J Anesth (2010) 24:143–145
DOI 10.1007/s00540-009-0839-z

CLINICAL REPORT

Suspected recurrent anaphylaxis in different forms during general anesthesia

Hirokazu Imanishi · Akira Kitamura · Kouichi Maruyama · Jun Ariyama · Hideyuki Nakagawa · Shinichi Nishibe · Masakazu Hayashida · Yutaka Usuda

Received: 17 June 2009 / Accepted: 3 September 2009 / Published online: 6 January 2010

Abstract We report on a patient who presented with recurrent severe shock during general anesthesia. The patient was a man scheduled for lung surgery whose first attack was a coronary spasm, which was followed by a second shock with severe bronchospasm and hypotension 4 weeks later. An elevated serum tryptase concentration was observed, and subsequent skin testing revealed negative reactions to some drugs administered in this case. This case serves to alert anesthetists to the possibility of some different forms of allergy and highlights the importance of rigorous investigation of all the reagents and phenomena.

Keywords Anaphylaxis · Shock · Recurrent · Coronary spasm · General anesthesia

Introduction

After induction of general anesthesia, we sometimes have hypotension before surgery. Most of those cases are due to the anesthetic drugs associated with myocardial depression and direct or indirect systemic vasodilation, and anaphylaxis is rare. Anaphylactic reactions are uncommon occurrences during anesthesia, and potentially life-threatening, so they require prompt recognition and immediate management. Although the incidence of anaphylaxis during anesthesia is unclear, it is estimated to occur in 1 in 6,000 to 1 in 10,000 anesthetic administrations [1–3]. As there are various forms of allergic reaction, it is sometimes hard to make a judgment that it is anaphylaxis. The diagnosis of an anaphylactic reaction, especially during anesthesia, may be challenging and must always be kept in mind.

We present a case of two severe hypotensive reactions in a man scheduled for lung surgery; the first being a coronary spasm, which was followed by a second shock with severe bronchospasm and hypotension. This case serves to alert anesthetists to the possibility of different forms of allergy and highlights the importance of rigorous investigation of all the reagents used when an anaphylactic reaction is suspected.

Case report

A 66-year-old, 65-kg, 165-cm-tall man was scheduled for a thoracotomy and resection of a right upper-lobe lung mass. He had hypertension and no history of coronary artery disease, and all the preoperative tests, including a chest radiograph and ECG, revealed no abnormalities. He had no known previous food or drug allergies, no predisposing factors to latex allergy, and no history of asthma, eczema, or hay fever. He had been hospitalized for a right hemicolectomy for colon cancer 6 months previously and had encountered no problems.

General anesthesia was induced with fentanyl and propofol, using rocuronium bromide for neuromuscular blockade. The patient was not premedicated. Epidural analgesia was established with 5 ml 1% lidocaine. The trachea was intubated with a left double-lumen endotracheal tube, and proper positioning was confirmed by bronchoscopy. Anesthesia was maintained with sevoflurane in oxygen-enriched air. The patient was then placed in the lateral

H. Imanishi · A. Kitamura (✉) · K. Maruyama · J. Ariyama · H. Nakagawa · S. Nishibe · M. Hayashida · Y. Usuda
Department of Anesthesiology,
Saitama International Medical Center,
Saitama Medical University, 1397-1 Yamane,
Hidaka, Saitama 350-1298, Japan
e-mail: kita5@saitama-med.ac.jp

decubitus position. Hemodynamic values remained stable for the first 20 min after the induction of anesthesia. Twenty minutes after the induction of anesthesia, antibiotics (1 g cefuroxime) and 0.2 μg kg^{-1} min^{-1} remifentanil were administered to the patient. Within 5 min the patient showed ST segment elevation on the lead II ECG soon after that his systolic blood pressure and heart rate had dropped from 100 to 30 mmHg and from 60 to 30 beats min^{-1}, respectively. Resuscitation commenced immediately with 0.5 mg boluses of intravenous epinephrine, and 0.5 mg boluses of intravenous isosorbide dinitrate following the diagnosis of the coronary spasms. The elevation of the ST segment observed on the ECG dissipated after 10 min, and the systolic blood pressure was maintained with a dopamine infusion (up to 10 μg kg^{-1} min^{-1} in the immediate resuscitation phase). Flushing or urticaria was not observed. The airway pressure was slightly elevated, about 20–25 cmH_2O. Surgery was suspended and the patient was transferred to the intensive care unit (ICU), and was extubated 3 h after admission into the ICU. He was investigated thoroughly, including by radiographical and angiographical examination, which revealed no abnormalities.

Four weeks after the first anesthesia, the same surgery plan was made. General anesthesia and epidural analgesia were induced in the same way as the first anesthesia. At 20 min after administration of 0.2 μg kg^{-1} min^{-1} remifentanil, the patient had the remarkable increase in airway pressure during volume-controlled ventilation, and the systolic blood pressure dropped from 100 to 50 mmHg. The ECG readings were unchanged. Other findings, for example flushing or urticaria, were not observed as in the previous anesthesia. For resuscitation, intravenous 0.5 mg epinephrine, 1,000 ml lactate Ringer's solution, and 100 mg hydrocortisone were immediately administered. Surgery was suspended again, and the patient was transferred to the ICU. The patient was weaned off ventilatory support after approximately 5 h, and made a full recovery. A venous sample was collected for serum tryptase analysis 2 h after the event. The patient's mast cell tryptase was 13.8 μg l^{-1} (normal range 3.0–6.0 μg l^{-1}). The patient was drug lymphocyte stimulation-tested (DLST) with cefuroxime, propofol, and lidocaine on the day, and skin-prick tested with remifentanil, fentanyl, and rocuronium bromide 2 months later. The reaction to these tests was negative to all drugs. After that, the patient finally canceled the operative therapy and selected radio and chemotherapy for the lung cancer by his own judgment.

Discussion

This case highlights some of the practical difficulties in the initial diagnosis and subsequent investigation of the cause of anaphylactic reaction during general anesthesia. The two occurrences of shock cannot be identified as anaphylaxis with only one positive result of serum tryptase level. However, the clinical course of severe hypotension with profound ST segment the first time, and severe hypotension with remarkably increased airway pressure, like a bronchospasm, the second time, made us diagnose anaphylactic shock. It was not possible to know that the first shock was due to anaphylaxis, because attacks of coronary artery spasm are frequently related to inadequate depth of anesthesia, the use of vasopressors, and vagal reflex, and are rarely associated with anaphylaxis. However, coronary spasm related to anaphylaxis is not without precedent [4, 5]. Severe vasodilatation with insufficient coronary blood flow in this case may have created a significant energy supply–demand imbalance in the myocardium. It might be reasonable to suspect that anaphylaxis itself was the cause of coronary spasm.

Several features of this case merit discussion. Initial presentation of anaphylaxis can vary, potentially involving numerous organ systems. The most common system involved is cardiovascular (hypotension, arrhythmia, myocardial depression, cardiovascular collapse), followed by cutaneous (flushing, urticaria) and respiratory (bronchospasm, laryngeal edema) manifestations [6]. The patient in this case did not show any cutaneous findings, so we could not recognize the shock at the first anesthesia as an anaphylactic reaction. The following day the patient underwent the second surgical operation under general anesthesia and was re-exposed to the same agents as the first anesthesia, resulting in bronchospasm and severe hypotension. A clinically indistinguishable syndrome, anaphylactoid reaction, can only be differentiated with later testing.

Detection of the causative drug in drug allergies is essential in order to prevent secondary allergic reactions and is also extremely important so that appropriate medical treatment can be administered when such reactions occur. Although the DLST method is safe for the patient, the rate of detection is not so high (40% or less) and the optimal timing of the testing is important. It might be better to perform the testing about 2 months after the episode. The suspicion of a drug-related anaphylactic shock was verified and confirmed by the elevated concentration of plasma tryptase. Tryptase, a protease released from activated mast cells, can be used as a marker of immune activation. An elevated serum tryptase concentration in blood drawn within several hours of the event can be helpful, although it cannot differentiate between anaphylaxis and an anaphylactoid reaction. A normal result, however, does not exclude these diagnoses [7].

The most valuable test to identify the drug responsible for an IgE-mediated anaphylactic reaction is skin testing.

Subsequent skin testing (performed according to the recommendations of Mertes et al. [8]) revealed negative reactions to three drugs administered in this case. A number of studies have demonstrated the usefulness of skin tests to retrospectively confirm allergy to some kinds of drugs [2]. Numerous agents have been identified as triggers of intraoperative anaphylaxis, the most common being neuromuscular blocking drugs and latex [6, 9]. A recent survey found that neuromuscular blocking drugs, most commonly rocuronium and succinylcholine, accounted for 58.2% of perioperative events [9]. These were followed by latex (16.2%), antibiotics (15.1%), colloids (4.0%), hypnotics (3.4%), and opioids (1.3%). Outside the perioperative period, insect stings and some foods (peanuts, shellfish, and tree nuts) are also common triggers.

We could not confirm the diagnosis of drug allergy by skin tests in this case, however the causative agent cannot always be identified. As the optimal timing of skin prick testing is four to 6 weeks after the episode, because of the consumption of IgE-antibody, the skin testing might be too late in this case. A retrospective survey comparing suspected causes with the result of subsequent testing found that, in 49 of 67 cases, the suspected agent did not match testing results [10]. Viewed in the course of anaphylactic reactions, remifentanil was suspected as the trigger in our case. The patient suffered shock several minutes after administration of remifentanil for the second time. There have been some reported cases of opioid-induced anaphylaxis [11, 12], in each of which the reaction presented as hypotension and urticaria. Opioid-induced anaphylaxis, however, is rare, and negative in the skin prick test in our case. While the skin prick test sometimes produce false-negatives, the possibility remains that remifentanil was the trigger of these phenomena.

We describe a patient who experienced intraoperative anaphylactic shock twice. The incidence of coronary artery spasm occurring in response to anaphylaxis is very low. This case serves to alert anesthetists to the possibility of different forms of allergy and highlights the importance of rigorous investigation of all the reagents used when an anaphylactic reaction is suspected.

References

1. Fisher MM, Baldo BA. Anaphylaxis during anaesthesia current aspects of diagnosis and prevention. Eur J Anaesthesiol. 1994; 11:263–84.
2. Laxenaire MC, The Members of the Writing Committee. Drugs and other agents involved in anaphylactic shock occurring during anaesthesia. A French multicenter epidemiological inquiry. Ann Fr Anesth Reanim. 1993;12:91–6.
3. Mertes PM, Laxenaire MC. Allergic reactions occurring during anaesthesia. Eur J Anaesthesiol. 2002;19:240–62.
4. Osugi T, Ueki R, Shimode N, Takara T, Tashiro C. Blood transfusion-induced anaphylaxis and coronary artery spasm during general anesthesia. J Anesth. 2008;22:457–9.
5. Fujita Y, Chikamatsu M, Kimura M, Toriumi T, Endoh S, Sari A. An anaphylactic reaction possibly associated with an intraoperative coronary spasm during general anesthesia. J Clin Anesth. 2001;13:221–6.
6. Laxenaire MC, Mertes PM. Anaphylaxis during anaesthesia. Results of a two-year survey in France. Br J Anaesth. 2001; 87:549–58.
7. Fisher NM, Baldo BA. Mast cell tryptase in anaesthetic anaphylactoid reactions. Br J Anaesth. 1998;80:26–9.
8. Mertes PM, Laxenaire MC, Lienhart A, Aberer W, Ring J, Pichler WJ, et al. Reducing the risk of anaphylaxis during anesthesia: guidelines for clinical practice. J Investig Allergol Clin Immunol. 2005;15:91–101.
9. Mertes PM, Laxenaire MC, Alla F. Anaphylactic and anaphylactoid reactions occurring during anesthesia in France in 1999–2000. Anesthesiology. 2003;99:536–45.
10. Kroigaard M, Garvey LH, Menne T, Husum B. Allergic reactions in anaesthesia: are suspected causes confirmed on subsequent testing? Br J Anaesth. 2005;95:468–71.
11. Zucker-Pinchoff B, Ramanayhan S. Anaphylactic reaction to epidural fentanyl. Anesthesiology. 1989;71:599–601.
12. Cummings KC 3rd, Arnaut K. Case report: Fentanyl-associated intraoperative anaphylaxis with pulmonary edema. Can J Anesth. 2007;54:301–6.