Case report of a child who may have developed anaphylaxis after ingesting raw horse meat by cross-reactivity of horse and cat pelt

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Pork-cat syndrome can occur in children younger than 10 years. A history of contact with animals since infancy and history of severe atopic dermatitis, which can promote epicutaneous sensitization to animal serum albumin, may be helpful in diagnosis. (J Allergy Clin Immunol Global 2023;2:100139.)

Key words: *Pork-cat syndrome, serum albumin, mammalian meat, anaphylaxis, children*

Abbreviation used
SPT: Skin prick test

The horse (*Equus caballus*) has been an important human partner since ancient times and has been used for farming, riding, and food. Its use as a food varies by region and culture. In the United Kingdom and Ireland, people never eat horse meat, whereas in France, The Netherlands, and Austria, it is consumed as beef or pork are. In Japan, horse meat is eaten in certain regions as part of the local cuisine. We found only 2 reported cases of allergy to horse meat. A 39-year-old woman with hamster-sensitized asthma developed lip swelling after consuming horse meat.[1] A 38-year-old woman with beagle dog–sensitized asthma developed edema of the lips and gums, laryngeal edema, and continuous cough after eating horse steak.[2] Here, we report the youngest known individual with horse meat allergy. A 9-year-old boy who had experienced mild exacerbations of his atopic dermatitis and asthma as a result of contact with cats later developed anaphylaxis after eating raw horse meat.

The patient had a history of atopic dermatitis, chicken egg allergy, asthma, and allergic rhinitis. He had had no history of anaphylaxis in response to egg and outgrew egg allergy at age 9 years. His asthma and atopic dermatitis were poorly controlled because he received only symptomatic treatment. Raised by a single parent, he spent weekdays at his grandmother's house and weekends at his father's home. Both homes had cats but no dog, and the boy had no daily contact with dogs elsewhere. He avoided direct contact with the cats as much as possible, but he and the cats did spend time in the same room. His grandmother cleaned her home every day, whereas his father did not. His eczema and asthma always worsened at his father's house.

He ate raw horse meat at a restaurant, and within 5 to 10 minutes—before eating any other food—he experienced oral pain, general urticaria, and wheezing. He was transported to a hospital by ambulance, where he exhibited seesaw breathing. He required 2 intramuscular adrenaline injections, inhalation of bronchodilators, and intravenous glucocorticoid and H1 antihistamine. The initial symptoms subsided; however, 22 hours later urticaria appeared on both lower extremities, and additional intravenous glucocorticoid and H1 antihistamine were administered. The boy had routinely consumed cooked pork, cooked beef, and cooked pork in the form of smoked processed meat products (ham, sausage, etc) without allergic symptoms, but he had never eaten raw pork or raw beef. He had also never eaten cooked horse meat.

The results of serum-specific IgE tests using the ImmunoCAP and ImmunoCAP Immuno-solid-phase Allergen Chip (ISAC) assay (Thermo Fisher Scientific, Waltham, Mass) were positive for cat dander, pork, beef, cat serum albumin (Fel d 2), swine serum albumin (Sus s 1), horse serum albumin (Equ c 3), and BSA (Bos d 6) but negative for Gal-alpha-1,3-Gal (α-gal) (see Table E1 in the Online Repository at www.jaci-global.org). Prick-to-prick tests with raw and cooked meat showed a wheal diameter of 3.8 × 4.3 mm with the histamine-positive control, 0 × 0 mm with the saline negative control, 2.7 × 2.7 mm with raw horse meat, and 1.9 × 1.9 mm with raw pork. The results of testing for cooked horse meat and pork were negative (ie, 0 × 0 mm [see Table E1]). Basophil activation tests using a commercial kit (Allergenicity Kit, Beckman Coulter, Tokyo, Japan) (see the Supplementary Methods in the Online Repository at www.jaci-global.org) indicated that raw horse meat extract enhanced CD203c expression on the patient's basophils, whereas a control

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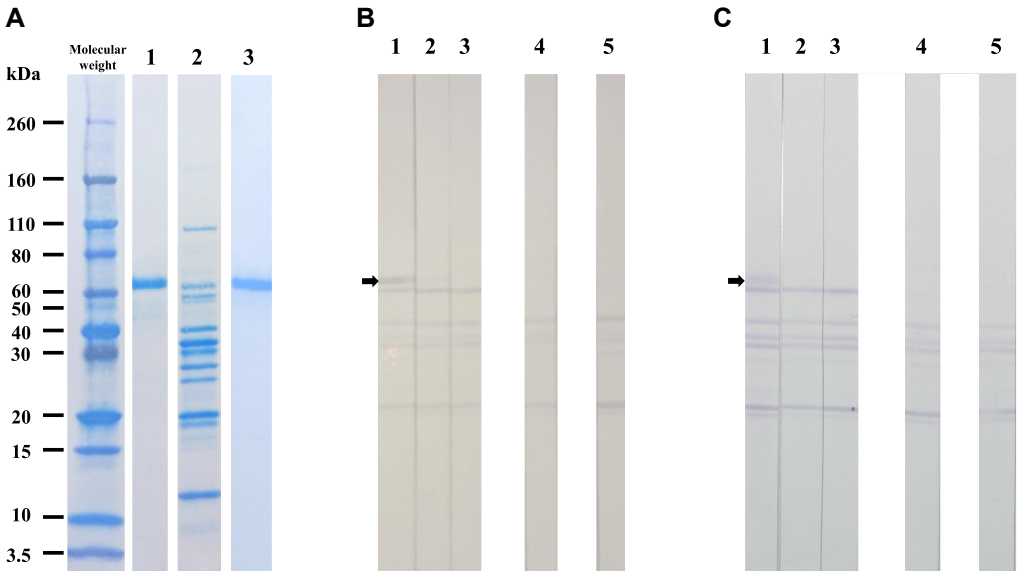

FIG 1. Western blotting and inhibition analyses of raw horse meat and cat pelt/Fel d 2. **A,** SDS-PAGE staining with Coomassie Brilliant Blue: allergenic extract of standardized cat pelt (*lane 1*), horse meat extract (*lane 2*), and Fel d 2 (*lane 3*). **B,** Inhibition assay for horse meat allergens: the patient's serum (*lane 1*), the patient's serum preincubated with cat pelt extract (0.1 μg, 2 μg) (*lanes 2 and 3*), and serum from an individual without allergy (*lanes 4 and 5*). **C,** Inhibition assay for horse meat allergens: the patient's serum (*lane 1*), the patient's serum preincubated with Fel d 2 (0.1 μg, 2 μg) (*lanes 2 and 3*), and serum from an individual without allergy (*lanes 4 and 5*).

subject's basophils showed no significant enhancement (see Table E1). Immunoblot analysis found that the patient's serum reacted with 1 of the main electrophoretic bands between 60 and 80 kDa from the raw horse meat extract (Fig 1, *B* [*lane 1*]); it corresponded to Equ c 3 with a molecular weight of 67 kDa. Serum from a healthy control did not react with that protein band (Fig 1, *B* [*lanes 4 and 5*]). An inhibition assay using cat pelt extract as an inhibitor showed concentration-dependent attenuation of binding of the patient's serum IgE to horse meat protein and natural Fel d 2 (Indoor Biotechnologies, Charlottesville, Vir). There was attenuation of binding of the patient's serum IgE to the horse meat protein from low concentrations, confirming cross-reactivity between Fel d 2 in cat pelt and horse meat protein (Fig 1, *B* and *C* [*lanes 2 and 3*]).

The patient refused to undergo oral food challenge. On the basis of the patient's medical history and the aforementioned examination findings, we concluded that this was a pediatric case of anaphylaxis caused by ingestion of raw horse meat, with the mechanism being the similar to that of pork-cat syndrome. We instructed the patient to avoid uncooked mammalian meat. He has since experienced no food-induced allergic symptoms.

An association between cat breeding and pork allergy is well known as pork-cat syndrome. The syndrome is characterized by sensitization to Fel d 2, mainly via the respiratory tract, and cross-reaction with Sus s 1, resulting in allergic symptoms after pork consumption.[3] Serum albumin is unstable to heat, so patients with pork-cat syndrome can often eat thoroughly cooked pork. Extensive cross-antigenicity between pets and mammalian meats has been demonstrated.[2,4-6] We surmise that our patient was initially sensitized to cats and then developed anaphylaxis in response to raw horse meat owing to a cross-antigenic reaction. The amino acid homology of serum albumin is 70% to 87% between cats and pigs and also among horses, dogs, cattle, and guinea pigs.[4] Because of multiple combinations of sensitizing sources, cross-reactive meats can cause allergic symptoms in at-risk subjects.[2,4-6] The patient was also sensitized to canine dander and the major canine allergen Can f 1; therefore, the possibility that the patient may have developed cross-antigenicity from dogs to horses, as previously reported, cannot be excluded. Unfortunately, additional inhibition assay cannot be performed on account of a lack of serum. However, because the patient had no history of contact with dogs and because cross-reactivity of lipocalins among species (in this case, Can f 1–Fel d 7) has been recognized, sensitization to Can f 1 may have been due to cross-reactive Fel d 7 in this patient who was highly sensitized to cat, although Fel d 7 was not included in the ISAC assay and we were not able to test Fel d 7 reactivity.

Pork-cat syndrome is rare, and the age of onset is considered to be mainly adolescence or later. We searched PubMed and CiNii Articles for English and Japanese reports published between January 1990 and May 2022, using *pork-cat syndrome* and *cat-pork syndrome* as search terms. We found 19 reported cases with details of the symptoms. Including our present patient, 4 cases were in children younger than 10 years (Table I).[7-9] All 4 patients were highly sensitized to cat dander, with extremely high Fel d 2 levels despite their young age. The 4 cases were characterized by daily contact with multiple cats and/or dogs since infancy and by poorly controlled atopic dermatitis that developed from infancy to early childhood. Of the 19 cases in total, atopic dermatitis was described as an underlying disease in only 3 cases in patients younger than 10 years. Those 3 patients may have been sensitized to airborne pet allergens from indoor dust via both the respiratory tract and the disrupted skin barrier in atopic

TABLE I. Clinical features and laboratory findings of previously reported pediatric cases of mammalian meat allergy due to cross-reactivity with mammalian serum albumin (in patients aged <10 years) and our present case

	Patient No.			
	1	2	3	Our present case
Age (y), no. (age of onset)	6 (6)	8 (8)	6 (3)	9 (9)
Sex	F	M	M	M
Underlying diseases	AD, AR	AD, BA	AD, BA, AR,	AD, FA (egg), BA, AR
Control of atopic dermatitis	Poor	Poor	ND	Poor
Animal exposure (no. of animals)	Cat (many)* Dog (1)	Cat (ND) Dog (ND)	Cat (3)	Cat (4)
Symptoms with cat (or dog) exposure	Skin itching	Skin itching	Urticaria	Asthma, eczema
Provocateur of allergic reaction	Pork, beef	Pork, beef, smoked pork, beef intestines	Pork, beef smoked pork, pork stomach	Raw horse meat
Clinical symptoms with meat	Skin itching, urticaria	Urticaria, respiratory symptoms, anaphylaxis (skin and respiratory symptoms)	Gastrointestinal symptoms, urticaria, respiratory symptoms	Anaphylaxis (skin/mucous membrane and respiratory symptoms)
Skin prick test†				
Cat dander	NA	+	ND	NA
Dog dander	NA	+	ND	NA
Pork				
Uncooked	+	+	+	+
Cooked	−	−	−	−
Beef				
Uncooked	+	+	+	−
Cooked	−	+	−	−
Horse meat				
Uncooked	ND	ND	ND	+
Cooked	ND	ND	ND	−
Total IgE level, (IU/mL)	7254	843	299	2209
Specific IgE level (UA/mL)/(ISU-E)‡				
Cat dander	34.2	27.3	67.3	882
Dog dander	≥100	48.9	ND	31.8
Pork	58.6	17.3	12.1	6.82
Beef	7.00	2.64	1.12	0.99
Fel d 2	≥100	62.1	99.8	49.2/50
Sus s 1	69.2	18.2	15.7	6.33
Can f 3	≥100	58.6	ND	/17
Bos d 6	ND	6.9	7.07	/2.5
Equ c 3	ND	ND	ND	/13
α-Gal	0.13	<0.1	<0.10	/<0.3
Cross-reactivity§	D	D	ND	D
Reference	Yamada et al[7]	Sagawa et al[8]	Kudo et al[9]	
Year published	2019	2021	2021	

AD, Atopic dermatitis; *α-Gal*, galactose-α–1,3-galactose; *AR*, allergic rhinitis; *BA*, bronchial asthma; *D*, determined; *F*, female; *FA*, food allergy; *ISU-E*, ISAC standardized units for detection of IgE antibodies; *M*, male; *NA*, not assessed; *ND*, not described.

*Patient 2 had many opportunities to come into contact with cats and dogs because his parents run a veterinary clinic on the first floor of their home.

†SPT-positive (+) defined as more than one-half of the wheal diameter of the positive control.

‡Specific IgE level measured using the ImmunoCAP assay (UA/mL)/ ImmunoCAP ISAC assay (ISU-E).

§Cross-reactivity between cat epithelia and pork meat was assessed by the inhibition test.

dermatitis. Early and close contact with multiple dogs and/or cats and the presence of uncontrolled atopic dermatitis may trigger development of this syndrome at a young age. We think that these are important clues pointing to pork-cat syndrome in young children with anaphylaxis of "unknown" cause. For patients with unusual anaphylaxis, physicians should not forget to ask about their histories of animal exposure and atopic dermatitis, especially in infancy.

Informed consent

The authors obtained the written consent of the patient's family for publication of this case.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

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REFERENCES

1. Cistero-Bahima A, Enrique E, San Miguel-Moncin MM, Alonso R, Bartra J, Fernandez-Parra B, et al. Meat allergy and cross-reactivity with hamster epithelium. Allergy 2003;58:161-2.
2. Morisset M, Arumugam K, Ollert M, Hilger C. Horse-meat allergy mediated by dog-allergy: a case report and review of the literature. Allergo J Int 2016;25:76-81.

3. Posthumus J, James HR, Lane CJ, Matos LA, Platts-Mills TA, Commins SP. Initial description of pork-cat syndrome in the United States. J Allergy Clin Immunol 2013; 131:923-5.
4. Chruszcz M, Mikolajczak K, Mank N, Majorek KA, Porebski PJ, Minor W. Serum albumins-unusual allergens. Biochim Biophys Acta 2013;1830:5375-81.
5. Curin M, Hilger C. Allergy to pets and new allergies to uncommon pets. Allergol Select 2017;1:214-21.
6. Hilger C, van Hage M, Kuehn A. Diagnosis of allergy to mammals and fish: cross-reactive vs. specific markers. Curr Allergy Asthma Rep 2017;17:64.
7. Yamada S, Matsubara K, Chinuki Y, Hori M, Masaki T. [Early childhood-onset pork-cat syndrome due to sensitization by both cats and dogs -a case report]. Arerugi 2019;68:1141-7.
8. Sagawa N, Inomata N, Suzuki K, Sano S, Watanabe Y, Aihara M. Pork-cat syndrome caused by ingestion of beef intestines in an 8-year-old child. Allergol Int 2021;70:395-7.
9. Kudo E, Takezaki S, Yamazaki T, Ito T, Hatakeyama K, Kawamura N, Sano H. Pork-cat syndrome repeating gastrointestinal symptoms triggered by pork or beef since three years old: a case report. J Jpn Pediatr Soc 2021;125:1194-8.