

Original article

Allergy to human seminal fluid: Cross-reactivity with dog dander

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Background: Human seminal plasma (HSP) allergy is uncommon, with symptoms ranging from vulvovaginal pruritus to life-threatening anaphylaxis. Although several seminal plasma allergens have been reported and their molecular masses have been estimated to range between 12 and 75 kd, the prostate-specific antigen (PSA) has recently been identified as a causative allergen. Given that in a large number of cases symptoms appeared during or after the first intercourse, a cross-reactivity phenomenon might be implicated.

Objective: We sought to assess the presence of IgE cross-reactivity among proteins from dog epithelium and HSP and to attempt to identify the allergens involved.

Methods: Forty-one patients with dog epithelium allergy were selected. One of them experienced anaphylaxis in contact with her husband's seminal plasma. Skin prick tests, serum specific IgE measurements, SDS-PAGE immunoblotting, and inhibition tests were performed to study the pattern of IgE-binding proteins and the potential cross-reactivity between HSP and dog epithelium. Mass spectrometry was carried out to identify the protein involved in allergy reactions.

Results: Twenty-four percent of the sera from patients with dog epithelium allergy recognized an IgE-binding band of 28 kd in HSP immunoblotting. Mass spectrometry identified this band as the PSA. SDS-PAGE immunoblotting-inhibition showed a complete IgE-binding inhibition when sera from these patients were preincubated with dog dander extract.

Conclusions: IgE cross-reactivity among proteins from dog dander and human PSA is demonstrated.

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Key words: Allergen characterization, cross-reactivity, dog epithelium allergy, human seminal plasma allergy, prostate-specific antigen

Abbreviations used

EAST:	Enzyme Allergo Sorbent Test
HSP:	Human seminal plasma
HSPA:	Human seminal plasma allergy
MALDI-TOF:	Matrix-assisted laser desorption/ionization-time of flight
MS:	Mass spectrometry
PSA:	Prostate-specific antigen

Human seminal plasma allergy (HSPA) in women is rare. Only 80 cases in the English literature have been reported since the first mention of HSPA in 1967 by Halpern et al.¹ The third decade of life has been found to be the most frequent period of appearance of this disorder, and an IgE-mediated response is the most common etiopathogenetic mechanism. In clinically sensitive subjects skin prick tests against human seminal plasma (HSP) produce a typical wheal-and-flare response, and a measurable serum specific IgE antibody has been detected.² Atopy status has been pointed out as an important predisposing factor to this infrequent phenomenon.³

In 40% of patients with HSPA, symptoms begin during or after the first sexual intercourse. Symptoms usually occur either immediately, during, or after coitus, and a gradual reduction in the time of onset of symptoms and a gradual worsening of symptoms over the course of time have been reported.⁴ The hypothesis that the sensitization agent would be an unknown antigen that cross-reacts with some of the proteins present in HSP was originally proposed by Halpern et al¹ several years ago, but until now, it has not been demonstrated. Another unclear point of this disease is whether the clinical manifestations occur only with one particular partner or if they appear after coitus with more than one sexual partner. Both situations have been reported, but there are many cases in which this information is lacking.²

Concerning the allergen involved, several IgE-binding antigens have been found, and their molecular masses were reported to range from 12 to 75 kd. However, there is no solid information concerning the precise characterization and origin of the responsible allergen, although a possible prostate origin has been suggested.¹

Recently, a case report demonstrated the presence of specific IgE antibodies against prostate-specific antigen (PSA) in the serum from a woman with HSPA.⁴ Despite technologic advances in recent years, few of the proteins detected in seminal fluid have been fully characterized. A comprehensive analysis of the peptide and protein components of human seminal fluid was performed by combining gel electrophoresis (1-dimensional

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and 2-dimensional) with matrix-assisted laser desorption/ionization–time of flight (MALDI-TOF)/mass spectrometry (MS), electrospray ionization (ESI) liquid chromatography/tandem mass spectrometry (LC/MS/MS), and database searching. The majority of the detected proteins were identified as modified forms of PSA, prostate acid phosphatase, Zn- α -2-glycoprotein, clusterin, semenogelin I, and semenogelin II.⁵

We have recently published the case of a 38-year-old nulligravida woman who experienced anaphylactic reactions after sexual intercourse with her husband since her first coitus. The husband had been her unique sexual partner. As a personal allergy history, she only mentioned bronchial asthma with sensitization to dog epithelium. The use of sperm barrier methods completely abolished the symptoms, but it was not acceptable at the time she wanted to become pregnant. The identification of the responsible allergen as a 28-kd allergen and the application of washed semen (free from this protein) in the artificial insemination allowed achievement of pregnancy and avoided an allergic reaction.⁶

This research was performed with the following objectives: (1) to characterize the 28-kd allergen involved in the case of HSPA previously reported,⁶ (2) to study the presence of cross-reactivity between this allergenic protein and some component of dog epithelium, and (3) to determine the percentage of patients with dog epithelium allergy in which serum IgE antibodies reacting with the 28-kd antigen from the HSP were present.

METHODS

Subjects

Between September 2004 and September 2005, all consecutive patients given diagnoses of dog epithelium hypersensitivity at the Allergy Department of Institut Universitari Dexeus (Barcelona, Spain) were eligible to participate in the study. The patients were selected based on a clear history of dog epithelium allergy and positive skin test responses against this allergenic source. Patients provided written informed consent, and the study was approved by the hospital ethics committee.

A short questionnaire was distributed among participants. The questionnaire was designed to collect the following information: age, sex, symptoms manifested by exposure to dog epithelium, symptoms manifested by exposure to other mammal epithelia, first clinical sensitization to mammal epithelium, treatment desensitization to dog epithelium, and symptoms experienced in contact with HSP.

Allergen sources and extracts

Seminal fluid was collected by condom from the partner of the patient with HSPA and was used to perform all the *in vitro* assays. Recombinant Can f 1 and recombinant Can f 2 (Department of Clinical Microbiology, University of Kuopio, Kuopio, Finland) was produced and purified, as previously described.⁷ Defatted dog epithelium and dog dander (Greer Laboratories, Lenoir, NC) were extracted by means of magnetic stirring during agitation in 50 mmol/L PBS at pH 7.5 for 4 hours at room temperature. The sample was centrifuged at 5600g for 30 minutes, and the supernatant was dialyzed against water. The dialyzed extract was filtered through a membrane with 0.22- μ m-diameter pores.

Skin prick test

Skin prick tests with dog epithelium (3 mg/mL) and dander (1.3 mg/mL) extracts and a panel of other mammal epithelia, including rat, mouse, hamster, cat, cow, pork, lamb, guinea pig, and rabbit (Bial-Aristegui, Bilbao, Spain), were performed according to a standard procedure⁸ on the volar side of the forearm by means of puncture with the Prick Lancettes Dome (Hollister-Stier, Spokane, Wash). One sterile device was used for each test. Histamine phosphate

(10 mg/mL) and sterile 0.9% saline were used as positive and negative controls, respectively. A mean wheal area of 7 mm² or greater compared with that elicited by the negative control 15 minutes after puncture was considered a positive response.

Specific IgE determination

Specific IgE measurement against human seminal fluid, dog epithelia, and dog dander was carried out by using the Enzyme Allergo Sorbent Test (EAST). The solid phase was obtained by coupling the seminal fluid (2 mg/mL) and dog extract (10 mg/mL) to the 6-mm-diameter cyanogen bromide-activated paper discs, as described by Ceska and Lunqvist.⁹ The EAST was performed, and results were expressed in accordance with the manufacturer's instructions (Specific IgE EIA kit; HYTEC, Hycor Biomedical Ltd, Penicuik, United Kingdom). A pool of sera from nonallergic subjects was used as a negative control.

SDS-PAGE immunoblotting and inhibition

SDS-PAGE was carried out according to the method of Laemmli¹⁰; 12.5% and 4% acrylamide were used for separating and stacking gels, respectively. Samples were dissolved in 0.125 mol/L HCl-Tris (pH 6.8) and were denatured with 0.1% SDS at 100°C for 5 minutes when nonreducing conditions were used. According to the technique of Bradford,¹¹ 20 μ g of protein was applied per lane.

After electrophoresis, gels were stained by means of diffusion in 0.1% Coomassie Brilliant Blue R-250 dissolved in methanol/acetic acid/distilled water (4:1:5). Separated protein bands were electrophoretically transferred to polyvinylidene difluoride, essentially as described by Towbin et al,¹² and blocked for 1 hour at room temperature with 0.1% Tween-20 and 5% fish collagen in Tris-buffered saline. Membranes were incubated overnight at 4°C with the patient's serum, followed by antihuman IgE–horseradish peroxidase conjugate incubation and detection with the chemoluminescence method, as recommended by the manufacturer (ECL-Plus; Amersham Pharmacia Biotech, Little Chalfont, Buck, United Kingdom).

When Western inhibition assays were performed, the patient's serum was preincubated with different inhibitor phases (dog epithelium or dog dander extracts) overnight at 4°C, and then membranes were incubated with the patient serum sample obtained.

EAST inhibition

EAST inhibition was performed according to methods reported by Yman et al.¹³ HSP was used as the solid phase, and the patient's serum was preincubated with dog dander extract (1.8 mg/mL) and Can f 1 and Can f 2 recombinant molecules at 120 μ g/mL (Department of Clinical Microbiology, University of Kuopio, Kuopio, Finland).

Protein identification and characterization by means of MS

The proteins of interest were identified by means of MS. The bands selected were cut out from the gels with a sterile scalpel and subjected to in-gel trypsin digestion according to the method of Shevchenko et al,¹⁴ with some modifications. The in-gel digests were purified as described by Gobom et al.¹⁵ Peptides were analyzed by using a Voyager-DE STR BioSpectrometry Workstation instrument (Applied Biosystems, Foster City, Calif), and positively charged ions were analyzed in reflector mode by using delayed extraction with the following settings: acceleration voltage of 20 kV, grid of 72%, delay time of 300 ns, 100 shots per spectrum, and mass range of 800 to 3500 d. Spectra were calibrated by using trypsin autolysis products, resulting in a mass accuracy of less than 50 ppm. Peptide fingerprinting was analyzed by using Data Explorer software (Applied Biosystems, Foster City, Calif). In addition, the identification was confirmed by means of MS/MS in a MALDI-TOF/TOF 14700 Protein Analyzer (Applied Biosystems). Protein identification was performed by searching a nonredundant protein sequence database (National Center for Biotechnology Information) with the Mascot program (<http://www.matrixscience.com>). The following parameters were

used: monoisotopic mass accuracy of less than 50 ppm, 1 missed cleavage, and allowed carbamidomethylation modifications of cysteine (complete), methionine, and pyroglutamic acid (partial).

Statistical analysis

Demographic, clinical, and laboratory data of patients with and without the 28-kd IgE-binding band recognition were compared. Categorical data are expressed as frequencies and percentages, and continuous data are presented as means and SDs. The χ^2 test, the Student *t* test, the Mann-Whitney *U* test, and Spearman correlation were used for the analysis of data. Statistical analysis was performed with SAS version 9.1.3 software (SAS Institute, Inc, Cary, NC). Statistical significance was set at a *P* value of less than .05.

RESULTS

The study population included 41 patients, 30 women and 11 men, aged between 7 and 67 years, who presented with a clear history of dog epithelium allergy with positive skin prick test responses to dog epithelium extracts, dog dander extracts, or both and with serum specific IgE to 1 or both allergenic sources of greater than 0.35 kU/L. There were no statistical differences between the groups of patients with and without HSP 28-kd IgE-binding band recognition regarding the mean age, sex, and clinical manifestations of dog allergy. In addition, 2 patients whose IgE recognized the protein of 28 kd presented with a sexual disease (HSPA in one and infertility of unknown cause in the other). The presence of sexual disorders was significantly more frequent among patients with 28-kd IgE-binding band recognition compared with that in the group without recognition of this protein (*P* < .0107). No case of sexual disease was observed among the population of patients with dog allergy who did not recognize the protein.

The percentage of patients with clinical symptoms related to dog allergy only and not allergy to other mammals was also significantly higher among those with serum specific IgE against the HSP 28-kd IgE-binding protein (*P* < .0004). Moreover, 80% of patients in this group were monosensitized to dog. The difference was statistically significant (*P* < .001).

The main demographic characteristics and allergy history of the study patients are summarized in Table I.

SDS-PAGE of HSP showed multiple protein bands with an apparent molecular mass ranging from 14 to 120 kd (Fig 1, A). IgE immunoblotting of this sample in nonreducing conditions and incubated with the serum of the woman with anaphylaxis revealed 2 IgE-binding bands, a clear band of 28 kd and a faint band of 32.7 kd. However, when reducing conditions were used, only a faint band of 34.6 kd was observed (Fig 1, B, and Fig 2, lane 29), indicating that after reduction of the disulfide bridges, the protein unfolds, and thus its apparent molecular mass increases. In nonreducing conditions similar results were obtained with 9 other sera from the studied group (9+1/41 [Fig 2, lanes 4, 10, 14, 16, 28, 29, 31, 36, 39, and 41] or 24% of the sera). An additional IgE-binding band of 53 kd was revealed with 3 of the sera, but it also appeared with sera from atopic patients with pollinosis who were not allergic to dog epithelium (data not shown).

The patient with clinical seminal fluid allergy had an IgE titer to complete HSP of 5 kU/L. Results in the other 9 patients with dog epithelium allergy who reacted to this band were as follows: 1.5, less than 0.35, less than 0.35, 0.7, 0.6, 0.4, less than 0.35, 1.5, and 3.4 kU/L. The serum from the anaphylactic patient showed the highest specific IgE level against HSP.

TABLE I. The main demographic characteristics and allergy history of the selected patients

	PSA recognition		<i>P</i> value
	No (n = 31)*	Yes (n = 10)*	
Age (y), mean (SD)	33.52 (14.17)	35.80 (9.35)	.637
Sex (female)	24 (77.4%)	6 (60.0%)	.279
Sexual disease	0 (0%)	2 (20.0%)	.010
Dog allergy			
Rhinoconjunctivitis	25 (81%)	5 (50%)	.057
Asthma	21 (67.7%)	6 (60.0%)	.653
Cutaneous	4 (12.9%)	1 (10.0%)	.807
Subclinical	1 (3.2%)	1 (10.0%)	.387
Other mammal allergy	18 (58.1%)	1 (10.0%)	<.001
Hyposensitization to dog	6 (19.4%)	3 (30.0%)	.480
Skin prick test to dog	31 (100.0%)	10 (100.0%)	NA
Skin prick test to cat	24 (77.4%)	2 (20.0%)	.001
Skin prick test to other epithelia	14 (45.2%)	3 (30.0%)	.473

NA, Not applicable.

*Descriptive statistics are presented as numbers (percentages) unless otherwise indicated.

EAST inhibition assays were performed with the serum from the patient with HSPA to investigate whether HSP proteins cross-reacted with Can f 1 and Can f 2, the 2 major dog epithelium allergens. The results showed that Can f 1 and Can f 2 recombinant allergens as inhibitors (120 μ g/mL) were not able to avoid any level of IgE-binding activity to seminal fluid, whereas in the same assay dog dander extract (1.8 mg/mL) produced a total inhibition (data not shown).

SDS-PAGE immunoblotting inhibition in nonreducing conditions showed a complete inhibition (both IgE-binding bands disappeared) when the serum of the anaphylactic patient was preincubated with dog dander extract at 1 mg/mL (Fig 3). A 5-fold concentration was necessary to obtain the same result with dog epithelium extract (data not shown). A similar inhibition result was obtained with the sera from patients 4, 36, 39, and 41 (data not shown).

The 28-kd IgE-binding band from the HSP was identified by means of MS and turned out to be the PSA. Sixty-five percent coverage was obtained by means of MALDI analysis, with 4 peptides identified. A score of 125 was generated by using the Mascot program, corresponding to human PSA. The MS/MS analyses of 3 peptides yielded the sequences IVGGWECEK, HSQPWQVLVASR, and AVCGGVLPQWVLTAAHCIR, which match with positions 1 to 9, 10 to 21, and 22 to 44 in the PSA sequence (Fig 4).

DISCUSSION

HSPA in women is rare. There is little information on the nature of the antigen involved in HSPA. The molecular mass of several seminal plasma allergens have been described ranging from 12 to 75 kd, but the origin of the allergens, as well as whether there is only 1 or multiple allergenic components involved in HSPA, is unclear.

Several years ago, Halpern et al¹ proposed that the allergy symptoms experienced by some women after their first sexual intercourse might be caused by a previous sensitization to unknown antigens that cross-react with HSP proteins; however, to our knowledge, this hypothesis has not been previously

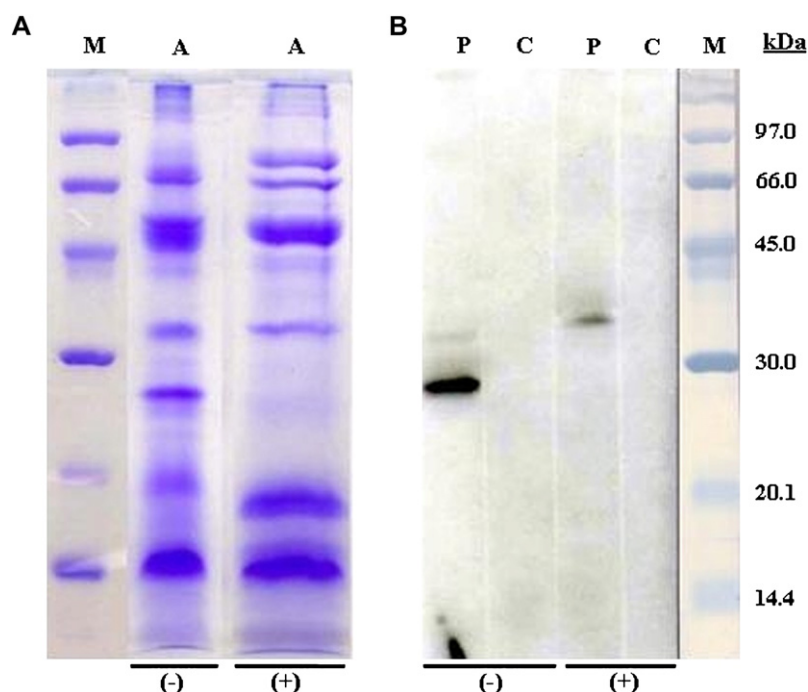


FIG 1. A, SDS-PAGE after Coomassie Brilliant Blue R-250 staining: lane A, HSP; lane M, molecular mass marker. B, IgE immunoblotting: lane P, patient serum; lane C, control serum (pool from nonatopic subject sera). The + and – symbols indicate the presence and absence of β-mercaptoethanol, respectively.

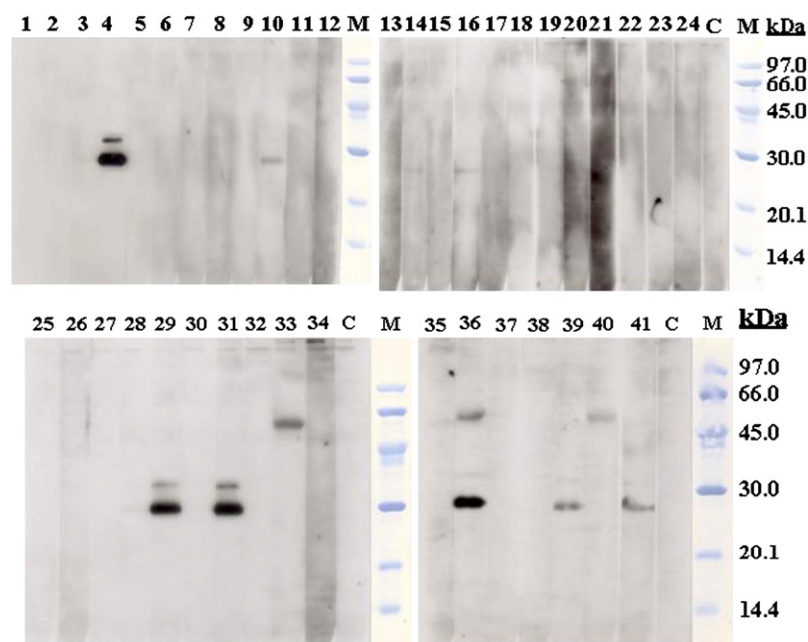


FIG 2. IgE immunoblotting: lanes 1–41, patient sera; lane C, control serum (pool from nonatopic subject sera); lane M, molecular mass markers. Samples are without β-mercaptoethanol.

demonstrated. Given that we encountered a patient with dog epithelium allergy who experienced an anaphylactic reaction in her first sexual intercourse, we examined the possibility of cross-reactions between both HSP and dog epithelium.

Dog allergens have been involved in mammal protein cross-reactivity. Can f 3, dog albumin, which is an important allergen

for up to 35% of patients with dog epithelium allergy, has been demonstrated to show IgE cross-reactivity with other serum albumins, such as cat, mouse, chicken, and rat albumin, and significantly with human albumin as well.^{16–19}

We identified and characterized by means of MS the responsible allergen in the HSP anaphylactic reaction here

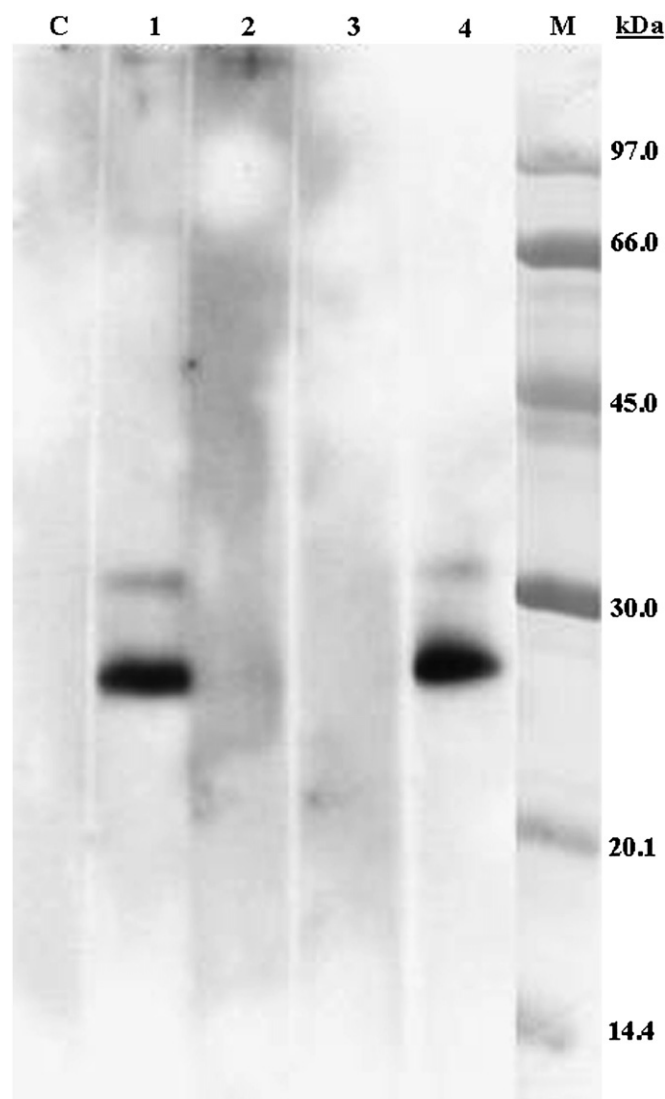


FIG 3. IgE immunoblotting inhibition: *lane C*, control serum (pool from nonatopic subject sera); *lane 1*, patient serum; *lane 2*, patient serum previously incubated with HSP; *lane 3*, patient serum previously incubated with dog dander extract; *lane 4*, patient serum previously incubated with lamb extract; *lane M*, molecular mass markers. Samples are without β -mercaptoethanol.

studied, and it turned to be the PSA, a kallikrein protein with serine protease activity that is present at levels of 0.5 to 2 mg/mL in HSP. The possible prostate origin of the HSP allergens, confirmed in our study by means of allergen characterization, was proposed by Levine et al²⁰ several years ago. They fractionated a pool of seminal plasma obtained from 4 vasectomized men, isolated a protein of 20 to 30 kD as the responsible allergen, and proposed its prostate origin because a filtered extract of prostate tissue caused positive cutaneous reactions in sensitized women.

The HSP immunoblot in nonreducing conditions carried out with the serum from the anaphylactic patient showed 2 IgE-binding bands of 28 and 32 kD, respectively. The 28-kD protein was identified as the mature form of the PSA. This enzyme is synthesized as a polypeptide of 261 amino acids (pre-pro-enzyme), which in its mature form consists of a single polypeptide

chain of 237 amino acids with 5 disulfide bridges that correspond to a molecular mass of approximately 26 kD. The backbone contains a carbohydrate moiety attached at asparagine 45 that increases the mass by another 2 to 3 kD to the total mature molecular mass of 28 kD, as we observed. The 32-kD IgE-binding band detected was one of the intermediate forms of the PSA, which is corroborated by the simultaneous disappearance of both IgE-binding bands in the blotting inhibition assay. The disappearance of the 28-kD IgE-binding band in the HSP immunoblotting under reducing conditions is in accordance with the presence of 5 disulfide bridges that maintain the tertiary structure of the protein.

Members of the kallikrein family are becoming of clinical interest because of their potential as prognostic biomarkers, particularly for hormone-dependent cancers. PSA or human kallikrein 3 has long been an effective biomarker for prostate cancer.²¹ There were 37 kallikreins described as allergens in animals and fungi, including dust mites, Hymenoptera, fungal species, and PSA belonging to the *Homo sapiens* group.²²

Surprisingly, the responsible allergen was a protein omnipresent in human prostate secretions; however, it is unclear why the number of women affected is very small. It might be postulated that the majority of female subjects might induce tolerance with current sexual intercourses and also through the participation of the complex homeostatic mechanism in the female genital tract that modulates recognition of antigens of HSP.²³ Although the exact prevalence of HSPA is unknown,²⁴ probably minor forms of this disorder, such as local reactions, are misdiagnosed as chronic vulvovaginitis.

The occurrence of allergic reactions to an antigen of human origin is always of biologic interest. The human body contains numerous endogenous proteins structurally related with others present in mammals, as described with lipocalins, and the immune system has to adapt to their presence. It has been proposed that under these conditions the immune response against the lipocalin allergens, which are structurally related to endogenous lipocalin proteins, might be the pathway to allergy in genetically predisposed persons.²⁵⁻²⁷ The same mechanism might be applied to other allergens with homologous endogenous counterparts, such as kallikreins.

Because of the low prevalence of allergy to HSP and after the cross-reactivity between HSP and dog dander in the first studied patient was demonstrated, blood samples from 40 other patients with dog allergy were collected. We carried out immunoblotting with HSP. The 28-kD IgE-binding band, identified as a PSA, was observed in 10 lanes. This represents a prevalence of 24.4% (10/41). There were significant statistical differences between the total population of patients with dog allergy and the group with dog allergy that recognizes the protein of 28 kD. Six of 10 of these patients were women, and 2 had a history of infertility. The HSP-specific IgE titers observed in the sera from these 2 women with infertility problems were among the highest detected (1.5 and 5 kU/L), and both revealed a strong 28-kD IgE-binding band in HSP Western blotting assay (Fig 2, lanes 4 and 29). The significance of this sensitization in male subjects is unknown.

The exact prevalence of dog allergy is unknown, but De Groot et al²⁸ found that in their own patient population, the incidence of dog dander allergy was 17% compared with an incidence of cat dander allergy of 24%. In a recent epidemiologic study carried out in Spain, an increased prevalence of sensitization to mammals' epithelia was observed. The mammal's epithelia represent the third most frequent cause of sensitization in rhinitis and

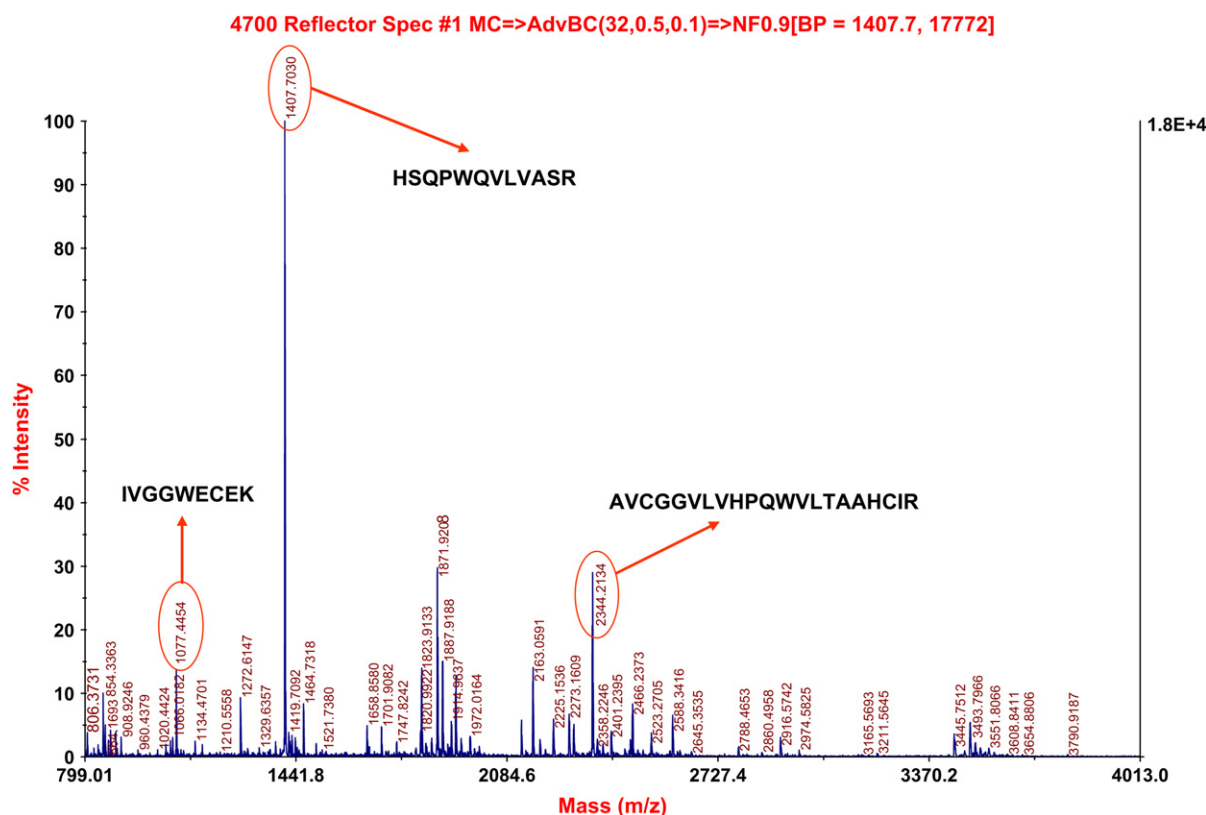


FIG 4. Identification by means of MS. Peptide fingerprinting of the 28-kd protein is shown. The signaled peaks were analyzed by means of MS/MS, obtaining the amino acid sequence.

asthma. In the subgroup of rhinitis, the most relevant epithelium was cat epithelium, followed by horse epithelium. Despite this, dogs were the animal most frequently present in the household of patients as a pet (25.9%), and no case of sensitization to dog epithelium among patients with rhinitis was observed. In the subgroup of patients with asthma, the most important sensitization to mammals' epithelia was also cat epithelium, followed by dog epithelium (15.3% and 13.7%, respectively).²⁹ Among the population with dog allergy, it is uncertain how many patients are monosensitized to dog. Many patients with cat allergy are also allergic to dog. It has been postulated that shared IgE epitopes of the major cat and dog allergens might provide an explanation for this clinical observation.³⁰ Recently, cross-reactivity between Fel d 1 and a protein from dog dander has been described. This is the first report demonstrating the presence of a Fel d 1-like allergen in dog dander extracts that might be responsible for *in vitro* double positivity to cat and dog.³¹ In our study in the group that recognized the 28-kd allergen of HSP, there were 8 (80%) of 10 patients monosensitized to dog compared with the other group, in which there were 7 of 31 (22.6%) monosensitized. We have not found any statistically significant relationship between HSP-specific IgE levels and the severity of dog allergy symptoms. However, because of the limited sample size, a correlation between higher IgE levels and the presence of asthma cannot be excluded. In fact, the *P* value was .095 (Mann-Whitney *U* test) when studying whether the IgE levels were higher in patients with asthma symptoms (either alone or associated to rhinoconjunctivitis). IgE levels presented a lineal correlation with the class global assessment ($P < .001$, $r = 0.98$, Spearman nonparametric correlation test).

The prevalence of monosensitization to dog epithelium found in the studied group is higher than that observed in daily practice. In this group there were 3 to 10 patients who followed a specific immunotherapy regimen to dog epithelium, in all cases with low response to this desensitization treatment. Probably these patients recognize some allergens that have not yet been characterized. The poor effectiveness of dog allergen-specific immunotherapy has been described by Lilja et al.³² The effect of immunotherapy with dog dander extract is less convincing than that with cat epithelium, and this might be caused by a less suitable extract, probably caused by the absence or low level of some of its allergens clinically relevant for some selected patients.

Two interesting points were the 5-fold concentration required with dog epithelium extract versus dog dander to produce the same IgE-binding inhibition on PSA immunoblotting and the higher specific IgE values detected against dog dander versus dog epithelium in those sera with detectable specific IgE against human seminal fluid (data not shown). Therefore the cross-reactive allergen is in a higher percentage in terms of weight in dander than in epithelium dog extract. This finding supports the hypothesis that the dog PSA cross-reactive protein is a dander protein, and we should test dog dander extract and not only dog epithelium to detect the kind of patients described in this article.

An interesting finding of the study was the fact that the cross-reactivity described is not with the major dog allergen (Can f 1/Can f 2).

In the current study we demonstrated the presence of cross-reactivity between HSP and dog dander and identified the HSP allergen involved as PSA. In addition, 24% of patients with dog

allergy showed serum specific IgE antibodies against the PSA from HSP. An increasing number of patients are needed to confirm these interesting preliminary findings.

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Clinical implications: Dog epithelium allergy might be a risk for HSP allergy.

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