Letter to the Editor

Initial description of pork-cat syndrome in the United States

To the Editor:

Despite meat being an important source of protein in Western diets, development of meat allergy is uncommon.[1] For mammalian meat, the extensive homology of proteins across mammalian species decreases the likelihood of creating a specific IgE (sIgE) response.[2,3] In fact, when clinically relevant reactivity to meats has been demonstrated, the results point to cross-reactivity (eg, serum albumin [SA] and actin) and not to a sensitization with meat-specific epitopes.[4] In keeping with this cross-reactivity, reports of IgE antibodies that bind various mammalian albumins do exist, notably pork-cat syndrome.[5,6] In this uncommon syndrome patients have an IgE antibody response specific for cat SA that cross-reacts with porcine albumin and can lead to severe or even fatal allergic reactions on occasions when pork is consumed.[5-7] Interestingly, the reported cases of pork-cat syndrome are largely European.

We have recently evaluated numerous patients with suspected "meat allergy"; in so doing, we have found and report here for the first time 8 cases of pork-cat syndrome in the United States. Representative clinical history and evaluations of 2 patients are described, including detailed IgE specificity and a clinical response to elimination diet, both of which strongly suggested the diagnosis. However, confirmatory food challenges were not performed in any of the 8 patients.

Published data regarding pork-cat syndrome have suggested that sensitization to cat SA represents the primary event in the development of the cross-reactive IgE.[6] In that investigation of sera from young patients in Luxembourg, it was shown that anti-cat SA IgE reactivity completely contained the anti-pork reactivity, whereas the reverse was not true.[6] The patients in that report were all selected on the basis of being highly allergic to cat, whereas the 8 subjects reported here each presented for evaluation of suspected meat allergy.

Patient E364 (Table I) reported symptoms of abdominal cramping, nausea, itching, and hives beginning 20 minutes after a meal of pork tenderloin, potatoes, and green beans. His abdominal symptoms worsened. He reported lightheadedness and was taken to the local emergency department, where he was treated for anaphylaxis. Given the proximity of his symptoms to the meal, a role for IgE antibody to galactose-α-1,3-galactose (α-gal) seemed unlikely. Positive immunoassay results to cat, dog, and pork without concomitant sensitization to beef or lamb prompted further investigation with SAs and gelatin (Table I). Positive results were obtained for cat and dog SA (Re220 and Re221, respectively), whereas results for bovine SA (Re204) were negative (Table I). Taken together, the results suggested that the anaphylactic reaction was triggered by pork because of cross-reacting IgE, which is consistent with pork-cat syndrome. The patient was advised to avoid eating pork and has been followed for 2 years without additional reactions.

A second illustrative case is that of patient T559, a 14-year-old girl. She presented with recurrent bouts of abdominal pain 30 to 45 minutes after a meal. The pain occurred 3 to 5 times a month over the course of 14 months and would resolve without treatment in 45 to 60 minutes. There was no associated nausea, vomiting, or diarrhea and no noticed changes in bowel movements. No association was made with a particular food or drink. On some occasions, the abdominal pain was accompanied by urticaria. Our work-up revealed the presence of sIgE to cat and dog albumin and pork, as shown in Table I (case 4), plus a negative result for sIgE antibody to alpha-gal. She was advised to remove pork from her diet but allowed to continue to eat beef. After 9 months of follow-up, no additional episodes of abdominal pain or urticaria were reported.

As Table I shows, this uncommon syndrome is similar to other food allergies in that a range of presentations are seen and the clinical symptoms are not consistently predicted by the titer of IgE to the allergen cat SA. Assessment of binding specificity was performed, as previously described,[8] on sera from 3 patients where sufficient quantity existed (Table II). The IgE response to cat SA and pork was significantly reduced by preincubation with cat albumin, whereas pork albumin and human albumin did not show significant inhibition of the cat SA response (Table II; note that porcine SA and human SA share 82% and 76% protein homology with cat SA, respectively[6]). The IgE response of the patients reported here shows similar specificity to published data and is also consistent with cat SA as the primary sensitizing antigen.[6]

There are 4 notable aspects to pork-cat syndrome that merit discussion. First, the sensitivity to pork does not arise early in life: most reported patients are older than age 8 years, with the majority being adults or teens.[5-7] It appears that the sensitization to cat SA develops over time, and therefore onset of a "new" food allergy in an older child or adult might prompt consideration of pork-cat syndrome.

Second, patients do not report reactions with each instance of eating pork. Both in the 3 patients described by Hilger et al[6] and in the 8 patients reported here, fresh meat or dried and smoked pork (ie, barbecue) were more consistent provocateurs of allergic reactions. However, well-cooked meat was associated with fewer reactions.

Third, reactions to pork begin soon after eating the meat. In many ways, the timing of these reactions is most helpful in differentiating pork-cat syndrome from delayed anaphylaxis caused by IgE to α-gal.[8] Both food allergies are IgE mediated, involve mammalian meat, and can show similar responses with certain skin tests and immunoassays; however, symptoms from pork-cat syndrome can occur rapidly and might initially present with oral pruritus during the meal. In general, reactions to pork begin within 30 to 45 minutes of consumption, often with gastrointestinal symptoms, such as abdominal cramping.

Fourth, the natural history of pork-cat syndrome is not well established, but it appears that the levels of sIgE to cat SA might slowly decrease over time.[9] Perhaps continued exposure to cat is important for maintaining the sensitization, and this might explain why certain patients can eventually consume pork again safely. In fact, existing data indicate that of appropriately sensitized patients, approximately 30% experience allergic symptoms in relation to pork consumption.[6]

Interestingly, whereas patients with IgE antibody to α-gal show positive immunoassay results to beef and pork, the cross-reactivity to bovine albumin in patients with pork-cat syndrome is variable. Thus certain patients with pork-cat syndrome report

TABLE I. Eight cases of pork-cat syndrome: subjects' characteristics and relevant sIgE profiles

	Subject no.							
	E364	E533	E572	T559	E584	T625	E710	E724
Sex	M	F	F	F	F	M	F	F
Age (y)	52	34	21	14	44	11	13	41
Symptoms with meat	ANA	OA/URT	OA/GI	URT	ANA	OA	ANA	OA/GI
Avoidance diet results	No episodes at 2 y	No episodes at 1.5 y	No episodes at 15 mo	No episodes at 9 mo	No episodes at 13 mo	Fewer episodes‡	No episodes at 1 y	Fewer episodes‡
Symptoms with cat or dog exposure	No	R	R, C, U	A	No	Yes	R, C	R
Animal exposure*	Cat	Cat, dog	Dog, horse	No	Cat, dog, guinea pig	Dog	Cat, dog	Cat
SPT, dog dander†	+	+	−	−	−	+	ND	ND
SPT, cat dander†	+	−	+	+	+	+	ND	ND
SPT, pork†	+	+	+	+	+	+	ND	ND
Total IgE (IU/mL)	83.4	252	328	791	42.3	1860	2619	133
sIgE (IU/mL) to:								
Cat albumin	2.28	98.8	12.3	9.96	4.18	2.33	130	26.8
Dog albumin	2.59	65.0	15.2	6.53	4.87	1.71	110	10.8
Bovine albumin	<0.35	6.79	1.92	4.76	<0.35	3.56	6.31	<0.35
Cat dander	3.74	33.8	5.71	121	3.87	23.6	155	17.7
Fel d 1	1.58	1.94	2.16	103	<0.35	ND	90.1	0.81
α-Gal	<0.35	<0.35	1.41	<0.35	<0.35	<0.35	<0.35	<0.35
Pork	0.65	13.2	7.10	7.96	0.53	42.8	43.8	3.40
Beef	<0.35	2.22	1.10	4.45	<0.35	0.91	2.62	<0.35

A, Asthma; *ANA*, anaphylaxis; *C*, conjunctivitis; *F*, female; *GI*, gastrointestinal symptoms; *M*, male; *ND*, not done; *OA*, oropharyngeal itching; *R*, rhinitis; *U*, urticaria; *URT*, urticaria.

*Defined as consistent exposure at home, work, or regular activity (eg, horseback riding). Note: Subject T559 had to limit animal exposure because of symptoms.

†A positive SPT response *(+)* is defined as a greater than 4-mm wheal with flare present, and a negative SPT response *(−)* is defined as a wheal of 4 mm or less.

‡Each subject reported symptoms when choosing to consume pork but denied episodes when following an avoidance diet.

TABLE II. Absorption of sera from pork-cat subjects using different mammalian albumins

Subject no.	sIgE (IU/mL)	Sepharose beads used for absorption*				
		Control	Cat	Pork	Dog	Human
E533	Cat albumin†	24.9	0.69	20.6	6.65	31.9
	Pork meat	6.37	0.36	0.39	<0.35	6.65
	Pork albumin	6.09	<0.35	<0.35	<0.35	6.09
E710	Cat albumin	51.3	1.58	30.2	6.05	47.3
	Pork meat	12.8	1.38	1.43	1.24	12.7
	Pork albumin	9.8	0.51	0.43	0.45	9.32
E724	Cat albumin	13.1	0.53	8.76	5.04	12.1
	Pork meat	1.65	<0.35	<0.35	<0.35	1.51
	Pork albumin	1.56	<0.35	<0.35	<0.35	1.34

*Each serum was diluted 1:2 or 1:4, and then 200 μL was absorbed for 4 hours with 40 μL of either Sepharose beads coated with the relevant albumin or uncoated blank beads. Sera were then assayed for sIgE to cat albumin (Re220), pork meat (f26), and pork albumin (e222) by using ImmunoCAP, as previously described.[8]

†Preincubation with α-gal or bovine gelatin did not affect the response to cat SA.

being able to tolerate beef, whereas others cannot,[6] and we have not advised beef avoidance unless patients report symptoms associated with eating beef. In the present group of subjects, only 1 (E710) specifically noted symptoms after eating beef, and she was advised to avoid both pork and beef.

If a careful history reveals the possibility that mammalian meat could be associated with episodes, we suggest performing immunoassay testing for sIgE to pork, beef, cat SA, and α-gal. Further investigations might be required, but this simple panel would identify patients whose symptoms were most likely to be explained by pork-cat syndrome. In summary, this represents the first report of patients identified in the United States with pork-cat syndrome in which sensitization to cat SA, which cross-reacts with pork albumin, can produce symptoms rapidly after the consumption of pork.

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