A Case of Pork-cat Syndrome That Developed as Food-dependent Exercise-induced Anaphylaxis

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Pork-cat syndrome is caused by immunoglobulin E (IgE)-mediated hypersensitivity to cat serum albumin, which cross-reacts with porcine serum albumin due to antigenic similarity between the 2 proteins (1). Its characteristic manifestation is generalized urticaria, angioedema, respiratory disturbance and anaphylactic shock after ingestion of pork, which is seen in subjects with cat dander allergy (1, 2).

By contrast, food-dependent exercise-induced anaphylaxis (FDEIA) is a distinct clinical entity characterized by development of systemic allergic reaction triggered when ingestion of food is followed by physical exercise (3). Patients usually eat causative foods without any symptoms. FDEIA is difficult to diagnose because the onset of symptoms varies greatly in terms of the threshold amount of food ingested and exercise intensity. Wheat and seafood are the most frequent causative foods in Japan (3). We report here a case of pork-cat syndrome, which developed as FDEIA, which was induced by exercise after eating pork.

CASE REPORT

A 13-year-old boy was referred to our hospital for 5 episodes of systemic urticaria and dyspnoea following intense exercise, running or playing basketball, after lunch. He developed allergic symptoms after approximately 10 min of intense exercise, with 30 min from lunch to onset of symptoms, and 6 h from breakfast to onset of symptoms. FDEIA caused by wheat was suspected, based on his history. However, serum-specific IgE test, skin-prick test and basophil activation test were all negative for wheat proteins. Detailed questions on his meals and living environment revealed that he had eaten pork ham and pork sausage at breakfast daily and had kept cats for a long time. Since a few years earlier, he had developed nasal discharge and nasal congestion when exposed to cats. Serum-specific IgE tests (measured by ImmunoCAP, Thermo Fisher Diagnostics, Tokyo, Japan) were negative for wheat, gluten and omega-5 gliadin, and positive for pork (40.1 kUA/l), beef (1.44 kUA/l), cat dander (137 kUA/l), dog dander (6.73 kUA/l), Sus s (pork albumin: 48.0 kUA/l) and Fel d 2 (cat albumin: >100 kUA/l). Specific IgE value for alpha-Gal, a major allergen of red meat allergy, was 0.36 kUA/l. Skin-prick tests showed positive reaction to commercial raw pork, pork sausage and cat hair allergen scratch extract (Torii Parmaceutical Co. Ltd, Tokyo, Japan) (**Fig. 1**). Western blotting revealed specific IgE against water-soluble beef protein, water-soluble pork protein, and mixture of hair and epithelium of *Felis domesticus* (ITEA Inc., Tokyo, Japan), showing approximately 60 kDa-bands (**Fig. 2**). To examine cross-reactivity between the water-soluble pork protein and the proteins of *Felis domesticus*, immunoblotting inhibition assay was performed (Fig. 2). The reaction of the IgE to water-soluble beef proteins, water-soluble pork proteins, and extract from hair and epithelium of *Felis domesticus* was inhibited in a dose-dependent manner by the extract from hair and epithelium of *Felis domesticus* when the patient's sera was pre-incubated with a series of extracts from hair and epithelium of *Felis domesticus*. From these observations, pork-cat syndrome was diagnosed. The patient was instructed not to exercise on the day he ate pork, and the allergic symptoms disappeared.

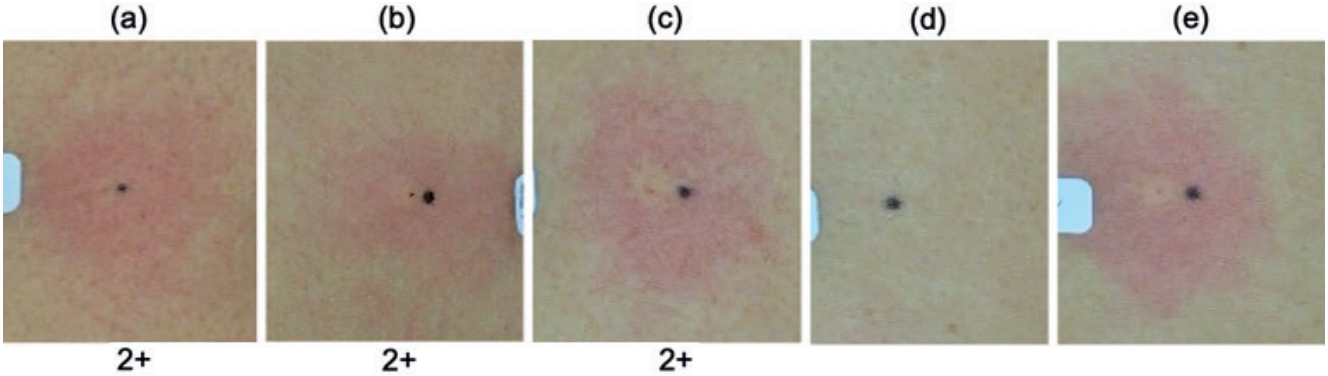

Fig. 1. Positive prick test results on (a) commercial raw pork, (b) pork sausage, and (c) cat hair allergen scratch extract (Torii Parmaceutical Co. Ltd, Tokyo, Japan). (d) Saline, (e) positive histamine controls (10 mg/ml). Reactions were read at 15 min, and responses were compared with positive histamine controls (10 mg/ml): 1+, 25% of the area of the wheal induced by the positive histamine control; 2+, 50%; 3+, 100%; 4+, 200%.

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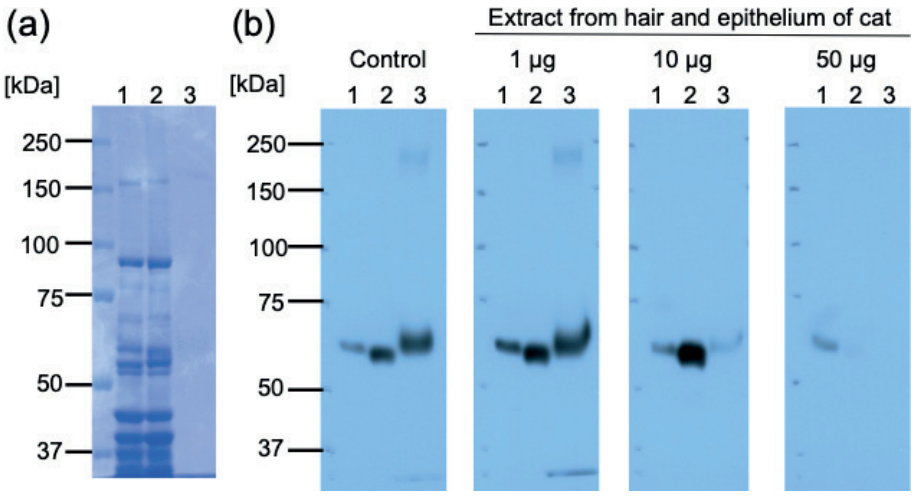

Fig. 2. Western blotting and immunoblot inhibition analyses of red meat proteins and extract from hair and epithelium of cat. (a) Gel stained with Coomassie Brilliant Blue; (b) Immunoglobulin E (IgE)-immunoblotting with the patient's sera. Lane 1: water-soluble beef proteins. Lane 2: water-soluble pork proteins. Lane 3: extract from hair and epithelium of *Felis domesticus*. Immunoblot inhibition assay was performed for determining cross-reactivity of pork proteins and extract from hair and epithelium of cat. Electrophoresed membranes were blotted against patient's sera without extract from hair and epithelium of cat (control) or with increasing amounts of extract from hair and epithelium of cat (1, 10, and 50 µg).

DISCUSSION

Pork-cat syndrome was first reported in 1994 (4). For its diagnosis, measurement of Sus s- and Fel d 2-specific IgE levels are useful (1, 5). Posthumus et al. (6) presented 4 points for clinical characteristics of pork-cat syndrome: (*i*) several years are required for cat dander-mediated sensitization;(*ii*) pork consumption does not always induce symptoms; raw or smoked pork ingestion causes marked symptoms, whereas there are few symptoms after heated pork ingestion; (*iii*) symptoms appear early after ingestion; and (*iv*) if the patient avoids cats in daily life, cat dander-specific IgE level may be reduced, facilitating safe ingestion of pork.

In the current patient: (*i*) symptoms of pork allergy appeared after 13 years of keeping a cat; (*ii*) when he developed allergic symptoms, he had not ingested cooked pork, but smoked pork, such as ham and sausage, both of which are compatible with the criterion of Posthumus et al. (6). However, point (*iii*) is not compatible, because his allergic symptoms appeared several hours after ingestion of pork. He developed urticaria and dyspnoea after lunch while exercising hard after having smoked pork at breakfast, as in the case of FDEIA. Since lunch on the day he developed allergic symptoms did not always contain pork, we assumed that the smoked pork in the breakfast was the cause. Although the time-lag between ingestion of pork and development of allergic symptoms was unclear, it is a characteristic feature in our case, which is different from previous reports. The reason for this is thought to be that absorption of sufficient quantity of allergens from the gastrointestinal tract is essential for eliciting allergic symptoms, as with wheat-dependent exercise-induced anaphylaxis (3). Considering point (*iv*), the boy was instructed to avoid keeping a cat, but he continued to do so, based on his wishes. Therefore, he avoids exercise on the day he eats pork and consequently does not develop allergic symptoms. In this case, a definitive diagnosis could only be made after asking about his lunch and breakfast dietary choices. As we have reported previously, α-Gal allergy, a major red meat allergy worldwide, is also a food allergy that develops several hours after ingestion (7). Therefore, when allergic symptoms are repeated, it is important to suspect food consumption a few hours before appearance of symptoms, as presented in this case.

The authors have no conflicts of interest to declare.

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