

PERINATAL/NEONATAL CASE PRESENTATION

Unexpected source of latex sensitization in a neonatal intensive care unit

RJ Wynn, A Boneberg and S Lakshminrusimha

Division of Neonatology, Department of Pediatrics, Women and Children's Hospital at Buffalo, State University of New York at Buffalo, Buffalo, NY, USA

We report a term infant with gastroschisis who presented with a systemic allergic reaction at a specific time of each day coinciding with infusion from a new preparation of total parenteral nutrition and intravenous lipid emulsion. The source of latex was traced to the rubber stopper of the lipid emulsion. We present this case to highlight the possibility of allergy from this unexpected source in a neonate.

Journal of Perinatology (2007) **27**, 586–588; doi:10.1038/sj.jp.7211793

Keywords: latex; allergy; intravenous lipid emulsion; stopper

Introduction

The immune system at birth is not adapted for post-natal life in several respects, including poor cell-mediated immunity, inability to produce certain immunoglobulin isotypes, poor inflammatory responses and impaired defenses against intracellular pathogens.¹ However, there appears to be a period in early life during which an infant is particularly susceptible to sensitization.² Allergy to natural rubber latex has increasingly become a concern among pediatric patients undergoing surgery in the first year of life³ and is highly prevalent among patients with spina bifida.^{4,5} Evidence of latex sensitization is observed in 48% of patients with meningomyelocele.⁶ Latex sensitization accounted for 27% of anaphylactic reactions during anesthesia in a French pediatric center.⁷ Very little information is available regarding the prevalence of latex allergy among patients without spina bifida in current neonatology text books. Many products in the neonatal intensive care unit can contain latex such as urinary collection devices, incubators, gloves, pads, drains, ambu bags and other respiratory equipments, disposable syringes with rubber plungers and ports on intravenous tubing.^{8,9} Many Children's hospitals (including our unit) have made attempts to become 'latex-safe' by removing all known sources of latex.¹⁰

We report a term infant with gastroschisis who presented with a systemic allergic reaction at a specific time of each day coinciding with infusion from a new preparation of total parenteral nutrition (TPN) and intravenous lipid emulsion. The source of latex was traced to the rubber stopper of the lipid emulsion. To our knowledge, this is the first report of latex allergy in a neonate secondary to a rubber stopper of parenteral nutrient solution.

Case

The patient was a baby girl born at term gestation by spontaneous vaginal delivery with gastroschisis. The intestines looked well perfused and were reduced into the abdominal cavity at the bedside. On day 2, the fascial defect in the abdominal wall was closed without use of latex precautions and a percutaneous intravenous catheter was placed for TPN.

Bilious emesis was noted on day 17 with a dilated loop of bowel on abdominal X-ray with a left shift on blood count. She was started on oxacillin, gentamicin and metronidazole. A new preparation of TPN and the third dose of oxacillin were infused at 1800 h. At 1900 h, red hives were noted on the infant's face, chest, abdomen and legs. An intravenous dose of diphenhydramine (Benadryl) was given. A few minutes later, she was noted to have stridor and periorbital edema. Intravenous dexamethasone and racemic epinephrine nebulization resolved stridor and rash. This reaction was presumed to be secondary to oxacillin. This antibiotic was discontinued and she was started on vancomycin.

The next day, she developed similar erythematous rash at 1930 h (1–2 h after an infusion of new preparation of TPN and second dose of vancomycin administered over 45 min). Vancomycin was discontinued for suspected 'red man' reaction. The following day, she again developed hives at 1915 h and received intravenous diphenhydramine. It was noted that allergic reaction occurred within 1–2 h of starting new TPN with a new set of intravenous tubing. After discussing with the pharmacist, it was discovered that the intravenous lipid emulsion (Liposyn III (20%), Hospira Inc., Lake Forest, IL, USA) has a latex stopper and latex allergy was suspected. On the following day, allergy/immunology

Correspondence: Dr S Lakshminrusimha, Division of Neonatology, Women and Children's Hospital of Buffalo, 219 Bryant St, Buffalo, NY 14222, USA.

E-mail: slakshmi@buffalo.edu

Received 6 February 2007; revised 15 May 2007; accepted 13 June 2007

consult was obtained and Liposyn was discontinued and parenteral nutrition tubing was changed. No further allergic reactions were noted. Four days later, Liposyn was restarted by drawing the lipid emulsion into a syringe and avoiding going through the latex stopper. The baby did not have any further allergic reactions during her hospital stay. On specific enquiry, patient's mother disclosed that she is allergic to latex. A radio-allergo sorbent test (RAST) for latex from the baby was negative.

Her upper gastrointestinal contrast study showed evidence of small bowel obstruction. She underwent exploratory laparotomy with lysis of adhesions, small bowel resection and primary end-to-end anastomosis. She slowly started tolerating maternal breast milk and was discharged home at 54 days of life.

Discussion

Latex comes from a milky sap in tropical rubber trees (*Hevea brasiliensis*).¹¹ The protein in latex can cause an allergic reaction in persons with significant cumulative latex exposure, such as those undergoing repeated surgeries, especially if they undergo surgeries early in life.³ Latex allergy can be mild or severe with angioedema, stridor and shock. It may even cause death.^{12,13}

The patient described in this case report underwent an abdominal surgery early in life without latex precautions. She was also exposed to latex through TPN. A positive maternal history of latex allergy was obtained only after similar allergy was diagnosed in the infant. Similar strong family history was observed among latex-sensitive infants without any surgical intervention in Japan.¹⁴ The etiology of allergic reaction was not clear for the first couple of days in our patient and was wrongly suspected to be antibiotic related. However, the precise timing of onset of allergic symptoms led us to suspect TPN as the source of allergen. The bags and tubing used for TPN (Baxter, Deerfield, IL, USA) were noted to be latex-free. However, intravenous lipid emulsion was noted to have a rubber stopper. We suspected that latex particles were contaminating the lipid emulsion while being drawn through the rubber stopper. Patient's symptoms disappeared when the lipid emulsion was drawn into a syringe without traversing the rubber stopper. Neither the package insert of Liposyn III nor the product's website (<http://www.hospira.com/Products/liposyn.aspx>, accessed on 28 January 2007) provided any caution that the stoppers were made of latex and that exposure to latex was possible through the use of this product. Hypersensitivity reactions to lipid emulsions have been described in adults. Some of these reactions are secondary to the presence of long-chain fatty acids derived from soybean¹⁵ or rare contamination of lipid emulsion by soybean or egg protein.¹⁶ Unlike reactions to latex, these reactions persist irrespective of how lipid emulsions are withdrawn and administered.

Latex is widely used in the manufacturing of packaging for pharmaceuticals and medical products because of its excellent

elasticity and durability.¹⁷ Medical devices containing natural rubber latex state a cautionary warning. However, this rule has largely remained a requirement focused on dipper rubber products (such as gloves and condoms), which have been shown to contain higher levels of releasable allergenic proteins than the dry, molded, natural rubber used in the packaging of medical devices. Questions have remained as to whether the dry natural rubber used in pharmaceutical vial closures release allergenic proteins, thereby creating an allergen exposure risk for latex-allergic patients. The current hospital practice by some pharmacy staff is to remove the vial closure before withdrawing the medication. By 'popping the top', pharmacists avoid puncturing the latex stopper and can withdraw medications into a glass or a latex-free plastic syringe for administration to a known latex-allergic patient.¹⁷ The practical consequences of this approach involve the technical difficulties of removing some closures and using an open system that increases the potential for microbial contamination.¹⁸ However, there are no published reports that clearly demonstrate a hypersensitivity reaction by administering a medication from a vial containing a latex enclosure.¹⁷ Primeau *et al.*¹⁹ conducted skin testing with solution stored in vials with either natural rubber or synthetic closures. The vials were either not punctured or punctured 40 times with a 21-G needle 12–24 h before testing. None of the normal subjects (non latex-allergic) showed any skin reaction to the test. Only 2/12 of latex-allergic patients reacted to testing from vials with rubber closures without puncture. However, 5/12 of latex-allergic patients reacted to testing from vials with rubber closure punctured.¹⁹ These results suggest that puncturing the rubber stopper increases the risk of allergy in latex-sensitive individuals. It is important to remember that the risk is not eliminated by avoiding puncturing of the rubber closure as latex allergen may leach from the closure into the medication during shipping or storage.¹⁷

A negative RAST to latex in our patient does not rule out latex allergy. These latex-specific IgE tests have low sensitivity with a false-negative rate of at least 20%.¹² Even in surgical pediatric patients with severe latex allergy, 2/35 of patients demonstrated negative *in vitro* tests for latex-specific IgE antibodies.²⁰ We decided not to proceed with more specific testing such as skin prick testing as the patient's symptoms improved with avoidance of exposure and also because of the risk of anaphylaxis with skin prick testing.

A series of allergic reactions (including deaths) from a latex tip for barium enemas resulted in withdrawal of this product in the United States.²¹ Similarly, alternative non-latex synthetic stoppers should be considered for medical packaging. We have been recently informed that Hospira is switching over to Liposyn with non-latex stoppers effective from March 2007.

To conclude, we report a case of latex allergy in a term neonate with gastroschisis following exposure to latex following exposure to a lipid emulsion solution with a rubber stopper. We present this

case to highlight the possibility of allergy from such a source (despite lack of mention about this possibility in the package insert) and also the benefit of discussion with family members and other health care professionals such as nurses and pharmacists in detecting the source of an allergen. Routinely asking about allergies in all patients and family members, a practice that was not employed in the patient presented except as an afterthought, should be considered in the neonatal intensive care unit.

References

- 1 Bjorksten B. The intrauterine and postnatal environments. *J Allergy Clin Immunol* 1999; **104**: 1119–1127.
- 2 Bjorksten B. The environment and sensitisation to allergens in early childhood. *Pediatr Allergy Immunol* 1997; **8**: 32–39.
- 3 Degenhardt P, Golla S, Wahn F, Niggemann B. Latex allergy in pediatric surgery is dependent on repeated operations in the first year of life. *J Pediatr Surg* 2001; **36**: 1535–1539.
- 4 Szepefalusi Z, Seidl R, Bernert G, Dietrich W, Spitzauer S, Urbanek R. Latex sensitization in spina bifida appears disease-associated. *J Pediatr* 1999; **134**: 344–348.
- 5 Pilcher J, Sogard L. Myelomeningocele, avocados, and rubber tree plants. *Neonatal Netw* 2005; **24**: 23–28.
- 6 Rendeli C, Nucera E, Ausili E, Tabacco F, Roncallo C, Pollastrini E *et al*. Latex sensitisation and allergy in children with myelomeningocele. *Childs Nerv Syst* 2006; **22**: 28–32.
- 7 Karila C, Brunet-Langot D, Labbez F, Jacqmarcq O, Ponvert C, Paupe J *et al*. Anaphylaxis during anesthesia: results of a 12-year survey at a French pediatric center. *Allergy* 2005; **60**: 828–834.
- 8 Moore A, McQuay H, Derry S, McQuay M, Moore M. Latex allergy. *Bandolier Journal* 1995, <http://www.jr2.ox.ac.uk/bandolier/bandopubs/NHSSLatex.html>.
- 9 Pennsylvania patient safety reporting system (PA-PSRS). Hidden sources of latex in healthcare products. *Patient Safety Advisory* 2004, http://www.psa.state.pa.us/psa/lib/psa/advisories/v1n2june2004/june2004vol12_article_a_hidden_sources_of_latex.pdf.
- 10 Bartoo C. Children's Hospital making move to latex-free materials. *The Reporter: Vanderbilt Medical Center* 2005, <http://www.mc.Vanderbilt.edu/reporter/index.html?ID=4148>.
- 11 Gunther KP, Nelitz M, Parsch K, Puhl W. Allergic reactions to latex in myelodysplasia: a review of the literature. *J Pediatr Orthop B* 2000; **9**: 180–184.
- 12 Reddy S. Latex allergy. *Am Fam Physician* 1998; **57**: 93–102.
- 13 Reddy S. Prevention and management of latex allergy. *JAMA* 1998; **279**: 911.
- 14 Kimata H. Latex allergy in infants younger than 1 year. *Clin Exp Allergy* 2004; **34**: 1910–1915.
- 15 Weidmann B, Lepique C, Heider A, Schmitz A, Niederle N. Hypersensitivity reactions to parenteral lipid solutions. *Support Care Cancer* 1997; **5**: 504–505.
- 16 Buchman AL, Ament ME. Comparative hypersensitivity in intravenous lipid emulsions. *JPEN J Parenter Enteral Nutr* 1991; **15**: 345–346.
- 17 Hamilton RG, Brown RH, Veltri MA, Feroli ER, Primeau MN, Schauble JF *et al*. Administering pharmaceuticals to latex-allergic patients from vials containing natural rubber latex closures. *Am J Health Syst Pharm* 2005; **62**: 1822–1827.
- 18 Association of Perioperative Registered Nurses. AORN latex guideline. *AORN J* 2004; **79**: 653–672.
- 19 Primeau MN, Adkinson Jr NF, Hamilton RG. Natural rubber pharmaceutical vial closures release latex allergens that produce skin reactions. *J Allergy Clin Immunol* 2001; **107**: 958–962.
- 20 Kwittken PL, Sweinberg SK, Campbell DE, Pawlowski NA. Latex hypersensitivity in children: clinical presentation and detection of latex-specific immunoglobulin E. *Pediatrics* 1995; **95**: 693–699.
- 21 Gelfand DW. Barium enemas, latex balloons, and anaphylactic reactions. *AJR Am J Roentgenol* 1991; **156**: 1–2.