Enterobacteraeaceae native joint septic arthritis

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Introduction:

- Native joint septic arthritis (NISA) is usually caused by Gram positive organisms.1
- Gram negative NISA is uncommon, and literature is frequently limited to gonococcal arthritis, despite Enterobacteriaceae-involved native joint septic arthritis (ENISA) being more prevalent.

Methods:

- ENISA and NENISA cases were obtained from a previously described retrospective, coding-based cohort of all patients aged ≥16 years admitted for NISA to Middlemore Hospital in South Auckland, New Zealand from 1 January 2009 to 31 Dec 2014.
- Cases were classified as ENISA if infecting organisms included Enterobacteriaceae, other cases were defined as NENISA. Microbiology results used were +/– a 3 days from admission or diagnosis.
- Fisher’s exact test was used for 2x2 contingency tables and Student’s t-test for comparison of means.
- p-values of ≤0.05 were considered statistically significant.

Results:

- The microbiology of ENISA is presented in Table 1

Microbiology

- Enterobacteriaceae were isolated in 7% (36/543) of NJSA
- Escherichia coli (10/36) was the most common organism followed by Enterobacter cloacae (8/36)
- ENISA was more likely to be polymicrobial (23/36, 64%), than NENISA (23/507, 8%) p<0.001
- Polymicrobial ENISA commonly involved Gram positive co-
- Demographics, co-morbidities, treatment and outcomes are presented in Table 2

Demographics

- Median age was 50 years (range 21-74)
- Males comprised 72% of ENISA cases

Co-morbidity

- Pre-existing immune compromise was more common in ENISA (7/36, 19%) than NENISA vs (42/507, 8%) p=0.0341
- Recent surgical intervention on the infected joint was more common in ENISA (9/36, 25%) than NENISA (39/507, 8%) p=0.0023
- Non-surgical trauma was not significantly associated with ENISA (13/36, 36% vs. 174/507, 34%, p=0.8568)

Clinical features

- Large joints were affected more commonly (26/36, 72%) than small joints (10/36, 28%). ENISA was less likely to affect small joints than NENISA (240/507, 47%) p=0.0247
- The most commonly infected joint was the knee (10/36, 28%), followed by the hip (5/36, 14%)

Complications

- Over half of ENISA cases (19/36, 53%) were complicated by local osteomyelitis, a greater proportion than NENISA (116/507, 23%) p=0.0002

Management

- Carbapenems and ciprofloxacin were the most frequently used antibiotics for ENISA
- Mean duration of antibiotic therapy for ENISA was 5.6 weeks
- ENISA cases required more surgical intervention (mean 2.6 operations) than NENISA (mean 1.5), p=0.0001

Outcomes

- ENISA was significantly associated with worse outcomes when compared to NENISA, including:
  - Treatment failure (19/36 (53%) vs. 76/507 (15%) p<0.001).
  - Amputation (7/36 (19%) vs. 9/507 (2%) p=0.0003)
  - Pathogen length of stay (mean 23 days vs. 13 days, p=0.0001).

Discussion:

- ENISA is associated with markedly poorer clinical outcomes than NENISA on multiple metrics. Potential contributors to poorer outcomes include previously recognised risk factors for poor outcomes in infection treatment:
  - Delay to effective antimicrobial therapy
  - Higher rates of immune suppression
  - Higher rates of large-joint infection

Given the poor outcomes, ENISA may require longer durations of targeted antimicrobial therapy (we suggest 6 weeks), and earlier/more aggressive surgical intervention than NENISA.

- Whilst ENISA is regarded as uncommon, Enterobacteriaceae were cultured in 7% of NISA, equating to one in fifteen cases, and one in 12 of large joint NISA cases
- Other studies report proportions of Gram negative septic arthritis from 6 to 50% 2-4 however inclusion criteria vary with some studies including prophyliktic joint infection, and in the study reporting 50%, Enterobacteriaceae comprised only 6% (Limmuthurolskul, personal communication)
- ENISA group included high rates of organisms with intrinsic or acquired resistance

Table 1: Microbiology of ENISA

<table>
<thead>
<tr>
<th>Organism</th>
<th>ENISA (N=36)</th>
<th>NENISA (N=507)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteriaceae</td>
<td>36 (100%)</td>
<td>445 (88%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>10 (28%)</td>
<td>22 (4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td>8 (22%)</td>
<td>6 (1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Proteus spp.</td>
<td>6 (17%)</td>
<td>27 (5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Serratia spp.</td>
<td>2 (6%)</td>
<td>10 (2%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Citrobacter spp.</td>
<td>1 (3%)</td>
<td>4 (1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Staphylococcus spp.</td>
<td>2 (6%)</td>
<td>9 (2%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Other</td>
<td>2 (6%)</td>
<td>9 (2%)</td>
<td>&lt;0.0001</td>
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Table 2: Clinical features, management and outcomes of ENJSA compared to NENJSA

<table>
<thead>
<tr>
<th>Feature</th>
<th>ENJSA (N=36)</th>
<th>NENJSA (N=507)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint involvement</td>
<td>36 (100%)</td>
<td>507 (100%)</td>
<td></td>
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<tr>
<td>Large joints</td>
<td>26 (72%)</td>
<td>435 (85%)</td>
<td>0.0341</td>
</tr>
<tr>
<td>Small joints</td>
<td>10 (28%)</td>
<td>72 (15%)</td>
<td>0.0247</td>
</tr>
<tr>
<td>Extra-articular infection</td>
<td>19 (53%)</td>
<td>116 (23%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Treatment failure</td>
<td>19 (53%)</td>
<td>76 (15%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Amputation</td>
<td>7 (19%)</td>
<td>9 (2%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mortality</td>
<td>9 (25%)</td>
<td>33 (6%)</td>
<td>0.0247</td>
</tr>
<tr>
<td>Length of admission in hospital</td>
<td>Mean 23 days</td>
<td>Mean 13 days</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Conclusion:

- Enterobacteriaceae are an uncommon but important cause of NISA. ENISA is more commonly polymicrobial, more frequently affects patients with immune compromise and recent surgical intervention, and is associated with markedly poorer outcomes than NENISA. More aggressive medical and surgical treatment may be necessary. Further studies of ENISA are required.

References:

2 De Serres L, student, SAB 2003, Final Year Project, Auckland University. Department of Infectious Diseases, Middlemore Hospital. Auckland, New Zealand.