

Anaphylaxis after Dental Treatment with a Formaldehyde-containing Tooth-filling Material

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Sir,

Formaldehyde is widely used in cosmetics, building materials and furniture, and is a well-known cause of contact dermatitis, occupational asthma, and sick-building syndrome (1, 2). Recently, a few cases of anaphylactic reactions to formaldehyde in patients with dental treatment have been reported (3–5). However, the mechanism of such reactions has not been precisely elucidated. We report here a patient who showed anaphylactic reactions after dental treatment with a formaldehyde-containing tooth-filling material, and demonstrate the release of histamine from basophils of this patient with formaldehyde-human serum albumin conjugates (formaldehyde-HSA).

CASE REPORT

A 31-year-old man who was engaged in the production of automobiles, who did not have a personal or family history of allergies, was treated with a formaldehyde-containing tooth filling (Formalin guaiacol FG neoTM), consisting of three liquids – formalin (40%), guaiacol (40%) and ethanol (20%). After 1 week, he was treated again in this way. Approximately 30 min later, he developed a generalized urticaria and experienced respiratory difficulty. He received oxygen and intravenous transfusion, and recovered after 3 h. The skin eruption gradually diminished and finally disappeared 2 days later. The intracutaneous test with 0.5×10^5 and 1×10^6 dilutions of 40% formaldehyde solution in saline was positive (wheal diameter 10 mm and 6 mm, respectively), whereas that with 1×10^7 , 1×10^8 and saline was negative (wheal diameter <2 mm). None of five healthy volunteers showed any reaction in these tests. The specific IgE value against formaldehyde was 17.0 UA/ml, class 3 (CAP-RAST Pharmacia and Upjohn), whereas total IgE was 239.0 IU/ml (normal range <321.4 IU/ml).

For laboratory analysis, a conjugate of formaldehyde with HSA was prepared as described by Karol et al. (6). Briefly, 4 ml of formaldehyde (12 mg/ml) was mixed with 1 ml of 0.01 M phosphate buffer (0.01 M $\text{NaH}_2\text{PO}_4 \times 2\text{H}_2\text{O}$, 0.01 M $\text{Na}_2\text{HPO}_4 \times 12\text{H}_2\text{O}$, pH 7.4) with 5% HSA and incubated for 30 min at 37°C. The solution was dialysed against 0.01 M phosphate buffer for 3 days at 4°C and used as such. Basophil-enriched leukocyte suspensions were prepared from 40 ml of venous blood from the patient as described by Hide et al. (7). They were aliquoted (11) in tubes containing the challenge stimuli: formaldehyde-HSA (≤ 6.95 mg/ml),

5% human serum albumin (6.95 mg/ml), goat anti-human IgE as positive control (0.67 µg/ml) (Seikagaku Co., Tokyo, Japan), or buffer alone. After incubation at 37°C for 40 min, the amount of histamine released into supernatants was measured by an automated fluorometric assay, as described previously (7).

Only the basophils of the patient released a large amount of histamine (44.0%) in response to formaldehyde-HSA (3.48 mg/ml). HSA induced no apparent release of histamine from either the patient's or healthy control's basophils (Fig. 1). Serial dilutions of formaldehyde-HSA formed a bell-shaped dose-response curve in the histamine release experiment with basophils of the patients (Fig. 2).

DISCUSSION

In the present case, we have demonstrated the presence of specific serum IgE and positive skin reaction to formaldehyde, suggesting that formaldehyde contained in tooth-filling material induced anaphylactic reaction after the dental treatment. The *in vitro* experiment revealed that formaldehyde-HSA induces the release of histamine specifically from the patient's basophils, in accordance with clinical observation.

Formaldehyde is commonly used for the treatment of dental caries. It is slowly released from root canal sealers, and permeates through cementum and blood after such treatments. Consequently, anaphylactic reaction to formaldehyde may not develop immediately

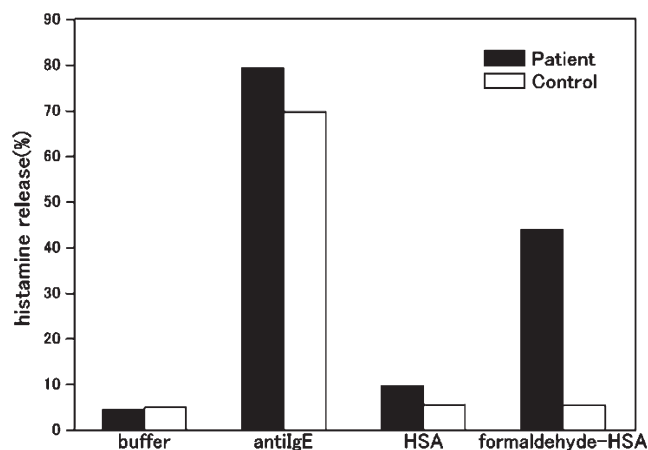


Fig. 1. Histamine release from basophils of the patient and a healthy volunteer (Control) in response to anti-IgE (0.34 µg/ml), human serum albumin (HSA, 3.48 mg/ml) and formaldehyde-HSA (3.48 mg/ml).

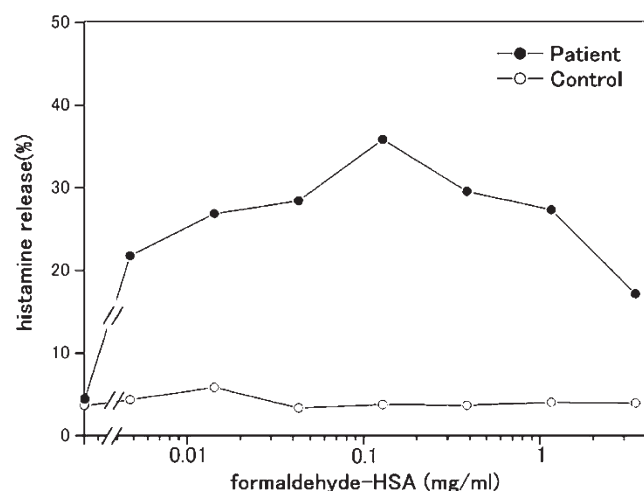


Fig. 2. Histamine release from basophils of the patient and a healthy volunteer (Control) with serial dilutions of formaldehyde-human serum albumin.

after the application of the material, rather later (3–5). As formaldehyde is included in many materials, such as building materials, furniture and paints, sensitization to formaldehyde can also take place during occupational exposure, and even during daily life by exposure to very low amounts of indoor formaldehyde. In the case reported here, sensitization may have occurred during dental treatment 1 week before, or through the patient's occupation – painting cars.

Recently, systemic reactions after dental treatment with formaldehyde-containing materials have been increasingly reported (3–5). The presence of specific serum IgE against formaldehyde has been taken as evidence for an anaphylactoid pathogenesis. However, such IgE was also detected in some patients with occupational asthma or sick-building syndrome who

have not developed anaphylactic reactions (1, 2). This suggests that the presence of specific serum IgE does not necessarily lead to anaphylactic reactions to formaldehyde. On the other hand, skin tests to formaldehyde are not standardized and positive skin reactions were observed only in few patients (3–5). In addition, skin tests with higher concentration of formaldehyde solution may provoke severe systemic reactions. We demonstrate here that a histamine release test with formaldehyde-HSA *in vitro* is a reliable and safe method for the diagnosis of anaphylaxis induced by formaldehyde.

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