Case Report

Formaldehyde-specific IgE-mediated Urticaria Due to Formaldehyde in a Room Environment

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Abstract

Formaldehyde is a primary skin-sensitizing agent inducing allergic contact dermatitis, and may induce immunological contact urticaria. However, there have been few reports on allergy associated with IgE. We describe here a case of formaldehyde-specific IgE mediated urticaria due to formaldehyde in a room environment.

A 35-year-old woman exhibited urticaria on her legs and face. Laboratory examination revealed elevated formaldehyde-specific IgE and non-specific IgE. Patch testing with formaldehyde was positive. The concentrations of formaldehyde in the rooms of her apartment were high.

Although inhalation challenge test was negative, we suspected that her urticaria resulted from IgE-mediated allergic reaction to formaldehyde in the rooms of her apartment.

Her symptoms gradually disappeared with thorough ventilation of the rooms of her apartment.

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—Key words—
formaldehyde, IgE, urticaria

Introduction

Recently, health problems such as allergy, headache, and sore throat due to chemical substances derived from building materials have been reported[1)~4)]. These problems are usually termed 'sick building syndrome' and formaldehyde is a representative cause of this syndrome[3)4)].

In patients with allergic reaction thought to be due to formaldehyde, elevated formaldehyde-specific IgE levels are seldom observed. Moreover, there have been few reports on allergic reaction associated with formaldehyde-specific IgE even in individuals handling formaldehyde occupationally. We report here a case of formaldehyde-specific IgE-mediated urticaria due to formaldehyde in a room environment.

Case

Ten months after a 35-year-old woman moved to a new apartment, she sometimes noted urticaria on her legs and face when she was at home. The frequency of urticaria gradually increased, and she also noted swollen lips and slight dyspnea. She experienced no symptoms outside of her apartment.

She underwent a medical examination by dermatologists and was diagnosed with stress-related urticaria. However, on medical examination by another physician, laboratory examination revealed elevated formaldehyde-specific IgE and non-specific IgE levels. She was a housewife and had not handled formaldehyde occupationally. Since her symptoms occurred after her move, she visited our hospital because she believed they resulted from her indoor environment.

Although no members of her family, including her husband and child, recognized a smell in the rooms of

Table 1 Results of indoor air quality investigation

	Formaldehyde (μg/m³)
Japanese-style room	150
Western-style room 1	90
Western-style room 2	120
Living room	100
Guideline value	< 100

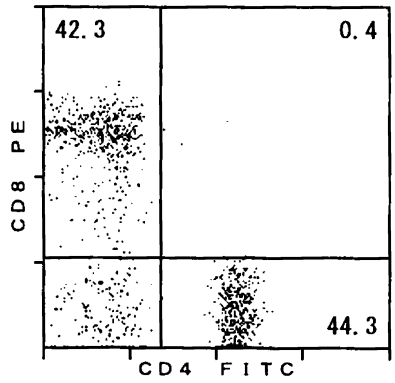

Fig. Two-color CD4/CD8 analysis (Dot plot). The vertical axis shows the fluorescent strength of CD4 and the horizontal axis shows the fluorescent strength of CD8.

Table 2 Two-color CD4/CD8 analysis

		Reference values
CD4 (−) CD8 (+)	42.3%	22.0−54.0
CD4 (−) CD8 (−)	13.0%	14.0−38.0
CD4 (+) CD8 (−)	44.3%	23.0−52.0
CD4 (+) CD8 (+)	0.4%	< 7.0
CD4/CD8 ratio	1.1%	0.40−2.30

Table 3 Results of measurement of hypothalamic-pituitary-adrenal axis hormones, interleukins, and substance P.

		Reference values
CRF	23.7 pg/ml	
ACTH	24.4 pg/ml	(7.4−55.7)
Cortisol	11.5 μg/dl	(4.0−18.3)
IL-1β	14 pg/ml	(< 10)
IL-2	< 0.8 U/ml	
IL-4	6.1 pg/ml	(< 6.0)
IL-5	< 5.0 pg/ml	(< 10)
IL-6	0.5 pg/ml	(< 4.0)
Substance P	25 pg/ml	

the apartment and none exhibited symptoms after the move, the formaldehyde concentrations in the rooms of her apartment were found to be higher than the guideline values for indoor air concentration of formaldehyde in Japan (Table 1).

From examination results at our hospital, she had no abnormal findings, including those of dermatological examination. Chest X-ray and electrocardiogram were both normal. WBC count was 3,800/μl (eosinophils 4.2%) and CRP was negative. Biochemical findings and results of urinalysis were all normal. However, nonspecific IgE was elevated to 317IU/ml (normal range: <173IU/ml) and formaldehyde-specific IgE (FEIA) was also positive (1.08UA/ml). Among other specific IgEs, only IgE for cedar pollen was positive on the MAST-26 assay.

Lymphocyte surface markers (two-color CD4/CD8), some chemical mediators such as interleukin (IL)-1β, 2, 4, 5, and 6, and hypothalamic-pituitary-adrenal axis hormones were measured. The results of two-color CD4/CD8 analysis were normal (Fig. and Table 2). The results of measurement of ILs and substance P are shown in Table 3. Although IL-1 and IL-4 levels were slightly elevated, levels of other ILs were within reference ranges. Substance P level was almost the same as normal levels previously reported[5)6)]. CRF, ACTH, and cortisol levels were 23.7pg/ml, 24.4pg/ml, and 11.5μg/dl, and not abnormal.

After receiving informed consent, we performed a formaldehyde inhalation test at 100μg/m³ for 15 minutes in a room with the area of 5m³. During the inhalation test, she noted a slight smell and headache, but exhibited no cutaneous symptoms during or after inhalation. Moreover, on pulmonary function testing, there were no significant differences in forced expiratory volume or the ratio of forced expiratory volume in one second before to after the challenge test (Table 4).

We also performed a patch test using 0.01% formaldehyde solution, with positive results after both 48 and 72 hours.

She had a past history of chronic eczema from childhood and took an H_1 blocker. However, she had experienced no symptoms of eczema for several years.

Although she exhibited no symptoms on examination, we diagnosed formaldehyde-specific IgE-mediated urticaria due to formaldehyde in a room environment on the basis of the following findings: 1) the formaldehyde levels in the rooms of her apartment were relatively high, and her symptoms appeared after moving to

Table 4 Pulmonary function tests

			Actual value	Predicted value	Percentage of predicted value
Pre-inhalation	VC	L	2.43	2.69	90.1%
	FVC	L	2.34	2.69	86.6%
	FEV1.0	L	1.99	2.45	80.9%
	FEV1.0%	%	85.01	82.71	102.7%
Post-inhalation	VC	L	2.49	2.69	92.3%
	FVC	L	2.25	2.69	83.4%
	FEV1.0	L	1.97	2.45	80.5%
	FEV1.0%	%	87.87	82.71	106.2%

the new apartment, 2) sensitization to formaldehyde was recognized, 3) there were no other substances to which sensitization was noted except cedar pollen, and 4) she was a housewife and has not handled formaldehyde occupationally.

Her symptoms gradually disappeared with thorough ventilation of the rooms of her apartment.

Discussion

Formaldehyde solution is a primary skin-sensitizing agent inducing allergic contact dermatitis (Type IV), and may induce immunological contact urticaria (Type I)[7]. Allergic reactions and the induction of asthma-like conditions have been reported following occupational exposure to it[8][9]. However, there are reports that asthma-like symptoms caused by formaldehyde are not due to allergic reaction[7][10]. Kramps et al.[11] mentioned that formaldehyde-specific IgE antibodies could be detected in only one of 86 serum samples from four groups of individuals exposed to formaldehyde by different routes and concentrations, and concluded that exposure to formaldehyde, even in relatively high concentrations, rarely evokes the production of specific IgE antibodies. Moreover, no RAST-positive findings for formaldehyde were observed in a group of subjects, 46% of whom had problems related to formaldehyde[12]. There is also a report that it is possible that clinical IgE-mediated allergy to gaseous formaldehyde does not exist, or that if it does exist it is extremely rare[13]. These reports suggest that although formaldehyde can cause IgE-mediated allergy, this condition is very rare.

In the present case, the patient's chief complaint was urticaria, and allergic urticaria typically involves IgE. The methods of determination of the causative agents of allergy include RAST, prick testing, basophil histamine-release testing, among others. There are reports that type I allergy tests sometimes yield false-positive or false-negative findings[14][15]. Therefore, for the present patient we performed a formaldehyde provocation challenge test to determine the causative agent, although no cutaneous symptoms appeared during or after inhalation. Although we were unable to obtain conclusive evidence that her urticaria resulted from formaldehyde, we believe that humoral immunity contributed to her urticaria.

The duration of challenge testing we performed was 15 minutes at around 100μg/m^3, and testing was performed twice over a three-month period. Since this patient was a housewife and had spent most of her time at home, further investigation is needed to determine whether the protocol for challenge testing we used had been appropriate.

Concerning patch testing, Trattner et al.[16] noted the lack of statistically significant difference in response between 1 and 2% levels with respect to allergic reactions, but reported that 2% yielded significantly more irritant reactions, and thus recommended a 1% patch test concentration for formaldehyde. There is a report that for the general population, dermal exposure to concentrations of formaldehyde in solution in the range of 1–2% is likely to cause skin irritation[7]. In the present case, we used 0.01% formaldehyde solution, and results were positive after both 48 and 72 hours. We therefore believe that cell-mediated immunity also played a role in this patient's urticaria. Based on her lifestyle, we strongly suspect that formaldehyde in her room environment was the cause of sensitization.

There is a report that the hypothalamic-pituitary-adrenal gland axis is affected by low concentrations of formaldehyde[17]. However, in the present case no abnormalities in hormone levels related to it were observed.

In addition, measurement of several factors related to allergic reaction, such as interleukins, lymphocyte surface markers, and substance P, revealed almost no abnormalities.

In the present case, testing for formaldehyde-specific IgE and patch testing with formaldehyde were positive. As noted above, this urticaria appears to have been the result of allergic reaction, and is thus very rare.

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室内環境中ホルムアルデヒドによるホルムアルデヒド特異的IgE関連蕁麻疹

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—キーワード—
ホルムアルデヒド，IgE，蕁麻疹

ホルムアルデヒドは，皮膚感作物質であり接触性蕁麻疹を引き起こしうる．しかしながら，IgEに関連したアレルギーに関する報告はわずかしかない．われわれは今回，室内環境中のホルムアルデヒドが原因と考えられるホルムアルデヒド特異的IgE関連蕁麻疹と考えられる症例を経験したので報告する．症例は35歳の女性で，新築マンションに転居後脚と顔に蕁麻疹を生じた．他院での検査にて，ホルムアルデヒド特異的IgEの上昇と非特異的IgEの上昇を認め，ホルムアルデヒドのパッチテストも陽性であった．自宅マンションの室内のホルムアルデヒド濃度は，厚生労働省の室内濃度指針値を超えていた．ホルムアルデヒド吸入負荷テストを行うも蕁麻疹は誘発されず陰性であったが，われわれは特異的IgEの上昇，パッチテスト陽性，室内のホルムアルデヒド濃度の結果からこの蕁麻疹がマンション内のホルムアルデヒドに対するIgEに関連したアレルギー反応であると考えた．その後部屋の換気を行い経過観察としたが，症状は生じていない．

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