Case Report

A critical incident report: Propofol triggered anaphylaxis

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ABSTRACT

Although propofol is one of the most commonly used drugs for induction of anaesthesia, it is not devoid of anaphylactic potential. Early detection of any suspected anaphylactic reaction during anaesthesia, prompt management, identification of the offending agent and prevention of exposure to the offending agent in the future is the responsibility of the anaesthesiologist. This is a case report of anaphylaxis to propofol at the induction of anaesthesia in a previously non-allergic 56 year-old man, planned to undergo laparoscopic nephrectomy, who responded to epinephrine infusion.

Key words: Anaphylaxis, epinephrine, propofol

INTRODUCTION

Anaphylaxis is an acute life-threatening systemic reaction that requires quick diagnosis and correct management to save the patient. Although it is a rare intraoperative complication, most drugs used in the perioperative period can lead to anaphylaxis. The incidence of anaphylaxis during anaesthesia has been estimated between 1 in 10,000 and 1 in 20,000.[1] The rate of mortality ranges between 3 and 9%. Ninety percent of the anaphylactic reactions occur at the time of induction of anaesthesia.[2]

Nowadays, propofol is the most widely used drug not only for induction of anaesthesia but also for sedation in various settings – short surgical procedures under total intravenous anaesthesia, intensive care settings and paediatric procedures. Propofol (2, 6 di-isopropylphenol) is currently formulated in a lipid vehicle containing soya bean oil, egg lecithin and glycerol. The incidence of anaphylactic reactions with this formulation has been reported as 1:60,000.[3] 1.2% of the cases of perioperative anaphylaxis in France have been reported to be caused by propofol.[4] Anaphylactic shock has also been reported in the European literature after first exposure to propofol.[5] We also report a case of anaphylaxis to propofol (Diprivan, 1% formulation in 10% soyabean oil containing disodium edetate glycerol and egg lecithin) after first exposure at the time of induction of anaesthesia.

CASE REPORT

A 56 year-old male patient, ASA I, weighing 64 kg, diagnosed as having right renal mass, was scheduled for elective laparoscopic nephrectomy. He had no past history of allergy to drugs and his physical examination and investigations (blood investigations, chest X-ray and electrocardiogram) were all within normal limits. General anaesthesia with endotracheal intubation was planned for the surgery. On arrival in the operation theatre, his non-invasive blood pressure was 120/80 mmHg, heart rate was 78/min and SpO_2 100% on room air were recorded.

After insertion of an 18G intravenous cannula in the dorsum of the hand, Inj. Magnamycin (Sulbactam and Cefoperazone) 1 g diluted in 10 ml of normal

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saline was injected slowly over 10 min and injection Amikacin sulphate 500 mg was given intravenous over 15 min in 100 ml normal saline. Because of some technical reasons there was a delay of 45 min before the induction of anaesthesia. During this time, the patient was haemodynamically stable with pulse of 70–75/min and BP 120/70 mmHg. At induction, fentanyl citrate 100 μg, propofol 80 mg and vecuronium bromide 6 mg was given to aid intubation. During the time positive-pressure ventilation was being given, the blood pressure dropped to 60/30 mmHg with tachycardia of 130–150 beats/min. The intravenous fluid infusion rate was increased and ephedrine 3 mg, repeated twice, was given intravenous. The trachea was intubated and the patient was ventilated with 100% O_2. Thereafter, a cutaneous rash was visible all over the body and the patient's lips, eyes, ears and hands appeared swollen and edematous. A provisional diagnosis of drug reaction was made and resuscitation was started. Injection adrenaline 0.2 mg intravenous bolus, Trendelenberg position, intravenous crystalloids 2–2.5 L over the next 2 h and injection hydrocortisone 200 mg intravenous were given. During this time, his systolic blood pressure was between 40 and 60 mmHg and diastolic blood pressure was 25–40 mmHg, even after a repeat dose of intravenous adrenaline 0.2 mg. Because the blood pressure was not responding, adrenaline infusion 0.05 μg/kg/min was started. After about 1.5 h, the patient's condition started improving and he became hemodynamically stable. The inotropic support was gradually withdrawn. The patient was mechanically ventilated till the blood pressure stabilized to 100/60 mmHg and pulse rate to 100/min. There was no evidence of bronchospasm and peak inspiratory pressure remained within normal limits. We confirmed absence of edema in the oral cavity, uvula and epiglottis by larygoscopic examination. When the patient was fully awake and there was sufficient leak around the deflated cuff, the trachea was extubated after 3 h with Cook's airway exchanger in trachea, which was subsequently removed after a few hours [Figure 1].

The surgery was postponed. The patient was kept under observation for 24 h in the post post-anaesthesia care unit and discharged home after 48 h.

Blood samples for plasma levels of lgE antibody were sent and the reported value was 350 ng/ml (normal reference value in our lab is less than 50 ng/ml). The patient underwent a skin test 3 weeks after the event. The skin test included skin prick test and intradermal test using saline as negative control and histamine as positive control. The prick test was performed on the anterior aspect of the forearm using a drop of undiluted propofol, vecuronium, amikacin, magnamycin, 10% intralipid and diluted fentanyl (1 in 10 dilution). It showed a positive response with propofol only. The intradermal test was then performed on the other forearm by injection of 0.02–0.05 ml of the diluted drugs in saline starting with a dilution of 1 in 1000 progressing to a dilution of 1 in 10. The intradermal test of propofol showed a positive response at 1 in 1000 dilution thus confirming our suspicion of anaphylaxis to propofol.

The same patient was again taken up for surgery 4 weeks later. This time, injection thiopentone sodium was used for induction instead of propofol while all other drugs were the same as that used for induction during the first time. The surgery and anaesthesia were uneventful [Figure 2] and the patient was discharged after 3 days.

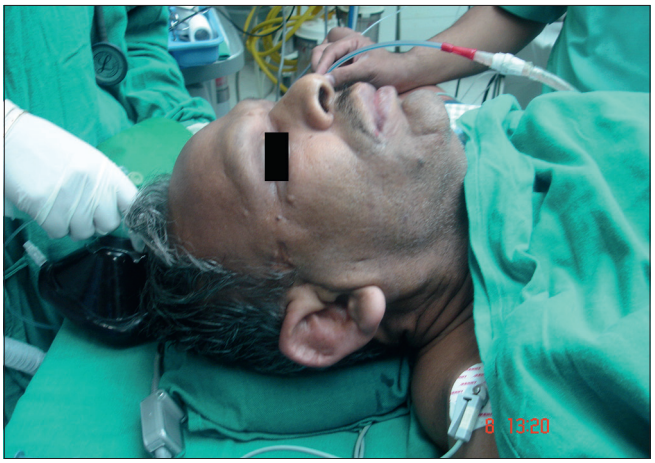

Figure 1: Patient after extubation with evident swelling over the ear lobule, periorbital tissues and lips

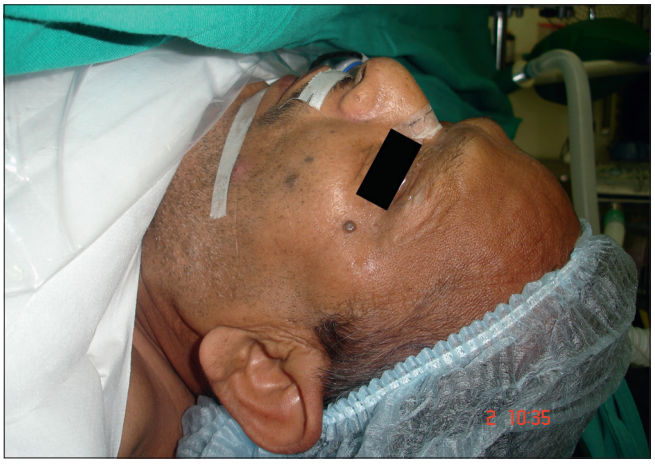

Figure 2: Patient during the second surgery with no evidence of anaphylaxis

DISCUSSION

Our suspicion of anaphylaxis was based on the presence of cutaneous rash all over the body, oedema over the face and upper limbs and severe hypotension not responding initially to intermittent doses of adrenaline. Serological testing for confirmation of anaphylactic reaction includes measurement of mast cell tryptase levels immediately after the event, 1 h later and 24 h later. Detection of the presence of IgE antibodies by the Radioallergosorbent test (RAST) measures the presence of specific IgE antibodies in the serum that bind to a disc coupled with the specific drug. RAST is highly specific, but sensitivity is low for most of the drugs.[6] Because there is no facility for measuring mast cell tryptase level and drug drug-specific IgE levels at our centre, we could not measure them. Although total IgE levels were raised significantly, this does not confirm anaphylaxis as drug-specific IgE levels could not be measured and, therefore, we went ahead with skin tests that are more specific than measuring IgE levels. Skin tests have global efficiency comparable to specific IgE assays.[7]

Skin tests remain the gold standard for IgE -mediated reactions. Ideally, the skin test should be performed 4–6 weeks after the event because of the risk of a false negative result. In our case, because of the semiemergent nature of case (renal tumour), it compelled us to carry out the test earlier. The patient and the surgeon were very keen to have the tumour removed at the earliest. If necessary, the skin test can be performed earlier, but if the results are negative, they require subsequent confirmation.

The skin prick test is easier and less traumatic to perform, but the intradermal test is more sensitive than the skin prick test; it carries a higher risk of inducing a false positive reaction and is more likely to cause systemic reactions.[6]

The detection of drug causing anaphylaxis is difficult because, at induction, multiple drugs are administered. Non-depolarizing muscle relaxant and latex are the leading cause of allergy. This patient was not exposed to latex and thus it was ruled out as a cause of anaphylaxis.[8]

Anaphylaxis due to propofol is rare; it has two potential allergenic molecules – the di-isopropyl side chain and phenol.[9] Propofol when given in an oil water emulsion equivalent to 10% intralipid provides 1.8–2.4 g/kg of intravenous lipids daily, which is within the range used in parentral nutrition. Therefore, the immunological test with 10% intralipid is carried out to rule out the lipid solvent as the allergenic molecule.[10] Many patients who develop anaphylaxis after first exposure may do so because of sensitivity to the di-isopropyl radical that is found in many dermatological products and lipid formulations. Thus, history of prior use of parenteral nutrition with intralipids and sensitivity to dermatological products is important. But, in this patient, skin tests with 10% intralipid were negative. Our patient had no history of allergies, but his anaphylactic reaction shows that sensitization can occur in normal persons who might have been exposed to phenolic group in the past. Allergic reactions to propofol upon re-exposure are because of the phenol group. There are many case reports of adverse reactions to propofol. Laxenaire in 1992[11] reported 14 cases of anaphylaxis to propofol, Oscar in 1992[9] reported a case of anaphylaxis after the third exposure to propofol, Nishiyama and Hanaoka in 2001[12] reported a case of propofol induced bronchoconstriction and McNcill in 2008[13] reported that 28% (14) cases had sensitization to propofol when he evaluated 50 patients with clinical episodes of anaesthesia-associated anaphylaxis. Most episodes of anaphylaxis usually respond to treatment with a single dose of epinephrine, but some cases who do not respond to single or intermittent doses may need epinephrine infusion[13] as in our case. There are reports of use of pure α-agonists and even vasopressin[14] in refractory cases. Although cardiovascular symptoms and bronchospasm are more frequent manifestations in IgE-dependent reactions, absence of respiratory symptoms as in our patient does not preclude the diagnosis of anaphylaxis.

The severity of clinical symptoms, positive skin prick test, intradermal test to propofol and absence of hypersensitivity during the second surgery when propofol was omitted definitely points to propofol as the causative agent.

Every patient with a suspected anaphylactic reaction during anaesthesia should be investigated to determine the allergic nature of the reaction and to identify the responsible drug with the aim of providing safe and documented advice for future administration of anaesthetic drugs.

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