Genomic analysis of Streptococcus agalactiae (group B Streptococcus) causing neonatal late-onset disease

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Background: Invasive Group B streptococcus (GBS) dominates as a cause of serious neonatal infection. Current strategies to reduce early onset GBS disease do not impact on late onset disease (LOD). A cluster of four LOD cases arose within 4 weeks in a single neonatal unit prompting prospective enhanced surveillance and genomic analyses of subsequent LOD cases.

Material/methods: Identified LOD GBS isolates were serotyped and whole genome sequenced using Illumina Hiseq platform. Additional contemporaneous GBS whole genome sequences (n=140) matched by serotype and MLST were used for comparative analysis. Antimicrobial resistance genes were determined from genomic sequences.

Results: The cluster comprised serotype V GBS isolates (n=4) belonging to ST1 and carrying tetM (resistance to tetracycline) and ermB (resistance to macrolides and lincosamides) antibiotic resistance
genes. Comparison with genomic data from contemporaneous ST1 GBS isolates indicated that neonatal and adult invasive strains were intermixing. Subsequent clusters of GBS LOD identified and confirmed genomically included cases due to serotype Ib (n=2), serotype III (n=2), and serotype Ia (n=3). Over 24 months, only a single serotype III LOD case could not be linked genomically to another case highlighting that horizontal transmission in the neonatal setting was the most common mode of acquisition for GBS LOD. All cluster isolates of serotype Ib and serotype III had tetM, while serotype Ia cluster isolates had tetM and msrD (resistance to macrolides). When compared with contemporaneous isolates of the same serotype and ST, neonatal and adult invasive strains were again observed to be intermixed.

**Conclusions:** Transmission routes for GBS in the nosocomial setting are poorly understood; in this study acquisition from common sources appears likely to explain almost all cases of GBS LOD. Large-scale genomic databases, which include longitudinally collected data from both disease-associated and carriage isolates can provide context for outbreak investigation and allow more certainty regarding transmission events. Carriage of tetM was frequent among adult and infant GBS isolates as commonly noted among human isolates. Importantly, isolates that cause adult invasive disease were demonstrated to be genomically similar to those causing neonatal infection supporting a common reservoir of disease.