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Anaphylactic reactions to measles–mumps–rubella vaccine in three children with allergies to hen’s egg and cow’s milk

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Keywords

Anaphylaxis, Egg protein, Food allergy, Measles–mumps–rubella vaccines, Vaccines – adverse reactions

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Received

30 August 2010; revised 27 December 2010; accepted 12 January 2011.

DOI:10.1111/j.1651-2227.2011.02165.x

ABSTRACT

Aim: Allergies to hen’s egg and cow’s milk are the most frequent food allergies in infancy and childhood. Current guidelines recommend safe administration of measles–mumps–rubella (MMR) vaccine in egg allergic patients.

Methods: We present three cases of anaphylaxis that we encountered after MMR vaccination in children sensitized to hen’s egg and cow’s milk.

Results: Even though MMR vaccine is generally known to be safe in children with egg allergy, there may still be isolated cases of anaphylaxis.

Conclusion: Therefore, we recommend that all children not only those who were sensitized to foods should receive the MMR vaccination in a setting that is equipped to deal with anaphylactic reactions. As stated by WHO in immunization safety surveillance, ‘Each vaccinator must have an emergency kit with adrenaline, and be familiar with its dosage and administration’.

Allergies to hen’s egg and cow’s milk are the most common food allergies in childhood with prevalences ranging from 1.6% to 3.2% (1,2) and 2.0% to 2.5% (2,3), respectively. Even though there is no report of reaction after measles–mumps–rubella (MMR) vaccine in cases with cow’s milk

allergy, Patja et al. (4) reported the positive immunospot results to cow’s milk in cases with reaction after MMR vaccine. For many years, administration of MMR vaccine to children with egg allergy has been a subject of debate because the vaccine is grown in cultures of fibroblasts derived from chick embryos. Later on, however, it was discovered that MMR vaccines do not contain significant amounts of detectable egg proteins and many of the reactions are in fact caused by gelatin allergy (5–7). Moreover, several studies have described that MMR vaccine can be

Abbreviations

MMR, Measles–mumps–rubella; IgE, Immunoglobulin E.

administrated to children with egg allergy uneventfully (4,5,8).

In this report, we describe anaphylactic reactions to MMR vaccine in three children who have allergies or are sensitized to hen's egg and cow's milk but not to gelatin to emphasize that there may still be cases of anaphylaxis after MMR vaccination. The diagnosis of egg or cow's milk allergy is made on the basis of a history of symptoms clearly associated with exposure to egg or cow's milk, and/or a clear improvement in symptoms with food avoidance and positive specific IgE response against food protein demonstrated by skin prick tests or serologic tests.

CASE 1

A 1-year-old girl presented with atopic eczema when she was 6 months old. Specific IgE levels to cow's milk and egg were 3.47 and 15.1 kU/L, respectively. She was placed on an elimination diet and did not consume egg- and cow's milk-containing food, and symptoms of eczema disappeared with egg and cow's milk avoidance before MMR vaccination. When she received MMR vaccine (Serum Institute of India, Hadapsar, Pune, India), she developed flushing, perioral pallor, cyanosis, respiratory distress and unresponsiveness, immediately. She was treated with epinephrine, hydroxyzine and methylprednisolone, and her symptoms resolved completely over the next 2 h. At the time period of anaphylaxis, following were the immune globulin E (IgE) levels to cow's milk: >100 kU/L, egg: 73.6 kU/L, gelatin: <0.35 kU/L and total IgE: 1695 kU/L (Pharmacia, Uppsala Sweden).

CASE 2

A 1-year-old boy presented with atopic eczema when he was 4 months old. Specific IgE levels to cow's milk and egg were 8.74 and 1.51 kU/L, respectively. He was prescribed an elimination diet and did not consume egg- and cow's milk-containing food, and symptoms of eczema disappeared with egg and cow's milk avoidance before MMR vaccination. After his first MMR vaccination (Serum Institute of India), he developed hives and facial flushing and vomiting within minutes. He was treated with high-flow oxygen, epinephrine and hydroxyzine. In 15 min, he developed increased sleep tendency. His eyes were initially fixed and then deviated leftward. Another dose of intramuscular epinephrine was applied. He developed mild perioral cyanosis. His heart rate ranged between 120 and 180 per minute. He was admitted to ICU. He recovered completely within 24 h. At the time period of anaphylaxis, following were the IgE levels to cow's milk: 3.34 kU/L, egg: 1.94 kU/L, gelatin: <0.35 kU/L and total IgE: 38 kU/L.

CASE 3

A 6-year-old girl had a history of anaphylaxis after her first MMR vaccination (Serum Institute of India) when she was 1 year old. She was admitted for her second dose of MMR vaccine. After the injection of 1/10 of the vaccine, she

developed angioedema, sneezing, wheezing, stridor and unconsciousness within minutes. She did not have hypotension or hypoxia. She was treated with high-flow oxygen, epinephrine, inhaled albuterol and methylprednisolone. Her symptoms resolved completely over the next 2 h. She had a history of milk, egg and beef allergy. At the time period of anaphylaxis, following were the IgE levels to cow's milk: 13.7 kU/L, egg: 0.77 kU/L, beef: 0.78 kU/L, gelatin: <0.35 kU/L and total IgE: 64 kU/L.

One year later, she had another episode of anaphylaxis following the ingestion of a small piece of cake containing milk and egg. At this time, IgE to cow's milk was 8.47 kU/L and to egg was 0.17 kU/L. None of our cases had a history of symptoms caused by gelatin-containing foods.

DISCUSSION

After the introduction of the MMR vaccine, there has been a continuous discussion about its administration to patients with egg allergy. Hypersensitivity to MMR vaccine has been described in children with allergy to hen's egg (9,10). Since 1963, several reports have shown that MMR vaccine can be safely administrated to children with hen's egg allergy. In one of the largest studies, Patja et al. (4) have shown that MMR vaccination causes 1 case of anaphylaxis, 1 urticaria and 0.3 asthma symptoms per 100 000 injections. Of the serum samples of 36 individuals with immediate or non-immediate reactions to MMR vaccine, 13.9% contained specific IgE to gelatin, 25.0% to egg, 22.2% to chicken and 47.2% to cow's milk in the immunospot.

Because measles vaccine is grown in the cultures of chick embryo fibroblasts, detectable amounts of egg-related antigens may be present in MMR vaccine. In fact, previous studies have reported the presence of trace amount of egg proteins, mostly ovalbumin, which are not sufficient to cause adverse allergic reactions (11). In favour of this claim, several examples of safe administration of the MMR vaccine to hundreds of children with known allergy to hen's egg have been reported. Under the light of these reports and considerations, American Academy of Pediatrics Committee on Infectious Diseases stated, 'children with egg allergy may routinely be given MMR, measles, or mumps vaccine without previous skin testing' (12). These reports and considerations were prepared in the light of the experiences with MMR vaccines produced in the United States or Europe.

Following the observation that allergic reactions after MMR occurred in individuals without egg allergy (8,11,13,14), different MMR components such as viral antigens, neomycin, sorbitol, gelatin and latex have undergone investigation. In 1993, Kelso et al. (6) and later various Japanese researchers have described reactions in children with anti-gelatin IgE antibodies (14,15). Pool et al. (7) have concluded that almost one-fourth of patients with reported anaphylaxis after MMR seem to have hypersensitivity to gelatin.

In this report, we describe three children who developed anaphylactic reactions following MMR vaccination. The

common characteristic of the children at the time of the anaphylactic reaction to MMR vaccine is the presence of specific IgE to egg and cow's milk and the absence of specific IgE to gelatin. Businco (16) denoted possible cross-reactivity between cow's milk and gelatin, but specific IgE to gelatin was absent in these children.

Eventually, specific IgE to egg became negative in two of our three cases. Therefore, it is not possible to attribute precisely the reactions to the presence of egg proteins in the vaccine. This observation points that even the tolerant children with low levels of positive specific IgE against egg may experience a reaction after vaccine. Furthermore, we do not have egg protein measurements in the lots that have been used for vaccination of these children. Therefore, we cannot claim a cause and effect relationship between egg allergy and MMR vaccination in our cases. Apparently, however, the reaction was caused by at least one component in the vaccine. The vaccines injected in Case 1 and Case 3 have the same lot numbers, which support the opinion that the vaccine may include some components causing reactions. Obviously, it would make sense to test these children with the vaccine. However, parents were reluctant and did not consent the procedure.

Whatever the underlying mechanism may be, these cases suggest the possibility of a clinical reaction to MMR vaccine in children sensitized to egg and cow's milk. This observation bears some resemblance to the report by Patja et al., which suggested that the patients who developed allergic reaction to MMR had positive specific IgE to gelatin, egg, chicken or cow's milk. In this report, reactions were also reported in cases who can tolerate egg. Therefore, the negative specific IgE to hen's egg in our patients in the course of their follow-up does not exclude the possibility of the anaphylactic reaction being caused by egg's protein.

Even though the mechanism remains undefined, our report suggests that children sensitized or allergic to food may develop reactions following MMR vaccination. Therefore, we recommend that all children not only those who were sensitized to foods should receive the MMR vaccination in a setting that is equipped to deal with anaphylactic reactions. As stated by WHO in immunization safety surveillance, 'Each vaccinator must have an emergency kit with adrenaline, and be familiar with its dosage and administration'.

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