



CASE REPORT

Anaphylaxis secondary to levobupivacaine

A. Gupta,¹ M. Fennelly,² V. Ramesh³ and K. Agyare²

1 Specialist Registrar in Anaesthesia, Royal Marsden Hospital, London, UK

2 Consultant in Anaesthesia and Intensive Care and 3 Consultant in Anaesthesia, Royal National Orthopaedic Hospital, Stanmore, UK

Summary

We describe the case of a 25-year-old woman presented for elective lumbar decompression and microdiscectomy who, towards the end of her surgery, developed clinical signs of anaphylaxis. Skin testing later confirmed sensitisation to levobupivacaine and possibly MediShield, an anti-adhesion gel used following microdiscectomy. This case is the first confirmed case report of anaphylaxis in response to levobupivacaine. It also highlights the possibility that multiple agents may simultaneously trigger a life-threatening reaction. Anaesthetists should remain alert to the use of potentially allergenic agents employed by surgeons.

Correspondence to: Dr A. Gupta

Email: anish147@gmail.com

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Anaphylaxis, the most severe type of allergic reaction, is a life-threatening clinical syndrome. While local anaesthetics do not feature among the well-known triggers to anaphylaxis, when reactions to them do occur, it is the ester compounds which are implicated more frequently than the amides, while preservatives used during manufacture are also implicated [1]. We describe what we believe to be the first reported case of an anaphylactic reaction to levobupivacaine.

Case Report

A 25-year-old woman presented with chronic back pain and was scheduled for elective lumbar decompression and microdiscectomy at L3/4. She was a controlled asthmatic (Step 2, British Thoracic Society guidelines) with polycystic ovarian disease and she also suffered from seasonal allergic rhinitis. Her past medical history included acute lymphoblastic leukaemia at the age of 4 years, treated with chemotherapy and radiotherapy. An echocardiogram from 2006 revealed good bi-ventricular function. She took salbutamol and beclomethasone inhalers to control her asthma, and paracetamol, codeine and loratidine as required. She had no history of allergy to any medication. She had previously been treated with a lumbar epidural

injection (using steroid, bupivacaine and lidocaine) without any adverse reactions. She avoided non-steroidal anti-inflammatory agents because of her asthma, but smoked 10–15 cigarettes per day.

Anaesthesia was induced using fentanyl and propofol (mixed with 1 ml lidocaine 2%). Intubation of the patient's trachea was facilitated by vecuronium and anaesthesia was maintained using sevoflurane in an oxygen and air mixture supplemented by a remifentanyl infusion. The patient was carefully moved into the prone position for the procedure. A dose of cefuroxime (our routine antibiotic prophylaxis) was administered once the patient was stable in theatre.

Before incision, 10 ml of bupivacaine 0.5% with 1:200 000 adrenaline was infiltrated by the surgeon. Latex gloves were used, as is routine. After an uneventful operation, the surgeon placed 3 ml MediShield gel (Medtronic UK Ltd) on to the exposed nerve root to reduce postoperative scarring. Following wound closure, 10 ml of levobupivacaine 0.5% was infiltrated for postoperative analgesia. Within 5 min, the airway pressures had increased from 28 cmH₂O to more than 50 cmH₂O. Simultaneously, the oxygenation saturation fell to 84%. The blood pressure dropped from a systolic pressure of 90–100 mmHg to

72 mmHg. Examination revealed widespread, bilateral expiratory wheeze and markedly reduced air entry, particularly on the left side. The patient was turned supine, and widespread wheals were observed.

The patient's trachea was re-intubated to exclude an obstructed tracheal tube, and intravenous ephedrine (6 mg plus 6 mg), hydrocortisone (200 mg), chlorpheniramine (10 mg) and 2 l Hartmann's solution were administered. Salbutamol (5 mg) was given via nebuliser. Remifentanyl and propofol infusions were commenced for transfer to the intensive care unit. Whilst in intensive care, the patient was sedated with midazolam and fentanyl infusions and an adrenaline infusion was required for 48 h. The cutaneous wheals and urticaria persisted for 36 h. Serial samples for serum tryptase levels were taken. Her stay in intensive care was complicated by pneumonia from day 2; however, the patient's trachea was extubated on day seven. She has made a full recovery, and has had a good result from her surgery.

Serum tryptase levels were $15 \mu\text{g.l}^{-1}$ at 2 h; $7 \mu\text{g.l}^{-1}$ at 4 h and $2 \mu\text{g.l}^{-1}$ at 26 h (normal range $0\text{--}14 \mu\text{g.l}^{-1}$), concentrations consistent with a diagnosis of anaphylaxis. On discharge, the patient was referred for allergy testing. Skin prick tests, conducted 12 weeks after the reaction, were performed against all the drugs that had been administered. The positive control produced a 3 mm wheal; the negative control (saline) did not produce a wheal. The common allergens latex, cefuroxime, vecuronium, iodine and chlorhexidine did not produce wheals. Morphine resulted in a 1-mm wheal, which was considered most likely to be a result of localised histamine release. The MediShield gel produced a 1-mm wheal. This test was repeated and subsequently produced 2-mm and 1-mm wheals. Levobupivacaine resulted in a 3-mm wheal after 30 min, while lignocaine 2% and bupivacaine 0.25% failed to produce any wheals. Serum IgE levels specific to penicillin were non-significantly raised (penicillin G $< 0.35 \text{ kUA.l}^{-1}$, penicillin V $< 0.35 \text{ kUA.l}^{-1}$; reference $0.00\text{--}0.35$).

The patient's case was reported to the Medicines and Healthcare Related Products Agency, to Abbott Laboratories Limited (Maidenhead, UK) as the manufacturer of levobupivacaine, and to Medtronic UK Limited (Watford, Hertfordshire), the manufacturers of MediShield gel.

Discussion

The true incidence of anaphylaxis during anaesthesia is unknown, but is thought to lie between 1 in 10 000

and 1 in 20 000 cases, with approximately 10% proving fatal [2]. It is not necessarily easy to diagnose; the biochemical mediators and pathways can vary, producing an array of clinical features. The effects usually resolve within 8 h, and recovery is complete. The management has been outlined in numerous texts [1].

As previous reactions do not predict the severity of subsequent incidents, all triggers should be identified and avoided [3]. Patients like ours, with a history of asthma, have an increased incidence of anaphylaxis [4]. In anaphylaxis during anaesthesia, the commonly encountered triggers are neuromuscular blocking agents, antibiotics, colloids and latex products [1, 5]. More recently, cases of anaphylaxis in response to chlorhexidine [6], steroids [7] and vasopressors [8] have been reported.

We present the first case of anaphylaxis to levobupivacaine. Our patient developed a sudden, severe deterioration in ventilatory function and moderate haemodynamic compromise during anaesthesia within 5 min of receiving levobupivacaine. Widespread cutaneous manifestations of anaphylaxis were evident, making anaphylaxis the most likely diagnosis. The diagnosis was supported by elevated tryptase concentrations and positive skin testing. A review of adverse drug reactions as reported to the Medicines and Healthcare products Regulatory Agency (MHRA) reveals a single anaphylactoid case out of a total of 114 adverse drug reactions and 53 adverse drug reports (from 11 March 2002 to 26 January 2011) [9]. Although the reporting of adverse drug reactions is voluntary, this suggests that anaphylaxis to levobupivacaine must be at least very rare. It also very probably suggests that under-reporting is a general problem.

This patient had previously been exposed to bupivacaine and lidocaine given as part of a lumbar epidural for chronic back pain. The manufacturer of levobupivacaine was contacted (Abbott Laboratories Limited). Excipients to their preparation of levobupivacaine include sodium chloride, sodium hydroxide and concentrated hydrochloric acid, substances not known to be common triggers for anaphylaxis. Compounds of polyethylene oxide and sodium carboxymethylcellulose have been used to prevent adhesions and tethering following discectomy since 2002. Various companies manufacture these gels; however, their safety is under constant review. A published non-randomised prospective case series failed to reveal any adverse incidents relating to the use of this compound [10].

We believe that the main trigger for the reaction in this patient was levobupivacaine. Although the

MediShield gel consistently produced a smaller, positive reaction to skin prick testing, it may have contributed something to the release of histamine. Our patient has been advised to avoid levobupivacaine and MediShield gel in the future, and has been offered a supervised challenge with lidocaine, which she is currently considering.

Anaesthetists should be aware of the possibility of two or more agents simultaneously precipitating an anaphylactic reaction, and hence of the importance of rigorous investigation to prevent re-exposure. Agents administered by surgical colleagues have the potential to cause allergic reactions and familiarity with these compounds is essential. Anaphylactic reactions to amide local anaesthetics are infrequent; there are no published case reports of anaphylaxis to levobupivacaine.

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Competing interests

None declared.

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