

Amalgam allergy associated with exacerbation of aspirin-intolerant asthma

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Summary

Background Aspirin-intolerant asthma can be induced not only by acidic analgesics (including acetylsalicylic acid), which effectively inhibit cyclo-oxygenase, but also by cross-reactivity with paraben, and other chemical additives.

Objective We examined whether amalgam allergy is involved in the pathogenesis of a aspirin-intolerant asthma.

Methods We present the first case of aspirin-intolerant asthma that improved after the removal of dental amalgam. In addition, we performed both the methacholine provocation testing and sulpyrine provocation testing before and after the removal of dental amalgam.

Results In addition, the methacholine concentration causing a 20% fall in FEV₁ in provocation tests rose significantly, though hypersensitivity to analgesics evaluated with sulpyrine provocation testing did not decrease. These results suggest that amalgam sensitization is involved in bronchial hyperresponsiveness in aspirin-intolerant asthma.

Conclusion Sensitivity to amalgam may cause exacerbation of aspirin-intolerant asthma in some patients. To the best of our knowledge, this is the first case report of amalgam allergy associated with aspirin-intolerant asthma.

Keywords: amalgam allergy, dental alloy, aspirin-intolerant asthma, bronchial hyperresponsiveness, methacholine provocation test, sulpyrine provocation test

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Introduction

Attacks of aspirin-intolerant asthma can be induced not only by acidic non-steroidal anti-inflammatory drugs (including acetylsalicylic acid, or aspirin), which effectively inhibit cyclo-oxygenase, but also by cross-reactivity of asthmatic attacks with paraben and other chemical additives. However, paraben does not have an anticyclo-oxygenase effect, and neither specific factors nor pathways of this cross-reactivity remain unclear [1].

In this case, we describe herein, amalgam allergy obviously exacerbated aspirin-intolerant asthma in one

patient, although amalgam is not thought to have an inhibitory effect on cyclo-oxygenase. To the best of our knowledge, this is the first report of amalgam allergy associated with aspirin-intolerant asthma.

Case report

A 36-year-old woman was referred to our medical centre for further evaluation of prolonged exacerbation of aspirin-intolerant asthma. Three years previously, having experienced nocturnal cough and mild shortness of breath once or twice a week, she had been diagnosed by her family physician with nonatopic bronchial asthma of unknown aetiology. The patient's condition was controlled well for 3 years with inhaled β -agonist on demand. However, for

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1 month before her referral to our medical centre, she suffered from nocturnal cough, shortness of breath, and wheezing almost every night. Her physician prescribed oral theophylline (400 mg/day) and clenbuterol hydrochloride (40 µg/day), but this treatment did not markedly alleviate her asthmatic symptoms.

When seen initially at our medical centre, the patient reported that she did not smoke, had no history of atopy, did not keep a bird as a pet, and had received no drug before exacerbation. Moreover, before the onset of bronchial asthma, she had had no history of recurrent cough, nocturnal cough, or exercised-induced bronchospasm suggestive of childhood asthma; however, she had experienced a severe asthmatic attack after taking analgesic medicine 2 years previously. Results of physical examination and chest radiography were normal. Eosinophil counts were normal in sputum and blood. Her total serum IgE level was 6.5 IU/L, and IgE-radioallergosorbent tests (RASTs) for 30 kinds of allergen were negative. Methacholine provocation testing gave results consistent with her obvious bronchial hyperresponsiveness: PC₂₀-methacholine was 0.31 mg/mL. Sulpyrine provocation testing performed to evaluate analgesic-intolerant reactions revealed hypersensitivity to analgesics with a PC₂₀-sulpyrine of 100 mg/mL.

The patient stated that a dental cavity had been filled with dental alloy at a dental clinic about 1 month before the asthma exacerbation and that the local gingiva had become swollen the next day. This episode raised the suspicion of a metal allergy to some component of the dental alloy.

Methods

Skin tests

Patch tests were performed according to the standard protocol of the International Contact Dermatitis Research Group, as previously described [2].

Methacholine provocation testing

Bronchial responsiveness was evaluated by methacholine provocation, as previously described [3].

Sulpyrine provocation testing

Sulpyrine provocation testing is widely used for diagnosis of aspirin-intolerant asthma. This testing was performed under conditions similar to those used for methacholine provocation testing, as previously described [3].

Results

The patch test series, a dental restorative material series, and a metal salt series revealed a strong erythematous papular

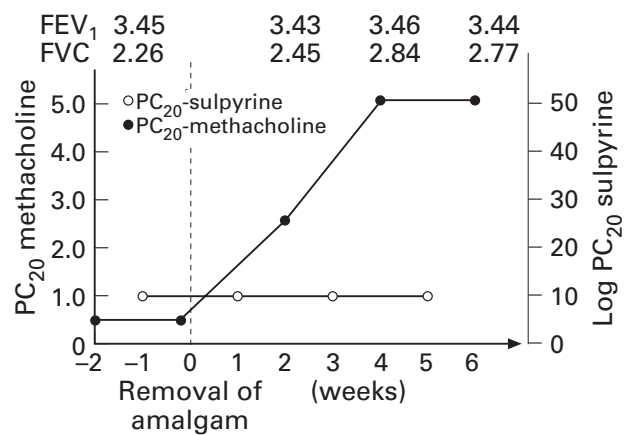


Fig. 1. Clinical course of patient with an exacerbation of aspirin-intolerant asthma related to amalgam allergy.

reaction to 5, 10, and 20% amalgam. Patch testing with 20% amalgam alloy without mercury also elicited a strong reaction. A patch test with either 0.1% mercuric chloride or 1% mercuric ammonium chloride yielded negative results. Also, other 19 metals including each single component of the amalgam (Ag, Sn, Cu) did not produce a positive skin test.

The patient's dentist confirmed that the dental alloys used to fill the patient's cavity were made of a silver-amalgam alloy (56% Ag, 29% Sn, 15% Cu, and <3% Hg). As a result of our evaluation, the dental alloys were removed from the patient's teeth. Two days later, despite no change in treatment, her condition improved and stabilized at the level maintained before the cavity was filled.

Every other week after the removal of the dental alloys, the patient underwent alternating methacholine and sulpyrine provocation testing under the same conditions as before. The marked improvement of his bronchial hyperresponsiveness was evidenced by a PC₂₀ methacholine of 5.0 mg/mL after 4 weeks (Fig. 1).

Although, either FEV₁ or FVC did not improve after removal of the dental amalgam, patient's condition improved, because exacerbated symptoms, such as nocturnal cough, shortness of breath, and wheezing, disappeared.

Discussion

Human exposures to mercury and the other main metal dental components of amalgam (Ag, Sn, Cu, and Zn) take place via inhalation of vapour, swallowing of corrosion products in saliva, and direct absorption into the blood stream from the oral cavity. Dental mercury amalgam disintegrates particularly slowly and can induce immune dysfunction [4]. Some reports indicated that main dental amalgam metals (such as Hg, Ag, Sn, Cu, and Zn) may

induce allergic or auto-immunity reactions. Still, other metals used in dental alloys (e.g. Ni, Co, or Pd) may also cause allergic diseases, including bronchial asthma [5].

Previous reports have suggested that dental amalgam is associated with the pathogenesis of allergy and immunodeficiency diseases, such as multiple sclerosis [6], multiple chemical sensitivities [7] and asthma [8]. Katsunuma *et al.* reported a case of exercise-induced anaphylaxis that was alleviated following the removal of dental amalgam. They also examined the increase in plasma histamine levels during exercise provocation test also improved. These findings suggest that sensitivity to metals may cause exercise-induced asthma in some patients [8].

The most useful method for the diagnosis of metal allergy is patch testing, because many false-positive results occur in *in vitro* assays, such as RAST [9]. To determine the metal which caused exacerbation in this patient, we performed patch tests according to the standard protocol of the International Contact Dermatitis Research Group, as previously described [2]. In the case described herein, the patient had an episode of asthma exacerbation that raised suspicion of a metal allergy to some component of dental alloy. This patient's dental alloy, which had been inserted only 1 month before the exacerbation of asthma, was dental amalgam contained <3% mercury, since the patient had no sensitization to mercury and other dental metals except amalgam. These findings showed the cause of exacerbation in this patient with asthma should not be either mercury toxicity, or sensitization to mercury and other single dental metal. We concluded that our patient had a clinically relevant exacerbation of bronchial asthma related to an allergic reaction to amalgam in dental alloy. Although amalgam produced a positive patch test in this patient, none of the components of the amalgam (Ag, Sn, Cu, Hg) produced a positive skin test when applied individually. The discrepancy may be due to an unknown minor component of the amalgam, an undescribed interaction between two or more components, or differences between allergic reactions in the lung and the skin. To determine the exact mechanism of this discrepancy, more studies will be needed.

The presence of amalgam did not affect the PC₂₀ sulphur dioxide, but obviously did affect the PC₂₀ methacholine. These results revealed that amalgam allergy does not affect hypersensitivity to analgesics, but did affect bronchial hyperresponsiveness in aspirin-intolerant asthma. In this case, patient's exacerbated symptoms improved rapidly (2 days) after removal of the dental amalgam. The exact reason the symptoms rapidly improved is still unproved, but one possibility is that the dental amalgam caused persistent bronchial inflammation, exacerbated bronchial hyperresponsiveness, and thus, symptoms of asthma were worsened.

At present, there is insufficient evidence to prove that immunological reactions resulting from amalgam metals are responsible for the local oral symptoms of certain individuals with dental amalgam, and there is no convincing evidence that dental metals are the cause of any allergic or immunodeficiency disease [5]. However, to the best of our knowledge, this is the first case report of amalgam allergy associated with aspirin-intolerant asthma. This case shows that metal allergy should be considered in the evaluation of this disease.

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