

The Approach to Conception for Women with Seminal Plasma Protein Hypersensitivity

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PROBLEM: Allergic reactions to human seminal plasma protein has become increasingly recognized in the medical community. Treatment for most allergic conditions usually begins with avoidance of the offending allergen. For women with seminal plasma protein hypersensitivity (SPH) who desire to conceive, this approach is unacceptable. We describe a case report of a woman with an SPH who desired to have unprotected intercourse in order to conceive.

METHODS: The patient underwent skin prick testing to her fiancé's fresh undiluted semen. Serum-specific IgG and IgE was performed by ELISA to the fiancé's whole seminal plasma and seminal plasma proteins (SPP). The patient underwent an intravaginal graded challenge to whole seminal fluid. Intrauterine insemination with washed spermatozoa was attempted but *in vitro* fertilization was subsequently required.

RESULTS: The patient had a positive prick test to whole seminal plasma but negative specific IgG and IgE ELISA to SPPs. An intravaginal graded challenge to whole seminal plasma was well tolerated. However, she experienced a subsequent severe local reaction after unprotected intercourse. She deferred treatment with systemic desensitization to relevant SPPs. She failed intrauterine insemination but successfully conceived with *in vitro* fertilization.

CONCLUSION: This case report emphasizes that SPH is not associated with sterility. It also indicates that whole seminal plasma graded challenge is not uniformly successful for the treatment of SPH.

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INTRODUCTION

Human seminal plasma protein hypersensitivity (SPH), although rare, is more common than previously recognized.¹ It was first reported by a Dutch gynecologist J.L.H. Specken in 1958.² Immunologic responses to seminal fluid antigens in women may result in local and/or systemic reactions.³ Symptoms may consist of diffuse urticaria, stridor, wheezing, vulvovaginal pain or burning, nausea, vomiting and facial, tongue, lip and/or laryngeal edema. These reactions typically occur within 30 min post-coitus. Although the etiology is not clearly defined, researchers believe that most reactions are IgE-mediated against glycoprotein antigens in seminal plasma.^{4,5} These glycoproteins are

mainly produced in the prostate gland and are present in all males. With most allergic conditions, avoidance is the treatment of choice. Abstinence or condom usage will prevent symptoms of SPH.

This approach, however, is unacceptable to many couples especially when the woman wants to conceive. Local subcutaneous injections with human seminal plasma proteins (SPP) has been successful and considered the gold standard for desensitizing patients with localized and/or systemic SPH; however, several case reports suggest that intravaginal graded challenge with whole seminal plasma may also be effective.^{5–9} Many women who desire unprotected intercourse in order to conceive are unable to afford the expense of systemic desensitization and do not respond to treatment with

seminal plasma intravaginal graded challenge. Therefore, alternative approaches to induce conception are necessary when treatment of this disorder is ineffective or not able to be implemented. We report a 25-year-old woman who failed whole seminal plasma intravaginal graded challenge but successfully conceived through *in vitro* fertilization.

CASE REPORT

A 25-year-old Caucasian woman engaged to be married presented to our clinic complaining of severe vaginal burning, pain and swelling within 1–5 min post-coitus. Her symptoms began 6 months prior, after having unprotected intercourse for the first time. The symptoms only occurred with unprotected intercourse and were completely prevented when her fiancé wore a condom. She did not experience systemic symptoms such as shortness of breath, wheezing, chest tightness, coughing, urticaria, diarrhea, dizziness or syncope. Underlying causes for these symptoms such as sexually transmitted diseases and chronic vulvovaginal candidiasis were excluded. She had no sexual relations with any other partner in the past. Her fiancé was not taking any over the counter/prescription medications nor eating foods to which she was sensitized when the reactions occurred.

Her past medical history was significant for spring seasonal allergies. She had previous reactions consisting of hives and shortness of breath after receiving penicillin and sulfonamides. She had no history of atopic dermatitis, asthma, or food allergies and there was no family history of atopy.

Physical examination was unremarkable. There was no evidence of dermatographism. Prick skin testing using appropriate negative and positive controls revealed sensitization to trees, grass and ragweed pollen in addition to dust mites, mold and cat allergen. Skin prick testing to a fresh specimen of the fiancé's undiluted semen elicited a 6-mm wheal with a 20-mm flare reaction. Similar testing performed on the fiancée as a control was negative. Serum-specific IgG and IgE performed by ELISA for both the patient and her fiancé in response to the fiancé's whole seminal plasma and SPP fractions were not elevated.

Seminal Plasma Desensitization

Using the protocol suggested by Matloff for intravaginal desensitization to whole seminal fluid,⁹ a fresh semen sample was obtained from the patient's fiancé and diluted with normal saline to concentrations of 1:10,000, 1:1000, 1:100, 1:10 and undiluted. Two milliliters of increasing concentrations of semen was deposited intravaginally at 20-min intervals over 2 hr.

Symptoms and vital signs including peak expiratory flow rates were monitored and remained unchanged throughout the procedure. The treatment was well tolerated without evidence of burning, pain, swelling or pruritus. The patient was instructed to have unprotected intercourse within 24 hr at home and if barring no reactions was to continue to have unprotected intercourse three times a week in order to maintain tolerance.

However, after unprotected intercourse, the female developed severe burning and swelling within 2 min of ejaculation. She was subsequently referred for systemic desensitization to relevant SPPs but elected not to pursue this treatment option.

Follow-up

As the patient could not tolerate unprotected sexual intercourse and wanted to conceive, intrauterine insemination using washed spermatozoa was initially attempted without success. She subsequently underwent *in vitro* fertilization, which resulted in conception and the birth of a healthy child.

DISCUSSION

This case report emphasizes two important points about SPH disorders. First, SPH is not associated with sterility. Secondly, whole seminal plasma graded intravaginal challenge is not uniformly successful for the treatment of SPH.

Our patient, as reported with other similar patients, had a positive response to skin prick testing to her fiancé's whole seminal plasma but serum-specific IgE to SPPs by ELISA could not be demonstrated.^{8,9} We found that a predictive response for successful desensitization is greatest when the woman elicits a positive skin test to relevant SPP in conjunction with serum-specific IgE to the SPP.¹⁰

The mechanism of this patient's localized urogenital reaction is unclear as she tolerated an intravaginal graded challenge to whole seminal plasma but developed symptoms immediately after natural intercourse. A positive skin test to whole seminal plasma in conjunction with negative serum-specific IgE antibody suggests that her reaction could have been induced by direct mast cell degranulation secondary to an unidentified histamine-releasing factor in seminal fluid, similar to what has been described with anaphylactoid reactions. Another plausible explanation why the patient did not experience a reaction after the controlled office graded intravaginal challenge was the lack of epithelial cell shedding in the vaginal vault as occurs during natural intercourse. This may have resulted in reduced localized and/systemic exposure

to the relevant SPPs responsible for her reaction. In the future, reproducing natural intercourse by disrupting the mucosal wall should be considered prior to initiating an intravaginal SPP graded challenge in order to determine whether this treatment is effective.

The treatment of SPH includes abstinence, the use of condoms, or desensitization. Couples attempting to get pregnant or who want normal sexual relations without the use of condoms typically pursue treatment. Subcutaneous desensitization, which requires fractionation of whole seminal plasma to remove large molecular weight proteins known to interfere with successful desensitization, is recognized as the gold standard for the treatment of patients with SPH. However, this treatment is very time consuming and can be cost prohibitive for many individuals. Furthermore, this treatment is not widely available to clinicians. A few case reports have reported successful intravaginal graded challenges using whole seminal plasma. This treatment approach is much easier for the allergist to administer and less cost prohibitive for the patient. Therefore, it seems logical that an intravaginal SPP graded challenge should be attempted prior to pursuing subcutaneous desensitization using fractionated SPP.

Regardless of which form of desensitization is pursued, women have been able to achieve pregnancy indicating that SPH is not typically associated with sterility.^{11,12} If intravaginal graded challenges to whole seminal plasma is unsuccessful and traditional SPP desensitization is not possible to perform, then artificial insemination with washed spermatozoa has been recommended to induce conception. Unfortunately, this approach is not always successful as was the case for our patient.¹³ However, she was able to conceive after in-vitro fertilization.

This case report confirms that sterility is not associated with SPH. Based on our experience, we recommend that women with SPH who want to achieve pregnancy first undergo an intravaginal graded challenge using their sexual partner's whole seminal plasma followed by subcutaneous desensitization to relevant SPP if the former approach proves unsuccessful. If both of these approaches are unsuccessful, an initial attempt should be made to induce

pregnancy by intrauterine artificial insemination using washed spermatozoa to remove any antigens responsible for SPH. Finally, if this approach also fails, and no other cause is identified for the patient's sterility, *in vitro* fertilization should be performed.

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