

## Allergy to Human Seminal Plasma: Case Report and Literature Review

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### Abstract

**Background:** Allergy to human seminal fluid (HSPA) is a rare condition, an IgE-mediated reaction to specific proteins therein. The symptoms occur within an hour after contact with semen and range from mild local to fatal systemic reactions. The mainstay treatment is avoidance of contact with semen.

**Objective:** To create awareness among health care providers on the phenomenon.

**Case:** A 21 year old girl presented with severe vulvar-vaginal pain, pruritus and swelling, which had developed about an hour after unprotected sexual intercourse. Previously she would experience mild to moderate genital burning sensation and pruritus. She had been treated for candidiasis on a number of occasions as a result, with no relief. A diagnosis of probable HSPA was made, for which she was counseled and advised to use condoms. She was put on antihistamines and the symptoms abated after about two days. She was followed up for six months during which period she was using condoms prophylactically and had not experienced any recurrences. Skin-prick allergy tests could not be done as the partner was uncooperative. We could not do IgE titres because of cost.

**Discussion/Conclusion:** Although HSPA has been documented in literature, few cases exist in the gynecologic literature. Local reactions may be misdiagnosed and mistreated as vulvo-vaginitis. There is need to improve awareness among health care providers as recognising this condition early will alleviate the stress and concerns that patients experience and enable providers to direct appropriate treatment.

### Introduction

Human seminal plasma allergy (HSPA) also referred to as human seminal plasma hypersensitivity (HSPH), is considered to be a rare phenomenon. It was first reported in 1958 from Germany, and by 2011 only about 80 cases had been documented in literature [1]. Since then a few more cases have been reported in the English literature, one of the more recent being by Sohn, et al. (2014) from China [2]. Bernstein, et al. (1997) [3] opined that the phenomenon is more common than hitherto reported, as many women with such symptoms either do not present to a health facility or when they do, are often misdiagnosed [3,4].

It is due to sensitization of the external female genitalia to seminal plasma proteins [5], most probably derived from the prostate or seminal vesicles [6], as vasectomy does not appear to prevent hypersensitivity reactions [7]. Disruption of the normal female genital tract immunomodulation is considered to be the pathophysiological process [8], although the actual mechanism is unclear.

The clinical manifestations are quite diverse. They include local genital reactions such as pruritus, pain, swelling and erythema, to systemic reactions such as urticaria, angioedema, shortness of breath, chest tightness, loss of consciousness and anaphylactic shock [9-11]. The symptoms develop within 30 minutes to an hour after exposure to semen or after sexual intercourse [7,12].

A careful detailed history to establish the temporal relationship between sexual contact and onset of the symptoms as well as exclusion of other possible causes of vulvo-vaginal symptoms is critical for a diagnosis of HSPA [13]. Absence of symptoms with prophylactic use of condoms is considered gold-standard for diagnosis thereof [1,7,14]. However for confirmation of the diagnosis serological tests for specific IgE to seminal proteins i.e. IgE titres, and/or a skin prick test using partner's semen or seminal fluid fractions are recommended [1,4].

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Avoidance of contact with seminal fluid through either abstinence, coitus interruptus, prophylactic antihistamines or condom use is considered appropriate treatment for local reactions and especially in those not desirous of a child or in non-permanent relationships. For systemic reactions immunotherapy through subcutaneous or intravaginal desensitization with the partner's seminal fluid may be preferred [1,7,8,15].

A probable case of human seminal plasma allergy presenting with severe local genital reactions, diagnosed on the basis of clinical presentation and managed with use of condoms prophylactically is presented. It is the first such case to be reported from sub-Saharan Africa region. The challenges in confirmatory diagnostic tests and management in our context are discussed.

### Case Report

A 21 year old, single African University student presented with severe vulvar-vaginal pain, pruritus and swelling of the labia about 18 hours after normal unprotected sexual intercourse with her boyfriend. The symptoms had started an hour or so after coitus. There was no history of vaginal discharge or bleeding and she did not have urinary symptoms. She had sexual debut at age 18, and this was her second boyfriend. She did not have similar experiences in her first relationship. She had only been sexually active with her second boyfriend for about six months. Prior to this she would get mild to moderate vaginal burning sensation and pruritus whenever they had unprotected sexual intercourse and had seen several doctors and each time she was treated for vulvar-vaginal candidiasis with no relief. The symptoms would abate a few days later, only to recur after unprotected sexual intercourse. She had no history of allergies or a family history thereof.

The only significant findings on clinical examination was labial swelling, the left more so than the right. There was no evidence of trauma and no discharge. She was otherwise in a good general condition, although a bit anxious and worried. A diagnosis of HSPA was suspected. She was counselled, explained the cause of her condition, given antihistamines and advised to abstain till the symptoms abated and thereafter use condoms all the time during sexual intercourse. The symptoms abated two days later. There was no recurrence during the six months of follow up as sexual intercourse was infrequent and they used condoms each time as advised. Attempts to do skin-prick allergy tests were unsuccessful as the partner was uncooperative. He refused to come to the clinic for counselling and to produce semen. She could not afford the cost for IgE titre test.

### Discussion

Human seminal plasma allergy (hypersensitivity) is defined as a spectrum of localized and/or systemic symptoms resulting from an IgE-mediated allergic reactions to specific allergens within the glycoprotein fraction of seminal [11,15]. The nature of the human seminal plasma allergens is still unknown, but several protein fractions, with molecular weights ranging from 12 000 to 75 000 Dalton, have been suggested as the possible allergens of human seminal plasma [6,7,11,16]. The pathophysiological process is not well understood. There are no known risk factors for developing seminal plasma hypersensitivity. Women who develop systemic symptoms are more frequently a topic [1]. The symptoms may develop after the very first sexual experience,

i.e. exposure to semen, in about 50% of cases [5,17], which is thought to be as a result of intrauterine sensitization from a twin pregnancy [18,19]. There have also been reports of cross-reaction with dog dander, epithelium or prostatic kallekrin [20-22]. It can also develop for the first time after repeated exposure to several partners' seminal fluids [23], or after an intercourse-free period such as following pregnancy and childbirth, hysterectomy or partial prostatectomy in the partner [13,16]. The presented patient developed the allergic reactions to seminal fluid in her second sexual relationship. She never experienced any problems in her first relationship. She did not have any obvious risk factors. There was an intercourse-free period of about a year between the two relationships.

The prevalence of HSPA remains unknown. Only slightly more than 80 cases have been documented in literature since the first case report in 1958. None of these has been from sub-Saharan Africa. This is perhaps the very first such case to be reported from the region.

The age of onset is usually 20-30 years. Shah, et al. (2004) in their review (n=74) noted that 61% of the patients were in their third decade of life [7]. In their study, Drouet, et al. (1997) (n=13), the ages ranged from 16 to 59 years, with 61.5% being aged  $\leq 30$  years [12]. It is reported that the younger women (<30 years) tend to have local reactions while the older (>30 year olds) tend to have systemic reactions [5,12]. The symptoms develop within an hour after coitus, worsen with time, peaking at about 24 hours, and abate usually two to three days later even if there is no treatment [2,7]. In some rare cases the symptoms may last up to 10 days [3].

The presented patient was 21 years old, had local genital reactions, i.e. vulvo-vaginal pain, pruritus and swelling, which developed about an hour after coitus and had worsened over time. The only significant finding on examination was swelling of the external genitalia. Reports indicate that in patients with local reactions the external genitalia is frequently normal, and if not, the typical findings are vulvar swelling and erythema [5].

A detailed history establishing the causal relationship between coitus, i.e. contact with seminal fluid and development of the symptoms is essential for making diagnosis. Complete avoidance of symptoms through abstinence, coitus interruptus or use of condoms is considered gold-standard for diagnosis [1,7,12-14]. The diagnosis may be confirmed by skin-prick allergy tests using partner's whole seminal fluid or fractionated seminal plasma proteins [1,4,7]. Other tests include identification and in vitro measurements of specific IgE antibodies [1,4,11,14,16]. These are however expensive and not readily available in developing countries. At the same time it is reported that these tests may be negative or equivocal [1,7]. IgE sensitivity is said to be about 50% [12]. Thus clinical diagnosis is considered more reliable, as stated above. In the case of the presented patient the diagnosis was made on clinical features, as the partner refused to produce a semen sample and she could afford an IgE identification and quantification tests.

The mainstay treatment modality for both local and systemic reactions is avoidance of contact with seminal fluid through abstinence, coitus interruptus or use of condoms [1,3,24]. Prophylactic use of anti-histamines or intravaginal cromoglycate may avert the symptoms [7,8,25]. The latter has however been

shown to have inconsistent results [7]. Antihistamines may not be a good option for those wanting to conceive as they have been shown to adversely affect ovulation and embryo implantation [26,27]. Other modalities, especially for those wanting to conceive or are not comfortable with or not able to use either of the above, include an intravaginal graded challenge using dilutions of whole seminal fluid, or subcutaneous desensitization to relevant fractionated seminal plasma proteins obtained from the woman's sexual partner [24,25]. The latter is reported to not only be effective but safer. Desensitization must be accompanied with regular and frequent unprotected sexual intercourse ideally every 48 hours, to maintain the cure [4]. As the presented young girl was not in a permanent relationship, did not wish to conceive, the partner refused to produce semen sample, and that she was comfortable with abstinence and use of condoms, these were considered adequate for the time being. She was however appraised of the fact that once HSPA develops it may persist even with future relationships [7,16], and may therefore require desensitization when she settles down i.e. gets married or is in long-term relationship to be able to conceive. Whereas HSPA does not cause infertility, some women may fail to conceive because of avoiding sexual abstinence, or use of condoms or as a result of side effects of antihistamines [26-28]. Women desiring to conceive may require desensitization, assisted reproduction through IUI using partner's washed spermatozoa [7,16,29,30].

## Conclusions and Recommendations

Although HSPA is considered a rare clinical condition due to paucity of published reports, it is nevertheless of significant public health concern. It affects young women at the peak of their sexual life, with potential impact on their sexual function and relationships. Diagnosis and treatment remain a challenge for developing countries and especially among young girls/women like the presented case, for various reasons, such as lack of awareness and access to skilled health care providers and cost implications. It may also be of medico-legal importance in case a woman developed anaphylactic shock and dies following sexual intercourse. The man may be accused of murder unknowingly. Fortunately there has not been a case of death due to HSPA to date.

Vulvo-vaginal complaints are very common among young sexually active women and one of the main reasons for seeking health care. HSPA may mimic chronic or recurrent vulvo-vaginitis and may therefore be misdiagnosed and wrongly treated. It may also be confused with contact dermatitis [29]. Genital allergy should be considered as a possible diagnosis in all patients with genital pruritus with no obvious features of infection or dermatosis and in whom symptoms do not abate or do worsen with treatment.

It is important therefore for health care providers to be aware of the phenomenon as recognising it early will alleviate the stress and concerns that patients experience and enable providers to direct appropriate treatment. There is also need for local research to determine the epidemiology, immunopathogenesis and treatment thereof.

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