

“NSAIDs-exacerbated urticaria/angio-oedema” using the “gold standard” oral provocation test, which yielded negative results for drug hypersensitivity.<sup>6</sup>

Thyroid autoantibodies (TA) have a prevalence of about 3–6% in the general population versus about 15–30% in chronic idiopathic urticaria (CIU) patients, suggesting that these two disorders are associated. The mechanisms for the apparent association between CIU and serological evidence of thyroid autoimmunity are not clear.<sup>9</sup> The effects of replacement treatment for hypothyroidism on clinical symptoms of urticaria are still controversial. Leznoff et al. reported that the L-thyroxine therapy improved clinical symptoms of CIU.<sup>10</sup> In our atopic patient, instead of NSAIDs hypersensitivity, the concurrence of HT might possibly be responsible for his urticaria/angio-oedema, which probably reflects a shared genetic predisposition toward the development of autoimmune disease. Also levothyroxine treatment had a positive influence on the clinical course of his urticaria.

This is a unique presentation of multifocal bullous FDE due to etodolac, which has not been previously described in the literature. We propose that etodolac should be added to the list of drugs causing multifocal bullous FDE, so that these lesions can be correctly recognised to indicate the appropriate therapy. This case also illustrates the importance of following the stepwise approach to the diagnosis of hypersensitivity to NSAIDs, both while taking the history as well as deciding on the implementation of diagnostic procedures.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this investigation.

**Confidentiality of data.** The authors declare that no patient data appear in this article.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

## Conflict of interest

The authors have no conflict of interests to declare.

## References

1. Sehgal VN, Srivastava G. Fixed drug eruption (FDE): changing scenario of incriminating drugs. *Int J Dermatol.* 2006;45:897–908.
2. Layton D, Marshall V, Boshier A, Friedmann P, Shakir SA. Serious skin reactions and selective COX-2 inhibitors: a case series from prescription-event monitoring in England. *Drug Saf.* 2006;29:687–96.
3. Yeo SN, Kang SJ, Lee AY. Nonpigmenting fixed drug eruption to etodolac. *Korean J Dermatol.* 1999;37:673–5.
4. Ozkaya E, Keles S. Etodolac-induced pigmenting fixed drug eruption. *Clin Exp Dermatol.* 2007;32:332–3.
5. Colombo G, Yacoub MR, Burastero SE, Garattini E, Girlanda S, Saporiti N, et al. Multiple drug hypersensitivity: insight into the underlying mechanism and correlation with autoimmune diseases. *Eur Ann Allergy Clin Immunol.* 2009;4:50–5.
6. Kowalski ML, Makowska JS, Blanca M, Bavbek S, Bochenek G, Bousquet J, et al. Hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs) - classification, diagnosis and management: review of the EAACI/ENDA and GA2LEN/HANNA. *Allergy.* 2011;66:818–29.
7. Shiohara T, Mizukawa Y. Fixed drug eruption: a disease mediated by self-inflicted responses of intraepidermal T cells. *Eur J Dermatol.* 2007;17:201–8.
8. Duarte AF, Correia O, Azevedo R, do Carmo Palmares M, Delgado L. Bullous fixed drug eruption to etoricoxib-further evidence of intraepidermal CD8+ T cell involvement. *Eur J Dermatol.* 2010;20:236–8.
9. Mozena JD, Tiñana A, Negri J, Steinke JW, Borish L. Lack of a role for cross-reacting anti-thyroid antibodies in chronic idiopathic urticaria. *J Invest Dermatol.* 2010;130:1860–5.
10. Leznoff A, Sussman GL. Syndrome of idiopathic chronic urticaria and angioedema with thyroid autoimmunity: a study of 90 patients. *J Allergy Clin Immunol.* 1989;84:66–71.

I. Koca Kalkan<sup>a,\*</sup>, A.F. Kalpaklioglu<sup>a</sup>, P. Atasoy<sup>b</sup>, A.A. Karabulut<sup>c</sup>

<sup>a</sup> Kirikkale University School of Medicine, Division of Immunologic and Allergic Diseases, Kirikkale, Turkey

<sup>b</sup> Kirikkale University School of Medicine, Department of Pathology, Kirikkale, Turkey

<sup>c</sup> Kirikkale University School of Medicine, Department of Dermatology, Kirikkale, Turkey

\*Corresponding author.

E-mail address: [ilkay.koca@gmail.com](mailto:ilkay.koca@gmail.com) (I. Koca Kalkan).

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## Anaphylactic reaction to bell pepper (*Capsicum annuum*) in a patient with a latex-fruit syndrome

To the Editor,

Bell pepper (*Capsicum annuum*) is a species belonging to the family of *Solanaceae*. This family is native of Central America and northern South America. Food allergy to some spices is relative frequent,<sup>1</sup> but very few cases of food allergy to

bell peppers have been described.<sup>2–7</sup> Besides, occupational allergy caused by exposure to bell pepper pollen in greenhouse workers has been published.<sup>8</sup>

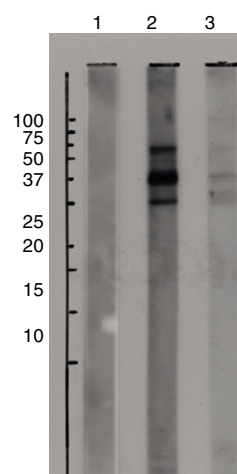
A 33-year-old woman experienced three episodes of facial, palpebral and oropharyngeal angio-oedema with difficulty in breathing and swallowing and generalised urticaria 10 min after eating raw green peppers (included in a salad, a pizza, and a typical Spanish dish called *gazpacho*, respectively). She progressively improved after treatment with corticosteroids and antihistamines. After these episodes she has tolerated the other implicated foods in these reac-

tions except for green and red bell peppers. She had been previously diagnosed in our department with rhinoconjunctivitis and moderate persistent asthma and latex allergy. After the last clinic reaction related with green peppers she has presented four similar clinic episodes. One after eating paprika (dried bell-pepper fruit) seasoned octopus, another one after eating chestnuts, walnuts and a fig and two others with a banana and an avocado, respectively. After the episode with paprika she has tolerated octopus. Before the first clinical episode with green bell pepper she suffered from pruritus and angio-oedema in hands after skin contact with green and red bell peppers, but she ate bell peppers without reaction.

We performed skin prick tests with common allergens (mites, pollens, moulds and epithelia), latex, birch pollen profilin, peach lipid transfer protein and a standard battery of foods (egg, milk, cereals, nuts, fish, fruits, meats, molluscs, crustaceans and vegetables) including paprika. Positive results for cat and dog epithelia, latex and paprika were found but were negative for the rest of the allergens tested, including walnut, chestnut and banana. Prick-by-prick tests were performed with green and red fresh peppers and they were positive with both (maximum wheals of 8 and 9 mm, respectively) and negative in 10 control subjects. Total serum IgE was elevated (282 IU/mL) and specific serum IgE detected by ImmunoCAP was positive for latex (1.82 kU/l) and banana (0.44 kU/l) but negative for chestnut and paprika. Specific IgE against an extensive panel of allergens included in the ImmunoCAP ISAC platform was positive for recombinant Hev b 6 (4.1 ISU), Fel d 1 (28 ISU), Fel d 4 (39 ISU), Can f 1 (18 ISU), Can f 2 (19 ISU) and native Mus m 1 (13 ISU) but negative for the rest of the included allergens. Specific IgE against chestnut (Cas s 5) and avocado (Pers a 1) chitinases were determined by the quantitative specific IgE assay ADVIA-Centaur resulting 0.23 and 0.07 kU/l, respectively.

Sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE) was performed with 16% acrylamide with green and red pepper extracts. After SDS-PAGE, the proteins were transferred to nitrocellulose by the method of Towbin et al.<sup>9</sup> Several bands were detected by immunoblotting for both extracts with molecular weights between 37 and 100 kDa (Fig. 1).

Oral Allergy Syndrome (OAS) with bell pepper has been described in very few patients.<sup>2,3</sup> Few other cases have been published reporting patients with angio-oedema or urticaria after bell pepper ingestion,<sup>4,5</sup> but in both publications there are not enough clinical data such as localisation or neither severity of the angio-oedema and/or urticaria nor the onset of these reactions. There is an article written in German reporting a case of anaphylaxis with raw bell pepper.<sup>6</sup> Callero et al. have very recently published a case of anaphylaxis with red bell pepper.<sup>7</sup> Nevertheless, the patient whom they describe was sensitised to pollens, and skin test and immunoblotting were only positive for red pepper but not for green pepper in contrast with our patient. Leitner et al. have studied 22 patients suffering from celery-birch-mugwort-spice syndrome.<sup>1</sup> They performed immunoblotting with a paprika extract, observing that 95% of patients recognised paprika allergens in the range of 23–50 kDa, but there are no data regarding neither the number of patients who suffered reactions after paprika



**Figure 1** Immunoblotting performed after transfer from SDS-PAGE with red and green peppers extracts. Lane 1: red and green pepper extracts without patient's serum. Lane 2: red pepper extract with patient's serum. Lane 3: green pepper extract with patient's serum.

or bell pepper ingestion nor the symptoms of those possible reactions.

We present a rare patient with several IgE-mediated anaphylactic reactions to raw green pepper and one similar reaction to paprika demonstrated by prick, prick-by-prick test and immunoblotting. In this woman clinical cross-reaction between bell pepper and paprika has been shown. Our patient is also sensitised to latex and some foods with well-known cross-reactivity with latex like chestnut and banana. She presented a very weak positive result for chestnut chitinase (Cas a 5) and a moderate/high positive result for the cross-reactive allergen hevein (Hev b 6). One of the bands present in the immunoblotting is near to 34 kDa, which is the molecular weight of Cas a 5. This could perhaps explain the latex-fruit syndrome suffered by this patient. To the best of our knowledge, this is the first patient described with anaphylactic reactions to raw green peppers and paprika in the context of a latex-fruit syndrome in a patient without pollen allergy.

## Ethical disclosures

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**Protection of human subjects and animals in research.** Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this investigation.

## Conflict of interests

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## References

1. Leitner A, Jensen-Jarolim E, Grimm R, Wüthrich B, Ebner H, Scheiner O, et al. Allergens in pepper and paprika. *Allergy*. 1998;53:36–41.
  2. Wagner S, Radauer C, Hafner C, Fuchs H, Jensen-Jarolim E, Wüthrich B, et al. Characterization of cross-reactive bell pepper allergens involved in the latex-fruit syndrome. *Clin Exp Allergy*. 2004;34:1739–46.
  3. Gallo R, Roncarolo D, Mistrello G. Cross-reactivity between latex and sweet pepper due to prohevein. *Allergy*. 1998;53:107–8.
  4. Jensen-Jarolim E, Santner B, Leitner A, Grimm R, Scheiner O, Ebner C, et al. Bell peppers (*Capsicum annuum*) express allergens (profilin, pathogenesis-related protein P23 and Bet V1) depending on the horticultural strain. *Int Arch Allergy Immunol*. 1998;116:103–9.
  5. Willeroide M, Fuchs H, Ballmer-Weber BK, Focke M, Susani M, Thalhamer J, et al. Cloning and molecular and immunological characterization of two new food allergens, Cap a 2 and Lyc e 1, profilins from bell pepper (*Capsicum annuum*) and tomato (*Lycopersicon esculentum*). *Int Arch Allergy Immunol*. 2003;131:245–55.
  6. Rüger RD, Wagner S, Simon JC, Treudler R. Severe type 1-allergy to raw bell pepper. *Hautarzt*. 2010;61:339–42.
  7. Callero A, Perez E, Ledesma A, Martínez-Tadeo JA, Hernández G, Rodríguez-Plata E, et al. A case report of bell pepper anaphylaxis: could 1, 3- $\beta$ -glucanase be the culprit allergen? *Ann Allergy Asthma Immunol*. 2012;109:474–5.
  8. Patiwaël JA, Jong NW, Burdorf A, Groot H, Gerth van Wijk R. Occupational allergy to bell pepper pollen in greenhouses in the Netherlands, an 8-year follow-up study. *Allergy*. 2010;65:1423–9.
  9. Towbin N, Staehelin T, Gordon J. Electrophoretic transfer of proteins from polyacrylamide gel to nitrocellulose sheets. Procedure and applications. *Proc Natl Acad Sci USA*. 1979;76:4350–4.
- J.M. García-Menaya<sup>a,\*</sup>, C. Cordobés-Durán<sup>b</sup>, P. Bobadilla-González<sup>a</sup>, A. Ledesma<sup>c</sup>, I. Pérez-Rangel<sup>a</sup>, S. Sánchez-Vega<sup>a</sup>, M.A. Zambonino<sup>a</sup>, S. Corrales-Vargas<sup>a</sup>
- <sup>a</sup> *Allergy Department, Infanta Cristina University Hospital, Badajoz, Spain*  
<sup>b</sup> *Allergy Department, General Hospital, Mérida, Spain*  
<sup>c</sup> *Biochemistry Research, Alk-Abelló, Madrid, Spain*
- \* Corresponding author.  
E-mail address: [jesusmiguelgarciamenaya@gmail.com](mailto:jesusmiguelgarciamenaya@gmail.com) (J.M. García-Menaya).
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