

Latex allergy in infants younger than 1 year

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Summary

Background The prevalence of latex allergy in children is increasing worldwide. Previous multiple operations or atopic predisposition are known risk factors. In contrast, only sporadic cases of latex allergy have been reported in infants younger than 1 year, and the causative latex-containing products or symptoms in young infants have not been studied in detail.

Objective The purpose of this study is to analyse the symptoms and risk factors of latex allergy in young infants.

Methods Cases of latex allergy in infants younger than 1 year were studied in detail. Clinical course, causative latex-containing products were spotted and detailed analysis for latex allergy in patients and patients' parents was performed.

Conclusion We report nine cases of latex allergy in infants younger than 1 year. None of them have any abnormality or previous operations. Six patients had atopic eczema/dermatitis syndrome, one patient had bronchial asthma, whereas two patients had no overt allergic diseases. Symptoms of latex allergy were wheezing, swelling of face or lips, facial rash, or anaphylaxis, and causative latex-containing products were teat, pacifier, nose cleaner, teether, balloon, or enema tube. All of the nine patients had positive skin prick test to latex and extract from causative latex-containing products, whereas eight patients had positive serum latex-specific IgE. Study for family history revealed that latex allergy was noted in either father or mother in six patients, in both father and mother in one patient, whereas no latex allergy was noted in parents in two patients. It should be noted that all of these patients had latex-induced symptoms at home. Latex allergy in young infants may not be unusual. Physicians should be aware of latex allergy, and care should be taken to avoid contact with latex in young infants, especially when there is family history for latex allergy.

Keywords atopic eczema/dermatitis syndrome, latex allergy, latex-specific IgE, nipple, skin prick test, swelling of face or lips, teether, wheezing, young infant

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Introduction

Several cases of latex allergy in children have been reported in the past, especially among those who have undergone multiple surgical procedures or have an atopic predisposition [1, 2]. However, only a few cases of latex allergy have been reported in infants younger than 1 year. It has previously been reported that latex pacifiers caused persistent cough in an 11-month-old infant, and a latex nipple caused episodic stridor and wheezing in a 2-month-old infant [3, 4]. However, these reports did not study allergic responses to extracts from pacifiers or nipples in patients. In addition, allergic responses to latex or latex-related allergens in the patients' family were not reported in detail [3, 4]. Here, we report nine cases of latex allergy in infants younger than 1 year. Detailed study of latex allergy and sensitization to other allergens in patients and parents will be discussed.

Subjects and methods

The characteristics of the nine patients are listed in Table 1. All of the patients were full-term born, and none of them had any abnormality or had had any surgical operations. Blood chemistry, including total protein, albumin, electrolytes, liver function tests, complement (CH50, C3, and C4) levels, and urine analysis were normal in all of them at the time of the presentation to the hospital. Chest radiographs and ultrasound scans for heart and neck showed no abnormality in patients 1, 2, 4, and 8.

Case reports

Patient 1 A 1.5-month-old female infant had been breastfed for first 14 days of life without difficulty. Thereafter, in addition to breastfeeding, she was partly bottle-fed with conventional cow's milk-based formula using a natural rubber latex teat without multiple washing. At the age of 22 days, the mother noticed noisy breathing upon bottle-feeding, but not upon breastfeeding. Since then, the mother noticed noisy breathing every time when the infant was bottle-fed.

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Table 1. Characteristics of patients with latex allergy

Patient no.	Age (months)	Sex	Allergic disease	Feeding	Major symptoms of latex allergy	Symptoms caused by
1	1.5	F	AEDS	Breast milk and formula	Wheezing	Teat
2	3.0	M	AEDS	Breast milk and formula	Wheezing	Teat
3	4.5	M	None	Breast milk	Swelling of face	Nose cleaner
4	5.0	F	AEDS	Breast milk	Wheezing	Pacifier
5	6.0	M	None	Formula	Facial rash	Teat
6	8.0	M	AEDS	Breast milk	Swelling of face	Pacifier
7	9.0	F	AEDS	Breast milk	Swelling of lips	Teether
8	10.0	F	BA	Formula	Anaphylaxis	Enema tube
9	10.5	M	AEDS	Formula	Swelling of face	Balloon

M, male; F, female; AEDS, atopic eczema/dermatitis syndrome; BA, bronchial asthma.

The noisy breathing occurred after several minutes of the start of bottle-feeding, and it resolved shortly after bottle-feeding was over. The mother switched the infant to a soy formula with the same natural rubber latex teat, but without any improvement. At the age of 32 days, the infant became pale and had dyspnoea upon bottle-feeding. Immediately, the mother took the infant to the local hospital. However, the symptoms resolved shortly without treatment. Eczema appeared on her face at the age of 40 days. She presented at our hospital at the age of 45 days.

Patient 2 A 3-month-old male infant had been breastfed for first 1 month of life without difficulty. Thereafter, in addition to breastfeeding, he was partially bottle-fed with conventional cow's milk-based formula using a teat composed of silicone and natural rubber latex, without multiple washing. At the age of 2 months, the mother noticed wheezing upon bottle-feeding, but not upon breastfeeding. At the age of 2.5 months, eczema appeared on his face. He presented at our hospital at the age of 3 months.

Patient 3 A 4.5-month-old male infant had been breastfed without difficulty. From the age of 3 months, the mother often used a natural rubber latex nose cleaner. At the age of 4 months, the mother noticed swelling of his face upon using the nose cleaner. The swelling of face subsided shortly without any treatment. Thereafter, the mother often noticed swelling of face upon using the nose cleaner. He presented at our hospital at the age of 4.5 months.

Patient 4 A 5-month-old female infant had been breastfed without difficulty. She used a natural latex pacifier from the age of 3 months. At the age of 4 months, the mother noticed wheezing when the infant used the pacifier. The mother did not notice wheezing when the child was fed. Wheezing resolved when she stopped using the pacifier. Eczema appeared on her face and trunks at the age of 4.5 months. She presented at our hospital at the age of 5 months.

Patient 5 A 6-month-old male infant had been breastfed for the first month of life without difficulty. Thereafter, the mother switched to bottle-feeding with conventional cow's milk-based formula using a natural rubber latex teat. At the age of 5 months, the mother noticed the development of a facial rash on bottle-feeding. The facial rash appeared several minutes after the start of feeding and resolved when feeding

was over. No swelling of face or lips was noted. Subsequently, the mother sometimes noticed facial rash on feeding. The mother also noticed a facial rash when he once ate banana at the age of 5.5 months. He presented at our hospital at the age of 6 months.

Patient 6 An 8-month-old male infant had been breastfed for the first 2 months of life without difficulty. At the age of 3 months, he had been using a natural rubber latex pacifier without washing. At the age of 7 months, the mother noticed swelling of his face when he used the same pacifier. Swelling of face subsided shortly without any treatment when he stopped using the pacifier. Thereafter, the mother often noticed swelling of face when he used the pacifier. At the age of 7.5 months, eczema appeared on his face. He presented at our hospital at the age of 8 months.

Patient 7 A 9-month-old female infant had been breastfed for 6 months without difficulty. At the age of 7 months, eczema appeared on her face and arms. A dermatologist diagnosed the symptoms as atopic eczema/dermatitis syndrome (AEDS) and treated her with a steroid ointment (clobetasone butylate). The infant did not use pacifiers, but she had been using a natural rubber teether since the age of 6 months. At the age of 8 months, the mother noticed swelling of infant's lips when she used the teether. Swelling of lips subsided shortly after removal of the teether. Thereafter, the mother noticed swelling of lips for several times. The infant presented at our hospital at the age of 9 months.

Patient 8 A 10-month-old female infant had been breastfed for the first 2 months of life without difficulty. Thereafter, the mother switched the infant to bottle-feeding with conventional cow's milk-based formula using a natural rubber latex teat. At the age of 8 months, the infant had her first asthmatic attack, which was treated by a paediatrician with the application of tulobuterol hydrochloride tape. Thereafter, the infant had frequent asthmatic attacks. At the age of 10 months, the infant was constipated, and the mother used a enema tube composed of silicone and natural rubber. Immediately after insertion of the tube, the infant developed a facial flush, periorbital oedema, wheezing, dyspnoea, and loss of consciousness. After being admitted to our hospital, treatment with oxygen, intravenous hydrocortisone, and the inhalation of procaterol hydrochloride and disodium cromoglicate restored her condition.

Patient 9 A 10.5-month-old male had been breastfed for 6 months without difficulty. Thereafter, the mother switched the infant to bottle-feeding with conventional cow's milk-based formula using a nipple composed of silicone and natural rubber. At the age of 7 months, eczema appeared on his face, which was diagnosed as AEDS by a dermatologist. At the age of 10.5 months, the infant played with a balloon. Immediately after contact with a balloon, his face was swollen. He presented at our hospital but by then the swelling of his face had subsided.

Investigations for latex allergy in patients and patients' parents

All tests were performed after obtaining informed consent. Latex (C-serum), control solution and histamine (10 mg/mL) (Sigma Chemical Co., St Louis, MO, USA) used for skin prick tests (SPTs) in patients and parents have been reported previously [5, 6]. Extracts from latex-containing products for SPT were prepared according to the method reported previously [7]. Briefly, latex-containing products, which patients used, were collected. They were natural rubber latex teats (patients 1 and 5), nipple composed of silicone and natural rubber (patient 2), natural rubber latex nose cleaner (patient 3), natural rubber latex pacifier (patients 4 and 6), natural rubber latex teether (patient 7), enema tube composed of silicone and natural rubber (patient 8), and balloon (patient 9). They were cut into 0.25–0.5 cm² pieces and were incubated in sterile physiological saline (1:5, w/v) at room temperature for 17 h. The extracts were then filtered through a Millipore filter (0.2 µm; WARO's Natural Science, Rochester, NY, USA) and freshly used for SPT [7].

SPTs were conducted on the volar surface of the forearms, and after 15 min the diameter of the weal was measured. The SPT results were assessed according to recommendations of European Academy of Allergology and Clinical Immunology (EAACI) [8]. The average diameter of each weal was established by measuring the longest diameter and the diameter perpendicular to it. Positive results were rated 4+ in the presence of a weal double the size of the weal induced by histamine, 3+ in the presence of a weal with the same diameter as the weal induced by histamine, 2+ if the average diameter was half of the weal induced by histamine, and 1+ if

the average diameter was less than half of the weal induced by histamine, and 0 if there was no weal. Only weals of 2+ or more were considered positive. All of the subjects were free from oral medication at the time of study. Serum latex-specific IgE was measured by CAP System RAST fluorescence-enzyme immunoassay (Pharmacia-UpJohn Corporation, Uppsala, Sweden). The assay is a solid-phase immunofluorometric assay in which IgE antibody is bound to latex allergosorbent and detected with β-galactosidase-labelled rabbit polyclonal anti-human IgE and 4-methylumbelliferyl-β-D-galactosidase substrate.

Investigations for other allergies in patients and parents

Sensitization to the commercial allergens, egg white, egg yolk, cow's milk, wheat, soy, rice, buckwheat, peanut, sesame, yeast, house dust mite (HDM), cat dander, dog dander, Japanese cedar pollen (JCP), ragweed, timothy, cocksfoot, candida or alternaria (Torii Pharmaceutical Co., Ltd, Tokyo) was performed by SPT as above. Sensitization to potato, tomato, kiwi, melon, banana, pineapple, peach, chestnut or apple was performed by prick-to-prick test. The SPT and prick-to-prick results were considered positive if the diameter of the weal by tested allergen was larger than half of the diameter of the weal induced by histamine [8].

Results and clinical course of the patients

Previous symptoms of latex allergy in patients' parents

Characteristics of patients' parents are shown in Table 2. Allergic diseases were noted in either father or mother in three patients, or in both parents in four patients, while no allergy was noted in parents in two patients. Symptoms of latex allergy were previously noted in either father or mother in six patients, in both father and mother in one patient, while no such symptoms were noted in parents in two patients.

Sensitization to latex in patients and parents

As shown in Table 3, all of the nine patients had positive SPT responses to both latex and extracts from latex products, while eight patients had elevated serum latex-specific IgE. On

Table 2. Characteristics of patients' parents

Patient no.	Father			Mother		
	Allergic disease	Major symptoms of latex allergy	Symptoms caused by	Allergic disease	Major symptoms of latex allergy	Symptoms caused by
1	OAS	Swelling of face	Balloon	AR	None	None
2	AR	Swelling of lips	Balloon	AEDS	None	None
3	None	None	None	None	None	None
4	None	None	None	AEDS	Urticaria on hands	Glove
5	BA	Urticaria on hands	Glove	AEDS	Urticaria on hands	Glove
6	AEDS	General urticaria	Glove	None	None	None
7	None	None	None	None	None	None
8	AR	None	None	OAS	Swelling of face	Balloon
9	None	None	None	AR	Urticaria on hands	Balloon

OAS, oral allergy syndrome; AR, allergic rhinitis; AEDS, atopic eczema/dermatitis syndrome; BA, bronchial asthma.

Table 3. Sensitization to latex in patients and parents

Patient no.	Patient			Father			Mother		
	SPT*		Latex FEIA†	SPT		Latex FEIA	SPT		Latex FEIA
	Latex	Extract		Latex	Extract		Latex	Extract	
1	3+	2+	0.95	4+	2+	23.4	0	0	<0.34
2	3+	2+	<0.34	3+	2+	12.6	0	0	<0.34
3	2+	2+	1.38	0	0	<0.34	0	0	<0.34
4	3+	2+	2.29	0	0	<0.34	3+	2+	6.29
5	2+	2+	1.97	3+	2+	4.37	3+	2+	7.53
6	3+	2+	3.60	3+	2+	58.5	0	0	<0.34
7	2+	2+	2.84	0	0	<0.34	0	0	<0.34
8	3+	2+	6.15	0	0	<0.34	4+	2+	18.42
9	2+	2+	3.26	0	0	<0.34	3+	2+	3.68

FEIA, fluorescence-enzyme immunoassay; SPT, skin prick test.

*SPT to latex or extracts from latex products. Positive results were rated as described in the text. Weal responses greater than 2+ were considered positive, while 0 indicates negative responses.

†Serum latex-specific IgE levels (IU/mL).

Table 4. Sensitization to other allergens in patients and parents

Patient no.	Patient Positive allergen*	Father Positive allergen	Mother Positive allergen
1	None	HDM, kiwi, melon	JCP, timothy, cocksfoot
2	Egg white, egg yolk	HDM, JCP, apple	HDM
3	None	None	None
4	Egg white, egg yolk	None	Peanut, HDM, JCP
5	Banana	HDM, alternaria	HDM, banana, chestnut
6	Egg white, egg yolk, wheat	HDM, kiwi, melon	HDM
7	Cow's milk, buckwheat	None	Peanut
8	HDM, cat dander, apple	HDM, JCP, ragweed	HDM, kiwi, banana, apple
9	Potato, tomato, sesame	None	HDM, JCP, melon

HDM, house dust mite, cat dander, dog dander; JCP, Japanese cedar pollen, ragweed, timothy, cocksfoot, candida or alternaria, while prick-by-prick test was performed by using potato, tomato, kiwi, melon, pineapple, peach, chestnut or apple.

*Skin prick test was performed by using commercial allergens, egg white, egg yolk, cow's milk, wheat, soy, rice, buckwheat, peanut, sesame, yeast.

the other hand, four fathers or four mothers had positive SPT responses to both latex and extracts from latex products, and all of these eight subjects had elevated serum latex-specific IgE.

Sensitization to other allergens in patients and parents

Sensitization to other allergens was investigated. As shown in Table 4, seven patients were sensitized to various allergens, including egg yolk, egg white, banana, wheat, cow's milk, buckwheat, HDM, cat dander, or apple. On the other hand, six fathers or eight mothers were sensitized to various allergens, including HDM, kiwi, melon, JCP, timothy, cocksfoot, apple, alternaria and ragweed. It should be noted that fathers of patients 1, 2, and 6, and mothers of patients 5, 8, and 9 were sensitized to various fruits. However, neither patient 3 nor his patient's parents were sensitized to these allergens.

Clinical course of the patients

Patient 1 The eczema was treated with application of a mixture of pinetar (Yoshida Pharmaceutical Co. Ltd, Tokyo, Japan) and zinc ointment, which is very effective for AEDS [9]. The mother stopped bottle-feeding, and breastfed the

infant without using latex-containing products, including pacifiers or rubber toys. Since the father was allergic to kiwi and melon, the mother avoided eating those fruits. Thereafter, eczema was markedly improved, and there had been no further wheezing associated with feeding. By 6 months of age, the infant was free from eczema or wheezing.

Patient 2 Because the mother had difficulty in lactation, she stopped breastfeeding and bottle-fed the infant with cow's milk-based formula by using 100% latex-free silicone teats. It was confirmed in preliminary study that the infant had negative SPT response to extract from this 100% latex-free silicone nipple. Eczema was treated with application of mixtures of pinetar and zinc ointment. By 4 months of age, the eczema was completely cured, and there was no wheezing associated with feeding. The infant is now 7 months old and is free from eczema or wheezing with continuous avoidance of latex products.

Patient 3 The mother breastfed the infant, while she avoided using a nose cleaner or other latex-containing product. By 7 months of age, the infant had been free from facial swelling or any other allergic symptoms.

Patient 4 The eczema was treated with the application of a mixture of pinetar and zinc ointment. The mother breastfed the infant and stopped eating egg-containing foods or peanut, and also avoided using a latex pacifier or other latex-containing products. Thereafter, the infant has been free from wheezing. Eczema was completely resolved at the age of 7 months. By 11 months of age, there had been no further wheezing with continued avoidance of latex-containing products.

Patient 5 The mother bottle-fed the infant with cow's milk-based formula using 100% latex-free silicone teats. The mother also avoided feeding the infant with banana. Thereafter, the infant has been free from facial rash. By 11 months of age, there had been no further symptoms associated with feeding.

Patient 6 Eczema was treated with application of mixtures of pinetar and zinc ointment. The mother breastfed the infant avoiding eating egg-containing foods or wheat, and also avoided latex pacifiers and other latex-containing products. By 9 months of age, eczema was improving markedly and there had been no swelling of face. He is now 15 months old, and is free from eczema and facial swelling with continued avoidance of latex-containing products and egg, while he can eat wheat without difficulty.

Patient 7 Eczema was treated with application of a mixture of pinetar and zinc ointment. The mother breastfed the infant avoiding cow's milk-containing foods, buckwheat or peanut, and also avoided using a teether or latex-containing products. By 11 months of age, the infant was free from eczema and swelling of lips. He is now 1.5 years old and has been free from allergic symptoms with continued avoidance of latex-containing products and buckwheat, but he tolerated cow's milk.

Patient 8 Bronchial asthma was treated with inhalation of disodium cromoglycate with procaterol hydrochloride administered using a nebulizer three times a day, and oral theophylline and pranlukast hydrate. The mother bottle-fed him with cow's milk-based formula, and avoided latex-containing products. The infant took normal food except apple, kiwi, or banana, without difficulty. By 12 months of age, the infant is free from asthmatic attacks, and oral theophylline and pranlukast hydrate have been discontinued. By 13 months of age, inhalation of disodium cromoglycate with procaterol hydrochloride was discontinued. By the age of 15 months, there had been no asthmatic attack or allergic symptoms by latex with continued avoidance of latex-containing products or latex-related fruits.

Patient 9 Eczema was treated with application of a mixture of pinetar and zinc ointment. The mother fed him regular meals avoiding sesame, potato, tomato, or melon, while she avoided latex-containing products. Since then, no swelling of face was noticed, and eczema was completely improved at the age of 12 months. By 16 months of age, he had been free from any allergic symptoms with continued avoidance of latex-related products.

Discussion

We report nine cases of latex allergy in infants less than 1 year old. All of the nine patients had positive responses to latex and extracts from latex-containing products by SPT, which confirmed the diagnosis. The levels of latex antigen in the extracts could not be measured because of degradation of latex protein. However, we obtained the same natural rubber latex teat, which Patient 1 used. The extract was made by incubating a new rubber latex teat in salt water for 30 min, 1 h, or 17 h. Then a SPT was conducted by using this extract in five adult volunteers with latex allergy. The diameter of the weals (mean $\pm$ SD, $n = 5$) using extracts incubated for 30 min, 1 h, and 17 h were 8 ± 2 mm, 9 ± 3 mm, and 13 ± 4 mm, respectively. These results indicate that longer incubation yields more latex antigen.

Although Patient 2 did not have serum latex-specific IgE at the time of study, this is not surprising. It was reported that even patients with severe clinical symptoms do not always have serum latex-specific IgE [10]. It should be noted that symptoms of latex allergy were wheezing, swelling of face or lips, facial rash or even anaphylaxis and all these symptoms were observed at home. None of the parents were aware of the latex allergy, although some had previously had symptoms caused by latex allergy.

It was previously reported that high-risk populations among children were individuals with spina bifida, bladder exstrophy, oesophageal atresia and previous operations [11–16]. In addition, atopic patients also belonged to a latex-allergy risk group, and a case of anaphylaxis was reported [17–19]. In our report, seven of nine patients were atopic, while Patients 3 and 5 had no overt allergic diseases. However, investigation of the parents revealed that four fathers out of nine and four mothers of nine had previous allergic symptoms induced by latex. Although Patient 5 had not yet overt allergic disease, both parents were allergic to latex. These results indicate that the family history is important for diagnosis of latex allergy. However, neither Patient 3 nor the patient's parents had overt allergic disease. Collectively, these results indicate that the prevalence of latex allergy in infants may be increasing even in non-risk groups.

Cases of latex allergy in young Japanese infants have not been reported before. We report nine cases of young infants with latex allergy in this study. Moreover, seven of these cases had one parent allergic to latex or in one case two parents who actually had latex allergy. This may be because of the fact that number of Japanese parents, who use latex products, may be increasing recently. Alternatively, since we are treating large number of allergic patients at our hospital, and since latex allergy is not known to Japanese general physicians, such allergic patients may be collected at our hospital. Patients with latex allergy come from various areas, including big cities and countryside. Hence epidemiological study is not possible.

Physicians should be aware of latex allergy, and care should be taken to avoid contact with latex in young infants, especially when there is a family history of latex allergy. Moreover, education of the latex allergy to general populations may be necessary.

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