

Human seminal plasma allergy: successful pregnancy after prophylactic anti-histamine treatment

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Human seminal plasma allergy is a rare phenomenon. Its clinical manifestations are diverse, and range from mild local pruritus to fatal anaphylaxis. Treatment varies with severity of the reactions: abstinence, condom usage or immunotherapy (subcutaneous or intravaginal) with seminal fluid. Local allergic reactions can be managed by prophylactic use of antihistamines or local cromolyn cream. A 33-year-old female visited the Asthma and Allergy Clinic in Seoul National University Bundang Hospital for the recurrent generalized urticarial reactions after sexual intercourse. She had been suffering from asthma, allergic rhinoconjunctivitis and atopic dermatitis for 10 years. She gave birth to a baby 6 months ago and no problem before. However, recently she began to recognize unexpected generalized urticaria that occurred after the sexual intercourse with husband. She wanted to have the second baby but hesitated because of the recurrent symptoms after the intercourse. She showed positive response to skin prick test with her husband's seminal fluid. The IgE-binding components were 15, 22, 28, and 35 kDa. Considering her moderate cutaneous reactions, we decided to try prophylactic treatments with oral anti-histamine one hour before sexual intercourse. She did not experience urticarial reactions with intercourse while oral anti-histamine was administered in advance. Finally, treatment outcome was successful, and the couple successfully gave birth to their second baby. We suppose that prophylactic antihistamine may be also applied in seminal plasma allergy patients if systemic reactions are limited to mild to moderate generalized urticaria.

Key words: Seminal fluid allergy; Urticaria; Semen; Hypersensitivity

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INTRODUCTION

Allergy to human seminal fluid is an uncommon phenomenon. It is usually considered to be an IgE-mediated hypersensitivity reaction to proteins in the seminal fluid. The clinical manifestations range from local pruritus to fatal anaphylactic reactions. Treatment can vary with severity of the reactions. Here we report a case of human seminal fluid allergy presenting as urticaria in which pregnancy was successful after prophylactic anti-histamine treatments.

CASE REPORT

A 33-year-old female visited the Asthma and Allergy Clinic in Seoul National University Bundang Hospital for the recurrent generalized urticarial reactions after sexual intercourse with her husband. She had been suffering from asthma, allergic rhinoconjunctivitis and atopic dermatitis for 10 years. She was married 8 years ago, and gave birth to a baby 6 months ago. She had no problem with the intercourse before. However, recently she began to recognize unexpected symptoms that occurred after the sexual intercourse with husband. The manifestation was generalized urticaria with immediate onset. She wanted to have the second baby but hesitated because of the recurrent symptoms after the intercourse.

Inhalant allergen skin prick tests were positive to *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, indoor molds, cat dander and dog dander. Seminal plasma from her husband was separated by centrifugation of semen at 5,000 rpm for 5 min at 4°C. Then skin prick test was performed using her husband's undiluted seminal plasma, and it yielded a positive reaction with a wheal diameter of 5 × 5 mm to semen. The positive control (1 mg/mL histamine; Allergopharma, Germany) resulted in a 3 × 3 mm wheal reaction, and the negative control (0.9% saline) did not show skin responses. To identify specific IgE and their binding components, sodium dodecyl sulfate-polyacrylamide gel electrophoresis immunoblotting was performed with seminal plasma from her husband and unrelated healthy controls. The immunoblotting revealed IgE-binding components of 15, 22, 28, and 35 kDa from her husband's seminal fluid. Common IgE-binding components reacted with other seminal fluid were 22, 28, and 35 kD (Fig. 1). Based on medical history and test results, the patient was diagnosed with hypersensitivity to seminal plasma. As the couple

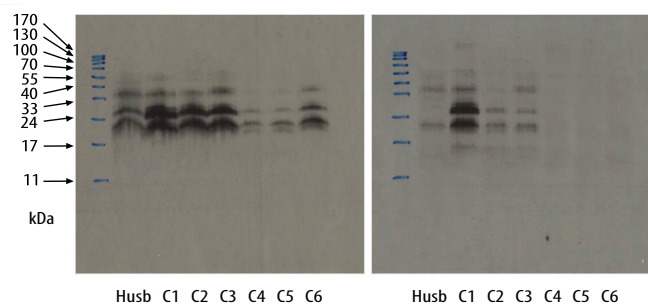


Fig. 1. Sodium dodecyl sulfate polyacrylamide gel electrophoresis and immunoblotting assay of seminal plasma from the patient's husband and unrelated healthy controls. Husb: husband, C: controls.

wanted to conceive another baby, various treatment options were discussed. Considering her moderate cutaneous reactions, we decided to try prophylactic treatments with oral anti-histamines (loratadine 10 mg once daily, Clarityne®; Schering-Plough, USA) one hour before sexual intercourse. She did not experience urticarial reactions with intercourse while oral anti-histamine was administered in advance. Finally, treatment outcome was successful, and the couple successfully gave birth to their second baby. After the birth, they did not want further conception. They were recommended to use condom protection and had no problem.

DISCUSSION

Human seminal plasma allergy is a rare disorder. In the literature, only more than 80 cases have been reported since the first English case report in 1967 by Halpern et al. [1]. Information on its prevalence is not available, but results from a questionnaire survey suggested that this hypersensitivity might be more common than previously recognized or reported [2].

The age of onset is usually between 20 and 30 years old. In a comprehensive review by Shah et al. [3], 61% of reported cases were in the third decade of life. Women over than 40 years old are less commonly affected. The clinical manifestations are diverse, but the reactions can be simply classified as local, systemic or both. Frequency of manifestations is one-third for each type of reaction. The local symptoms are commonly vulvar and vaginal itching, burning, pain, swelling, and erythema. The systemic reactions include generalized itching, urticaria, angioedema, respiratory distress, rhinitis symptoms, or fatal anaphylactic shock. A case of fixed eruption has been also described [4]. The time of onset is

mostly within 1 h, and only 13% developed between 1 and 15 h [3]. Thus, most of human seminal plasma hypersensitivity reactions are considered as classical IgE-mediated reactions. Although rare, cases also have been described for type III or IV hypersensitivity reactions [4, 5]. Symptoms resolve spontaneously in more than half of the cases, but severe reactions often required emergency interventions [3]. Atopic background may be associated with increased risk of human seminal plasma allergy [3].

Interestingly, 40% of seminal plasma allergy patients experienced hypersensitivity reactions on their first sexual intercourse [6]. Thus, the possibility has been raised that sensitization to an unknown allergen may cross-react with allergens in human seminal fluid. In this regard, a recent work by Basagaña et al. [7] was outstanding as they suggested that sensitization to dog epithelium may be a risk factor for human seminal plasma allergy. They demonstrated IgE cross-reactivity between dog allergen and the prostate-specific antigen. Another remarkable work by Mattsson et al. [8] identified that prostatic kallikrein is a major dog allergen, and that it is a key culprit in cross-sensitization and IgE-mediated seminal fluid allergy. Interestingly, our case was also sensitized to dog epithelium and had a history of dog breeding, but she developed urticarial reactions after a gap of time since first intercourse. It is unclear whether cross-sensitization existed between dog epithelium and seminal fluid allergens in this patient.

The diagnosis is based on careful history taking. Condom test can be diagnostic by demonstrating that symptoms of seminal fluid allergy can be abolished with condom usage [9]. Possible sensitizations to other antigens (latex, lubricants, or contraceptives) also should be evaluated [10]. Differential diagnosis includes contact dermatitis, candida or bacterial vulvovaginitis, coitus-linked asthma, 'honeymoon rhinitis', anxiety, irritant reactions or latex allergy [3, 10, 11]. However, *in vivo* skin tests are the most important for the diagnosis. Among 71 patients reviewed by Shah et al. [3], 93% of skin tested patients showed positive responses. For skin testing, the first step is to obtain a fresh ejaculate from their husbands or sexual partners. The sample needs to be liquefied at room temperature for 30 min, and then centrifugation is to be carried out to separate spermatozoa and seminal plasma [11]. Most reactions are known to develop with seminal plasma fractions [10]. *In vitro* measurements for specific IgE antibody include radioallergosorbent tests and enzyme-linked immunosorbent assays [6, 12]. Commercial kits for specific IgE tests are available, but their clinical utility is still uncertain [11]. Identification of allergens can be performed by electrophoresis, chromatographic separation and IgE immunoblotting assays [9, 10, 13, 14]. It has

been suggested that 14–75 kDa proteins of seminal fluid could be the IgE binding components [15, 16]. We have previously reported a middle aged woman with severe seminal fluid allergy. In that case, the common IgE-binding components were 15, 28, 35, 45, 90 kDa and the specific IgE-binding components to her husband's seminal fluid were 13, 26, and 30 kDa [14]. Regarding present case, 28, and 35 kDa could be the common IgE-binding components.

For treatment, avoidance is the mainstay. Exposure can be prevented by abstinence or condom usage. Improvements in clinical and skin test responses have been reported after the condom usages for 6 to 12 months [17]. However, in cases hoping for pregnancy, desensitization can be considered as a useful treatment option. Various immunotherapy protocols have been tried since the first report in 1967 by Halpern et al. [1]. Rush immunotherapy protocols have been also performed successfully by subcutaneous or intravaginal route [18, 19]. Following desensitization, a regular schedule of sexual intercourse or exposure to human seminal plasma needs to be maintained every 2–3 days to continue tolerance status [11]. In patients with local reactions, allergic symptoms can be managed by prophylactic usage of antihistamines or local cromolyn cream. However, to our knowledge, no cases have been reported for a patient with systemic reactions that achieved successful pregnancy only with prophylactic antihistamine treatments. We suppose that prophylactic antihistamine may be also applied in seminal plasma allergy patients if systemic reactions are limited to mild to moderate generalized urticaria.

In summary, we report a case of human seminal plasma allergy in which pregnancy was successful. The diagnosis was based on clinical history and skin tests. Mild to moderate urticarial cases may be prophylactically managed with oral anti-histamines to achieve pregnancy.

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