

Adverse Anesthetic Reaction: Confirming the Cause

Abstract

A report of a 38-year-old female with a history of local anesthetic hypersensitivity and positive allergy test to articaine but not mepivacaine is presented. Recurrent swelling and rash after a medical procedure using selected local anesthetics led both patient and family physician to suspect a universal local anesthetic 'allergy.' However, further investigation including consultation with an allergist suggested a diagnosis of chronic urticaria. Common adverse reactions associated with local anesthesia are reviewed. Dentists are encouraged to be familiar with various reaction manifestations and management. Patients who exhibit drug reactions should not necessarily be mislabelled 'allergic' without a proper history or referral investigation; necessary dental care could otherwise be significantly delayed.

Introduction

Although true allergy to amide dental local anesthetics is very rare¹, it is not uncommon that patients present with such a concern. Due to their safe and effective profile, amide local anesthetics (lidocaine, mepivacaine, prilocaine and articaine) are currently the main analgesic modality for dental treatment. It is prudent that general dental practitioners be able to differentiate whether the 'allergy' presented by a patient is a life-threatening anaphylactic reaction or if it is consistent with a possible adverse reaction commonly associated with local anesthetic administration.^{2,3} Such reactions, often due to

systemic toxicity and patient anxiety, can usually be prevented by proper injection technique and stress reduction strategies; those associated with anaphylactic or idiopathic reactions, although rare, may be severe⁴ and require emergency response as well as further investigation. Before refusing treatment or subjecting patients to general anesthesia for dental treatment, practitioners administering local anesthetics must be able to adequately investigate and diagnose a patient's reaction, or refer appropriately if the diagnosis is unclear.⁵⁻⁷

This case report describes the complex work-up process of a patient with history of 'allergic reaction to local

anesthetics.' Attention is drawn to the abnormal hypersensitivity reaction described and patient's strong belief in her 'allergy'. Detailed history, ongoing differential diagnosis and interdisciplinary consultation proved to be helpful in the case management.

Initial Presentation

A 38-year-old female was referred to our hospital-based dental clinic by her community dental practitioner due to 'allergy/anaphylaxis to local anesthesia' and 'not suitable for non-hospital surgery facility'. When first seen in February 2008, the patient expressed frustration at not being able to obtain dental care despite visiting

multiple offices since moving to the local community in 2006.

The physical exam revealed a 70-kg Caucasian female of normal build with normal baseline vital signs. She wore a medical alert bracelet documenting a list of allergies and hypoglycemia. The bracelet tracking hotline was contacted and confirmed that all information listed on the bracelet was provided by the patient herself and not by any medical authority.

Dental History

The dental history indicated the patient received routine dental care with local anesthesia prior to the 'reaction' and allergy diagnosis in 2002. Between 2002 and 2006, she had multiple general anesthetics for dental treatment, with one episode of hypoglycemia intra-operatively. Currently, the patient's chief concern included generalized sensitivity to temperature prohibiting routine dental prophylaxis, lost and chipped fillings and a specific desire to complete needed dental work prior to a planned pregnancy. Oral examination revealed a heavily restored dentition with fractured and stained posterior Class II & V composite restorations and mild abrasion lesions.

Medical History

The medical history, confirmed with the patient's physician, was significant for anaphylaxis to local anesthetics and reactive hypoglycemia during general anesthesia. Other adverse drug reactions included a rash upon exposure to ciprofloxacin, demerol and sulfa; 'hyper' reaction to codeine and localized swelling to bee sting. Medication included two different topical steroid ointments as well as an EpiPen, as required, and a proton-pump inhibitor Pantoprazole.

An allergy consultation report (dated 2002; received in June 2008) stated:

- Patient's narration of her initial reaction to local anesthetic in 2002: "[She] had facial and tongue swelling and a slight wheeze with urticaria coming on about 10 hours after dental work. She was seen in Emergency and was treated with Epinephrine, Benadryl and prednisone for three days."
- Patient has atopic predisposition. Allergy test to dental local anesthetics resulted in a "positive reaction to ultracaine (articaine) but negative to scandonest and carbocaine (both are mepivacaine)."
- Consultant's opinion: "The reaction to dental anesthesia is not a true IgE mediated phase I atopic allergy — it is a mixture between a sensitive individual and an actual drug response."

It was recommended that if the patient takes prescribed antihistamine medication before and after a dental procedure, it should be sufficient to prevent further reactions.

Thus far, the information described an atopic female with non-Type I allergy reaction to local anesthetics. The allergy test result indicated mepivacaine (preferably plain without vasoconstrictor and antioxidant) could be a safe choice.

Clinical Findings

Unfortunately despite a detailed explanation, the patient refused the use of any dental local anesthetics (including mepivacaine). She recalled a separate episode following the allergy test: an outpatient skin incision and drainage procedure was performed under local anesthesia. Several hours later, she suffered severe regional swelling that required an emergency hospital visit and high dose steroid medication. The latter subsequently promoted a surgical wound infection and prolonged healing. Such a debilitating experience (although without any significant airway obstruction or cardiovascular collapse) convinced

the patient she is allergic to all types of local anesthetic despite allergy testing and premedication. The patient's current physician agreed with her and recommended she have absolutely no local anesthesia in the future.

The patient returned to clinic in August 2008 complaining of worsening sensitivity and demanding prompt treatment. She was again reminded that she did not have true immune-mediated allergy to dental local anesthetics. Still, the possibility of Type IV delayed hypersensitivity could not be eliminated and the suspected culprit, in my view, was the methylparaben preservative. Methylparaben is a known allergen and it's no longer included in single dose dental local anesthetic carpules since the 1980s.² To definitively isolate the causative agent of this hypersensitivity, such that life long involvement of deep sedation or general anesthesia for routine dentistry could be eliminated, it was suggested the patient have another allergy consultation, to which she agreed.

In the circumstances — long wait time before seeing an allergist, leaking restorations, family planning — one procedural sedation appointment (using possibly diphenhydramine one percent as an adjunct local anesthetic) was agreed and scheduled in early October 2008, allowing adequate time for communication with the patient's new physician.

Two weeks later, the patient reported that several hours after her last dental examination, which involved no local anesthetic, she developed a rash on her left jaw which worsened over the next day despite antihistamine intake. After 48 hours, the rash and swelling progressed to the right face and a local emergency physician prescribed a five day-course of oral prednisone, which helped. The definitive cause of her symptoms remained

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Table 1
Immunologic and Non-Immunologic Drug Reactions Associated with Dental Local Anesthetics (LA)

Type	Example	Comment	Emergency Management
Immunologic			
Type I reaction (Ig E mediated)	Anaphylaxis from any LA agent <ul style="list-style-type: none"> • previous exposure — no reaction • repeated exposure leads to rapid severe local or generalized reaction characterized by urticaria, angioedema, bronchospasm, cardiorespiratory collapse 	Prevention is the goal. <ul style="list-style-type: none"> • Avoid exposure to agent proven to cause anaphylactic reaction • Definitive allergy test to identify allergenic agents and any agent with cross-reactivity 	<ul style="list-style-type: none"> • Oxygen • Epinephrine 0.3-0.5mg IM Q10 15min. • Ambulance to hospital
Type IV reaction (delayed, cell-mediated)	Contact Allergy: <ul style="list-style-type: none"> • Cutaneous swelling/ eczematous eruption 2-7 days post injection • No urticaria, laryngeal edema or bronchospasm¹⁷⁻²⁰ 	Consultation & allergy testing to: <ul style="list-style-type: none"> • exclude other possible offending agents (latex or other ingredients in a dental cartridge) and other etiology • identify LA agents that do not have cross-reactivity to allergen. • consider preservative-free and bisulfite-free LA 	<ul style="list-style-type: none"> • Mild skin response may require no treatment or can be managed with oral antihistamine.
Non-Immunologic Predictable			
Pharmacologic Side Effect	<ul style="list-style-type: none"> • Exaggerated systemic response (severe hypertension or cardiovascular accident) to epinephrine in patient taking non-selective beta-blockers • Tachycardia or hypertension and sense of palpitation associated with inadvertent vascular injection of LA containing epinephrine. 	<ul style="list-style-type: none"> • Review of patient's medical history and choice of LA agent • Limit the amount of epinephrine used in patient with pre-existing cardiac problem. • Maximum dose of epinephrine 0.018 – 0.036mg (1-2 cartridges 2% lidocaine 100,000) 	<ul style="list-style-type: none"> • Monitor vital signs, explain and reassure of short effect. • If blood pressure rises significantly use sublingual nitroglycerin, oxygen and contact emergency medical response as necessary
Drug Overdose	<ul style="list-style-type: none"> • Tremors, muscle twitching or convulsion post-LA administration • Usually followed by a period of lethargy, unresponsiveness & muscular weakness. 	<ul style="list-style-type: none"> • Limit dose according to patient's age and health status • Proper injection technique, with aspiration • Limit amount of dental work per appointment 	<ul style="list-style-type: none"> • Effects usually transient • Monitor and maintain patient's Airway-Breathing-Circulation and protect patient from injury.
Non-Immunologic Unpredictable			
Idiosyncratic	<p>Psychogenic reaction:</p> <ul style="list-style-type: none"> • Short-term tremor/seizure of multiple limbs immediately following a relatively small dose injection with altered level of consciousness and hypotension⁶ <p>Anaphylactoid response:⁴</p> <ul style="list-style-type: none"> • Tachycardia or hypertension., hyperventilation and tetany^{7, 21} • Methemoglobinaemia associated with prilocaine in susceptible patient² • Dizziness, tinnitus, diplopia or seizure after "smaller than maximum dose".¹⁶ 	<ul style="list-style-type: none"> • Review patient's health history, event record and relationship associated with LA allergy incident to help identify nature of reaction • Total dose of LA (esp. prilocaine) be calculated carefully and not to exceed recommended maximum dose. • Use stress reduction strategies Inject slowly and aspirate carefully • Sensible choice of agent and dose limitation according to patient's age, co-morbidities & weight 	<ul style="list-style-type: none"> • Patient education and reassurance essential.²² • In severe cases, anaphylaxis management protocol may be required. • Anxiolysis or even sedation may be indicated for management⁷
Iatrogenic	<ul style="list-style-type: none"> • Physical damage to nerve/vessel when inserting needle. • Post-operative paresthesia²³ or failure to obtain anaesthesia 	<ul style="list-style-type: none"> • Careful technique (including aspiration) and choice of anesthetic agents 	<ul style="list-style-type: none"> • Proper patient follow up and referral.

unknown. Upon further questioning, she revealed similar episodes of jaw and facial rash/swelling had occurred several times within the past nine months without any apparent trigger event. The patient was investigated for possibility of food allergy, but diet-changing efforts remained futile. She suspected that the old, "leaky" white dental filling material was the cause of her facial rash and was thus anxious to have replacements completed as soon as possible. Patient was again informed that hypersensitivity to dental material is also extremely rare; and if that is the case, her facial rash and swelling would be more severe post-dental restoration procedure due to exposure. Dental treatment will therefore mean using an alternative, possibly less esthetic material. In addition, communication with the physician is essential for proper pre- and post-dental appointment management.

Inter-Professional Communication

One letter was sent to the patient's current physician, clarifying the issues, outlining the dental treatment and sedation plan and confirming the future allergy consultation. The physician did not feel it necessary to delay dental treatment pending the results of the allergy consultation. A second letter was sent to the local allergist, detailing the patient's allergy history, previous allergy consultation report, recent conflicting facial swelling episodes, and my suspicion of an allergy to local anesthetic additives. Allergy tests were requested for all available dental local anesthetics as well as dental materials.

Treatment

The patient returned in October 2008. The allergist confirmed that:

- a) There was no evidence of allergy to dental local anesthetics and no contraindication to their use;
- b) The patient has chronic urticaria. The current medical literature implicates an underlying auto-immune pathophysiology for her skin condition; chronic urticaria is often aggravated by NSAIDs and narcotic analgesics and it was recommended to avoid the use of these medications within the context of any future dental procedures;
- c) No allergy testing to dental resin material was able to be performed.
- d) Having objective evidence against allergy is hoped to be helpful in guiding her future perception of these problems.

After another explanation of how chronic urticaria affected her past dental experience, the patient was then more receptive to the fact that she is not allergic to local anesthetics. An intraoral injection was performed, the patient's vital signs were continuously monitored and full resuscitative equipment and nursing staff was readily available. 1.0 cc of two percent lidocaine with 1:100,000 epinephrine was

infiltrated into the mucobuccal fold to facilitate restorative procedures. The patient remained relaxed and vital signs remained stable throughout the 40-minute procedure. Upon discharge, instruction was given to contact the clinic should post-operative hives or swelling occur. A follow-up phone call four days later revealed a pleasantly surprised, asymptomatic patient. A regular antihistamine regimen was followed and the patient made an appointment with her family dentist to complete treatment.

Discussion

Urticaria, characterised by the rapid appearance of wheals and/or angioedema, is typically recognized as a manifestation of an immune mediated anaphylactic reaction, but it may also appear with pseudo-allergic reactions⁸, or as a heterogeneous disease entity on its own⁹ making diagnosis and proper treatment difficult. The latter entity turns out to be the etiology of this case report.

Unlike angioedema associated with a Type I allergic reaction, the angioedema of chronic urticaria usually does not cause life threatening upper airway obstruction.

The etiology for spontaneous urticaria remains diverse and patient specific, although pseudoallergens such as

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drugs (i.e. penicillin; NSAID) or food additives (aromatic compounds in vegetables and wine), infection (viral), chronic non-infectious inflammatory process and stress have been identified as a cause of urticaria in certain patients. The mechanism involves anti-IgE receptor auto-antibodies that directly stimulate mast cells to release inflammatory mediators, causing urticaria. Thyroid auto-antibodies are also associated with chronic urticaria. Type I-allergic reactions are only rarely responsible for the development of chronic urticaria.

The patient reported was an interesting case wherein signs and symptoms of chronic urticaria manifested in close proximity (hours to days) to dental/medical procedures involving local anesthetic administration, convincing the patient that she was allergic to all types of local anesthetics. Urticaria manifested days after dental examination led both operator and patient to suspect a delayed-hypersensitivity reaction to “leaky” resin dental materials. These and other unpredictable spontaneous episodes of rash and cutaneous swellings guided the author to consult an allergist for confirmation. Prior to this, the patient’s misconception of a local anesthetic allergy remained unrectified by other health-care providers despite the 2002 allergy consultation that clearly eliminated an IgE mediated response. Secondly, it was interesting to see that the positive allergy skin prick test result for articaine was not reproduced upon second skin testing in 2008. This might be due to the unpredictable nature of urticaria, or to the low sensitivity of skin tests toward a positive allergy result.¹⁰⁻¹² Direct challenge with lidocaine + vasoconstrictor induced no immediate or delayed symptoms, thus definitively ruling out an allergic reaction to lidocaine local anesthetic.

This case signifies the importance of proper local anesthetic ‘allergy’ diagnosis and patient education by means of:

- a detailed history

- a repeated firm reassurance to address the patient’s fears
- a proper interdisciplinary referral to confirm or establish a diagnosis

Although a large amount of time was spent in patient management and inter-professional communications, the patient is currently not anxious about dental treatment, no longer requires dental treatment in hospital setting under sedation or general anaesthesia and understands she does not have an allergy to dental anesthetics.

Conclusion

Adverse reactions to local anesthetics are uncommon and true immune mediated allergic reactions to amide local anesthetic are extremely rare (less than one percent of all adverse reactions associated with local anesthetics¹³). Most dentists will at some point encounter a patient who presents with a history of ‘allergy’ to local anesthesia. When this happens, dental practitioners should be able to identify whether the patient suffered an adverse reaction or a true allergic reaction that requires further investigation.

The vast majority of adverse systemic reactions to local anesthetic are caused by anxiety, an associated psychomotor response or inadvertent intravascular injection⁷ that should not be mistaken for a true allergic reaction. Practitioners are encouraged to review local anesthesia pharmacology, clinical techniques and associated adverse reactions.¹⁴ Although by no means being complete, common adverse drug reactions associated with local anesthesia and suggestions on management strategy are provided in Table 1. A patient should not be labelled as having allergy to local anesthetic until proven. Misdiagnosing preventable adverse reactions as allergy may, as in this case, only confuse the patient and other practitioners and delaying care due to “inability to treat” is a major disservice to patients with the potential for severe consequences.^{15,16} 

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