

A Case of Seminal Fluid Allergy Successfully Treated with Immunotherapy in a One-day Rush Procedure

Bart W. Boom, Albert W. van Toorenenbergen**, Geesje Nierop* and
Jan-Gerrit van der Schroeff

Abstract

A 28-year-old woman was treated for seminal fluid allergy with immunotherapy using a one-day 'rush' procedure. Apart from minor anaphylactic symptoms, no serious side effects were noted during or after hyposensitization or boosting. Five weeks after the start of the hyposensitization, she was free of symptoms after unprotected coitus.

Abbreviations: SF: seminal fluid, SFA: seminal fluid allergy, RAST: radioallergosorbent test, HRT: histamine-release test

Key words: seminal fluid allergy; immunotherapy; rush method

Introduction

Immediate type hypersensitivity to seminal fluid (SF) is an infrequent but well-documented syndrome. Most woman suffering from seminal fluid allergy (SFA) have an atopic constitution, which facilitates acquisition of IgE-mediated disease (1-6). The causative antigen is a glycoprotein with a molecular weight between 12.4 and 30 kD, which is mainly, if not totally, from prostatic origin (7, 8). This antigen is present in SF of all men, which should be stressed to the patient.

In mild cases, symptoms can be prevented by antihistaminic drugs or intravaginal use of cromoglycate-containing creams (9), but severe cases demand avoidance of all contact with SF and thus require the use of condoms or abstinence from sexual intercourse. Since these alternatives are not very attractive for long periods of time and can even be hazardous, as in the case of a ruptured condom, more

definite and causal treatments have been sought. Specific immunotherapy ('hyposensitization') can offer a reasonable alternative to some patients with SFA. Both classical and rush methods of hyposensitization have been tried with variable and unpredictable results (1, 4, 10-13).

A uniform hyposensitization protocol for the 'average patient' is hard to recommend, since too many variables are involved. Both the immunologic status of the patient prior to immunotherapy and the frequency of contact with SF once immunotolerance has been established are important parameters that are difficult to manipulate. Inevitably, the choice of a hyposensitization scheme is subjective, depending largely on individual circumstances.

In this report we present the case of a woman who was treated successfully for SFA by using a one-day rush hyposensitization scheme.

Patient and Methods

A 28-year-old unmarried woman was referred for evaluation of anaphylactic symptoms occurring minutes after sexual intercourse. She had experienced mild urticarial reactions after unprotected sexual intercourse for the last two years. The last three months, the reactions had aggravated, leading to generalized urticaria, dyspnoea, palpitations,

Received July 10, 1990; accepted for publication March 15, 1991.

Departments of Dermatology and *Lung Disease, University Hospital Leiden and **Laboratory of Allergy, University Hospital Dijkzigt, Rotterdam, The Netherlands.

Reprint requests to: B.W. Boom, M.D., Department of Dermatology, University Hospital Leiden, P.O. Box 9600, 2300 RC Leiden, The Netherlands.

Table 1. Intracutaneous tests with seminal fluid (SP)

No	Concentration	Reaction
1	SP 10^{-8}	—
2	SP 10^{-7}	+
3	SP 10^{-6}	+
4	SP 10^{-5}	++
5	SP 10^{-4}	+++
6	SP 10^{-3}	+++
7	SP 10^{-2}	+++
8	SP 10^{-1}	+++
9	SP as is	ND
10	NaCl 0.9%	+
11	histamine 0.01%	+++

ND indicates not done.

Table 2. Hyposensitization scheme: Dosages (ml) and concentrations of seminal fluid (SF) given at 20 minute intervals

Concentration	Dosages				
SF 10^{-5}	0.3	0.6	1.0		
SF 10^{-4}	0.3	0.6	1.0		
SF 10^{-3}	0.3	0.6	1.0		
SF 10^{-2}	0.2	0.4	0.6	0.8	1.0
SF 10^{-1}	0.2	0.4	0.6*	0.8	1.0
SF as is	0.2	0.4	0.6	0.8	1.0

*point at which the hyposensitization procedure was broken off.

dizziness, and faintness. Localized urticarial swelling occurred 15–30 minutes after skin contact with ejaculate. When condoms were used, none of the above symptoms were noted.

The patient and her family had a medical history of atopic disease. Occasionally, she still suffered from mild atopic dermatitis in the face and on the flexural sites of the extremities.

Laboratory investigations

Masturbated SF from her sexual partner was depleted from spermatozoa by filtration through a 22 μ m Millipore filter, diluted in saline, and used for intracutaneous tests. Results are shown in Table 1. Whealing was present up to a dilution of 1:100,000 (Fig. 1).

Total serum IgE was 942 IU/L. A radioallergo-sorbent test (RAST) for specific IgE antibodies against SF was negative. A histamine-release test

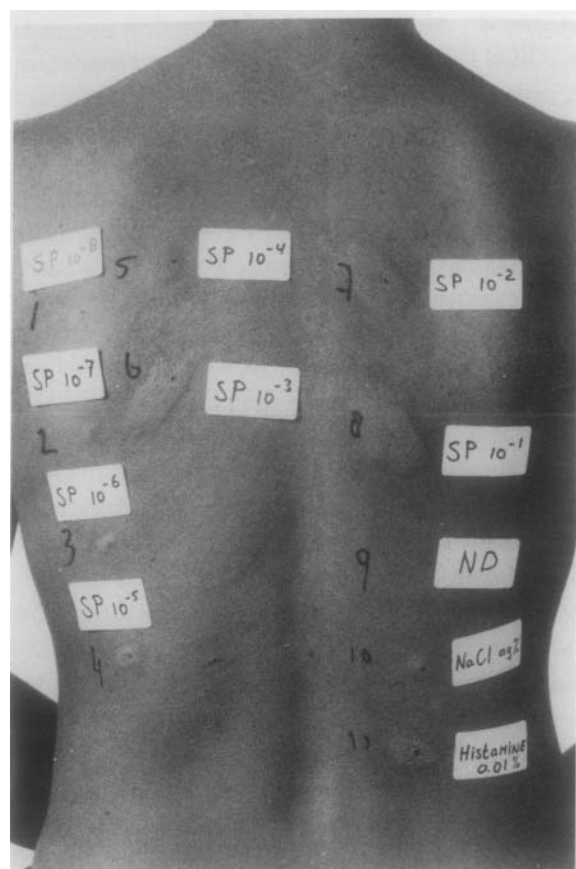


Fig. 1. Intracutaneous tests with seminal fluid (SP), showing whealing up to a dilution of 10^{-5} .

(HRT) with SF was positive up to a dilution of 1:100,000.

Hyposensitization protocol

SF was prepared as indicated, dissolved in saline, and vortexed. Dilutions of SF were prepared up to 1:100,000. On the day of the hyposensitization, the patient was hospitalized in an intensive care unit of our hospital.

Thirty minutes prior to the first injection with SF, 2 mg clemastine was administered intravenously. Subcutaneous injections with SF were given every twenty minutes in the upper legs. Dosages and concentrations are shown in Table 2.

Booster injections were planned weekly after hyposensitization with the highest possible dose reached at the day of hyposensitization.

Blocking antibodies

IgG antibodies directed against SF were measured by protein-A assay (14). In brief, 0.1 ml SF, dialyzed against distilled water, was coupled to 100 mg CNBr-

Table 3. Measurement of IgG against seminal fluid (SF) in serum from two patients with SF allergy and in 3 controls

	% binding pA
Patient A	20.9 (a) 30.3 (b)
Patient B	3.1
Control 1	3.0
Control 2	4.4
Control 3	2.1

Percentages of patient A are given 6 weeks prior (a) and 7 months after (b) immunotherapy with SF.

The values are corrected for the blank value (no patient serum added), which was 16% binding of radiolabelled protein-A (pA).

activated Sepharose 4B (Pharmacia, Woerden, The Netherlands) according to the manufacturer's instructions. Per test, 0.5 mg SF-agarose was incubated with 0.05 ml patient serum diluted 1:40. After four hours of incubation and three washes, ^{125}I -labelled protein-A (Dupont Biotechnology Systems, Den Bosch, The Netherlands) was added. After an overnight incubation, non-bound radioactivity was washed away. The results were expressed as percentage binding of the total amount of radio-labelled protein-A added.

Results

The hyposensitization procedure did not give any problems until the dosage of 0.2 ml SF diluted 1:10 was reached. At this dosage the patient developed a dry cough and minimal dyspnoea. These symptoms receded after 2 mg clemastine was given intravenously. At a dose of 0.6 ml SF diluted 1:10, dyspnoea developed again. In few minutes, facial edema and generalized erythema of the skin developed. Pre-existent eczematous lesions on the flexural sites of the extremities seemed to flare. At this point, the hyposensitization procedure was broken off. Hydrocortisone 100 mg was administered intravenously and the larynx of the patient was sprayed with salbutamol. All symptoms faded gradually, but one and a half hours later an urticarial exanthema developed, pre-

dominantly on the extremities. The exanthema faded after another 100 mg hydrocortisone was administered intravenously. Six hours after the last injection with SF the patient was completely free of symptoms.

A week after the hyposensitization, the patient received a booster injection of SF (0.4 ml, diluted 1:10). On this occasion only a slight late phase reaction (erythema, itch) was noted for which no treatment was necessary. A second booster with the same dosage was given after two weeks.

The first unprotected coitus was performed at home three weeks after the start of the hyposensitization. The patient was well instructed and equipped with an emergency kit containing epinephrine and clemastine for intramuscular use. Thirty minutes before sexual contact, she took 2 mg clemastine. A few minutes after intravaginal ejaculation, she experienced mild itchiness and redness of the face. Additional medication was not needed. No late phase reactions were observed. In the following days, coitus were performed without antihistamines. Since this did not give any more severe problems, it was decided to stop further boosting. Five weeks after the start of the hyposensitization, the patient was free of symptoms on intravaginal contact with ejaculate. However, on skin contact with SF, she may still experience itching and a local urticarial reaction. These features have not been changed in a follow-up period of over two years.

The results of the tests on blocking antibodies are shown in Table 3. All values were corrected for the blank value (no patient serum added), which was 16% binding of radiolabelled protein-A. Serum samples from the patient (A) were taken six weeks prior (a) and seven months after (b) the hyposensitization procedure and compared with serum from another patient with SFA (B) and three healthy non-atopic controls. After the hyposensitization, a clear rise in protein-A binding was observed, indicating an increase in blocking antibodies.

Discussion

The strict relationship of the symptoms to coital behaviour makes the diagnosis SFA easy, if one is acquainted with its existence. An easy and reliable confirmation can be made with intracutaneous tests with SF. If possible, a RAST and HRT should be performed to further support the IgE-mediated nature of SFA.

The negative RAST in our patient suggests that most of the present specific IgE antibodies against SF were bound to membranes of basophils and mast cells. Shapiro (15) presented a similar case with borderline elevation in serum IgE antibodies to crude seminal plasma as detected in the RAST, but with a significant increase in IgE antibodies to a particularly purified seminal plasma fraction. Technical inaccuracies in our assay could be excluded by comparison with blood samples of another patient with SFA, as described in detail elsewhere (16).

Theoretically, a positive intracutaneous test and HRT together with a negative RAST could be caused by non-allergic effects of SF components on vasoactive amine containing cells. The good response to immunotherapy, however, almost excludes this possibility.

Most often, SFA is quite an embarrassing affliction for the patient. Depending on the severity of symptoms, there can be great anxiety, which cannot easily be overcome by practical but potentially hazardous measures like the use of antihistaminic drugs or the use of condoms. Antihistamines do not guarantee sexual intercourse without problems. Moreover, the planning that is needed if antihistamines are used is an obvious disadvantage. The continuous use of condoms may be a problem for some couples, and rupture of a condom can be dangerous, since IgE antibodies to seminal fluid can remain present for years (8).

In our view, the best therapeutic option for a sexually active woman with SFA is immunotherapy. Although the effect of immunotherapy is well documented in several IgE-mediated allergic conditions, its mechanisms of action are still unclear. Working mechanisms that have been postulated include the induction of

allergen-specific IgG antibodies ('blocking antibodies') and their relation to IgG subclass, reduction of IgE synthesis and modulation of mediator production, or susceptibility of certain inflammatory cells (17).

The first report on hyposensitization for SFA dates from 1967 by Halpern et al. (1). Hyposensitization for 2 years in the classical way did not alter the patient's reaction to sexual intercourse. Classical hyposensitization, however, has been effective in other patients (5, 10, 13). Friedman et al. (11) describe a patient in whom immunotherapy attenuated the severity of the allergic reaction. The first successful rush hyposensitization was reported by Frisch et al. (12). They used a 5 day-rush hyposensitization protocol with supplementary injections with SF in a final frequency of twice a month. No allergic symptoms were noted on unprotected sexual intercourse after 7 weeks. Nine months later, the hyposensitization was stopped.

We prefer rush hyposensitization to the classical method, since the nature of the problem asks for a quick solution. The dangers of this type of hyposensitization procedure do not have to be greater than the dangers of any of the alternatives. The setting of a rush hyposensitization requires full facilities for cardiopulmonary resuscitation in order to react immediately to any problem of anaphylactic origin as necessary (18). Of course, hyposensitization with unknown human biologic components bears potential risks, but so far no serious adverse reactions to immunotherapy with SF have been noted.

Unfortunately, our patient was unwilling to cooperate in further laboratory testing after completion of the immunotherapy. Apart from repetition of the test on blocking antibodies, no confirmation could be obtained for our clinical findings. Tests on blocking antibodies, however, showed a rise after hyposensitization. Fennerty et al. (19) recently showed that subjects responding to immunotherapy had significantly higher pre- and post-treatment allergen-specific IgG levels than did non-responders. The presence of IgG antibodies to SF prior to the start of hyposensitization may have influenced the response in our patient. The

high protein-A binding of the blank value (16%) is probably caused by agarose-coupled IgG from SF. Human semen contains IgG at a concentration of approximately 1% of the concentration of human serum (20).

After hyposensitization, frequent and regular contact with SF seems to be necessary to maintain 'immunity'. A minimum frequency, however, is hard to indicate. Friedman's patient, who had been treated successfully with classical immunotherapy, suffered from an exacerbation after a discontinuation of sexual intercourse for 2 weeks. Reinstitution of sexual intercourse at regular intervals again established complete remission of symptoms.

An optimal strategy for immunotherapy is one that combines a maximum of safety and efficacy with a minimum of discomfort to the patient. In general, such a strategy is difficult to define. The successful one-day hyposensitization in our patient indicates that, at least in some patients, the outlines of a hyposensitization protocol can be defined quite sharply.

References

- Halpern BN, Ky T, Robert B: Clinical and immunological study of an exceptional case of reaginic type sensitization to human seminal fluid, *Immunology*, **12**: 247-258, 1967.
- Siraganian RP, Schenkein I, Levine BB: Immunologic studies of a patient with seminal plasma allergy, *Clin Immunol Immunopathol*, **4**: 59-66, 1975.
- Pevny I, Peter G, Schulze K: Spermaallergie vom anaphylaktischen Typ, *Hautarzt*, **29**: 525-530, 1978.
- Mathias CGT, Frick OL, Caldwell TM, Yunginger JW, Maibach HI: Immediate hypersensitivity to seminal fluid and atopic dermatitis, *Arch Dermatol*, **116**: 209-212, 1980.
- Bernstein IL, Englander BE, Gallagher JS, Nathan P, Marcus ZH: Localized and systemic hypersensitivity reactions to human seminal fluid, *Ann Intern Med*, **94**: 459-465, 1981.
- Presti ME, Druce HM: Hypersensitivity reactions to human seminal plasma, *Ann Allergy*, **63**: 477-482, 1989.
- Voorhorst R: Female allergy to seminal fluid, *Ann Allergy*, **41**: 252, 1978.
- Kooistra JB, Yunginger JW, Santrach PJ, Clark JW: *In vitro* studies of human seminal plasma allergy, *J Allergy Clin Immunol*, **66**: 148-154, 1980.
- Goldenhersh MJ, Saxon A: Seminal fluid hypersensitivity (SFH): a new approach (abstract), *Ann Allergy*, **62**: 256, 1989.
- Mathias CG, Frick OL: Immunotherapy in seminal fluid allergy, *J Allergy Clin Immunol*, **63**: 173, 1979.
- Friedman SA, Bernstein IL, Enrione M, Marcus ZH: Successful long-term immunotherapy for human seminal plasma anaphylaxis, *JAMA*, **251**: 2684-2687, 1984.
- Frisch C, Pujade-Lauraine MD, Leynadier F, Dry J: Rush hyposensitization for allergy to seminal plasma, *Lancet*, **i**: 1073, 1984.
- Ohman JL, Malkiel S, Lewis S, Lorusso JR: Allergy to seminal fluid: characterization of the allergen and experience with immunotherapy, *J Allergy Clin Immunol*, **85**: 103-107, 1990.
- Hamilton R, Adkinson NF: Quantitation of antigen-specific IgG in human serum, *J Immunol*, **124**: 2966-2971, 1980.
- Shapiro SS, Kooistra JB, Schwartz D, Yunginger JW, Haning RV: Induction of pregnancy in a woman with seminal plasma allergy, *Fertil Steril*, **36**: 405-407, 1981.
- Boom BW, Van Toorenenbergen AW, Van der Schroeff JG: Spermaplasma-allergie, *Ned Tijdschr Geneesk*, **130**: 265-267, 1986.
- Bousquet J, Michel FB: Specific immunotherapy, *Allergy*, **43**, suppl. 8: 16-22, 1988.
- Warner JO, Kerr FW: Hyposensitization, *Br Med J*, **294**: 1179-1180, 1987.
- Fennerty AG, Jones KP, Davies BH, Fifield R, Edwards J: Immunological changes associated with a successful outcome of pollen immunotherapy, *Allergy*, **43**: 415-419, 1988.
- Rümke P: The origin of immunoglobulins in semen, *Clin Exp Immunol*, **17**: 287-297, 1974.