CASE REPORT

Manifestation of intraoperative anaphylactic shock along with latex allergy : a pediatric case report

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Abstract : Natural rubber latex (NRL) allergy is one of the most important causes of severe anaphylaxis during medical intervention. We report a pediatric case of latex allergy with multiple surgical histories. A 12-year-old girl developed anaphylactic shock during the pyeloplasty for ureteropelvic junction restenosis. Latex gloves or medications used during the surgery were suspected to be the cause of anaphylactic shock. We diagnosed her latex allergy on the basis of the results that serum latex-specific IgE, skin prick tests of extract from NRL gloves and recombinant Hev b 6.02 solution were positive. Basophil activation test of NRL gloves was also positive, supporting the diagnosis of immediate allergic reactions caused by NRL. It was speculated that a history of multiple surgeries in infancy became a trigger of sensitization to latex in this patient. Reoperation after the diagnosis of NRL allergy was carried out in a latex-free environment and completed without any allergic symptoms. It would be necessary to perform the pre-screening of latex allergy to prevent the onset of latex allergy especially in the patients with multiple surgical histories. J. Med. Invest. 65 : 292-295, August, 2018

Keywords **:** *latex allergy, anaphylaxis, latex-specific IgE, skin prick test, basophil activation test*

INTRODUCTION

Patients with IgE-mediated natural rubber latex (NRL) allergy are sensitized by proteins contained in the natural rubber and cause immediate allergic reactions after the exposure to natural rubber products. Health care workers, patients with spina bifida, multi-operated patients and atopic individuals are known as high-risk populations of NRL allergy (1-4).

The diagnosis of NRL allergy has been performed based on the clinical history of allergic symptoms on NRL exposure, a positive skin prick test (SPT) with a latex extract and a positive latex-specific IgE. Recently, the utility of component-resolved diagnosis (CRD) (5) and basophil activation test (BAT) (6, 7) in the diagnosis of NRL have also been reported.

Here we report a pediatric case of NRL allergy with the manifestation of intraoperative anaphylactic shock.

CASE PRESENTATION

A 12-year-old girl with right ureteropelvic junction restenosis underwent renal pyeloplasty and WJ stenting in general anesthesia. Increased airway pressure, desaturation (SpO2 80%), erythema and urticaria in her face and neck, hypotension (45/13 mmHg) appeared after 88 minutes of starting general anesthesia (after 47 minutes of starting surgery). She was given a diagnosis of anaphylactic shock and intravenous adrenaline, hydrocortisone and chlorpheniramine were administrated. The allergic symptoms improved and the surgery was completed as scheduled. Multiple urticaria recurred 3.5 hours after the administration of sulbactam/ampicillin (SBT/ABPC) after surgery, however, they improved after the administration of olopatadine and famotidine. The course of symptoms and medication in her perioperative period is shown in Fig. 1.

She was introduced to our department at 7 days after the operation for the further examination of anaphylactic shock. She had five surgical histories in infancy to a congenital bilateral hydronephrosis caused by ureteropelvic junction stenosis and an intussusception caused by ileal heterotopic pancreas. Although she had a history of hospitalization with asthma attack at 5 year of age, she had no history of food allergy. Regarding her family history of allergic diseases, her father had a history of childhood asthma. On physical examination, urticaria had already disap-

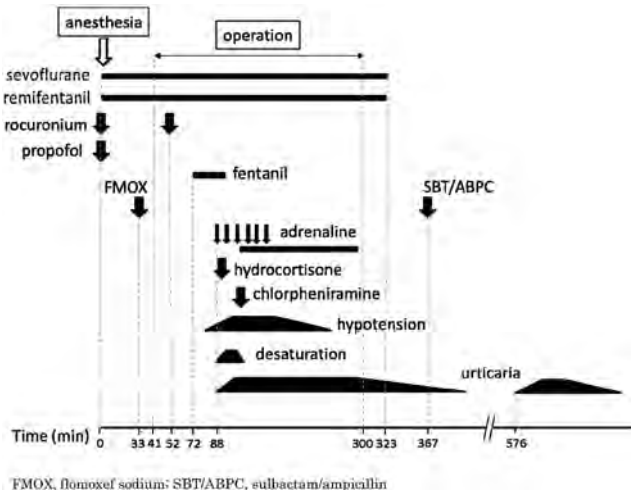

Figure 1. The course of symptoms and medication in the perioperative period
FMOX, flomoxef sodium ; SBT/ABPC, sulbactam/ampicillin

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peared and there were no abnormal findings except the operative scar on the right flank. The drugs administered during surgery and NRL gloves which the surgeons had used were suspected as the cause of her anaphylactic shock.

A blood laboratory test showed the following : white blood cell (WBC) count ; 5100/mm^3 (Eosinophils, 16.0%) ; total IgE, 278.1 IU/L ; latex-specific IgE, > 100 UA/mL ; banana-specific IgE, 0.68 UA/mL ; avocado-specific IgE, 0.86 UA/mL ; kiwi-specific IgE 0.38 UA/mL.

We performed skin tests of suspected drugs and latex at more than one month after anaphylactic shock. The concentration of drug used in skin tests was based on ENDA/EAACI Skin test concentrations for systemically administered drugs (8). Skin tests of remifentanil, rocuronium, propofol, fentanyl, flomoxef sodium (FOMX) and SBT/ABPC were negative except for intradermal test (IDT) of propofol (Table 1). Regarding SPT of latex, latex gloves (Triflex® Sterile Latex Powdered Surgical Gloves, Cardinal Health, Waukegan, USA), which was used during the surgery, extract was negative, however, other latex gloves (Glovex Eco® Latex Exam Gloves, Terumo Beiersdorf, Tokyo, Japan), which is known to contain high residual latex protein, extract and recombinant Hev b 6.02 (BIOMAY, Produktions-und Handels AG Vienna Competence Center, Vienna, Austria) were both positive (Table 2).

BAT using FMOX, SBT/ABPC, latex rubber gloves, and nitrile rubber gloves was conducted by BML, INC., Tokyo, Japan. Nitrile rubber gloves, which are frequently used in medical care, were selected to eliminate non-specific responses by rubber gloves and to evaluate the future risk of allergic reactions induced by nitrile. Single dosage of antibiotics (1 g of FMOX and 1.5 g of SBT/ABPC), 0.2 g of latex nitrile rubber gloves (Triflex®) and nitrile rubber gloves were suspended in 31.25 mL of PBS, respectively, and filtered after sonication to prepare 4-fold dilution series (1/31.25, 1/125, 1/500). These were diluted 10-fold (1/312.5, 1/1250, 1/5000) with whole blood and the same amount of RPMI. Time of incubation was 1 hour and 24 hours for FMOX and SBT/ABPC, 20 minutes for latex and nitrile rubber gloves, respectively. After additional reaction of CD3-PC7, CRTH2 (CD294-FITC), CD203c-PE antibody solution, CD203c expression of all basophils (CD3-CRTH2+) was analyzed by flow cytometer. The cut-off value for positive tests was set at 15% CD203c-positive basophils, in line with the manufacturer's instructions. The level of basophil activation was expressed as %CD203c-positive basophils above the threshold set in the negative control (2.5%). In our case, basophil activation percentage of latex gloves was positive, whereas those of FMOX, SBT/ABPC and nitrile rubber glove were negative (Table 3). Drug-induced lymphocyte stimulation test (DLST) of FMOX and SBT/ABPC were also negative.

From the results above, she was given a diagnosis of NRL allergy and her anaphylaxis during the surgery was considered to be caused by latex gloves. Prick to prick tests of banana, avocado, kiwi and chestnut, which were known as causative food of latex-fruit syndrome, were negative (Table 2).

Removal of WJ stent after 5 months from anaphylaxis was performed using latex-free products under general anesthesia and completed without any allergic symptoms.

DISCUSSION

The perioperative incidence of anaphylaxis ranges from 1 : 5000 to 1 : 25000 (9, 10). Muscle relaxant, latex and antibiotics are known to be the major causative drugs of anaphylaxis under general anesthesia (11, 12). We examined the cause of anaphylaxis using skin tests with suspected drugs and latex gloves, latex-specific IgE and BAT. Regarding the skin tests of perioperative drugs, only IDT of propofol was positive. IDT of propofol in the present case was conducted at 1 mg/mL (1/10 of therapeutic concentration), which was maximum nonirritating test concentration in ENDA/EAACI Skin test concentrations for systemically administered drugs. However, there are difficulties in the interpretation of this result because intrinsic histamine releasing activity is more marked on IDT than SPT, increasing the potential for false-positive results and reducing the specificity of the test (13). In this patient, there was no history of propofol administration in the previous general anesthesia and the result of IDT might be due to a false positive reaction by propofol directly stimulating mast cells to release chemical mediators. Propofol contains soy and egg components ; thus, we also cannot deny the possibility of IDT result being affected if this patient exhibited sensitization to soy or egg. However, we are convinced that this patient is not allergic to soy or egg because she has ingested sufficient amounts of these products in her daily life without any allergic symptoms. We did not perform SPT and measure allergen-specific IgE level of soy and egg because the significance of confirming sensitization to soy and egg for diagnosing allergies is considered to be poor in this patient. However, to the best of our knowledge, the reports of no connection between hypersensitivity to propofol and allergy/sensitization to soy or egg (14, 15) also support that soy and egg components in

Table 1. Summary of skin prick test and intradermal test in suspected drugs

	SPT		IDT	
Drugs	Concentration (mg/mL)	Wheal diameter (long diameter × short diameter, mm)	Concentration (mg/mL)	Wheal diameter/ Erythema diameter (long diameter × short diameter, mm)
Remifentanil	0.05	3 × 3	0.005	6 × 5 / 6 × 5
Fentanil	0.05	3 × 2	0.005	0 × 0 / 0 × 0
Rocuronium	10	4 × 3	0.05	8 × 8 / 8 × 8
Propofol	10	3 × 3	0.1	10 × 9 / 24 × 22
FMOX	2	3 × 2	2	0 × 0 / 2 × 2
SBT/ABPC	2	1 × 1	2	0 × 0 / 5 × 4
Saline (negative control)		3 × 2		0 × 0 / 3 × 3

Mean wheal diameter ≧ 3 mm compared with the negative control in the SPT, mean wheal diameter ≥ 9 mm or mean erythema diameter ≥ 20 mm in the IDT, were defined as positive, respectively.
SPT, skin prick test ; IDT, intradermal test ; FMOX, flomoxef sodium ; SBT/ABPC, sulbactam/ampicillin

Table 2. Skin prick tests of latex gloves, recombinant Hev b 6.02 solution, and fruits related to latex-fruit syndrome

Allergen	Wheal diameter (long diameter × short diameter, mm)
Latex glove (Triflex®)	6 × 5
Latex glove (Glovex Eco®)	18 × 8
recombinant Hev b 6.02 (0.1 mg/dL)	7 × 7
Banana (prick to prick)	4 × 4
Avocado (prick to prick)	3 × 3
Kiwi (prick to prick)	4 × 3
Chestnut (prick to prick)	2 × 2
Saline (negative control)	3 × 3

Mean wheal diameter ≧ 3 mm compared with the negative control was defined as positive.

Table 3. Summary of the basophil activation test

Allergen	Incubation time	Concentration	Activation percentage (%)
FMOX, 1 g	1 h	1/312.5	0
		1/1250	0
		1/5000	0
	24 h	1/312.5	1.4
		1/1250	0
		1/5000	0
SBT/ABPC, 1.5 g	1 h	1/312.5	0
		1/1250	0
		1/5000	0
	24 h	1/312.5	0
		1/1250	0
		1/5000	0
NRL glove (Triflex®), 0.2 g	20 min	1/312.5	32.4
		1/1250	37.6
		1/5000	38.9
Nitrile rubber glove, 0.2 g	20 min	1/312.5	5.1
		1/1250	4.4
		1/5000	3.5

The cutoff value for positive tests was set at 15% CD203c-positive basophils as per the manufacturer's instructions. Activation percentages of positive control (anti-IgE antibody) and negative control (PBS) were 2.5% and 12.8%, respectively. FMOX, flomoxef sodium ; SBT/ABPC, sulbactam/ampicillin ; NRL, natural rubber latex

propofol did not cause anaphylaxis in our patient. Moreover, approximately 90% of anaphylactic reactions during anesthesia occur within minutes of induction (16). The onset of anaphylaxis after 88 minutes from administration of propofol also suggests that it is not a cause of anaphylaxis in this patient. However, the possibility of being an anaphylactoid reaction caused by propofol could not be completely excluded, therefore, the induction of anesthesia in her reoperation after anaphylaxis was performed without the use of propofol.

Michalska-Krzanowska G reported that the typical allergic reaction to latex occurred 30-60 min after the onset of surgical procedure and was rarely observed during the induction of anesthesia (17). This is consistent with our case, where allergic symptoms developed 47 min after initiating the surgery.

In the diagnosis of latex allergy, the measurement of serum latex-specific IgE using a crude extract latex allergen and SPT using latex glove extract are commonly performed. However, the sensitivity and specificity of serum latex specific IgE are reported to be 67%-83% and 87%-94%, respectively, in the diagnosis of latex allergy (18). Actually, some populations who have positive latex crude-specific IgE do not appear any allergic symptoms at the use of latex products.

We identified the cause of her intraoperative anaphylaxis as latex on the basis of positive results of latex-specific IgE, SPT of latex glove extract and recombinant Hev b 6.02, BAT of latex gloves. While the result in SPT of latex glove extract with high amount of residual protein was positive, that of latex glove extract used during surgery was negative in this case. It was presumably because the latex gloves used during surgery contained less amount of residual latex allergen. Powders on the surface of natural rubber gloves adsorb water-soluble proteins contained in latex. Both the elution of the latex powder into the body fluids including blood and the absorption through mucosal surfaces in direct contact of NRL gloves to the internal organ could lead to anaphylaxis in the laparotomy operation, even if the amount of residual latex protein was small.

Fifteen kinds of latex allergens components, Hev b 1-15, have been identified and the diagnosis using these for the improvement of diagnostic accuracy has been reported. True latex allergy patients have high sensitization rate to Hev b 5 (acidic latex protein), Hev b 6.01 (prohevein) and Hev b 6.02 (hevein), which are well-known major allergen components from Hevea brasiliensis (natural rubber tree). Health care workers who developed latex allergy due to percutaneous sensitization via NRL gloves show the high sensitization rates to Hev b 5 and Hev b 6.02 (19, 20). Hydrophobic proteins bound to rubber particles, such as Hev b 1 (rubber elongation factor) and Hev b 3 (small rubber particle protein), have been reported to be very important allergens among the children with spina bifida (21). We demonstrated that our patient was sensitized to Hev b 6.02, which was speculated to be due to latex gloves used during multiple surgeries in infancy.

Hev b 6.02 are also known as important causative components of latex-fruit syndrome (22). Because of the high similarity of the amino acid sequence between these and class 1 chitinase contained in banana, avocado, kiwi, chestnut and so on, IgEs to these may cause cross-reactivity (22). Neither allergic symptoms nor positive SPT to these fruits were shown in our patient, we need to pay attention to the development of her latex-fruit syndrome in the future.

In the diagnosis of latex allergy, the utility of BAT has also been reported (6, 7). BAT is an inspection method that detect the activation of basophils, which are the major effector cells in peripheral blood as well as mast cells in the tissue in immediate hypersensitivity reaction, by flow cytometry utilizing that the expression of basophil-specific cell surface markers is enhanced depending on the activation of basophils. In this case, SPT in latex glove extracts used in the surgery was negative, however, the enhancement of CD203c expression on basophils was shown in BAT. The sensitivity and specificity of BAT for NRL are reported to be 96.65% and 100%, respectively (6). Although SPT and provocation test with latex gloves also have high diagnostic accuracy of latex allergy, the risk of inducing anaphylaxis is a disadvantage especially in severe cases. Therefore, the combination of BAT and allergen-specific IgE determination could be useful as first-line in vitro diagnostic tests in patients with NRL allergy (6). Further studies would be needed regarding the diagnostic utility of BAT in latex allergy.

The cause of postoperative erythema and urticaria in this patient was considered to be the biphasic reaction of preceding anaphylaxis induced by latex, not by SBT/ABPC, because of negative results in skin tests, BAT and DLST of SBT/ABPC.

In conclusion, the combination of latex-specific IgE, SPT and BAT were useful for the diagnosis of latex allergy in a 12-year-old girl who caused intraoperative anaphylactic shock in general anesthesia. It would be necessary to perform the pre-screening of latex allergy and the surgery under a latex-free environment to prevent the onset of latex allergy in the patients with multiple surgical histories.

CONFLICT OF INTEREST

None of the authors have any conflict of interest to declare.

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