

CASE REPORT

Successful pregnancy by insemination of spermatozoa in a woman with a human seminal plasma allergy: should in vitro fertilization be considered first?

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Objective: To raise the possibility that pregnancy can be obtained by assisted reproductive techniques in patients with human seminal plasma allergy.

Design: Case report.

Setting: University hospital.

Patient(s): A woman consulted for a 3-year primary infertility. She reported lack of intercourse because of a seminal plasma allergy.

Intervention(s): One intrauterine insemination associated with antihistamine treatment was performed with carefully washed spermatozoa.

Result(s): Immediately after the insemination, the patient had an allergic reaction treated by steroids. Fortunately, this single attempt led to a successful pregnancy, and the patient gave birth to a healthy girl.

Conclusion(s): Pregnancies can be obtained in patients with seminal plasma hypersensitivity by means of intrauterine insemination. However, serious complications may occur after performing intrauterine insemination, which is not a totally reliable method to prevent an allergic reaction. Thus a multidisciplinary team should follow such patients carefully and watch for the potential risks and side effects. In vitro fertilization may represent the more cautious option. (Fertil Steril® 2010; ■: ■–■. ©2010 by American Society for Reproductive Medicine.)

Key Words: Allergy, seminal plasma, intrauterine insemination, assisted reproductive techniques (ART), infertility, pregnancy

Human seminal plasma allergy is a rare disorder, even though this phenomenon probably is underestimated (1). Up till now, 80 cases (2) were described in the literature, since the first publication in 1958 by Specken (3). Human seminal plasma allergy has various clinical presentations, classified as local or systemic, ranging from vulvovaginitis to anaphylactic reaction. In typical cases, patients have an immune reaction dependent on IgE antibodies (type I hypersensitivity) and have symptoms during or soon after sexual intercourse. The use of condoms seems to be the easiest method to avoid symptoms but is unsuitable for couples who want to conceive. Few alternatives are offered to them: desensitization for the responsible antigen or assisted reproductive techniques (ART). Indeed, pregnancies can be achieved by intrauterine insemination (IUI) with washed spermatozoa. So far, only three successful attempts of IUI have been documented. We report a new case of successful

pregnancy, obtained by insemination of spermatozoa in a woman with human seminal plasma allergy.

CASE REPORT

A 26-year-old woman consulted for primary infertility of 3 years' duration. She had no particular medical history, except an atopic background: asthma, allergy to dust mite and pollens. Results of her infertility investigations were normal. However, she reported the lack of unprotected sexual intercourse because of a seminal plasma allergy. Her 25-year-old husband had no medical or surgical history, except for phimosis operated on during childhood. His sperm analysis, performed after 3 days of abstinence, showed normal concentration ($29 \times 10^6/\text{mL}$ spermatozoa) and moderate asthenoteratozoospermia according to the World Health Organization criteria (motility a + b: 35%, typical morphology: 21%) (4). Sperm selection by migration on a Puresperm (Nidacon, Mölndal, Sweden) gradient (45%, 90%) led to the recovery of 6.12×10^6 motile spermatozoa (motility a + b: 70%), a number appropriate for all ART techniques.

The first allergic episode occurred immediately after unprotected intercourse with her husband. The woman had expiratory dyspnea with sibilant noises, nasal obstruction, and a generalized and pruriginous erythema. Rapid clinical improvement was obtained after

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a treatment by corticoids, antihistamines, and bronchodilators (methylprednisolone, cetirizine, and terbutaline). This initial event was followed by two similar episodes in the following years, after unprotected sexual intercourse with the same partner. Skin prick tests were performed in the allergy department of our hospital by measuring the diameters of the allergen-induced papule and erythema. The tests were considered positive when the papule's diameter was equal to or greater than the diameter of the positive control (histamine 10 mg/mL) or at least 3 mm greater than the diameter of the negative control (saline solution) (5). The patient had a significant reaction to the seminal fluid of her partner (positive control: 5–35 mm, negative control: 0–0 mm, patient: 12–55 mm after 10 minutes only). The couple was advised always to use condoms to prevent the development of serious allergic reactions.

Four years after the first allergic episode, the patient and her partner consulted, wishing to become parents. New skin prick tests were performed: a test with total sperm and another with prepared spermatozoa. The sperm preparation consisted in separating sperm cells from seminal plasma and selecting the spermatozoa according to their motility and density. Separation was made over a discontinuous Puresperm gradient (45% and 90%) by centrifugation at 400 to 600 × g. The pellet was carefully washed with Ferticult (Ferti-Pro, Beernem, Belgium) to remove seminal plasma allergens. This sperm preparation, routinely used for IUI, was checked in the patient. The results still confirmed a seminal plasma allergy (positive control: 11–45 mm, negative control: 0–0 mm, patient: 9–45 mm). Skin prick tests performed with washed spermatozoa were also positive (positive control: 7–25, negative control: 0–0, patient: 3–20). We knew this patient already had had IUI in another medical center. The patient had reacted mildly to the sperm preparation with vaginal pruritus, but the attempt failed. The couple was highly motivated to try another IUI. After multidisciplinary discussions and patient counseling, it was decided to proceed with a new attempt under antihistamine cover.

Ovarian stimulation was performed with purified human FSH (1125 IU). Ovulation was triggered on day 16 by hCG (Ovitrelle; Merck Serono, Geneva, Switzerland) when ultrasound showed two well-sized ovarian follicles (15 and 21 mm). Sperm preparation was realized with a Puresperm gradient (45% and 90%) by centrifugation at 400 to 600 × g. The pellet of selected spermatozoa was washed carefully twice to try to eliminate the maximum amount of seminal fluid and antigens responsible for the allergy. A volume of 400 µL of BM1 medium (ElliosBiomed, Paris, France) containing 2.7×10^6 motile spermatozoa was introduced in the uterine cavity of the patient, who had taken an antihistamine compound (cetirizine 10 mg) 1 hour before. Nevertheless, 15 minutes after the IUI, pruritus and a general edematous reaction developed. Symptoms were controlled quickly by corticotherapy, and she left the hospital 4 hours later. It turned out to be a successful attempt as the patient became pregnant and gave birth to a healthy girl.

DISCUSSION

The first case of human seminal plasma allergy was described in 1958 by Specken (3), a German gynecologist. Nine years later,

Halpern et al. (6) reported the first case published in the English literature. In 2004, Shah and Panjabi (2) recorded in a review approximately 80 reported cases of hypersensitivity to semen. However, this phenomenon seems to be more frequent and probably underdiagnosed. Indeed, it is sometimes difficult to differentiate between hypersensitivity to seminal plasma and other allergies (allergy to latex, lubricants, and spermicides). Absence of symptoms when patients use condoms is a strong criterion in favor of a true intolerance to seminal plasma. Patients are often young (20–30 years old) (2) and have typically a history of atopic disease. Human seminal plasma allergy usually occurs with more than one sexual partner. In the literature, only three cases were described with a specific partner (7–9). The antigen responsible for the antibodies' response in human seminal plasma allergy is not identified. It belongs to a heterogeneous family of glycoproteins present in the seminal fluid and is probably of prostatic origin (10). Allergens have been identified between 12 and 75 kDa (11). Skin prick tests are used to diagnose human seminal plasma allergy, as IgE-mediated immune response is the most common mechanism to explain the symptoms, as in this case report. However, type III or IV immune response also is described in the literature (12, 13).

Pregnancies can be obtained in these patients by ART. In 1981, Shapiro et al. (14) published the first pregnancy obtained in a patient allergic to seminal plasma after IUI. Seven cycles of IUI had been necessary to lead finally to the birth of twins. Another case was reported in 1999 by a Japanese team (15) and described a 29-year-old woman whose seminal plasma allergy was confirmed by skin prick tests. The sperm preparation for IUI was performed with a density gradient and washed before insemination. No allergic reaction was observed, but six cycles were necessary before obtaining a pregnancy. The last known successful attempt was described in 2006 (16). The 38-year-old patient presented with a serious anaphylactic reaction, after unprotected sexual intercourse. Four cycles with IUI were necessary to obtain an evolutive pregnancy.

In our case report, the recorded patient was pregnant at the second attempt of IUI (the first one in our center), but allergic symptoms, requiring fast IV steroids, immediately developed after insemination. One might hypothesize that some seminal fluid and traces of allergens remained after the sperm preparation. It could be wise, in such allergic patients, to consider IVF directly to avoid serious allergic symptoms, particularly when skin prick test results remain positive despite sperm washing. In vitro fertilization, although more complex than IUI for such young and fertile patients, may be recommended because it makes it possible for them to obtain a pregnancy without any contact with the sperm of their partners.

CONCLUSION

Pregnancies can be obtained in patients with seminal plasma hypersensitivity by means of ART. However, serious troubles may occur after performing an IUI, which does not reliably prevent an allergic reaction. This is why multidisciplinary teams must follow these patients carefully and watch for the potential side effects. To use IVF instead may be more cautious.

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