

Latex allergy in subjects who had undergone multiple surgical procedures for bladder exstrophy: relationship with clinical intervention and atopic diseases

G. RICCI, A. GENTILI*, F. DI LORENZO†, F. RIGHETTI‡, A. PIGNA*, M. MASI and R. DE CASTRO

Departments of Paediatrics, *Anaesthesia-Intensive Care, †Paediatric Surgery and the ‡Central Laboratory, University of Bologna, S. Orsola-Malpighi Hospital, Bologna, Italy

Objective To evaluate the prevalence of latex sensitization in a group of patients with bladder exstrophy, and to determine the role of associated risk factors, e.g. atopy, and the number and duration of surgical and anaesthetic procedures.

Patients and methods The study comprised 17 patients (15 children and two young adults) affected by bladder exstrophy who had undergone multiple surgical procedures. Skin-prick tests and specific immunoglobulin-E (IgE) assays against latex, food allergens cross-reacting with latex and inhalant allergens were carried out.

Results Twelve patients showed latex sensitization and five showed symptoms related to latex exposure, the most common of which was contact urticaria (four of the symptomatic patients). Intraoperative anaphylactic reaction had led to life-threatening events in only one child. Latex-specific IgE determined both by the prick test and assay was positive in all those with symptoms. Specific IgEs against inhalant allergens and

foods were present in four of five symptomatic patients. In the seven sensitized patients with no clinical symptoms, the assay was positive in all, while the skin-prick test was positive only in four; specific IgEs against inhalant allergens were present in three of the seven. In the five patients not allergic and not latex-sensitized, only one showed allergic sensitization against grass pollen and mite allergen. None of the children without latex antibodies had symptoms of latex allergy. Symptomatic patients had undergone significantly more hours of surgery, more cystography and had used intermittent catheterization for longer than those with no symptoms.

Conclusion A third of patients with bladder exstrophy showed latex symptoms and another third had latex sensitization. Multiple surgical procedures and atopy play a major role in the development of latex hypersensitivity

Keywords Latex allergy, latex sensitization, bladder exstrophy

Introduction

Latex allergy is a significant medical problem that is progressively increasing. Three major groups are more likely to have allergic reactions; (i) children with spina bifida or urogenital malformations who have been repeatedly exposed to contact with latex since the first day of life through multiple surgical procedures; (ii) healthcare workers and other workers with occupational exposure to latex; and (iii) subjects with allergy to food that cross-reacts with latex allergens. From published reports, patients with spina bifida are the group at the highest risk of sensitization to latex proteins; the frequency of symptoms related to latex allergy is variable, at 18–50%, with sensitization in up to 72% [1–6].

Although very young children with spina bifida can be sensitized to latex by surgery during the first days of

life, some patients can tolerate several operations with no sensitization. In a study by Ziyhan *et al.* [7] of children with spinal dysraphism, repeated surgery alone did not seem to be responsible for the high incidence of latex sensitivity in these patients.

In addition to repeated exposure to gloves and other latex products, atopy seems to be a determinant for the development of latex sensitization. Recent work by Mazon *et al.* [8] showed that the number of operations and personal history of atopy were the main risk factors for latex-related symptoms. However, in the same report, the authors noted that in a few patients with urological malformations the prevalence of latex sensitization was 18%, slightly lower than that in patients with spina bifida.

Thus the aim of the present study was to evaluate the prevalence of latex sensitization in a group of patients with the same genito-urinary defect, bladder exstrophy; moreover, we assessed the role of associated risk factors,

Accepted for publication 31 August 1999

e.g. atopy, and the number and duration of surgical and anaesthetic procedures.

Patients and methods

The study included 17 patients (15 children, mean age 7.9 years, range 2–12, and two young adults; four females and 13 males) affected by bladder exstrophy, who underwent surgical procedures in our paediatric departments. Informed consent was obtained from the patients or parents before the beginning of the study.

Allergometric assessment

Skin-prick tests (Laboratorio Lofarma, Rome, Italy) were performed in all patients for latex, food allergens (kiwi fruit, apple, pear, chestnut, avocado, cherry, plum, melon, banana, apricot, peach, tomatoes, potatoes, peanut), inhalant allergens (grass pollen, cat, dog, *Dermatophagoides pteronyssinus*, *D. farinae*) and positive (histamine) and negative (saline) controls. Allergens eliciting a mean weal diameter of ≥ 3 mm than the negative control were considered positive. The patients had not taken antihistamines of any type for at least 7 days before the prick tests and no side-effects were apparent during the tests.

Circulating specific IgE antibody was determined using the RAST CAP-System (Pharmacia, Uppsala, Sweden) for latex, food allergens (kiwi fruit, apple, pear, chestnut, avocado, banana, apricot, peach, tomatoes, potatoes and peanut), and inhalant allergens (grass pollen, cat, dog, *D. pteronyssinus* and *D. farinae*). The patient was considered sensitized if the IgE antibody concentrations were >0.4 kU/L (i.e. CAP class 1).

Surgical and anaesthetic procedures

To repair the bladder exstrophy, all patients were treated with a multistage approach, as proposed by Jeffs *et al.* [9]; all underwent the first surgical step with initial bladder closure (within the first 48 h with no osteotomy) followed by epispadias and bladder neck repair later (epispadias repair at 12–18 months and bladder neck reconstruction at 4–8 years). In these patients there had been two unsuccessful attempts at bladder closure, 11 operations for epispadias repair [10], seven cases of bladder augmentation using enterocystoplasty (five gastric-patch) and in three patients the augmentation was in conjunction with the creation of a Mitrofanoff [11] channel.

Continence was achieved by bladder neck reconstruction using the Young–Dees–Leadbetter [12] technique in seven patients; one had undergone a cosmetic procedure [13] to obtain a normal-looking mons veneris. Ten

patients are continent using CISC but three patients require revision of the continence system. The surgical, endoscopic and radiological interventions were often carried out under general anaesthesia.

The factors analysed were: the numbers of operations, the total duration of surgery, number of intensive care hospitalizations, the number of days in intensive care, the number of cystographic assessments, and the number and duration of contacts with Penrose drainage. Student's *t*-test, Fisher's exact test and the chi-squared test were used to compare categorical variables.

Results

Of 17 patients, 12 were sensitized and five insensitive to latex; of those sensitized, five showed symptoms related to latex exposure and another seven showed specific latex sensitization (Table 1). There were more males than females in the study group, but there was no significant difference in sex ratio among the three sensitivity groups. The symptoms occurred after latex exposure, from direct contact or inhalation of airborne allergens (Table 1); intraoperative anaphylactic reactions had led to life-threatening events only in one child. Latex products causing reactions were: balloons (three cases), gloves (two cases), toys, elastic bands and a foot appliance (one case).

To analyse the influence of atopy and of surgical procedures, the patients were divided into three subgroups: group 1, latex symptomatic (five patients); group 2, asymptomatic but latex-sensitized (seven); and group 3, those not allergic or sensitized (five). In group 1, latex-specific IgE determined both by the prick test and RAST was positive in all patients; the clinical severity did not correlate with a higher latex-specific IgE titre. Specific IgE against inhalant allergens and against foods were present in four patients; all four were positive against grass pollen. Three children also had food allergy reactions, against peach in two, cherry in two and chestnut in one; allergic respiratory diseases were present in two patients.

In group 2, latex-specific IgE determined by the RAST were positive in all, while the skin-prick tests were positive only in four. Specific IgE against inhalant allergens was present in three patients and all three were positive against mite allergens, associated in one with grass allergen positivity; food sensitization was present in two patients. None had food allergy reactions but there was allergic respiratory disease in one patient.

In group 3, one patient had allergic sensitization against grass pollen and mite allergen, with symptoms of allergic conjunctivitis; the others had normal reactions. None of the children without latex antibodies had symptoms of latex allergy.

Table 1 Details, allergy test results and occurrence of clinical symptoms in 17 patients who had undergone multiple surgical procedures for bladder exstrophy

Patient no.	Sex/age (years)	Skin-prick test (mean diameter of weal, mm)	Latex RAST (kU/L)	Total IgE (UI/L)	Allergic disease*	Symptoms from latex products*
Group 1						
1	F/10	6	3.65	nd		+: Rh
2	M/10	10	>100	624	As, FA	+: CU, L/F sw, As, Wh, Rh, Ex
3	M/6	5	32.9	nd	Rh, conjunctivitis	+: CU, L/F sw,
4	M/16	4	2.04	106	Rh, FA	+: CU, L/F sw, DU
5	M/10	10	17	nd	Rh, As, FA	+: CU, L/F sw, As, Wh, Rh, An
Group 2						
6	F/25	0	0.54	<8	–	–
7	M/4	0	0.8	50	As	–
8	M/12	5	52.1	127	–	–
9	F/3	4	8.36	20	–	–
10	F/11	0	0.55	20	–	–
11	M/11	4	1.85	nd	As	–
12	M/9	5	9.01	917	–	–
Group 3						
13	M/8	0	0	38	–	–
14	M/2	0	0	144	–	–
15	M/10	0	0	15	–	–
16	M/5	0	0	nd	–	–
17	M/6	0	0	11	Conjunctivitis	v

*FA, food allergy; DU, diffuse urticaria; CU, contact urticaria; L/F sw, lip and facial swelling; An, anaphylactic reaction; Rh, rhinitis/nasal obstruction; As, asthma; Wh, wheezing; Ex, foot eczema (delayed reaction).

All patients had undergone at least three operations to rebuild the bladder and usually several additional operations; the maximum was 12 (mean 6.5, sd 2.8); males had undergone as many operations (mean 6.2, sd 2.5) as females (mean 6.5, sd 3.8). Patients in group 1 had undergone more operations, total hours of operation, intensive care hospitalizations, cystographic assessments, Penrose drainage, and years of CISC (Table 2), but only the total duration of surgery, years of intermittent catheterization and number of cystographic assessments were significantly greater than in the other groups.

Discussion

A high proportion of children with spina bifida have symptoms related to latex allergy (up to half), with latex sensitization in 72% of patients [1–6]. Urogenital malformations are associated with latex sensitization although there are no homogeneous data reported. In patients affected by spina bifida, Mazon *et al.* [8] reported latex sensitization up to 71%; on the contrary, the same authors report a lower prevalence of sensitization (18%) in patients with urological malformations.

Bladder exstrophy requires multiple surgical treatments in the first days of life, as does spina bifida. The age of first exposure to latex allergen seems crucial for

the development of sensitization, as observed by Konz *et al.* [14], who assessed patients who had undergone multiple operations, the first being as adults. To our knowledge, the published data concern patients affected by genito-urinary defects of many types, with no distinction amongst them. In the present study, patients with the same urogenital malformation were selected, to obtain more homogeneous data from those with similar clinical problems and surgical procedures.

About a third of the present patients with bladder exstrophy showed symptoms related to latex allergy (29%) and 71% showed sensitization. The latter group included those with Class 1 RAST positivity and a negative skin-prick test. If sensitized patients with a positive Class 1 RAST are excluded, the percentage of sensitized patients decreased to 53%. However, there were more latex-sensitized patients with no clinical symptoms; the absence of clinical reactions does not guarantee the exclusion of future clinical symptoms.

Symptomatic patients had a higher specific IgE titre than sensitized patients; the child who had had an anaphylactic reaction did not have the highest titre. There was also one patient with a high specific IgE titre in the sensitized asymptomatic group. Thus the latex antibody concentration was not predictive of the appearance of severe allergic reactions during surgical

Table 2 Potential risk factors in subjects with bladder exstrophy

Risk factor	Group		
	1 (n = 5)	2 (n = 7)	3 (n = 5)
Mean (sd) age, years	10.8 (3.4)	10.8 (7.5)	6.8 (2.9)
Number with			
Inhalant allergen positivity (≥ 1)	4	3	1
Food allergen positivity (≥ 1)	4	2	0
Symptoms related to inhalant allergen	3	2	1
Symptoms related to food allergens	3	0	0
Mean (sd)			
Number of operations	7.8 (2.2)	6.8 (3.2)	4.8 (2.1)
Total hours of operations	39.4 (6.6)*	31.1 (14.4)	18.0 (7.3)*
Number of intensive care hospitalizations	1.4 (1.1)	1.0 (1.1)	0.6 (0.5)
Number of days in intensive care	4.8 (5.0)	3.0 (3.7)	7.0 (6.5)
Years of intermittent catheterization	5.6 (2.8)†	4.2 (5.5)	0.6 (1.3)†
Number of cystographic assessments	4.8 (1.3)‡	3.0 (2.8)	2.2 (1.6)‡
Number of Penrose drainage episodes	2.2 (0.4)	2.0 (0.1)	1.8 (0.4)
Days of Penrose drainage	22.8 (30.8)	7.2 (1.7)	5.0 (1.4)

* $P < 0.001$; † $P < 0.007$; ‡ $P < 0.002$.

procedures, as reported by Kremer *et al.* [15], and partly in contrast with the data of Bernardini *et al.* [16], who considered a value of 3.5 kU/L as predictive of the appearance of symptoms related to latex.

The most frequently reported symptom was contact urticaria, lip and facial swelling (four of five symptomatic patients), as observed in other studies [17,18]. The reactions observed were mild except for the patient who had had anaphylactic shock during surgery. The highest prevalence of symptoms occurred in patients with other associated atopic diseases: atopy was present in four of the patients in group 1, in two of those in group 2 and in one of those in group 3. This is in accord with several studies showing a higher prevalence of atopic children among latex sensitized patients with spina bifida, but contrasts with other recent work [10].

There was some clinical cross-reactivity to fruit, as noted by others [16,17,19]; food allergy towards peach, cherry and chestnut occurred only in symptomatic patients; we were unable to determine if food allergy preceded the latex symptoms or vice versa. Probably the atopic status may lower the threshold of sensitization for the appearance of clinical reactions.

There were more surgical interventions in group 1 and a significant difference in the total hours of surgery compared with group 3. Other factors that may have potentiated latex exposure are prolonged postoperative placement of indwelling urinary catheters and repeated cystography. Patients who were asymptomatic and not atopic were also younger; we cannot suggest an explanation for this and further evaluation during the follow-up, associated with other observations, may provide an explanation for this difference. Early and repeated expo-

sure to latex seems sufficient to induce sensitization even in patients who are not atopic, but the clinical symptoms are most apparent when patients are atopic.

The proportion of patients with bladder exstrophy who were sensitized was the same as that in patients with spina bifida and therefore the same the preventive procedures should be adopted, as proposed by Kremer *et al.* [20]. The latter study noted that no patients became sensitized to latex after the establishment of a latex-free operating theatre and perioperative management. Thus, we suggest that contact with latex proteins should be avoided in patients with bladder exstrophy, from the first surgical intervention.

References

- 1 Pearson ML, Cloe JS, Jarvis WR. How common is latex allergy: a survey of children with myelodysplasia. *Dev Med Child Neurol* 1994; **36**: 64–9
- 2 Kelly JK, Kurup V, Zacharisen M, Fink JN. Skin and serologic testing in the diagnosis of latex allergy. *J Allergy Clin Immunol* 1993; **91**: 1140–5
- 3 Ellsworth PI, Merguerian PA, Klein RB, Rozycki AA. Evaluation and risk factors of latex allergy in spina bifida patients: is it preventable? *J Urol* 1993; **150**: 691–3
- 4 Moneret-Vautrin Da Beaudouin E, Widmer S *et al.* Prospective study of risk factors in natural rubber hypersensitivity. *J Allergy Clin Immunol* 1993; **92**: 668–77
- 5 Tossi LL, Slater JE, Shaer C, Mostello LA. Latex allergy in spina bifida patients: prevalence and surgical implications. *J Pediatr Orthop* 1993; **13**: 709–12
- 6 Michael T, Niggeman B, Moers A, Seidel U, Wahn U. Risk factors for latex allergy in patients with spina bifida. *Clin Exp Allergy* 1996; **26**: 934–9

- 7 Ziylian HO, Ander AH, Alp T *et al.* Latex allergy in patients with spinal dysraphism: the role of multiple surgery. *Br J Urol* 1997; **78**: 777–9
- 8 Mazon A, Nieto A, Estornell F, Nieto A, Reig C, Garcia-Ibarra F. Factors that influence the presence of symptoms caused by latex allergy in children with spina bifida. *J Allergy Clin Immunol* 1997; **99**: 600–4
- 9 Jeffs RD, Charrois R, Many M, Jurianz AR. Primary closure of exstrophied bladder. In Scott R Jr, ed, *Current Controversies in Urologic Management*, Chapt 14 Essay 1 Philadelphia: WB Saunders Co., 1972: 235–43
- 10 Ransley PG, Duffy PG, Wollin M. Bladder exstrophy closure and epispadias repair. In *Operative Surgery — Paediatric Surgery*, 4th edn, Edinburgh: Butterworths, 1986: 620
- 11 Mitrofanoff P. Cystostomie continente trans-appendiculaire dans le traitement des vessies neurologiques. *Chir Pediatr* 1980; **21**: 297–305
- 12 Ahmed S, Fouda-Neel K, Borghol M. Continence after bladder-neck reconstruction in patients with bladder exstrophy and pubic diastasis. *Br J Urol* 1996; **77**: 896–9
- 13 Marconi F, Messina P, Pavanello P, De Castro R. Cosmetic reconstruction of mons veneris and lower abdominal wall by skin expansion as the last stage of surgical treatment of bladder exstrophy: a report of three cases. *Plastic Reconstr Surg* 1993; **91**: 551
- 14 Konz KR, Chia JK, Kurup VP, Resnik A, Fink JN. Comparison of latex hypersensitivity among patients with neurological defects. *J Allergy Clin Immunol* 1995; **95**: 950–4
- 15 Kremer R, Hoppe A, Korsch E, Kleine-Diepenbruck U, Blaker F. Natural rubber latex allergy: prevalence and risk factors in patients with spina bifida compared with atopic children and controls. *Eur J Pediatr* 1998; **157**: 13–6
- 16 Bernardini R, Novembre E, Lombardi E *et al.* Risk factors for latex allergy in patients with spina bifida and latex sensitization. *Clin Exp Allergy* 1999; in press
- 17 Turjanmaa K, Alenius H, Makijnen-Kiljunen Reunala T, Palosuo T. Natural rubber latex allergy. *Allergy* 1996; **51**: 593–602
- 18 Ylitalo L, Turjanmaa K, Palosuo T, Reunala T. Natural rubber latex allergy in children who had not undergone surgery and children who had undergone multiple operations. *J Allergy Clin Immunol* 1997; **100**: 606–12
- 19 Blanco C, Carillo T, Castillo R, Quiralta J, Cuevas M. Latex allergy: clinical features and cross-reactivity with fruits. *Ann Allergy* 1994; **73**: 309–14
- 20 Kremer R, Kleine-Diepenbruck U, Hoppe A, Blaker F. Latex allergy in spina bifida patients- prevention by primary prophylaxis. *Allergy* 1998; **53**: 709–11

Authors

G. Ricci, MD, Paediatrician.

A. Gentili, MD, Anesthesiologist.

F. Di Lorenzo, MD, Paediatric Surgeon.

F. Righetti, MD, Clinical Pathologist.

A. Pigna, MD, Anesthesiologist.

M. Masi, MD, Paediatrician.

R. De Castro, MD, Paediatric Surgeon.

Correspondence: Dr G. Ricci, Department of Paediatrics, University of Bologna, Via Massarenti 11–40138, Bologna, Italy. e-mail: ricci@med.unibo.it