

RESEARCH LETTER

Prevalence of allergy to human seminal fluid among women with allergy to male dog and sensitization to Can f 5

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To the Editor:

The number of households with pets is progressively increasing. The amount of registered dogs in our country arises up to over 5 million, and they are currently the main pet.¹ It is estimated that 27% of European adults coming to the clinic for suspected allergy to inhalant allergens are sensitized to dogs,² and mammal epithelia are the third cause of rhinitis and asthma after dust mites and pollen in Spain.³ To date, 7 dog allergens have been described: most of them belong to the lipocalin family (Can f 1, Can f 2, Can f 4 and Can f 6), one is an albumin (Can f 3), another one is a recently reported MD2-like lipid² (Can f 7), and Can f 5 is a 28 kDa protein prostatic kallikrein secreted mainly by male dog urine, dander and epithelium, which cross-reacts with prostate-specific antigen (PSA) of human seminal plasma (HSP).^{4,5} In view of the high number of patients sensitized to Can f 5, which has been lately considered as a major allergen,^{2,6} and the potential consequences in females, we wanted to know the prevalence of allergic symptoms to HSP during intercourse among women sensitized to Can f 5.

Twenty-seven women with male dog at home who consecutively attended to our clinic complaining of respiratory symptoms after exposure to the animal, and with a positive (≥ 3 mm) skin prick tests to dog epithelium (ALK Allergologisk Laboratorium A/S, Horsholm,

Denmark), were included. Total IgE, specific IgE (sIgE) to dog epithelium, sIgE to Can f 1, Can f 2, Can f 3 and Can f 5 levels (Thermo Fisher, Waltham, Massachusetts, USA) were performed in all the patients' sera. Each of the women included was asked about the presence of symptoms during sexual relationships. Human seminal plasma extract from a healthy donor was analysed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), showing protein bands ranging from 200 to 6 kDa. SDS-PAGE IgE immunoblotting assays in nonreducing conditions (without 2-mercaptoethanol) with HSP revealed a double IgE-reactivity band of approximately 28/30 kDa in 11 patients, and to a 17 kDa band in 1 patient (Figure 1). See all these results in Table 1. The 30 kDa, 28 kDa and 17 kDa protein bands of the HSP extract were manually excised from the gel, digested with trypsin and analysed by matrix-assisted laser desorption/ionization time of flight and liquid chromatography coupled to tandem mass spectrometry (MS/MS). Protein identification was performed by searching a nonredundant protein sequence database (National Center for Biotechnology Information) using the Mascot program (<http://www.matrixscience.com>). When compared with the databases, the analysis of the resulting peptides by MS or MS/MS corresponded to PSA both the 28 kDa and 30 kDa proteins, and to prolactin the 17 kDa band.

As it might be expected in a series with only women with male dogs included, Can f 5 seems to be a major allergen: 22/27 (81.4%) were sensitized (≥ 0.1 kU_A/L) to Can f 5, and 5/20 (25%) were

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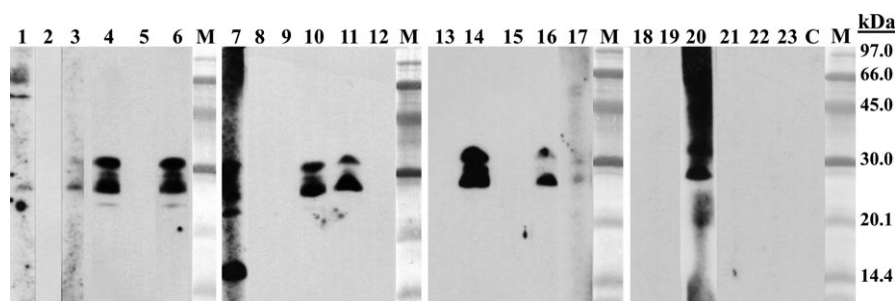


FIGURE 1 Identification of IgE-binding proteins in the human seminal plasma (HSP) extract. Lines 1 to 23, SDS-PAGE IgE immunoblotting with HSP with each patient's serum. Line C, SDS-PAGE IgE immunoblotting with HSP with controls sera (pool of sera from non-atopic subjects). Line M, molecular weight marker. Line kDa, kilo Dalton

TABLE 1 Baseline characteristics of the population

Pt	Age (y)	Symptoms with dog	Other sensitizations	Total IgE (kU/L)	slgE dog (kU _A /L)	slgE Can f 1 (kU _A /L)	slgE Can f 2 (kU _A /L)	slgE Can f 3 (kU _A /L)	slgE Can f 5 (kU _A /L)	Intercourse symptoms	SDS-PAGE ^a (kDa)
1	63	R/A	C, P, D, M	649	67	9.1	NA	NA	5	No	28
2	30	A	C, P, D	609	3.6	0	NA	NA	0	Yes ^b	None
3	42	R	C, P	42	2.6	0	NA	NA	15.6	No	28/30
4	20	R/A	C, P, M	1115	>100	15.4	14.6	19.8	>100	Yes ^b	28/30
5	43	R/A	P	67	0.7	0	0	0	1	Yes ^b	None
6	34	R/A	C, P, M	653	16.7	9.8	5.3	0.2	1.8	Yes ^b	28/30
7	29	R	C, P, D, M	47	1.8	0	0	0	0.4	No	17, 28/30
8	23	R/A	P	75	0.2	0	0	0	0	No	None
9	26	R	C, P	377	9.4	0	0	0	1.8	No	None
10	50	R	C, P	225	19.9	1.1	0.6	0	49.7	Yes ^b	28/30
11	20	R/A	C, P, M	288	19.3	0	0	0	54.5	Yes ^b	28/30
12	41	R/A	C, P	NA	0.4	0	0	0	0	No	None
13	29	R/A	C	225	10.9	7.8	0.5	2.5	7.5	No	None
14	31	A	C, P	492	17.9	0	3.5	0	4.3	NK ^c	28/30
15	36	R	P, D	88	15.5	4.3	16.7	0	2.2	No	None
16	45	R/A	C, P	297	41.9	11	7.4	7.2	10.3	No	28/30
17	31	A	C, P	35	7.7	0	0	0	17.6	No	28/30
18	51	R/A	P, D	163	11.9	1.4	1.3	0	2.4	Yes ^b	None
19	24	R/A	C, P	1607	32.3	8.2	7.6	0	5.8	No	None
20	13	R	C, P	2512	>100	47.4	60.7	0.2	49	NK ^c	28/30
21	57	R/A	C	114	12.7	0.3	1.8	0.1	1.4	No	None
22	29	R/A	C, P	947	33.6	24	11.2	0	9.2	No	None
23	32	R	C, P	85	3.9	2.3	3	0	2.9	No	None
24	64	R	P	213	1	1	NA	NA	0	No	NA
25	40	R	C, P, D, M	67	3.2	2.6	NA	NA	0.2	Yes ^b	NA ^d
26	16	R/A	C, P, M	1375	5.3	0	NA	NA	0	NK ^c	NA
27	30	R/A	C, P, D, M	661	NA	5.1	NA	NA	1.6	No	NA

A, asthma; C, cat; D, dust mites; M, moulds; NA, not available; NK, not known; P, pollen; R, rhinitis; slgE, specific IgE.

^aMolecular weight of the IgE-binding band of each patient.

^bThey all referred genital pruritus with no additional symptoms associated. Condoms were recommended in patients 4, 6, 10 and 11, and symptoms were prevented in all of them.

^cPatients 14 and 26 used condoms in their intercourse, and patient 20 had never had sexual relations.

^dThe patient refused to continue in the study but consented to use her data.

monosensitized to this allergen in 7 patients all the sIgE to dog components could not be carried out. These rates do not differ with previous reports including men and women with male and female dogs.^{2,6} We also found a wide spectrum of sensitization to the different dog components—59% to Can f 1, 65% to Can f 2 and 30% to Can f 3—also in accordance with previous series.^{2,6} Regarding the main objective of this work—to know the prevalence of allergy to HSP in women sensitized to Can f 5—8 patients reported symptoms during intercourse: 1 (pt. 2) was not sensitized to Can f 5, 1 (pt. 25) was sensitized to Can f 5 but did not undergo additional in vitro studies, and 2 (pts. 5 and 18) also sensitized to Can f 5 showed no serum-IgE reactivity with HSP in the SDS-PAGE immunoblotting assay. In 4 of 22 (18.1%), symptoms with HSP seemed to be related with allergy to Can f 5 as immunoblotting showed serum-IgE reactivity to PSA. Mean levels of sIgE to Can f 5 and total IgE in these women (n = 4) were 51.7 and 570.2 kU/L, respectively (sIgE > 100 kU_A/L in pt. 4 was considered as 101 kU_A/L). The same values in patients with serum-IgE reactivity to PSA in immunoblotting assay but without intercourse symptoms (n = 5) were 9.7 and 214 kU/L, respectively; and in patients sensitized to Can f 5 without symptoms and no IgE reactivity to PSA in immunoblotting (n = 8), mean levels were 4 and 513 kU/L, respectively.

Several relevant conclusions arise from the results of this work. The most striking one is the high prevalence of allergy to HSP among women who attended to our clinic complaining of respiratory symptoms with male dogs and sensitized to Can f 5, which rose up to 18.1% (95% CI: 5.1%, 40.2%). The presence of allergic symptoms to human seminal fluid among sensitized patients to kallikrein might be related to the levels of sIgE of Can f 5. Although it is not statistically significant ($P > 0.05$)—probably due to the small number of patients in each group—PSA allergic women had higher levels of sIgE against Can f 5 than those asymptomatic and with IgE reactivity in the SDS-PAGE, and this latter group had higher levels than patients only sensitized to Can f 5 and without IgE reactivity in the immunoblotting. Another relevant issue seems to be the lack of knowledge in the current composition of the diagnostic and therapeutic dog extracts. As reported elsewhere,^{2,6} Can f 5 seems to be a major allergen and the profile of sensitization to the different dog components is diverse.⁶ Current natural dog allergen extracts show considerable heterogeneity in their composition which complicates the accuracy of the diagnosis.⁷ Besides, dog immunotherapy might not always be an effective option since the presence of Can f 5 in the composition of the extract or its quantity—or any other of the considered as minor allergens—is unknown.^{6,8} Finally, one patient (no. 7) showed IgE reactivity with prolactin, a 17 kDa protein secreted from the pituitary gland. Physiologic levels of prolactin in males enhance luteinizing hormone receptors in Leydig cells, resulting in testosterone secretion, which leads to spermatogenesis.⁹

In the light of the results obtained, it would be appropriate to ask the patients with dog allergy about symptomatology during intercourse apart from respiratory symptoms, especially in women

with higher titres of sIgE to Can f 5. Besides, it is mandatory to thorough research in the composition of diagnostic and therapeutic dog extracts, in order to be able to provide helpful tools to allergic patients.

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CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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