

Human Seminal Plasma Protein Allergy: A Diagnosis Rarely Considered

Barbara Glaser Ludman, RN, MS, FNP

■ Women with seminal plasma protein allergy (SPPA) have an immunologic response to human semen. Symptoms vary from local inflammation and pruritus to systemic anaphylaxis after exposure. The first case was documented in Germany in 1958. Prevalence is difficult to determine because of the sensitive nature of the symptoms and resultant underreporting. The immunologic etiology of the allergy is not clearly understood; however, it is thought to be an IgE-mediated response from mast cells. Patients with SPPA often have recurrent vaginitis associated with intercourse and are unresponsive to traditional therapies. The gold standard of diagnosis is absence of symptoms with condom use. Treatments include cromolyn vaginal cream for local reactions and immunotherapy with human seminal plasma. Treatment success has been varied. The implications and impact of SPPA on sexuality and reproduction are significant, and this allergy should be added to the provider's list of differential diagnoses for recurrent vaginitis in sexually active women. *JOGNN* 28, 359-363; 1999.

Accepted: January, 1999

Seminal plasma protein allergy (SPPA) is an immunologic response to human semen. Symptoms vary from localized irritation and inflammation to systemic anaphylaxis. The first reported case of SPPA was documented by Specken in Germany in 1958 (DeCuyper, Bogaerts, Vandekerckhove, & Gunst, 1996). Presti and Druce (1989) did a worldwide literature search of reported cases from 1958 to 1989 and found 32 cases. The prevalence is thought to be higher because of underreporting and lack of recognition by the medical community. Bernstein, Sugumaran, Bernstein, and

Bernstein (1997) conducted a prevalence study by sending out 1,073 questionnaires to women with symptoms such as local vaginal pain or systemic reactions in association with intercourse or exposure to semen. All the questionnaires were returned. The results indicated that 24.8% of the respondents had possible SPPA and 12.1% had probable SPPA, confirming that the allergy may be more prevalent than previously thought. While it may not be common, health care providers should be aware of the symptoms, treatment, and sequelae of human seminal plasma protein allergy. The literature on this topic is limited and primarily addressed in immunology and dermatology texts. Obstetric and gynecologic references to SPPA are limited and frequently outdated. Patients with symptoms suggestive of SPPA often are referred to immunologists or dermatologists for diagnosis and treatment.

Etiology

Although the cellular etiology is not clearly defined, several researchers have examined the

The incidence of human semen allergy is probably higher than reported because of lack of recognition in the medical community and underreporting by patients.

immunologic response to seminal fluid. It is thought to be an IgE-mediated reaction against the glycoprotein antigens in seminal plasma (Bernstein, Herd, Bernstein, Korbee, & Bernstein, 1993). These glycoproteins are produced in the prostate gland and are present in all males (Mathias, Frick, Caldwell, Yunginer, & Maibach, 1980). Antigens from the glycoproteins of seminal fluid bind to basophils and mast cells, causing histamine release and inducing an immediate hypersensitivity (Ebo, Stevens, Bridts, and Declerck, 1995; Witkin, Jeremiads, & Ledger, 1988). Some researchers have found a relationship between atopic disorders and SPPA (Friedman, Bernstein, Enrione, & Marcus, 1984; Mathias et al., 1980). In a study of 32 women with SPPA, Presti and Druce (1989) found that 59.4% had a history of atopy (eczema, asthma, rhinorrhea, and seasonal allergies) and 37.5% had a family history of atopy. In the Bernstein, Sugumaran, et al. (1997) prevalence study, 50.8% of those patients with probable SPPA had a history of atopy. Although a significant correlation appears to exist between atopic history and SPPA, atopy is not a prerequisite for SPPA (Ebo et al., 1995). In atopic females, seminal transfer of drug and food allergies have been reported. In one case, a male partner being treated with dicloxacillin for a skin infection had intercourse with a woman who was allergic to penicillin. She developed diffuse urticaria after intercourse. Further episodes were avoided by using condoms until her partner completed his course of antibiotics (Bernstein, Sugumaran, et al., 1997). In another case, a woman with allergies to walnuts developed diffuse urticaria and throat swelling minutes after having intercourse with a partner who had ingested walnuts shortly before intercourse (Jones, 1991).

Although the average time of onset in reported cases ranges from 20 to 30 minutes, variations exist (Bernstein, Bernstein, & Bernstein, 1997).

Signs and Symptoms

Reactions usually are classified as local or systemic. Local reactions include postcoital onset of vaginal burning, itching, edema, erythema, and possible vesicles. Onset may vary, with some women experiencing symptoms after first exposure to semen and others after numerous exposures. As with other allergic responses, onset does not necessarily occur with the first exposure to the allergen but rather an immunologic response may develop over time (S. Matloff, personal communication, March 25, 1998). When symptoms occur, the reaction usually is immediate. Duration may range from minutes to weeks. Some women find that symptoms resolve quicker with bathing. Allergic response has been confirmed with allergy skin testing, using the partner's seminal plasma (Bernstein, Englander, Gallagher, Nathan, &

Local reactions to SPPA include postcoital onset of vaginal burning, itching, edema, erythema, and possible vesicles. Systemic reactions are more serious and may include diffuse urticaria; angioedema of the face; respiratory compromise; pelvic pain; nausea; vomiting; diarrhea; general malaise; hypotension; and circulatory failure, although no fatalities have been reported.

Marcus, 1981; Friedman et al., 1984; Mathias et al., 1980; Matloff, 1993). Resolution with condom use is considered the gold standard of diagnosis for SPPA (Bernstein et al., 1997; Bosso, Aiken, & Simon, 1991; DeCuyper et al., 1996; Ebo et al., 1995; Matloff, 1993; Witkin et al., 1988).

The course of the allergy is unpredictable and variable. Symptoms may resolve over time (Chang, 1976; Jones, 1991) or may progress and worsen (Bernstein, Bernstein, et al., 1997).

Because multiple differential diagnoses exist for vulvovaginal erythema, excoriation, and inflammation (see Table 1), it is important to rule out infection and other potential sources of vulvovaginitis. Recurrent allergic *Candida* vulvovaginitis has been described in the literature. Women with recurrent vulvovaginal *Candida* infections appear to develop a localized hypersensitivity to *Candida albicans* (Witkin, 1987). Although vaginitis caused by *Candida albicans* and vaginitis caused by seminal plasma protein both appear to be IgE-mediated reactions, the literature does not suggest a relationship between the two. It should be noted that the differential diagnoses listed in Table 1 can occur exclusively or in conjunction with one another. A thorough sexual history is an important part of the patient's workup in the definitive diagnosis of SPPA.

Women with systemic reactions, a more serious condition, may have any of the following symptoms: diffuse urticaria; angioedema of the face, tongue, lips, and throat; stridor; wheezing; dyspnea; pelvic and vulvovaginal pain; nausea; vomiting; diarrhea; general malaise; hypotension, and circulatory failure. No fatalities have been reported as a consequence of SPPA (Bernstein, Bernstein, et al., 1997).

TABLE 1
Differential Diagnoses for Human Seminal Plasma Protein Allergy

- Contact dermatitis caused by diaphragms, condoms, lotions, spermicides, or lubricants
- Vaginal structural abnormalities (imperforate hymen, small introitus)
- Vaginal exposure to chemicals, such as those in soaps, toilet paper, and sanitary napkins
- Infection (bacterial vaginosis, *Trichomoniasis*, *Candida*)
- Sexually transmitted disease (gonorrhea, syphilis, *Chlamydia*, herpes)
- Lichen sclerosus
- Atrophic vaginitis
- Mechanical stimulation (vulvar edema secondary to vibratory stimulators)
- Latex allergy

Note: From *Contact Urticaria Syndrome* (p. 246), edited by S. Amin, A. Lahti, & H. Maibach, 1997, Boca Raton, FL: CRC Press. Copyright 1997 by CRC Press. Adapted with permission.

Case Report

A 23-year-old woman, married for 6 months, presented to her primary provider with vulvar burning and throbbing after intercourse, lasting 30 to 45 minutes, which improved upon showering. Symptoms had persisted for 6 months before she sought medical assistance. Upon examination by her primary provider, she was noted to have vulvar and labial erythema with a moderate amount of white, creamy discharge in the vagina. Vaginal pH was 4.0; potassium hydroxide and saline wet mounts were negative, as were tests for vaginal infections and sexually transmitted diseases. The patient and her spouse had used condoms consistently before marriage, and she had had no signs or symptoms of irritation. The primary provider prescribed a baking soda douche once a day for 2 days and Mycolog (E. Fougera & Company, Melville, NY) topical ointment. The woman was asked to refrain from intercourse for 1 week to allow the vaginal area to heal and to return for gynecologic consultation if her symptoms persisted. Approximately 1 month later, the patient and her husband returned with no improvement of symptoms. The nurse practitioner in the clinic recognized these symptoms as potential localized semen allergy and referred the patient to an immunologist where treatment was initiated with a 4% cromolyn vaginal cream.

Treatment

While no large-scale studies have been reported examining the efficacy of treatments, several researchers

have reported varying degrees of success with different treatment options (see Table 2). It should be noted that abstinence and condoms are not always viable options for some patients. Lifestyle and family planning should be considered when determining individual therapies for patients. If SPPA is suspected, patients can be referred to an immunologist for skin testing to confirm the diagnosis. For local reactions, Bosso et al. (1991) describe the use of 4% cromolyn sodium powder dissolved into an inert water-based cream. One teaspoon (5 ml) of the cream was applied to the vaginal canal via applicator 30 minutes before exposure to semen. The patient experienced no initial local reactions and was symptom-free at a 6-month follow-up. Cromolyn 4% vaginal cream continues to be one method of treatment for local reactions.

In a study by Chang (1976), complete relief of local symptoms was accomplished in one patient by using 25 mg of Benadryl (Rugby Lab, Norcross, GA) orally 30 minutes before intercourse. A second patient obtained partial relief of symptoms by taking Benadryl before intercourse. Bernstein, Bernstein, et al. (1997) also report varying success with the use of oral antihistamines 30 to 60 minutes before intercourse for the treatment of patients with systemic and local reactions. Best, Walters, and Adelman (1988) report one case successfully treated with mefenamic acid, a nonsteroidal anti-inflammatory with known prostaglandin inhibition. The patient was given 500 mg 2 hours before intercourse and every 4 hours as needed after intercourse. This particular patient did not have evidence of IgE-mediated hypersensitivity based on negative skin testing, but instead, probable prostaglandin involvement.

Local desensitization also was performed with success (Matloff, 1993) by depositing increasing concentrations of the partner's semen into the vaginal canal every 20 minutes for 4 doses, the last dose being undiluted. This method was successful as long as the patient and partner engaged in frequent intercourse (every 24–48 hours). Symptoms returned after a 10-day period

TABLE 2
Treatment Options

Abstinence
 Condoms
 Vaginal desensitization with partner's semen
 Immunotherapy
 Antihistamines
 Cromolyn vaginal cream

of abstinence. The procedure was repeated, and intercourse was resumed on a frequent basis without reaction (Matloff, 1993). Because of the frequency of intercourse required for success in this treatment, practicality of this method is questionable for many couples. This procedure, however, can be considered for patients wishing to conceive (DeCuyper et al., 1996).

For systemic reactions, immunotherapy has been attempted with success (Bernstein, Gallagher, Friedman, & Marcus, 1985; Friedman et al., 1984; Jones, 1991; Ohman, Malkiel, Lewis, & Lorusso, 1990). Desensitization is accomplished by introducing seminal plasma protein intradermally over a varying period of time. For treatment to be successful, it was necessary to have intercourse at least twice weekly or symptoms returned. For couples who were unable to maintain this level of frequency, Bernstein describes freezing pools of fresh semen ejaculates which could then be instilled into the vagina by the patient in the absence of her partner (Bernstein, Bernstein, et al., 1997).

Nursing Implications

Vulvovaginitis is a common complaint in a vast majority of practices. Because of the sensitive nature of the problem, patients may be reluctant to discuss it in detail with their health care providers. A sensitive approach, patience, and insight into the potential implications on a relationship by the provider may facilitate a more detailed coital history and discussion. Because SPPA is not well-reported in the literature and may well be more prevalent than the cases documented, it is important for providers to consider it when evaluating patients with postcoital vulvovaginitis and postcoital atopic symptoms. The potential for emotional stress associated with SPPA is rarely discussed in the medical literature. It is important to assess each patient's emotional well-being and the allergy's impact on her current and future relationships. Referral to counseling or mental health services may be indicated. It also would be advantageous to include the woman's partner in consultations to allow for open communication and exchange of information.

It is important for providers to include seminal plasma protein allergy on their list of differential diagnoses when patients present with postcoital vulvovaginitis or other atopic reactions following intercourse.

Further research on SPPA is needed to evaluate the emotional as well as physical implications of this diagnosis.

Conclusion

While SPPA is not a common problem, it is serious enough to warrant consideration when evaluating a woman for vulvovaginitis, atopic reactions, or dyspareunia. Because of the underreporting of this condition, a thorough, sensitively obtained history and physical examination will help to evaluate potential patients with SPPA. Absence of symptoms with condom use is a reliable diagnostic tool. Referral to an immunologist for further testing is recommended if SPPA is suspected.

REFERENCES

- Bernstein, J. A., Bernstein, D. I., & Bernstein, I. L. (1997). Seminal plasma hypersensitivity. In S. Amin, A. Lahti, & H. Maibach (Eds.), *Contact urticaria syndrome* (pp. 251-259). Boca Raton, FL: CRC Press.
- Bernstein, J. A., Sugumaran, R., Bernstein, D. I., & Bernstein, I. L. (1997). Prevalence of human seminal plasma hypersensitivity among symptomatic women. *Annals of Allergy, Asthma & Immunology*, 78, 54-58.
- Bernstein, J. A., Herd, Z. A., Bernstein, D. I., Korbee, L., & Bernstein, I. L. (1993). Evaluation and treatment of localized vaginal immunoglobulin E-mediated hypersensitivity to human seminal plasma. *Obstetrics and Gynecology*, 82, 667.
- Bernstein, I. L., Gallagher, J. S., Friedman, S. A., & Marcus, Z. H. (1985). Standardized immunotherapy protocol for IgE-mediated anaphylaxis to human seminal plasma. *Contraception, Gynecology and Obstetrics*, 14, 151-159.
- Bernstein, I. L., Englander, B. E., Gallagher, J. S., Nathan, P., & Marcus, Z. (1981). Localized and systemic hypersensitivity reactions to human seminal fluid. *Annals of Internal Medicine*, 94, 459-465.
- Best, C. L., Walters, C., & Adelman, D. C. (1988). Fixed cutaneous eruptions to seminal-plasma challenge: A case report. *Fertility and Sterility*, 50(3), 532-534.
- Bosso, J. V., Aiken, M. J., & Simon, R. A. (1991). Successful prevention of local and cutaneous hypersensitivity reactions to seminal fluid with intravaginal cromolyn. *Allergy Proceedings*, 12, 114-116.
- Chang, T. (1976). Familial allergic seminal vulvovaginitis. *American Journal of Obstetrics and Gynecology*, 126(4), 442-444.
- DeCuyper, C., Bogearts, Y., Vandekerckhove, F., & Gunst, J. (1996). Intravaginal desensitization and successful pregnancy in a woman with seminal fluid allergy. *Journal of Allergy and Clinical Immunology*, 97, 1427-1428.
- Ebo, D. G., Stevens, W. J., Bridts, C. H., & DeClerck, L. S. (1995). Human seminal plasma anaphylaxis (HSPA): Case report and literature review. *Allergy*, 50(9), 747-750.

- Friedman, S., Bernstein, I. L., Enrione, M., & Marcus, Z. H. (1984). Successful long-term immunotherapy for human seminal plasma anaphylaxis. *Journal of the American Medical Association*, 251, 2684-2687.
- Jones, W. R. (1991). Allergy to coitus. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 31, 137.
- Mathias, C. G., Frick, O. L., Caldwell, T. M., Yunginger, J. W., & Maibach, H. I. (1980). Immediate hypersensitivity to seminal fluid and atopic dermatitis. *Archives of Dermatology*, 116, 209-212.
- Matloff, S. M. (1993). Local intravaginal desensitization to seminal fluid. *Journal of Allergy and Clinical Immunology*, 91, 1230-1231.
- Ohman, J. L., Malkiel, S., Lewis, S., & Lorusso, J. R. (1990). Allergy to human seminal fluid: Characterization of the allergen and experience with immunotherapy. *Journal of Allergy and Clinical Immunology*, 85, 103-107.
- Presti, M. P., & Druce, H. M. (1989). Hypersensitivity reactions to human seminal plasma. *Annals of Allergy*, 63, 477.
- Witkin, S. S., Jeremiads, J., & Ledger, W. J. (1988). Recurrent vaginitis as a result of sexual transmission of IgE antibodies. *American Journal of Obstetrics and Gynecology*, 159, 32-36.
- Witkin, S. S. (1987). Immunology of recurrent vaginitis. *American Journal of Reproductive Immunology and Microbiology*, 15(1), 34-37.
- Barbara Glaser Ludman is a nurse practitioner in high risk obstetrics at Brigham and Women's Hospital Center for Women and Newborns in Boston, MA.*
- Address for correspondence: Barbara Glaser Ludman, RN, MS, FNP, Brigham and Women's Hospital, Department of OB/Gyn, 75 Francis Street, Boston, MA 02115.*