrest 4%, bronchospasm 44.2%, cutaneous symptoms 69.9%, and angioedema 11.7%.[4] Our patient presented with hypotension and bronchospasm but no cutaneous signs.

Anesthetic allergy databases reveal that the incidence of reactions to particular drugs reflects their level of use.[5] Reactions to newer agents such as rocuronium have increased whereas reactions to older agents such as thiopentone have fallen[6]. The most commonly involved drugs and substances involved in allergic reactions during anaesthesia are:

- Neuromuscular blocking agents 60-65% [6]
- Latex 13% [7]
- Antibiotics 8.6% [7]
- Colloids 4.7 % [8]
- Induction agents 3.6 %
- Benzodiazepines 2 %
- Opioids 1.7 %
- Other agents (protamine, methylene blue etc.) 2.5 % [9]

In our patient all of the induction drugs could have potentially caused the reaction, but the timing of administration favors the antibiotics.

Antibiotics are one of the common causes of perioperative anaphylaxis. In a French study the reported incidence of reactions was reported to be as high as 15% while in UK antibiotics were responsible for about 8.6% of perioperative anaphylaxis.

Among antibiotics, penicillin's and cephalosporin's are most frequently involved in hypersensitivity reactions and there is cross reactivity of about 8 % between penicillin and cephalosporin due to the common β lactam ring.[10] In a recent meta-analysis it has been shown that patients who are allergic to penicillin or amoxicillin have a higher incidence of allergic reactions to first generation cephalosporin and cefamandole, but not with second and third generation.[11] Other antibiotic associated with peri-operative anaphylaxis is vancomycin,[12] and if administered rapidly can result in life threatening non-allergic reactions. This is thought to be mediated by direct histamine release and myocardial depression

.Current peri-operative antibiotic practice is to administer antibiotics intravenously at induction of anaesthesia and immediately before surgical incision. Recent data suggests that administration as near to the incision time as possible may not be optimal. Administration 30 minutes to 1 hour prior to the incision may be more ideal. In a large multi-centre report involving 4472 patients in 29 hospitals, the timing of the administration of perioperative antibiotics was studied involving cardiac, hip-knee arthroplasty and hysterectomy cases. The best protection from infection was seen when the antibiotic was given within the first 60 minutes before incision.[13] We therefore recommend a change of practice in administering antibiotics in the pre-induction period so that difficulty in diagnosing antibiotic related anaphylaxis can be avoided in an anaesthetized patient.

Investigation of anaphylaxis is both immediate and delayed. Immediate investigation includes measurement of serum tryptase concentration. Tryptase is a neutral serine protease found in mast cells released upon degranulation of mast cells. The rise and fall in serum concentration of tryptase would confirm the clinical diagnosis. Three samples should be sent to the laboratory.

1. First sample immediately after the reaction
2. Second sample1 hour after the reaction
3. Third sample between 6 to 24 hoursIn our patient the diagnosis was confirmed by the raised tryptase levels.

Later investigations include skin testing for allergens to confirm the causative agent. Any patient who has suspected anaphylactic reaction should have full investigations. It is responsibility of the anesthetist who administered drugs

during an allergic reaction that these tests are performed and patient referred to an allergy center with all the relevant details.

Anaphylaxis Drill: Early diagnosis and specific management improves the outcome of this fatal but manageable condition. AAGBI (Association of Anesthetists for Great Britain and Ireland) has come up with specific guidelines for the management of suspected anaphylaxis.[14] These management guidelines presuppose that the patient is in the care of an appropriately trained anaesthetsit and full resuscitation facilities and appropriate vital signs monitors are available. Although management should be tailored to the individual patient, there is consensus that adrenaline should be given as early as possible. In addition to having alpha-agonist activity, adrenaline is a valuable beta agonist, which is inotropic, and a bronchodilator, and reduces further mediator release. Other causes of hypotension or difficulty in ventilation should be excluded, for example a misplaced tracheal tube or equipment failure.

CONCLUSION

In conclusion early diagnosis and specific management improves the outcome of this fatal but manageable condition. AAGBI (The Association of Anesthetists of Great Britain and Ireland) has already published specific guidelines for the management of suspected anaphylaxis[14]. We recommend that all anesthetists should make themselves familiar with these guidelines and they should be immediately available in all places where anaesthesia is being administered.

We also recommend that antibiotics be administered in the preinduction period.

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