

Session: 66. Molecular and Genomic Epidemiology of Resistant Pathogens

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Background. Ventriculoperitoneal (VP) shunt is one of the commonest procedures in neurosurgical practice. A significant problem encountered in shunt procedures is infection, with infection rate ranging from 2 to 27%, often with poor outcome. The objectives of the study were to retrospectively evaluate the infection rate associated with central nervous system (CNS) shunts, assess the frequency of the pathogens as well as their antibiotic sensitivity pattern to aim at suitable prophylaxis.

Methods. Materials and Methods. Retrospective study conducted in the Microbiology Department, SGPGI, Lucknow from December 2017 to August 2018. A total of 168 CSF samples were received with a suspected shunt infection. Samples were analyzed by wet mount, India ink, gram stain and inoculated on blood agar and MacConkey agar. Identification and AST were done by MALDI-TOF system (VITEK-MS) and Vitek 2.0 automated sensitivity system.

Results. During the study period, 37/168(22.02%) CSF were positive by culture. Most frequently isolated pathogen was *Acinetobacter baumannii* 20/37(54.05%), followed by *Staphylococcus aureus* 06/37 (16.20%), *Enterococcus faecalis* 04/37(10.81%) coagulase negative staphylococci- CONS 04/37(10.81%), *Klebsiella pneumoniae* 2/37 (5.40%) and *Escherichia coli* 1/37(2.70%). 100% of *A. baumannii* and *E. coli* strains were found to be XDR and carbapenem-resistant showing susceptibility to minocycline and colistin only. All strains of *K. pneumoniae* were MDR. 66.7% *S. aureus* were MRSA and showed 100% resistance to fluoroquinolone. A similar pattern was seen in CONS. 25% of Enterococci were found to be vancomycin resistant.

Conclusion. Discussion and Conclusion. The antibiotic sensitivity pattern suggests aminoglycosides, colistin and vancomycin to be a better choice of antibiotics either prophylactically/therapeutically, which may result in effective sterilization of the CSF. Infections following VP shunt procedure are secondary to catheter blockage complicating the results of surgery and are associated with high morbidity and mortality rates.

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634. Incidence of vanC-Mediated Vancomycin-Resistant Enterococcus Bloodstream Infections at Children's Hospital of Colorado and Implications for Empiric Enterococcal Therapy

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Background. The most well-known Enterococcal species, *E. faecium* and *E. faecalis*, can harbor high-level vancomycin resistance mediated by acquired *vanA* and *vanB* operons. However, other Enterococcal species such as *E. gallinarum* and *E. casseliflavus* (VCE), harbor intrinsic low-level vancomycin resistance mediated by an intrinsic *vanC* operon, and the incidence of these pathogens among pediatric patients is not clear. As the antibiotic resistance pattern of VCE is different than *E. faecium* and *E. faecalis*, a high prevalence of VCE may have implications for antibiotic therapy. We describe the incidence and susceptibility of VCE bloodstream infections at a large children's hospital and compare to *E. faecalis* and *E. faecium*.

Methods. Positive blood culture results from 2013 to 2018 were obtained from the Children's Hospital of Colorado data warehouse. All first-time positive cultures for Enterococcus were analyzed for species, susceptibility, and hospital unit location. First-time positive was defined as being at least 2 weeks after any previous positive Enterococcus blood culture. Susceptibilities were categorized by clinical laboratories standards institute (CLSI) guidelines.

Results. Of 240 positive isolates, 7% were ampicillin susceptible and vancomycin nonsusceptible (resistant or intermediate), vs. 6% that were ampicillin resistant and vancomycin susceptible. An additional 3% of isolates were not susceptible to either antibiotic; all of these were *E. faecium*. VCE accounted for 12% of our isolates while *E. faecalis* and *E. faecium* accounted for 66% and 16%, respectively. All VCE were susceptible to ampicillin, but 52% were nonsusceptible to vancomycin. VCE incidence, ampicillin resistance, and vancomycin nonsusceptibility were most prevalent in our hematology, oncology, and bone marrow transplant (BMT) units.

Conclusion. At our institution, an as yet unspicied Enterococcus is equally likely to be ampicillin susceptible and vancomycin nonsusceptible as ampicillin resistant and vancomycin susceptible. This is driven by a significant incidence of VCE, especially on our hematology, oncology, and BMT units. Therefore, vancomycin may not provide adequate empiric Enterococcal coverage on these units, and the addition of ampicillin will be recommended.

Table 1: Enterococcal blood stream infections from 2013-2018 categorized by Enterococcus species and susceptibility to vancomycin and ampicillin

Species	Total # (% of total)	Vancomycin Susceptible and Ampicillin Susceptible (% of species)	Vancomycin non-Susceptible and Ampicillin Susceptible (% of species)	Vancomycin Susceptible and Ampicillin Resistant (% of species)	Vancomycin non-Susceptible and Ampicillin Resistant (% of species)
Enterococcus (all)	240	202 (84)	16 (7)	15 (6)	7 (3)
<i>Enterococcus</i> spp. (unidentified)	7 (3)	6 (86)	0	1 (14)	0
<i>Enterococcus avium</i>	1 (0.5)	1 (100)	0	0	0
<i>Enterococcus casseliflavus</i>	13 (5.5)	10 (77)	3 (23)	0	0
<i>Enterococcus durans</i>	3 (1)	2 (67)	1 (33)	0	0
<i>Enterococcus faecalis</i>	159 (66)	159 (100)	0	0	0
<i>Enterococcus faecium</i>	39 (16)	18 (46)	0	14 (36)	7 (18)
<i>Enterococcus gallinarum</i>	16 (7)	4 (25)	12 (75)	0	0
<i>Enterococcus hirae</i>	2 (1)	2 (100)	0	0	0

Table 2: Enterococcal blood infections from 2013-2018 categorized by hospital unit and susceptibility to vancomycin and ampicillin

Unit	Total # (% of total)	Vancomycin Susceptible and Ampicillin Susceptible (% of unit)	Vancomycin non-Susceptible and Ampicillin Susceptible (% of unit)	Vancomycin Susceptible and Ampicillin Resistant (% of unit)	Vancomycin non-Susceptible and Ampicillin Resistant (% of unit)
All	240	202 (84)	15 (6)	16 (7)	7 (3)
CICU/CPCU	20 (8)	19 (95)	1 (5)	0	0
HEM/ONC/BMT	54 (23)	29 (54)	9 (16.5)	10 (18.5)	6 (11)
NICU	49 (20)	49 (100)	0	0	0
PICU	26 (11)	22 (84.5)	1 (4)	2 (7.5)	1 (4)
MED	91 (38)	83 (91)	4 (4.5)	4 (4.5)	0

Cardiac Intensive Care Unit (CICU); Cardiac Progressive Care Unit (CPCU); Hematology, Oncology, and Bone Marrow Transplant Units (HEM/ONC/BMT); Neonatal Intensive Care Unit (NICU); Pediatric Intensive Care Unit (PICU); General Medical Unit (MED)

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635. Genomic Evolution and Progression of Antimicrobial Resistance in a Series of Extensively Drug-Resistant *Pseudomonas aeruginosa* (XDR-Pa) Isolates from a Cystic Fibrosis Lung Transplant Recipient

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Background. Chronic respiratory infection due to extensively drug-resistant *Pseudomonas aeruginosa* (XDR-Pa) is a significant cause of mortality in cystic fibrosis (CF) patients. The CF respiratory anatomy, chronic antibiotic use, and PA colonization creates a milieu for high evolutionary pressure and genetic diversity. We sought to explore the progression of antibiotic resistance and genome evolution of XDR-Pa in a longitudinal series of isolates collected from an 18-year-old CF patient who underwent lung transplantation.

Methods. Consecutive respiratory isolates were collected from December 2016 to March 2018. Standard disk diffusion methods were used to evaluate antimicrobial susceptibility. Whole-genome sequencing (WGS) data were obtained on an Illumina NextSeq and assembled. Variants were identified using the GATK HaplotypeCaller and their functional impact was determined using snpEff. Maximum likelihood phylogenetic trees were constructed using MEGA and BEAST. Panther was used to test for enrichment of Gene Ontology functional categories among mutated genes.

Results. Phylogenetic analysis of complete genome sequences showed that 18 isolates formed a monophyletic group. Analysis using BEAST showed that genomes shared a common ancestor that was present prior to transplant. Over 300 single nucleotide variants and small insertion-deletion mutations were found, in comparison with a reconstruction of the ancestral sequence (Figure 1). Shared patterns of antibiotic susceptibility profiles were largely concordant with phylogenetic clustering and trended toward a decrease in susceptibility over time. Two different frameshift mutations in the DNA mismatch repair gene *mutL* were found in 15 genomes and these exhibited an increased rate of transition to transversion mutations, consistent with a hypermutator phenotype.

Conclusion. WGS of XDR-Pa identified variations in antibiotic resistance and virulence genes. Changes in *mutL* likely accelerated the accumulation of mutations. Multiple related sub-groups of strains appear to have been circulating prior to transplant and continued to diverge during the treatment period. Correlating antibiotic pressure, susceptibility profiles, and WGS in XDR-Pa from a single patient reveals the clinical impact of genomic evolution in CF.

