CASE REPORT

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Neisseria gonorrhoeae and *Chlamydia trachomatis* coinfection in a 20-year-old man with recurrent urethritis: a case report

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ABSTRACT

Introduction: *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are the two pathogens most commonly reported to cause sexually transmitted infections (STIs) worldwide. Coinfection between these two pathogens has been widely reported, but the incidence is still rarely reported due to challenges in diagnosis to prove the involvement of the two pathogens simultaneously. The molecular diagnostic approach is an effective option for this case and optimizing this method will able to help clinicians deciding management for the patients and prevent the spreading of the disease. This study aimed to present a case of *N. gonorrhoeae* and *C. trachomatis* coinfection in a 20-year-old man with recurrent urethritis.

Case Description: A 20-year-old man presented to the Dermatology and Venereology clinic at Dr. RSUP. Sardjito with purulent discharge from the penis started a week prior. From the anamnesis and physical examination, the doctors suspected this patient with *N. gonorrhoeae* infection. *N. gonorrhoeae* was detected by microscopic examination, culture, and Real-Time Polymerase Chain Reaction (RT-PCR) examination, while *C. trachomatis* was also detected in RT-PCR. The patient was treated with azithromycin 1-gram single dose and cefixime 400 mg single dose.

Discussion: The World Health Organization (WHO) reported that the incidence of STIs is always increasing. Most STIs are usually asymptomatic, but it can be presented as urethritis in male patients. For females, it can be given as leucorrhoea, pelvic inflammatory disease (PID), or other pregnancy complications. *N. gonorrhoeae* and *C. trachomatis* are the two main pathogens always reported annually and often found as coinfection. Due to the virulence factors of these bacteria, *N. gonorrhoeae* and *C. trachomatis* are very hard to diagnose with conventional culture methods, and the molecular approach is now an effective option to detect them and help prevent recurrence.

Conclusion: Coinfection of *N. gonorrhoeae* and *C. trachomatis* is a case that is quite often encountered in clinical practice, but the incidence is rarely reported due to supporting examination methods to help confirm the presence of these two microorganisms are still limited. In cases of suspected infection by *N. gonorrhoeae*, *C. trachomatis*, or both simultaneously, the most recommended microbiological examination is to use molecular diagnostics such as PCR.

Keywords: *Chlamydia trachomatis,* coinfection, *Neisseria gonorrhoeae,* sexually transmitted infections.
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INTRODUCTION

Sexually transmitted infections (STIs) are one of the health problems that are of significant concern to WHO in relation to their prevalence, morbidity, and complications. Data from WHO in 2020 estimates that around 374 million new cases occur every year throughout the world, with the most common causes being Chlamydia (129 million), gonorrhea (82 million), syphilis (7.1 million), and trichomoniasis (156 million).[1] Most STIs are asymptomatic or mildly symptomatic, so individuals who are infected are not aware of it, and they have the potential to spread the infection.

Neisseria gonorrhoeae and *Chlamydia trachomatis* are the two most commonly reported pathogens responsible for STIs globally. Coinfections involving these pathogens have been extensively documented, including in Indonesia; however, the incidence remains underreported due to diagnostic challenges in simultaneously identifying both pathogens. Enhancing microbiological diagnostic technologies, particularly molecular-based methods, is crucial for controlling their spread, preventing early complications, and mitigating the emergence of antibiotic resistance.[2]

Here, we describe a case of the recurrent sexually transmitted disease in a 20-year-old man caused by *N. gonorrhoeae* and *C. trachomatis* coinfection in RSUP Dr. Sardjito Dermatology-Venereology outpatient clinic unit, diagnosed by Gram-staining, culture, and polymerase

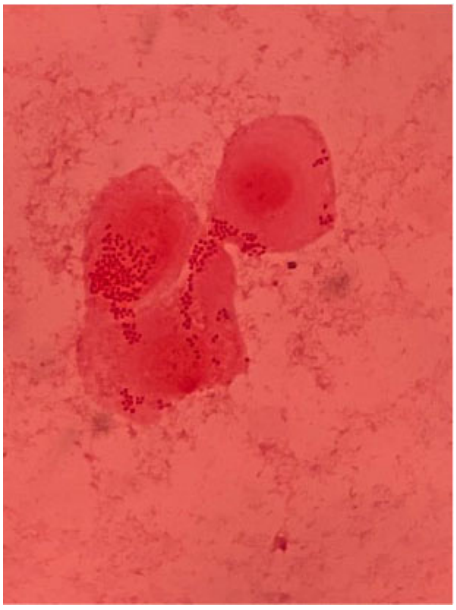

Figure 1. Direct microscopic examination from the urethral swab specimen showing diplococcus Gram-negative intracellular bacteria.

chain reaction (PCR) in the microbiology laboratory. We present the history of illness, risk factors, microbiology examination, and management of the patient.

CASE DESCRIPTION

A 20-year-old man presented to the Dermatology and Venereology Clinic at RSUP Dr. Sardjito Yogyakarta with a one-week history of purulent penile discharge, accompanied by a burning sensation and pain during urination. He reported no wounds, itching, or abnormalities in the surrounding area and denied experiencing fever or other symptoms. In the past six months, he had two similar episodes, for which he was diagnosed with gonorrhea and treated with a single oral dose of azithromycin (1 gram) and cefixime (800 mg), along with doxycycline (100 mg twice daily) for 7 days. His symptoms improved after completing the medication, and he discontinued further follow-up.

The patient reported being sexually active with non-regular female partners, including commercial sex workers. One week prior to symptom onset, he had unprotected sexual intercourse with a female partner. He denied any history of genital wounds, ulcers, significant weight loss, or recurrent mouth sores. Additionally, he reported no history of diabetes mellitus, chronic infections, hospitalization, HIV, medication allergies, or other underlying conditions.

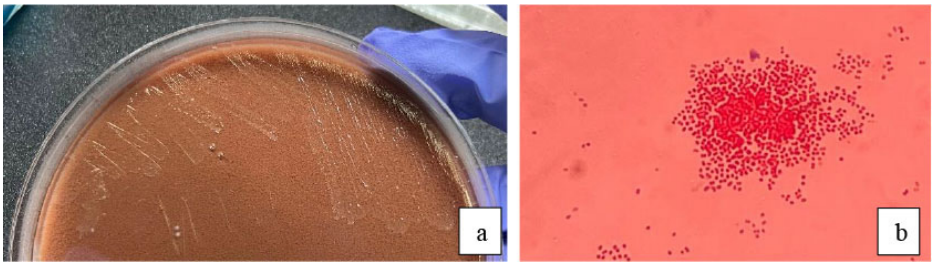

Figure 2. (a) Culture on chocolate agar after 1x24 hours incubation obtained a small round and transparent colony; (b) Visualization of diplococcus Gram-negative bacteria from the isolate by Gram staining.

On physical examination, the patient's vital signs were within normal limits. Mucopurulent discharge was observed from the external urethral orifice upon milking. Swab samples were collected for microscopic examination, bacterial culture, and real-time PCR (RT-PCR) testing. The RT-PCR targeted the porA pseudogene for *N. gonorrhoeae* and the cryptic plasmid for *C. trachomatis*. Microscopic examination of the Gram-stained specimen revealed 3–5 epithelial cells per field, 10–20 polymorphonuclear cells per field, and intracellular Gram-negative diplococci (Figure 1). Bacterial culture on chocolate and Thayer-Martin agar showed small, round, transparent colonies, which were confirmed as Gram-negative diplococci via Gram staining (Figure 2). However, no growth of Gram-negative diplococci was observed on blood agar or MacConkey agar media. RT-PCR results were positive for *N. gonorrhoeae* with a cycle threshold (CT) value of 29.36 and *C. trachomatis* with a CT value of 28.12. The patient was diagnosed with gonorrheal urethritis and treated with a single oral dose of azithromycin (1 gram) and cefixime (400 mg).

DISCUSSION

STI is a group of infections caused by viruses, bacteria, fungi, or parasites that can be spread through sexual contact. Since many STIs are asymptomatic, a person may be infected without realizing it. Sexual intercourse, including vaginal, anal, and oral sex, is known to spread over 30 distinct bacteria, viruses, and parasites. Some STIs can be passed from mother to child during nursing and childbirth. The highest prevalence of STIs is gonorrhea, chlamydia, trichomoniasis, syphilis, hepatitis B, herpes simplex virus (HSV), HIV, and human papillomavirus (HPV). The first four are currently treatable, and the remaining four remain incurable viral illnesses.[1] One STI often leads to another STI because of the patient's sexual activities. Congenital abnormalities, low birth weight, stillbirth, and neonatal conjunctivitis are the main concerns for pregnant women with STIs. STIs, including chlamydia and gonorrhea, are also the leading causes of pelvic inflammatory disease and infertility in women.[1]

Gonorrhea is a sexually transmitted disease caused by the bacteria Neisseria gonorrhoeae. It usually infects the exposed mucosa. In 2022, the Centers for Disease Control and Prevention (CDC) reported the incidence of gonorrhea in the United States as about 648.056 new cases.[2] Data from Global Progress WHO 2021 reported about 82,4 million new cases of gonorrhea happened worldwide in 2020, with the highest prevalence in the African region.[3] Estimates of gonorrhea in adult women and men in Indonesia use estimates from the WHO South Asian Regional Office (SEARO) due to a lack of data from the general population. The overall estimate for women and men aged 15-49 years was 0.7% and 0.6% in 2016.[4]

Neisseria gonorrhoeae is a Gram-negative coccus bacteria that usually appears in pairs (diplococcus). *Neisseria gonorrhoeae* has several antigenic structures that play a role in attachment, virulence, and defense against the host immune system. Multiple peptidoglycan-degrading activities also have been

described in *N. gonorrhoeae*, including that of lytic transglycosylases, endopeptidases, and an N-acetylglucosaminidase, but the significant autolytic activity has been ascribed to an N-acetylmuramyl-L-alanine amidase, and this mechanism mainly occur when this bacteria exposed to the unfavorable condition. These enzymes also play an important role in its difficulties in growing on regular mediums such as blood agar and MacConkey agar.[5]

Chlamydia is a sexually transmitted infection caused by the bacteria *Chlamydia trachomatis*. The 26 countries of the European Union reported 434,184 cases of chlamydia infection in 2019. The infection index included a rate of 157 per 100,000 population. Denmark, Iceland, and Norway occupy the highest figures from the European Union countries and the United Kingdom, with 300 cases per 100,000 population and accounting for 83% of cases in 2019. The estimated prevalence of chlamydia based on WHO SEARO in 2016 in women and men aged 15-49 years is 1.5% and 1.2%.[4] *C. trachomatis* has a cell wall structure that resembles Gram-negative bacteria, with a thick lipid composition including lipopolysaccharide. Because of its very small genome size, Chlamydia bacteria depend on host cells to obtain energy and grow, which is why they are called obligate intracellular bacteria and can't be cultivated in regular medium.[6] *C. trachomatis* serovar D-K is known to be one of the most common causes of sexually transmitted infections, especially in developed countries.[7]

Patients diagnosed with gonorrhea are often reported to have other sexually transmitted infections at the same time. The most common coinfections are gonorrhoea and chlamydia. Coinfection of these two diseases is also closely related to a previous history of STI. In 1982, the CDC stated that chlamydia occurred in 45% of gonorrhea patients.[8] Adolescents and young adults have a higher risk of experiencing coinfection because of the high rate of changing sexual partners and the lack of use of protection in sexual relations. Homosexual men are also at higher risk of coinfection compared to heterosexual men. Coinfection is also thought to be associated with an increased risk of re-infection with both chlamydia and gonorrhea when diagnostic tests are carried out again within a period of 6 weeks to 6 months. Research shows that each STI may increase susceptibility and/or transmission to another STI infection, and bacterial loads may be increased in chlamydia and gonorrhea infections when compared with gonorrhea infection alone.[9] Chlamydia and gonorrhea infections have an incubation period. Most infections with these two diseases are asymptomatic. The incubation period lasts 2-7 days for gonorrhea and 2-6 weeks for chlamydia. The clinical manifestations of the two are often similar and difficult to differentiate. The most frequent clinical manifestation in men is urethritis, characterized by dysuria, urethral pruritis, and discharge. Chlamydia and gonorrhea can cause acute epididymitis with symptoms of unilateral testicular pain and swelling. Cervicitis in women is often asymptomatic; symptoms that appear can include abnormal vaginal discharge or intermenstrual bleeding. Physical examination may reveal purulent endocervical discharge or continuous endocervical bleeding. Pelvic inflammatory disease (PID) occurs in approximately 15% of cases, with symptoms of pelvic or abdominal pain, dyspareunia, or abnormal uterine bleeding.[10]

In cases of urethritis with suspected coinfection of *N. gonorrhoeae* with *C. trachomatis*, the recommended sample is a urethral swab or urine first thing in the morning collected in a sterile container. The supporting examination that is considered the most efficient is using a molecular approach because of its high level of sensitivity and can be carried out in one sample to detect both pathogens. Routine antimicrobial susceptibility testing (AST) is not needed; it is only indicated in patients who have failed therapy. The gold standard for AST *N. gonorrhoeae* is using the MIC agar dilution method from the Clinical Laboratory and Standards Institute (CLSI).[11]

Gram staining is primarily performed as a diagnosis of urethritis in symptomatic men because of its high specificity. Gram staining has low specificity in women because of the high probability of non-pathogenic Gram-negative diplococci appearing in cervical secretions. Another examination that can be done is culture. Culture is often used in cases of resistant infections to assess antibiotic susceptibility testing. The sensitivity of culture ranges from 72-95%. The disadvantage of culture is that results do not appear until 48 hours, and the sensitivity of culture is reduced to 65-85% in asymptomatic patients, as opposed to higher molecular methods.[12]

The use of nucleic acid amplification testing (NAAT) or molecular method is recommended as a method for diagnosing genital or extragenital infections, both symptomatic and asymptomatic, caused by *N. gonorrhoeae* and *C. trachomatis* which are often co-infectious pathogens. This method is more commonly performed because it is faster and has high sensitivity. Molecular methods can be performed on a variety of urogenital samples, including swabs from endocervical, vaginal, urethral, and urine. Real-time polymerase chain reaction (RT-PCR) is one of the molecular methods used to detect pathogens causing STI. The result of this diagnostic method is presented as a cycle threshold (CT) value sigmoid curve. The CT Value in RT-PCR is the number of target-specific amplification cycles detected and crosses the threshold line. The lower CT value means less cycle number needed to reach the threshold line, and that can also infer the more microorganism load in the sample.[13] The disadvantages of using molecular methods are that they cannot detect sensitivity to antibiotics, that they require trained experts, and that they are relatively expensive.[12]

Treatment of patients with STIs prevents further complications and widespread transmission. Reinfection must be prevented by stopping sexual activity until all sexual partners have been treated completely. Patients with chlamydia should also be tested for HIV, gonorrhea, and syphilis.[14]

This study has several limitations. The patient discontinued follow-up, preventing further evaluation of disease progression and microbial growth. Consequently, additional examinations could not be conducted. Furthermore, the patient did not provide a comprehensive sexual history, including the number of sexual partners, history of same-gender

relationships, or other relevant sexual behaviors, resulting in incomplete data for analysis.

CONCLUSION

This report describes a recurrent sexually transmitted infection in a 20-year-old male caused by *N. gonorrhoeae* and *C. trachomatis* coinfection. Diagnosis at the RSUP Dr. Sardjito Outpatient Clinic was made using bacterial culture and RT-PCR. These pathogens are the most commonly reported STIs globally, with coinfections often underreported due to limited diagnostic methods. PCR is the preferred approach for confirming such infections, while antimicrobial susceptibility testing is reserved for treatment-resistant cases. Adopting healthy sexual practices is essential for preventing STIs and recurrence.

PATIENT'S INFORMED CONSENT

The patient has agreed and signed the written informed consent to this study publication.

FUNDING

There is nothing to declare.

AUTHOR CONTRIBUTION

All authors contributed equally to this study's writing and publication.

CONFLICT OF INTEREST

All authors declare that there is no conflict of interest regarding this study publication.

REFERENCES

1. (WHO) WHO. Sexually Transmitted Infections [Internet]. 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis)?gad_source=1&gclid=CjwKCAiAivGuBhBEEiwAWiFmYfv7NuyKdKUI4BVpFyabokkooy-HAJalbsbd9Xpe77ujzJFVQaX4exoCw68QAvD_BwE
2. CDC. Sexually Transmitted Infections Surveillance [Internet]. 2022. Available from: https://www.cdc.gov/std/statistics/2022/default.htm
3. (WHO) WHO. Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021 [Internet]. Vol. 53, Who. 2021. 1689–1699 p. Available from: https://www.who.int/publications/i/item/9789240027077
4. Kementerian Kesehatan Republik Indonesia. Estimasi Infeksi Menular Seksual Indonesia. Afriana N, Nisa TM, editors. Jakarta: Kementerian Kesehatan Republik Indonesia; 2021.
5. Garcia DL, Dillard JP. AmiC functions as an N-acetylmuramyl-L-alanine amidase necessary for cell separation and can promote autolysis in Neisseria gonorrhoeae. J Bacteriol. 2006;188(20):7211–21.
6. Jones CA, Hadfield J, Thomson NR, Cleary DW, Marsh P, Clarke IN, et al. The nature and extent of plasmid variation in chlamydia trachomatis. Microorganisms. 2020;8(3):1–20.
7. Carroll KC, Butel JS, Morse SA, Mietzner T. Jawetz-Melnick-Adelbergs-Medical-Microbiology. In: Medical Microbiology. 27th ed. McGraw-Hill Education; 2017.
8. Dionne-odom J, Workowski K, Perlowski C, Taylor SN, Mayer KH, Mcneil CJ, et al. Coinfection with Chlamydial and Gonorrheal Infection among US Adults with Early Syphilis. 2023;49(8):1–8.
9. Barati Sedeh F, Thomsen SF, Larsen HK, Westh H, Saladorasmussen K. Sex-associated risk factors for co-infection with chlamydia trachomatis and neisseria gonorrhoea among patients presenting to a sexually transmitted infection clinic. Acta Derm Venereol. 2021;101(1):1–7.
10. Van Ommen CE, Malleson S, Grennan T. A practical approach to the diagnosis and management of chlamydia and gonorrhea. C Can Med Assoc J. 2023;195(24):E844–9.
11. Leber A. Clinical Microbiology Procedures Handbook. 4th ed. Washington: ASM Press; 2016.
12. Khalil G Ghanem. Clinical manifestations and diagnosis of Neisseria gonorrhoeae infection in adults and adolescents - UpToDate. Uptodate. 2018;1–24.
13. Coyle P V., Al Molawi NH, Kacem MABH, El Kahlout RA, Al Kuwari E, Al Khal A, et al. Reporting of RT-PCR cycle threshold (Ct) values during the first wave of COVID-19 in Qatar improved result interpretation in clinical and public health settings. J Med Microbiol. 2022;71(5):1–7.
14. WHO. Guidelines For The Management Of Symptomatic Sexually Transmitted Infections. Guidelines for the management of symptomatic sexually transmitted infections. 2021. 216 p.