

Fatal Anaphylaxis to Atracurium: A Case Report

Jan Schumacher, MD, PhD

A 52-year-old patient was scheduled for a cystoscopy. Anesthesia was induced by intravenous injection of fentanyl and propofol. After administration of atracurium, he became bradycardic and suffered a cardiac arrest. Despite prolonged cardiopulmonary resuscitation, the patient could not be revived. Electrolytes and hemoglobin levels were normal, and a transthoracic echocardiogram showed no signs of pericardial effusions or of any left ventricular contraction. The postmortem found no pathology. However, mast cell tryptase was raised significantly, indicating fatal anaphylaxis. Having presented no classic clinical signs, this case is a reminder that rapid cardiovascular collapse can be the sole clinical feature of anaphylaxis. (A&A Practice. XXX;XXX:00–00.)

Neuromuscular blocking drugs (NMBDs) account for most cases of anaphylaxis during the perioperative period.^{1,2} The most common clinical signs are flushing, urticaria, tachycardia, hypotension, and bronchospasm. We present a case of severe intraoperative anaphylaxis with epinephrine-unresponsive circulatory shock. Written consent to use existing protected health information was granted by the mother of the deceased.

CASE DESCRIPTION

A 52-year-old patient was scheduled for a cystoscopy, retrograde x-ray studies of the native ureters, and bladder biopsies. Medical history was significant for end-stage renal disease secondary to familial glomerulonephritis and renal allograft dysfunction. As part of the workup for a second kidney transplant, a cardiac stress test was recently performed, which showed no evidence of significant reversible perfusion changes in the heart. Left ventricular ejection fraction was an estimated 67% at rest and 52% at stress. The patient was on long-term warfarin after deep venous thrombosis and was therefore considered a high risk for thrombotic events. Before surgery, warfarin was switched to heparin. The use of thromboembolism-deterrent stockings was contraindicated due to suspected peripheral arterial disease; however, intermittent pneumatic compression-boots for intraoperative embolic prophylaxis were used. The most recent general anesthetic for a thyroidectomy was uneventful. The patient denied any allergies, myocardial infarcts, strokes, diabetes mellitus, asthma, or smoking. Home medications were significant for propranolol and thyroxine. Vital signs as well as electrolyte and hemoglobin levels were within normal range on the day before surgery.

Monitoring according to national standards was established. The electrocardiogram showed a sinus rhythm of 61 bpm and normal repolarization, and his noninvasive blood pressure was 140/90 mm Hg. Anesthesia was induced by

intravenous injection of 150 µg of fentanyl and a cumulative dose of 200 mg propofol. Subsequently, a laryngeal mask airway was inserted and correct placement was confirmed by successful ventilation with 2.1% sevoflurane in oxygen. A postinduction blood pressure was taken and was unchanged at 140/90 mm Hg. The patient was transferred onto the operating table and his legs were elevated into the lithotomy position. After that maneuver, the patient coughed and anesthesia was deepened by an increase in sevoflurane concentration and the injection of 25 mg of atracurium. After the administration of atracurium, the patient became bradycardic (45 bpm) and 600 µg of atropine were administered intravenously. He subsequently became severely hypotensive (60/40 mm Hg), and his carotid pulse was not palpable. A bolus of 1 mg of intravenous epinephrine was administered. He had normal gas exchange, normal airway pressures, normal breath sounds, and equal air entry. A second dose of 600 µg of atropine was administered and a crash call was sent. The sevoflurane administration was stopped and the inspired oxygen concentration was increased to 100%. The surgical team commenced chest compressions, and the patient received another milligram of epinephrine intravenously. Subsequently, the laryngeal mask airway was exchanged to an endotracheal tube. The patient had a pulseless electrical activity (PEA) arrest diagnosed. He received more epinephrine during uninterrupted cardiopulmonary resuscitation. The first arterial blood gas was taken via a freshly inserted arterial line. The potassium level was 4.97 mmol/L, and his hemoglobin level was 125.4 g/L. A subsequent arterial blood gas was taken 15 minutes later and showed no abnormal electrolyte values. A central line was inserted and revealed a central venous pressure of 15 mm Hg, and an epinephrine infusion was started via this line. A promptly obtained transthoracic echocardiogram showed no impairments. Noninvasive transcutaneous pacing via external chest electrodes was unsuccessful. Despite major and prolonged efforts for 60 minutes, we could not revive the patient.

The internal examination during the postmortem found no signs of thromboembolic events and no significant coronary artery disease. However, the heart was enlarged (580 g) and myocardial scarring was detected. The toxicology report revealed normal plasma levels of 0.3 µg/mL propofol, 0.001 µg/mL fentanyl, and traces of laudanosine. However, a significantly increased mast cell tryptase of 102 µg/L was detected. After a coroner's inquest with expert

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witnesses from a national protein reference unit, the verdict was fatal anaphylaxis to atracurium.

DISCUSSION

During the incident, the patient presented none of the classical clinical signs of anaphylaxis, that is, bronchospasm, tachycardia, or a skin rash. The key feature was hypotension accompanied by bradycardia, PEA arrest, and finally asystole. Even high doses of epinephrine and uninterrupted chest compressions failed to reestablish cardiac output. This case is a reminder that rapid cardiovascular collapse can be the sole clinical feature of a fatal anaphylaxis to atracurium.

NMBDs account for most cases of perioperative anaphylaxis and are usually associated with the classic clinical signs of flushing or urticaria, tachycardia, or bronchospasm.^{1,2} However, in 10% of cases, bradycardia or hypotension may be the sole clinical feature.^{3,4} Patients taking β -blocking drugs may suffer a more severe reaction, and some of these reactions may be refractory to conventional therapy.⁴ The patient had unintentionally omitted his morning dose of propranolol, and his heart rate before induction of anesthesia and during anesthesia ranged from 61 to 70 bpm; a β -blocker overdose and any need for glucagon treatment were dismissed by the team of 3 attending anesthesiologists. Equally, because bradycardia was the leading feature of the arrest, H1/H2 blockade or vasopressin was not necessarily indicated according to the European Resuscitation Guidelines.⁵ The patient received 60 minutes of chest compressions, and 5 boluses of epinephrine, followed by a continuous epinephrine infusion, as well as external cardiac pacing but remained in refractory PEA arrest. Although the use of noninvasive transcutaneous pacing is not part of the treatment algorithm for PEA arrest, it might be beneficial in toxic exposure or electrolyte abnormalities.⁵

Cardiocirculatory arrest as the initial manifestation of anaphylaxis is usually triggered by extreme vasodilation that impairs venous filling followed by myocardial ischemia and PEA. The lack of circulatory volume ends in epinephrine-unresponsive shock.⁶ It is also described that during anaphylaxis, histamine, leukotrienes, platelet-activating factor, and other mediators released from cardiac mast cells might contribute to vasoconstriction and coronary artery spasm.⁷

The pathology results were not able to distinguish between an anaphylactic or an anaphylactoid reaction. Because our patient had been exposed to atracurium during previous general anesthetics, an IgE-mediated reaction is more likely.⁸ However, Immunoglobulin E-mediated reactions can also occur in patients with no previous exposure to the drugs. The quaternary ammonium moiety common to many NMBDs is also common in many environmental chemicals, and sensitization may occur before exposure

to NMBDs.⁸ Anaphylactic reactions to atracurium are also known after direct activation of mast cells, not involving antigen binding to IgE, and that monomeric IgE under certain conditions can also cause degranulation and the release of mediators such as histamine, prostaglandins, proteoglycans, and cytokines, leading to the clinical manifestations of anaphylaxis.⁸ A recent retrospective, observational cohort study of intraoperative anaphylaxis to NMBDs by Reddy et al⁹ implicated rocuronium as a significantly more potent trigger than atracurium. The implications of his results, however, have been debated by other authors.¹⁰

We assume that, in our case, the patient's concomitant medication and his preexisting myocardial pathology contributed to the fatal outcome. This case is a reminder that rapid cardiovascular collapse can be the sole clinical feature of anaphylaxis. ■■

DISCLOSURES

Name: Jan Schumacher, MD, PhD.

Contribution: This author collected and analyzed all of the data, and wrote the manuscript.

This manuscript was handled by: BobbieJean Sweitzer, MD, FACP.

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