

Clinical Communications

First reported allergic reaction in the United States to pili nut (*Canarium ovatum*)

Elizabeth J. Cho, BS, and Angela L. Chang, MD

Clinical Implications

- This is the first documented allergic reaction to pili nut in the United States. Pili nut is in the same phylogenetic order as cashew and pistachio and hypothesized to be cross-reactive with cashew and/or pistachio.

We describe the first documented case of an allergic reaction in the United States to pili nut (*Canarium ovatum*) in a 2-year-old female child of Caucasian descent with mild atopic dermatitis, egg allergy, and newly diagnosed cashew and pistachio allergy.

Around 6 months of age, she developed hives and emesis with scrambled egg introduction. Skin prick testing to egg extract at 7 months of age was positive with 9 mm wheal and 28 mm flare (9/28) with adequate saline and histamine controls and egg white specific IgE of 1.32 kU/L. She passed a baked egg muffin oral food challenge (OFC) at 15 months and continued frequent ingestion of baked egg-containing foods with avoidance of other forms of egg (due to family preference). She did not have any other known allergies.

At 2 years of age, the patient was in her usual state of health. She was introduced to a plant-based, nondairy yogurt and also ingested cereal and milk that she tolerates on a daily basis. The yogurt ingredient label reads as follows: coconut (water, cream, and powder), strawberry, plantains, pili nut, cassava root powder, lime juice, salt, and live cultures. The allergen label stated that the yogurt contained pili nut and coconut; there was no precautionary allergen labeling. Within 5 minutes of ingesting approximately 2 ounces of yogurt, she developed hives on her face. In the next 10 minutes, she developed rhinorrhea and coughing. She was treated with diphenhydramine 25 mg and an epinephrine autoinjector 0.15 mg and was taken to a local emergency department by ambulance. She received famotidine and prednisolone and was discharged after 3 hours of observation with a 3-day course of prednisolone.

At a later date, the patient was referred back to Pediatric Allergy for evaluation of the recent allergic reaction. The family stated that the patient had previously tolerated all other ingredients of the yogurt, including coconut, strawberry, plantains, cassava (in tapioca in the remote past), and lime. In addition to baked egg-containing foods, she also tolerated cow's milk, wheat, soy, peanut, some tree nuts (almond, walnut, pine nut), fish, and shellfish. She had not yet ingested other tree nuts, including cashew and pistachio, in part because the mother has cashew, pistachio, and pecan allergies. Skin prick testing was performed using extracts to egg white, coconut, hazelnut, pecan, cashew, and pistachio, with prick-prick testing performed to

Brazil nut, macadamia nut, pine nut, and pili nut. Saline and histamine controls were adequate. The patient had positive skin prick test results to cashew (16/26), pistachio (21/34), and pili nut (4/16). All other skin tests were negative, including coconut. Serum testing revealed egg white IgE of 0.25 kU/L, cashew IgE of 65.6 kU/L with Ana o 3 60.2 kU/L, and pistachio IgE of 53.4 kU/L. To definitively evaluate for pili nut allergy, the family was offered an OFC but declined given the recent reaction and history of tolerance of all other ingredients in the yogurt.

Pili nuts were originally found and cultivated in the Bicol region of the Philippines, where they are traditionally consumed as glazed candies and in desserts. They recently entered the Western diet and are available in the plant-based yogurt, whole nuts, and nut butters. They have been popularized through the ketogenic diet.

Although the Food and Drug Administration (FDA) categorizes pili nut as a tree nut, a recent report from the National Academies of Sciences recommended that consideration be given to removing a subset of tree nuts including pili nuts from the FDA's categorization due to a lack of data supporting their allergenicity.¹ Phylogenetically, pili nut, cashew, and pistachio are in the Sapindales order, but pili nut is the Burseraceae family, whereas cashew and pistachio are in the Anacardiaceae family.² The major allergens in cashew are Ana o 1, Ana o 2, and Ana o 3 seed storage proteins, and Ana o 3 is thought to be a good predictor for clinical cashew allergy.^{3,4} Although the 11S globulin has been identified as the main pili nut storage protein, no studies have been performed to determine cross-reactivity with cashew, pistachio, or other tree nuts.⁵

Pili nut was the most likely cause of this patient's anaphylaxis because she had tolerated all of the other ingredients before and had subsequently tolerated coconut again. It remains unclear how she developed sensitization to pili nut, as she had no known prior exposure. In general, hypothesized routes of sensitization include cutaneous contact, *in utero* transfer, breastfeeding exposure, or through cross-reacting allergens. Given that pili nut, cashew, and pistachio are in the same phylogenetic order, we hypothesize that these nuts are cross-reactive, and the patient likely developed the reaction due to extreme sensitivity to cashew and pistachio, as evidenced by her large positive skin tests and significantly elevated cashew, Ana o 3, and pistachio IgE levels. It is less likely that she developed cutaneous sensitization to pili nut as no one else in the family had consumed it before, including the mother who did not ingest the yogurt.

Limitations to the case include the lack of a pili nut OFC, possible cross-contamination of the food, inability to fully exclude cassava allergy due to the patient's limited exposure to tapioca, and a lack of evidence supporting clear cross-reactivity between pili nut and cashew and/or pistachio. Representatives from the yogurt company disclosed that no other tree nuts, including cashew and pistachio, are present in the manufacturing facility, but it is possible that the ingredients themselves had some cross-contamination.

To our knowledge, this is the first probable pili nut allergy in the United States. More work is needed to better understand the prevalence of pili nut allergy and if allergen labeling is warranted.

As pili nut is gaining popularity in the Western diet and cashew and pistachio allergies are increasing in prevalence, inhibition immunoassays are needed to determine if there is cross-reactivity between these nuts.³ We hope to increase awareness of this tree nut and its potential allergenicity to decrease unexpected allergic reactions to pili nuts.

Department of Pediatrics, UCSF Benioff Children's Hospital, University of California, San Francisco, San Francisco, Calif

No funding was received for this work.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication February 29, 2020; revised August 28, 2020; accepted for publication August 31, 2020.

Available online ■ ■

Corresponding author: Angela L. Chang, MD, University of California, San Francisco, Box 0434, 550 16th St, San Francisco, CA 94158. E-mail: angela.chang@ucsf.edu.

2213-2198

Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaip.2020.08.062>

REFERENCES

1. National Academies of Sciences, Engineering, and Medicine. Finding a Path to Safety in Food Allergy: Assessment of the Global Burden, Causes, Prevention, Management, and Public Policy. Washington, DC: The National Academies Press; 2017.
2. Cho CY, Oles C, Nowatzke W, Oliver K, Garber EAE. Cross-reactivity profiles of legumes and tree nuts using the xMAP® multiplex food allergen detection assay. *Anal Bioanal Chem* 2017;409:5999-6014.
3. Van Der Valk JPM, Dubois AEJ, Gerth Van Wijk R, Wichers HJ, De Jong NW. Systematic review on cashew nut allergy. *Allergy* 2014;69:692-8.
4. Lange L, Lasota L, Finger A, Vlajnic D, Büsing S, Meister J, et al. Ana o 3-specific IgE is a good predictor for clinically relevant cashew allergy in children. *Allergy* 2017;72:598-603.
5. Marcone MR, Kakuda Y, Jahaniaval F, Yada RY, Montevirgen LS. Characterization of the proteins of pili nut (*Canarium ovatum*, Engl.). *Plant Foods Hum Nutr* 2002;57:107-20.