

Pistachio allergens: the long journey between mother and daughter

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The protective and beneficial effect of breastfeeding on neonate global health is widely accepted. However, whether breastfeeding protects against the development of allergies remains controversial [1]. It has been hypothesized that early sensitization to food allergens may be due to breastfeeding ingestion, although it can also be intrauterine or transcutaneous.

We present an exceptional case of a 2-year-old girl who develops facial wheals during some breast milk feedings. She presents a history of cow's milk allergy, currently resolved, and egg allergy. The child had completed food diversification and continued to receive breastfeeding on demand. She had no personal history of atopic dermatitis or asthma. At 22 months of age, the patient presented two episodes of facial hives during breastfeeding that were resolved spontaneously within two hours. These events occurred separated by two months, and she tolerated the intermediate feedings of breast milk. Both times, the mother had eaten a large quantity of pistachios an hour earlier. The patient had previously tolerated almond milk, crushed hazelnuts and sesame; no other nuts had been introduced into the diet.

Breast milk was collected to analyze if the possible presence of pistachio allergens inside could be really capable of inducing and immediate allergy reaction after its ingestion. Considering that the time from ingestion to peak concentration in breast milk

after the ingestion for peanuts, eggs, milk and wheat described in literature is around 1 to 6 hours[2,3] and usually are quickly cleared from breast milk [4], the mother was instructed to consume 100g of pistachio 12, 5 and 1 hour before the collection of 150 ml of breast milk (PBM1h). Subsequently, another 150 ml of breast milk was collected after 24 hours of pistachio intake (PBM24h). A written informed consent document was provided by the mother before beginning the study.

Skin prick tests (SPT) with commercial nut extracts (Leti Pharma Laboratories, Madrid, Spain) and skin prick-prick tests (SPPT) with corresponding collected samples of PBM1h and PBM24h were performed. Total and specific serum IgE (sIgE) to nuts, and peanut, walnut and cashew proteins, were determined by ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden), considering positive values above 0.35 kU_A/L. SPT (mm) were positive for pistachio (12), cashew (11) and walnut (3). Histamine (4), negative control (0). Total serum IgE (30.1kU/L), pistachio (0.99kU/L), cashew (0.39kU/L), walnut (0.6kU/L), peanut (0.09kU/L), rAna o 3(0.42kU/L), rJug r 1(0.49kU/L), rJug r 3(0.01kU/L), rPru p 3(0.01kU/L). SPPT to PBM1h and PBM24h were negative.

An SDS-PAGE IgE immunoblot analysis was performed with patient serum detecting six bands in the pistachio extract with approximate molecular weights of 70, 55, 40, 34, 32, and 28 kDa, and two IgE bands of 55 and 28 kDa in cashew extract (Figure 1, panel 1). Figure 1, panel 2 represents the SDS-PAGE IgE immunoblot analysis incubated with negative control serum.

To clarify the diagnosis, an oral challenge with PBM1h was performed. Breast milk was administered by syringe to avoid skin contact. Ten minutes after the first dose of

breast milk (10ml) was given, the patient developed facial and neck erythema and wheals, which subsided spontaneously after 20 minutes. After instructing the mother to follow a pistachio- and cashew-free diet, the patient had no further reactions with breast milk feedings.

To date, different food allergens have been shown to be present in breast milk. In different studies, ovalbumin has been detected in 59-74% of breast milk samples, cow's milk β -lactoglobulin in 53-63% [2] and peanut proteins in about 48% [4]. Also, ovomucoid [2], alpha-S1-casein [5], gliadin [3] has been among the main allergens described. Pastor-Vargas et al., developed an antibody array capable to detect ten major food allergens in breast milk, demonstrating that a high number of the allergens studied were detected in most of the samples obtained [6]. In our case, although we're lacking proper mass spectrometry-based identification, the 55kDa band detected could correspond to Pis v 3 (vicilin), and the 32 kDa band with Pis v 2 (legumin), both already described.

Eczema, colic, diarrhea and vomiting are frequent symptoms in exclusively breastfed infants, but few cases of food allergy during exclusive breastfeeding have been reported.

Monti *et al.*, described a case of anaphylaxis in a 4-months-old infant with atopic dermatitis after ingestion of breast milk, whose mother had previously eaten trout [7].

The infant had positive IgE against trout and turbot. González de Olano *et al.* reported a case of allergy after the first ingestion of garlic in a 9-month-old infant without atopy history. However, sensitization through breastfeeding could not be confirmed because garlic allergens were not identified in breastmilk [8].

Finally, Martin Muñoz *et al.* reported 5 infants who developed symptoms during breastfeeding in which the presence of specific IgE to allergens that had not been previously introduced in the diet (milk, egg and peanut) was demonstrated. After instructing to eliminate these foods from the mother's diet, the children did not present any more symptoms during lactation [9].

We present a case of an immediate allergic reaction after breastfeeding due to pistachio allergy. Based on the clinical data and the results of the challenge with breast milk, we suggest the hypothesis of a possible pistachio sensitization via breastfeeding

A negative SPPT with PBM1h and PBM24h could be justified by the possibility that it did not contain enough allergen for a positive prick but did contain enough allergen for a positive challenge (PBM1h).

Declaration of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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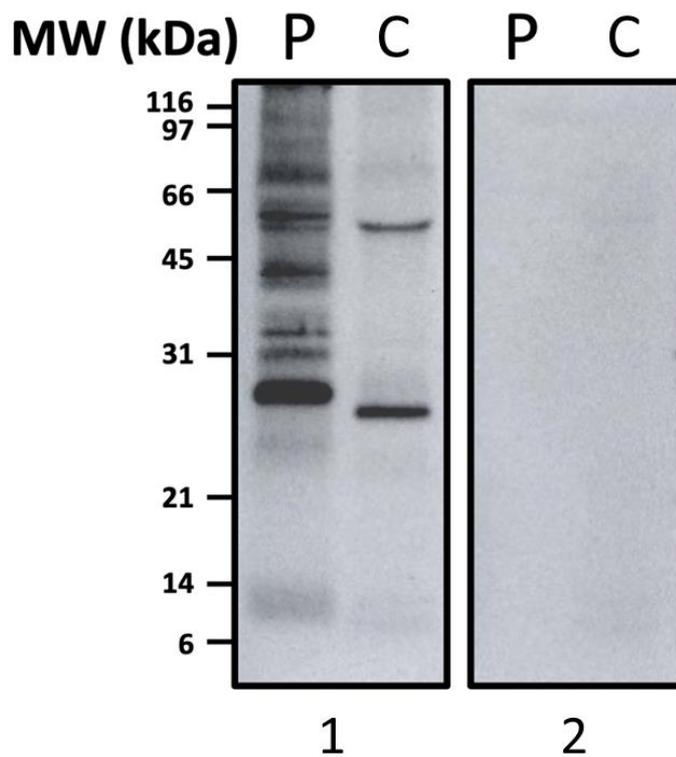
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Figure 1. IgE immunoblot assay with pistachio and cashew extracts.



Panel 1: incubated with patient's serum.

Panel 2: Incubated with negative control serum.

C, cashew extract; **MW,** molecular weight; **P,** pistachio extract.