Management of deep postoperative shoulder infections: is there a role for open biopsy during staged treatment?

Alan L. Zhang, MD, Brian T. Feeley, MD, Brian S. Schwartz, MD, Teddy T. Chung, C. Benjamin Ma, MD*

Department of Orthopaedic Surgery, University of California San Francisco, San Francisco, CA, USA

Background: Despite the gold standard treatment of 2-stage exchange arthroplasty, reinfection after periprosthetic shoulder infections and periarticular osteomyelitis can be as high as 37%. This study describes a protocol to detect persistent deep shoulder infection before revision arthroplasty.

Methods: Patients who presented with periprosthetic shoulder infections and osteomyelitis after previous surgery were treated with a standardized protocol of irrigation and debridement (I&D), removal of implants, antibiotic cement spacer placement, and pathogen-directed antibiotic therapy for 6 weeks. After completion of antibiotics and resolution of clinical symptoms, specimens were obtained from an open biopsy performed in the operating room, followed by revision arthroplasty at a later date if final cultures were without evidence of infection. If evidence of infection persisted, then another course of I&D and antibiotic treatment was performed. American Shoulder and Elbow Surgeon scores were used to evaluate clinical outcomes.

Results: Eighteen patients were included between 2005 and 2012. The most common pathogens isolated were Propionibacterium acnes (44%), Staphylococcus epidermidis (39%), and S aureus (22%). Four patients (22%) had evidence of persistent infection on specimens from open biopsy and required subsequent rounds of I&D before replantation. The infecting pathogen in 75% of patients with persistent infection was P acnes, and 38% of patients with P acnes infection had recurrence. Mean follow-up of 24 months showed no signs of recurrent infection in any patient and an average American Shoulder and Elbow Surgeon score of 71.

Conclusion: Despite prior staged treatment for deep postoperative shoulder infections, specimens obtained from open biopsy before replantation detected a persistent infection rate of 22% in all patients and 38% in patients with P acnes infection, which may indicate a role for this procedure in the prevention of recurrent infections.

Level of evidence: Level IV, Case Series, Treatment Study.

Keywords: Deep shoulder infection; open biopsy; recurrent infection; shoulder arthroplasty

Periprosthetic shoulder infections, although less common than periprosthetic infections after total knee or hip arthroplasty, can have devastating effects. The reported incidence of infection after primary anatomic total shoulder arthroplasty (TSA) ranges between 0.4% and 3% and can be as high as 5% for reverse TSA (RTSA). When...
shoulder arthroplasty infection does occur, the current accepted treatment algorithm includes explant of the infected prostheses, followed by antibiotic cement spacer placement and at least a 6-week course of antibiotic therapy before reimplantation of a new prosthesis.\textsuperscript{4,16,18,19} Reinfection rates of between 0\% and 37\% have been reported after a 2-stage revision.\textsuperscript{16,18} In addition, \textit{Propionibacterium acnes}, a pathogen that can be difficult to diagnose and eradicate, is the primary pathogen in up to 20\% of shoulder arthroplasty infections.\textsuperscript{7,20}

Because TSA is becoming more common in the United States,\textsuperscript{14} further investigation is necessary to properly treat deep postoperative joint infections that may arise as a complication. In this study, we evaluated our single-institution protocol for treatment of periprosthetic joint infections and periarticular osteomyelitis. This protocol consists of explantation of the infected prosthesis, antibiotic spacer placement, and antibiotic treatment for 6 weeks, followed by culture of specimens from open biopsy to ensure eradication of infection before a new shoulder prosthesis is reimplanted. We hypothesized that this would be an effective method for the detection of persistent deep shoulder infections despite standard treatment with 2-stage exchange arthroplasty and would subsequently decrease recurrent infection rates.

**Methods**

This study consisted first of removal of all previous hardware through a standard deltopectoral approach once the deep infection was diagnosed by a combination of clinical signs and various diagnostic methods, including deep draining sinus, purulent drainage from the wound, erythema, abnormal white blood cell (WBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), computed tomography, magnetic resonance imaging, and joint aspiration. This was followed by a thorough debridement of necrotic and infected tissue, and copious irrigation with antibiotic saline solution. A resection arthroplasty of the humeral head was performed in the setting of osteomyelitis of the humeral head, diagnosed through magnetic resonance or computed tomography imaging and in some cases with a bone biopsy specimen, if there had not already been a humeral prosthesis. Any previous cement was removed with osteotomes or an ultrasonic bone cement removal device. Antibiotic-impregnated cement consisting of 1 gram vancomycin and 1.2 grams tobramycin for every bag of polymethyl methacrylate was used to space the joint before the wound was closed (Fig. 1).

After surgical therapy, patients were administered pathogen-directed antibiotic therapy, as determined by infectious diseases specialists, for at least 6 weeks. Patients were re-examined a minimum of 4 weeks after completion of this course of antibiotic therapy. After resolution of clinical signs of infection and normalization of CRP and ESR, the patients underwent an open biopsy and limited debridement in the operating room.

This procedure consisted of using the previous deltopectoral incision and deep dissection until the antibiotic spacer and bone junction was visualized. At this point, a specimen of the surrounding soft tissue and bone was obtained and sent for cultures, and a limited debridement of scar tissue was performed. At least 3 cultures were taken at each procedure and held between 7 and 14 days, according to hospital protocol, to evaluate for bacterial growth and to decrease the risk of skin contamination. If the results of the cultures of the open biopsy specimens were negative, then the patient was scheduled for reimplantation of a shoulder prosthesis with removal of the antibiotic spacer. However, if the culture results were positive for an organism, then the patient underwent another formal irrigation and debridement (I&D) with exchange of the antibiotic spacer and another 6-week course of directed antibiotic therapy. This process was repeated until cultures from the open biopsy specimen were negative.

This treatment algorithm was performed on 18 patients affected with deep shoulder infections at our institution from 2005 through 2012. The patients were monitored in the clinic after completion of the treatment protocol and replantation of new shoulder components for up to 3 years. American Shoulder and Elbow Surgery (ASES) scores, range of motion, and pain levels were recorded during follow-up, and analysis of variance testing was used to determine statistical significance, with significance set at \( P < .05 \).

**Results**

During the study period, 18 patients (15 men and 3 women) presented with evidence of periprosthetic joint infection or osteomyelitis after shoulder surgery. Five of the 18 infections occurred at our institution between 2005 and 2012, and the index procedures in other 13 patients occurred at other hospitals. Mean patient age was 69 years (range, 52-88 years). The mean follow-up was 24 months (range, 12-
Bacillus (11%), and epidermidis (39%), Staphylococcus recovered bacteria (50%), followed by acnes in 8, replanted with a RTSA. The patient's third open biopsy were negative, and he was patient had positive cultures again at his third biopsy and patients, and their prosthesis was able to be replanted. One antibiotic therapy. After a second course of therapy, specific who underwent the treatment according to the protocol, 4 (22%) continued to have positive cultures from specimens obtained at the first open biopsy and required another course of formal I&D, spacer exchange, and a 6-week course of antibiotic therapy. After a second course of therapy, specimens from repeat biopsies were sterile for 3 of these 4 patients, and their prosthesis was able to be replaced. One patient had positive cultures again at his third biopsy and required a third round of surgical and antibiotic therapy according to the protocol. Results from specimens from this patient's third open biopsy were negative, and he was replanted with a RTSA.

Among these patients with shoulder arthroplasty infection who underwent the treatment according to the protocol, 4 (22%) continued to have positive cultures from specimens obtained at the first open biopsy and required another course of formal I&D, spacer exchange, and a 6-week course of antibiotic therapy. After a second course of therapy, specimens from repeat biopsies were sterile for 3 of these 4 patients, and their prosthesis was able to be replaced. One patient had positive cultures again at his third biopsy and required a third round of surgical and antibiotic therapy according to the protocol. Results from specimens from this patient's third open biopsy were negative, and he was replanted with a RTSA.

Among our 18 patients, Propionibacterium species (P acnes in 8, P avidum in 1) were the most commonly recovered bacteria (50%), followed by Staphylococcus epidermidis (39%), S aureus (22%), gram-negative rods (11%), and Bacillus species (6%). More than 1 pathogen was present in 22% of patients (Table I). Propionibacterium acnes was present in 3 of the 4 patients (75%) who required multiple biopsies and I&Ds. Among the 3 patients with residual infection who required an additional course of treatment according to the protocol, 1 grew P acnes, 1 grew P acnes and S epidermidis, and 1 grew S epidermidis alone. The patient who required 2 subsequent I&Ds after the initial explant was positive for P acnes at both of the repeat biopsies. In these 4 patients, the culture of each subsequent open biopsy specimen grew the same organism as the original culture. Overall, the recurrence rate in patients who had P acnes infection was 38%.

At the most recent follow-up, all 18 patients were infection free, with average shoulder forward flexion (FF) of 127°, abduction (Abd) of 116°, external rotation (ER) of 33° and internal rotation (IR) to L2. Fifteen patients were pain free; 1 patient had pain scale score of 2 of 10, 1 had 3 of 10, and 1 reported 5 of 10. The average ASES score for the 18 patients was 71 (range, 50-100). When analyzing the 4 patients who had multiple biopsies, the average ASES score was 78, the average range of motion was FF, 142°; Abd, 140°; ER, 39°; and IR, L2. By analysis of variance testing, these results showed no statistical difference compared with those of the 14 patients who had only 1 biopsy (P = .40).

Discussion

In this study, we presented our institution’s protocol for treatment of deep periprosthetic infection and periarticular osteomyelitis of the shoulder. When the open biopsy before replantation protocol was used, 22% of patients had persistent deep infections despite the standard treatment with explant, I&D, antibiotic spacer, and intravenous (IV) antibiotics for 6 weeks. This amounted to a 22% rate of persistent infection despite the current gold standard treatment and absence of clinical symptoms as well as normalization of infection laboratory results. These patients would have likely had a recurrence of periprosthetic joint infection had the prosthesis been replanted without undergoing the biopsy. The prosthesis was replanted successfully in all 18 patients in this study, and all remained free of infection at an average follow-up of 24 months, with an average ASES score of 71. Thus, this protocol may represent an approach that can limit the rate of recurrence after periprosthetic shoulder infections.

The reported incidence of infection after primary anatomic TSA ranges between 0.4% and 3% and can be as high as 5% for RTSA.1-3,8,9,13,17 In addition, recurrent infection rates can be as high as 37%, despite the gold standard treatment of 2-stage revision.18 One reason for this high recurrent infection rate is the difficulty of detecting persistent infections with current techniques. A recent study by Grosso et al12 showed that frozen sections taken at the time of revision shoulder arthroplasty had a low sensitivity for detection of infection (67%) and an even lower sensitivity for detection of P acnes (50%). Our results indicate that taking tissue samples and then holding them for culture before replantation is more accurate than taking frozen sections at the time of replantation and is one reason why we do not perform frozen sections as part of our protocol.

With respect to the timing of the open biopsy, after the index removal of hardware for periprosthetic infection or resection arthroplasty for periarticular osteomyelitis along with placement of an antibiotic spacer, we then give culture-specific IV antibiotics for 6 weeks. After the 6-week IV antibiotic treatment is completed, we then allow for a 4-week antibiotic holiday period before returning for an open biopsy. The delay between the removal of implants and open biopsy is to allow for a full 6-week course of IV antibiotic treatment in an attempt to eradicate the deep infection and then allow for a 4-week antibiotic holiday to prevent any false-negative culture results for the IV antibiotic treatment.

Further, we do not believe that the antibiotic spacer influenced any culture results. The elution of antibiotics and more specifically vancomycin, which is preferably used
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>Gender</th>
<th>Type of infection</th>
<th>Culture results</th>
<th>Open biopsies until clear of infection (No.)</th>
<th>Replanted prosthesis</th>
<th>Follow-up (mon)</th>
<th>ASES score</th>
<th>Shoulder range of motion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>73</td>
<td>M</td>
<td>Infected RTSA</td>
<td>P. acnes</td>
<td>3</td>
<td>Right, RTSA</td>
<td>12</td>
<td>68</td>
<td>160 (FF), 150 (Abd), 40 (ER), L5 (IR)</td>
</tr>
<tr>
<td>2</td>
<td>64</td>
<td>F</td>
<td>Infected TSA</td>
<td>P. acnes</td>
<td>2</td>
<td>Left, RTSA</td>
<td>24</td>
<td>50</td>
<td>130 (FF), 130 (Abd), 70 (ER), T12 (IR)</td>
</tr>
<tr>
<td>3</td>
<td>61</td>
<td>M</td>
<td>Infected TSA</td>
<td>P. acnes and S. epidermidis</td>
<td>2</td>
<td>Left, RTSA</td>
<td>36</td>
<td>100</td>
<td>160 (FF), 140 (Abd), 10 (ER), L1 (IR)</td>
</tr>
<tr>
<td>4</td>
<td>80</td>
<td>M</td>
<td>Infected RCR</td>
<td>S. epidermidis</td>
<td>2</td>
<td>Left, RTSA</td>
<td>36</td>
<td>92</td>
<td>120 (FF), 140 (Abd), 35 (ER), L1 (IR)</td>
</tr>
<tr>
<td>5</td>
<td>52</td>
<td>F</td>
<td>Infected RTSA</td>
<td>P. aeruginosa</td>
<td>1</td>
<td>Left, RTSA</td>
<td>12</td>
<td>47</td>
<td>170 (FF), 130 (Abd), 10 (ER), S2 (IR)</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
<td>M</td>
<td>Infected RCR</td>
<td>P. acnes, S. aureus,</td>
<td>1</td>
<td>Left, RTSA</td>
<td>12</td>
<td>95</td>
<td>140 (FF), 110 (Abd), 30 (ER), T12 (IR)</td>
</tr>
<tr>
<td>7</td>
<td>65</td>
<td>M</td>
<td>Infected Hemi</td>
<td>S. epidermidis</td>
<td>1</td>
<td>Right, RTSA</td>
<td>12</td>
<td>52</td>
<td>110 (FF), 100 (Abd), 5 (ER), S2 (IR)</td>
</tr>
<tr>
<td>8</td>
<td>74</td>
<td>M</td>
<td>Infected RCR</td>
<td>S. epidermidis</td>
<td>1</td>
<td>Left, RTSA</td>
<td>24</td>
<td>67</td>
<td>110 (FF), 117 (Abd), 0 (ER), S1 (IR)</td>
</tr>
<tr>
<td>9</td>
<td>59</td>
<td>M</td>
<td>Infected RTSA</td>
<td>Bacillus spp</td>
<td>1</td>
<td>Left, RTSA</td>
<td>36</td>
<td>88</td>
<td>140 (FF), 85 (Abd), 0 (ER), T11 (IR)</td>
</tr>
<tr>
<td>10</td>
<td>83</td>
<td>M</td>
<td>Infected Hemi</td>
<td>Serratia marcescens, P. acnes, S. aureus</td>
<td>1</td>
<td>Left, TSA</td>
<td>36</td>
<td>67</td>
<td>140 (FF), 120 (Abd), 60 (ER), T12 (IR)</td>
</tr>
<tr>
<td>11</td>
<td>88</td>
<td>M</td>
<td>Infected ORIF</td>
<td>P. avidum</td>
<td>1</td>
<td>Left, RTSA</td>
<td>24</td>
<td>52</td>
<td>130 (FF), 110 (Abd), 20 (ER), T12 (IR)</td>
</tr>
<tr>
<td>12</td>
<td>74</td>
<td>M</td>
<td>Infected TSA</td>
<td>P. acnes</td>
<td>1</td>
<td>Right, RTSA</td>
<td>24</td>
<td>72</td>
<td>80 (FF), 90 (Abd), 30 (ER), T11 (IR)</td>
</tr>
<tr>
<td>13</td>
<td>54</td>
<td>F</td>
<td>Infected RCR</td>
<td>S. epidermidis</td>
<td>1</td>
<td>Left, Hemi</td>
<td>12</td>
<td>67</td>
<td>50 (FF), 60 (Abd), 60 (ER), T12 (IR)</td>
</tr>
<tr>
<td>14</td>
<td>62</td>
<td>M</td>
<td>Infected RCR</td>
<td>P. acnes</td>
<td>1</td>
<td>Right, RTSA</td>
<td>24</td>
<td>85</td>
<td>140 (FF), 140 (Abd), 80 (ER), T12 (IR)</td>
</tr>
<tr>
<td>15</td>
<td>72</td>
<td>M</td>
<td>Infected TSA</td>
<td>P. acnes, S. epidermidis</td>
<td>1</td>
<td>Left, RTSA</td>
<td>12</td>
<td>50</td>
<td>90 (FF), 80 (Abd), 30 (ER), S2 (IR)</td>
</tr>
<tr>
<td>16</td>
<td>75</td>
<td>M</td>
<td>Infected Hemi</td>
<td>S. aureus</td>
<td>1</td>
<td>R Hemi</td>
<td>36</td>
<td>68</td>
<td>140 (FF), 110 (Abd), 80 (ER), T12 (IR)</td>
</tr>
<tr>
<td>17</td>
<td>77</td>
<td>M</td>
<td>Infected TSA</td>
<td>S. aureus</td>
<td>1</td>
<td>L Hemi</td>
<td>36</td>
<td>88</td>
<td>140 (FF), 130 (Abd), 45 (ER), T12 (IR)</td>
</tr>
<tr>
<td>18</td>
<td>72</td>
<td>M</td>
<td>Infected RCR</td>
<td>S. epidermidis</td>
<td>1</td>
<td>R RTSA</td>
<td>24</td>
<td>82</td>
<td>140 (FF), 142 (Abd), 30 (ER), L1 (IR)</td>
</tr>
</tbody>
</table>

NOTE. Shoulder range of motion: FF, Abd, and ER are in degrees (*°*); IR are vertebral levels reaching behind the back (BTB).

Abd, abduction; ASES, American Shoulder and Elbow Surgeons; ER, external rotation; F, female; FF, forward flexion; Hemi, hemiarthroplasty of humeral head; IR, internal rotation; M, male; ORIF, proximal humerus open reduction internal fixation; P. acnes, Propionibacterium acnes; RCR, rotator cuff repair; RTSA, reverse total shoulder arthroplasty; S. aureus, Staphylococcus aureus; S. epidermidis, Staphylococcus epidermidis; TSA, total shoulder arthroplasty.
at our institution, from a cement spacer is highest in the first 8 days and then drops off significantly, as reported by Galvez-Lopez et al.11 Any persistent infection that remains at the open biopsy point should therefore have avoided any significant effects of the antibiotic spacer as well as the previous 6-week course of IV antibiotics.

The mean follow-up for the 18 patients was 2 years. At the most recent follow-up, all 18 patients were free of infection, with average shoulder FF of 127°, Abd of 116°, ER of 33°, and IR to L2, and an average ASES score of 71 (range, 50-100). These results are comparable to those of recent outcomes after shoulder arthroplasty.6 Cuff et al6 reported average ASES scores after RTSA in 112 patients were 77, with FF of 118°, Abd of 110°, and ER of 28°. There was no relationship between the original infection, whether it was in hemiarthroplasty, TSA, RTSA, or osteomyelitis after rotator cuff repair, and outcomes after replantation. This indicates that patients with previous deep infections, when finally replanted with a prosthesis, achieved good clinical results similar to patients without a previous infection and that the additional operative procedure of an open biopsy did not cause greater morbidity. Further, the number of biopsies and I&Ds did not correlate with the clinical outcome, because the average ASES score and range of motion of the 4 patients who underwent more than 1 round of biopsy showed no statistical difference from the rest of the group. Although we recognize the potential detrimental effects of additional surgery, including lengthened time without an implant, higher costs, scarring, and risks associated with more surgeries, the ultimate clinical outcome may be improved with this protocol, and total costs and morbidity may be decreased by preventing replantation of hardware in a persistently infected patient.

Of the 4 patients with persistent infections found in specimens of the open biopsy, 3 were clear of infection after another course of I&D, spacer exchange, and IV antibiotics for 6 weeks. One of the 4 patients had positive culture results at the second open biopsy and required 1 more round of I&D, spacer exchange, and IV antibiotics before the infection cleared. The average age of these 4 patients was 70 years (range, 61-80 years), and average follow-up was 27 months (range, 12-36 months). All 4 patients had no clinical signs of infection and initially elevated infection markers (WBC, ESR, and CRP) that had normalized after their initial treatment course before the first open biopsy. Two patients had infected TSAs, 1 patient had an infected RTSA, and 1 had a deep periarticular osteomyelitis infection after rotator cuff repair. The patient who required 2 subsequent I&Ds after the index procedure was positive for \( P \) acnes and was treated with vancomycin, followed by rifampin and daptomycin, and 1 grew \( S \) epidermidis and was treated with meropenem and moxifloxacin, followed by linezolid. All 4 patients were treated with culture-specific antibiotics and eventually their RTSA was replanted. The average ASES score for these 4 patients was 78, which was not significantly different from the average score of 69 for other 14 patients (\( P = .40 \)). Because \( P \) acnes was present in 3 of the 4 patients (75%) who required multiple biopsies and I&Ds, this pathogen may be a risk factor for recurrent infection. Therefore, periprosthetic joint infections that are culture positive for \( P \) acnes may have additional benefit from an open biopsy before replantation of a prosthesis.

In addition, a large proportion of shoulder infections are known to be caused by \( P \) acnes (20%), which has been reported to be more difficult to diagnose and eradicate,7,20 and, more recently, even implicated as a cause in glenohumeral arthropathy by Levy et al.15 In this study, \( P \) acnes was isolated in 8 of 18 patients (44%) and 3 of these 8 patients (38%) would need multiple rounds of I&D before the infection was eradicated. These can be isolated cases of \( P \) acnes (50%) or polymicrobial infections (50%), but \( P \) acnes was one of the pathogens in all microbial cases. Further, 7 of 8 patients with \( P \) acnes infections in this series were men, which may be a trend that necessitates further investigation. These results further substantiate the difficulties of treating \( P \) acnes infections and the need for development of improved protocols.

Limitations of this study include the small sample size of 18 patients and the relatively short follow-up of 2 years. Yet, the purpose of the study was to show that there may be value in using open biopsy to obtain specimens during staged treatment, and its ability to detect persistent infections in 22% of patients in this cohort gives cause for further investigation. The benefits and drawbacks of an added operative procedure in reducing recurrent deep shoulder infections can be better elucidated with a larger cohort and longer follow-up. This is a future aim, because our institution will continue to collect data using this treatment protocol on periprosthetic shoulder infections. Further, comparing the results of a shoulder aspiration with the results of performing a full open biopsy may be beneficial. If accurate cultures can be obtained from the aspiration, then that may be a less invasive form of sampling for persistent deep infections.

**Conclusion**

We present a protocol of open biopsy before replant of shoulder prostheses for patients with previous deep postoperative infections. In doing so, we detected a persistent infection rate of 22% in all patients and 38% in patients with \( P \) acnes infection despite prior staged
treatment and resolution of clinical symptoms, which may indicate a role for open biopsy in the prevention of recurrent infections.

Disclaimer

Dr Ma received educational support and research support from Zimmer, Inc. The other authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

References