Daptomycin Non-Susceptible MRSA Bacteremia: A Case Report

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Background

Staphylococcus aureus[1, 2, 3]

• One of the most common pathogens causing community-acquired and nosocomial infections

• Has rapidly developed resistance to many antibiotics:

	Methicillin	Vancomycin	Linezolid	Daptomycin	Ceftaroline
Antibiotic introduced:	1960	1972	2000	2003	2010
First isolate of S. aureus resistance:	1962	2002	2001	2005	2011

Daptomycin [2]

- Bactericidal cyclic lipopeptide antibiotic
- Possesses negative charge which attracts calcium to form cationic complex
- Interacts with negatively charged phospholipid heads on bacterial cell membranes, leading to membrane depolarization and cell death

Daptomycin non-susceptible (DNS) *S. aureus* [2, 4, 5]

- Extremely rare - About 60 clinical cases reported
- Defined by an MIC greater than 1 mcg/mL
- Potential mechanisms include:
  - Changes in cell membrane and cell wall structure alter daptomycin's permeability[2]
    - Overexpression and dysregulation of *dltA* transcription increases *D*-alanylated teichoic acid content in the cell wall
    - *mprF* mutation leads to partially neutral charge of cell membrane
  - Vancomycin intermediate *S. aureus* (VISA) and vancomycin resistant *S. aureus* (VRSA) may predispose patients to develop DNS *S. aureus*[2]
- Have seen increased resistance with lower doses[4, 5]
  - 4 to 6 mg/kg/day has higher rates of DNS *S. aureus*
  - Experts recommend doses ≥ 8mg/kg/day especially for bacteremia

Patient Case

History of Present Illness:

- 44 year old female transferred from outside hospital
- Complains of several days of worsening cough and abdominal pain, chronic weight loss and sweats, and hemoptysis
- Blood cultures at outside hospital grew pan-sensitive *Klebsiella pneumoniae* & coagulase negative *Staphylococcus*
  - Likely source: PICC line, which was removed

Height : 66 in **Weight :** 70 kg **CrCl :** ~57 ml/min

135	105	13	76
3.6	17	1.2	

	8.3	
34.6		333
	26	

Neutrophils: 62%
Bands: 15%

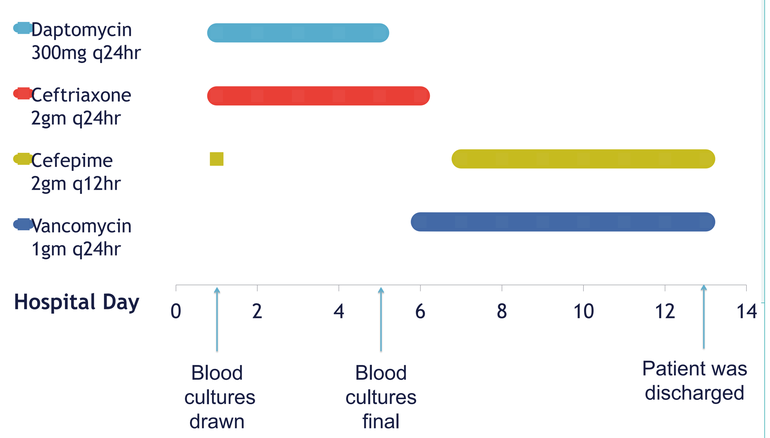
PMH:
- Recent hospitalization for MRSA pneumonia and sepsis s/p 4 weeks of vancomycin therapy
- HIV

Allergies:
- Bactrim: Steven's Johnson Syndrome
- Vancomycin: Reported throat swelling

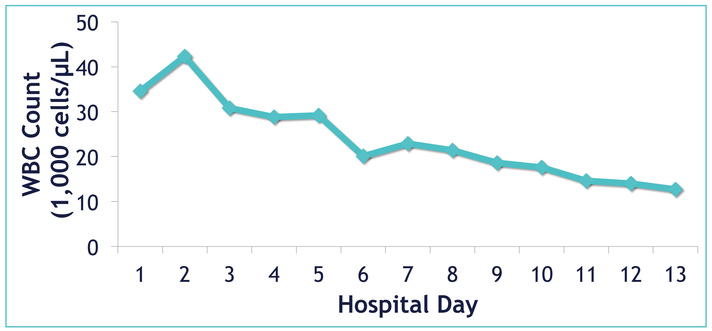
Patient Case

Antibiotic Course:

- Continued cefepime 2gm IV q12hr from outside hospital
- Added daptomycin 300mg (~4mg/kg) IV q24h for positive blood culture from outside hospital



Blood Culture Results: *Staphylococcus aureus*		
	MIC	Interpretation
Clindamycin	>2	Resistant
Erythromycin	>4	Resistant
Oxacillin	>2	Resistant
Rifampin	≤0.5	Susceptible
Tetracycline	2	Susceptible
Trimeth/sulfa	≤1/19	Susceptible
Vancomycin	1	Susceptible
Daptomycin MIC by E Test (mcg/mL)	3.0	Nonsusceptible



Discharge:

Discharge Plan
- Patient transferred to another facility
- Daptomycin 500mg (~8 mg/kg) IV q24hr
- Aztreonam 2gm IV q8hr

Treatment Options

To date, there have been no randomized controlled trials studying the treatment of DNS *S. aureus*, but treatment options have been discussed in case reports and *in vitro* studies

Daptomycin in combination with a beta-lactam[6-8]

- Beta-lactams enhance activity of daptomycin
  - Seen with oxacillin, nafcillin, ceftaroline
  - Due to enhanced daptomycin binding to cell wall when used in combination with beta-lactams
  - Likely occurs through a reduction in net positive membrane surface charge (may be linked to release of wall teichoic acid)

Telavancin[9]

- PK/PD models show that it maintains activity in its susceptible range and is bactericidal against DNS *S. aureus*

Discussion

- Patient was discharged on daptomycin and aztreonam
  - Aztreonam was used as continuation of therapy for *Klebsiella pneumoniae* bacteremia
  - Aztreonam only has coverage against gram negative pathogens and will not enhance the activity of daptomycin as has been shown with the anti-staphylococcal penicillins and ceftaroline
- Daptomycin dose was increased from 300mg (~4mg/kg) q24h to 500mg (~8mg/kg) q24h to possibly overcome the resistance
- Total duration of antibiotics and clinical outcome is unknown due to transfer out of the health system

Disclosure Panel

Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation

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