

Seminal plasma hypersensitivity: Clinical and histopathologic features in a multipara woman

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Clinical Implications

- Vulvovaginal provocation with allergen followed by colposcopy has not been evaluated to provide a suitable mean of assessing allergic vulvovaginitis. We identify a case of seminal plasma hypersensitivity with colposcopic and histopathological control following vulvovaginal exposure after coitus.

TO THE EDITOR:

Seminal plasma hypersensitivity (SPH) in women is a rare condition characterized by a local or systemic immunologic reaction against glycoprotein antigens in seminal plasma that should be distinguished from hypersensitivity to latex, spermicidal agents, or lubricants. Its prevalence is unknown and in most of the cases may be underdiagnosed. Only about 90 cases have been documented in English literature.¹ Jover et al² published the first case in Spain in 1993. Current evidence suggests that systemic SPH is mostly mediated by IgE against seminal plasma antigens. In contrast, localized SPH does not elicit significant seminal plasma-specific IgE response, suggesting a role of potential non-IgE-mediated mechanisms underlying this clinical condition.^{3,4} The presence of proteases in seminal plasma could explain this non-IgE-mediated response. It is known that the proteases can disrupt the epithelial permeability barrier and activate protease-activated receptors on epithelial cells, augmenting epithelial barrier dysfunction and increasing localized mucosal inflammation independent of specific IgE responses.^{4,5} Moreover, semen protease prostate-specific antigen has been identified and characterized as a causative allergen of SPH and has shown cross-reactivity with Can f 5.⁶ The clinical features of SPH are diverse and vary from weak reactions, such as vaginal itching after coitus, to systemic reactions, such as systemic urticaria or even anaphylactic shock, which can be life-threatening. There is an immediate reaction after coitus that can sometimes be delayed (1-15 hours). This reaction is resolved spontaneously or by treatment within 24 hours, and is prevented by using condoms. Local reactions may persist for days and even weeks.

We present the case of a 44-year-old multiparous woman with a history of hepatitis A during childhood, rhinitis and mild/intermittent cough, and cholinergic urticaria with local SPH. Our objective is to describe the clinical and histopathological

characteristics, as well as possible immune mechanisms, following vulvovaginal exposure after coitus.

Following her first sexual encounter at age 14 years and subsequent relations with different partners, the patient referred swelling and vulvovaginal pain at 90 to 120 minutes reaching greater intensity at 7 to 24 hours, with a burning sensation and abdominopelvic pain that spontaneously disappeared after 24 to 48 hours. These symptoms were aggravated if intercourse was repeated in the first days after the act but did not appear if *coitus interruptus* or condoms were used. In the last year, there were immediately associated buccal stinging and burning, ocular hyperemia, and a maculopapular rash on the abdomen after the ejaculate contacted skin and mucous membranes.

An *in vitro* and *in vivo* study involving the patient and her current partner was initiated, with prior informed consent from both parties. The *in vitro* study included the assessing of IgG, IgM, IgA, and total IgE; serum tryptase; and serology, urine sediment, and semen culture to discard transmissible infectious diseases. Specific IgE for common inhalants and foodstuff was assessed because of her rhinitis and mild/intermittent cough. Seminal fluid (from 5 different sources) was also assessed by SDS-PAGE immunoblotting. The *in vivo* study consisted of prick test for common inhalants, foodstuffs, latex, and pan-allergens (such as profilin, tropomyosin, polcalcin, and lipid transfer protein); prick-to-prick test with prawns, saliva, serum, sperm, whole semen, and seminal plasma; patch test for common allergens and whole semen; rubbing test on abdominal skin for whole semen; and colposcopy, cytology, and immunohistochemical examination. Assessments were basal and postcoital at 90 minutes and 24 hours.

Hematological and urine test results were normal in both subjects, including infectious serology. No specific IgE was detected for common inhalants, foodstuffs, latex, and seminal fluid from different sources. However, specific IgE for prawn and dust mites was detected. In addition, no antisperm antibodies or specific IgG against seminal fluid were detected. Prick test results for common inhalants, foodstuffs, latex, and panallergens were negative; prick-to-prick test was positive for whole semen (wheal diameter of 6 × 6 mm), seminal plasma (5 × 6 mm, with erythema), histamine (7 × 7 mm), and prawns, being negative for whole semen in the partner; patch test was positive for nickel and negative for whole semen; and rubbing test showed local wheals at 30 minutes with whole semen. No IgE reactive proteins were detected by immunoblotting.

Immunohistochemical study of vagina and vulva displayed an increase in intraepithelial and stromal CD3-positive T lymphocytes (Figure 1). Colposcopy at 90 minutes and 24 hours revealed severe vaginismus with dehydrated edematous mucosa. Speculum was difficult to introduce. Genital biopsy showed minimal increase in T cells, mast cells, and eosinophils at 90 minutes in the vagina and cervix, with a further increase in the vulva, vagina, and cervix, as well as stromal and dermal edema at 24 hours (Table 1).

The patient was diagnosed with local IgE-mediated SPH with recurrent vaginitis and contact urticaria and with a type I-mediated response, proven by medical history, prick test, and histopathology studies. Although prophylactic treatment with

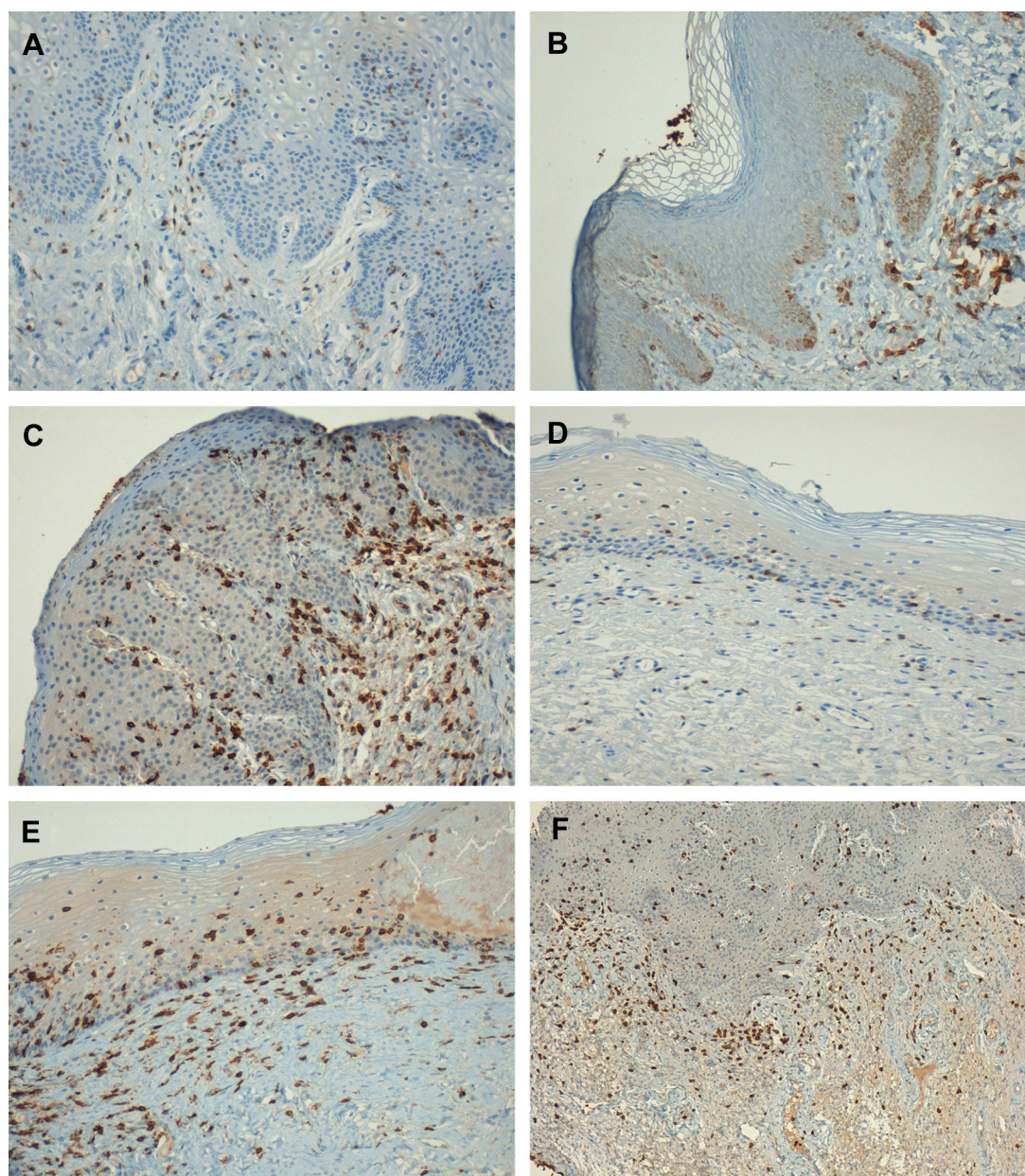


FIGURE 1. Immunohistochemical study in vulva and vagina after exposure to seminal fluid. Vulva study: **A**, Basal, 11 lymphocytes per hpf. **B**, 90 minutes, 12 lymphocytes/hpf. **C**, 24 hours, 52 lymphocytes/hpf. Vagina study: **D**, Basal, 8 lymphocytes/hpf. **E**, 90 minutes, 25 lymphocytes/hpf. **F**, 24 hours, 53 lymphocytes/hpf. All micrographs show intraepithelial and stromal CD3-positive T lymphocytes (20× magnification).

antihistamine or cromolyn has proven to be successful in other cases,^{7,8} montelukast, cetirizine, and 4% topical cromolyn did not protect our patient. In addition, the patient refused gradual intravaginal desensitization, despite its success in up to 72% of local reactions.¹ Nevertheless, the use of condoms has proved to be effective in our patient.

Avoidance of semen is effective in managing SPH, but it may not be acceptable by women who want to have a normal sexual relationship and/or who desire to conceive.⁹ According to the algorithm proposed by Bernstein,⁹ treatment strategies include preintercourse use of H1/H2 antagonists, leukotriene-modifying agents, and/or nonsteroidal anti-inflammatory

drugs. If premedication is not effective, gradual intravaginal desensitization with whole seminal fluid could be tried. For women with IgE-mediated SPH, subcutaneous immunotherapy using relevant seminal plasma proteins isolated by fractionation of whole seminal fluid has proven to be effective. The recommendation to our patient was the use of condoms.

To our knowledge, this is the first case of SPH with colposcopic and histopathological control following vulvovaginal exposure after coitus, as well as local manifestations after oral sex. Although the diagnostic role of genital biopsy is limited, the histopathological study proved useful for this case, providing a suitable mean of assessing recurrent allergic vulvovaginitis.

TABLE I. Biopsy study in vulva, vagina, and cervix

Time of study	Cervix	Vagina	Vulva
Basal	• 4 T lymphocytes/hpf • <1 mast cell/hpf	• 8 T lymphocytes/hpf • 1 mast cell/hpf	• 11 T lymphocytes/hpf • 1 mast cell/hpf
90 min	• 22 T lymphocytes/hpf • 3 mast cells/hpf	• 25 T lymphocytes/hpf • 7 mast cells/hpf	• 12 T lymphocytes/hpf • 3 mast cells/hpf
24 h	• 25 PMN/hpf • 41 T lymphocytes/hpf • 7 mast cells/hpf • 10 eosinophils/hpf	• 98 PMN/hpf • 53 T lymphocytes/hpf • 7 mast cells/hpf • 9 eosinophils/hpf	• 20 PMN/hpf • 52 T lymphocytes/hpf • 5 mast cells/hpf • 1 eosinophil/hpf

PMN, Polymorphonuclear neutrophils.

However, these findings are quite specific for recurrent allergic vulvovaginitis. It is unknown if they apply to non-IgE-mediated local reactions to seminal plasma. More studies are needed to know the immunological mechanism implicated.

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