Diagnosis and Management of Infection in Revision Shoulder Arthroplasty

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Conflict of Interest

• DePuy – Synthes – Royalty
• DJO – Consulting and Royalties
• Tornier Royalties
• Custom Orthopaedic Solutions Equity
• Lippincott WW – Royalties
• None relevant to this presentation
Infection: Incidence

- Generally reported to be less than 1% in primary anatomic TSA
- Higher in reverse TSA about 2-3%
  - Reasons: older patients prior surgery, larger dead space, hematoma
- Revision arthroplasty: 3-10% depending upon series


Infection: Incidence

- Late infections (greater than one year post) are most common
- Incidence is likely more than reported
  - Many revision are not accurately diagnosed
  - Indolent pathogens
  - Incomplete pre and intraoperative evaluation
  - Diagnosis of mechanical loosening but is infection
  - Loose humeral stem within 5 years of surgery should be considered infected until proven otherwise
Timing of Diagnosis

- Many are diagnosed months to years after the surgery
- Indolent pathogens
  - P. acne is most common
  - 70% of larger series
Clinical Findings Vary: Pathogen and Host Specific

- Pain most common and may be only finding
- Local soft tissue findings rare
  - Draining, erythema, sinus (rare)
  - Hematoma – assoc. high incidence of + cx
    - Cheung et al, 2008
- Systemic findings rare
  - fever, chills, malaise

In most cases local or systematic findings of infection are subtle or nonexistent
Classic Laboratory Diagnoses

• Pre op synovial aspirate
  – Useful if positive
  – Negative aspirate does not always correlate with tissue cultures (20%)
  – Many cases of P acne have a dry tap

• Serology: Serum Inflammatory Markers
  – ESR, CRP and IL-6
  – Useful if positive: High specificity with clinical suspicion
  – Often negative with infection: Low sensitivity
Imaging Diagnoses

• Radiographs
  – Loose component within 5 years if placed correctly should consider infection until proven otherwise’
  – Most loose stems are infected

• Nuclear medicine scans
  – Low predicative value in the setting of a loose component
Pathogens

• Gram positives most common
  – Propriobacterium Acne most common infection greater than 3 months post op
  – Staph epidermidis
  – Staph aureus
P. Acne

- Normal skin flora: in skin and around hair follicles: more comment in men (Lives in the skin)
- Anaerobic gram positive rods
- Preferential site: Axilla, chest and back
- Sensitive to most antibiotics
- Need to maintain high index of suspicion for all failed shoulder replacements even those that have functioned well for many years

- Time to culture:
  - Anaerobic,
  - Aerobic and
  - Enriched broth
  - At least 14 days
“The Incidence of Propionibacterium Acnes in Open Shoulder Surgery”

– June 2015 Mook et al, - Duke group
– 117 surgeries: All cultured and held for 14 days
  • Patient with no prior surgery
  • Patients with prior surgery
  • Sterile culture to serve as control
Results

• No previous surgery had 18% + cultures
• Previous surgery had 26% + cultures
• Sterile control had 13% + cultures
Their conclusions

• “Our data show that every + culture does not represent a true infection”

• “The presence of a commensal relationship between P. Acnes and the shoulder cannot be excluded”

• “Long hold cultures can be false +”
Results: Infection classification

Relationship of Days until Detection and Infection Classification

Definite

Probable

Probable Contaminant

Days until culture growth

Mean = (4.2 days $\pm$ 1.7)

Mean = (8.2 days $\pm$ 5.8)

P = 0.037
Results: Infection Probability Over Time

Predicted Probabilities Based on Proportional Odds Model

**For each doubling in the number of days until detection, the odds of having a contaminant increased by a factor of .5 (p = 0.019)**
P. Acne

• Hold pre operative antibiotics (controversial)
• Pre operative testing to include aspirate
  – Fluid aspirate less likely to be positive than tissue samples
  – Arthroscopic tissue biopsy
• Intra – operative tissue samples for culture from at least three preferable five sites around the prosthetic:
  – Capsule,
  – Membrane between the humeral and glenoid component,
  – Joint fluid,
  – Periprosthetic tissue
P. Acne: Clinical Exam

- Pain
- No systemic findings
- Sometimes no loosening but some lucent lines
- Some have subtle non blanching skin redness around the shoulder
- Intra – operative tissue may have areas of softer or edematous tissue around the implant
Newer Tests: Synovial Alpha –Defensin (Synovasure™)

- Antibacterial peptides that represent a part of the innate immune system
- Expression of α-defensins in synovial fluid in prosthetic shoulder joint infection
## Results

Diagnostic parameters of α-defensin compared to conventional tests.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>C-reactive protein</th>
<th>Erythrocyte sedimentation rate</th>
<th>α-defensin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimized cut-off</td>
<td>0.35 mg/dL</td>
<td>22 mm/hr</td>
<td>0.48 ug/mL</td>
</tr>
<tr>
<td>Area Under the Curve</td>
<td>0.69</td>
<td>0.69</td>
<td>0.78</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>71</td>
<td>43</td>
<td>63</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>67</td>
<td>90</td>
<td>95</td>
</tr>
<tr>
<td>Positive Likelihood ratio†</td>
<td>2.1</td>
<td>4.3</td>
<td>12.1</td>
</tr>
<tr>
<td>Negative likelihood ratio‡</td>
<td>0.43</td>
<td>0.63</td>
<td>0.38</td>
</tr>
</tbody>
</table>

†A value > 5 is considered useful for ruling-in infection
‡A value < 0.2 is considered useful for ruling-out infection
Newer Tests
Synovial Interleukin-6

- Pro-inflammatory cytokine
  - Regulator of acute and chronic phase
  - Favors a transition from neutrophil to monocyte
  - Presence is critical for the persistence of inflammation\(^4,5\)

Results: **ROC curve**

**CONTROLS**
20 underwent arthroscopic rotator cuff repair and fluid was obtained for analysis

**REVISIONS**
32 patients underwent revision shoulder arthroplasty and fluid was obtained for analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Current Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.87</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.90</td>
</tr>
<tr>
<td>Positive Likelihood ratio†</td>
<td>8.45</td>
</tr>
<tr>
<td>Negative likelihood ratio‡</td>
<td>0.15</td>
</tr>
</tbody>
</table>

†A value > 5 is considered useful for ruling-in infection
‡A value < 0.2 is considered useful for ruling-out infection

Cut off: 359.3 pg/mL
Results: Clinical Diagnosis
Treatment Options: Chronic Infection

1. Suppressive antibiotic and prosthetic retention: Rarely Considered or Successful
2. Debridement, synovectomy, antibiotics and prosthetic retention: Rarely Successful
3. Resection arthroplasty: Rarely Accepted
4. Single stage re-implantation with IV antibiotics: Rarely planned as first choice, common unanticipated outcome
5. Two stage re-implantation with spacer and IV antibiotics: Preferred treatment best results but high morbidity.
Resection Arthroplasty

- Patient with poor health and low anticipated activity level
- Modest functional outcome
  - Waist level function
- Usually pain relief and cure of infection
- Improved management w/ less diagnostic delay

Maynou C, 2006
Two Stage Revision

- Component removal
- Cement- antibiotic spacer (vanco and tobra)
- IV antibiotics (6 wks)
- Exchange prosthetic arthroplasty at 3 months, repeat w/u
Infection after shoulder arthroplasty.

- Of 2512 primary and 222 revision prosthetic shoulders, 19 primary and 7 revision shoulder arthroplasties deep periprosthetic infection.
- 7 primary shoulder arthroplasties and 1 with a revision were referred with deep periprosthetic infection.
- The average time to diagnosis of infection was 3.5 years (range, 0-14.8 years).

Sperling JW; Kozak TK; Hanssen AD; Cofield RH CORR 2001 Jan;(382):206-16
Infection after shoulder arthroplasty.

- **Group I**
  - 21 resection arthroplasty, 6/21 had recurrent infection.
- **Group II**
  - 6 debridement and prosthetic retention, 3/6 reinfection and underwent a resection arthroplasty.
- **Group III**
  - 2 shoulders who had removal of the prosthesis, debridement, and immediate reimplantation, 1 had reinfection with resection arthroplasty
- **Group IV**
  - 3 shoulders had removal of the prosthesis, debridement, and delayed reimplantation.
  - No Reinfection.
Infection after shoulder arthroplasty.

• At final followup, patients with a prosthesis in situ had better pain relief and shoulder function than patients treated with resection arthroplasty.

• Delayed reimplantation best chance for pain relief, eradication of infection, and maintenance of shoulder function.

Sperling JW; Kozak TK; Hanssen AD; Cofield RH CORR 2001 Jan;(382):206-16
Personal Experience
Two Stage Exchange Experience

• 27 infected arthroplasty cases treated by two stage revision one surgeon JPI from 2001-2009

• First stage- resection of prosthesis
  – Post op IV antibiotics for 6-8 weeks
  – Off antibiotics avg 6 weeks and then culture, ESR, WBC diff

• Antibiotic spacer for avg 12 weeks

• Second stage – re-implantation arthroplasty +/- bone graft

Sebasan et al CORR 2011
<table>
<thead>
<tr>
<th></th>
<th>All Patients (n=27)</th>
<th>Stage 2: Reverse (n=16)</th>
<th>Stage 2: Hemi (n=9)</th>
<th>Stage 2 Reverse vs. Stage 2 Hemi p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications</td>
<td>8/27 (30)</td>
<td>7/16 (44)</td>
<td>1/9 (11)</td>
<td>P=0.09</td>
</tr>
<tr>
<td>Postop FF (degrees)</td>
<td>117.5 (31.5)</td>
<td>122.3 (32.1)</td>
<td>110.0 (34.3)</td>
<td>P=0.38</td>
</tr>
<tr>
<td>Postop ER (degrees)</td>
<td>24.4 (11.1)</td>
<td>25.0 (5.3)</td>
<td>22.2 (19.2)</td>
<td>P=0.76</td>
</tr>
<tr>
<td>Baseline PENN</td>
<td>23.1 (19.2)</td>
<td>24.9 (22.3)</td>
<td>22.1 (13.3)</td>
<td>P=0.77</td>
</tr>
<tr>
<td>Last Follow-Up (months)</td>
<td>25.9 (20.6)</td>
<td>27.3 (19.9)</td>
<td>24.2 (25.8)</td>
<td>P=0.79</td>
</tr>
<tr>
<td>Last Follow-Up PENN</td>
<td>58.4 (22.4)</td>
<td>61.6 (19.3)</td>
<td>54.8 (29.1)</td>
<td>P=0.58</td>
</tr>
</tbody>
</table>
One Stage Revision
Is it every appropriate or effective?
Clinical Scenario

• A patient is determined to require revision surgery for mechanical failure of a shoulder implant
• Patient undergoes a successful revision surgery, with routine intra-operative tissue samples sent into microbiology
• A few days later, after patient is dismissed from the hospital, microbiology calls to report that one of the tissue samples was positive for *Propionibacterium acnes*
• Since patient had no pre operative or intra-operative evidence for infection besides the intra-operative culture, what is the next step?
Methods

• 187 patients undergoing revision surgery
  - 48 with at least one positive intraoperative culture
  - 17 without signs of a clinical infection
  - 31 with signs of a clinical infection
Results

• Only 1 of the 17 patients (5.9%) with a positive intraoperative culture developed a subsequent clinical infection
  – Interestingly, this was from a patient with a culture originally labeled as a contaminant
• The most common pathogen cultured at revision surgery was Propionibacterium acnes (10/17, 56%)
  – followed by coagulase negative Staphylococcus species (6/17, 35%)
• ESR and CRP were within normal levels for all 17 patients
Results

• For the 31 patients treated for clinical infections with two stage revision and at least 6 weeks of IV antibiotics after the first stage,
  - 5 (16%) had minor complications related to antibiotic therapy,
  - 1 acquired a *C. difficile* infection

• Low virulence and clinically unexpected infections treated with only one stage revision without long term post operative antibiotics have a low risk for recurrent infection.
Conclusion

• Low virulence and clinically unexpected infections treated with only one stage revision without long term post operative antibiotics have a low risk for recurrent infection.
After a one stage revision

- Keep patient on oral antibiotics until final culture results
- Clindmycin or doxycycline is preferred to cover P. Acne
Unexpected Positive Cultures

- More than one positive culture or
- One of four positive with 7 days or less
  - IF through full debridement with antibiotic cement all components
    - Consider no additional antibiotics
  - IF Incomplete removal then
    - 6 weeks IV antibiotics
    - Consider extended antibiotics
Recommendations: Diagnosis

• Serum for ESR an CRP
  – If positive likely infection assuming not inflammatory arthritis
  – If negative poor predictor

• Synovial Fluid culture, α defensin and IL6
  – If positive two stage revision
  – If negative one stage revision

• Minimum 4 tissue samples from both sides of the joint
Thank You for Your Attention