Prognostic Utility of Whole Genome Sequencing and PCR in Post-procedure Endophthalmitis

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Disclosures

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Summary

• Pathogen-negative and *S. epidermidis* endophthalmitis have better outcome than non-*S. Epidermidis* cases

• Bacterial load identified by WGS in non-*S. Epidermidis* cases are inversely associated with clinical outcome

• TTV is a significant risk factor for needing a secondary PPV

• Molecular data may be important predictors of poor clinical outcome
Introduction

- Approximately 30% of post-CE endophthalmitis is culture-negative
- qPCR 30% culture negative
- Up to 2/3 post-injection endophthalmitis culture-negative

Han et al. AJO 1996
Joseph et al. AJP 2012
Shah et al. Ophthalmology 2011
Emerging techniques for pathogen discovery in endophthalmitis

Bryan K. Hong¹, Cecilia S. Lee², Russell N. Van Gelder², and Sunir J. Garg¹

• Culture, 16S PCR, and BRiSK provide complementary information
• Culture-negative endophthalmitis cases do not have detectable bacterial DNA
Torque Teno Virus

- Small (3.8 kb), single-stranded DNA anellovirus
- Nearly ubiquitous
  - Viremia 2/3
- Associated with numerous chronic inflammatory conditions
  - MS, SLE, pulmonary fibrosis, asthma
  - SHAPU
• All culture- samples showed at least trace evidence of TTV, as did some culture+
• Viral loads of Torque Teno virus varied but in some cases were extremely high (>10^7/ml)
Purpose

• Is TTV, along with other molecular data, associated with clinical outcome?
Methods

• Post procedure endophthalmitis cases recruited prospectively
• Standard culture, quantitative PCR (qPCR) and whole genome sequencing (WGS) performed
• Outcomes: baseline, week 1, week 4, week 12
Results

50 eyes:
24 culture-positive cases
26 culture-negative cases
<table>
<thead>
<tr>
<th></th>
<th>Culture positive (n=24)</th>
<th>Culture negative (n=26)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age (range)</strong></td>
<td>67 (44-85)</td>
<td>72 (36-98)</td>
<td>0.84</td>
</tr>
<tr>
<td><strong>Male, n (%)</strong></td>
<td>14 (58)</td>
<td>12 (46)</td>
<td>0.41</td>
</tr>
<tr>
<td><strong>Intravitreal injections</strong></td>
<td>16 (67)</td>
<td>14 (54)</td>
<td>0.43</td>
</tr>
<tr>
<td><strong>Cataract surgeries</strong></td>
<td>2 (8)</td>
<td>6 (23)</td>
<td>0.43</td>
</tr>
<tr>
<td><strong>Median days to presentation (range)</strong></td>
<td>5 (1-30)</td>
<td>8 (1-42)</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Median baseline VA, logMAR</strong></td>
<td>2.4 (HM)</td>
<td>2.4 (HM)</td>
<td>0.74</td>
</tr>
<tr>
<td><strong>TTV presence (%)</strong></td>
<td>8/22 (36)</td>
<td>15/25 (60)</td>
<td>0.15</td>
</tr>
</tbody>
</table>
• Of the 24 culture + cases, WGS identified the cultured bacteria in 3/4
• WGS identified potential pathogens in 8/22 (36%) culture-negative cases
  • (S. epidermidis (n=7) and Pseudomonas fluorescens (n=1))
Culture + vs - doesn’t predict outcome

P-value 0.448

Culture positive

Culture negative
Better VA if culture - or S. epi vs other bacteria

P-value 0.021
Pathogen Load

- Pathogen load for S. epi did not impact visual acuity
- However, higher baseline pathogen load for non S. epi was associated with worse vision at month 1 and 3
Torque Teno Virus

• TTV present in 8/22 (36%) of culture-positive and in 15/25 (60%) of culture-negative cases (p=0.147)
TTV and Secondary PPV

- 10/23 (43%) in TTV+ group
- 3/24 (13%) in TTV- group
- OR 5.2 (95%CI 1.07, 34.82, p=0.02)

All 5 cases that developed RD were TTV+
Culture & TTV negative

Culture & TTV positive

1 - Secondary PPV probability

Days since the endophthalmitis diagnosis

p = 0.0092
Conclusions

- Pathogen-negative and *S. epidermidis* endophthalmitis have better outcome than non-*S. Epidermidis* cases
- Bacterial load identified by WGS in non-*S. Epidermidis* cases are inversely associated with clinical outcome
- TTV is a significant risk factor for needing a secondary PPV
- Molecular data may be important predictors of poor clinical outcome
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