

# Anaphylactic Reaction with The Measles-Mumps-Rubella Vaccine in A Patient with Cow's Milk Allergy

## *İnek Sütü Alerjisi Olan Bir Hastada Kızamık-Kabakulak-Kızamıkçık Aşısı İle Anafilaktik Reaksiyon*

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### Özet

Dünya çapında çocuklarda en yaygın görülen gıda alerjisi inek sütü alerjisidir. İnek sütü proteinlerinden en bilinen alerjenler kazein, alfa-laktalbumin ve beta-laktoglobulindir. Lactalbumin hidrolizat, Hindistan menşeli kızamık kabakulak kızamıkçık (MMR) aşısında stabilizatör olarak kullanılır. MMR aşısının farklı ticari formları mevcuttur. Bir formda stabilizatör olarak neomisin kullanılırken, diğer formda laktalbumin hidrolizat kullanılır. İnek sütü alerjisi nedeniyle izlenen ve Hindistan menşeli MMR aşısı sonrası anafilaksi gelişen bir hastayı sunuyoruz. İnek sütü anafilaksi öyküsü olan, aile sağlığı merkezinde rutin aşı takvimine göre aşılı uygulanan 4 yaşında kız hastamızın aşidan 1 dakika sonra hışırtı ve öksürme şikayeti başladı. Hasta acil servise (aşidan sonraki 10 dakika içinde) şiddetli solunum sıkıntısı ve interkostal çekilmeler ile başvurdu. Hastaya 5 dakika aryla 3 doz intramusküler adrenalin, intravenöz feniramin ve metilprednizolon ve inhaler kısa etkili beta agonist uygulandı. Hastane başvurusundan yaklaşık 40 dakika sonra semptomlar geriledi. İnek sütü anafilaksisi öyküsü olan ve laktalbumin-spesifik immunoglobulin E değeri 61,3 kU/L olan hastamızda MMR aşısı ile anafilaktik reaksiyon gelişmesi aşının içerdiği laktalbumin ile ilişkili gibi görünmektedir. Bilinen besin alerjisi olan hastaların takibinde aileler ve hekimler etiket okuma konusunda titiz davranmalıdır.

**Anahtar kelimeler:** Anafilaksi, inek sütü, laktalbumin hidrolizatı, kızamık aşısı, kabakulak aşısı

### Abstract

**Objective:** The most common food allergy in children worldwide is cow's milk allergy. The most known allergens from cow's milk proteins are casein, alpha-lactalbumin, and beta-lactoglobulin. Lactalbumin hydrolysate is used as a stabilizer in the measles mumps rubella (MMR) vaccine originating in India. Different commercial forms of the MMR vaccine are available. While neomycin stabilizes, lactalbumin hydrolysate is used in the other form. We present a patient who was followed up for cow's milk allergy and developed anaphylaxis after the MMR vaccine originating from India. A 4-year-old girl with a history of anaphylaxis with cow's milk whose vaccinations were applied by the routine vaccination schedule in the family health center. Sneezing and urticaria started 1 minute after immunization. The patient presented to the emergency department (within 10 minutes after vaccination) with severe respiratory distress and intercostal retractions. The patient was administered three doses of intramuscular adrenaline, 5 minutes apart, intravenous pheniramine and methylprednisolone, and a nebulizer short-acting beta agonist. Symptoms regressed approximately 40 minutes after hospitalization. In our patient with a history of cow's milk anaphylaxis and lactalbumin-specific immunoglobulin E value of 61.3 kU/L, anaphylactic reaction with MMR vaccine seems to be related to the lactalbumin contained in the vaccine. Families and physicians should be meticulous about reading labels in the follow-up of patients with known food allergies.

**Keywords:** Cow's milk, anaphylaxis, lactalbumin hydrolysate, measles mumps, rubella vaccine

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**Submission date:** 20.06.2023

**Acceptance date:** 22.01.2024

**DOI:** 10.17517/ksutfd.1317061

## INTRODUCTION

The incidence of food allergies is increasing worldwide. Studies have shown that the frequency of food allergies in the pediatric age group is between 1% and 10% (1). Cow's milk allergy is the most common food allergy in children. Its incidence in early childhood is approximately 3% (2). Cow's milk contains at least 20 protein components that induce antibody production. The most commonly known are casein and whey proteins. Caseins make up 76%-86% of cow's milk protein. Whey proteins contain  $\alpha$ -lactalbumin,  $\beta$ -lactoglobulin, bovine serum albumin, bovine immunoglobulins, and small amounts of lactoferrin, transferrin, lipase, and esterase proteins (3). Lactalbumin hydrolysate is obtained from whey and acts as an adjuvant in vaccines, increasing the immune response to the antigen (4).

In the vaccination program of the Ministry of Health in Türkiye, the measles mumps rubella (MMR) vaccine is administered in the 12th and 48th months, with an additional dose in the 9th month in regions with epidemic risk (5). The MMR vaccine is imported to our country under different brands, which use different stabilizers. Some strains in the Priorix® vaccine are produced in chicken embryo cells. The MMR vaccine produced by the Serum Institute of India contains partially hydrolyzed gelatin, sorbitol, L-histidine, L-Alanine, tricine, L-arginine hydrochloride, and lactalbumin hydrolysate as stabilizers.

Our article presents a patient with severe cow's milk allergy who continues on a cow's milk diet and had anaphylaxis after the MMR vaccine.

## CASE REPORT

A 4-year-old female patient followed up with a cow's milk protein allergy. There has been a history of anaphylaxis against cow's milk during a food challenge test performed when she was two years old. The patient developed urticaria 15 minutes after drinking 50 ml of milk in the 6th step of the test, followed by sneezing, coughing, and wheezing. The patient was accepted as

anaphylaxis, and the test was terminated. Adrenaline was administered intramuscularly, and pheniramine was administered intravenously. The patient's symptoms regressed. An adrenaline autoinjector report was issued. Cow's milk diet was continued.

The patient was called from the family health center for the routine vaccination schedule, and vaccinations were made. She started sneezing and urticaria 1 minute after the vaccine. Then she said that her throat was sore, and she started coughing. Within 5 minutes, she fainted slightly. The family could not apply the adrenaline autoinjector because they did not have it. When the patient came to the emergency room (within 10 minutes after vaccination), she had severe respiratory distress and intercostal retractions. Oxygen saturation was measured at 76%. Her blood pressure is normal. The patient was considered anaphylaxis because she developed two systemic findings, such as urticaria and respiratory distress, after contact with an agent to which she was not known to be allergic. The patient was administered three doses of intramuscular adrenaline, intravenous pheniramine, and methylprednisolone, salbutamol nebulizer with an interval of 5 minutes. The emergency physician consulted the patient by telephone. The patient's symptoms regressed approximately 40 minutes after admission to the hospital. The patient was discharged after 24 hours of hospitalization.

The family physician who administered the vaccine to the patient was reached. It was learned that the patient received the MMR vaccine from India. It was stated in the package insert of the vaccine that it contains lactalbumin hydrolysate as a stabilizer. The patient's alpha-lactalbumin-specific IgE value during anaphylaxis was 61.3 kU/L (negative: <0.35 kU/L) (Table 1). Our patient had no history of symptoms caused by eggs and gelatin-containing foods (e.g., gelibon).

Permission was obtained from the family to share the patient's laboratory results and clinic. The family stated they were very sorry that they did not carry the adrenaline autoinjector and that the vaccine contained milk protein.

**Table 1. Cow's Milk Specific Ige Values of The Patient**

	Beta Lactoglobulin (kU/L)**	Alpha Lactalbumin (kU/L)**	Casein (kU/L)**	Cow's milk (kU/L)**
23.9.2020	8,58	8.04	-	-
25.11.2022	14,3	-	-	-
12.1.2023*	9,9	61,3	27,5	49,2
6.4.2023	19,8	86,8	50,8	>100

\* The last values measured before anaphylaxis. The patient was vaccinated on 13.2.2023 and had anaphylaxis.

\*\*Reference value: negative: <0,35 kU/L, positive: >0,35 kU/L

The vaccine company was informed about the side effects caused by the vaccine through the Turkish Pharmacovigilance Center.

## DISCUSSION

MMR vaccine is included in our country's routine childhood vaccination program and many other countries. It provides immunity against vaccine-preventable diseases. Since it is a live vaccine administered to millions of children in repeated doses, close studies are conducted on the allergy and side effect profile. Shu *et al.* conducted a study to prospectively monitor adverse events following mass measles vaccinations in China. Reactions were divided into allergic reactions and serious adverse events. The incidence of anaphylaxis reaction was estimated at 6.5 per million for the attenuated measles vaccine. Out of 14.3 million vaccinations, 1 case of acute disseminated encephalomyelitis, idiopathic thrombocytopenic purpura, and 28 cases of Henoch-Schonlein purpura cases were reported. The total incidence of serious adverse events after vaccination was 2.14 per million doses (6).

Allergic reactions that may occur with the MMR vaccine in children with egg allergy are more known. Priorix<sup>®</sup> vaccine consists of live attenuated measles virus (Schwarz), live attenuated mumps virus (RIT 4385, derived by Jeryl Lynn), and live attenuated rubella virus (Wistar RA 27/3). The first two strains were produced in chicken embryo cells and may contain egg protein. Until now, many studies have evaluated the relationship between egg allergy and the MMR vaccine. It was concluded that the MMR vaccine can be administered without hospitalization if there is no history of egg anaphylaxis in patients with egg allergy who have not reacted to the previous vaccine (7-9).

In a case series from our country, Yavuz *et al.* reported that anaphylaxis developed after MMR vaccine administration in three infants with cow's milk and egg allergy. It was stated that these cases were followed without symptoms with milk and egg elimination, and they had anaphylaxis immediately after vaccination with the MMR vaccine (Serum Institute, Hadapsar, Pune, India). The authors suggested that egg-specific IgE levels were low in two cases, egg allergies returned to normal over time, and the reactions seen in children were unrelated to possible egg protein found in the vaccine. Ultimately, the authors stated that another vaccine molecule could cause the reactions (10).

Caseins are suspended in the micelle complex and presented to the immune system through Peyer's patches. At the same time, whey proteins quickly pass

through the intestinal epithelium due to their easily soluble feature. As a result, caseins have more significant potential to induce antibody response, including IgE, than whey proteins; however, when looking at animal models sensitive to casein and whey protein, the possibility of triggering a systemic allergic reaction after re-exposure to whey proteins is higher than caseins. This is probably due to the rapid absorption of whey proteins from the intestinal epithelium (3). Formulas with whey hydrolysate, once given to children with cow's milk allergy, are no longer preferred because they cause allergic reactions in children. Ragno *et al.* showed that two of 15 children with cow's milk allergy experienced an allergic reaction to a formula containing lactalbumin hydrolysate (11). Nilsson *et al.* reported that a three-year-old child was allergic to a formula containing lactalbumin hydrolysate (12).

In another article, Uysal *et al.* reported that their 9-month-old patient with cow's milk allergy developed anaphylaxis with the MMR vaccine (Serum Institute, Hadapsar, Pune, India). The authors think that the low milk protein level, lactalbumin hydrolysate, in the vaccine causes anaphylaxis in the patient (13). Like Uysal *et al.*, we believe that the anaphylactic reaction with the MMR vaccine (Serum Institute, Hadapsar, Pune, India) in our patient with milk allergy is related to the content of lactalbumin hydrolysate in the vaccine.

It is a known fact that food allergies increase gradually in childhood. We recommend not using nutritional proteins as a stabilizer in childhood vaccines. In addition, families and physicians of children with food allergies should read the label, and families of children with a previous history of food-related anaphylaxis should be cautious about carrying an adrenaline auto-injector with them.

**Conflicts of Interest:** None

**Consent Form:** An informed consent form was taken from the patient's family.

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