SHORT COMMUNICATION

Two New Strains of Drug-resistant Neisseria gonorrhoeae in a Bisexual Man having Sex with Men in Wroclaw, Poland

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Submitted Jan 4, 2024. Accepted after revision Apr 3, 2024
Published Apr 24, 2024. DOI: 10.2340/actadv.v104.35658. Acta Derm Venereol 2024; 104: adv35658.

Antimicrobial resistance of *Neisseria gonorrhoeae* (NG) is an increasing public health problem, highlighted by the fact that NG has been declared a "high" priority pathogen by the World Health Organization (WHO) for research and development of new antibiotics (1). To date, according to the PubMLST database, the isolate count of NG is 24,849, including 13,441 isolates in Europe (2). There is no evidence that the new strains cause more serious disease. However, due to high rates of gonorrhoea and rapid evolution of NG resistance, treatment failures have to be anticipated in the near future (3). Here we present a patient infected with 2 new strains of drug-resistant NG.

CASE REPORT

A 31-year-old bisexual man having sex with men (MSM) using on-demand pre-exposure prophylaxis (PrEP) for HIV was admitted to a local HIV outpatient clinic due to urethritis, bloody rectal discharge, rectal pain, and tenesmus. He reported having these symptoms for the last 7 days. There were no other abnormalities on physical examination. In the last month he reported sexual contacts with his wife and 3 men in Poland. No condoms were used during oral, vaginal and anal contacts, while PrEP was used inconsistently. He denied substance use and chemsex. Oropharyngeal, urethral, and rectal swabs were collected for PCR and culture. PCR-based pooled 3-site screening for *NG* and *Chlamydia trachomatis* was positive. Ceftriaxone 1 g i.m. plus azithromycin 2 g p.o. as single doses, as well as doxycycline 2x100 mg p.o. for 7 days, were given. *NG* cultures were positive from rectal and urethral swabs with isolates of different antimicrobial susceptibility. Antimicrobial susceptibility testing of NG isolates included 6 antimicrobials (ceftriaxone, cefixime, azithromycin, ciprofloxacin, tetracycline, and benzylpenicillin). Minimum inhibitory concentrations (MICs; mg/L) were determined using Etest on gonococcal isolates. Rectal NG was resistant to penicillin, ciprofloxacin, and tetracycline while urethral isolate was resistant to ciprofloxacin. Strains comparison was performed using multilocus sequence typing. The *NG* multi-antigen sequence typing (NG-MAST) method was based on PCR amplification and sequence analysis of the gonococcal porB and tbpB genes and subsequent characterization of specific sequence types (ST) of the studied strains.

Table I. Details of the strains included in the study

No	Isolate	PubMLST isolate id	porB allele	tbpB allele	Sequence type
1	NG75U	141487	12130	3283*	22792*
2	NG75A	141488	8931	3282*	22793*

* New allele/sequence type.

Retrieved sequences for the 2 strains (NG75A, NG75U) were uploaded to the PubMLST.org website (4). Obtained alleles, profiles, and isolates were subject to submission. Complete and characterized data of the strains are listed in **Table I**.

We have confirmed infection with 2 new strains of NG. Symptoms resolved several days after treatment was started. Additionally, the patient was diagnosed with syphilis and early HIV infection (screening HIV Ag/Ab test and quantitative HIV-RNA results were both positive). One day before onset of symptoms he had sexual contact with his 8-week pregnant wife and she was also diagnosed with NG infection; however, she was asymptomatic. Ceftriaxone 1 g i.m. single-dose monotherapy was used and recovery was confirmed with test of cure 4 weeks later. The wife's HIV/p24 and syphilis ELISA results were all negative; however, she received treatment for syphilis at the same time as her husband to avoid reinfection due to the diagnostic window. She was retested for syphilis 4 and 6 weeks later and the result were negative. She was retested also for HIV (ELISA 4th generation assay and quantitative HIV-RNA) 4 and 6 weeks after the last sexual contact with her husband and all these results were negative, so HIV infection could be excluded.

DISCUSSION

NG is the second most commonly reported bacterial STI in Europe (5). MSM are more likely to be diagnosed with NG than the general population. Several factors may contribute to higher rates of STIs among MSM, including number of partners, younger age, condomless sex, group sex, and chemsex (6). Condom use among MSM has decreased, partly due to PrEP use and U=U campaigns (undetectable= untransmissible) (7). HIV-infected patients who achieve and maintain undetectable

(below 200 copies/mL per protocol) HIV viral load while on combined antiretroviral therapy do not transmit the infection to their sexual partners. This has led to a desired sexual emancipation and in effect an increase in the number of partners and decrease in condom use. Gonorrhoea symptoms may vary by anatomical site: urethral infection is usually symptomatic, whereas rectal and oropharyngeal infections are frequently asymptomatic. Triple-site testing should remain the gold standard to prevent onward transmission. Moreover, this case highlights the importance of performing cultures as antimicrobial susceptibility patterns may differ with anatomical sites, especially among high-risk MSM. To our knowledge this is the first confirmed infection with 2 new strains of NG with different antimicrobial susceptibilities in Poland. To date, only a few such case reports have been described in the literature. Successful treatment reduces the risk of complications such as pelvic inflammatory disease, epididymitis, infertility, first-trimester miscarriage, and ectopic pregnancy, and decreases the risk of HIV transmission (8). According to the WHO, the antimicrobial resistance of NG has increased rapidly in recent years and has led to reduced treatment options (9). In 2020, 23 European Union/ European Economic Area (EU/EEA) member states participated in the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) and reported a continued decreasing trend in levels of cefixime resistance, the persistent rise in ciprofloxacin resistance, and a significant increase in the proportion of isolates with azithromycin resistance, along with the detection of 1 ceftriaxone-resistant isolate (10). Trends in susceptibility also for the antimicrobials tested in Euro-GASP pose a serious threat to the treatment and control of gonorrhoea (10). In total, 3,291 isolates were tested; the majority of specimens were from male patients (84.4%). Among cases with reported sex and sexual orientation (55.0%), 46.8% were MSM, 28.1% were females, and 25.1% were heterosexual males (10). Continuously high and rising azithromycin resistance is concerning for the future effectiveness of any ceftriaxone plus azithromycin dual therapy and begs the question of whether Europe should adopt the approach of ceftriaxone monotherapy for NG. Additionally, azithromycin resistance may lead to therapeutic difficulties in patients with beta-lactam allergy. To date no significant number of ceftriaxone and/or cefixime resistant isolates have been reported (11). Only early detection of emerging resistant strains, prevention, and treatment, including an enhanced focus on key populations, can reduce the impact of NG on public health.

ACKNOWLEDGEMENTS

The study was approved by the Wroclaw Medical University Ethics Committee. Informed consent was obtained from the patient involved in the study.

The authors have no conflicts of interest to declare.

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