

Patient Report

Two cases of anaphylactic reaction to gelatin induced by a chloral hydrate suppository

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An accumulating number of reports have pointed out the importance of gelatin allergy in young children, which sometimes leads to a fatal outcome due to anaphylaxis.^{1,2} In Japan, most vaccines have been replaced with gelatin-free forms, whereas gelatin is still contained in many drugs and baby foods. Therefore, it is necessary to be aware of gelatin-containing products. We have experienced two patients with anaphylactic symptoms induced by a chloral hydrate suppository, which contained gelatin, used for sedation before an electroencephalography (EEG) examination. Here, we present the clinical course of the patients and discuss the acquisition and mechanism of gelatin allergy.

Case report

Case 1

A 2-year-old girl was referred to our hospital for close examinations for three episodes of febrile convulsion. She had a family history of allergic rhinitis and atopic dermatitis. She had been bottle-fed, and had frequently taken gelatin-containing jelly since the age of 1. She had never demonstrated any allergic symptoms. She received vaccines for poliomyelitis, diphtheria-pertussis-tetanus (DPT), rubella and Bacille Calmette-Guérin (BCG), some of which contained gelatin (Fig. 1), without any side-effects. Before the EEG examination, a suppository was inserted containing 500 mg of chloral hydrate for sedation. Thirty minutes after its administration, a cough developed and urticaria of the whole-body appeared. She was successfully treated with an antihistamine (hydroxyzine) and hydrocortisone. The laboratory examinations

revealed a high total IgE level (275 IU/mL) and a gelatin-specific IgE antibody (1.99 UA/mL, class 2). The skin prick test for chloral hydrate (5 µg/mL) was negative. She avoided intake of gelatin containing foods afterwards. One year later, her total IgE level went up to 779 IU/mL, whereas the gelatin-specific IgE became negative (<0.35 UA/mL).

Case 2

A 4-year-old boy suffered from febrile convulsions twice. He had wheezing repeatedly with upper respiratory infections since the age of 1 and was diagnosed with bronchial asthma. His family members had no history of allergic disorders. His past nutrition was mixed-feeding, and almost every day he had taken rice that was boiled with vitamin supplements packed in a gelatin capsule since 5 months of age. He received gelatin-containing vaccines without any side-effects (Fig. 1). A 500 mg chloral hydrate suppository was administered at the time of an EEG examination. Thirty minutes after administration of the suppository, coughing, wheezing, rhinorrhea, sneezing and urticaria on the face and both lower extremities appeared. The wheezing was successfully treated with inhalation of a β_2 stimulant, and the other symptoms disappeared spontaneously. His total IgE level was 3690 IU/mL, and the gelatin-specific IgE antibody level was >100 UA/mL (class 6). His specific IgE against egg-whites, milk, wheat and rice was 0.54 UA/mL, 2.77 UA/mL, <0.35 UA/mL and <0.35 UA/mL, respectively. Skin tests for gelatin or chloral hydrate were not performed, because parents' informed consent was not available.

Discussion

In this report, we have demonstrated two patients with anaphylactic symptoms after the administration of a chloral hydrate suppository containing a large amount of gelatin. To our knowledge, there is no report indicating that chloral hydrate itself induces anaphylactic reaction. Furthermore, our two

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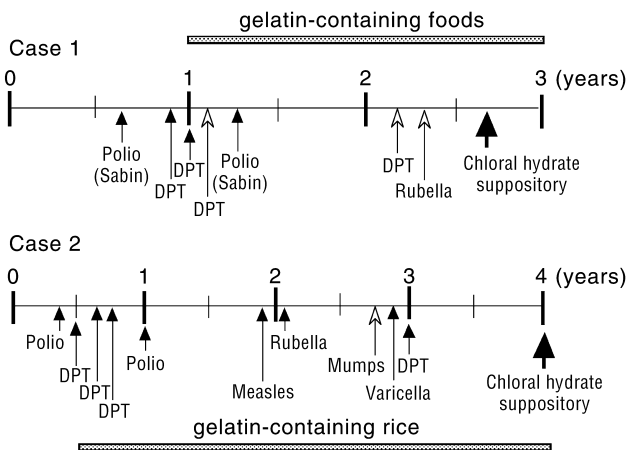


Fig. 1 History of immunization and intake of gelatin-containing foods. Closed arrows mean gelatin-containing vaccines or suppository, and open arrows mean gelatin-free vaccines.

cases had had no chance of sensitization to chloral hydrate before the administration of the suppository and the skin test for chloral hydrate of case 1 was negative. Although an allergen-challenge test for gelatin and chloral hydrate was not performed because of its potential danger to life and for ethical reasons, the results of the clinical course and the radio-allergosorbent test strongly suggested that the anaphylactic symptoms were induced by gelatin rather than chloral hydrate.

There were several common characteristics in these two patients. First, both patients had an atopic background. Second, they had received vaccinations with gelatin-containing products in their first year of life. Third, they had frequently taken gelatin-containing foods and additives since an early infantile age. Finally, they did not show any hypersensitivity to gelatin-containing foods or vaccines, and the first anaphylactic reaction appeared after the administration of the gelatin-containing suppository. These findings suggest that gelatin-containing vaccines and foods during early childhood play a role in allergic sensitization against gelatin, but were insufficient for inducing allergic symptoms.

In Japan, the guideline for the vaccination schedule was amended in 1994. Since then, the DPT vaccine has been generally inoculated in infants under 1 year. Although the amount of gelatin in a DPT vaccine is small (Table 1), the inoculation starts at an early infantile period and is carried out over four times. Moreover, the vaccine contains aluminum hydroxide, a strong adjuvant.³ As repeated injections of small dosages of allergen with aluminum hydroxide result in IgE production in experimental animals, the vaccination schedule may trigger an allergic sensitization to gelatin.⁴ Gelatin-free vaccines are thus important for reducing gelatin allergy, and gelatin has been removed from DTP and rubella vaccines since 1999, although the measles vaccines still contain a considerable amount of gelatin.

Table 1 Dose of gelatin in vaccine and chloral hydrate suppository

	Dose	Source of gelatin
Vaccine	(w/v%)	Case 1, Case 2
Measles	0.2–0.5	Bovine bone
Rubella	0.2–0.5	Bovine bone
Varicella	0.2	Bovine bone
Polio (Sabin)	≤ 0.0075	Bovine bone
DPT	≤ 0.0067	Bovine bone
Chloral hydrate suppository (mg)		
250 mg	196	Bovine bone
500 mg	231	Bovine bone

Data of vaccine supplied in 1997–98. DPT, diphtheria-pertussis-tetanus; w/v, weight/volume.

Gelatin-containing baby foods may also play an important role in allergic sensitization to gelatin in young children. It may be worthy, especially for atopic infants, to pay attention to such foods.

The pharmacological effects of the suppository appear within 10–30 min, and the blood concentration of chloral hydrate reaches a peak approximately 30 min after administration. Therefore, it is likely that gelatin melts in the rectum and is absorbed within 10 min after administration. As shown in Table 1, a chloral hydrate suppository contains gelatin 80 times more than vaccines, so that the amount of gelatin absorbed from a chloral hydrate suppository might be enough to trigger anaphylactic reaction, whereas that of vaccines would have been under the threshold of the reaction. Although the patients did not show any allergic reactions against gelatin-containing foods, the quality and the quantity of the gelatin antigens from foods may be reduced and modified by a digestive process in the gastrointestinal tract.⁵ In contrast, the antigenicity of the gelatin absorbed from the chloral hydrate suppository may be intact because it is absorbed directly through rectal mucosa.

It is suggested that the accumulation of risk factors such as genetic background, gelatin-containing vaccines and foods, induced the allergic sensitization against gelatin and that the gelatin-containing suppositories triggered the hypersensitive reaction. As chloral hydrate suppositories are used frequently to sedate children during various examinations, the gelatin-free form is desirable. It is possible that patients with an allergy against various foods may also have a gelatin allergy. It has been recommended to examine the gelatin-specific IgE level of these patients properly to prevent gelatin-induced anaphylactic shock. It has also been shown that a history of vaccinations with gelatin-containing vaccines without side reaction could not rule out the possibility of anaphylaxis by a chloral hydrate suppository.

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