A Case of Rectal *Ureaplasma* Infection and Implications for Testing in Young Men Who Have Sex with Men: The P18 Cohort Study

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Abstract

Ureaplasma is a significant cause of nongonococcal urethritis. This is a case of rectal *Ureaplasma* found on culture in a young man who has sex with men not previously reported in the literature. Nucleic acid amplification tests are now standard of care for sexually transmitted infection testing, but they do not test for *Ureaplasma* and, therefore, may be missing important infections. *Ureaplasma* could have important implications in urethritis and rectal HIV transmission among men who have sex with men engaging in condomless anal intercourse. Further study of *Ureaplasma*'s role as a rectal pathogen may be warranted.

Keywords: health screening, HIV/AIDS, men who have sex with men (MSM), sexually transmitted infection (STI), testing

Introduction

A LARGE COHORT STUDY being conducted in New York City is evaluating syndemic production (i.e., the development of mutually reinforcing conditions that negatively affect health outcomes) among young men who have sex with men (YMSM) as they transition into adulthood.¹ This is a case report of one study participant, from whom we gathered information about his demographics, healthcare access, sexually transmitted infection (STI) history, and sexual behaviors in the 6 months before assessment. In addition, per the study protocol, he was tested for syphilis, gonorrhea, chlamydia, and HIV.

Historically, culture methods were the reference standard against which diagnostic tests for STIs were compared. More recently, nucleic acid amplification tests (NAATs) have been shown to be more sensitive and specific for gonorrhea and chlamydia than culture methods, and in 2014, these became the standard for detection of gonorrhea and chlamydia.² In our study, we obtained a urine sample to test for urethral gonorrhea and chlamydia by rRNA detection. However, NAATs are more expensive than culture methods, and because of the financial constraints of our grant, this study employed culture methods to test for pharyngeal and rectal gonorrhea and chla-

mydia. In doing so, we incidentally identified a participant with rectal *Ureaplasma* on culture. Because of laboratory testing procedures and because *Ureaplasma* was not an expected culture result, the exact species was not determined before the laboratory disposed of the specimen.

We present this case because it highlights the fact that the new standard use of NAATs for gonorrhea and chlamydia alone may be missing infections that culture methods or expanded NAATs would otherwise identify. YMSM are at increased risk of HIV transmission, and rectal gonorrhea and chlamydia infections are associated with an increase in HIV transmission in YMSM.³ The concern is that potentially mucosal disrupting rectal infections, such as *Ureaplasma* species, may similarly increase the risk of HIV transmission, and detection may be important in YMSM.

Clinical Case

The volunteer participant was a 21-year-old who was born in the United States and self-identified as a white gay man. At the time of the study, he was a college undergraduate student, had stable housing for the past 6 months, and an annual income of <\$4900 before taxes, with sex as his biggest source of income. He stated that his general health was "very good" and he had

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medical insurance, although he did not have a primary care physician or access care in the past 12 months. He self-reported no history of genital/anal warts or human papillomavirus (HPV), and stated that he would “probably not” receive an HPV vaccine in the next year. He reported never being tested for Hepatitis C virus (HCV), gonorrhea, chlamydia, syphilis, or HIV. He knew of HIV postexposure prophylaxis and preexposure prophylaxis, but had never taken them. When asked how likely he thought he was to become infected with HIV, he reported that it was “possible” (equivalent to 3 on a scale of 1–5).

In the past 6 months, he only had sex with men. During this time, he had 35 casual partners with whom he had anal and oral sex, and self-reported no steady partners. He had condomless insertive anal sex six times with four partners, and condomless receptive anal sex two times with two partners. He received money for sex but self-reported not giving or receiving drugs for sex. In the past 6 months, he had not asked any clients to use condoms. He did not know the HIV status of the majority of his sexual partners. It is unknown whether the participant had clinical symptoms as these questions are beyond the scope of our study.

The participant had a negative pharyngeal culture, negative urethral NAAT for gonorrhea and chlamydia, and negative syphilis and HIV testing. However, his anal culture grew only *Ureaplasma* species. The presence of rectal *Ureaplasma* would have gone undetected if the clinical standard NAAT for gonorrhea and chlamydia alone had been used. In addition, because his urethral sample was limited to NAAT for gonorrhea and chlamydia, it is unknown whether he had a urethral *Ureaplasma* infection. The participant was notified of his results and linked to outside medical treatment.

The participant provided his consent to participate in the P18 study and, in accordance with the NYU institutional review board, University Committee on Activities Involving Human Subjects, his consent extends to this article. In addition, identifying information about this specific participant was removed from the article.

Discussion

Ureaplasma is a bacterium that is transmitted sexually or by vertical transmission. Although it is a common organism in the genitourinary tract of asymptomatic men, it is also thought to be a cause of nongonococcal urethritis (NGU), prostatitis, reactive arthritis, and spermatic dysfunction.^{4–6} Urethritis is the most common reason men present to STI clinics in the United States, and multiple studies show that *Ureaplasma urealyticum* is among the top 5 etiologies, accounting for 4%–5% of all urethritis, and up to 13% of all those with NGU.^{7–9} In another study, *Ureaplasma* rates were not significantly different between asymptomatic men and men with NGU, but when differentiated between *U. urealyticum* and *Ureaplasma parvum*, *U. urealyticum* was significantly associated with NGU, whereas *U. parvum* was not.¹⁰ Therefore, *U. urealyticum* may cause morbidity and should be considered in diagnosis and treatment of NGU.

The Centers for Disease Control and Prevention (CDC) recommends that all men who have sex with men (MSM) are tested annually (or every 3–6 months, if at “increased risk”) for HIV, syphilis, urethral, rectal, and pharyngeal gonorrhea, and urethral and rectal chlamydia.¹¹ However, a standard NAAT does not include testing for *Mycoplasma* or

Ureaplasma and, thus, *Ureaplasma* infections will not be detected. There are limited data on the incidence and pathology of *Ureaplasma* species at extragenital sites. When thought to be a cause of NGU, it is generally treated similarly to urethral chlamydia.¹¹ However, there is substantial evidence that more than 50% of chlamydia and gonorrhea infections in MSM are at nonurethral sites, and would be missed if we only screened MSM with urethral specimens.¹² Although this participant’s infection was detected using culture methods, *Ureaplasma* can also be detected molecularly.^{13,14} There are some data that NAATs may be more sensitive than standard culture (sensitivity=92.4%, specificity=94.8% in one study of vaginal specimens).¹⁵ Given the significant incidence of *Ureaplasma* as etiology for NGU and the significance of extragenital STIs in MSM, further research on the value of screening for urethral and rectal *Ureaplasma* infections in YMSM is merited, especially for those engaging in condomless anal intercourse.

STIs associated with increased risk of HIV transmission are of particular interest in our patient population. MSM engaging in condomless anal intercourse with HIV positive partners are more susceptible to HIV transmission, especially those with partners with high viral loads.¹⁶ Plasma viral load is used to monitor HIV-positive patients’ responsiveness to antiretroviral therapy. It is regarded as a measure of infectivity potential, with lower viral loads greatly reducing the risk of HIV transmission.¹⁷ However, when evaluating the risk of transmission through sex, it is important to differentiate between viral load in genital secretions (semen in men) and viral load in the peripheral blood. Although there are conflicting data, some studies indicate that in HIV-positive people with active urethral infections, there is viral load discordance (higher viral loads in semen than in blood), thought to be because of compartmentalized shedding of HIV in the genital tract.¹⁸ This higher viral load is thought to increase the risk of HIV transmission sexually. Additional studies show that STIs are associated with increased risk of an HIV-negative partner seroconverting when exposed to HIV (likely because of increased number of activated CD4⁺ T cells at the site of infection).^{19–21} It has also been shown that HIV-negative MSM with rectal infections are at higher risk of HIV transmission than MSM without rectal infections.³ Therefore, active STIs in either serodiscordant partners may increase the risk of HIV seroconversion and should be given special attention among patients at high risk of HIV exposure. In the past 30 days, our participant engaged in condomless anal intercourse with two partners with unknown HIV status, and had rectal *Ureaplasma* infection, which raises the question of whether he is at increased risk of HIV seroconversion.

Conclusion

This is a case of rectal *Ureaplasma* infection, not previously described in the literature. Given the incidence of NGU caused by *U. urealyticum*, this has important implications for MSM who are engaging in condomless anal intercourse. Although NAAT has been shown to be more sensitive and specific for gonorrhea and chlamydia than culture methods, it fails to test for other potentially important causes of NGU, such as *Ureaplasma* and *Mycoplasma*. *U. urealyticum* is a significant cause of NGU, and although there are little data on rectal *Ureaplasma* infection, it may

have important implications in urethritis and rectal transmission among MSM engaging in condomless anal intercourse. Furthermore, it may increase the HIV transmission risk in an already vulnerable population. This case highlights the importance of additional research into incidence and prevalence of *Ureaplasma* and any link to increases in HIV transmission when present either in the urethra or in the rectum. More data are needed to fully illuminate the health implications of *Ureaplasma* infections in this population, and whether additional screening, testing, or treatment is needed for MSM infected with *Ureaplasma*.

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