Detection of Sexually Transmitted Pathogens in Patients with Hematospermia

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Abstract

Background: Although the current literature attributes most cases of hematospermia to an infectious agent, identification of the specific pathogens involved has been limited.

Objectives: To determine the prevalence of different pathogens in patients presenting with hematospermia to our sexually transmitted disease clinic.

Methods: Between January 1999 and January 2000, 16 patients presented to our STD clinic with hematospermia after other non-infectious pathologies had been excluded by a referring physician. After obtaining informed consent, subjects completed a questionnaire addressing symptoms and sexual behavior. First-void urine samples, as well as genitourinary and serum specimens were tested for *Chlamydia trachomatis, Ureaplasma urealyticum* and herpes simplex virus. Standard bacterial cultures were also performed.

Results: Laboratory testing detected a pathogen in 12 of the 16 males presenting with hematospermia. The sexually transmitted pathogens detected were herpes simplex virus in 5 patients (42%), *Chlamydia trachomatis* in 4 (33%), *Enterococcus fecalis* in 2 (17%), and *Ureaplasma urealyticum* in 1 (8%). In all cases in which a pathogen was identified, the appropriate antimicrobial agent was administered. Symptoms resolved for each patient following antimicrobial therapy. During a 1 year follow-up, all 12 patients remained free of disease.

Conclusions: Recent advances in microbiologic diagnostic techniques have facilitated the detection of pathogens in patients with hematospermia, thereby enhancing the efficacy of treatment.

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Hematospermia, or hemospermia, is the presence of fresh or altered blood in the ejaculate. The condition may result from various pathologies affecting the male genitourinary tract, including the testes, prostate, vas deferens, seminal vesicles, urethra, and the accessory sexual glands and ducts. It can occur as a single episode or over a period, with or without recurrence, and may even become chronic with blood persisting in the semen for years. In general, hematospermia is a benign condition that typically resolves spontaneously, in contrast to other pathologies associated with blood in bodily fluids [1]. The condition can, however, be alarming to patients and their spouses who, when faced with symptoms, will invariably seek prompt medical attention [2].

As can be seen in Table 1, the etiology of hematospermia is vast, potentially involving several mechanisms, depending on the anatomic site, disease process or iatrogenic cause. As a general rule, most cases in the middle-aged group (<40 years of age) are benign, while unsuspected malignancy and diseases of the prostate may occur in older men (>40 years) [3]. Recent advances in laboratory diagnostic testing and imaging have enabled us to identify a cause in many cases that would have once been thought to be idiopathic or "essential." It was recently estimated that infectious or inflammatory disorders account for 39% of cases of hematospermia [4].

Although the current literature attributes most cases of hematospermia to an infectious agent, the identification of specific pathogens has been limited [1–4]. In those limited studies where an infectious etiology was identified, *Mycobacterium tuberculosis, Neisseria gonorrhoeae* and *Schistosoma haematobium* were among the most common. In addition, isolated reports have linked hematospermia with *Staphylococcus aureus* and cytomegalovirus infection [5–7].

At present, therefore, little is known about the prevalence of specific infectious agents in hematospermia. We evaluated the prevalence of different pathogens in patients with hematospermia in whom a referring physician excluded non-infectious pathology.

Patients and Methods

The Bnai Zion Medical Center STD clinic provides care to approximately 350 patients per year from the metropolitan Haifa area and northern Israel. Sixteen patients with a recent history of hematospermia who sought care at the clinic were prospectively enrolled in our study from January 1999 to January 2000. Most of the individuals (12/16) were young, sexually active males. Non-infectious etiologies of hematospermia were excluded by the referring physician (either a urologist or a primary care physician) through a history, physical examination, urinalysis, urine culture, urine cytology, complete blood count with coagulation profile, and imaging modalities (ultrasound, computerized tomography or magnetic resonance imaging) where warranted.

After giving informed consent for testing for a variety of sexually transmitted diseases, patients were asked to complete a questionnaire addressing sexual behavior. A physical examination of the genitalia was performed and genitourinary and serum specimens collected. Urethral secretions and discharge were obtained follow-

* The first two authors contributed equally.

STD = sexually transmitted disease

Table 1. Causes of hematospermia

Prostate	Urethra	Seminal vesicle	Trauma	Infectious	Systemic	Iatrogenic
Adenomatous polyps	Benign polyps	Amyloidosis	Local nerve block	Bilharziasis	Cirrhosis of liver	High frequency ultrasound
Benign prostatic hyperplasia	Condylomata	Calculi	Perineal	Epididymo-orchitis	Hypertension	Prostate biopsy
Calculi	Stricture	Carcinoma	Self-instrumentation	Seminal vasculitis	Hemophilia	Prostatic injections
Carcinoma	Urethritis	Cysts	Testicular	Tuberculosis	Leukemia	Post-hemorrhoidal sclerotherapy
Prostatitis	Utricular cysts	Diverticula		Urethritis	Lymphoma	Post-orchiectomy
Sarcoma		Leiomyoma			Purpura	Post-prostate cryosurgery or brachytherapy
Telangiectasia		Obstruction			Scurvy	Post-vasectomy
Varices					Von Willebrand's disease	Ureteral stents

Table 2. Laboratory methods and source of specimen for each microorganism

Infectious agent	Source of specimen	Diagnostic test
N. gonorrhoeae	Urethra	Stained smear
		Selective culture (Hylabs, Rehovot, Israel)
C. trachomatis	First-catch urine	PCR (Amplicor, Roche Diagnostic Systems)
U. urealyticum	Semen	Selective culture (Mycofast, France)
Mycoplasma hominis	Semen	Selective culture (Mycofast, France)
Trichomonas vaginalis	Urethra	Saline wet mount
	Semen	Selective culture (Hylabs, Rehovot, Israel)
Herpes simplex	Serology	HSV-1&2 IgG ELISA (Gull Laboratories, USA)
	Urethra	Antigen Detection (Dako, IDEIA, UK)
	Semen	Nested PCR[15]
Other sexually transmitted pathogens tested for:		
Treponema pallidum	Serology	VDRL
		TPHA (Biokit, SA, Spain)
Hepatitis B virus	Serology	Anti-HBc Ag (Abbott Labs, IL,USA)
Human immuno-deficiency virus	Serology	ELISA (Abbott Labs, IL, USA)

ing a prostate massage by insertion of narrow shafted dacron-tipped swabs 2–3 cm into the urethra. The swabs were then placed into transport vials (Copan, Italy), and the specimens were transported and processed immediately. A first morning semen sample was plated on selective media to culture *Neisseria gonorrhoeae*. The specimen was also analyzed for *Ureaplasma urealyticum*. First-voided urine, 30–50 ml, was collected and stored at 4°C until polymerase chain reaction testing for *Chlamydia trachomatis*. HSV-1 and HSV-2 type-specific seropositivity was tested by enzyme-linked immunosorbent assay. HSV antigen detection was performed from urethral swabs. PCR testing for HSV DNA was available for only one patient. A full list of the laboratory methods and source of specimen for each microorganism is summarized in Table 2.

HSV = herpes simplex virus
PCR = polymerase chain reaction

Results

Sixteen urethral, first-voiding urine, serum and semen specimens were available for laboratory evaluation. The age range of the patients was 17–66 years (median 33 years), with 4 patients (25%) over 40 years old. Eight (50%) were Israeli Jews, 6 (38%) were Israeli Arabs, and 2 (13%) were foreigners. Thirteen patients (81%) reported having two or fewer sexual partners in the last 6 months. All patients reported to be heterosexual. Two patients reported that they seldom use condoms, while all others reported that they never use condoms.

Hematospermia was the only current symptom among all 16 patients. All patients specifically denied experiencing testicular pain, sex-organ itching or lesions, epididymal pain, proctitis, arthritis, lymphadenopathy, perineal lesions, or testicular atrophy. However, two patients described the presence of a sex-organ lesion in the past, while one claimed that he suffered from prostatism and dysuria. Twelve patients (75%) complained of recurrent bouts of hematospermia over periods ranging from 1 month to more than 2 years. Two patients were not sure of the exact duration of the symptoms, while the remainder complained of hematospermia that had lasted for less than a month.

An etiologic agent was detected in 12 patients (75%). Herpes simplex virus was found in 5 (42%) of these patients, *C. trachomatis* in 4 (33%), *Enterococcus fecalis* in 2 (17%), and *U. urealyticum* in 1 (8%). No pathogen was detected in the other four patients. Of the five patients with positive serology for HSV, four were seropositive for HSV-2 and one for HSV-1. Herpes antigen was positive from the urethral swab of the HSV-1-seropositive patient. A semen sample for one patient was available for PCR DNA analysis, and was positive for HSV-2. *N. gonorrhoeae* was neither cultured nor detected by PCR in any of the semen or urine specimens, respectively. The characteristics, etiologic agents isolated, and laboratory methods in all 12 cases are summarized in Table 3.

Table 3. Patient characteristics and etiologic agent Isolated

Patient	Age	Duration of hemato-spermia (wk)	No. of partners in the last 6 months	Finding	Confirmatory diagnostic test
1	31	104	5	HSV-2	**Serology:** (+) IgM and IgG **Antigen detection:** Negative **PCR DNA of semen:** N/A **Other:** sex-organ lesion in the medical history
2	35	250	1	HSV-2	**Serology:** (+) IgM and IgG **Antigen detection:** Negative **PCR DNA of semen:** N/A
3	32	104	1	HSV-1	**Serology:** (+) IgM and IgG **Antigen detection:** Positive **PCR DNA of semen:** N/A
4	31	10	1	HSV-2	**Serology:** (+) IgM and IgG **Antigen detection:** Negative **PCR DNA of semen:** N/A
5	66	30	1	HSV-2	**Serology:** (+) IgM and IgG **Antigen detection:** Negative **PCR DNA of semen:** Positive
6	30	104	1	*C. trachomatis*	(+) PCR
7	17	150	0	*C. trachomatis*	(+) PCR
8	40	1	1	*C. trachomatis*	(+) PCR
9	60	4	1	*C. trachomatis*	(+) PCR
10	33	104	5	*U. urealyticum*	(+) culture of semen
11	35	10	1	*E. fecalis*	(+) culture of semen
12	33	4	1	*E. fecalis*	(+) culture of semen

Ig = immunoglobulin.

In each case where a pathogen was identified, the appropriate antimicrobial agent was administered. The treatment protocol was valacyclovir (500 mg twice a day for 10 days) for HSV-2, doxycycline (100 mg twice daily for 10 days) for *C. trachomatis* and *U. urealyticum*, and amoxicillin (500 mg three times a day for 7 days) for *Enterococcus fecalis*. Symptoms resolved for each patient following antimicrobial therapy. During the 1 year follow-up all 12 patients remained free of disease. The five patients for whom no pathogen was identified were referred to a urologist for further evaluation.

Discussion

Hematospermia has a vast number of possible etiologies, but evaluation of patients usually reveals an infectious or idiopathic cause. In cases where symptoms occur without an associated structural or functional impairment, the condition is usually self-limiting and will resolve spontaneously. Consequently, an extensive workup is generally not conducted. However, hematospermia can persist for years, with the accompanying emotional strain on the patient and his sexual partner [2]. Therefore, even in self-limiting cases it may be prudent to pursue the etiology.

Our study examined 16 patients in whom possible non-infectious causes of hematospermia were excluded and a full STD workup was performed. In 12 of the 16 cases an infectious agent was identified as a possible cause for hematospermia. Before recent advances in microbiologic assays and techniques, these cases might have been labeled as 'essential' or idiopathic, or attributed to a disease like tuberculosis. Today however, advances in PCR and serology enabling the detection of *C. trachomatis* and HSV, respectively, may offer new explanations for an old disease. The management of those cases of hematospermia in which a STD pathogen is detected is potentially greatly simplified: Antimicrobial therapy may afford a relatively simple and effective intervention, thereby eliminating much stress and anxiety for patients and their sexual partners.

In our sample group, herpes simplex virus and *C. trachomatis* were the most common pathogens isolated when an etiologic agent could be detected. Weidner et al. [8] also identified *C. trachomatis and U. urealyticum* in patients with hematospermia. However, in their series all patients suffered from prostatitis, which may explain their conclusion that these pathogens were uncommon in hematospermia without an underlying genitourinary infection. Our results demonstrate that these agents may cause hematospermia in the absence of an underlying genitourinary infectious focus (e.g., non-gonococcal urethritis, prostatitis, epididymitis).

It has been estimated that about 60% of patients infected with HSV-2 have atypical manifestations of the disease that are unrecognized or under-diagnosed by the physician and the patient [9,10]. Thus, individuals with HSV-2 seropositivity shed virus with or without the presence of genital ulcerations or a previous history of the classic genital lesions [11,12]. Given that many individuals are unaware of their HSV status, they would not attribute their hematospermia to herpes infection. Our laboratory detection of HSV, reflecting either past or recent infection, among patients with hematospermia lends itself to the possibility that hematospermia may in fact be yet another atypical manifestation of herpes infection. Indeed, in patients 3 and 5, laboratory findings of antigen detection and PCR, respectively, reflect a recent HSV infection/reactivation coincident with their hematospermia.

Asymptomatic infection may also occur in patients with *C. trachomatis*. Patient no. 7, 17 years old, tested PCR-positive for this pathogen yet denied any sexual activity in the 6 months preceding the laboratory testing. The most likely explanation for this finding is that this individual contracted chlamydia in the "past," and it was not diagnosed because the patient was asymptomatic.

Some authors have shown that age plays a significant role in the workup of patients with hematospermia [13]. Multiple reports during the past decade reflect the trend that most patients under age 40 have an infectious or idiopathic etiology and require simple diagnostic modalities, while patients over 40 tend to have more serious etiologies and require more sophisticated diagnostic tests [13,14]. Our report revealed a wide age range (17–66 years) for hematospermia, with 12 (75%) of 16 patients being 40 years old or

younger. Our data are consistent with the literature, which shows that in most patients with hematospermia under the age of 40, an infectious or inflammatory disorder is the underlying cause of the disease. However, although age can play a significant role in the choice of diagnostic procedures, we recommend that a thorough sexual history and past history of an STD or a partner with a STD be obtained regardless of the age at presentation.

Infection has been reported to be one of the most common causes of hematospermia. It has been postulated that most patients with hematospermia have seminal vasculitis of an infectious origin [15]. However, the agents causing this symptom have not been well studied. Our findings suggest that recent advances in microbiologic diagnostic techniques may be used to facilitate the detection of pathogens in these patients, thereby enhancing the efficacy of treatment. In this regard, a thorough history of a patient's sexual history in conjunction with new microbiologic assays and imaging techniques can reduce the likelihood that cases of hematospermia will be labeled as idiopathic when in fact an etiology can be readily identified. With the identification of a specific pathogen, appropriate treatment may be initiated prior to the onset of any psychosocial complications. Consequently, a diagnostic workup for sexually transmitted pathogens should be pursued in those cases in which the underlying pathology of hematospermia is unknown.

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