

Natural Rubber Latex Allergy-Pearls and Pitfalls: Review

DOĞAL KAUÇUK LATEKS ALLERJİSİ

Öner ÖZDEMİR, MD,^a Emin METE, MD^b

^aDivision of Allergy and Immunology, Department of Pediatrics, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH, USA

^bDivision of Allergy, Department of Pediatrics, Fatih University, Medical Faculty, ANKARA

Abstract

A case of natural rubber latex allergy is briefly described. The clinical characteristics, pathogenesis, diagnosis and management of this disease are discussed followed by clinical pearls and pitfalls for the practicing allergist. Natural rubber latex allergy is now considered the most frequent cause of occupational allergy in healthcare workers. Dipped latex products can trigger urticaria, angioedema, and anaphylaxis after cutaneous or mucosal exposure. Adsorbed latex allergens in powdered gloves also may cause rhino-conjunctivitis and asthma. In the pathogenesis, immediate- and delayed- type hypersensitivity reactions play a major role. Diagnostic tools are ImmunoCAP, skin prick test and provocation test as required. Treatment is simply based on avoidance as well as symptomatic treatment. New treatment modalities e.g. immunotherapy with hypoallergenic hevein and anti-IgE are underway.

Key Words: Latex hypersensitivity; immunotherapy; hevein

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Özet

Doğal kauçuk lateks allerjisi olan bir olgu kısaca takdim edildi. Hastalığın klinik karakteristikleri, patogenezi, teşhis ve tedavisi tartışılırken, allerji pratiği ile uğraşanlar için konunun ipuçları ve dikkat edilmesi gereken noktalar üzerinde duruldu. Doğal lateks allerjisinin sağlık çalışanlarında görülen meslek allerjileri içinde en sık rastlanılanı olduğu düşünülmektedir. Deri ve mukozanın lateks ile kontamine olmuş ürünlere maruz kalması ürtiker, anjiyoödem ve anafilaksiyi tetikleyebilir. Pudralı eldivenlere absorbe olan lateks allerjenler rinokonjunktivit ve astıma sebebiyet verebilir. Patogeneizde erken ve geç tip aşırı duyarlılık reaksiyonları önemli rol oynamaktadır. Gerekirse yapılması gereken tanısal testler immünoCAP, deri prik testler ve provokasyon testleridir. Tedavi semptomların giderilmesi ve allerjiden kaçınılması esasına dayanır. Hipoallerjenik hevein ile immünoterapi ve anti-IgE tedavileri gibi yeni tedavi yöntemleri üzerinde çalışılmaktadır.

Anahtar Kelimeler: Lateks allerjisi; immünoterapi; hevein

A 36-year-old female surgical nurse presented with a 2-year history of increasing breathing difficulty. She was very healthy until 6 years ago, when she noted a pruritic, erythematous rash on her hands whenever she wore latex gloves. This rash was associated with latex glove use and even persisted after using steroid creams for 10 days. A couple of years later, the rash involved her arms and she developed a peri-

odic, nonproductive cough, and wheezing when she used powdered latex gloves. She did reasonably well until recently but her symptoms worsened and she experienced dyspnea within 20 minutes of wearing latex gloves during surgery. Symptoms sustained throughout the work-hours and improved when she left work. Skin biopsy of her rash revealed changes consistent with contact dermatitis. Although ImmunoCAP test for latex IgE antibody was negative, skin prick test was positive to latex glove extracts. She gave a history of perioral pruritus when she ate banana. Her examination was remarkable for expiratory wheezing and erythematous urticarial rash on both hands. Respiratory symptoms completely resolved after she changed her job and started to work in another

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Yazışma Adresi/Correspondence: Emin METE, MD
Fatih University, Medical Faculty
Division of Allergy, Department of Pediatrics, ANKARA
metee@hotmail.com

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clinic. Her contact dermatitis also improved when she wore latex-free gloves at work. Which of the following statements are correct?

A- Healthcare workers are likely to be sensitized to latex Hev b-2 /-5 /-6, and -7 allergens; however, Hev b -1 and -3 are the responsible latex allergens in spina bifida patients.

B- Although latex allergy is not associated with dipped latex products; hard rubber products are mostly responsible for allergies.

C- Hev b 1, class I chitinase, is the culprit allergen in latex-fruit syndrome.

D- Latex-mold syndrome describes the cross-sensitization between molds and latex allergens e.g. Hev b -9 and -10.

E- The sensitization risk tends to decrease in repeatedly operated children.

Natural rubber latex (NRL) allergy now is considered the most frequent cause of occupational allergy of healthcare workers. NRL sensitization prevalence ranges from 2-10% in general vs. up to 17% in health care workers.¹ A study evaluating latex allergy among operating room personnel in Turkey showed skin prick test positivity to latex in 9.22%.² Nowadays; its prevalence is increasing in non-healthcare occupations as well as reported non-occupational cases.

NRL, used in the manufacture of latex gloves, is derived from the milky sap of the rubber tree, *Hevea brasiliensis*. Dipped NRL products e.g. gloves and balloons are responsible for most of the allergic reactions. Dry rubber latex products e.g. vial stoppers are rarely responsible for NRL allergy. Similarly, synthetic rubber products pose no risks to sensitized persons. The major source of allergen in health care settings is powdered latex gloves.

NRL allergy is more complex than many others and is attributable to at least 13 latex allergens. Hev b 6.02, Hev b 5, Hev b 3, and Hev b 1 are known as main allergens detectable in latex gloves.³

High risk groups include atopics, females, health care workers, patients with pre-existing

hand eczema and chronic renal failure or congenital anomaly (spina bifida) requiring recurrent surgery, and all persons regularly contacting with NRL products.

Clinical Characteristics

NRL allergy can be categorized as allergic (Ig-E mediated/type-I or delayed/type-IV) or non-allergic e.g. irritational. Ig-E mediated hypersensitivity reactions to NRL products include contact urticaria and angioedema after cutaneous, mucosal or visceral exposure. Adsorbed latex allergens in powdered gloves may cause rhinoconjunctivitis and asthma. Latex-associated asthma is limited largely to those exposed to latex aerosols and is estimated to affect 2.5% of health care and manufacturing workers.^{1,4} Anaphylaxis, the most feared complication, may occur after contacting with gloves, balloons, catheters, squash racquets, and latex-containing hair adhesive.⁵

Allergic contact dermatitis (ACD) is the most common immune-mediated reaction to latex gloves. It is a delayed hypersensitivity due to exposure to the chemical additives or endotoxins, which may be present as contaminants. The most common culprits are accelerators, especially thiurams and carbamates.⁶ Features of ACD are pruritic rash (urticaria), swelling, blistering, weeping, and crusting; and symptoms occur from several hours to several days after exposure. Nevertheless, a comparative evaluation of type 1 latex hypersensitivity in patients with chronic urticaria showed that the frequency of latex hypersensitivity in chronic urticaria patients is no higher than that in healthy individuals.⁷ Irritant contact dermatitis (ICD) often involves the webbed spaces between the fingers and it is not an allergic reaction, contrary to ACD. It usually is caused by multiple irritants, such as hand washing, friction, or other irritating chemicals.

IgE-mediated reactions to a wide variety of foods, mainly fruits [latex-fruit/food syndrome] occur in 20% to 60% of latex-allergic patients⁸ Structural homologies are known between major latex allergen Hev b 6 and wheat germ agglutinin and between endochitinases in avocado and banana. Four

well-known foods frequently causing allergy in latex allergic persons are avocado, banana, kiwi, and chestnut. Primary sensitization to latex profilin, Hev b 8, in the majority of cases takes place via pollen (ragweed and grasses) profilins. Furthermore, cross-reactivity between latex and molds was also described [mold-latex allergy syndrome].⁹

Pathogenesis

As mentioned earlier; reactions to NRL can be classified into 2 main groups: Allergic (type-I or type-IV) and non-allergic e.g. ICD. However, concomitant type IV and type I allergies may occur in the same patient. Regrettably, ICD may also make the individual allergic to NRL.

ACD is a delayed hypersensitivity reaction caused by exposure to the accelerators. This exposure causes the activation and release of lymphokines by sensitized T lymphocytes rather than to the latex itself. The immediate-type hypersensitivity is the most serious reaction and relies on previous sensitization to NRL antigens.

Diagnosis

Diagnosis of latex allergy requires a history of exacerbation of symptoms after exposure to NRL products and showing sensitization by latex-specific IgE antibodies, skin or patch or challenge testing. Although skin prick testing (SPT) is the initial diagnostic procedure in Europe, latex-specific IgE measurement is the first-line diagnostic test in U.S. Specific IgE antibodies can be studied by ImmunoCAP (The Pharmacia CAP System RAST), AlaSTAT fluorescence enzyme immunoassay (FEIA), and HY-TEC enzyme immunoassay (EIA).¹⁰ The flow cytometric basophil activation test was also found to be valuable. However, in vitro lymphocyte transformation to NRL is too insensitive.

Allergists in U.S. frequently perform SPT with extracts of NRL products (usually gloves), which vary widely in their allergen contents. When there is a discrepancy between SPT and specific IgE tests or history, NRL allergy can be confirmed by the 'Wear/Use Test'.¹ Contact dermatitis patients deserve not only to be patch-tested with rubber chemi-

cals (T.R.U.E. test) but also be tested for immediate sensitivity, and if results are negative, to be patch-tested with ammonia-free NRL or gloves.¹¹

Nasal and bronchial inhalation challenge tests have been used to document the allergenicity of crude latex or individual latex proteins.

Management

Since spontaneous desensitization is not likely to occur, optimal management of NRL allergy involves reducing contact with latex products, and minimizing exposure to latex aeroallergens (latex free environment) as well as education concerning cross-reacting allergens. Prevention of sensitization in workplace includes increased use of non-latex, powder-free, low-protein latex gloves in addition to cleaning of carpets and upholstered furniture.

Urticaria and asthma usually respond to standard care. Steroids and antihistaminics can be used for pre-operative prophylaxis but this is not a substitute for avoidance. Despite reported successful sublingual desensitization, specific immunotherapy is still lacking. Recently hypoallergenic Hev b -5/-6 proteins and anti-IgE antibodies are tried.¹²

Nonsensitized individuals in high-risk groups should use nonlatex synthetic or low allergenic gloves as well as polyurethane and deproteinized latex condoms. Oil-based hand creams should not be used while using latex gloves, but concomitant hand eczema should be treated. Latex-allergic patients should wear Medic-Alert bracelets and patients with systemic symptoms should carry epinephrine syringes.

Answers to the Questions

- A. Correct
- B. Wrong
- C. Wrong
- D. Correct
- E. Wrong

Pearls

- The initial screening test for NRL allergy is CAP test in US, but latex skin test is the gold standard and more sensitive, when done properly.

- Contact urticaria is the most common presenting symptom of NRL allergy and often is the only sign of IgE-mediated reaction.
- NRL allergy is the second most frequent cause of anaphylaxis during anesthesia.
- The most frequent latex glove-associated skin reaction is ICD.
- Oat starch powder is less allergenic than cornstarch and cotton fluffs in the latex gloves.

Pitfalls

- Hand creams applied before donning gloves actually increase the risk of sensitization to NRL.
- Observed milk allergy in latex allergic patients is associated with casein that is sometimes added in the manufacture of NRL.
- Nonsterile latex gloves contain higher allergen levels than sterile ones.
- Even if the patient's history of latex allergy is limited to skin manifestations there is still potential for inducing a systemic reaction.
- Anaphylaxis due to latex allergy is responsible for two fifths of intraoperative anaphylaxis and mostly encountered in obstetrics/gynecologic interventions.

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