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Communication:

Anaphylaxis and generalized urticaria from eating Chinese bayberry fruit*

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Chinese bayberry *Myrica rubra* is a very popular fruit in southeastern China. In spite of its wide consumption, no allergies to this fruit have been reported previously. Here we report on a 40-year-old woman suffering from anaphylaxis to Chinese bayberry fruit. Prick-prick skin tests revealed strong reactions to fresh Chinese bayberry fruits as well as to peach, and weaker reactions to some other fruits including apple, melon, and banana. ImmunoCAP analysis revealed identical titers of specific IgE (4.3 kU_A/L) to peach extract and its lipid transfer protein (LTP, rPru p 3), which was confirmed by detection of a 9 kD band following immunoblotting. Immunoblot analysis with Chinese bayberry extract gave bands of 22, 45, and 90 kD, but no 9 kD band was recognized. There was also no evidence of LTP recognition for loquat (36 kD) or melon (24 kD). This first report of a severe allergic reaction to Chinese bayberry fruit in a patient with LTP-mediated peach allergy indicates that other as yet unidentified non-pollen related fruit allergens are involved in this new severe fruit allergy.

Key words: Chinese bayberry, Fruit allergy, Anaphylaxis

1 Introduction

In China, fruit allergy is becoming a major health problem due to the dramatic increase in production and consumption of various fruits. The spread of local exotic fruits to a wider area may lead to the occurrence of previously unreported fruit allergies. Chinese bayberry (*Myrica rubra*), belonging to the family Myricaceae and the order Fagales, is a native Chinese subtropical fruit with high anthocyanin content for which health promoting properties have been claimed (Chen *et al.*, 2010; Yang *et al*., 2011; Zhang *et al.*, 2011). It is a very popular fruit consumed in China mostly fresh or as juice for more than 7000 years (Xie *et al.*, 2008; Jiao *et al*., 2012). In recent years its processed products have increasingly been exported to Europe and North America. In spite of its wide consumption, no allergies to this fruit have been reported previously.

A native *Myrica cerifera* bayberry (or wax-myrtle), within the same genus, has been reported as a tree pollen allergen source in USA (Prince and Meyer, 1977). Since this genus belongs to the order Fagales to which birch trees also belong, the involvement of PR10 (Bet v 1-like) and/or profilin has been considered (Jacinto *et al.*, 1992). In this paper we report on a patient suffering anaphylaxis to Chinese bayberry together with mild allergy to other fruits.

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2 Case description

A 40-year-old Chinese woman received emergency treatment at the allergy department of our hospital after suffering anaphylaxis induced by eating Chinese bayberry fruit. The patient had no atopic family background and no history of rhinoconjunctivitis or asthma, but she had experienced episodes of food allergy as a young child. She claimed to have had allergic reactions to baby bok choy (*Brassica rapa* var. Chinensis) as a very young child, as a consequence of which she avoided most vegetables and fruits. At ten years of age, she slowly started eating vegetables and fruits again, such as white Chinese cabbage and tomato, if no symptoms occurred. She continued to avoid banana and celery, because they induced severe oral allergy syndrome (OAS). Apple, peach, loquat, and Chinese bayberry were tolerated until three years ago when she experienced an episode of systemic urticaria within 5 min after eating peach and Chinese bayberry fruit. She also then felt uncomfortable eating apple, plum, loquat, banana, and melon, but tolerated watermelon and kiwi. During the same period, washing rice resulted in contact urticaria on her hands and eyelids. One year later, trying one Chinese bayberry again, she developed anaphylaxis that was resolved only after emergency treatment. On that occasion, skin prick tests for reaction to mites, molds, mixed pollen, and animal dander were all negative (ALK-Abelló A/S, Horsholm, Denmark).

One year later, this patient was enrolled for further skin test studies and serum IgE analysis. Strong positive skin tests were observed with two Chinese bayberry fruit cultivars ('Shuijing' and 'Dongkui') and peach extract. She also showed a mild reaction to fresh peach, apple, and melon fruits and washing water of rice, as well as Chinese bayberry juice, but not bayberry extract (Table 1). Specific IgE measurements by ImmunoCAP (Thermo-Fisher, Uppsala, Sweden) revealed an elevated total serum IgE (451.4 kU_A/L), and specific IgE titers against peach, melon, and mugwort pollen extract of 4.3, 0.7, and 1.2 kU_A/L, respectively. Single component ImmunoCAP analysis demonstrated specific IgE against rPru p 3 was 4.3 kU_A/L and nArt v 3 IgE was 0.4 kU_A/L. rPru p 1 (Bet v 1 homologue), rPru p 4 (profilin), and rArt v 1 IgE were negative (<0.35 kU_A/L) (peach and mugwort sIgE data are from patient S24 reported by Gao *et al*. (2012)). Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE)/immunoblotting with protein extracts from peach fruit peel (cv. 'Yulu'), Chinese bayberry whole fruit (*Myrica rubra* cv. 'Biqi'), loquat peel (*Eriobotrya japonica* cv. 'Ninghaibai'), and melon flesh was carried out to investigate which individual allergens may be involved in the reactions to Chinese bayberry and other fruits. With peach, a putative LTP band at 9 kD was detected, which is in agreement with the positive rPru p 3 CAP result. Surprisingly, with Chinese bayberry there was no recognition of a 9-kD LTP band, but instead three as yet unidentified bands were found at 22, 45 and 90 kD, indicating that the bayberry allergy of this patient is not a cross-reactive phenomenon induced by Pru p 3 primary sensitization. With loquat a 36-kD band was detected, and with melon, a 24-kD band (Fig. 1). Written consent was obtained from the patient and this study was approved by the local ethics committee (authorization No. 2011-R-1, the Second Affiliated Hospital, School of Medicine, Zhejiang University, China).

Table 1 Skin prick test with different fresh materials and protein extracts

Allergen source	Wheal size (mm)	Times of the positive control
Chinese bayberry cv. Shuijing	15×11	3.44
Chinese bayberry cv. Dongkui	13×11	2.98
Chinese bayberry cv. Biqi	11×7	1.60
Chinese bayberry juice	12×4	1.00
Peach	10×6	1.25
Melon	15×5	1.56
Apple cv. Fuji	8×8	1.33
Banana	6×5	0.63
Litchi	3×3	0.19
Rice washing water	14×8	2.12
Peach extract, 400 μg/ml	18×20	7.50
Peach extract, 40 μg/ml	15×14	4.58
Peach extract, 4 μg/ml	17×10	3.14
Chinese bayberry extract, 25 μg/ml	3×3	0.19
Histamine, 10 mg/ml	8×6	1.00
Negative control (Saline)	0	

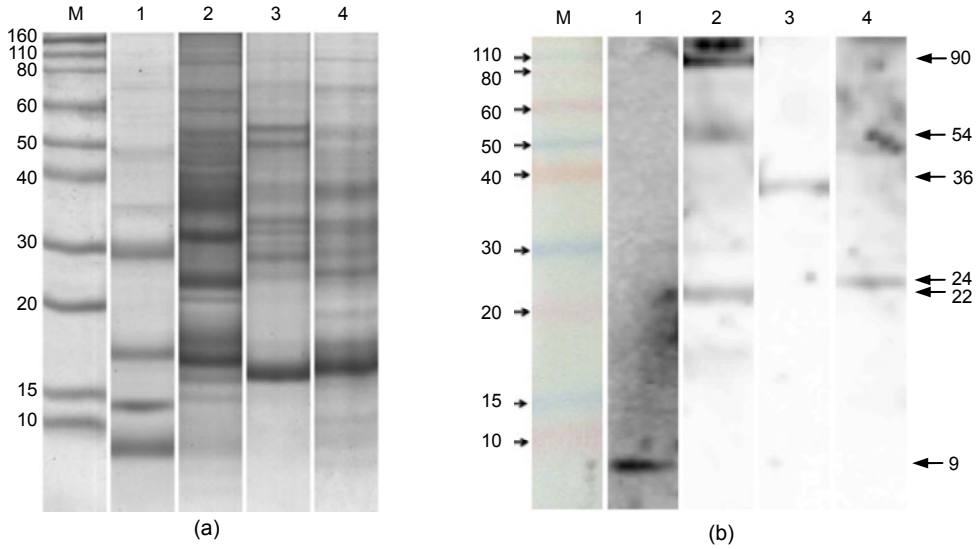

Fig. 1 Electrophoresis and Western blots of four allergenic fruit protein extracts

(a) SDS-PAGE of protein extracts from fruits; (b) Immunoblots with the patient serum. M: protein molecular weight marker in kD (invitrogen LC5800); 1: peach (cv. Yulu, peel); 2: Chinese bayberry (*Myrica rubra* cv. Biqi, whole fruit); 3: Loquat (*Eriobotrya japonica* cv. Ninghaibai, peel); 4: melon flesh

3 Discussion

In Europe, fresh fruits have been found to be the most frequent cause of food allergies in patients over five years of age (Fernández-Rivas *et al.*, 2008). Usually these allergies are considered to result from primary sensitization to pollen or latex, but peach LTP has been described as the primary sensitizer responsible for often severe peach allergy and cross-reactivity to other fruits and vegetables and even to pollen (Rossi *et al.*, 2009; Schulten *et al.*, 2011). Peach allergy patients in China have been classified into two groups: a larger group frequently reported in north China resulting from high exposure and strong sensitization to mugwort pollen LTP, and a smaller group in south China resulting from peach fruit LTP sensitization (Gao *et al.*, 2012). This case belongs to the south China peach allergy group, but there was no evidence of LTP recognition with Chinese bayberry, loquat or melon fruit extracts. From an "expressed-sequence tag" (EST) survey of bayberry fruit, it was found that the fruit contains at least two isoforms of LTP, a longer one with 66.3% amino acid identity to Pru p 3.01 and a shorter one with 29.5% identity. Neither appears to be recognized by cross-reactive Pru p 3 specific IgE. Negative single component Pru p 1 and Pru p 4 CAP and immunoblot results suggested that PR-10 (Bet v 1 homologues) and profilin are also not the allergens for this patient. One of the identified bands of 22 kD corresponds to the molecular weight (M_W) of the reported fruit allergen thaumatin-like protein (TLP) (Breiteneder, 2004). The fact that its putative encoding gene is abundantly expressed during bayberry fruit ripening (unpublished data) warrants further studies into a possible role for a TLP in the bayberry fruit allergy. With preliminary skin prick tests showing possible allergenicity differences among Chinese bayberry cultivars (Table 1), further in vitro and in vivo testings with more patients and cultivars are planned to select hypoallergenic cultivars using similar approaches to that used in apple (Gao and Gilissen, 2011).

In conclusion, to the best of our knowledge, this is the first case report of severe allergy to Chinese bayberry. Further molecular characterization of the allergens involved in the allergy to this exotic fruit is needed. Research on other fruit TLP allergens provides useful references (Gavrović-Jankulović *et al.*, 2002; Breiteneder, 2004).

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