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IgE-mediated hypersensitivity reaction to lignocaine – a case report

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Abstract. We report a 7 year old girl who developed ipsilateral left facial swelling immediately after lignocaine injection. Skin prick test showed positive reaction to pure 2% lignocaine hydrochloride and to lignocaine oral dental gel. Specific Immunoglobulin E (Ig E) to lignocaine was detected. Lignocaine is a commonly used anaesthetic agent mainly as local anaesthesia. However type I hypersensitivity to lignocaine is rare and there have been very few cases reported in the literature.

INTRODUCTION

Local anaesthetics are widely used in dentistry as they allow a variety of procedures to be performed safely and comfortably. Local anaesthetics were divided into two groups: (i) amide-derivatives of xylidine and toluidine group (lidocaine, lignocaine, mepivacaine, prilocaine) and (ii) ester or benzoic and aminobenzoic derivatives (cocaine, benzocaine, procaine, tetracaine, butacaine) (Lu, 2002).

The first synthetic procaine was introduced in 1904 and lignocaine was introduced into clinical practice in 1946 (Curley *et al.*, 1986). Lignocaine are produced in several forms: solution for injection, suppository (antihemorrhoidal preparation), lignocaine ointment, sunburn cream (Curley *et al.*, 1986) and dermal creams EMLA (Eutectic mixture of lignocaine and prilocaine). Although lignocaine injections are generally well tolerated, there are reports of adverse reactions to these agents (Ball, 1999; Rood, 2000; Berkun *et al.*, 2003).

In clinical practice, adverse reactions after local anaesthesia injections are frequently attributed to toxic events, psychogenic, idiosyncratic or allergy (type I or type IV) (Ball,1999). True allergic reaction is extremely rare (Rood, 2000). Only a few cases of type I immediate hypersensitivity reaction (Chin & Fellner, 1980; Chiu *et al.*, 2004) and type IV delayed hypersensitivity (Evans *et al.*, 2002; Mackley *et al.*, 2003) to lignocaine have been reported in the literature.

Clinical features of type I allergy tend to occur within minutes of giving injection and may present with lip, tongue and periorbital swelling (angioedema), agitation, generalized itching particularly of the hands and feet, urticaria and wheezing (Ball, 1999). A classic anaphylaxis would cause laryngeal oedema, bronchospasm and hypotension.

PATIENT AND METHODS

A 7 year old child was referred from a dental clinic for ipsilateral facial swelling following a dental procedure. She developed left upper facial swelling immediately after she was given oral lignocaine dental gel and lignocaine HCl (2% lignocaine HCl + adrenaline) injection to the upper anterior region of her mouth.

She was given intravenous antihistamine and the swelling subsided on the same day when the patient was already at home. This episode was not associated with urticaria, laryngeal oedema, bronchospasm and hypotension. She had no past history of bronchial asthma, atopic eczema or drug allergy except for one episode of urticaria of unknown origin when she was 4 year old. She had never been given local anesthetics agents in the past. There was strong family history of urticaria in her sibling and angioedema in her father. Due to the fact that the swelling was at the site where local anaesthetics was given, it was thought that the patient could have had a reaction to either 2% lignocaine HCl + adrenaline, oral lignocaine dental gel or latex glove used during the procedure.

Skin prick test (SPT) was carried out with 2% lignocaine HCl + adrenaline, pure 2% lignocaine HCl, lignocaine oral dental gel and latex (Alk Abello, Spain). Histamine and phosphate buffered saline was used as positive and negative controls, respectively. SPT results were read after 15 minutes. Weal of 3 mm and above was considered as positive result. Blood pressure and vital signs were monitored closely throughout the SPT session. 10 minutes after SPT was performed, she developed pruritic erythematous rash over the right eyebrow and left earlobe. This was followed by urticaria scattered over her back. There was no facial or lip swelling, laryngeal oedema or bronchospasm.

Blood pressure, vital signs and oxygen saturation remained normal through out the test. She responded immediately to oral antihistamine (cetirizine 5mg) and was observed closely in the allergy clinic. There were no further systemic allergic symptoms. She was uneventfully discharged from the hospital the same day with oral antihistamines and steroids.

Immunoblot (dot blot method) for specific IgE to lignocaine was performed using the patient's serum according to the method described by Vila *et al.* (2001). Serum from a non-allergic individual was used as a negative control. Briefly, 10 µg of either lignocaine gel or 2% lignocaine HCl in 100 µl phosphate buffered saline was applied to nitrocellulose membrane discs in a 96-well microplate, followed by overnight incubation. The discs were washed, blocked in 5% non-fat milk in tris buffered saline (TBS) and then incubated with patient's serum. This was followed by incubation in biotinylated goat antihuman IgE (Kirkergaard and Perry Laboratory, UK), and incubation in streptavidin-conjugated alkaline phosphatase (BioRad, USA). After the final wash, the discs were developed with Alkaline Phosphatase Conjugate Substrate kit (BioRad, USA) to detect the bound IgE.

Specific IgE to latex was measured using UniCAP 100 (Pharmacia Diagnostic Sweden) following the manufacturers instructions.

RESULTS

The SPT revealed positive reaction to pure 2% lignocaine HCl and lignocaine oral dental gel. She also developed urticaria after 10 minutes of carrying out the test. We did not proceed to intradermal test since the SPT was positive and the child had urticaria. SPT and specific IgE to latex were negative. Full blood count, serum complement C3 and C4 levels were all within normal range. Immunoblot test demonstrated positive dot-blot reaction to both 2% lignocaine HCl and lignocaine oral dental gel (Figure 1).

DISCUSSION

Lignocaine is routinely used in dental practice for pain control. Adverse reactions to local anaesthesia are uncommon (Jackson *et al.*, 1994). However it is probably under-reported as various surveys estimate that only 10-15% of serious adverse reactions are reported (Ball, 1999). Overdosage has been implicated as the most common cause of local anaesthetic adverse reactions (Macy, 2003). Less than 1% of adverse reactions

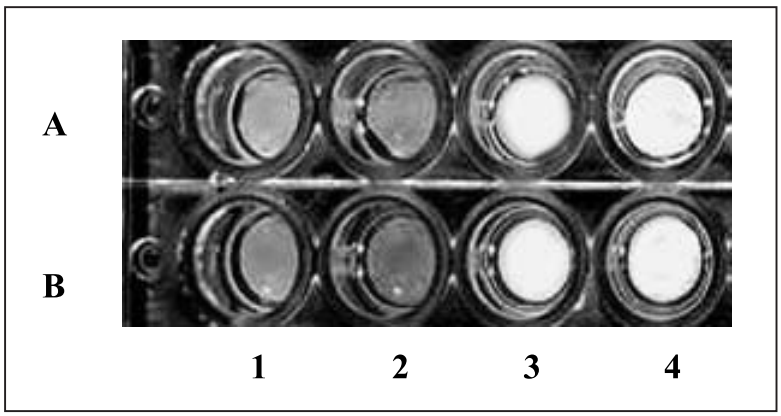

Figure 1. Well 1 and 2 showed positive dot-blot test of patient's sample for both lignocaine and lignocaine oral dental gel, well 3 and 4 are negative control and blank, respectively.
A – Lignocaine injection solution
B – Lignocaine oral dental gel
1 – Patient's serum (diluted 1:1)
2 – Patient's serum (undiluted)
3 – Negative control; 4 – Blank (no serum)

caused by local anaesthetic drugs are due to true allergy (Giovannitti & Bennett, 1979).

Allergic responses to lignocaine (amide local anaesthesia) used in dentistry are extremely rare (Brown *et al.*, 1982; Rood, 2000). It has been noted that the amide class of local anesthesia is significantly less allergenic than the ester type. There is also limited cross-reactivity between amide local analgesic agents (Ball, 1999).

Allergy to local anaesthetics may be type I, immediate hypersensitivity reaction which is mediated by IgE antibodies or type IV, delayed hypersensitivity reaction mediated by sensitized lymphocytes. Lignocaine has been reported responsible for immediate type I hypersensitivity reaction which includes urticaria, angioedema, and anaphylaxis on a number of occasion (Shields, 1972; Chin & Fellner, 1980; Chiu *et al.*, 2004). Whalen (1996) reported a type IV hypersensitivity reaction in a patient with localized, pruritic, vesiculobullous delayed-type hypersensitivity reaction on the dorsum of the hand 12 hours after lignocaine injection. Patch test confirmed this sensitivity. Breit & Rueff (2001), reported a man who developed pruritus, swelling, and erythema at lidocaine injection sites. His skin test including intradermal test were negative at 20 minutes but intradermal test results were positive at 48 hours, thus indicating type IV hypersensitivity reaction.

Diagnosis of type I drug allergy includes a complete medical history and history of atopy. The commonest diagnostic test for drug allergy is SPT. IgE-mediated reaction can be demonstrated by a positive skin prick test and/or intradermal test. For suspected lignocaine allergy, latex allergy testing could be considered, particularly if the history is suggestive (Macy, 2003). Latex allergy can be diagnosed by SPT or detection of specific IgE to latex. SPT and intradermal tests should be performed 4-6 weeks after the reaction, in a specialist environment with intensive care facilities, since the tests themselves can induce anaphylaxis very rarely (Demoly & Bousquet, 2002).

Intradermal test are usually carried out when the SPT is negative. Intradermal test is performed initially at the lowest dose dilution with progressive increasing

dose later (Waton *et al.*, 2004). In addition, detection of drug specific IgE can be helpful.

Drug Provocation Test (DPT) with the suspected drug is performed only if case history, skin test, laboratory test give equivocal results. Some centres, however consider it as gold standard in the diagnosis of drug allergy (Weiss & Adkinson, 1998; Gomes *et al.*, 2004).

In this case report, the diagnosis of type I lignocaine allergy was made based on the suggestive clinical finding and demonstration of specific IgE by SPT as well as *in vitro* test.

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