Anaphylaxis associated with, but not caused by, extradural bupivacaine

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Summary
Identifying anaphylaxis and determining its cause during anaesthesia can be very difficult. We describe a patient who suffered a life-threatening reaction which was diagnosed originally as being caused by bupivacaine. Subsequent investigation and enquiry showed that this was not so and suggested latex as the likely true cause. (Br. J. Anaesth. 1997; 78: 224–226)

Key words

Allergy to amide local anaesthetics is rare, but has been reported. More common is the patient who is labelled as being allergic to these drugs when this is not the case. Given the significance of the diagnosis, and the problems it produces for dental treatment in particular, it is essential to confirm the true situation in such patients. The following case report illustrates these issues.

Case report
A 33-yr-old woman with a history of immune complex disease, but no evidence of vasculitis, presented for elective Caesarean section. She was not receiving any medication and had no drug allergies. She had previously undergone an emergency Caesarean section under uneventful extradural block with bupivacaine and was happy to receive the same anaesthetic again.

Approximately 1 h before the procedure she received 30 ml of sodium citrate 0.3 mol litre−1 and ranitidine 300 mg, but no sedative medication. On arrival in the anaesthetic room, her systolic arterial pressure was 120 mm Hg and heart rate 90 beat min−1. An extradural catheter was inserted at the fourth lumbar interspace and a total of 18 ml of 0.5% bupivacaine was injected in increments. At 25 min a bilateral block to T2 had developed, but surgery was delayed by an emergency elsewhere. During the interval she was kept in the left lateral position, arterial pressure decreasing only to 105 mm Hg and heart rate remaining unchanged. At 40 min, preparations for surgery began with urethral catheterization in the wedged, supine position. Immediately after catheterization her arterial pressure decreased to 70 mm Hg systolic, but responded initially to increments of i.v. ephedrine. However, she then became nauseated, vomited and developed persistent hypotension. Surgery was started and she required 2200 ml of i.v. crystalloid and increments of ephedrine and metaraminol to maintain systolic pressure at 100 mm Hg before delivery. The baby was born in good condition (Apgar score 9 at 1 and 5 min) 13 min after skin incision.

After delivery the patient became acutely breathless and clinically cyanosed, and arterial pressure could not be recorded, although peripheral pulses were palpable. She lost consciousness and her trachea was intubated after administration of suxamethonium 100 mg. I.v. frusemide and increments of adrenaline were administered for suspected pulmonary oedema and left ventricular failure. She remained hypotensive (systolic arterial pressure 65 mm Hg) and tachycardic (150 beat min−1) and at this point developed a generalized erythematous rash. During the procedure she lost an estimated 500 ml of blood and received Syntocinon 10 u. At the end of the operation she was transferred to the intensive therapy unit where artificial ventilation was continued. Arterial pressure responded to 2800 ml of colloid and 1 u. of red cell concentrate. She was noted to have marked peripheral oedema. Coagulation screens remained normal throughout and there was no evidence of amniotic fluid in the maternal blood samples. Her trachea was extubated 5 h after admission to the unit and the following day she was transferred to the postnatal ward where her subsequent recovery was uneventful.

An anaphylactic drug reaction was considered as the explanation for this event and advice was sought from the National Adverse Anaesthetic Reactions Advisory Service, Sheffield. Blood samples for radioallergosorbent tests were obtained and that for suxamethonium was negative. No test was available for bupivacaine, but a diagnosis of a specific reaction to bupivacaine was thought likely and the patient was advised to avoid future exposure to bupivacaine.

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was considered that intradermal testing would not be helpful.

Subsequent to this event, dental work was carried out uneventfully (as it had been previously) using 3% prilocaine with octopressin, but then local infiltration for further treatment was performed using 2% lignocaine with adrenaline 1 in 80 000. After this the patient developed a severe headache which was probably an adrenaline reaction, but she was concerned that she was experiencing allergy to yet another local anaesthetic drug and was referred, some 7 yr after the original event, to the anaesthetic department for further investigation.

A review of her medical and dental notes was undertaken and revealed that she was known to the dentists to be allergic to latex, but this information was not in the medical notes. Given this fact, and the temporal relationship of the original collapse to insertion of the bladder catheter, it was felt that the latter was the more likely cause of the acute event. Investigations revealed that latex catheters were in routine use in the labour unit at the time of the reaction. Challenge testing with local anaesthetic drugs was agreed with the patient to eliminate them as the cause of her problem and so that further dental treatment could proceed. With appropriate safeguards a series of intradermal injections was performed. At 10-min intervals 0.1-ml increments of normal saline, 0.01% lignocaine, 0.1% lignocaine, 0.05% bupivacaine, 0.5% bupivacaine and 0.5% prilocaine with methyl paraben were injected. The test drugs produced no more erythema than the saline control, and therefore 1% lignocaine 1 ml was injected s.c. before, finally, 0.5% bupivacaine 1 ml was given i.v. There was no reaction.

Discussion

An adverse reaction to a local anaesthetic agent may result from the systemic effects of the drug or the nerve block it produces, an allergic reaction to some component of the solution, a vasovagal reaction to the situation, or may be temporally, but not causally, related to administration of local anaesthetic. This patient was stable for 40 min before developing hypotension and subsequent loss of consciousness. Systemic toxicity, inadvertent spinal anaesthesia and allergy to some component of the local anaesthetic solution are unlikely as all would be expected to present within minutes of drug administration. The patient did not become bradycardic and this makes a vasovagal event unlikely also. Extensive sympathetic block could produce some of the features seen, but would not explain the generalized erythematous rash or the later oedema, and arterial pressure was stable until preparation for surgery. Turning her to the supine wedged position for catheterization might have compromised arterial pressure, but would not have produced the other features. Hypotension, respiratory difficulty and rash are compatible with an immunological reaction and we propose that this was in response to either the antiseptic (Hibitane) or the urethral catheter, with ranitidine therapy and extensive sympathetic block compounding the situation. Syntocinon might cause such a reaction, but none was administered until well after it had commenced. Reports of allergy to skin antiseptics are beginning to appear and latex allergy is well documented. Given that she is now known to be allergic to latex this seems the most likely cause of the reaction. More recently she was accidentally exposed to latex and developed skin oedema and swelling at the point of contact. A further deterioration in her condition occurred after delivery and Syntocinon could have contributed to this.

In this patient, anaphylaxis was diagnosed with the onset of the rash. The diagnosis is easy when cardiovascular collapse is immediately associated with bronchospasm and cutaneous signs, but the latter only appear in 65% of cases. The differential diagnosis of these symptoms in the absence of cutaneous manifestations is difficult and includes not only anaphylaxis, but also drug overdose, haemorrhage, air, emboli, bronchial intubation, aspiration, etc. Fortunately, and despite difficulties in diagnosis, treatment is often the same: adequate oxygenation, with sympathomimetic drugs and i.v. fluids. If anaphylaxis is thought possible, potential antigens must be sought and exposure terminated. This patient eventually responded to treatment, but recovery took several hours, probably because the urinary catheter was not suspected as the cause and was left in situ. There are no investigations that can be performed during a reaction that aid diagnosis or acute management, but estimation of serum tryptase concentration approximately 1 h after onset is helpful in the subsequent investigation. This test was not available at the time of our patient’s reaction. After the patient’s recovery a detailed history of the event, and examination of all past notes, should be undertaken in an attempt to ascertain the cause of the reaction. If our patient’s latex allergy had been documented in her medical notes she would not have been exposed to latex and one of the drugs she received would not have been blamed for the reaction.

If the history suggests anaphylaxis rather than anaesthetic misadventure, or serum tryptase concentration is increased, skin prick testing, as recommended by the recently published Association of Anaesthetists’ Guidelines (Anaphylactic Reactions Associated with Anaesthesia) may be undertaken to try and establish the cause of the reaction. These guidelines recommend that all reagents administered around the time of the reaction should be used in testing, in addition to a range of agents that may be used in the future. Our patient was challenge tested with local anaesthetic agents because of her concern about continued use. There was no real benefit for her in being tested for latex or Syntocinon, which she had refused in any case. There is ample clinical evidence from her dental attendances that she reacts to latex with skin swelling and oedema, and testing would have exposed her to a small, but real risk of life-threatening anaphylaxis. She intends having no more children and so will not be exposed again to Syntocinon.

Intravascular injection is not recommended in routine testing because a severe response is likely if the true antigen is injected. In this patient’s case
intravascular injection with bupivacaine was performed because she expressed a wish to be certain that she was not allergic to this drug. It was felt that this was a safe procedure because there had been no reaction to intradermal bupivacaine and the history clearly suggested latex as the true cause of the original problem, although Syntocinon cannot be totally excluded from a contributory role. The testing did prove definitively that the patient was not allergic to local anaesthetic drugs, and the case illustrates clearly the need to consider all aetiological possibilities when anaphylaxis occurs during anaesthesia.

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References