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REPORT OF A MULTI-SPECIES OUTBREAK OF VIM-PRODUCING CARBAPENEM-RESISTANT ORGANISMS IN A BURN UNIT AND SUBSEQUENT EXPERIENCE USING NOVEL B-LACTAM ANTIBIOTICS FOR TREATMENT

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BACKGROUND

- The incidence of carbapenem-resistant organisms (CROs) has increased over the past 3 decades.
- Carbapenem-resistance due to metallo-β-lactamases (MBLs) such as the Verona integron-encoded metallo-β-lactamase (VIM) are particularly problematic due to the limited treatment options.
- Two newer treatment options for these infections are cefiderocol and the combination of aztreonam with ceftazidime-avibactam.
- Cefiderocol is less susceptible to hydrolysis by carbapenemases and novel in its mechanism to promote active uptake by hijacking bacterial iron transport systems while the combination of aztreonam and ceftazidime-avibactam has shown success both *in vitro* and *in vivo* in treating infections due to MBLs.
- We describe a multi-species outbreak of VIM-producing CROs (VIM CROs) in a tertiary care hospital along with our experience using novel β-lactam antibiotics for treatment.

METHODS

- A retrospective chart review was conducted of patients treated in the Vanderbilt University Medical Center (VUMC) Vanderbilt Burn Center, a 25-bed level I burn unit.
- A case was defined as any patient with a documented history of a VIM CRO isolated from either a blood or a tissue culture taken directly from an infected site between November 2021 and May 2022.
- Antimicrobial susceptibility testing was performed on the Phoenix (BD, Sparks, MD) using the NMIC-306 panels
- MICs in the not susceptible range were confirmed by ETEST (bioMerieux, Durham, NC).
- Cefiderocol testing was performed using a Sensititre panel, and all cefiderocol resistant isolates were confirmed (along with the susceptible isolates from the same patient) by testing at LSI laboratories.
- Carbapenemase testing was performed using the Carba-5 lateral flow assay (Hardy, Santa Ana, CA).
- The data was analyzed using secure REDcap and excel files.

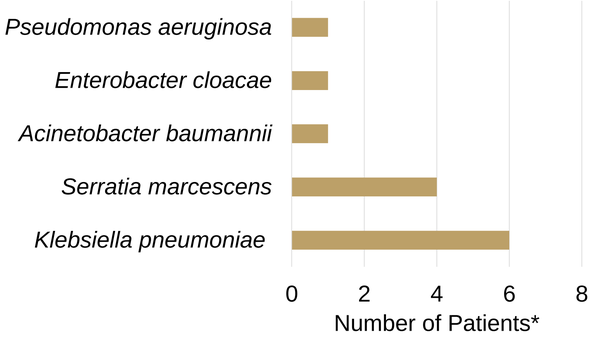
RESULTS

Table 1. Characteristics of Burn Patients with Infections due to VIM CROs (n=9)

Median Age, in years (range)	38 (19-81)
Gender, n (%)	
Male	7 (78)
Female	2 (22)
Median Total Body Surface Area of Burn, percent (range)	40 (13-65)
Median Length of Stay, in days	75 (32-157)
Median Length of Stay Prior to Isolation of CRO, in days	25 (8-45)
Median Number of Surgeries[a] During Hospitalization (range)	12 (1-16)
Associated Bacteremia due to a CRO, n (%)	4 (44)
Mean Pitt Bacteremia Score at Time of Initial CRO Isolation (range)[b]	2.3 (0-6)
Among Surviving Patients (n=8)	1.9 (0-4)
Mortality, n (%)[c]	
Within 30 days of Initial CRO Isolation	1 (11)
Within 30 days of Hospital Discharge	1 (11)
Among Patients with Bacteremia	1 (25)

[a]Includes only amputation or debridement surgeries occurring in an operating room
[b]Highest Pitt Bacteremia Score calculated for the 24 hr period during which the initial VIM-producing CRO was isolated from a patient
[c]Single patient death in this study was attributed to a subsequent fungal infection with fungemia

Figure 1. Frequency with which various VIM CROs were isolated from patients



*Total is greater than total # of patients as 3 patients had multiple species isolated

Figure 2. Breakdown of Treatment Strategies Employed

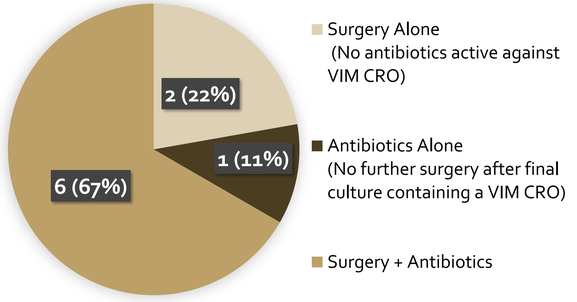
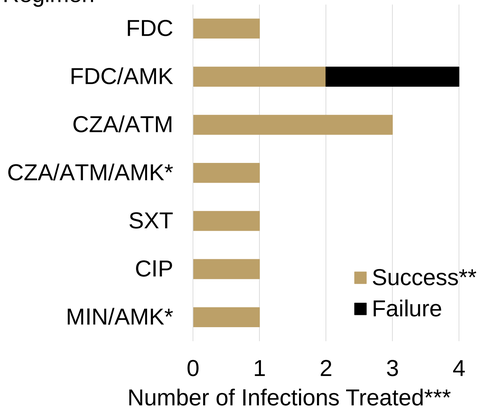


Figure 3. Treatment Outcomes Based on Antibiotic Regimen



*Includes a patient treated with salvage therapy after FDC failure in each group

**Success was defined as resolution of fever and/or clearance of VIM CRO on subsequent culture from infected site

***Total is greater than total # of patients because treatment courses for salvage therapy and two patients who had multiple separate VIM CRO infections during hospitalization are included separately

FDC – cefiderocol, CZA – ceftazidime/avibactam, ATM – aztreonam, SXT – trimethoprim/sulfamethoxazole, CIP – ciprofloxacin, MIN – minocycline, AMK – amikacin

CONCLUSIONS

- MBLs such as VIM have the potential for multi-species spread throughout hospital units even in the absence of carbapenem selection pressure.
- >40% of patients had bacteremia and cefiderocol-resistance developed in 40% of patients treated with cefiderocol, however, mortality remained low.
- While newer β-lactam antibiotics remain an exciting addition to our armamentarium, we must remain diligent in monitoring for rapid development of resistance.

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