

- British parents, teachers and children. *J Abnorm Child Psychol.* 2010;38:1179–1191.
- [8] Annesi-Maesano I, Zhou C, Baiz N, et al. Externalizing and internalizing behavioural problems related to asthma in school children. *Allergy.* 2013;68:1471–1474.

- [9] Lien L, Green K, Thoresen M, Bjertness E. Atopic conditions and mental health problems: a 3-year follow-up study. *Eur Child Adolesc Psychiatry.* 2010;19:705–713.
- [10] DunnGalvin A, Gaffney A, Hourihane JO. Developmental pathways in food allergy: a new theoretical framework. *Allergy.* 2009;64:560–568.

## First case of airborne-induced anaphylaxis triggered by fruit



The common fig (*Ficus carica*) is the fruit of the fig tree, a species of the genus *Ficus* from the Moraceae family. Although native to southwestern Asia, it has been cultivated since ancient times in the Mediterranean basin, where it is often consumed.

Few allergic reactions to fig have been reported. Symptoms have ranged from oral allergy syndrome to anaphylaxis, always occurring after ingestion<sup>1,2</sup> and mainly in patients sensitized to weeping fig (*Ficus benjamina*), which is often used in homes as a decorative plant.<sup>3</sup> We present the case of a patient with anaphylaxis after manipulating, not eating, figs. In addition, we found a sensitizing protein not previously described.

The patient was a 10-year-old boy who was playing and handling figs under a fig tree (striking them with a racket as if they were tennis balls), but he did not eat them. He suddenly presented itching on the upper limbs and face, sneezing, eyelid and lip edema, followed by dysphagia, coughing with dyspnea, and audible wheezing but without dizziness. He was immediately taken to the emergency department, where he was diagnosed with anaphylaxis and treated with intramuscular adrenalin, dexchlorpheniramine, and methylprednisolone. He showed improvement after 30 minutes and the episode resolved in 2 hours. The patient was referred to his pediatrician, who prescribed a preloaded auto-injector of adrenalin and referred him to our allergy service. A possible insect bite was ruled out because the parents denied that their son had ever been bitten by a tick, they lived in an urban environment, and on physical examination no sting was found. The patient denied any food ingestion or the administration of any drug in the previous 8 hours. The parents denied that their son had ever eaten a fig. The parents referred to the fact that their son often played in a garden where there is a fig tree, and that a few months previously he presented an episode of skin lesions that were diagnosed as acute urticaria in the emergency department and successfully treated with intramuscular dexchlorpheniramine. At that time the episode was not associated with a specific trigger.

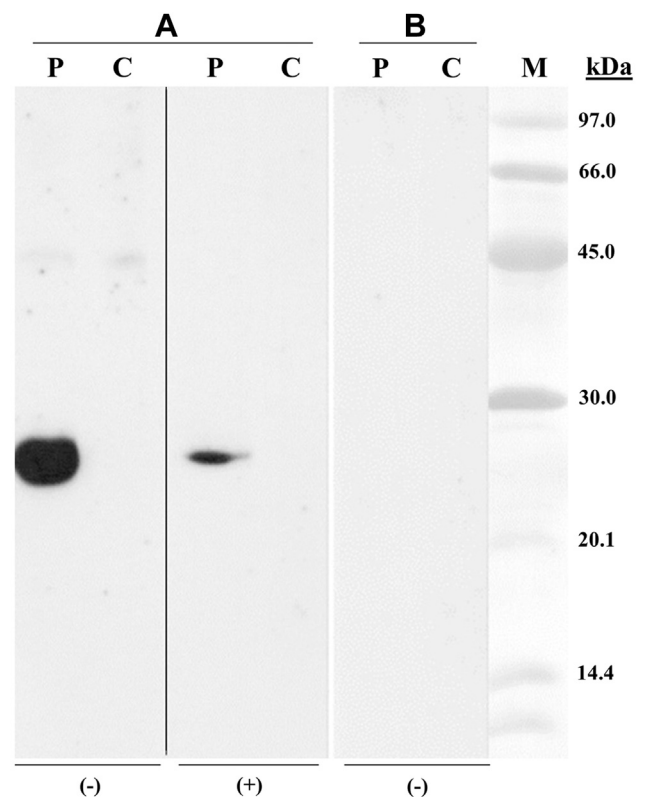
Skin prick tests were performed with a common battery of aeroallergens (house dust mites, fungal spores, grass and tree pollens, and animal epithelia; ALK-Abelló, Madrid, Spain) and food allergens (milk, egg, cereals, fruits, nuts, vegetables, legumes, fish, seafood, and spices), the results of which were positive only for olive tree pollen. The parents provided a fig and a leaf from the implicated fig tree. An extract of the fig and leaf (1/10 w/v) was obtained. The prick-prick test result of the fig was positive (7 × 7 mm) for the patient and negative for 5 atopic controls. Skin prick test results with the fig and fig leaf extracts also were positive for the patient and negative for the controls.

The in vitro study (ImmunoCAP, ThermoScientific, Barcelona, Spain) showed a total IgE level of 93.6 kU/L, a tryptase level of 4.12 mgA/L, and a fig-specific IgE level of 15.5 kUA/L. Specific IgE test reactions to mulberry, latex, and rHev (1.3, 6.01, and 6.02), galactose- $\alpha$ (1.3)-galactose, and bee, *Polistes*, and *Vespula* venoms were negative (<0.35 kUA/L). The patient had never eaten mulberries and denied having symptoms after contact with latex.

An ISAC assay (ImmunoCAP, ThermoScientific) was negative for all 112 available allergens except Ole e 1 (including profilins, polcalcins, and lipid transfer proteins).

Sodium dodecylsulfate polyacrylamide gel electrophoresis immunoblotting with the fig extract under reducing and non-reducing conditions showed a 28-kDa IgE binding band (which was much more intense under nonreducing conditions; Fig 1). This protein was identified as a cysteine protease by tandem mass spectrometry as previously described<sup>4</sup> in the proteomic service of the Complutense University of Madrid, a member of the ProteoRed Network. To study the presence of serum-specific IgE against ficin, a well-known cysteine protease from the fig tree, sodium dodecylsulfate polyacrylamide gel electrophoresis immunoblotting (under nonreducing conditions) was performed with ficin; results were negative (Fig 1). Because ficin is derived from fig latex, the specific IgE was detected by immunoblotting, and the IgE-reactive band was absent in the immunoblots of the fig leaf and branch extracts (results not shown), we judged that the cysteine protease detected could not be ficin.

Cysteine proteases have been previously described as allergens in several allergenic sources. They behave as allergens when ingested and inhaled. Some examples are Der p 1 (24 kDa); Blo t 1



**Figure 1.** Sodium dodecylsulfate polyacrylamide gel electrophoresis immunoblotting. (A) Extract from fig. (B) Ficin from fig tree. Lane P, patient serum; lane C, control serum (pool of sera from nonatopic subjects). (–) Samples without 2-mercaptoethanol, (+) samples with 2-mercaptoethanol.

**Disclosures:** Authors have nothing to report.

(39 kDa); Amb a 11 (37 kDa); Ana c 2 (25 kDa); Car p 1 (23.5 kDa), and Act d 1 (30 kDa; [www.allergome.org](http://www.allergome.org)). Some investigators have stated that proteases, even at a low dose, can act as an adjuvant in T-helper cell type 2 respiratory responses.<sup>5</sup>

Until now, 4 fig allergens have been described: Fic c 1, a PR-10 molecule<sup>6</sup>; Fic c 4, a profilin; a Fic lipid transfer protein<sup>7</sup>; and Fic c, ficin, a cysteine protease. This last protein was isolated and characterized in 1968,<sup>8</sup> but thus far it has not been sequenced. Protease allergens can activate airway mucosal responses, thus increasing the allergenicity<sup>9</sup> and making them capable of inducing severe reactions.

We have identified an IgE-binding protein with cysteine protease activity that had not been previously described. Prior sensitization could have occurred in the same manner because the patient had previously played with and handled figs on several occasions; on one of these occasions he developed an episode of urticaria, although it was not then attributed to fig. Some fig fragments could have reached the oral mucosa. Although the patient and his parents denied this possibility, it is impossible to exclude it. Food airborne anaphylactic reactions are unusual and most are related to cooked foods owing to aerosolized or vaporized particles.<sup>10</sup> In the present case, the implicated food was the native fig, probably owing to sprayed particles induced by its manipulation.

In conclusion, we present an exceptional case of airborne anaphylaxis to an uncooked food, triggered by a fig, and induced by a new protein that has not yet been described. To our knowledge, this is the first case of airborne anaphylaxis caused by a fruit.

Eva M. Macías, MD, PhD\*  
Omar Sierra-Salgado, MD†  
Borja Bartolomé, BSc, PhD‡  
Carlos Pastor-Vargas, PhD§  
Francisco J. Muñoz-Bellido, MD, PhD\*  
Ignacio Dávila, MD, PhD\*

\*Allergy Department  
University Hospital of Salamanca-IBSAL

†Allergy Department  
University Hospital of Salamanca  
Salamanca, Spain

‡R&D Department  
Bial-Aristegui  
Bilbao, Spain

§Department of Immunology  
Instituto de Investigación Sanitaria  
Fundación Jiménez Díaz  
Madrid, Spain  
[evammacias@usal.es](mailto:evammacias@usal.es)

## References

- [1] Dechamp C, Bessot JC, Pauli G, Deviller P. First report of anaphylactic reaction after fig (*Ficus carica*) ingestion. *Allergy*. 1995;50:514–516.
- [2] Oei HD, Tjiook SB. A case report of an anaphylactic reaction after fig (*Ficus carica*) ingestion. *Allergy*. 1998;53:85.
- [3] Gandolfo M, Baeza M, De Barrio M. Anaphylaxis after eating figs. *Allergy*. 2001;56:462–463.
- [4] Pastor C, Cuesta-Herranz J, Cases B, et al. Identification of major allergens in watermelon. *Int Arch Allergy Immunol*. 2009;149:291–298.
- [5] Cunningham PT, Elliot CE, Lenzo JC, et al. Sensitizing and Th2 adjuvant activity of cysteine protease allergens. *Int Arch Allergy Immunol*. 2012;158:347–358.
- [6] Hemmer W, Focke M, Marzban G, Swoboda I, Jarisch R, Laimer M. Identification of Bet v 1–related allergens in fig and other *Moraceae* fruits. *Clin Exp Allergy*. 2010;40:679–687.
- [7] Asero R, Mistrello G, Roncarolo D, Amato S. Detection of some safe plant-derived foods for LTP-allergic patients. *Int Arch Allergy Immunol*. 2007;144:57–63.
- [8] Englund PT, King TP, Craig LC, Walti A. Studies on ficin. I. Its isolation and characterization. *Biochemistry*. 1968;7:163–175.
- [9] Jacquet A. Interactions of airway epithelium with protease allergens in the allergic response. *Clin Exp Allergy*. 2011;41:305–311.
- [10] Fiocchi A, Bouygue GR, Restani P, Gaiaschi A, Terracciano L, Martelli A. Anaphylaxis to rice by inhalation. *J Allergy Clin Immunol*. 2003;111:193–195.

## Poor utility of the atopy patch test in infants with fresh rectal bleeding



In healthy small infants with fresh rectal bleeding, the first suspicion may be food protein–induced proctocolitis (FPIP), which is a benign inflammatory colitis that results from a non–IgE-mediated immune reaction to ingested foreign proteins, mainly, cow's milk protein.<sup>1–5</sup> In clinical practice, 3 criteria need to be fulfilled for an FPIP diagnosis: (1) small and fresh rectal bleeding in a relatively healthy neonate for more than 4 days, (2) no other causes of rectal bleeding, and (3) the disappearance of rectal blood after changing diet.<sup>2–4</sup> Recently, some publications have suggested the need for an oral food challenge (OFC) and the recurrence of rectal bleeding to confirm FPIP.<sup>1,5</sup>

The food atopy patch test (APT) has been used by many researchers as a tool to help the diagnosis of non–IgE-mediated food allergies.<sup>6</sup> Controversial results are found in previous studies, but only a few discuss its utility in FPIP.<sup>5,6</sup> The aim of our study was to evaluate the utility of a cow's milk APT in infants with fresh rectal bleeding with FPIP criteria compared with the OFC.

Thirty-one infants with small and fresh rectal bleeding were recruited from the Food Allergy Clinic of the Universidade Federal de Uberlândia between March 2013 and February 2014. Inclusion criteria were signing the informed consent form and fulfilling criteria for FPIP. The exclusion criteria were another diagnosis characterized by rectal bleeding, such as anal fissure.

The study was designed in 3 stages. First, a food elimination test was performed for 4 weeks when FPIP was suspected. In formula-fed patients, their diet was changed to an amino acid–based elemental formula. Second, in breastfeeding mothers, cow's milk was eliminated from the diet, and a cow's milk APT was performed. Third, an OFC was performed for the confirmation of FPIP.

The cow's milk APT was performed using fresh cow's milk,<sup>6</sup> 2 g of powdered skim cow's milk with 2 g of petrolatum vehicle,<sup>6</sup> and 2 g of powdered skim cow's milk with 2 mL of isotonic saline solution vehicle.<sup>7</sup> These preparations were attached to 8-mm Finn chambers, which were adhered to the upper region of the patient's back and removed after 48 hours, and the reading was performed 24 hours after. The same researcher performed and read all APTs following the technique described previously.

The European Society for Paediatric Gastroenterology Hepatology and Nutrition Gastrointestinal Committee recommend an open OFC when objective symptoms were expected, as in the case of small and fresh rectal bleeding.<sup>5</sup> In-patient OFCs were performed by administering crescent doses of cow's milk–based infant formula (10 mL, 20 mL, 30 mL, and 40 mL) every 20 minutes. After discharge, the patients received cow's milk formula as a replacement to amino acid–based elemental formula. In exclusively breastfeeding mothers, cow's milk was reintroduced from the diet. The patients were evaluated 2 times after OFC (1 and 4 weeks after

**Disclosures:** Authors have nothing to disclose.