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1233. Serious Toxicities During Antimicrobial Therapy for Disseminated Nocardia Infection in Solid Organ Transplant Recipients

Christopher Saling, MD[1]; Sabirah N. Kasule, MD[1]; Holenarasipur R. Vikram, MD[2]; [1]Mayo Clinic in Arizona, PHOENIX, Arizona; [2]Mayo Clinic hospital, Phoenix, Arizona, Phoenix, AZ

Session: P-72. Resistance Mechanisms

Background. Management of disseminated *Nocardia* (NC) infection in transplant recipients requires prolonged antimicrobial therapy. Treatment can be particularly challenging if NC is resistant to standard agents. Drug toxicities can further limit options. We present a series of transplant patients with multi-drug resistant, disseminated NC infection complicated by serious adverse reactions to sequential antimicrobials.

Methods. This is a prospective review monitoring response to treatment of disseminated NC as well as adverse events to therapies.

Results. The first case is a 66-year old heart transplant patient who presented with fever and cough. Investigations revealed *N. otitidiscaviarum* lung lesion and multiple brain abscesses. Trimethoprim-sulfamethoxazole (TMP-SMX) and linezolid were started empirically. NC was fully susceptible to linezolid only, and intermediate to quinolones and tobramycin. Linezolid was switched to ciprofloxacin due to ongoing cytopenia, and dose of TMP-SMX was reduced due to renal insufficiency. Repeat brain MRI showed enlarging abscesses; regimen was changed to linezolid and moxifloxacin. Severe peripheral neuropathy led to linezolid discontinuation and initiation of high-dose doxycycline plus moxifloxacin. One year into therapy, he presented with a large aortic dissection. His long-term quinolone therapy was felt to be contributory. He underwent aortic stent placement and remains on doxycycline monotherapy. The second case is a 74-year old female renal transplant patient who presented with fevers. A perinephric abscess was found which grew *N. farcinica* resistant to floroquinolones and clarithromycin, and intermediate to doxycycline. Further imaging also revealed pulmonary and brain involvement. TMP-SMX was started but soon switched to linezolid due to acute kidney injury. One month later she presented with severe thrombocytopenia and subdural hematoma thought to be secondary to linezolid. She died despite surgery.

Conclusion. This series illustrates challenges encountered in the treatment of disseminated NC infection in transplant recipients. Multidrug resistant NC coupled with serious toxicities of therapies often severely limits treatment options. Counseling patients and closely monitoring for adverse events is essential.

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1234. Can Susceptibility to One Carbapenem be Conferred to Another? Frequency of Discordance in Gram-negative Clinical Isolates

Pam M. Ku, PharmD, BCPS[1]; Diana A. Hobbs, PhD[2]; Melissa Gilmore, n/a[3]; Athena L. Hobbs, PharmD, BCIDP[4]; [1]Augusta University Medical Center, Augusta, Georgia; [2]Washington University School of Medicine, St. Louis, Missouri; [3]Baptist Memorial Hospital, Columbus, Mississippi; [4]Methodist University Hospital, Memphis, Tennessee

Session: P-72. Resistance Mechanisms

Background. Carbapenem-Resistant Enterobacterales (CRE) and Carbapenem-Resistant *Pseudomonas aeruginosa* (CRPA) can exhibit resistance to one carbapenem while remaining susceptible to another. While case reports describing discrepant carbapenem susceptibilities are available, the authors are unaware of any literature reporting aggregate carbapenem susceptibility discrepancies at a hospital level.

Methods. Susceptibility data from April 1, 2017 - December 31, 2017 was extracted through an antibiogram report for a 706-bed hospital. Ertapenem, imipenem-cilastatin, and meropenem susceptibilities were captured and compared for common Enterobacterales and *Pseudomonas aeruginosa*. Organism identification was performed using Matrix Assisted Laser Desorption Ionization-Time of Flight (MALDI-TOF) mass spectrometry. Antibiotic susceptibility testing was performed using BD Phoenix™. Carbapenem susceptibilities were interpreted using the most updated Clinical and Laboratory Standards Institute (CLSI) breakpoints at the time of assessment (2021). Carbapenem discordance was defined as an organism being susceptible to one carbapenem and non- susceptible (intermediate or resistant) to another. Approval was obtained from the institution's Institutional Review Board.

Results. Meropenem proved to be the most active antimicrobial for all organisms (Figure 1). Carbapenem susceptibility discordance ranged from 0%-23.8% (Table 1). There was a significant difference in the incidence of discordance between Enterobacterales and *Pseudomonas aeruginosa* isolates (2.6% vs. 6.1%, $p < 0.001$). Of the 20 *Pseudomonas aeruginosa* isolates with discordant carbapenem susceptibilities, 70% were meropenem susceptible/imipenem non-susceptible and 30% were imipenem susceptible/meropenem non-susceptible. The most common site for discordance was urine for both Enterobacterales and *Pseudomonas aeruginosa*. However, while there was a significant rate of discordance between sites for *Pseudomonas* isolates, this was not the case for Enterobacterales (Table 2).

Figure 1: Carbapenem Susceptibility by Isolate

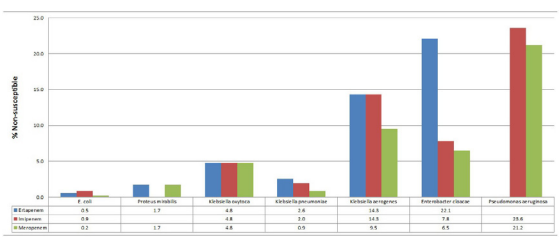

Table 1: Frequency of Carbapenem Discordance

	Total Number of Isolates (n)	Number of Discordant Isolates (n)	Percentage of Discordant Isolates (%)
Enterobacterales	1524	40	2.6
E. coli	920	11	1.2
Proteus mirabilis	115	2	1.7
Klebsiella oxytoca	42	0	0.0
Klebsiella pneumoniae	349	9	2.6
Klebsiella aerogenes	21	5	23.8
Enterobacter cloacae	77	13	16.9
Pseudomonas aeruginosa	326	20	6.1

Table 2: Frequency of Carbapenem Discordance by Site

	Blood n (%)	Urine n (%)	Sputum/BAL n (%)	Wound n (%)	Sterile n (%)	Misc. n (%)	P-value
Enterobacterales (n=40)	3 (7.5)	21 (52.5)	6 (15)	6 (15)	1 (2.5)	3 (7.5)	0.12
Pseudomonas aeruginosa (n=20)	2 (10)	14 (70)	3 (15)	1 (5)	0 (0)	0 (0)	<0.005

Conclusion. Due to the wide range of susceptibility discordance, clinical implications can be drastic if an institution is relying on susceptibility of one carbapenem to confer susceptibility to another carbapenem.

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1235. Roles of Tetracyclines for Treatment of *Stenotrophomonas maltophilia* Pneumonia

Taha Alhayani, PharmD[1]; Carolyn Philpott, PharmD[2]; Siyun Liao, PharmD, PhD, BCPS, BCIDP[3]; Anthony Gentene, PharmD[2]; Eric Mueller, PharmD[2]; [1]Trihealth Good Samaritan Hospital, Cincinnati, Ohio; [2]UC Health, Cincinnati, Ohio; [3]UC Health-University of Cincinnati Medical Center, Cincinnati, OH

Session: P-72. Resistance Mechanisms

Background. *Stenotrophomonas maltophilia* is a multidrug resistant organism with limited antibiotic treatment options. Sulfamethoxazole-trimethoprim (TMP-SMZ) is considered first line agent based on *in vitro* studies and clinical evidence. Minocycline has been showed to be active on *in vitro* studies and also has been explored in small retrospective studies However, doxycycline in the same class has variable in susceptibility in *in vitro* studies and has not been evaluated for efficacy in treatment of *S. maltophilia* infections The purpose of this research is to compare minocycline and doxycycline to TMP-SMZ for treatment of *S. maltophilia* pneumonia.

Methods. This retrospective, multi-center study evaluated hospitalized patients treated for *S. maltophilia* pneumonia with minocycline, doxycycline, or TMP-SMZ for clinical success, microbiologic success, and recurrence or reinfection within 30 days that required treatment. The inclusion criteria were patients ≥18 years old with *S. maltophilia* confirmed on respiratory culture from January 2013 to November 2020. Patients were classified as treatment with tetracyclines (minocycline or doxycycline) or TMP-SMZ based on definitive agent used for ≥50% of the treatment course and a minimum of four days. Patients with *S. maltophilia* resistant or intermediate to definitive therapy, and patients with combination therapy for treatment for *S. maltophilia* pneumonia were excluded.

Results. A total of 21 patients were included in tetracyclines group and 59 patients included in TMP-SMZ group. There was no difference in clinical success (28.6% vs. 25.4%; P = 0.994) or microbiologic success (n=28, 55.6% vs. 66.4%; P= 0.677) between tetracyclines and TMP-SMZ, respectively. Recurrence or reinfection requiring treatment (n=24) was higher in the tetracyclines group but not statistically significant compared to TMP-SMZ (66.7% vs. 26.7%; P= 0.092). A subgroup analysis showed no difference between doxycycline, minocycline, and TMP-SMZ for these three aims.

Conclusion. Clinical and microbiologic success were similar in patients treated with tetracyclines compared to TMP-SMZ for *S. maltophilia* pneumonia. This data suggests minocycline and doxycycline may be an option to treat *S. maltophilia* pneumonia, but conclusive clinical data continues to be lacking.

Disclosures. **Anthony Gentene, PharmD**, **advisory board with Theravance Biopharma and Mylan** (Consultant)

1236. Update on the *In Vitro* Activity of Ceftaroline against *Staphylococcus aureus* from United States (US) Medical Centers Stratified by Infection Type (2018-2020)

Helio S. Sader, MD, PhD, FIDSA[1]; Mariana Castanheira, PhD[1]; Mariana Castanheira, PhD[1]; Leonard R. Duncan, PhD[1]; Rodrigo E. Mendes, PhD[1]; [1]JMI Laboratories, North Liberty, Iowa

Session: P-72. Resistance Mechanisms

Background. Ceftaroline was initially approved by the US FDA in 2010 to treat skin and skin structure infection (SSSI) and community-acquired bacterial pneumonia (CABP). FDA approval was extended in 2015 to treat patients with SSSI and CABP who developed bacteremia. Moreover, ceftaroline has also been used off-label to treat other infection types. We evaluated the *in vitro* activity of ceftaroline against *S. aureus* isolated in US medical centers in 2018-2020.

Methods. A total of 9,268 *S. aureus* isolates were consecutively collected from 33 US medical centers in 2018-2020 and susceptibility tested by broth microdilution method against ceftaroline and comparators. Results were stratified by infection type and resistance profile.

Results. Ceftaroline ($MIC_{50/90}$, 0.25/1 mg/L) susceptibility (S) ranged from 98.5% (SSSI) to 95.4% (pneumonia; 97.2% overall [Table]). Ceftaroline retained potent activity and broad spectrum against methicillin-resistant *S. aureus* (MRSA; 41.9% of isolates), with S rates varying from 96.3% (SSSI) to 89.2% (pneumonia; 93.4% overall). Overall S rate to erythromycin (ERY), levofloxacin (LEV), tetracycline (TET), and trimethoprim-sulfamethoxazole (TMP-SMX) were 44.0%, 67.9%, 94.1%, and 97.5%, respectively. Ceftaroline retained good activity against *S. aureus* resistant to ERY (94.8%S), LEV (91.4%S), TET (92.3%S), and/or TMP-SMX (98.7%S). Among the resistant subsets, ceftaroline S rates were generally highest among isolates from SSSI (93.1-100.0%), followed by other infections (81.8-100.0%), bloodstream infections (BSI; 89.4-96.2%), and pneumonia (86.6-98.1%); overall susceptibility was highest among TMP-SMX-R isolates (98.7%), followed by ERY-R (94.8%), MRSA (93.4%), TET-R (92.3%), and LEV-R (91.4%) isolates. Dalbavancin (MIC_{90}, 0.03 mg/L), teicoplanin (MIC_{90}, 0.5 mg/L), and vancomycin (MIC_{90}, 1 mg/L) exhibited complete activity (100.0%S), whereas daptomycin (MIC_{90}, 0.5 mg/L) and linezolid (MIC_{90}, 2 mg/L) were active against >99.9% of isolates.

Conclusion. Ceftaroline remained very active against contemporary (2018-2020) *S. aureus* from US medical centers, independent of infection type. Ceftaroline retained good activity against MRSA and isolates resistant to ERY, LEV, TET, and/or TMP-SMX.

Resistant	% Susceptible to Ceftaroline by Infection Type (no. tested)				
subset	SSSI	Pneumonia	BSI	Other sites	All combined
All isolates	98.5 (4,343)	95.4 (2,260)	96.6 (2,235)	97.4 (430)	97.2 (9,268)
MRSA	96.3 (1,831)	89.2 (959)	91.8 (922)	93.7 (175)	93.4 (3,887)
ERY-R	97.2 (2,251)	91.2 (1,164)	93.6 (1,152)	94.9 (217)	94.8 (4,784)
LEV-R	95.1 (1,312)	86.6 (767)	89.4 (718)	92.5 (147)	91.4 (2,944)
TET-R	93.1 (233)	90.8 (120)	93.3 (89)	81.8 (11)	92.3 (453)
TMP-SMX-R	100.0 (111)	98.1 (52)	96.2 (52)	100.0 (13)	98.7 (228)

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