

# Anaphylaxis to Baked Milk: A Case Presentation and Review of Literature

Andrew O'Keefe, MD, Christine Lejtenyi, MD, Moshe Ben-Shoshan, MD, MSc\*

Division of Pediatric Allergy and Clinical Immunology, Department of Pediatrics, McGill University Health Center, Quebec, Canada

## Abstract

**Introduction:** Milk allergy is the most common food allergy among young children, affecting 2% to 8.4% of children. Most (75%) milk-allergic children are able to tolerate milk protein that has been denatured through heating. In addition, most children will outgrow their milk allergy, with 79% tolerating milk by age 16 years. The inclusion of extensively heated milk, or baked milk, in the diet is important as it improves quality of life and may hasten tolerance to milk in its usual pasteurized form.

**Case presentation:** We describe a 17 year-old male with long-standing history of milk allergy, who strictly avoids milk products. Upon challenge with baked milk, he developed severe anaphylaxis including hypotension, necessitating treatment with epinephrine, supplemental oxygen, IV fluids, and salbutamol.

**Conclusion:** Anaphylaxis to milk, even in extensively heated forms, can be a life threatening problem and appropriate management is crucial. Food challenge remains the gold-standard for the diagnosis of food allergy. While investigations such as skin prick testing and specific IgE levels can help stratify risk, there is limited data available for these regarding baked milk. Baked milk challenge is an important diagnostic test as tolerance to baked milk improves quality of life and hastens resolution of milk allergy. Food challenges are safe, but carry the risk of inducing severe anaphylaxis. As such, food challenges must be carried out in a setting where these reactions can be managed appropriately.

## Introduction

Milk allergy is the most common food allergy among young children, affecting 2% of children and up to 8.4% of those with atopic dermatitis [1,2]. Previously, milk allergic children were advised to strictly avoid foods that contain milk and traces of milk products. However, more recent studies demonstrated that 75% of milk allergic children are able to tolerate extensively heated (baked) milk products [3]. Distinguishing patients who tolerate baked milk is important, as they are able to liberalize their diet and improve their quality of life. Moreover, there is evidence that inclusion of baked milk in the diet accelerates resolution of cow's milk allergy. Kim et al. found that subjects who tolerated baked-milk were 28 times more likely to become unheated-milk tolerant compared to baked-milk reactive subjects [4]. It is thought that heated proteins act as a "natural immunotherapy" and thus hasten tolerance in milk allergic individuals. Examination of specific IgE and IgG<sub>4</sub> profiles in baked milk tolerant subjects supports this theory [4].

In addition, although many infants with milk allergy will outgrow the allergy, the natural history of milk allergy appears to be changing. In 1990, Host and Halcken demonstrated a 75% resolution of milk allergy by 3 years [5], whereas a study in 2007 demonstrated a rate of 79% by age 16 years [6].

## Case Presentation

A 17 year old male with known milk and peanut allergy as well as eosinophilic esophagitis underwent an open food challenge to baked milk in the Allergy Clinic. Prior to challenge he had been avoiding milk since infancy, including all products containing milk. At age 3 he had anaphylaxis to bread containing milk. Previous investigations revealed a Skin Prick Test (SPT) to milk extract with wheal measuring 9 mm and 30 mm erythema. Specific IgE to milk was 1.88 kUa/L. On the day of the challenge, SPT using dairy containing baked goods (muffin baked with milk to be used for oral challenge) resulted in an 8mm wheal and 23mm flare. His eosinophilic esophagitis was well controlled on Flovent, 250 mcg/day, and he had some mild rhinitis but was otherwise well with no pathological findings on physical exam.

For the challenge, we used muffins that had been prepared at

home, containing 1 cup of milk for 8 muffins, baked at 350 minutes. The patient tolerated the initial dose of 1 teaspoon of muffin and was advanced to 1 1/2 teaspoons. A few minutes after ingestion he developed erythematous, pruritic skin, abdominal pain and nausea as well as chest tightness and a general sense of malaise. There was no sign of respiratory distress, and his vital signs were stable (Respiratory Rate (RR) 18 breaths/minute, Heart Rate (HR) 68 beats/minute, and Blood Pressure (BP) 120/70 mmHg). As such, he was treated with 0.3 mg epinephrine Intra Muscularly (IM). Following treatment there was minimal improvement in his symptoms, and his physical examination remained unchanged so a second dose of epinephrine (0.3 mg, IM) was administered 30 minutes later. He began to feel some improvement in his symptoms, and was treated with 50 mg hydroxyzine orally. Subsequently, he began to vomit profusely and developed urticaria. Upon sitting to vomit, he felt lightheaded and was found to be hypotensive at 80/50 mmHg. He was placed in the recumbent position and his blood pressure improved, initially only to 85/60 mmHg, then to 106/50 mmHg. He was transferred to the emergency room for further management (Figure 1). On arrival in ER his vitals were BP 113/74 mmHg, HR 115 beats/minute, RR 24 breaths/minute and O<sub>2</sub> saturation 97% in room air. On examination he had generalized erythema and decreased air entry bilaterally at the base of the lungs, though no wheeze. He was treated with intravenous fluids normal saline (N/S bolus 1200 mL, then D<sub>5</sub>NS 105 mL/hr), as well as nebulized salbutamol (1 mL in 2.5 mL N/S), and solucortef (65 mg, IV). His air entry improved and

**\*Corresponding author:** Moshe Ben Shoshan, MD, MSc, Division of Pediatric Allergy and Clinical Immunology, Department of Pediatrics, The Montreal Children's Hospital, McGill University Health Center, Montreal, Quebec, Canada, Tel: 514-412-4400(23151); E-mail: [moshebenshoshan@gmail.com](mailto:moshebenshoshan@gmail.com)

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**Figure 1:** On arrival in the emergency room, the patient was flushed, with an urticarial rash.

he remained well during at 8 hour observation period, after which he was discharged home. A tryptase level drawn during the reaction was found to be elevated, at 29.8 micrograms/liter. Tryptase level drawn 3 weeks after reaction were within normal limits (2.3 micrograms/liter).

## Discussion of Case and Literature Review

Cow Milk (including baked milk) allergy (CM) is a major cause of anaphylaxis and accounts for up to 13% of fatal food-induced anaphylaxis [7]. Up to 50% of anaphylactic reactions to milk are due to accidental exposure in individuals who are known to have milk allergy [8]. Appropriate diagnosis and prompt management of milk allergy is crucial. Although initial studies suggest that up to 75% of children will become milk tolerant by 3 years [5], recent studies have shown a later acquisition of tolerance to CM in a subset of patients [6]. Milk allergy can be divided into two broad phenotypes: baked-milk tolerant subjects with transient milk allergy who produce IgE to conformational, heat-labile epitopes, and baked-milk reactive subjects with persistent milk allergy who produce IgE to sequential, heat-stable epitopes [4]. It is important to recognize that children reactive to baked milk have a more severe phenotype of cow milk allergy, with a higher risk of severe anaphylaxis and a more protracted course [9]. The development of an allergic reaction after baked milk ingestion involving more than one organ system meets the diagnosis criteria of anaphylaxis in this patient [1]. Elevated tryptase level, a mast cell mediator, supports this diagnosis [2,3].

Although it is crucial to differentiate between these two groups of individuals with milk allergy, there is little data published regarding the utility of skin tests or specific IgEs in these patients. In 2012, Bartnikas et al. found that there was no statistically significant difference in milk protein skin or blood specific IgE test results among children who passed or failed baked milk challenges [10]. In a larger cohort, Ford et al. reported that subjects who were baked milk reactive had higher levels of casein-specific IgE, greater levels of basophil reactivity, and larger wheal diameter in SPT than did baked-milk tolerant subjects [11]. Recently it was suggested that casein-specific IgE levels may be helpful and that a concentration of less than 0.94 kU<sub>A</sub>/L (negative decision point) indicates a very low risk of reacting to baked milk [9]. However, these tests are not yet available for routine clinical use. As such, food challenge, or provocation testing, remains the gold-standard for the diagnosis of food allergy.

Our patient has comorbid eosinophilic esophagitis (EoE), a chronic disease characterized by eosinophilic inflammation of the esophagus [12]. Although food is considered an important trigger with milk, egg, wheat, and soy listed as the most common foods, identification of the specific food triggers remains a challenge [13]. There is little data published on whether baked-milk is tolerated by subjects with cow's milk mediated EoE (CMME). In a small cohort, Leung et al. reported that 73% of CMME (n=11/15) maintained histologic remission of their EoE after baked milk had been reintroduced to the diet for 6 weeks [14].

Our patient demonstrated severe anaphylaxis during baked-milk challenge including hypotension, a very rare occurrence. Mauro et al. reviewed 526 food challenges, where 48.3% of subjects reacted. None of the subjects in their cohort had cardiovascular symptoms [15]. Prompt administration of intramuscular epinephrine is the treatment of choice for any anaphylactic reaction [16,17]. Patients diagnosed with baked milk allergy should avoid all milk and dairy products diligently [18], and carry an epinephrine auto-injector at all times [19].

In conclusion, milk allergy in general and baked milk allergy in particular is an important life threatening condition. Baked-milk challenge remains the only way to distinguish baked-milk tolerant from reactive subjects, and is an important step in the management of these patients. Most patients are able to tolerate baked milk thus liberalizing their diet, improving their quality of life and hastening resolution of their allergy. Food challenge is safe, but must be undertaken in a facility that can manage potential complications.

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