

The Role of Molecular Allergens in the Diagnosis of Cat-Pork Syndrome: An Unusual Case Report



O Papel dos Alergénios Moleculares no Diagnóstico de Síndrome Gato-Porco: A Propósito de um Caso Clínico Raro

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ABSTRACT

Cat-pork syndrome is a rare condition, with few cases reported in the literature. This syndrome is justified by the homology between serum albumins from cat and pork. Evidence suggests that a primary sensitization to cat serum albumin Fel d 2 occurs, followed by allergic reactions after ingestion of pork meat containing serum albumin Sus s 1. Due to homology between other mammalian serum albumins, reactions with other meats can also be present. We report a well-documented case report of a patient with cat-pork syndrome, with initial mild and non-specific manifestations to well-cooked pork that were overlooked. Component resolved diagnosis was essential to establish the diagnosis, which confirmed the involvement of Fed 2 and Sus s 1, but less relevant in helping to define avoidance diets, since the sensitization profile was not in accordance with clinical manifestations.

Keywords: Cats/immunology; Food Hypersensitivity/immunology; Meat/adverse effects; Serum Albumin/immunology; Swine/immunology

RESUMO

A síndrome do gato-porco é rara, com poucos casos relatados na literatura. Esta patologia é justificada pela homologia entre albuminas séricas de gato e de porco. A evidência sugere que ocorre uma sensibilização primária à albumina sérica de gato Fel d 2, seguida por reações alérgicas após a ingestão de carne de porco contendo albumina sérica Sus s 1. Devido à homologia com outras albuminas séricas de mamíferos, reações com outras carnes também podem ocorrer. Reportamos um caso clínico bem documentado de uma doente com síndrome do gato-porco, com sintomas clínicos ligeiros e inespecíficos com ingestão de carne de porco cozinhada, que foram desvalorizados. O diagnóstico por componentes moleculares foi fundamental para estabelecer o diagnóstico, confirmando o envolvimento do Fed 2 e do Sus s 1, mas foi, no entanto, menos relevante na definição de dietas e evicção, uma vez que o perfil de sensibilização não se mostrou concordante com as manifestações clínicas.

Palavras-chave: Albumina Sérica/immunologia; Carne/efeitos adversos; Gato/immunologia; Hipersensibilidade Alimentar/immunologia; Suíno/immunologia

INTRODUCTION

Cat-pork syndrome is a rare condition, with few case reports from Europe published.¹⁻⁵ In this syndrome, patients develop respiratory symptoms to cat epithelium followed by food allergy symptoms with pork ingestion, due to cross-reactivity between serum albumins present in both of these animals.¹⁻⁸ Cross-reactivity can occur because serum albumins are highly conserved across many animals, including mammals.^{7,9-11} About 1% to 3% of patients that are allergic to cats seem to be at risk of pork meat allergy associated with this mechanism.^{4,7,9} More recently, the serum albumins Fed 2 (minor cat allergen) and Sus 1 (major pork allergen) were identified as the molecular compounds involved.⁷ We report a well-documented rare case of a patient with cat-pork syndrome, and explore, in terms of diagnosis and management, the role of component resolved diagnosis (CRD), a diagnostic approach that uses purified native or recombinant allergens to detect the sIgE antibody response against an individual allergenic molecule.

CASE REPORT

We report a case of a 51-year-old female, with a history of intermittent moderate-severe allergic rhinitis and intermittent asthma when exposed to cats, since childhood. She was referred to our allergy department with a history of several episodes of intense generalized pruritus, occurring a few minutes after the ingestion of well-cooked pork meat, in the previous year. She previously tolerated pork meat and also tolerated other meats and derived products, namely, beef, lamb, cow's milk, chicken, turkey and hen's egg.

Skin prick tests (SPT) (Roxall, Spain) with fur animals and meat extracts and skin prick-to-prick tests (SPPT) with cooked pork were performed, both in accordance with the European Academy of Allergy and Clinical Immunology (EAACI) guidelines, and which were considered positive when the mean diameter of the wheal was ≥ 3 mm. SPT were positive to cat (10 mm) and pork (5.5 mm) and SPPT was positive to raw (9 mm) and well-cooked (8 mm) pork meat.

Serum IgE (sIgE) were determined by ImmunoCAP[®] and ImmunoCAP ISAC-112[®] (ThermoFisher, Sweden), in

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Table 1 – Results of sIgE (complete extract and components), and inhibition with rFel d 2 and nSus s 1 (as inhibitors) determined by ImmunoCAP® and ISAC®. ISAC® Standardized Units (ISU-E) Level: < 0.3 Undetectable; 0.3 - 0.9 Low; 1-14.9 Moderate / High; Very High ≥15.

sIgE ImmunoCAP®	(kU _A /l)	Inhibited with “sponge” e220: rFel d 2 (kU _A /L)	Inhibited with “sponge” e222: nSus s 1 (kU _A /L)
IgE cat dander (e1)	66.0	50.50 (23% inhibition)	70.70 (0% inhibition)
IgE pork meat (f26)	10.2	2.73 (73% inhibition)	3.08 (70% inhibition)
IgE cow's milk (f2)	3.79	2.76 (27% inhibition)	3.55 (6% inhibition)
IgE beef meat (f27)	1.84	0.83 (45% inhibition)	0.94 (49% inhibition)
IgE rFel d 2 (e220)	53.9	9.68 (82% inhibition)	38.60 (28% inhibition)
IgE nSus s 1 (e222)	11.1	3.70 (67% inhibition)	3.44 (69% inhibition)
IgE nBos d 6 (e204)	4.32	1.45 (66% inhibition)	2.65 (39% inhibition)
sIgE ISAC-112®	(ISU-E)	Inhibited with “sponge” e204: Fel d 2 (ISU-E)	
Fel d 2 (albumin)	30.0	15.0 (50% inhibition)	
Can f 3 (albumin)	21.0	11.0 (48% inhibition)	
Equ c 3 (albumin)	12.0	3.8 (68% inhibition)	
Bos d 6 (albumin)	1.8	1.0 (44% inhibition)	
Fel d 1	3.8	5.6 (0% inhibition)	
Fel d 4	12.0	16.0 (0% inhibition)	
Can f 1	1.1	1.7 (0% inhibition)	
Can f 5	0.6	0.7 (0% inhibition)	
Bos d lactoferrin	1.9	2.4 (0% inhibition)	
Cup a 1	0.4	0.4 (0% inhibition)	

accordance with the manufacturer's instructions. Values of sIgE > 0.35 kUA/l for ImmunoCAP® and > 0.3 ISU-E for ImmunoCAP ISAC-112® were considered positive.

sIgE were positive to cat/pork extracts, Fel d 2 and Sus s 1. ImmunoCAP ISAC® showed positivity's to some other serum albumins, particularly, Can f 3, Equ c 3, Gal d 5 and Bos d 6 (Table 1).

ImmunoCAP®- inhibition assay, which is a useful tool to identify the allergen of primary sensitization of cross-reactive allergens, was also performed. Patient serum was incubated with a *sponge* of ImmunoCAP e220 (rFel d 2) and e222 (nSus s 1). Percentages of inhibition when pork meat was used in solid phase were 73% with Fel d 2 and 70% with Sus s 1 (Table 1).

SDS PAGE immunoblotting, with 2-mercaptoetanol, identified an IgE binding band of 66kDa in pork extract (Fig. 1).

A strict pork-free diet was initiated, and no more episodes occurred. Months later, the patient accidentally ingested smoked pork and few minutes later, urticaria, dyspnea and wheezing occurred. Cofactors were not involved, namely, exercise, NSAIDs or alcohol ingestion. After this episode, no more accidental ingestions occurred, and she maintains a strict pork-free diet without symptoms.

DISCUSSION

We present a rare case of a patient with cat-pork syndrome which is, to our knowledge, the first one exploring the molecular allergens involved and their role in the diagnosis

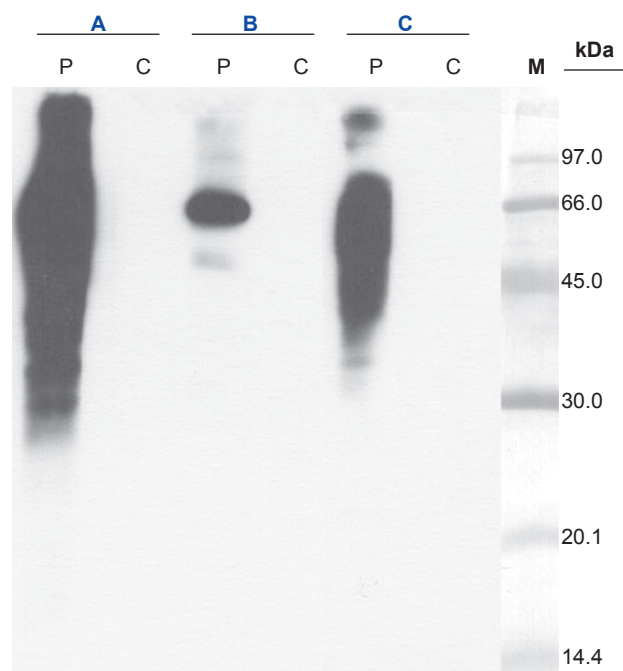


Figure 1 – SDS-PAGE Immunoblotting. (A) Cat dander extract (B) Pork meat extract (C) Purified cat albumin (Fel d 2). Lane P: patient serum; Lane C: control serum (pool of sera from non atopic subjects); M: molecular mass standard.

and management of this condition.

We were able to establish the diagnosis based on a suggestive clinical history supported by skin tests, immunoblotting and CRD. CRD was essential to document the serum

albumins involved - Fel d 2 and Sus s 1. Oral challenges were protracted since the diagnosis was extremely likely.

In terms of clinical history, this patient had a history of respiratory symptoms to cat dander for several years, without symptoms associated with pork meat ingestion. This is in agreement with the literature, which supports that cat-pork syndrome commonly occurs later in life and primary sensitization is due to cat dander.^{1,3,4,6} In this patient, symptoms with pork meat ingestion were initially mild and non-specific, which led to them being overlooked for a long time. This could be explained by the fact that the patient only ingested well-done pork meat and serum albumins are heat-labile proteins, being absent/less present in these forms.⁷ This fact can also justify the higher percentage of patients sensitized to Fel d 2, when compared with patients diagnosed with cat-pork syndrome. However, this case highlights that serum albumins can still remain in their whole form in well-done cooked meat, so caution is still needed. A strict pork-free diet seems to be a safer approach. Later on, a severe reaction after an accidental ingestion of smoked pork occurred, which strongly supports the diagnosis and reinforces the importance of promptly establishing it, since fatal reactions can occur.

Apart from Fel d 2 and Sus s 1, other serum albumins were documented by CRD, namely, Can f 3, Bos d 6, Gal d 5 and Equ c 3. Regardless of these sensitizations, the patient reported no reaction with the ingestion of other meats or derivatives. This fact reinforces that the sensitization profile should not determine avoidance diets, making CRD less useful in defining clinically relevant cross-reactivity, and supporting the importance of a detailed clinical history and proper evaluation of these patients in Allergy departments. Even though it was not the case of our patient so far, cross-reactivity between mammalian meats can occur, so patients should always be aware of this possibility.

IgE-inhibition assays were quite important for reaching the diagnosis, since they demonstrated that serum albumin sensitization justified the allergy to pork meat, as demonstrated by high inhibition of sIgE to pork with Fel d 2 and Sus s 1. This assay also favored the role of Fel d 2 as a primary sensitizer, since it was the one with the highest levels and the one in which greater inhibitions of cat/pork were achieved.

Due to their relevance in meat allergy, α -Gal and Bos d 6 were also considered as culprit allergens. However, clinical

history supported by CRD allowed to rule out both.

So far, avoidance diets are the only available option in these patients. Since the molecular allergens involved are well-documented, we question if specific immunotherapy containing Fel d 2 in a significant amount could improve this condition. However, more studies are needed to support this approach.

CONCLUSION

Despite its rarity, cat-pork syndrome can occur even when associated with well-done pork meat ingestion. Severe reactions may happen, reinforcing the importance of an early diagnosis and proper reference to an Allergy department. CRD seem to be of extreme importance in establishing a diagnosis of cat-pork syndrome but less relevant in helping to define avoidance diets, since the sensitization profile is not always in accordance with clinical manifestations.

AUTHORS CONTRIBUTION

JBL: Conception of the work, analysis and interpretation of data, draft of the manuscript, approval of the final version.

MLH, BB, LC: Critical review of the paper, approval of the final version.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

All authors report no competing interests.

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