Allergy to local anaesthetic: the importance of thorough investigation

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A case report is presented which highlights the importance of a good history in arriving at the correct diagnosis in cases where allergy to local anaesthetic is suspected. Management of the patient is discussed and the topic of 'adverse reaction' briefly reviewed.

In brief

- The paper emphasises the need for prompt and appropriate referral, a thorough history and the need to send samples of potential allergens. This streamlines future investigations.
- Caution needs to be exercised in the use of root canal medicaments.
- Referral to a local allergy specialist is desirable where such allergy is suspected.

Allergy to local anaesthetic is considered rare. True immunological reaction represents only 1% of adverse reactions to local anaesthetic.[1] Adverse reactions can be type A (pharmacological) or type B (idiosyncratic). Type A reactions are dose-dependent and predictable from the drug's pharmacology and represent 80% of all adverse reactions. As such, this type of reaction is not relevant to local anaesthetic administration so long as the drug is delivered correctly and within recommended dose parameters. Idiosyncratic reactions are less common but potentially more serious in so far as such reactions are not predictable from the drug's pharmacology.[2] Type 1 hypersensitivity reactions belong to this category. Immunological reaction is one of several mechanisms for such idiosyncratic reactions.[3] Other mechanisms are cited in Table 1.

Traditionally, reaction to local anaesthetic compounds has been categorised under three headings, these being allergic, toxic and autonomic. All patients have some degree of autonomic response to injections, ranging from sweating and slight tachycardia to syncope. The autonomic reaction can be secondary to the local anaesthetic vasoconstrictor effect or be caused by the patient's own endogenous autonomic/psychological reaction to the experience. Such symptoms, however, are generally short-lived and respond readily to simple supportive measures. Toxic reactions are less common and are most frequently seen with rapid intra-vascular injection of anaesthetic, overdose or in those patients who have problems with eliminating or metabolising the anaesthetic. The neurological and cardiovascular consequences of overdose are well understood.[4] These can be minimised by staying within safe dosage parameters and using safe injection techniques.

The authors would like to highlight the importance of obtaining a good history from both the patient and the dentist in cases where allergy to local anaesthetic is suspected. It may be that questioning will reveal a number of potential allergens. The consequences of genuine allergy to local anaesthetic are serious with regards to the patient's future management and prompt identification of the aetiological agent(s) is to be recommended. This case report highlights one such case and shows the value of prompt referral, not only in the case of the patient's immediate medical management but also in the prevention of future complications secondary to mis-diagnosis. Prompt referral is essential if all the relevant facts and implicated materials are to be gathered and analysed.

Case Report

A 74-year-old lady attended casualty with a swollen upper lip. Some 72 hours previously, she had seen her dentist with toothache relating to the ⌊1 and was prescribed amoxycillin. At 13:00 hours on the day of her return appointment she was given an infiltration of local anaesthetic to this area. An extirpation was performed, and the root canal was medicated with sodium hypochlorite and sealed with a temporary dressing. The lady recalled having a pain in her lip after the local was given. Her upper lip began to swell steadily, according to her, during the next 8 hours to the point that she called in the emergency doctor who referred her immediately to the casualty department with a diagnosis of angioedema or facial cellulitis. She had never previously had an adverse reaction to a local anaesthetic injection and felt that the swelling represented an allergic reaction.

On examination in the casualty department she was found to have severe facial swelling (Figs 1 and 2) but was apyrexial and had no other systemic signs or symptoms. Exactly 10 hours had lapsed since the injection. It was felt at the time that this might represent an adverse reaction to

Table 1 Types of idiosyncratic drug reaction

- Immunological eg Hypersensitivity reactions 1–4
- Pharmaceutical variation eg Reaction to certain isomeric variations of the drug
- Abnormalities in drug metabolism eg enzyme deficiencies such as glucose 6 phosphate dehydrogenase (primaquine induced haemolysis) or N-acetyl transferase in the case of slow acetylators
- Drug-drug interaction
- Receptor abnormality eg malignant hyperthermia
- Multifactorial reactions

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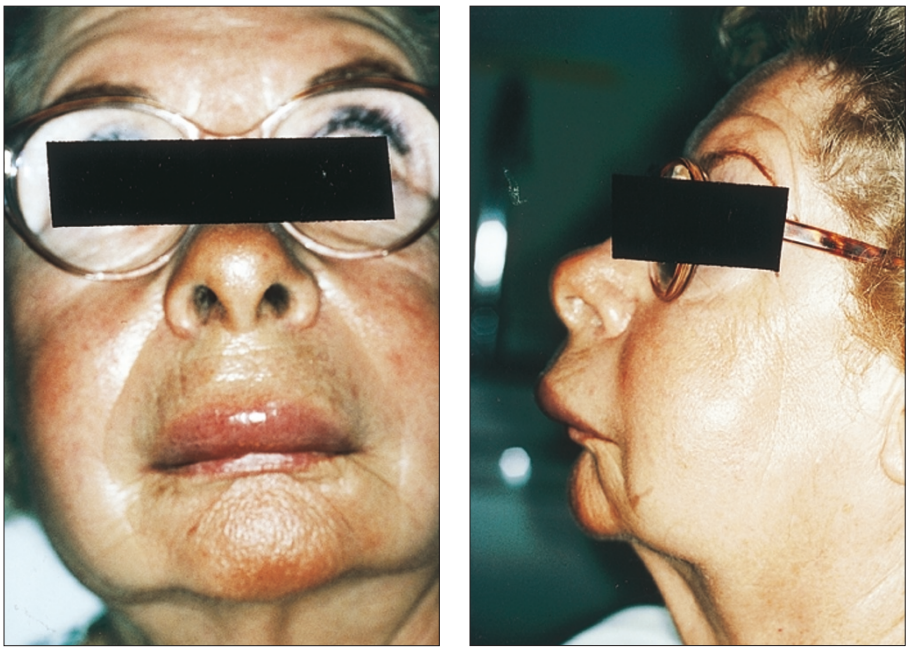

Fig. 1 (left) Frontal view of patient's swollen lip, (right) lateral profile view of patient's swollen lip

the local anaesthetic. The appearances were in keeping with angioedema but the possibility of a severe cellulitis was also high on the list of differential diagnoses. Radiographs failed to indicate a localised cause for the swelling. Her presentation was discussed over the phone with the consultant oral & maxillofacial surgeon. Intravenous access was established and she was given 8 mg of Dexamethasone via the cannula in casualty.

She was admitted to the ward and treated with regular doses of intra-venous dexamethasone, oral amoxycillin and metronidazole. Though prescribed analgesics, the patient did not have need of them. The case was discussed with a biochemist and recommendations were given concerning appropriate blood tests. All of the recommended tests were carried out on the samples taken at the time of admission, some 10 hours after the local anaesthetic injection. As well as routine blood tests, an assay was also performed for complement C3/4 and C1q esterase inhibitor and IgE levels. Latex specific IgE levels were not measured, as allergy to latex was felt highly unlikely. The patient had been exposed to latex gloves at many previous visits to her dentist without any reaction. The response witnessed was localised tending to reinforce the idea that latex related allergy was unlikely. C1q esterase levels were normal; suggesting that hereditary angioedema (HAE) was unlikely as the cause of the swelling. As C4 and C1q levels were normal during the acute episode of swelling, the diagnosis of HAE was excluded. The total IgE level was slightly raised at 114 IU/ml (normal adult range, 0–81 IU/ml), suggesting that the patient had an atopic tendency ie a propensity to produce IgE in response to an antigenic challenge. Serial plasma tryptase and urinary methyl-histamine levels were not performed. This was an important omission, as these tests would have helped in establishing the nature of the response witnessed in the patient. The importance of this issue is dealt with in the discussion section.

She remained in hospital for 5 days until the swelling had subsided sufficiently so that it was judged safe for her to return home. In that time she had been on IV dexamethasone for 72 hours. Her response to this was rapid and as a result this medication was withdrawn after the first three doses, but the swelling rapidly recurred necessitating reinstitution of the steroid regime. This suggested the presence of a persistent antigenic or inflammatory stimulus.

Skin prick testing (SPT) was performed, as an outpatient procedure; one month after the patient was discharged from hospital. The patient had not been treated with any anti-histamines during the acute episode of swelling (may cause false-negative results in skin prick testing). However, appropriate negative (normal saline) and positive (0.1% histamine) controls were included. Satisfactory results were obtained from these controls, ie no wheal from negative control (excludes dermatographism), and 4 mm wheal from positive control, indicating that the test procedure was giving valid results. The batch of local anaesthetic used by the dentist was tested by pinprick and intradermal bleb injection. Comparisons were made between this, the controls and separate injections of preservative-free local anaesthetic, methyl paraben and metabisulfite. Dilutions of 1/1000, 1/100 were tested prior to using the undiluted stocks. The patient was observed for 15–30 minutes between each testing for signs of an allergic reaction. Intra-muscular adrenaline and full resuscitation facilities were available in case of an anaphylactic response. Hydrocortisone ointment was also available to use on the skin sites if the patient was to experience any itching or discomfort locally.

There was no reaction to any of the tested substances. It was therefore concluded that the reaction originally experienced by the patient was secondary to the medicament used to treat the extirpated pulp chamber. Unfortunately this material used was not available for testing and the diagnosis was therefore one by exclusion. The lady's dental practitioner was informed of the diagnosis so that the medicament could be avoided in future in her case. The Committee for Safety in Medicines was informed of the findings.

Discussion

In this case allergy to local anaesthetic was eventually excluded. The most likely cause for the reaction was the use of hypochlorite for medicating the canal. Such complications have been previously recorded in the literature either by escape of hypochlorite through a perforation,[5] or through the apex.[6] There is no evidence in this case that a perforation was produced, though egress of hypochlorite through the apex of the tooth may have been sufficient to produce the reaction witnessed. Skin testing of hypochlorite was considered in this case, however, the sub-dermal or intra-dermal injection of what is in effect bleach was thought to be needlessly pragmatic. The diagnosis was therefore one of exclusion. The chances of such a complication are thought to be small, but care is urged in terms of the quantity and way in which such medicaments are used.

Allergic reactions are classified as type 1, 2, 3 (immediate reactions) or 4 (delayed reaction). Of these reactions only types 1 and 4 are clinically significant to local anaesthetic allergy. Type 2 and 3 reactions are exceedingly rare, though have been reported.[7] Type 1 reactions are mediated by specific IgE antibodies causing degranulation of mast cells and basophils causing a localised or generalised reaction. Such

reactions are termed as angioedema if localised, and anaphylaxis if generalised. Symptoms and treatment of type 4 (delayed hypersensitivity) reactions are similar to type 1 reactions, though these tend to be localised to the injection site. Type 4 reactions are the most prominent with local anaesthetics and are mediated by sensitised T-cells known as memory cells. These cells release lymphokines on secondary exposure to the antigen, which mediate inflammatory cascade reactions. True allergic responses are very rare, forming less than 1% of adverse reactions to local anaesthetic. Most reactions are in fact toxic or autonomic in nature.

In cases of suspected acute allergic reactions associated with anaesthesia, it is recommended that investigations are performed according to the recent guidelines published by the Association of Anaesthetists of Great Britain and Ireland and the British Society of Allergy and Clinical Immunology.[8] Initially, patients should have complement C3, C4 and C1q esterase performed to exclude hereditary angioneurotic oedema (HAE). Serial plasma tryptase levels and a spot urinary methyl histamine level are the most accurate way to assess whether mast cell degranulation has occurred. An acute increase in these levels indicates a type 1 or 4 hypersensitivity response. Though IgE mediates type 1 hypersensitivity responses, increased levels of IgE in themselves do not constitute a type 1 response unless they are shown to be specific to the suspected allergens. At best, a raised non-specific IgE level will only indicate that a patient has an atopic tendency, as in this case. For completeness, latex specific IgE should have been performed in this case, though at the time the clinicians involved felt that there was little indication given the history. The omission of plasma tryptase testing was unfortunate in this case, though it did not ultimately influence outcome. This highlights the importance of appropriate consultation when faced with such rare situations.

Whenever skin prick testing (SPT) is performed, it is important to include a negative (normal saline) and positive (0.1% histamine). For example, some individuals have dermatographism, a condition in which any pressure exerted on the skin, such as the lancet used to perform SPT, may cause a wheal and flare response. Others may have inadvertently taken anti-histamine treatment recently, either knowingly, or as part of a cold-remedy and this will of course generate false negative results. The controls cater for either event.

SPT may be performed soon after the acute event, although it is usually recommended to wait for 4–6 weeks after the reaction, as levels of the relevant specific IgE may be temporarily lowered as the IgE antibody itself is involved in mediating the acute allergic response. It is also important that any anti-histamine treatment be stopped at least 3 days before the test is performed, since these drugs will prevent a positive wheal response, which is caused by histamine released into the skin. However, very long acting anti-histamines such as Astemizole need a 4-week washout period. In this case no antihistamines were used. An adequate positive control histamine response in the SPT panel shows that antihistamine treatment (if occurring) is not interfering with the SPT results.

An appropriately trained practitioner should perform all allergy testing. This case has clearly shown the need for careful liaison with a clinician experienced in clinical immunology and allergy testing. Though the testing itself may be performed, as in this case, by a clinician that has run allergy clinics in the past, the authors feel that such tests are best performed in a dedicated setting where such work is routinely performed. This is especially the case when dealing with a rarely encountered clinical problem. As in this case, full resuscitation equipment and trained staff should be at hand.

Conclusion

In cases were anaesthetic allergy is implicated, prompt referral and treatment is indicated. Control of the reaction and prevention of secondary infection are the initial priorities. It is essential to obtain an accurate history of events from the patient and the dentist, and obtain samples of the materials implicated in the adverse reaction. These may then be stored in suitable conditions. Appropriately timed blood tests should be performed in consultation with a specialist who has knowledge of allergy testing. Referral to an allergy clinic is recommended at an early stage so that allergy testing can be performed safely and effectively. The field of allergy testing is a complex one and the author strongly feels that it is inappropriate for such tests to be performed by those who have only occasional exposure to such situations. Moreover, clinics that regularly deal in such problems are in a better position to deal adeptly with possible complications that ensue.

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