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Letter to the Editor

A case of human seminal plasma allergy sensitized with dog prostatic kallikrein, Can f 5

Dear Editor,

Human seminal plasma allergy (HSPA) is a rare phenomenon in women that was first described by Specken in 1958¹ and which was thought to be an allergic reaction to a specific protein in seminal plasma. The clinical responses vary from local reactions (e.g., vulvar and vaginal itching and erythema) to life-threatening anaphylaxis. While the mechanism underlying HSPA is unclear, prostate-specific antigen (PSA) is thought to be a causative allergen.^{2,3} We describe a patient with HSPA who developed anaphylaxis after coitus.

A 37-year-old woman presented with a history of anaphylactic reaction 30 min after sexual intercourse with her husband. She developed general urticaria, swelling of her lips and eyelids, cough and dyspnea. She took oral antihistamines, and the symptoms disappeared within several hours. She experienced vulvar and cutaneous itching, erythema and swelling immediately after contact with seminal fluid a few months before developing the anaphylactic reaction. The use of a condom during sexual intercourse prevented these symptoms. Her medical history included chronic thyroiditis.

She was treated with levothyroxine sodium and was symptom-free. She had only experienced mild atopic dermatitis in early infancy and had no eczema when she was referred to our hospital. She experienced an extrauterine pregnancy at 21 years of age. A laboratory examination revealed a total serum IgE titer of 158 IU/ml. Her specific IgE antibody levels for dog dander, cat dander, human seminal fluid, and latex, as determined using an ImmunoCAP system (Phadia, Uppsala, Sweden), were 13.00 UA/mL, 1.39UA/mL, 1.02UA/mL, and 0.1 > UA/mL, respectively. A skin prick test was performed using seminal fluid from her husband. When the average wheal diameter induced by the allergen was >50% of the positive control response induced by histamine hydrochloride at 10 mg/ml, the result was considered positive. The results were positive for 10- and 100-fold diluted seminal fluid (wheal diameters, 6 × 6 and 6 × 5 mm, respectively; positive control [10 mg/ml histamine hydrochloride]: wheal diameter, 6 × 6 mm; negative control [saline]: wheal diameter, 0 × 0 mm).

She developed cough and pruritic erythema on her thigh 15 min after the prick test. Antihistamines were administered intravenously and the symptoms disappeared within 30 min. Next, seminal fluid from her husband was separated into spermatozoa and seminal plasma by a percol gradient technique, and the spermatozoa were washed three times with sperm wash media. A skin prick test was performed using spermatozoa, seminal plasma, percol and

sperm wash media (Fig. 1). The results were positive for 10- to 10000-fold diluted seminal plasma and negative for spermatozoa, percol and sperm wash media. The skin prick test with spermatozoa showed little wheal formation, but large erythema of 20 × 20 mm in diameter. We considered that contamination of the spermatozoa sample by seminal plasma caused the erythematous reaction after washing the spermatozoa 3 times, as even 10000-fold diluted seminal plasma showed a strong wheal reaction. The diagnosis was HSPA, and condom use during sexual intercourse prevented the onset of further symptoms. She wants to become pregnant and is undergoing *in vitro* fertilization.

HSPA is considered an IgE-mediated immediate-type allergic reaction. The diagnosis is based on the patient's clinical history and is made by ruling out other specific causes of hypersensitivity, including latex and food allergies. HSPA can be completely prevented by using a condom. Treatment of HSPA involves subcutaneous or intravaginal desensitization with relevant fractionated seminal plasma proteins.⁴ Recently, Omalizumab, a monoclonal antibody to human IgE, was found to be effective in a patient with HSPA.⁵ Our patient decided to undergo *in vitro* fertilization because artificial insemination is not a completely reliable means of preventing allergic reactions, and severe allergic reactions have been reported immediately after artificial insemination.⁶

Although no definitive risk factors have been identified, a previous report found that 84% of patients with HSPA had an atopic background, as was the case with our patient. Interestingly, approximately 40% of HSPA cases occur after first-time intercourse.⁷ It has been proposed that a common protein cross-reacting with PSA may explain the high incidence of cases after first-time intercourse. Since our patient experienced an extrauterine pregnancy, she always made her partner use a condom for contraception. She didn't have any symptoms after contact with seminal fluid before having a male dog in her workplace. She developed an anaphylactic reaction within 30 min after her husband ejaculated intravaginally without using a condom for the first time since that point.

Detailed history-taking revealed that the patient was a barber and had experienced severe hand eczema several years previously. She frequently experienced erythema, wheal and swelling of her hands after making contact with a male dog at her workplace. It has recently been reported that a prostatic kallikrein protein isolated from dog urine and dog dander extract (Can f 5), is 55–60% structurally homologous with human PSA and can cross-react with human PSA.^{3,8} The IgE antibody levels in our patient against Can f 1, Can f 2, Can f 3, and Can f 5 (dog allergen components), as determined using the ImmunoCAP system, were <0.1 UA/mL, <0.1 UA/mL, 12.4UA/mL, and 28.1 UA/mL, respectively. Can f 1, to

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	Wheal diameter (mm)
① seminal plasma (1/10)	8.5×7
② seminal plasma (1/100)	5×7
③ seminal plasma (1/1000)	6×4
④ seminal plasma (1/10000)	5×4
⑤ spermatozoa	2×2
⑥ histamine hydrochloride	7×8
⑦ saline	1×2
⑧ percol	0×0
⑨ sperm wash media	0×0



Fig. 1. Results of a prick test. Positive results were obtained from diluted seminal plasma samples, and negative results were obtained from spermatozoa, percol and sperm wash media samples. Spermatozoa showed little wheal development but an erythematous reaction.

which >50% of individuals with dog allergy respond, is considered the most important dog allergen component. Our patient was negative for Can f 1 but positive for Can f 5. Thus, we hypothesize that our patient was sensitized to Can f 5 through the barrier-disrupted skin of her hands and then presented with HSPA due to cross-reactivity between Can f 5 and human PSA.

To our knowledge, there have been few reports of HSPA in which IgE antibodies against Can f 5 were detected^{3,8,9} and this is the first report describing the possible development of HSPA through epicutaneous sensitization with Can f 5. Similar case reports are required to clarify whether or not HSPA is caused by cross-reactivity between Can f 5 and human PSA.

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Conflict of interest

The authors have no conflict of interest to declare.

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References

- Specken JLH. A strange case of allergy in gynecology. *Ned Tijdschr Verloskd Gynaecol* 1958;**58**:314–8.
- Weidinger S, Mayerhofer A, Raemsch R, Ring J, Köhn FM. Prostate-specific antigen as allergen in human seminal plasma allergy. *J Allergy Clin Immunol* 2006;**117**:213–5.
- Basagaña M, Bartolomé B, Pastor C, Torres F, Alonso R, Vivanco F, et al. Allergy to human seminal fluid: cross-reactivity with dog dander. *J Allergy Clin Immunol* 2008;**121**:233–9.
- Sublett JW, Bernstein JA. Seminal plasma hypersensitivity reactions: an updated review. *Mt Sinai J Med* 2011;**78**:803–9.
- Burguete-Cabanas MT, Fajardo-Ramirez OR, Yesaki R, Estrada-Maganas R, Salazar-Meza S, Rios-Chavez O, et al. Omalizumab for hypersensitive reaction to seminal plasma: a case report. *Allergol Int* 2018;**67**:278–9.
- Sohn SW, Lee HS, Yoon YS, Park HS. Successful intravaginal desensitization in a woman with seminal plasma anaphylaxis after artificial insemination failure. *J Invest Allergol Clin Immunol* 2014;**24**:276–7.
- Shah A, Panjabi C. Human seminal plasma allergy: a review of a rare phenomenon. *Clin Exp Allergy* 2004;**34**:827–38.
- Mattsson L, Lundgren T, Everberg H, Larsson H, Lidholm J. Prostatic kallikrein: a new major dog allergen. *J Allergy Clin Immunol* 2009;**123**:362–8.
- Basagaña M, Bartolomé B, Pastor-Vargas C, Mattsson L, Lidholm J, Labrador-Horrillo M. Involvement of can f 5 in a case of human seminal plasma allergy. *Int Arch Allergy Immunol* 2012;**159**:143–6.

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