PVL-\textit{Staph aureus}- just a skin/soft tissue problem?

Layla Mohammadi
Lead Pharmacist, Antimicrobials
Lewisham Healthcare NHS Trust
Neonatal Case History

- Neonate born at 26 +2 gestation
- Spontaneous onset of preterm labour
- Presumed sepsis, respiratory distress
- Empirical benzylpenicillin and gentamicin initiated
- Blood cultures –ve
- Positive clinical and biochemical response to 6/7Abx
Day 19

- 3 episodes of bradycardia / desaturation
- ? Sepsis
- CRP < 5
- Teicoplanin / gentamicin initiated (long line in situ)
- Small swelling / erythema noticed on R arm (previous cannula site)
- Blood cultures from day 19 reported –ve on day 21 so Abx stopped
• Day 29
  – Distended abdomen & dilated loops of large and small bowel
  – Desaturating on CPAP and bradycardic
  – CRP ↑
  – ? NEC
  – Teicoplanin, gentamicin and metronidazole started
• Day 32
  – Baby found to be MRSA +ve on regular Control of Infection (COI) screening
  – ICN advised for mum be screened
Day 31
- Gram +ve coccis grown from B/C and line tip despite Teicoplanin therapy
- Transthoracic ECHO normal
- Abx switched to vancomycin and cefotaxime

Day 32
- MRSA bacteraemia confirmed

Day 34
- Further deterioration
- BC still +ve
- MRSA shows increased MICs to teicoplanin and vancomycin
What could be causing this neonate’s ongoing sepsis?

What further investigations are required?
Potential Diagnosis at this stage - ?
PVL Staph aureus

How could this diagnosis be confirmed / ruled out?

What would the empirical treatment options be for PVL-Staph aureus infection?
Meropenem, linezolid, rifampicin and vancomycin combination initiated

What role do each of these agents play in treating PVL-SA?
Day 38
* MRSA confirmed to be PVL positive
  - Patient clinically improving
  - CRP decreasing
  - Meropenem stopped

Day 39
- Clinically well but CRP increasing and BC from previous day still growing gram +ve cocci (3rd positive result)
What are your thoughts on further management?

What additional treatment options could be considered?

What further investigations should be considered at this stage?
Day 39

- Antibiotics switched to daptomycin, gentamicin and linezolid
- Literature search and expert neonatal advice sought regarding daptomycin dosing and levels
Day 41

* Mum’s LSCS scar swab MRSA +
* Conversation between ICN and mum reveals that mum had repeated boils on back of ear in 2010
* Conversation with GP reveals that ear swab in 2010 had grown PVL-MRSA

How would you manage mum now that these results are available?
What additional screening may be considered?
* Day 41-45
  * Clindamycin added to Abx regimen
  * No deep seated source of PVL MRSA infection found
    - US of swelling on R arm found to be normal
    - Trans-oesophageal ECHO normal
    - Full body MRI scan - Osteomyelitis ruled out
  * All other neonates on ward screened and found to be MRSA –ve
  * Decision made that staff screening not required in view of mum being identified as index case
Ongoing management

- **Day 45**
  - Blood culture remains positive

- **Day 51**
  - First negative blood culture

- **Day 53**
  - Patient clinically improving and CRP ↓
  - Day 14 of daptomycin combination
  - CK level 214, LFTs ↑
  - Daptomycin dose decreased to 10mg/kg once daily wrt CK
  - Linezolid stopped wrt to LFTs

- **Day 54-62**
  - Clinical improvement
  - LFTs and CK ↓
Clindamycin stopped day 62
Daptomycin and gentamicin continued for 4/52 from date of first negative BC
Baby made full recovery
Discharged home on day 88
PVL- *Staph aureus*
What is it?

- PVL - Panton-Valentine Leukocidin
- Toxin that destroys white blood cells
- Virulence factor in some *Staph aureus* strains
- First detected in 1900s
- Seen in UK since 1950s
- Genes encoding for PVL found in < 2% of *Staph aureus*
- Can have PVL MSSA and MRSA
- Mainly associated with community strains
Mostly causes abscesses/boils that require incision and drainage and/or antibiotics

Analysis of SRU data revealed 65% of *S. aureus* from such infections are PVL-positive

1/3 of infections associated with recurrent episodes of infection

From 2006 onwards majority of PVL-SA identified have been susceptible to methicillin

Cases are mainly sporadic and community-associated

Outbreaks in healthcare settings have been observed in England and abroad
### Number of PVL–SA identified by the HPA's Staphylococcus Reference Unit (SRU)

<table>
<thead>
<tr>
<th>Year</th>
<th>No (%) PVL-MSSA</th>
<th>No (%) PVL-MRSA</th>
<th>Total PVL-SA</th>
<th>Relative year on year change</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>107 (48%)</td>
<td>117 (52%)</td>
<td>224</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>337 (58%)</td>
<td>159 (32%)</td>
<td>496</td>
<td>+2.2 fold</td>
</tr>
<tr>
<td>2007</td>
<td>729 (60%)</td>
<td>477 (40%)</td>
<td>1206</td>
<td>+2.4 fold</td>
</tr>
<tr>
<td>2008</td>
<td>1013 (58%)</td>
<td>724 (42%)</td>
<td>1737</td>
<td>+1.4 fold</td>
</tr>
<tr>
<td>2009</td>
<td>1573 (61.5%)</td>
<td>984 (38.5%)</td>
<td>2557</td>
<td>+5.4 fold</td>
</tr>
<tr>
<td>2010</td>
<td>1178 (53%)</td>
<td>1049 (47%)</td>
<td>2227</td>
<td>-0.87 fold</td>
</tr>
</tbody>
</table>

Thought to be due to labs testing their own samples
Other Clinical Features of PVL-SA

- Necrotising haemorrhagic pneumonia (may be following a ‘flu-like’ illness)
  - May affect otherwise young, fit healthy people
- Necrotising fasciitis
  - Osteomyelitis, septic arthritis, and pyomyositis
  - Purpura fulminans
Following settings have been identified as high risk for transmission from an individual colonised or infected with PVL-MRSA:

- households
- close contact sports e.g. wrestling, american football, rugby, judo
- military training camps
- gyms
- prisons
MSSA or MRSA from patients with the following clinical features should be considered for PVL-testing:

- boils or abscesses, especially where recurrent
- necrotising skin and soft tissue infections
- necrotising pneumonia, purpura fulminans or necrotising fasciitis
- isolates from close contacts of PVL cases
• MSSA or MRSA isolated from suspected cases should be referred to the SRU at HPA Colindale for:
  – toxin gene profiling
  – PCR-based assay performed daily and completed within a working day.
  – If cases are urgent, results will be telephoned to the submitting laboratory
  – Even if PVL testing is performed locally, isolates must be sent to the Reference Unit for further toxin testing and typing
• Minor SSTIs (furunculosis, folliculitis, small abscesses/boils without cellulitis)
  – Do not need systemic antibiotic treatment unless the patient is immunocompromised, an infant or deteriorating clinically.
  – Incision and drainage is the optimal management for abscesses
• Moderate SSTIs including cellulitis and larger abscesses (especially those > 5cm)
  – should be treated with oral anti-staphylococcal antibiotics in addition to drainage

HPA guidance - Management of PVL-SA infection
Empirical antibiotics for moderate SSTI

• For moderate SSTI with MSSA:
  – Flucloxacillin 500mg qds or clindamycin 450 mg qds

• When PVL-MRSA is suspected and hospital admission is not warranted:
  – Rifampicin 300mg bd PLUS doxycycline (not for children <12 y)
• Or
  – Rifampicin 300mg bd PLUS fusidic acid 500mg tds (care needed with regards to resistance developing and hepatotoxicity)
• Or
  – Rifampicin 300 mg bd PLUS trimethoprim 200 mg bd
• Or
  – Clindamycin 450 mg qds
• **Total course length 5-7 days**
Empirical management for severe infections

- Parenteral vancomycin, teicoplanin, daptomycin or linezolid
- Tigecycline may also offer broader polymicrobial cover
- No evidence that any one agent is superior
- In severe infections with features of toxic shock, necrotising fasciitis, or purpura fulminans consider using two or three agents such as:
  - **Linezolid 600mg bd combined with clindamycin 1.2 - 1.8g qds +/- rifampicin 600mg bd**
- Based on in-vitro synergy and ability of linezolid and clindamycin to switch off toxin production
Empirical management for severe infections

- Consider IVIG 2g/kg
- IV flucloxacillin is not recommended
  - concerns that at concentrations just above the MIC, flucloxacillin may increase PVL production
- Refer to HPA guidance for details on additional clinical management and supportive measures
Osteomyelitis/deep seated infections (BSAC guidelines)

**First line** - Teicoplanin or Vancomycin

PLUS either
- gentamicin
or
- rifampicin
or
- sodium fusidate

**Second line** - linezolid
or
- off label usage of daptomycin
or
- tigecycline
Special considerations in children

- Consider PVL-SA infection in the following situations:
  - **Severe sepsis**: if patient or close family contact has current, or a history of, recurrent boils/abscesses or skin infections, and there are bone or joint infection, necrotising pneumonia, deep venous thrombosis, purpura fulminans
  - **Pneumonia**: if there is preceding “flu-like” illness, haemoptysis, multilobular infiltrates, bone or joint infection, leukopenia/neutropenia or patient or close family contact has current, or a history of, recurrent boils/abscesses or skin infections
Decolonisation of patients and close contacts

* Required for all infected patients and close/household contacts (see HPA guidance)
* Nasal mupirocin and antiseptic bodywash such as chlorhexidine (aqueous solution required for neonates and children)
* 5 day course length
* For patients with active infection- start after acute infection has resolved
HPA guidance on diagnosis and management of PVL-SA can be found at:

http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1218699411960