J Anesth (2011) 25:606–608
DOI 10.1007/s00540-011-1148-x

CLINICAL REPORT

Anaphylaxis to pantoprazole during general anesthesia

Hou-Chuan Lai · Shih-Wei Hsu · Chueng-He Lu · Hsin-I Ma · Chen-Hwan Cherng · Nan-Kai Hung · Ching-Tang Wu

Received: 8 March 2011 / Accepted: 6 April 2011 / Published online: 29 May 2011

Abstract The most frequent causes of anaphylaxis during anesthesia are neuromuscular blocking agents, antibiotics, and latex. Proton pump inhibitors (PPI) are widely used during major surgery for the prevention of stress ulcers, but cases of perioperative anaphylactic reactions to these have rarely been reported. We present a 50-year-old male patient who experienced an episode of anaphylaxis with hypoxemia, hypotension, tachycardia, and generalized erythema after intravenous injection of pantoprazole 40 mg and methylprednisolone 1 g during general anesthesia. After resuscitation, the patient recovered without any sequelae. Six months after the surgery, a skin test was positive to pantoprazole.

Keywords Anaphylaxis · Proton pump inhibitors · Pantoprazole · Steroid · Anesthesia

Introduction

The incidence of anaphylaxis during anesthesia ranges from 1 in 13,000 to 1 in 3,180, and the rate of mortality ranges between 3% and 9% [1]. Among these, neuromuscular blocking agents are most frequently involved, followed by latex and antibiotics [1]. Proton pump inhibitors (PPI) are widely used for the prevention of stress ulcers during major surgery [2], with a low incidence of adverse reactions, such as nausea, diarrhea, dizziness, headache, hyperglycemia, Stevens–Johnson syndrome, and anaphylaxis [3]. An anaphylactic reaction to pantoprazole is very rare. To our knowledge, there is no report in the literature of anaphylaxis to pantoprazole during anesthesia. Here, we report a patient who experienced pantoprazole-induced anaphylaxis during general anesthesia (GA) despite the concurrent use of steroids.

Case report

A previously healthy, 50-year-old, 60-kg, 170-cm man was scheduled for elective microdiscectomy, L5–S1, under GA. The patient did not take any premedication before the surgery. Routine anesthetic monitoring including electrocardiography (lead II), pulse oximetry, and noninvasive blood pressure was prescribed before induction. The patient received IV fentanyl 2 μg/kg, dexamethasone 5 mg, and 2% lidocaine 1.5 mg/kg before anesthesia. Total intravenous anesthesia was induced with continuous infusion of propofol (Fresfol 1%) using the Schneider kinetic model target-controlled infusion (TCI) system with an effect-site concentration (Ce) of 4.0 μg/ml. When the patient lost consciousness, 0.6 mg/kg rocuronium was given. Anesthesia was maintained using TCI with propofol and an oxygen flow of 0.3 l/min without air mix. Propofol was adjusted to keep the auditory evoked potential index (AAI) between 15 and 25 during maintenance of anesthesia. Fentanyl 50 μg IV every 40 min was prescribed for attenuating surgical pain. Ventilation rate and maximum airway pressure were adjusted to maintain end-tidal carbon

H.-C. Lai · C.-H. Lu · C.-H. Cherng · N.-K. Hung · C.-T. Wu (✉)
Department of Anesthesiology, Tri-Service General Hospital and National Defense Medical Center, #325, Section 2, Chenggung Road, Neihu 114, Taipei, Taiwan, Republic of China
e-mail: wuchingtang@msn.com

S.-W. Hsu · H.-I. Ma
Department of Neurosurgery, Tri-Service General Hospital and National Defense Medical Center, Taipei, Taiwan, Republic of China

dioxide ($EtCO_2$) pressure at 35–45 mmHg. Rocuronium (10 mg IV) was given as required by the return of neuromuscular function as confirmed by train-of-four (TOF) peripheral nerve stimulation. The patient received 1 g cefazolin as a prophylactic antibiotic after anesthesia induction. No skin rash or changes in vital signs occurred after induction.

The procedure was performed smoothly for 70 min until IV infusion with pantoprazole 40 mg over 2 min for prevention of stress ulcers [2] and methylprednisolone 1 g for prevention of neuropathic limb edema, administered simultaneously [4]. Five minutes after administration of pantoprazole and methylprednisolone, the patient developed hypoxemia ($SpO_2 = 89\%$), hypotension (systolic blood pressure < 80 mmHg), and tachycardia (120–130 beats/min); airway pressure was 4–28 cm H_2O, $EtCO_2$ pressure was 38 mmHg, and generalized erythema was noted over the back and face. The patient was successfully resuscitated with 100% oxygen, ephedrine 20 mg, and saline infusion 1,000 ml. His symptoms gradually improved after resuscitation, so his elective surgery was completed. The entire period under anesthesia was 3 h. The patient was transferred to the intensive care unit (ICU) after the surgery. Five hours after arrival in the ICU, no edema of the larynx and airway was observed, the patient was hemodynamically stable, and the endotracheal tube was removed without any complications. One day later, he was transferred to the ordinary ward and discharged without any sequelae 2 days later. Six months later, a skin prick test with pantoprazole (4 mg/ml) was performed on the volar side of the forearm. A positive reaction (wheal, 25 mm) was observed 20 min later. Histamine (10 mg/ml) was used as a positive control, and normal saline was used as a negative control.

Discussion

Neuromuscular blocking agents and antibiotics represent the most frequent substances causing perioperative anaphylaxis [1]. However, in this case, the antibiotic and muscle relaxant did not seem to be the cause of the anaphylaxis, because the anaphylaxis occurred 70 min after their administration. Moreover, the patient received the same muscle relaxant and antibiotic after resuscitation, but no recurrence of anaphylaxis was noted. In addition, there are indeed cases reported in the literature of anaphylaxis to steroids [5, 6]. However, the patient received dexamethasone 5 mg at induction, and anaphylaxis occurred 70 min after induction. Hydrocortisone sodium succinate 200 mg was also administered after resuscitation, but no recurrence of anaphylaxis was noted. From this point of view, steroids seemed not to cause anaphylaxis. The immediate development of anaphylaxis in response to pantoprazole and the result of the skin prick test were highly suggestive of pantoprazole-induced anaphylaxis during anesthesia.

Anaphylaxis to PPI has rarely been described. Anaphylaxis to oral pantoprazole has been reported for 4 patients [7–10]. In addition, previous reports [11–13] described 3 patients who developed anaphylaxis to omeprazole with positive skin prick tests. Lobera and his colleagues [14] demonstrated that there was a cross-reactivity between PPIs in 9 patients who experienced an anaphylactic reaction to oral pantoprazole, omeprazole, and lansoprazole. Therefore, until now, only 16 patients have been reported to suffer anaphylaxis to PPIs [7–14], and these reactions did not occur during anesthesia.

The clinical presentations include hypoxemia, hypotension, tachycardia, and generalized erythema. The diagnosis relies on tryptase measurements at the time of the reaction or skin prick tests or specific immunoglobulin (Ig)E or basophil activation assays [1]. We did not measure tryptase within 2 h or 24 h later because of our limited facility; also, the patient refused it. However, we performed a skin prick test. Treatment consists of instant interruption of contact with possible antigens, 100% oxygen, intubation, adrenaline, and volume expansion [15]. Steroids are used to treat anaphylaxis, although there is no convincing evidence of their effectiveness [16, 17]. In this case, however, prophylactic steroid did not prevent pantoprazole-induced anaphylaxis during GA, consistent with the observation of Kwittken et al. [18], who observed perioperative latex hypersensitivity reactions despite prophylactic steroid. Nevertheless, this aspect needs further study for verification.

In conclusion, anesthetists should be alert when PPIs are used. Although anaphylaxis caused by pantoprazole is rare, it remains a potential cause of perioperative anaphylaxis despite the concurrent use of steroids.

References

1. Moneret-Vautrin DA, Mertes PM. Anaphylaxis to general anesthetics. Chem Immunol Allergy. 2010;95:180–9.
2. Pang SH, Graham DY. A clinical guide to using intravenous proton-pump inhibitors in reflux and peptic ulcers. Ther Adv Gastroenterol. 2010;3:11–22.
3. Dekel R, Morse C, Fass R. The role of proton pump inhibitors in gastro-oesophageal reflux disease. Drugs. 2004;64:277–95.
4. Kingery WS, Guo T, Agashe GS, Davies MF, Clark JD, Maze M. Glucocorticoid inhibition of neuropathic limb edema and cutaneous neurogenic extravasation. Brain Res. 2001;913:140–8.
5. Shirahata A, Matsumiya A, Saito M, Ishibashi K, Kigawa G, Nemoto H, Sanada Y, Hibi K, Kou Y, Watanabe R. A case of advanced breast cancer with anaphylaxis-like reaction after intravenous administration of dexamethasone. Gan To Kagaku Ryoho. 2009;36:1383–5.

6. Steiner UC, Gentinetta T, Hausmann O, Pichler WJ. IgE-mediated anaphylaxis to intraarticular glucocorticoid preparations. Am J Roentgenol. 2009;193:156–7.
7. Natch S, Vinks Mh, Voogt AK, Mees EB, Meyboo RH. Anaphylactic rections to proton pump inhibitors. Ann Pharmacother. 2000;34:474–6.
8. Fardet L, Izzedine H, Ciroldi M, Tiev KP, Cabane J. Pantoprazole-induced recurrent anaphylactic shock. Am J Gastroenterol. 2002;97:2933.
9. Kaatz M, Bauer A, Hipler C, Elsner P. Nonallergic anaphylaxis to pantoprazole. Allergy. 2002;57:184.
10. Kollmeier AP, Eddleston J, Zuraw BL, Christiansen SC. Recurrent anaphylaxis linked to pantoprazole. J Allergy Clin Immunol. 2004;114:975–7.
11. González P, Soriano V, López P, Niveiro E. Anaphylaxis to proton pump inhibitors. Allergol Immunopathol. 2002;30:342–3.
12. Galindo PA, Borja J, Feo F, Gómez E, García R, Cabrera M, Martinez C. Anaphylaxis to omeprazole. Ann Allergy Asthma Immunol. 1999;82:52–4.
13. Ottenwanger JP, Phaff RAS, Vermeulen EGJ, Stricker BHC. Anaphylaxis to omeprazole. J Allergy Clin Immunol. 1996;97:1413–4.
14. Lobera T, Navarro B, Del Pozo MD, González I, Blasco A, Escudero R, Venturini M, Alarcón E. Nine cases of omeprazole allergy: cross-reactivity between proton pump inhibitors. J Invest Allergol Clin Immunol. 2009;19:57–60.
15. Soetens FM. Anaphylaxis during anesthesia: diagnosis and treatment. Acta Anaesthesiol Belg. 2004;55:229–37.
16. Whiteside M, Fletcher A. Anaphylactic shock: no time to think. J R Coll Physicians Edinb. 2010;40:145–7.
17. Choo KJ, Simons FE, Sheikh A. Glucocorticoids for the treatment of anaphylaxis: Cochrane systematic review. Allergy. 2010;65:1205–11.
18. Kwittken PL, Becker J, Oyefara B, Danziger R, Pawlowski NA, Sweinberg S. Latex hypersensitivity reactions despite prophylaxis. Allergy Proc. 1992;13:123.