

Correspondence

Anaphylaxis to levobupivacaine? Maybe...

We read with great interest the case report by Gupta et al. [1]. One of the positive elements of the paper is the documentation of an anaphylactic mechanism through demonstration of sequentially raised serum tryptase levels, but we feel two other elements of the report appear to provide weaker evidence.

Firstly, the skin tests were prick tests; these are less sensitive than intradermal tests [1]. Moreover, the diameter of the positive control wheal was just 3 mm with a negative control of 0 mm. This makes interpretation of wheals ≤ 3 mm difficult because in order to have a positive reaction, the tested drug must provoke a wheal at least 3 mm more than the control. In addition, the drug concentrations used in the prick tests were not mentioned.

Secondly, the IgE dose of penicillin G and V is insufficient to exclude an IgE-mediated sensitisation to penicillins or cephalosporins [2]. The sensitivity of specific IgE to penicillins varies between 15 and 25% depending on the observed clinical manifestations. These in vitro tests are not sufficient to study the

cross-reactivity between penicillins and cephalosporins.

We believe this report would have been more persuasive if the authors had demonstrated a strongly positive intradermal reaction to a 1:10 000 or even a 1:1000 dilution of levobupivacaine. The interpretation of the MediShield gel (Medtronic UK Ltd., Watford, UK) prick test is not significant (1–2 mm wheals).

We would conclude that an allergy to levobupivacaine cannot be excluded but it is far from proven. A sensitisation to another substance was not excluded because the authors did not perform intradermal testing. If intradermal testing with levobupivacaine had been done and had been negative, a provocation test would have been necessary to implicate it positively as the cause of anaphylaxis.

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Anaphylaxis to levobupivacaine - probably not

We read with interest the article by Gupta et al. describing a case of suspected anaphylaxis to levobupivacaine [1]. We have reservations concerning the authors' conclusions that the event was triggered by the administration of levobupivacaine and additionally that the clinical features were exacerbated by co-administration of MediShield gel. Although the diagnosis of anaphylaxis is likely, alternative diagnoses and alternative trigger agents should be considered.

Widespread urticaria was observed when the surgical drapes were removed and the patient was returned to the supine position. It is

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possible that these cutaneous features developed unnoticed before the administration of levobupivacaine. The agent with the highest pre-test probability of being the causative agent was cefuroxime. Although a skin prick test with cefuroxime was negative, this may have been a false-negative result. It is our experience and the experience of other specialist centres that the sensitivity of a skin prick test in diagnosing antibiotic allergy is relatively poor and it is often necessary to proceed to intradermal testing. The sensitivity of tests for specific IgE to penicillins is even lower in cephalosporin allergy.

Idiopathic urticaria is surprisingly common and this diagnosis should also be discussed. Urticaria can arise for many reasons and, on its own, is not suggestive of anaphylaxis. Urticaria is common in the context of infection and pneumonia was confirmed two days later. Mast cell tryptase can be elevated in any cause of mast cell degranulation including urticarial reactions and the direct non-immune effect of many drugs in the absence of anaphylaxis.

The respiratory features comprised elevation of airway pressures, reduced air entry to the left lung and wheeze. The patient's condition began to respond when the tracheal tube was changed. Bronchial migration of the tracheal tube during the surgical procedure would explain all the respiratory features and this possibility should also be considered.

We have concerns regarding the criteria for a positive skin prick test used by the authors. The skin wheal produced by levobupivacaine was only 3 mm in diameter, which makes this a borderline result. Guidelines

recommend that a test should be considered positive only when the diameter of the wheal is at least 2–3 mm greater than the negative control [2, 3]. Interpretation of skin prick tests in drug allergy requires considerable experience; there is no reference to involvement of an immunologist or allergist in the interpretation of these tests. Skin testing in suspected local anaesthetic allergy has a good negative predictive value. The positive predictive value is difficult to ascertain as positive skin responses are very uncommon and when patients with positive skin tests are challenged, systemic responses have not been confirmed [4].

The authors state that the skin prick test with MediShield gel was associated with 1- and 2-mm wheals. These findings represent an unequivocally negative result and MediShield should not be considered as contributing to the reaction.

The evidence the authors presented for amide local anaesthetic type-1 hypersensitivity was based solely on anecdotal reports and, in this case, alternative diagnoses should be explored with greater rigour. Based on the information provided we are unable to conclude that anaphylaxis occurred in response to the administration of levobupivacaine.

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A reply

We thank Drs Scholtes, Pirson, Harper and Garcez for their comments about our article [1]. We discussed the issues raised with our allergy centre specialists and this is our joint response.

We referred our patient to a recognised allergy centre, listed in the AAGBI booklet [2]. The skin prick test with levobupivacaine did yield a reaction 3 mm greater than the negative control, which is defined as a positive result by this allergy centre. The same concentration of the drug was used in the skin prick test as was used during the clinical situation (0.25%). In the presence of a positive skin prick test, and given the severity of the patient's reaction, we felt that an intradermal test would not change the patient's management and held a small but significant risk of reaction, that we deemed was an unnecessary risk to the patient.

With respect to the penicillin and cephalosporin testing, the timing