

IMMUNOGLOBULIN E-MEDIATED SEVERE ALLERGY TO HUMAN SEMINAL PLASMA*

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Two women with allergy to human seminal plasma are described. Both patients had generalized and local allergic symptoms, i.e., hypotension, asthmatic dyspnea, urticaria, and vaginal swelling, beginning within a few minutes of intercourse. The antigen causing the reaction in these patients was common to all seminal plasmas examined. Most of the antigenic activity was shown to be present in one protein band detected by acrylamide gel electrophoresis. The seminal plasma reaction was mediated through an immunoglobulin E (IgE) antibody. Passive transfer of the hypersensitivity with the serum of both patients was successful, and the radioallergo-sorbent test showed that the serum of the first patient contained IgE specific to seminal plasma.

An allergic reaction to human seminal plasma is a rarely reported phenomenon. The first case was described by Halpern et al.¹ in 1967. Subsequent reports have presented five women with this allergy.²⁻⁴ All patients had symptoms typical of an immediate allergic reaction. In the most severe form there was anaphylaxis with loss of consciousness, asthma, and generalized urticaria beginning within minutes of intercourse.¹ The patients also had local symptoms including vaginal itching and swelling. A familial occurrence of this allergy has been described recently.⁵ Three members of a family had only local symptoms, and the term "allergic seminal vulvovaginitis" has been proposed.

It is clear that the antigen in seminal plasma is a basic protein, probably of prostatic origin, which seems to be common to all men.¹⁻⁶ The antibody which mediates the seminal plasma re-

action appears to be immunoglobulin E (IgE). In skin tests it produces a wheal and flare reaction, is transferable with the Prausnitz-Küstner test, and causes in vitro histamine release from basophils.⁷

In this report we describe two patients with a severe form of this allergy. The antigen was characterized by acrylamide gel electrophoresis, and the antibody was shown to be IgE by the radioallergosorbent test (RAST).

CASE HISTORIES

The first patient (A. G.) was a 31-year-old unmarried woman. At the age of 26 she noticed vaginal itching, swelling, and generalized urticaria soon after intercourse. The symptoms faded within 8 hours. The patient thought that the reaction was due to semen and thereafter a condom was used. The next intercourse without a condom occurred 6 months later. Within a few minutes of ejaculation she exhibited an anaphylactoid reaction. She did not lose consciousness but did feel faint. In the hospital emergency room her systolic blood pressure was 60 mm Hg and she had generalized urticaria. The symptoms dis-

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appeared within 4 hours after the intravenous administration of corticosteroids.

At the age of 28 she exhibited her third allergic reaction, now after intercourse with a second partner. Five minutes after ejaculation she had difficulty in breathing, a sensation of throat swelling, and generalized and vaginal pruritus. She did not lose consciousness but again a fall in blood pressure was noted. She also had respiratory obstruction, facial edema, and generalized urticaria. She was given corticosteroids intravenously and was hospitalized overnight. The next day facial edema persisted but other symptoms had faded. Since this third episode the patient has had intercourse many times with a third partner. A condom has always been used and no more reactions have occurred.

This patient had had atopic eczema since childhood and allergic rhinitis to house dust for a few years. Her brother had hay fever. Her parents, who are cousins, were asymptomatic. The patient had menstruated irregularly but no gynecologic abnormalities had been found.

The second patient (A. R.) was a 31-year-old married woman with no history of previous allergy or other diseases. She had one sister who had chronic rhinitis, possibly of allergic origin. She had been married for 10 years. Because of lower back pain and difficulties in becoming pregnant, she consulted a gynecologist at the age of 26. Endometriosis was suspected and she was given lynestrenol (5 mg/day) for 6 months. After that she became pregnant and was delivered of a girl at term. A second child, a boy, was born 1½ years later, and an intrauterine device (TCu-200) was subsequently inserted. Soon afterward she noticed vaginal itching, swelling, and local urticaria on the abdomen after every intercourse. The symptoms gradually became more severe, and the couple minimized the frequency of intercourse to one or two times per month. Despite this measure the symptoms became more severe. The patient now experienced swelling in her throat and had difficulties in breathing. She was treated with antihistamines without success.

One and one-half years after the symptoms had begun she exhibited such a severe postcoital reaction that she sought help from a hospital. She

felt confused and had difficulty in breathing. In the emergency room, respiratory obstruction, generalized urticaria, and periorbital edema were noted. She was given corticosteroids intramuscularly. The symptoms abated gradually.

The main symptoms of this patient are listed in Table 1. Usually they were somewhat milder before menstruation. This patient also noted that urticaria developed if semen touched her skin.

METHODS

Skin Tests. Skin scratch and intradermal tests were performed on the arms or on the back. In the first experiments, fresh, whole semen samples from the partners and from another donor were used. Later, ejaculates were centrifuged to separate the spermatozoa from the seminal plasma, which was kept frozen at -20°C . Micro-pore-filtered, pooled seminal plasma from three to eight healthy donors, diluted with phosphate-buffered saline (pH 7.0) containing 0.4% phenol, was used in titrations of seminal plasma antigen. Histamine and diluent served as controls.

Passive transfer of the antibody (Prausnitz-Küstner test) with the sera of the patients was achieved by injecting 0.1 ml of serum into the skin of two healthy recipients. Challenge was performed after 24 hours with 0.05 ml of seminal plasma. A reading was taken after 1 hour. Serum from an atopic woman and diluent were used as controls.

Electrophoresis. Samples of pooled seminal plasma (200 μl) were separated by using polyacrylamide gel electrophoresis.⁸ The separating gel buffer used was 0.75 M Tris-glycine, pH 8.9. The acrylamide concentration was 7.5%. The electrophoresis was run for 5 hours at 2.5 mA/tube. After this the gels were sliced transversely, and the slices (5 mm thick) were eluted in physiologic saline. After standing overnight at 4°C , the eluates were used in intradermal tests.

IgE Determinations. Serum total IgE was determined by using the Phadebas IgE kit (Pharmacia Diagnostics, Uppsala, Sweden). Serum IgE specific to seminal plasma proteins was determined with the radioallergosorbent test.⁹ The proteins from pooled seminal plasma were coupled to

TABLE 1. *The Course of Symptoms in a Patient with Allergy to Human Seminal Plasma*

Symptom	Time after exposure			
	5 min-½ hr	½ hr-2 hr	2 hr-6 hr	6 hr-12 hr
Asthmatic dyspnea, sensation of swelling in throat	+	+	—	—
Vaginal pruritus, swelling	+	+	+	—
Generalized urticaria appearing first on the abdomen	—	+	+	+

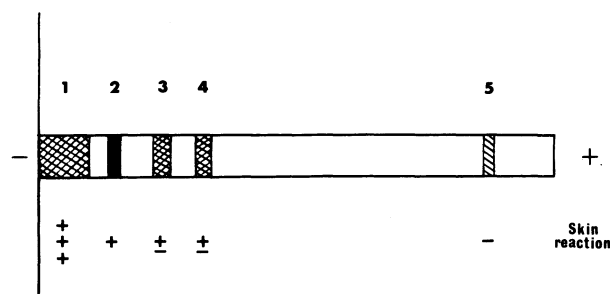


FIG. 1. Acrylamide gel electrophoresis of human seminal plasma. Diagrammatic representation of the protein bands and corresponding intensity of the immediate skin reaction.

cyanogen bromide-activated paper discs.¹⁰ Other reagents were obtained from Phadebas RAST kits. A semiquantitative RAST score (0 to 4) based on the commercial reference system was used for the interpretation of the results. The score 0 indicates the absence of detectable IgE antibody to seminal plasma antigen.

RESULTS

Skin Tests. In scratch tests both patients had strong, immediate reactions (wheal, flare, and pseudopods) to whole semen and undiluted seminal plasma. A seminal plasma dilution of 10^{-1} gave a somewhat weaker positive reaction and a dilution of 10^{-2} gave a weakly positive reaction in both patients. Washed spermatozoa did not elicit any reaction. Seven healthy control subjects gave negative results when tested with whole semen and undiluted seminal plasma.

Intradermal tests were positive with seminal plasma at dilutions of 10^{-5} in the first patient and 10^{-6} in the second patient. Three healthy control subjects and twelve females with urticaria gave negative results when tested with dilutions of 10^{-1} and 10^{-2} .

Prausnitz-Küstner tests were positive with undiluted serum and serum diluted 10^{-1} from each patient. The 10^{-2} dilution and controls gave negative results.

Electrophoresis. Acrylamide gel electrophoresis of the proteins of seminal plasma revealed a total of five bands (Fig. 1). The eluate which contained the proteins of band 1 gave the strongest positive reaction (+++) in the intradermal test. The eluate from band 2 gave a weakly positive reaction (+); the others yielded uncertain or negative results.

IgE Determinations. The results of the IgE determinations are shown in Table 2. The total serum IgE level was elevated in the first patient

TABLE 2. IgE Determinations in Patients with Allergy to Human Seminal Plasma

Patient	Serum total IgE	Seminal plasma antigen		Serum seminal plasma-specific IgE	
		Pool no.	Volume/disc	Count	RAST score
	<i>U/ml</i>		<i>μl</i>	<i>% reference</i>	
A. G.	1100	3	10	13	1
		4	200	14	1
		5	10	13	1
		5	50	14	1
		5	200	13	1
			0	2	0
A. R.	90	3	10	5	0
		3	50	6	0
		3	200	5	0
		4	10	4	0
		4	50	5	0
		4	200	5	0
Control	1200	3	200	3	0
		4	10	4	0
			0	3	0

(A. G.) and normal in the second patient (A. R.). A significant amount of IgE (RAST score 1) specific to seminal plasma proteins was found in the serum of the first patient. This antibody could not be detected (RAST score 0) in the serum of the second patient or in the serum of an atopic control patient with an elevated serum total IgE level (Table 2). A reference group of 12 women with urticaria and 10 women examined for infertility were also negative for IgE specific to seminal plasma.

Other Laboratory Tests. Agglutinating or immobilizing antibodies to spermatozoa were not found in the sera of patients with an allergy to seminal plasma. The patients had no antinuclear antibodies, tissue-specific autoantibodies, or antibodies to human leukocytes or thrombocytes. The serum concentration of immunoglobulin M (1.67 gm/liter) was slightly elevated in the first patient and that of IgG (21.72 gm/liter) was slightly elevated in the second patient.

DISCUSSION

All patients with an allergy to seminal plasma described thus far have had allergic reactions of the immediate type. They have also had other allergies of this type, or at least an atopic family history. The antigen in seminal plasma seems to be common to all men. All allergic patients have had positive skin test reactions to all of the human seminal plasmas tested. One allergic patient had had intercourse with several men, and allergic manifestations had occurred with every partner.⁴ In individuals with severe allergy to seminal plasma, positive intradermal tests at

dilutions of 10^{-5} to 10^{-7} have been reported.¹⁻³ The findings in both of our patients are in agreement with those mentioned above.

Earlier studies^{2, 3, 6} have shown that the seminal plasma antigen is a basic protein with a molecular weight of 14,000 to 30,000. When seminal plasma was separated in this study by using acrylamide gel electrophoresis, most of the antigenic activity was found in the band closest to the cathode. This indicates that the protein causing the allergy may have been the same in both of our patients.

The antibody to seminal plasma was demonstrable with the Prausnitz-Küstner test in the serum of our patients at dilutions comparable to those used in earlier studies.^{1, 6} In addition, IgE specific to seminal plasma was detected with the RAST in the serum of our first patient. This indicates that the allergic reaction is mediated through an IgE antibody. Earlier efforts with this method failed to demonstrate the antibody.⁴ We also failed to detect IgE antibody with the RAST in the serum of our second patient, although she had skin test results similar to those of our first patient.

Both of our patients had local and generalized symptoms which are known to occur in the severe forms of this allergy. It is clear that most women with severe forms of this allergy would probably recognize the immediate temporal association of explosive symptoms with intercourse, as did both of our patients. They related their suspicions to their gynecologists. In one subject the intra-uterine device was suspected to be somehow responsible for the trouble. However, both patients were first referred for allergologic examinations by the emergency units of hospitals.

Seminal plasma allergy is not a disease which is easily recognized.⁵ Therefore, the actual incidence may be more common, especially in local forms. Allergy with mild local symptoms can insidiously progress to severe allergy, as was shown by our

second patient. Proper diagnosis and the elimination of the antigen through the use of a condom are of great importance to the well-being of patients affected. The best and easiest way to confirm the diagnosis seems to be through skin testing with whole semen or seminal plasma. Prophylactic antihistamines may help in mild allergy⁵ but do not seem to be effective in the severe forms. The use of a condom prevented all symptoms in both of our patients. Hyposensitization has not succeeded,¹ and when the patient has been sensitized the allergy seems to last for years. The risk of anaphylaxis has inhibited fertilization of one of our patients, but infertility per se due to this allergy has not been reported.

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