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Characterization of multi-drug non-susceptible/resistant *Neisseria gonorrhoeae* isolates from Massachusetts, 2022

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Background

In 2022, CDC STD Laboratory Reference and Research Branch (SLRRB) initiated support for public health laboratories to build capacity for *Neisseria gonorrhoeae* (GC) gradient strip antimicrobial susceptibility testing (AST). Shortly after commencing these activities, the Massachusetts Department of Public Health reported a gonorrhea case from which two morphologically distinct colonies were isolated from urine and were determined to be non-susceptible to ceftriaxone, the recommended treatment for gonorrhea.

Aim/Methods

SLRRB sought to confirm the identity and susceptibility profiles of the isolates and perform genomic characterization by whole-genome sequencing.

Results

Minimum inhibitory concentrations (MICs) for both isolates were non-susceptible to ceftriaxone (1 µg/mL), cefixime (>1 µg/mL), and azithromycin (2 µg/mL), and resistant to ciprofloxacin (16 µg/mL), tetracycline (2 µg/mL), and penicillin (32 µg/mL). Antimicrobial resistance markers associated with reduced susceptibility or resistance for all of the mentioned antibiotics were identified in the whole-genome sequences, including the mosaic penA-60.001 allele which contributes to cephalosporin non-susceptibility. Only an mtrR promoter A deletion and an MtrD R714H variant were identified that are linked to elevated azithromycin MICs; mtrR-CDE operon was 99% identical to reference FA19. A retrospective search of over 16000 GC sequences from 01/2018-06/2022 found MtrD R714H occurring only 19 times and associating with AZM MICs 0.5-8 µg/mL. Among all published international isolates carrying penA-60.001, the MA isolates did not phylogenetically cluster with FC428 related clones but did cluster with recent isolates from the UK of the same MLST-8123. Among all international MLST-8123 isolates, the MA and UK isolates clustered within an emerging international sub-lineage. Other recent MLST-8123 isolates from the US (GISP 2021 – 2022) clustered separately, did not carry penA-60.001, and were susceptible to cephalosporins.

Conclusions

While no epidemiological links could be made to the MA case, the isolates are in an international lineage with isolates identified in Asia or with links to travel to Asia. The azithromycin MIC=2µg/mL, often associated with a mosaic mtr operon in recent GISP datasets, appears to result from a few SNPs in the mtr operon. Monitoring for similar isolates and MLST-8123/penA-60.001 isolates continues through GISP, SURRG, and enhanced culture and AST being carried out in MA.