Daptomycin Non-Susceptible MRSA Bacteremia: A Case Report
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Background
Staphylococcus aureus1, 2, 3
• One of the most common pathogens causing community-acquired and nosocomial infections
• Has rapidly developed resistance to many antibiotics:
  - Methicillin-resistant
  - Vancomycin-resistant
  - Linezolid-resistant
  - Daptomycin-resistant
  - Cefepime-resistant
  - First isolate of S. aureus introduced: 1962

Daptomycin2
• Bactericidal cyclic lipopeptide antibiotic
• Positively charged group which attracts calcium to form cationic complex
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• Interacts with negatively charged phospholipid heads on bacterial cell membranes, leading to membrane depolarization and cell death
• Possesses negative charge which attracts calcium to form cationic complex
• Bactericidal cyclic lipopeptide antibiotic
• Has rapidly developed resistance to many antibiotics:
  - Blood cultures at outside hospital grew pan-sensitive Staphylococcus aureus
  - Weight loss and sweats, and hemoptysis
  - Complains of several days of worsening cough and abdominal pain
  - Chronic membranes, leading to membrane depolarization and cell death
  - Changes in cell membrane and cell wall structure alter daptomycin’s binding.
  - Overexpression and dysregulation of dltA transcription increases D-alanylated teichoic acid in the cell wall
  - mpf mutation leads to partial neutral charge of cell membrane
  - Vancomycin intermediate S. aureus (VISA) and vancomycin resistant S. aureus (VRSA) may predispose patients to develop DNS S. aureus2
  - Have seen increased resistance with lower doses1, 5
    - 4 to 6 mg/kg/day has higher rates of DNS S. aureus
    - Experts recommend doses ≥8mg/kg/day especially for bacteraemia

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

Hospital Day
Blood cultures drawn
Blood cultures final
Patient was discharged

Blood Culture Results:

<table>
<thead>
<tr>
<th>Staphylococcus aureus</th>
<th>MIC</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycin</td>
<td>&gt;2</td>
<td>Resistant</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>&gt;4</td>
<td>Resistant</td>
</tr>
<tr>
<td>Oxacillin</td>
<td>&gt;2</td>
<td>Resistant</td>
</tr>
<tr>
<td>Rifampin</td>
<td>≤0.5</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>2</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Trinem/sulfamethoxazole</td>
<td>≤1/19</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>MIC by E Test (mcg/mL)</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Discharge:
- Patient transferred to another facility
- Daptomycin 500mg (~8mg/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-lactam1, 4, 6
- Beta-lactams enhance activity of daptomycin
- Seen with oxacillin, nafcillin, cefazolin
- 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)

Telavancin6
- PKPD 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 bacteraemia
  - 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 cefazolin
  - 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

References