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ORIGINAL ARTICLE

Asthma Caused by Human Seminal Plasma Allergy

Ashok Shah, M.D.,^{1,*} Chandramani Panjabi, M.D.,¹
and A. B. Singh, Ph.D.²

¹Department of Respiratory Medicine, Vallabhbhai Patel
Chest Institute, University of Delhi, Delhi, India

²Institute of Genomics and Integrative Biology (formerly known as Centre for
Biochemical Technology), Delhi University Campus, Delhi, India

ABSTRACT

Human seminal plasma allergy (HSPA) in women is a rare phenomenon and can be life-threatening. Hypersensitivity reactions occur during or immediately after coitus and are usually caused by sensitization to proteins in the seminal fluid. This can be very distressing for the patients and their partners. Young, married female patients with episodic asthma dating to their marriage with a history of difficulty in conceiving were specifically asked for local and systemic symptoms chronologically related to coitus. This methodology was adopted keeping in view our social conditions and sensitive nature of the information sought. Two patients thus detected were evaluated further. Condom usage, on our advice, abolished both local and systemic postcoital symptoms. Both patients tested positive to intradermal skin test with the seminal plasma antigen (SPA) derived from their respective husbands and, in patient 1, was accompanied by intense burning, irritation, and itching of the skin. Specific IgE against SPA was demonstrated in the serum of both patients. Elevated levels of total IgE were also detected. A high index of suspicion is needed to diagnose HSPA, especially the local forms, which can easily be overlooked due to patient embarrassment and lack of physician awareness.

Key Words: Human seminal plasma allergy; Asthma; Infertility.

INTRODUCTION

Hypersensitivity reaction to seminal plasma in women is an exceptionally rare phenomenon and is

termed as human seminal plasma allergy (HSPA). It is usually caused by sensitization to male seminal fluid proteins and occurs during or immediately after intercourse. This is thought to be mediated

*Correspondence: Ashok Shah, M.D., Professor of Respiratory Medicine, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi 110 007, P.O. Box 2101, India; Fax: +91-11-27667420; E-mail: ashokshah99@yahoo.com.

by the classical IgE-mediated pathophysiological mechanism.

This little known disorder was first recognized by the Dutch gynecologist Specken (1) in 1958. This was followed by the first English language report in 1967, from France, by Halpern et al. (2). Since then sporadic cases have documented the existence of this extremely rare disorder in the West. The first report from the Asian continent was documented by us in 1988 (3). Subsequently, one case each has been described recently from Japan (4) and Korea (5). We report two cases of this unusual condition who presented as asthmatics.

METHODS

Young, married female patients who presented in our outpatient department with episodic asthma and/or rhinitis dating to their marriage were also interrogated for an obstetric history. Those with a history of difficulty in conceiving were specifically asked for local and systemic symptoms that were chronologically related to coitus. This methodology was adopted to gain the patients' confidence, keeping in view our social conditions and the sensitive nature of the information sought. We were able to detect two patients with history suggestive of HSPA who were being treated as asthmatics.

Patient 1

A 25-year-old woman, married for 1½ years, was referred to our institute for evaluation of a 4-year history of dry cough and rhinitis. She also complained of episodic breathlessness, which had started 2 months after marriage. Her symptoms had progressively worsened and had increased in frequency and severity. Surprisingly, she remained relatively symptom-free during visits to her parental home when unaccompanied by her husband. There was no family history of atopy. On interrogation, she revealed that she had severe itching, burning, and pain in the vaginal area after coitus with her husband, her only sexual partner, since consummation of marriage. These symptoms, which occurred with every coitus, commenced immediately after ejaculation and abated spontaneously within half an hour of onset. Wheezing dyspnea also occurred after intercourse and this too lasted for about half an hour before subsiding gradually. She also suffered from severe itching and burning whenever her husband's seminal fluid came in contact with her skin. Neither partner was taking any medication or using any

topical ointment, nor did they ever use a condom. The patient had three first-trimester spontaneous abortions prior to referral.

Patient 2

The second patient, a 23-year-old woman, presented to us with a 5-year history of cough, breathlessness, and wheezing, occurring episodically, usually following an episode of rhinitis. She had been married for 5 years and her symptoms had commenced immediately after marriage. The patient related her initial symptoms to wheat dust exposure, which were aggravated by exertion and cold temperatures. Nocturnal exacerbations were also common. However, further interrogation revealed a definite association of her symptoms with coitus, dating back to her first intercourse with her husband, her only sexual partner. Worsening of rhinitis, cough, wheezing, and breathlessness were accompanied by local perineal itching and burning during and/or immediately after sexual intercourse. The symptoms occurred with every coitus and would last for about 15 minutes before subsiding spontaneously. In this case, too, symptoms eased considerably whenever she visited her parental home without her husband. Although the patient has a 3-year-old child, she gave a history of an elective abortion 2 years back. Following this, an intrauterine device was inserted, which was removed after a year. A third conception, 1 year prior to referral, resulted in a child who died 22 days after birth. The couple had never used condoms. The patient's mother and son were also asthmatics.

Physical Examination and Routine Investigations

Clinical assessment of both patients was done along with routine haemogram, urinalysis, roentgenograms of the chest, as well as the paranasal sinuses and spirometry. Routine intradermal skin testing with the usual set of aeroallergens was also done.

Specific Investigations

Keeping in mind the possibility of HSPA, the following investigations were carried out:

1. Condom test: Condom usage was advised to both couples and the patients were requested to record their postcoital symptoms.

2. Intradermal skin testing with seminal plasma antigen: Fresh semen was obtained from each patient's husband for preparing the seminal plasma antigen (SPA). The semen samples were processed as per methods adopted by us earlier (3). The SPA was diluted with buffered saline (BS) to get dilutions of 1:1, 1:4, 1:100, and 1:500 v/v. Intradermal tests were performed on the patients with serial dilutions of the SPA of their respective husbands along with a negative control (BS) and a positive control (histamine, 100 µg/mL). The tests were also done on the husbands of both patients with their respective SPA.
3. Specific IgE against husband's SPA in the patient's serum by ELISA.
4. Total serum IgE level by ELISA.

RESULTS

Clinical data of the patients is summarized in Table 1. Apart from bilateral polyphonic rhonchi on chest auscultation, physical examination in both patients was unremarkable. Routine haemograms, urinalysis, and roentgenograms of the chest as well as paranasal sinuses did not detect any abnormality

in either patient. Spirometry, however, revealed moderately severe airway obstruction with significant reversibility in both patients. Intradermal skin tests with the routine set of local allergens detected marked positivity to the pollen antigen of *Morus alba* in patient 1, while patient 2 had a positive skin reaction to the pollen of *Pennisetum typhoides* and cockroach antigen.

Specific Investigations

Both patients recorded that their postcoital symptoms, local as well as systemic, were abolished completely with condom usage. The relief in local symptoms was highlighted by the patients. In both cases, the husbands were unaware of the nature of the local symptoms in their spouses. Patient 1 had markedly positive skin reactions to 1:1 and 1:4 dilutions of her husband's SPA and complained of intense burning, irritation, and itching immediately after the test, while patient 2 tested positive to 1:1, 1:4, and 1:100 dilutions of her husband's SPA (Table 2). Identical tests on the husbands of both patients were uniformly negative. The sizes of the wheal with 1:1 dilution of the SPA in husbands of both patients were considered negative in view of the high concentration of the antigen (1:1) and the size of the negative as well

Table 1. Clinical profile of the patients.

	Patient 1	Patient 2
Age (years)	25	23
Duration of illness (years)	4	5
Duration of marriage (years)	1.5	5
Duration of symptoms of HSPA (years)	1.5	5
Number of children	0	1
Postcoital symptoms		
Local		
Itching	+	+
Burning	+	+
Pain	+	—
Systemic		
Breathlessness	+	+
Wheeze	+	+
Cough	+	+
Rhinitis	+	+
Onset of symptoms	Immediately after coitus	During coitus
Spontaneous resolution of symptoms—local and systemic (minutes)	30	15
Prevention of symptoms by condom usage	Yes	Yes

Table 2. Results of intradermal tests with husbands' SPA on the patients and controls (respective husbands)^a.

	Histamine	Buffered saline	1:500	1:100	1:4	1:1
Patient 1						
Wheal	11 × 9	2 × 3	5 × 4	6 × 6	9 × 8	10 × 11
Erythema	31 × 33	—	17 × 18	20 × 22	26 × 25	35 × 35
(Grade)	(++)	(-)	(+)	(+)	(++)	(++)
Husband of patient 1						
Wheal	13 × 14	3 × 3	^b	2 × 3	6 × 7	7 × 7
Erythema	25 × 26	—		6 × 7	11 × 10	10 × 10
(Grade)	(++)	(-)		(-)	(-)	(-)
Patient 2						
Wheal	7 × 8	2 × 2	^b	6 × 8	9 × 10	11 × 13
Erythema	20 × 18	—		12 × 15	16 × 18	22 × 25
(Grade)	(++)	(-)		(++)	(++)	(+++)
Husband of patient 2						
Wheal	14 × 10	4 × 3	^b	1 × 1	4 × 5	6 × 6
Erythema	27 × 29	—		7 × 8	12 × 10	10 × 11
(Grade)	(++)	(-)		(-)	(-)	(-)

^aAll figures in millimeters.^bTest not performed.

as positive controls. The sera of both patients demonstrated significantly higher levels of specific IgE antibodies against the SPA of their respective husbands (> 30%, as compared to control samples). Elevated levels of total IgE in the sera of both patients were also recorded (patient 1: 1800 IU/mL, patient 2: 780 IU/mL, normal values: < 180 IU/mL). With symptomatic relief, both patients were lost to follow-up.

DISCUSSION

Human seminal plasma allergy, a rarely considered diagnosis, is often underreported by the patients. This entity in women needs to be distinguished from other forms of coitus-linked asthma including post-coital asthma (6) and condom-induced asthma (7). Both patients who exhibited the classical symptomatology of HSPA presented to us as asthmatic subjects (8). The diagnosis of HSPA was only established because of a high index of suspicion.

Our patients reported the occurrence of symptoms ever since their first coitus with their husbands, their only sexual partners. Symptoms in HSPA can range from local pruritis to life-threatening anaphylaxis and can thus be classified as either local or systemic. Patients can present with either local or systemic symptoms, or a combination of both. Progress from local symptoms to systemic symptoms has also been reported (3). In patient 1, progression

of symptoms from local to systemic occurred 2 months after the initial occurrence of local symptoms with the first coitus; while in patient 2, the local and systemic symptoms started simultaneously with the first coitus.

In our patients, commencement of symptoms of HSPA since the first intercourse conforms to several earlier reports (2,3). Some authors have also reported a temporal relationship between seminal fluid allergy and coitus during or immediately after pregnancy (9), insertion of an intrauterine device (10), and, in one case each, hysterectomy (11) and menopause (12).

A history of infertility has been regarded as an important clue for the diagnosis of HSPA. Successful induction of pregnancy with seminal fluid-free spermatozoa has been achieved in two patients (4,13). It was thought that pregnancy was not recorded after identification of HSPA (13). However, familial allergic seminal vulvovaginitis was reported by Chang (14) in 1976 in which the local form was seen in a mother and her three daughters. All four women in the family had experienced discomfort from contact with seminal fluid beginning from their first sexual intercourse. The mother could not tolerate coitus more frequently than once every third day because of local reactions. The eldest daughter, who was then 33, also had two children. Voorhorst (15) reported a patient with postcoital itching of genital areas that started between two pregnancies, but after the birth of the second child the symptoms worsened considerably. Blair and Parish (16) also reported a

Asthma Due to Human Seminal Plasma Allergy

129

patient who developed HSPA after the fourth pregnancy but had a successful full-term normal delivery subsequently. In patient 1, there was a history of three first-trimester spontaneous abortions; while patient 2 had conceived three times in spite of having symptoms of HSPA.

Contrary to our earlier report (3), both patients had an atopic background. Patient 1 had a personal history of atopic disease. Patient 2 also had a family background. Atopy is reported to be a consistent risk factor for the development of HSPA (17).

The diagnosis of HSPA was established on the basis of complete resolution of symptoms with condom usage and positive skin test with the SPA of their respective husbands. This was further confirmed by the presence of specific IgE to seminal plasma proteins. The *in vivo* skin test with the partner's SPA is considered to be more reliable than the *in vitro* immunologic methods because reliable, sensitive, specific IgE assays are not available (17).

The local forms of HSPA frequently go unrecognized as they are often misdiagnosed as vulvovaginitis (18). Patients with episodic allergic manifestations and a history of difficulty in conceiving should be evaluated sensitively for temporal relationship of symptoms with coitus. Note that HSPA can easily be overlooked due to patient embarrassment and lack of physician awareness, especially in our social conditions and busy outpatient departments.

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