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Review

Cross-Reactions and Biomedical Innovations: Challenges and Prospects in Managing Pork-Cat Syndrome

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SUMMARY

Pork-Cat Syndrome (PCS), initially identified in 1994, exemplifies cross-reactive allergic reactions between certain foods and inhalant allergens, notably between feline serum albumin (Fel d 2) and porcine serum albumin (Sus s 1). This review explores the syndrome's pathophysiology, clinical patterns, diagnostic methods, and therapeutic options, aiming to serve as a reference for allergists. PCS arises from IgE-mediated sensitization to Fel d 2, leading to reactions upon consuming pork due to cross-reactivity with Sus s 1. Unlike delayed meat allergies such as Alpha-Gal Syndrome, the symptoms of PCS manifest rapidly after exposure, often following secondary contact with cat allergens. The syndrome's incidence reflects regional dietary habits and exposure to primary allergens, with variability suggesting differences in cat dander exposure and pork consumption practices. Diagnosis involves patient history, specific IgE serum measurements for cat and pig allergens, and molecular diagnostics to highlight cross-reactivity potential. Therapeutic approaches focus on allergen avoidance and emergency management for acute reactions, with no established desensitization protocols due to the syndrome's unique cross-reactivity nature. Clinical and diagnostic challenges stem from the syndrome's rapid symptom onset and the need for precise allergenic testing to confirm cross-reactivity. The review underscores the intricate dynamics between inhalant and food allergens, requiring comprehensive allergological analysis for effective management. It highlights the importance of considering potential cross-allergies in medical and surgical contexts, particularly with products containing bovine serum albumin, due to shared epitopes with Fel d 2. Advances in molecular diagnostics facilitate targeted therapeutic approaches, optimizing clinical outcomes for affected patients. PCS exemplifies the complex interplay between dietary practices, environmental exposures, and allergenic cross-reactivity, emphasizing ongoing research to unravel these interactions and develop specific therapeutic strategies.

KEYWORDS: pediatric allergology, Pork-Cat Syndrome, cross-reaction

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INTRODUCTION

First identified in 1994 by Drouet et al. [1], Pork-cat syndrome epitomizes the paradigm for studying cross-reactive allergic reactions between certain foods and inhalant allergens. This condition is determined by an IgE-mediated immunological response against a 66 kDa antigen, feline serum albumin, which exhibits cross-reactivity with porcine serum albumin.

Meat consumption, especially pork, had already doubled by the late 20th century [2]. Globally,

red meat accounts for 60% of total meat consumption, equating to 34.1 kg per capita annually [3]. In Korea, where pork is particularly favored and its consumption is on the rise, a study among an urban school population reported a 1.9% incidence of pork allergy [4]. In a study conducted in Spain on meat allergy sensitivity in 57 individuals with food allergies, a prevalent reactivity to IgE against pork was noted. Over half of the participants, representing 58%, exhibited allergic reactions to both raw and cooked pork. Among these, some responded only to raw meat, others only to cooked meat, and a third group to both forms of pork [5].

Previously considered rare, the reported variability in the incidence of Pork-Cat Syndrome may reflect regional and environmental differences in exposure to the primary allergen, cat dander, and various pork consumption habits. Between 14% and 23% of individuals allergic to cats have specific IgE to Fel d 2, and among these, approximately 1-3% may develop clinical symptoms after consuming pork [6].

This review aims to summarize current scientific evidence on Pork-Cat Syndrome, delving into pathophysiological mechanisms, observed clinical patterns, standardized diagnostic methods, and available therapeutic options. It seeks to serve as a reference for allergists to facilitate the identification and management of this complex syndrome in clinical practice.

PATHOPHYSIOLOGY AND CLINICAL PRESENTATION

Pork-Cat Syndrome arises from an IgE-mediated immunological sensitization to feline serum albumin (Fel d 2), leading to cross-reactivity with porcine serum albumin (Sus s 1). This sensitization predominantly occurs through inhalation exposure to cat dander, underscoring the intricate interaction between inhalant and food allergies. Molecular biology studies have identified key epitopes involved in the allergenicity of these proteins, showing significant conservation between species [7;8].

The clinical manifestations of this syndrome range from mild reactions such as urticaria and angioedema to more severe conditions such as anaphylaxis [9]. Symptoms appear rapidly, distinguishing this syndrome from other forms of delayed meat allergies, such as Alpha-Gal Syndrome, which is an allergic reaction to a sugar (Galactose-α-1,3-Galactose) found in non-primate mammalian meats, including red meat and some derivatives, with symptoms manifesting 3 to 6 hours after ingestion [10;11]. Pork-Cat Syndrome develops following secondary exposure to cat allergens, whereas Alpha-Gal sensitization is often associated with tick bites. This tick is the Ixodes scapularis in the United States, also known as the deer tick or black-legged tick. In Europe and Australia, sensitization can be mainly attributed to Ixodes ricinus and Ixodes holocyclus ticks, respectively [12]. These ticks can transfer, through their bite, Alpha-Gal antigen (Galactose-α-1,3-Galactose) to humans, triggering potential sensitization to this sugar and leading to the development of the syndrome. The differential diagnosis between Pork-Cat Syndrome and Alpha-Gal Syndrome, besides the different times of onset of symptoms, is based on various aspects, including:

- Clinical and dietary history: A detailed patient history can provide valuable clues. In Pork-Cat Syndrome, patients often report a pre-existing allergy to cats. For Alpha-Gal Syndrome, patients might describe reactions following the consumption of red meat or have a positive history of tick bites;
- Specific allergenic tests: for Pork-Cat Syndrome, skin prick tests or serological tests for specific IgE against cat and pork serum albumin are performed. The presence of specific IgE to Fel d 2 or Sus s 1 may indicate potential cross-reactivity. For Alpha-Gal Syndrome, specific IgE to the Galactose-α-1,3-Galactose (Alpha-Gal) antigen is detected through serological tests;
- Oral provocation tests with suspected foods can be considered. Due to the risk of serious reactions these tests should be conducted under strict medical supervision;
- Evaluation of reactions to other products: Alpha-Gal Syndrome can also cause reactions to products containing gelatin, a common derivative in some pharmaceutical and vaccine production processes [13]. The global prevalence of α-Gal allergy has shown a dramatic increase [14], with an estimated 10% of the US population having high IgE titers against α-Gal [15].

Diagnosis of Pork-Cat Syndrome involves comprehensive patient history, supported by skin prick tests and specific IgE serum measurements for both cat and pig allergens. Molecular diagnostics play a pivotal role, highlighting specific IgE to Fel d 2 as a marker for potential cross-reactivity with pork, and similarly for Sus s 1 [16,17]. Currently, there are no universally recognized prognostic markers to accurately predict the severity of clinical manifestations or the persistence of the allergy over time. However, a study utilizing data from 779 children randomly selected from the BAMSE birth cohort at ages 4, 8, and 16 years, measured specific IgE levels not only for cat but also for dog using ImmunoCAP, and for specific allergenic molecules using an ISAC technology-based microarray. Polysensitization to three or more allergenic molecules of cat or dog was a better longitudinal indicator of symptoms than IgE tests with cat or dog allergen extracts. Sensitization to Fel d 1 was associated with an increased likelihood of developing cat allergy symptoms and allergic asthma during adolescence. Further data are needed to confirm the role of this protein as a significant prognostic marker for patient health [18].

DISCUSSION

The mechanism underlying Pork-Cat Syndrome, which involves an IgE-mediated reaction to feline serum albumin (Fel d 2) with subsequent cross-reactivity to suine albumin (Sus s 1), is exemplified in the clinical cases discussed below. The ingestion of beef viscera in an 8-year-old child sensitized to Fel d 2 [9] led to immediate allergic manifestations, demonstrating that some animal tissues, despite being cooked, retain allergenicity.

The effect of heat on the allergenicity of beef and bovine serum albumin (BSA) was studied in 10 children positive for skin prick tests (SPT) for raw and cooked meat. The diagnosis of meat allergy was confirmed during a double-blind, placebo-controlled food challenge (DBPCFC) with 180 g of beef cooked for 5 minutes at 100°C. SPTs were performed with homogenized beef, lyophilized beef, and heated and unheated BSA. All children were SPT-positive for unheated BSA. Seven were positive for heated BSA, one for lyophilized beef, and none for homogenized beef. DBPCFCs were negative for homogenized and lyophilized beef, positive for unheated BSA in five patients, and positive for heated albumin in four children. Therefore, heating reduces sensitization to beef and BSA, but does not abolish reactivity to albumin under household conditions. However, thermally treated and industrially sterilized homogenized beef and lyophilized beef may be suitable substitutes in cases of beef meat allergy [19].

In the case of an 8-year-old child [14], skin tests showed reactivity only to roasted beef viscera. Specific IgE tests detected sensitivity to pork serum, beef, cow's milk, cat and dog dander, and specific components such as Sus s 1, Fel d 2, Can f 3, and Bos d 6, but not to α-Gal. Immunoblotting confirmed cross-reactivity between swine, bovine, cat, and dog allergens. The method utilizes electrophoresis to separate proteins based on their molecular weight, which are then transferred onto a nitrocellulose or polyvinylidene difluoride (PVDF) membrane. Subsequently, the membrane is incubated with sera from patients allergic to cats. Detection of specific IgE to serum albumins of different species is achieved using anti-IgE antibodies conjugated to enzymes or fluorophores, thus enabling the identification of protein-level cross-allergic reactions among the mentioned species [6]. The child, who had a history of atopic dermatitis and asthma and lived with a cat and a dog, developed generalized urticaria, cough, and wheezing 15 minutes after eating roasted beef intestines. A study revealed that sensitization to Fel d 1 and Fel d 4 allergens is closely correlated (with a p-value less than 0.05) with the occurrence of respiratory wheezing in children with atopic dermatitis, as well as an increased risk of developing asthma during adolescence. In contrast, sensitization to Fel d 2 showed no significant relationship with respiratory manifestations in these patients. Therefore, it is essential to accurately distinguish between the different allergenic components of cats during the assessment of sensitizations and their clinical consequences in children with atopic conditions, highlighting the critical importance of Fel d 1 and Fel d 4, unlike Fel d 2, in the genesis of respiratory wheezing and potentially in the development of asthma [20].

Figure 1 depicts a flow chart illustrating the mechanism of allergic sensitization to cat dander, distinguishing between the response to allergens Fel d 1 and Fel d 2. On one hand, sensitization to Fel d 1 manifests with a specific allergic reaction to cats without further cross-reactivity. On the other hand, reactivity to Fel d 2 is linked both to Pork-Cat Syndrome, in the presence of specific antibodies to swine albumin, and to a marker of allergy to dairy and beef products, indicated by reactivity to Bos d 6. A detailed understanding of these pathways is crucial for a correct diagnostic approach to allergies.

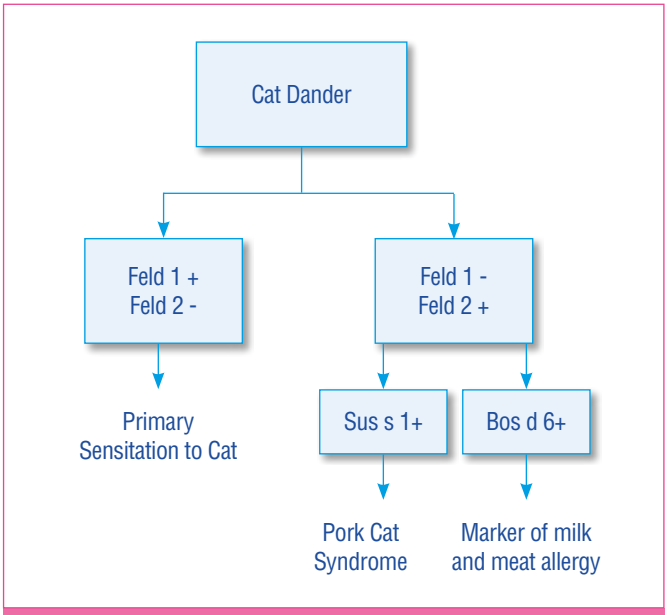

FIGURE 1. Pathways of Allergenic Sensitization: Cat Dander and Associated Allergens.

It is important to consider the variety of clinical presentations of Pork-Cat Syndrome, which can manifest with typical immediate symptoms or with less clear and more atypical ones such as FDEIA, i.e, exercise-induced anaphylaxis dependent on food ingestion [21]. In particular, the case of the adolescent illustrates that physical exercise can exacerbate the allergic response in the presence of specific allergens, an aspect that may be overlooked during conventional evaluation. The patient developed systemic urticaria and dyspnea after engaging in intense physical activity following the consumption of a meal that included pork. Although initially suspected to be caused by wheat-induced FDEIA, further investigations revealed specific sensitization to pork, beef, cat and dog dander, Sus s 1 (pig albumin), and Fel d 2 (cat albumin), with positive specific IgE tests. Immunoblotting analysis confirmed the presence of specific IgE against soluble pig proteins and cross-reactivity with cat proteins. The patient was advised to avoid physical exercise immediately after consuming pork and to be cautious of cofactors (NSAIDs, alcohol, viral infections). Preventing FDEIA requires close collaboration between the patient, family, healthcare providers, and, if applicable, school or sports personnel, to ensure a safe environment and minimize the risk of severe reactions [22].

Understanding these clinical cases and analyzing Pork-Cat Syndrome requires a review of current diagnostic and therapeutic practices. Preventing anaphylactic reactions in patients sensitized to Fel d 2 should also involve the selection of safe medical devices for sensitized patients [23]. BSA is indeed contained in various medical devices, such as some types of tissue adhesives used for vascular repair surgeries. Indeed, the case of a 53-year-old man is described who developed an

anaphylactic reaction during surgery for the repair of an abdominal aortic aneurysm. The reaction was triggered by the application of BioGlue®, a BSA and glutaraldehyde-based adhesive used to seal the suture line on the supraceliac aorta. The diagnosis of IgE-mediated BSA allergy was confirmed through the temporal coincidence between adhesive application and symptom onset, tryptase levels, skin test results, and the patient's clinical history. The latter included episodes of rhino-conjunctivitis after exposure to cats and digestive disorders following the consumption of lamb or pork. Further tests showed that primary sensitization was due to feline serum albumin (Fel d 2), leading to cross-reactivity with other mammalian serum albumins, including bovine, resulting in an anaphylactic reaction to the tissue adhesive used during the operation. This case highlights the importance of considering potential cross-allergies and the need to preoperatively evaluate specific IgE levels for feline serum albumin in cat-allergic patients in order to avoid the use of tissue adhesives containing BSA whenever possible.
Therefore, close collaboration between allergists and surgeons is necessary to identify at-risk patients and select safe materials for use in medical and surgical settings. The ability to identify specific sensitization profiles through molecular tests allows for the prediction and prevention of potential reactions, using appropriate sealing materials and ensuring patient safety.

But the surgical sector is not the only one that utilizes bovine proteins. BSA is used in vaccine production processes for its nutrient properties in cell cultures and as a stabilizer in some vaccine formulations. Considering the possibility of allergic reactions, the World Health Organization (WHO) has established that the maximum allowable limit of BSA per vaccine dose is 50 ng [24]. In line with these guidelines, the industry is moving towards the use of animal-component-free cell culture systems and towards reducing or eliminating such materials in production processes to improve vaccine safety and acceptability.

Vaccines such as DTP-IPV/Hib (Pentacel) [25], Hepatitis A vaccine (Vaqta) [26], Japanese encephalitis vaccine (Ixiaro) [27] use BSA as an excipient. In the Ixiaro vaccine's package insert, hypersensitivity to BSA is listed as a contraindication. This contraindication may arise from the production process, or the excipients used, which may include or come into contact with BSA in quantities sufficient to pose risks to individuals with allergies to this protein. Transparency regarding these components addresses the need to prevent adverse reactions in individuals sensitive to BSA.
The Pentacel and VAQTA vaccines, although produced on matrices containing proteins, do not mention the quantity of BSA contained, nor the presence of an actual contraindication to their administration for patients allergic to BSA, in their package inserts.
Finally, it is important to note that vaccine production practices are constantly evolving with the aim of minimizing the presence of potentially allergenic components. Patients with a history of significant allergies should consult a healthcare professional to assess the risk before vaccine administration.

Regarding contamination with bovine proteins, Andreas et al. [28] report a case of type I anaphylactic reaction in a patient treated with autologous dendritic cells generated in vitro and cultured in a medium containing fetal bovine serum (FBS). During phase I immunotherapeutic treatment for melanoma, one of the 16 patients developed an anaphylactic reaction after vaccination with these cells. Investigation of pre- and post-vaccination serum samples revealed the presence of antibodies against FBS and BSA, with a significantly increased specific IgE response only in the patient who experienced anaphylaxis.

The reported case highlights the risks associated with the use of FBS in cell culture for therapeutic applications, particularly due to the potential sensitization and development of anaphylactic reactions to xenogeneic proteins such as BSA. The other six patients, in fact, developed IgG and IgM antibodies against FBS and BSA after vaccination, none of whom experienced anaphylactic reactions, indicating that the anaphylactic reaction was mediated by specific IgE antibodies to BSA. Therefore, great care must be taken in selecting culture media in the preparation of cells for therapeutic purposes to prevent antibody responses to foreign proteins and anaphylactic reactions.
Other data in the literature underline that FBS is the most widely used growth supplement added to in vitro cell cultures and is employed in a variety of research and industrial applications, including vaccine production. During vaccine development, FBS is particularly effective as a culture medium supplement to promote viral replication. However, it is important to note that FBS does not actually exist within the final vaccine; rather, its macromolecular proteins are broken down by cells to be used as nutrients, and its growth factors stimulate the proliferation of desired cells. Significant variations in production methods and specific ingredients may occur depending on the vaccine and the manufacturer.

To date, no allergic reactions have been reported for individuals with Pork-Cat Syndrome undergoing these types of vaccinations [29].

Recent biotechnological advancements have led to the development of innovative nanoparticles, such as combined hydroxyapatite (HA), BSA, and paclitaxel (PTX) nanoparticles, designed for the controlled release of antitumor drugs directly into the tumor site. These nanoparticles represent a promising advancement in adjuvant therapy for osteosarcoma, offering both targeted antitumor actions and promoting bone repair [30]. However, in evaluating the use of such innovative treatments, it is crucial to consider the implications for patients with allergies.
This condition, characterized by IgE-mediated allergic reactions to specific albumin components present in both cats (Fel d 2) and pigs (and by extension, in bovine proteins such as BSA), raises concerns regarding the safety of using nanoparticles containing BSA in these patients. The possibility that individuals with this syndrome may develop potentially severe allergic reactions following exposure to

BSA through such nanoparticles requires careful risk assessment. Faced with these challenges, it is imperative for researchers and clinicians engaged in the development of nanoparticle-based treatments for osteosarcoma to evaluate alternatives to BSA or adopt rigorous protocols for monitoring and managing potential allergic reactions in patients with Pork-Cat Syndrome. This may include pre-treatment sensitivity testing specific to BSA and the preparation of detailed emergency plans to manage any adverse reactions.

Bovine milk proteins are known for their moisturizing properties and are extracted from milk and partially hydrolyzed to modify their structure and allergenic properties. There are several beauty products on the market that exploit these properties of bovine proteins. A group of experts examined 16 ingredients derived from bovine milk proteins, which are predominantly used as conditioning agents for skin and hair in personal care products. Despite their known allergenicity, bovine milk proteins have not demonstrated immediate hypersensitivity reactions after topical use [31].
Furthermore, studies on genotoxicity and carcinogenicity indicate that they may even have tumor-suppressive properties. Renea RE. et al exposed female Sprague-Dawley rats to diets containing either casein (CAS) or whey protein hydrolysate (WPH) starting from the fourth day of gestation. After weaning, the offspring were fed the same diet as their mothers for their entire lives. At 50 days of age, the rats were treated with N-methyl-N-nitrosourea to induce mammary carcinogenesis. The results showed that lifelong exposure to WPH, compared to CAS, reduced the incidence of mammary tumors [32]. Further studies are certainly needed to evaluate the safety of BSA use in other sectors and contexts for individuals affected by pork-cat syndrome.

MANAGEMENT

Scientific research confirms that feline serum albumin, Fel d 2, is a minor allergen despite being an important component present in cat fur. All cats possess this allergen. Serum albumin shows a high sequence identity with albumins from other mammals, such as the dog (Can f 3), pig (Sus s 1), cattle (Bos d 6), and horse (Equ c 3), with an average of 75%-85%. This makes Fel d 2 a useful biomarker for a high risk of cross-reactivity with other serum albumins. Approximately 15%-25% of cat-allergic patients are sensitized to feline albumin, and this sensitization is associated with moderate/severe rhinitis and asthma diagnoses. [33]

It is surprising that allergic patients develop specific IgE responses against animal albumins, given that these proteins show a sequence similarity of over 70% with human serum albumin (HSA), the most abundant protein in human blood. The sequence of cat albumin (Fel d 2) and dog albumin (Can f 3) has an identity of 82% and 80% respectively with HSA. This raises questions about immunotolerance and possible IgE sensitization to Fel d 2 and Can f 3 due to minimal differences in sequences compared to HSA, which could lead to the development of specific T and B cell responses to these albumins [34]. These studies confirm the importance of considering cross-sensitizations between albumins of different mammals in the management of allergic patients, especially in medical and surgical contexts where products containing BSA, such as tissue adhesives, may be used.

Table I shows the alignment between the Sus S 1 protein and homologous proteins from various species. Those data were collected from the project "SDAP 2.0 - Structural Database of Allergenic Proteins". For example, Fel d 2 (cat) and Bos d 6 (bovine) show 79% identity with Sus S 1, suggesting the possibility of cross-reactivity in sensitized individuals. Instead, the E-value, or expectation value, is a key parameter used in sequence alignment analyses. This value provides a statistical measure of the significance of the alignment found between two sequences. In simple terms, the E-value helps distinguish between alignments that occur due to true evolutionary similarity (homology) and those that occur by pure chance. A low E-value (close to zero) indicates that the alignment is highly significant and is unlikely to be due to chance. This suggests

TABLE I. Alignment between homologous protein to Sus S 1. Alignment made with FASTA version 36.3.8. As explained in the FASTA manual, the bit score is equivalent to the bit score reported by BLAST. A 1 bit increase in score corresponds to a 2-fold reduction in expectation, and a 10-bit increase implies 1000-fold lower expectation. Sequences with E values < 0.01 are almost always homologous. All FASTA search sequence alignments are printed in Blast format where Query is input sequence, and Sbjct is sequence found in the database.

UniProt Name	Name	Length	Opt	Bits Score	E-Value	Identities (%)	Positives (%)	Gaps (%)
P49064	Fel d 2	608	3386	778.0	0	483/607 (79%)	546/607 (89%)	1/607 (0%)
P02769	Bos d 6	607	3451	792.0	0	485/607 (79%)	549/607 (90%)	0/607 (0%)
P49822	Can f 3	608	3379	776.4	0	476/606 (78%)	543/606 (89%)	1/606 (0%)
CAA52194	Equ c 3	607	3295	757.3	6.6e-220	464/607 (76%)	531/607 (87%)	0/607 (0%)
CAA43098	Gal d 5	615	2032	469.4	3.1e-133	267/606 (44%)	408/606 (67%)	5/606 (0%)
Q6WDN9	Cav p 4.0101	608	3181	731.3	4.4e-212	445/607 (73%)	527/607 (86%)	1/607 (0%)

a strong evolutionary and functional relationship between the compared sequences. Conversely, a high E-value suggests that the alignment may not be significant and may have occurred by chance. Gal d 5 shows only 44% identity and 67% positivity with Sus S 1 in a sequence alignment; therefore, it can be concluded that, compared to other examined proteins (such as Fel d 2, Bos d 6, and Can f 3), Gal d 5 shows lower sequence homology with Sus S 1. These levels of identity and positivity suggest moderate similarity, which may not be sufficient to indicate strong homology or a direct evolutionary relationship. The protein showing the highest sequence similarity with Sus S 1 (swine albumin) is Bos d 6 (bovine albumin), with 79% identity and 90% positivity in sequence alignment. These high values of identity and positivity indicate a strong similarity between the two protein sequences, suggesting a close evolutionary or functional relationship between swine and bovine albumins.
The 79% identity means that approximately four-fifths of the amino acids in these sequences are identical when aligned, while 90% positivity indicates that in addition to the identity percentage, there is also a high similarity in the chemical and physical properties of the amino acids composing the two proteins, even though they are not identical. This strong similarity may reflect similar biological functions and, in the context of allergies, can explain the possibility of cross-reactivity between bovine and pig allergens in sensitized individuals.

This high homology between Sus S 1 and Bos d 6 underscores the importance of considering potential cross-reactivities in allergy diagnoses and in advising patients regarding the avoidance of specific foods or exposures to certain allergens. These data provide molecular support to the clinical observation that patients with allergies to particular animal proteins may experience cross-allergic reactions when exposed to other allergens with similar protein structures.

Patients affected by Pork-Cat Syndrome should avoid consuming pork meat and, potentially, other animals that share similar epitopes with feline serum albumin due to cross-reactivity. These primarily include:

- Pork meat: The main allergen involved in Pork-Cat Syndrome is pig serum albumin (Sus s 1), so pork meat in all its forms (fresh, cooked, processed) should be avoided;
- Pork-based products: Deli meats, sausages, and other processed products containing pork meat or derivatives should be excluded from the diet;
- Foods that may contain traces of pork meat: it is important to carefully read food labels to identify those that may contain traces of pork meat or derivatives, even when they are not the main ingredient.

In addition to pork meat, some patients may need to consider avoiding:

- Meat from other mammals: Although the main issue concerns pork meat, cross-reactivity with serum albumin from other mammals could theoretically extend dietary restrictions to meats such as beef, veal, and perhaps lamb. However, the need to avoid these meats varies from person to person and should be individually assessed based on clinical reactions and allergy test results.

Environments such as butcher shops and restaurant kitchens may pose a risk due to potential cross-contamination. Patients should be aware of this risk when dining out or purchasing prepared foods. For sensitive individuals, it is crucial to read food labels to identify possible traces of pork meat, considering that even skin contact and inhalation during handling of raw meat can constitute exposure pathways.

Management of diet in Pork-Cat Syndrome requires particular attention and, in some cases, collaboration with a dietitian to ensure that the diet remains balanced and nutritious despite the restrictions.

Pharmacotherapy for acute reactions and the provision of emergency action plans, including self-injectable epinephrine, are essential.

Currently, the scientific literature does not provide significant evidence or consolidated protocols regarding the feasibility or effectiveness of specific desensitization for this condition. The unique nature of cross-reactivity in this syndrome poses a challenge in directly translating desensitization approaches used for other food or inhalant allergies.

Future research could explore desensitization protocols or tolerance induction specific to this unique allergic syndrome.

CONCLUSIONS

Pork-Cat Syndrome highlights the intricate dynamics between inhalant and food allergens, emphasizing the need for meticulous allergological analysis to overcome diagnostic difficulties and therapeutic complexities. Analysis of clinical cases combined with advances in molecular diagnostic methodologies underscores the importance of adopting a comprehensive and informed strategy in patient management, integrating understanding of molecular components with observed clinical manifestations. It is crucial for allergy specialists to pay attention to patients undergoing procedures requiring use of specific adhesive materials to mitigate the risk of serious adverse reactions. Molecular diagnostics become crucial, allowing for targeted therapeutic approaches and effective prevention of allergic reactions, especially in specialized clinical settings. A thorough understanding of the molecular characteristics and clinical manifestations of this syndrome enables healthcare professionals to significantly optimize clinical outcomes and improve the quality of life of affected patients. Continued research is imperative to unravel the complexities of allergic cross-reactivity between different allergens and to formulate specific therapeutic strategies that may open new perspectives in the treatment of Pork-Cat Syndrome.

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Authors' contribution
C.I., V.T., G.M.: conceptualized the project. C.I., V.T, G.M.: wrote the first draft. All authors revised the manuscript and approved the final version.

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