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Prevalence of reduced susceptibility to 3rd generation cephalosporins in Neisseria meningitidis in the United States from 2017 to 2021

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Background

Neisseria meningitidis (Nm) is responsible for severe invasive meningococcal disease (IMD) with approximately 10-15% case fatality. In most countries, including the United States, the antibiotics recommended for treatment of IMD are penicillins, ampicillins and third generation cephalosporins (3GCs) and the emergence of Nm resistance to these antibiotics is of great concern. Nm resistance to 3GCs is very rare, however, recently, reduced susceptibility to 3GCs has been increasingly observed throughout the world. Although information regarding the specific mechanism and genetic origin is limited, it has been suggested that acquisition of certain penA alleles, including penA327, make Nm less susceptible to 3GCs. Our previous report found only 1 penA327 isolate from 2012 to 2016 among U.S. genomic surveillance data, which highlights the need of continues monitoring of prevalence of this allele.

Aim/Methods

Whole-genome sequencing (WGS) is performed on all invasive Nm isolates received through CDC surveillance programs. Sequencing data is analyzed using the Bacterial Meningitis Genome Analysis Platform (BMGAP) and provides information on the penA allele for a specified isolate. These data were examined to identify penA327 from the isolates sequenced from 2017 to 2021. To establish a relationship between the presence of penA327 and reduced 3GC susceptibility, an antimicrobial susceptibility testing (AST) was performed on isolates harboring penA327 and genetically closely related isolates with other penA alleles. The resistance minimum inhibitory concentrations (MICs) for cefotaxime and ceftriaxone are greater than 0.12 µg/mL.

Results

A total of 1162 U.S. invasive Nm isolates received from 2017 to 2021 were sequenced. A total of 11 isolates were identified with penA327, all serogroup C. Eight were clonal complex 11 (CC11), sequence type 11 (ST11), 2 were CC11, ST14609, and 1 was a new ST/CC. Four isolates had MICs of 0.12 µg/mL for cefotaxime, though all had MICs < 0.06 for ceftriaxone.

Conclusions

This finding indicates a recent surge of penA327 prevalence in invasive Nm in the United States. Additional analyses are being performed to better understand relatedness, the mutations underlying reduced cefotaxime susceptibility, and to better define the MIC range for penA327 isolates, as the lowest cefotaxime concentration in our AST panel is < 0.06.