ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Intravaginal desensitization in a woman with IgE-mediated allergy to seminal fluid: a case report

Dessensibilização intravaginal em uma mulher com alergia mediada por IgE ao fluido seminal: um relato de caso

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ABSTRACT

Semen allergy is an IgE-mediated disease in which patients develop several clinical symptoms, whether local or systemic, subsequent to contact with the components of their partner's seminal fluid. Although uncommon, this allergy can have a major psychological impact on the lives of patients and their partners, which should be considered in the treatment decision-making. Treatment options include actions aimed at preventing the patient's contact with semen or interventions with specific desensitization using the sexual partner's seminal fluid. We report the case of a patient with a diagnosis of semen allergy who was treated with an intravaginal desensitization protocol to her partner's seminal fluid. This treatment allowed her to have an active sexual life, without the need for a barrier method, with the possibility of pregnancy if desired.

Keywords: Semen, hypersensitivity, immunologic desensitization.

RESUMO

A alergia ao sêmen é uma doença mediada por IgE, na qual a paciente apresenta diversos sintomas clínicos, localizados ou sistêmicos, após contato com os componentes do liquido seminal do parceiro. Apesar de não ser comum, esta alergia pode gerar um grande impacto psicológico na vida da paciente e de seu parceiro, o que deve ser considerado no momento da escolha do tratamento. As opções terapêuticas englobam, além das ações que visam prevenir o contato da paciente com o sêmen, a possibilidade de intervenção com a dessensibilização específica utilizando o fluido seminal do parceiro sexual. No presente relato, descrevemos o caso de uma paciente com diagnóstico de alergia ao sêmen, tratada com um protocolo de dessensibilização intravaginal ao líquido seminal de seu parceiro. Este tratamento possibilitou a ela ter uma vida sexual ativa, sem necessidade de uso de método de barreira, além da possibilidade de gestação.

Descritores: Sêmen, hipersensibilidade, dessensibilização imunológica.

Introduction

Semen allergy, also known as seminal plasma hypersensitivity, is a disease with uncertain incidence, manifesting with diverse clinical symptoms after contact with protein components present in the seminal fluid of a sexual partner. It is estimated that the incidence of this condition is higher than reported, and it is an underdiagnosed and underreported disease. Its prevalence is estimated at around 40,000 women in the USA.[1-3]

Semen allergy is mediated by IgE to specific proteins present in seminal plasma, not to sperm, and can occur at the first sexual intercourse or throughout

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sexual life.[1,2,4] Women with semen allergies may present with signs and symptoms ranging from localized to systemic. Local manifestations are often underdiagnosed, manifesting as burning and pain, angioedema, erythema and hives, as well as vaginal discharge and vulvar and vaginal itching.[1,3,5]

Systemic respiratory tract symptoms range from rhinorrhea and nasal obstruction to dyspnea and/or wheezing. Other possible symptoms in the gastrointestinal tract include vomiting or diarrhea, while pruritus and/or generalized hives can occur on the skin. Pelvic pain and malaise can also be observed. Some cases progress to severe anaphylaxis, with circulatory shock and loss of consciousness. Most reactions occur < 1 h after unprotected sexual intercourse. Some authors report a higher incidence of systemic than local manifestations. Symptoms proportionally increase in severity with recurrent exposure, and the interval between contact and symptom onset may gradually shorten.[1,3]

The mechanism of sensitization is not yet completely clear, but it is believed that IgE-mediated allergy occurs after exposure to proteins present in seminal fluid. Other rare cases, compatible with type III and IV hypersensitivity, have also been reported. Seminal plasma is rich in minerals, spermine, free amino acids, prostaglandins and enzymes. The prostate is the main source of seminal fluid proteins, and a prostate-specific antigen, 33-34 kD glycoprotein, is the most relevant sensitizer. Other proteins, not yet as well characterized, may also be involved. Reports of vasectomized men who induced reactions reinforce the findings implicating seminal plasma proteins in hypersensitivity reactions. However, in rare cases, spermatozoa have been identified as inducers of a cell-mediated reaction.[2,3,6]

Diagnosis is based on clinical history associated with IgE sensitization to seminal proteins, i.e. a reproducible immediate reaction after direct contact with semen during unprotected sexual intercourse. Elements that corroborate clinical suspicion include a lack of reaction during condom-protected intercourse and recurrent reaction after a ruptured condom. Sensitization to seminal fluid proteins is proven through in vivo or in vitro immunological tests, such as specific IgE to seminal plasma antigens or immediate skin tests, such as a prick test or an intradermal test.[5] Differential diagnoses include other coital-related disorders, such as IgE-mediated allergy to latex, contact dermatitis to latex-based condoms, spermicidal lotions or lubricants, exogenous allergens (such as foods or drugs) the partner has ingested, and even infectious conditions such as infectious vulvovaginitis and sexually transmitted diseases.[1,3]

Treatment may be preventive or interventional and must also consider psychological aspects. The couple should be advised to prevent exposure to the allergen by using barrier methods, such as condoms, and/or abstaining from intercourse. Coitus interruptus is not very safe and should not be recommended. Some patients (e.g., those considering pregnancy) may be considered for desensitization treatment.[5] The patient and her partner should also be advised about emergency measures after accidental exposure to semen, including self-injectable epinephrine for anaphylaxis.[5] Using antihistamines before sexual intercourse may help prevent mild, local post-coital reactions.[6]

An interesting therapeutic option for patients with IgE-mediated hypersensitivity to semen is specific desensitization using the seminal fluid of their sexual partner. There are several desensitization protocols in the literature, either subcutaneously or intravaginally.[2] The advantages of intravaginal desensitization over the subcutaneous route include greater ease, less complexity in processing the material, and the possibility of performing the procedure in a single day.[6]

In this report, we describe the case of a patient diagnosed with IgE-mediated hypersensitivity to her partner's semen, who underwent intravaginal desensitization.

Case report

A 29-year-old patient had a history suggestive of immediate reaction after unprotected vaginal intercourse, although skin contact was tolerated. She had been with a sole partner for 5 years, but reported no signs or symptoms during or after sexual intercourse in the first 3 years. In the last 2 years, on average 5 min after unprotected sexual intercourse, she began to experience reactions. Initially, they were mild, such as a runny nose, itching and nasal congestion, with spontaneous improvement after a few hours. However, the severity progressively increased, culminating in anaphylaxis, which manifested as dyspnea, wheezing, bilateral eyelid angioedema, and widespread hives. On this occasion, the patient did not seek emergency care, but self-medicated with fexofenadine 180 mg and albuterol spray 100 µg, which resulted in considerable

improvement, except for the eyelid edema, which lasted until the following day.

After anaphylaxis, the patient used the withdrawal method for almost 2 years, during which some episodes of sneezing and mild nasal itching occurred, although they improved in less than 1 h after using oral antihistamines. She was then advised to have intercourse only using condoms and was referred for desensitization assessment.

Prior to the investigation of IgE-mediated allergy to seminal plasma, some additional tests were requested for the patient and her partner to prevent transmissible diseases (Table 1). The patient was instructed to avoid contact with semen by using a condom during sexual intercourse.

To confirm the allergy, the partner's semen was used to perform a titrated prick test, as described previously.[7] The collected semen was centrifuged at room temperature for 10 min at 4000 rpm to separate the seminal plasma from the sperm. After centrifugation, the sperm were discarded and the seminal plasma was used for the prick test and subsequent desensitization. The prick test was performed using the seminal plasma titrated in decimal dilutions. The results, shown in Table 2, were positive for seminal plasma at dilutions of 1:10 and pure.

Desensitization followed the same protocol, using previously frozen seminal plasma.[7] On the day of desensitization, the seminal plasma was thawed at room temperature, and decimal dilutions were prepared with 0.9% saline solution, from 1:10 to 1:1,000,000. The patient was placed on a stretcher in the lithotomy position, with a pillow under the buttocks, tilting the pelvis to prevent leakage of the injected liquid during the procedure.

According to protocol[7], a plastic syringe without a needle or lubrication was used to administer 3 mL of each dilution intravaginally at 15-min intervals. The 1:1,000,000 solution was used first, without incident; approximately 5 min later, the 1:100,000 dilution was applied and the patient developed mild nasal itching, which resolved spontaneously in approximately 10 min. Again, approximately 5 min after the 1:10,000 dilution was applied, the patient developed wheals on her trunk and she was medicated with oral bilastine 40 mg. Since the reaction was mild, the applications were continued as planned. Complete remission of the wheals occurred approximately 20 min after antihistamine treatment. The remaining dilutions, 1:1000, 1:10, and pure semen, were administered at 15-min intervals and were uneventful, even during the subsequent 90 min observation period. The patient was then discharged, instructed to have unprotected sexual intercourse 2 to 3 times a week, and was given an action plan for possible reactions. If this schedule was interrupted, such as during travel, the patient was instructed to freeze a sufficient quantity of semen and apply it intravaginally 2 to 3 times a week.[6]

Seven months after desensitization, the patient continued having unprotected intercourse twice a week, with rare episodes of sneezing and nasal itching occurring approximately 5 minutes after intercourse, which spontaneously improved in less than 1 h.

Table 1
Complementary examinations

Patient	Partner
HBsAg: 0,54 (VR - reag > 1)	HBsAg: 0,76 (VR - reag > 1)
HBeAg: NR	
Anti-HBe: NR	
Anti-HBs: 14,19 (VR - reag > 10)	Anti-HBs: 845,6 (VR - reag > 10)
Anti-HCV: NR	Anti-HCV: 0,04
Anti-HIV 1 e 2: NR	Anti-HIV 1 e 2: NR
HTLV 1 e 2: NR	

Table 2
Titrated prick test

Material	Result
Seminal plasma 1:10.000	0
Seminal plasma 1:1000	0
Seminal plasma 1:100	0
Seminal plasma 1:10	3x3 mm
Pure seminal plasma	4x4 mm
Positive control (histamine)	7x7 mm
Negative control	0

However, one episode of dyspnea and wheezing occurred immediately after intercourse, for which the patient used fexofenadine 180 mg and albuterol spray, resulting in rapid improvement. Currently, and unlike the original treatment plan[6], the patient has sexual intercourse every 7 to 10 days, with no further episodes of systemic allergic reactions. On rare occasions, the patient experiences sneezing and mild nasal itching immediately after intercourse, treated with antihistamines, resulting in rapid and complete remission.

Discussion

The patient in this case suffered from an immediate type allergy after unprotected sexual intercourse, which began after 3 years of her relationship with the same partner, with no previous history of similar symptoms with other partners. According to the literature, in around 41% of cases the reaction occurs immediately upon first exposure, suggesting that these patients may be sensitized prior to first contact with human semen. However, in other reports, patients developed the allergy after varying periods of intercourse with the same partner or when they changed sexual partners.[6,8-10]

One as yet unproven explanation for first-contact reaction is cross-reactivity with some common protein structurally similar to prostate-specific antigens. Prostatic kallikrein isolated from dog urine has been reported to have about 80% structural homology to human prostate-specific antigens. Thus, sensitization may occur through previous exposure to dog urine.[2]

It is likely that, once a semen allergy has developed, it will occur with different partners. However, as in this case, a comparison could not be established since the patient has had a relationship with only one partner and there are ethical impediments to performing a skin test using seminal material from other men, in addition to the fact that specific IgE tests for seminal fluid have not been clinically validated and their negative and positive predictive values are unknown.[6]

Although effective, avoiding contact with the proteins in seminal fluid through condom use and sexual abstinence can present an obstacle for patients who wish to conceive and it can interfere in the relationship between partners. Thus, for patients who wish to become pregnant, desensitization is a relevant therapeutic alternative.[2,3] Another option would be artificial insemination.[11]

Semen desensitization can be performed either subcutaneously or intravaginally. However, subcutaneous desensitization requires more complex sample processing, limiting its use. Observational studies have shown good results from rapid vaginal semen desensitization, with a reduction in local and

systemic reactions. For this reason, patients who are unable to become pregnant after completing desensitization should be investigated for infertility.6 For the patient described in this report, we chose to perform intravaginal desensitization due to its greater ease as an outpatient treatment, our familiarity with the protocols, and to reduce the risk of systemic reactions.

A number of intravaginal desensitization protocols have been published, many of which use 2 mL of seminal fluid administered intravaginally every 15 to 20 minutes, starting at a dilution of 1:1000, progressing to 1:100, to 1:10, and then to the undiluted material. For patients who have had more severe reactions, other protocols begin with higher dilutions of 1:10,000, 1:100,000, or 1:1,000,000. In the present case, we began with a dilution of 1:1,000,000 due to the patient's history of systemic reactions, including anaphylaxis. There are also intravaginal desensitization protocols involving fractionation of semen components, in which high molecular weight proteins are eliminated. The fractionation procedure is the same as that of subcutaneous desensitization.[12] The literature suggests that the high molecular weight components of seminal fluid may have immunosuppressive action and could attenuate the efficacy of immunotherapy with unprocessed semen.[7]

In interventional therapy, such as semen desensitization, whether subcutaneous or intravaginal, the couple must be advised of the possible risks, which could range from local to systemic symptoms due to an IgE-mediated response. Thus, the couple is to be provided guidance on emergency measures in case of a reaction.[5]

After the desensitization procedure, the patient should be advised to have unprotected intercourse regularly (every 72 h) to promote immunological tolerance and avoid the recurrence of previous symptoms. Intravaginal application of semen samples may be considered when the partner is absent for more than 72 h.[12] Non-barrier contraceptive methods, such as oral contraceptives or intrauterine devices, should be used in patients who do not desire pregnancy.

Although the patient was instructed to have unprotected sexual intercourse every 2 or 3 days to maintain desensitization, as previously described[7], this frequency was only followed in the first 2 months. Soon afterwards, the interval was extended to once every 7 to 10 days. Despite recommendations to the contrary, decreasing the frequency of sexual intercourse in the present case did not result in serious systemic events after intercourse. Although tolerated by the patient, longer intervals are not recommended. According to the literature, intervals longer than 72 h between unprotected episodes of sexual intercourse could result in decreased or lost immunological tolerance and, consequently, a return of local and/or systemic symptoms.[6] Additionally, cofactors, such as infections, might lead to a lower tolerance threshold and an increased risk of severe reaction. Therefore, patients and their partners should be provided with an emergency action plan, including instruction on the use of self-injectable epinephrine in cases of anaphylaxis.[11]

Conclusions

IgE-mediated semen allergy, although uncommon, can have a major impact on patients and their partners due to the risk of serious symptoms from accidental exposure and the impossibility of pregnancy. Therefore, in addition to being considered a safe and effective method, specific desensitization to seminal fluid can reduce the psychological impact of the disease on the couple's life.

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