

Acute urticaria due to dental eugenol

M. Bhalla, G. P. Thami*

Key words: dental; eugenol; urticaria.

EUGENOL IS A *para*-substituted phenolic compound that is commonly used in various cosmetics, foods and dental materials (1). In dentistry eugenol is used as an impression material, in periodontal packs, and in various sealers. As a

primary irritant and sensitizer it is known to cause contact urticaria as well as chronic urticaria (1, 2).

A 32-year-old woman presented with severely pruritic, erythematous wheals of 12 h duration that were all over her body. She had been fitted with a temporary dental bridge on the previous morning, and developed an urticarial rash in the evening. Cutaneous examination revealed extensive blanchable wheals of various shapes and sizes. There was no angioedema or mucosal involvement. A provisional diagnosis of acute urticaria due to dental material was made.

Treatment with chlorpheniramine maleate 8 mg 6-hourly and prednisolone 1 mg/kg bodyweight per day failed to control the urticaria for next 2 days until the dental bridge and sealer were removed. There was temporary exacerbation of urticaria at the time of removal of the dental bridge, which gradually subsided over 3–4 days. Her dentist revealed that the dental intervention included fixing a polymethyl methacrylate bridge with zinc oxide–eugenol

sealer. No local anesthetics or any other drugs or chemicals were used.

A skin prick test (SPT) done 2 weeks later was positive for eugenol (10%) and negative for zinc oxide (10%) and polymethyl methacrylate (10%). She was advised not to have eugenol in future dental treatments. No relapse or recurrence was observed during 3 months follow-up. SPT in another two subjects undergoing similar dental interventions with eugenol showed negative results.

Eugenol (4 allyl-2-methoxy phenol; $C_{10}H_{12}O_2$) is naturally present in different concentrations in oil of carnation (80%), pimento oil (80%), oil of bay (60%), oil of cloves (85%) and oil of cinnamon (10%) (1). Cements and liners have antiseptic and anesthetic properties with a palliative action on the dental pulp (3). These sealers may also be used as lubricants or as fillers in teeth. Zinc oxide and eugenol undergo a combination of chemical and physical reactions to yield a hardened mass of zinc eugenate. Small amounts of free zinc oxide and eugenol remain trapped in the matrix of the long sheath of eugenate and are released slowly during setting over a period of several days. Zinc eugenate can also be slowly decomposed by water to release minute quantities of zinc oxide and eugenol (3).

Eugenol is known to cause contact urticaria, characterized clinically by development of an immediate wheal-and-flare response on intact skin coming into direct contact (2). Acute urticaria has rapid onset and disappearance and is usually regarded as an allergic reaction (4). Eugenol has an inhibitory action on the cyclooxygenase pathway of arachidonic acid metabolism and may cause urticaria by its direct pharmacological action similar to other cyclooxygenase inhibitors (e.g. aspirin and other nonsteroidal anti-inflammatory drugs) (5).

Strong temporal correlation of onset of urticaria with dental intervention, continued presence of urticaria despite therapy, its resolution after removal of the dental bridge and sealer, and positive SPT to eugenol confirmed the etiological role of eugenol in acute urticaria in this case. The immunological mechanism in this patient was apparently an immediate-type IgE-mediated hypersensitivity reaction, so it was considered unsafe to rechallenge orally.

Although contact and chronic urticaria have previously been described with eugenol, this is the first report of acute urticaria.

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Anaphylaxis during negative penicillin skin prick testing confirmed by elevated serum tryptase

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Key words: anaphylaxis; mastocytosis; penicillin allergy; skin prick tests; tryptase.

A 42-year-old woman was referred to allergological evaluation because of an episode of cutaneous pruritus, hypotension and loss of consciousness which appeared 5 min after the intake of 500 mg of amoxicillin for pharyngitis. Physical examination (including skin evaluation) was unremarkable. Haematological and biochemical analysis, electrocardiogram (ECG), chest X-ray, abdominal ultrasound and cerebral computed tomography (CT) scan were normal. A negative tilt test ruled out an neurocardiogenic syncope. Total immunoglobulin E (IgE) was 4.03 UI/ml. Specific IgE (CAP-System; Pharmacia, Sweden) and histamine release test (HRT) by a fluorimetric method to benzylpenicilloyl, fenoxymethylpenicilloyl, amoxicillin and ampicillin were negative. Specific IgE to anisakis, latex, food and common inhalant allergens were all negative.

After obtaining written informed consent, skin prick tests (SPTs) were performed with BPO, MDM (Allergopharma Merck, Germany), benzylpenicillin 10 000 IU/ml, and amoxicillin 25 mg/ml (Beecham, Spain). At 15 min, the patient started feeling pruritus and nausea, but no skin response was observed at the site of SPTs with penicillin determinants, although the histamine control was positive. Suddenly she started vomiting, felt faintness, and presented

An exceptional case of anaphylaxis without skin involvement induced by penicillin skin prick testing is reported.

hypotension (systolic was 60 mmHg, diastolic was undetectable), which was resolved rapidly with epinephrine and endovenose saline. Serum total tryptase level (UniCAP-Tryptase; Pharmacia & Upjohn) was 180 ng/mL in a blood sample taken at 30 min of the reaction and 69 ng/mL at 90 min (normal < 13.5 ng/mL) and it decreased in the next few hours. One month later, the serum tryptase level was 17.3 ng/mL, and CAP to penicillin determinants was again negative. Follow-up of serum tryptase levels for 18 months after the reaction showed similar values. Skin responsiveness was later assessed by a positive SPT codein.

Systemic reactions after skin testing with betalactams can occur in patients with high sensitivity. Penicillin and amoxicillin are the drugs more frequently involved (1, 2). Although exceptional, skin involvement may be absent in anaphylaxis, specially in the severest reactions (3, 4).

This is an exceptional case of an anaphylactic shock without skin involvement induced by amoxicillin and by skin prick testing with penicillin determinants. Although penicillin SPTs turned out to be negative, as well as serum specific IgE, the rise of serum tryptase during the reaction suggested a generalized mast-cell (MC) activation and confirmed drug anaphylaxis. Other authors have also shown the usefulness of tryptase determination in the diagnosis of systemic anaphylaxis (5, 6). It is remarkable that the extraordinary severity of the reaction is induced by a minimally invasive technique such as SPTs. To the best of our knowledge, no other cases of similar characteristics have been reported.

It has been described that underlying mastocytosis may predispose to anaphylactic and anaphylactoid reactions (7, 8). The UniCAP-Tryptase fluorimunoassay detects both α -tryptase and β -tryptase. α -Tryptase is constitutively secreted by MC and β -tryptase is released during MC activation. The high value detected in the acute phase of the reaction (180 ng/mL) reflects the magnitude of the MC activation and it would consist of (mainly) β -tryptase. The serial tryptase determinations

performed after the reaction which would reflect α -tryptase levels, showed low constant values (ranging from 17.3 to 12.8 ng/mL). According to Kanthawatana et al. (8), these follow-up values would rule an underlying mastocytosis in our patient.

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Aspirin intolerance in boy with primary ciliary dyskinesia

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Key words: aspirin intolerance; cyclooxygenase; primary ciliary dyskinesia; provocation test; selective COX₂-inhibitor.

ASPIRIN INTOLERANCE occurs in 5–20% of adult asthmatics but it is rare in children. Cyclooxygenase (COX) plays a major role in the pathogenesis of aspirin intolerance. Aspirin and other nonsteroidal antiinflammatory drugs (NSAIDs) unselectively inhibit the COX pathway, inducing synthesis of leukotriene A₄ (LTA₄) and thus resulting in a strong proinflammatory response (1).

A 12-year-old Moroccan boy was evaluated for recurrent episodes of bronchial obstruction. On examination he showed nasal congestion, rhinorrhoea, and wheezing. Laboratory tests and complete allergologic work-up revealed eosinophilia (34%) and an eosinophilic cationic protein level of 95.2 µg/l (normal range 4.4–11.3 µg/l), but otherwise normal findings. Lung function tests showed bronchial obstruction (forced expiratory volume in 1 s, FEV₁ 54%). Cystic fibrosis was ruled out because of normal sweat chloride values, genetic analysis, and normal intestinal current in rectum samples. In the chest roentgenogram, bronchiectasis was detected in both lower lobes; paranasal CT scans revealed polyposis nasi. Transmission electron microscopy of bronchial biopsy tissue showed no inner dynein arms, and a numeric aberration of peripheral microtubules, so leading to the diagnosis of primary ciliary dyskinesia (PCD).

Despite antiobstructive treatment (2) the boy was admitted to our hospital seven times for recurrent bronchospasm in an 18-month period. On one occasion

mechanical ventilation was needed 30 min after treatment with 500 mg of oral acetaminophen. After negative skin prick tests and cellular allergen stimulation tests for aspirin-lysin, acetaminophen and rofecoxib, we performed a double-blind placebo-controlled oral provocation test (DBPCPT) with aspirin (3,4). Forty minutes after application of 50 mg aspirin, peak flow declined by 50%, and oxygen saturation fell to 88%. With extensive antiobstructive treatment the patient recovered within 2 h. There was no reaction to the placebo. Cross-reactivity to a selective COX₂ inhibitor, rofecoxib, was ruled out by another DBPCPT.

The diagnosis of NSAID intolerance is based on thorough medical history and provocation tests, while in-vitro tests apparently have a low diagnostic yield. NSAID intolerance may occur after ingestion of unselective COX inhibitors (e.g. acetaminophen, aspirin) as well as selective COX₂ inhibitors (5). However, recent studies suggest that the selective COX₂ inhibitor rofecoxib may be a safe alternative for analgesic and antiphlogistic treatment of people with NSAID intolerance (4). Despite severe reactions to aspirin our patient tolerated rofecoxib.

Although the boy presented with a nonspecific clinical triad of NSAID intolerance (rhinitis, nasal polyps, bronchial asthma) (6), and recurrent severe attacks of bronchospasm not attributable to the diagnosis of PCD alone, it was not until oral provocation that this cause of pulmonary obstructive disease was detected.

Clearly, NSAID intolerance must be considered in cases of intractable bronchial asthma and recurrent obstructive exacerbations—even in children.

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Double allergy to the same drug in the same patient

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Key words: delayed allergy, immediate allergy, LTT, penicillin.

Penicillin and related antibiotics with the β-Lactam ring represent a typical example of allergy-inducing drugs (1). These antibiotics are involved both in IgE-mediated and delayed hypersensitivity reactions. The coexistence of both delayed and immediate reaction in the same patient to the same drug can be

Co-existing IgE-mediated and delayed allergy to penicillin-G in the same patient.

Table 1. Lymphocyte transformation test (LTT)

Penicillin-G		Ampicillin		Amoxicillin	
µg/ml	SI	µg/ml	SI	µg/ml	SI
1000	29	500	1.1	500	3.7
500	18	200	0.7	200	1.64
200	13	100	0.3	100	1.2

Proliferative responses are expressed as mean stimulation index (SI): ratio of cpm with and without antigen in triplicate culture.

considered a very uncommon event (2). In this study, we report the immunological evaluations in a patient where a delayed and immediate reactivity to penicillin-G coexisted.

We describe the case of a 59-year-old woman who complained of pruritus, generalized urticaria and facial angioedema 1 day after oral intake of amoxicillin 500 mg. Furthermore, the patient's historic data reported that a maculopapular rash, followed by loss of consciousness, occurred during penicillin-G treatment, about 1 year previously. She had no personal or family history of atopic disease, chronic sinusitis, nasal polyps nor other drug sensitivity. She was not taking any concomitant therapy at the time of her adverse reaction. Two years after the first reaction, the patient was referred to our allergy clinic for the aetiological diagnosis.

After obtaining the patient's written consent, we carried out a skin test with 6×10^{-5} mm/l, benzylpenicilloyl polylysine (BPO) (Allergopen, Reinbek, Germany), 2×10^{-2} mm/l minor determinant mixture containing benzylpenicillin and benzylpenicilloate (Allergopen), penicillin-G, ampicillin and amoxicillin, as well as patch tests with the last three drugs. An immediate reaction to benzylpenicilloyl polylysine and penicillin-G was observed at the 20-min reading (wheals had maximum diameters of 10 and 7 mm, respectively). The immediate reaction disappeared within an hour. Surprisingly, about 24 h after the test, itching and erythematous patches developed at the injection sites of penicillin-G (maximum diameters of 7 and 16 mm, at concentrations of 100 and 10 000 IU, respectively), ampicillin (maximum diameter of 6 mm, at a concentration of 20 mg) and amoxicillin

(maximum diameter of 11 mm, at a concentration of 20 mg), whereas no reaction was observed at the injection sites of benzylpenicilloyl polylysine (BPO) and the minor determinant mixture. Patch tests were performed with penicillin-G (5000 IU/g petrolatum), ampicillin, and amoxicillin (5% in petrolatum) as described (3, 4). A strong delayed hypersensitivity to penicillin-G (+ + +) and a slight reaction to amoxicillin (+) was observed at the 48 and 72 h readings.

Assays (UniCAP specific IgE; Pharmacia & Upjohn, Uppsala, Sweden) for specific IgE to penicilloyl G gave a positive result (10.9 kU/l), whereas penicilloyl V, ampicilloyl, amoxicilloyl and cefaclor were negative (<0.35 kU/l).

To document the T cell involvement in our case further, we measured the proliferative T cell response to penicillin-G, ampicillin and amoxicillin *in vitro* by the so-called lymphocyte transformation test (LTT) (5, 6). As Table 1 shows, the stimulation of PBMC with penicillin-G led to a strong proliferative response, whereas a weak proliferation was observed with amoxicillin.

Clinical findings, *in vitro* test and proliferation studies indicate the presence of both delayed and IgE-mediated hypersensitivity to penicillin-G in our subject. Similarly, Romano et al., in an elegant report, described a case with both a type-I allergy to cephaloridine and a type-IV hypersensitivity to ampicillin (2). To our knowledge the presence of a double type of reactivity to the same drug in the same patient has never been described.

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Meat allergy and cross-reactivity with hamster epithelium

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Key words: albumin allergy; epithelia allergy; hamster allergy; horse allergy; meat allergy.

SOME CLINICAL observations have revealed an association between allergy

Epithelia inhalation allergy Linked with meat allergy.

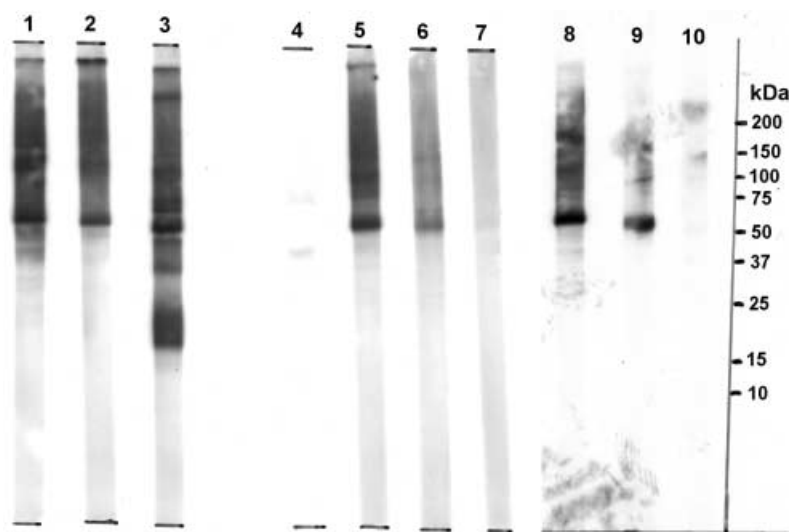


Figure 1. IgE-immunoblotting after SDS-PAGE of different epithelium and meat extracts. Lane 1, hamster epithelium; lane 2, Guinea pig epithelium; lane 3, cat epithelium; lane 4, negative control; lane 5, rabbit meat; lane 6, beef; lane 7, chicken meat; lane 8, horse meat; lane 9, bovine serum albumin; lane 10, negative control.

to epithelia and allergy to meat known as the pork–cat syndrome. A common allergen, serum albumin, has been found in people affected by this (1, 2). Secretion of allergens into the environment by mammals and pets is an important cause of IgE antibody responses, and a risk factor for asthma development (3, 4). We report the case of a woman with asthma related to hamster exposure, and with food allergy due to horse meat.

A 39-year-old woman referred a recent episode of lip angioedema after eating horse meat. She tolerated other types of meat. She had experienced asthma due to cat epithelia and oral pruritus after ingesting rabbit meat as a child. Since the introduction of a hamster at home in the previous year, she has suffered from asthma.

Skin prick tests (SPT) to common inhalant allergens were positive to cat and dog. SPT to different animal epithelia were positive to hamster and Guinea pig. SPT with fresh foods were positive to beef, pork, rabbit and horse meat and negative to poultry meat.

Immunoblotting with cat, hamster and Guinea pig epithelia, and with beef, rabbit, and horse-meat extracts showed an IgE-binding protein band of ~65 kDa, with the same electrophoretic mobility as bovine serum albumin (Fig. 1). This band was not observed in

chicken meat. IgE cross-reactivity between hamster epithelium and horse meat was studied by RAST inhibition and a partial inhibition of ~30% was obtained.

This case is interesting because the patient began with asthma related to cat exposure, and later the meat allergy appeared. After avoiding exposure to cats the patient was able to tolerate meat. After the second exposure to epithelium (from the hamster), she developed asthma and oral syndrome to horse meat. RAST inhibition studies between hamster epithelia and horse meat demonstrated a partial cross-reactivity, for which serum albumin may be responsible. IgE-immunoblotting to different types of meat confirmed recognition of rabbit, cow, and horse albumins but not to chicken albumin α -livetin. Surprisingly, despite previous reactions to rabbit meat and the immunoblotting results, the patient now tolerated rabbit meat as well as beef. Although serum albumins from various species are highly homologous, a significant variability in IgE reactivities has been observed (3). This might explain why this woman did not tolerate horse meat, although she did tolerate other types of meat.

In conclusion, a partial cross-reactivity between horse meat and hamster epithelium has been demonstrated using RAST

inhibition. The meat allergy is probably caused by previous exposure to mammal epithelia.

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Treatment of bullous pemphigoid with a leukotriene receptor antagonist

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THE EFFECTS OF leukotriene receptor antagonists are complementary to those of inhaled corticosteroids, and they can be tapered in patients with bronchial asthma. We describe a case of blister healing with

A beneficial role in reducing the dosage of glucocorticoid?

bullous pemphigoid by the use of a leukotriene receptor antagonist.

A 59-year-old woman with bronchial asthma was admitted to the University Hospital for systemic blisters. Blister formation was remarkable, particularly in the oral cavity. A diagnosis of bullous pemphigoid was made after skin biopsy, and the patient was given prednisolone at 90 mg/day. Once remission was obtained, prednisolone was gradually tapered to 12.5 mg/day. However, recurrence of blisters and asthma exacerbation occurred at this dose, at which point the dosage of prednisolone was raised to 15 mg/day.

Although complete remission of bullous pemphigoid was obtained on prednisolone at 15 mg/day, her asthma worsened. She received oral leukotriene receptor antagonist pranlukast 450 mg/day for asthma treatment. Given that her asthma was well controlled and prednisolone was reduced to 7.5 mg/day without further recurrence of blisters, it was suggested that pranlukast might have an inhibitory effect on blister formation.

To investigate the effect of pranlukast on bullous pemphigoid, the administration of pranlukast was discontinued from the morning, while the patient continued to receive prednisolone at 7.5 mg/day. Blister formation with bleeding occurred again in the evening of the same day in the oral cavity, and readministration of pranlukast was found to completely suppress it.

To our knowledge, this is the first report describing the efficacy of leukotriene receptor antagonists for treatment of bullous pemphigoid. Bullous pemphigoid is a systemic disease affecting the subepidermis of the skin and mucosa, and autoimmune reaction is believed to lead to blister formation in the basal layer (1).

Although glucocorticoids are the most effective agents for controlling the disease, a variety of adverse effects make its long-term use difficult. Immunosuppressive drugs used for treatment of bullous pemphigoid also have adverse effects. Peptide-leukotrienes are thought to be important mediators involved in the etiology of asthma. However, peptide-leukotrienes are also reported to be involved in blister formation, based on their ability to increase plasma leakage

from vessels (2) and the significant levels of leukotriene C₄ observed in the blister fluids of pemphigoid patients (3). Findings in this patient suggest that leukotriene receptor antagonists may have a beneficial role in reducing the dosage of glucocorticoid to control bullous pemphigoid.

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Winging of the scapula – an unusual cause

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Key words: benzylpenicillin; brachial plexus neuritis; differential diagnosis; electromyography; human; male.

This report discusses a case of scapula winging caused by an allergic response to the administration of antibiotics. Winging of

the scapula is an uncommon condition and although an allergic association has been previously suggested (1), this has not been previously reported.

A 31-year-old man presented as an emergency, with a 6-month history of fatigue, lethargy, weight loss, and more recently fever and night sweats. He was generally fit. In particular he was not an atopic individual, with no past history of allergies. Examination revealed an early diastolic murmur. Echocardiography demonstrated a thickened bicuspid aortic valve consistent with endocarditis. Serial blood cultures grew *Streptococci*. He was started with benzylpenicillin and gentamicin, with considerable improvement.

Approximately 2 weeks later he developed bilateral shoulder pain and a fine erythematous rash over trunk and neck. This was confidently diagnosed as an allergic response to benzylpenicillin, confirmed by the microbiologist. The penicillin was stopped and the rash and shoulder pains resolved. However, winging of the right scapula was clearly evident, exacerbated by provocation of the serratus anterior muscle in protraction. There was no distal neurovascular deficit. Other tests of the shoulder girdle musculature were normal.

Neurophysiological studies were performed 6 weeks following the onset of winging. Needle electromyography of the long thoracic nerve demonstrated active denervation and no recruited potentials. The conclusion was that he had a long thoracic palsy. The neurologist performing this investigation reported that this was highly suggestive of brachial plexopathy (neuralgic amyotrophy) caused by an immune response to antibiotics.

The serratus anterior muscle is innervated segmentally by the long thoracic nerve, which is formed from the C5, 6 and 7 nerve roots. The function of the muscle is to protract the scapula whilst maintaining contact with the chest wall. Winging of the scapula occurs with paralysis of the muscle, allowing the vertebral border to protrude posteriorly.

Perlmutter and Leffert (2) reviewed the literature regarding the cause of serratus anterior paralysis. They found episodes following sporting activities, acute traumatic and traction injuries, in association with viral illness, brachial neuritis and iatrogenic injury following

A case of scapula winging caused by an allergic response to the administration of antibiotics.

decompression of the thoracic outlet. Johnson and Kendall (1), in 1955, noted the causes as listed above, including exposure to cold, and the injection of sera, vaccines and antibiotics.

Parsonage and Turner (3) described a form of brachial plexus neuropathy as neuralgic amyotrophy. This condition is typified by acute shoulder pain, which resolves spontaneously. The pain is followed after a variable period by weakness of at least one of the shoulder girdle muscles. The aetiology of this condition is unclear although an infective or immunological cause is proposed. A number of series have been reported (4, 5, 6).

The patient that we have presented in this report developed scapula winging and shoulder pain simultaneously with the onset of an allergic response to antibiotics. There was no history of antecedent trauma. The diagnosis has been strongly supported by the neurophysiological investigations undertaken

at that time. Whilst this aetiology has been previously proposed, we have found no other recorded case in the world literature.

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