Arthroscopic Tissue Culture for the Evaluation of Periprosthetic Shoulder Infection

Matthew F. Dilisio, MD, Lindsay R. Miller, MPH, Jon J.P. Warner, MD, and Laurence D. Higgins, MD

Investigation performed at the Boston Shoulder Institute, Brigham and Women’s Hospital/Massachusetts General Hospital/Harvard Medical School, Boston, Massachusetts

Background: Periprosthetic shoulder infections can be difficult to diagnose. The purpose of this study was to investigate the utility of arthroscopic tissue culture for the diagnosis of infection following shoulder arthroplasty. Our hypothesis was that culture of arthroscopic biopsy tissue is a more reliable method than fluoroscopically guided shoulder aspiration for diagnosing such infection.

Methods: A retrospective review identified patients who had undergone culture of arthroscopic biopsy tissue during the evaluation of a possible chronic periprosthetic shoulder infection. The culture results of the arthroscopic biopsies were compared with those of fluoroscopically guided glenohumeral aspiration and open tissue biopsy samples obtained at the time of revision surgery.

Results: Nineteen patients had undergone arthroscopic biopsy to evaluate a painful shoulder arthroplasty for infection. All subsequently underwent revision surgery, and 41% of those with culture results at that time had a positive result, which included Propionibacterium acnes in each case. All arthroscopic biopsy culture results were consistent with the culture results obtained during the revision surgery, yielding 100% sensitivity, specificity, positive predictive value, and negative predictive value. In contrast, fluoroscopically guided glenohumeral aspiration yielded a sensitivity of 16.7%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 58.3%.

Conclusions: Arthroscopic tissue biopsy is a reliable method for diagnosing periprosthetic shoulder infection and identifying the causative organism.

Level of Evidence: Diagnostic Level I. See Instructions for Authors for a complete description of levels of evidence.

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Periprosthetic joint infection can be a devastating complication of arthroplasty, with substantial associated morbidity and cost. With the projected increase in the number of joint arthroplasties performed in the United States over the next twenty years, the societal burden of prosthetic joint infections will likely increase. The evaluation of a painful prosthetic joint routinely involves a patient history, physical examination, and inflammatory markers in peripheral blood if infection is in the differential diagnosis. Joint aspiration is routinely performed to evaluate the synovial fluid for evidence of infection.

Although a reliable algorithm for the evaluation of chronic infection in a prosthetic joint has been established in the total knee and hip arthroplasty literature, the same is not true for shoulder arthroplasty. The biologic milieu of the shoulder differs from that of the hip and knee, as evidenced by the bacteria that are commonly identified in periprosthetic shoulder infections.

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A commentary by Joaquin Sanchez-Sotelo, MD, PhD, is linked to the online version of this article at jbjs.org.
Specifically, *Propionibacterium acnes* is preferentially identified in periprosthetic shoulder infections compared with periprosthetic knee or hip infections. This bacterium can be very difficult to isolate in routine laboratory cultures. In addition, routine blood tests have demonstrated poor sensitivity and specificity for detecting periprosthetic shoulder infections, in contrast to reports in the hip and knee arthroplasty literature. An algorithm that involves joint aspiration may not be as reliable in the shoulder as in the hip and knee, and a more sensitive and specific method of identifying the causative organism may be more advantageous.

Some studies have indicated that arthroscopic biopsy of a prosthetic joint may be a more accurate method for diagnosing infection. Obtaining tissue rather than aspirated synovial fluid for culture may more likely identify bacteria such as *P. acnes*, which may be difficult to culture and often exists as an intracellular...
organism. The purpose of the present study was to investigate the utility of arthroscopic biopsy for diagnosing infection following shoulder arthroplasty. Our hypothesis was that arthroscopic biopsy is a reliable method for making such a diagnosis.

Materials and Methods

A retrospective review identified all patients who had undergone shoulder arthroplasty and subsequently had tissue obtained during arthroscopy and cultured for the evaluation of possible infection during a five-year period by the two senior authors (L.D.H. and J.J.P.W.). Institutional review board approval was obtained prior to data collection for the study. Inclusion criteria were a patient age of at least eighteen years at the time of the arthroscopic biopsy and any type of painful index anatomic shoulder arthroplasty that required revision surgery. Patients were excluded if they had no recorded culture results for the arthroscopically obtained tissue, an acute postoperative infection within six months after surgery, or follow-up of less than three months after arthroscopic biopsy. If arthroscopic biopsy was performed on multiple occasions in the same shoulder, only the initial diagnostic biopsy was included in the analysis. The senior authors evaluated approximately 350 painful shoulder arthroplasties performed during the study time period. Arthroscopy was performed in patients for whom the diagnosis of periprosthetic infection could not be reasonably confirmed or refuted by the patient history, physical examination, imaging studies, and laboratory data.

Patient demographic data included sex, referral from another surgeon, age at the time of the index arthroplasty and of the arthroscopic biopsy, type of index and revision procedures, and number of prior shoulder procedures performed. Preoperative patient data included pain on a visual analog scale (VAS) running from 0 to 10 and function as measured with the subjective shoulder value (SSV), which runs from 0% to 100%\textsuperscript{21,22}. Preoperative laboratory data included the white blood-cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) level.

All fluoroscopically guided glenohumeral aspirations were performed by a board-certified radiologist with fellowship training in musculoskeletal radiology. No local anesthetic was used within the glenohumeral joint, and contrast was utilized to confirm the intra-articular location. Arthroscopic tissue biopsies were performed according to a previously described technique\textsuperscript{18}. The patient was in the beach-chair position, and a pneumatic arm holder was used. After examination under anesthesia, a standard anterior portal was established through the rotator interval immediately superior to the subscapularis tendon with use of spinal needle localization. A sequential diagnostic arthroscopy was then performed with an arthroscopic probe to evaluate glenoid stability, the presence of synovitis or metallosis, loose bodies, scar tissue, and the status of the rotator cuff (Figs. 1-A through 1-D). Any tissue with an abnormal appearance was biopsied, generally through the anterior portal with use of an arthroscopic basket punch, grasper, or pituitary rongeur. Tissue exhibiting synovitis was often found at the margins of the glenoid component and was cultured. At least three tissue specimens, all of which had been in contact with the prosthesis, were routinely obtained from separate areas and cultured\textsuperscript{23}. The arthroscope was then redirected into the subacromial space, and a standard subacromial diagnostic arthroscopy was performed. If any tissue with an abnormal appearance was evident in the subacromial space, this was also biopsied and cultured. At least three tissue specimens, all of which had been in contact with the prosthesis, were routinely obtained from separate areas and cultured\textsuperscript{23}. The arthroscope was then redirected into the subacromial space, and a standard subacromial diagnostic arthroscopy was performed. If any tissue with an abnormal appearance was evident in the subacromial space, this was also biopsied and cultured. The procedure represented a diagnostic tool, and no therapeutic arthroscopic maneuvers were performed at the time of surgery. Prophylactic antibiotics were not administered until after tissue had been obtained for culture. Postoperatively, a simple arm sling was used for one week, after which active and passive motion was allowed. All procedures were performed on an outpatient basis.

Each tissue specimen was placed directly into a sterile BBL Port-A-Cul specimen tube (Becton, Dickinson and Company, Franklin Lakes, New Jersey).
on the surgical field and transported immediately to the microbiology laboratory for aerobic and anaerobic culture. Each specimen was immediately processed by the laboratory and inoculated on the following media: 5% sheep blood agar, chocolate agar, MacConkey agar, thioglycollate agar, Columbia agar with blood, Brucella agar with blood, anaerobic LKV (laked blood, kanamycin, vancomycin) agar, and thioglycollate agar with hemin and vitamin K. Specimens were incubated at 35°C to 37°C, either in 5% to 7% CO₂ (aerobic cultures) or anaerobically. Cultures were examined every twenty-four to forty-eight hours for growth. All fluid and tissue specimens were submitted to the microbiology laboratory for culture with deliberate instructions to hold the cultures for at least twenty-one days to specifically identify *P. acnes* if it was present.

The primary outcome measures were the culture results of the aspirations, the arthroscopic biopsies, and the open biopsies at the time of revision surgery. The type of organism identified and the time to a positive culture were tabulated, along with the results of the arthroscopic tissue biopsy samples of the revision surgery; both had a prior positive arthroscopic biopsy and were treated as infected. *P. acnes* was identified in the intraoperative open biopsy cultures of all seventeen patients who had a positive arthroscopic biopsy, and the ten patients with a negative arthroscopic biopsy also had a negative open biopsy. This resulted in a sensitivity, specificity, positive predictive value, and negative predictive value of 100% for arthroscopic biopsy. In the single patient with a positive fluoroscopically guided aspiration culture, *P. acnes* was also identified in the cultures from both of the other specimen types (those from the arthroscopic and open tissue biopsies). Fluoroscopically guided aspiration did not identify *P. acnes* in five of the six patients with positive cultures from both arthroscopic and open tissue biopsies. This resulted in a sensitivity of 16.7%,

*The values are given as the mean and the standard deviation, with the range in parentheses.*

| TABLE III Preoperative Patient Pain and Function and Pre-Biopsy Laboratory Values* |
|----------------------------------|---------------------------------|-------------------------------|-------------------|
| VAS pain                         | 8.87 ± 1.19 (6.0-10.0)          | SSV (%)                       | 27.92 ± 18.27 (10.0-60.0) |
| WBC (10⁴ cells/μL)               | 8.4 ± 3.30 (1.6-14.2)           | ESR (mm/hr)                   | 16.5 ± 12.89 (5.0-40.0)  |
| CRP (mg/L)                       | 9.6 ± 7.80 (0.2-21.2)           |

*The values are given as the mean and the standard deviation, with the range in parentheses.*

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**Results**

Nineteen patients (eight female and eleven male) who had undergone arthroscopic biopsy to evaluate a painful shoulder arthroplasty for infection were identified. Fourteen had been referred from another surgeon to the two senior authors after the index arthroplasty. The mean age at the time of the index arthroplasty was 56.7 years, and the mean interval (and standard deviation) between the index arthroplasty and the arthroscopic biopsy was 3.0 ± 2.0 years (range, 0.7 to 7.7 years) (Table I). The index procedure had been total shoulder arthroplasty (TSA) in fourteen patients, hemiarthroplasty in four, and hemiarthroplasty with biologic glenoid resurfacing in one (Table II). The affected shoulder had undergone a mean of 2.5 ± 1.4 surgical procedures (range, one to six procedures) prior to the arthroscopy. Three patients had undergone a formal revision arthroplasty prior to evaluation. The mean preoperative VAS pain score was 8.9 ± 1.2 (range, 6 to 10), and the SSV was 27.9% ± 18.3% (range, 10% to 60%). The mean preoperative WBC count was 8.4 ± 3.3 × 10⁴ cells/μL (range, 1.6 to 14.2 × 10⁴ cells/μL; normal, 4.5 to 11 × 10⁴ cells/μL), the ESR was 16.5 ± 12.9 mm/hr (range, 5.0 to 40.0 mm/hr; normal, 0 to 17 mm/hr), and the CRP level was 9.6 ± 7.8 mg/L (range, 0.2 to 21.2 mg/L; normal, 0 to 8 mg/L) (Table III). None of the patients in the study population had concomitant elevation of the WBC, ESR, and CRP values.

Preoperative fluoroscopically guided glenohumeral aspiration was performed in fourteen of the nineteen patients. Only one (7%) of these fourteen patients had a positive culture of the aspirate, and the identified organism was *P. acnes*. Bacteria were identified in the arthroscopic tissue biopsy samples from nine (47%) of the nineteen patients. *P. acnes* was the identified organism in all nine cases, with concomitant growth of *Staphylococcus capitis* ssp. *ureolyticus* and *Enterococcus faecalis* in one specimen from one shoulder. *P. acnes* was identified at a mean of 10.1 ± 3.8 days (range, 5 to 18 days). Revision surgery was performed in all nineteen patients. Tissue was obtained intraoperatively and cultured for at least seven days in seventeen of the nineteen patients. Bacteria were identified in seven (41%) of these patients, and *P. acnes* was the identified organism in all seven cases (Table IV; see Appendix).

Two of the nineteen patients did not undergo biopsy during the revision surgery; both had a prior positive arthroscopic biopsy and were treated as infected. *P. acnes* was identified in the intraoperative open biopsy cultures of all seven patients who had a positive arthroscopic biopsy, and the ten patients with a negative arthroscopic biopsy also had a negative open biopsy. This resulted in a sensitivity, specificity, positive predictive value, and negative predictive value of 100% for arthroscopic biopsy. In the single patient with a positive fluoroscopically guided aspiration culture, *P. acnes* was also identified in the cultures from both of the other specimen types (those from the arthroscopic and open tissue biopsies). Fluoroscopically guided aspiration did not identify *P. acnes* in five of the six patients with positive cultures from both arthroscopic and open tissue biopsies. This resulted in a sensitivity of 16.7%,
TABLE IV Arthroscopic Biopsy, Aspiration, and Revision Surgery Biopsy Cultures

<table>
<thead>
<tr>
<th></th>
<th>Aspiration</th>
<th>Arthroscopic Biopsy</th>
<th>Open Biopsy at Revision</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>14</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>No. (%) with positive culture*</td>
<td>1 (7)</td>
<td>9 (47)</td>
<td>7 (41)</td>
</tr>
<tr>
<td>\textit{P. acnes}</td>
<td>1</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>\textit{Staphylococcus capitis ssp. ureolyticus}</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>\textit{Enterococcus faecalis}</td>
<td></td>
<td>1</td>
<td></td>
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</tbody>
</table>

*The mean time to a positive culture was 10.1 ± 3.79 days (range, 5 to 18 days).

There were no identified complications as a result of any of the arthroscopic biopsies. The mean time from the arthroscopic biopsy to the latest clinical follow-up was 23.6 ± 16.7 months (range, 4.4 to 53.3 months). All of the patients with a negative arthroscopic biopsy who subsequently underwent a single-stage revision had no clinical evidence of infection at the time of the latest follow-up.

**Discussion**

The principal results of this series demonstrate that arthroscopic tissue biopsy for the evaluation of infection following shoulder arthroplasty is an accurate method for diagnosing periprosthetic \textit{P. acnes} shoulder infections. Using the culture results from the open biopsies as the standard for comparison, culture of arthroscopically obtained tissue demonstrated 100% sensitivity, specificity, positive predictive value, and negative predictive value for identifying periprosthetic shoulder infection. This is in sharp contrast to the findings for fluoroscopically guided glenohumeral aspiration, which failed to identify \textit{P. acnes} in five of the six patients with a positive culture from both arthroscopic and open tissue biopsies.

Little published literature is available on the utility of arthroscopic biopsy in the evaluation of potential infection following shoulder arthroplasty. Morman et al. reviewed two patients in whom an arthroscopic biopsy identified a chronic \textit{P. acnes} periprosthetic shoulder infection after shoulder aspiration cultures demonstrated no growth even though the laboratory was specifically looking for \textit{P. acnes}\textsuperscript{13}. Because it is the senior authors’ experience that glenohumeral joint aspiration has low sensitivity for diagnosing periprosthetic shoulder infection, arthroscopic biopsy has become a routine step in the evaluation and treatment of our patients with a painful prosthetic shoulder when infection is suspected. Both the accuracy of the arthroscopic biopsy procedure and the insensitivity of fluoroscopically guided glenohumeral aspiration for identifying periprosthetic shoulder infection demonstrated in the present study support this practice. There were no complications as a result of the arthroscopic biopsy procedure, which supports its safety. Although we routinely prefer to perform arthroscopic tissue biopsy and culture in questionable cases, we will proceed directly to open biopsy and culture and antibiotic-impregnated cement spacer placement in those cases in which there is obvious implant

specificity of 100%, positive predictive value of 100%, and negative predictive value of 58.3% for the fluoroscopically guided aspiration (see Appendix).

All nineteen patients underwent revision surgery. Complete removal of the prosthetic components and placement of a custom antibiotic spacer was performed in eight of the nine patients with a positive arthroscopic tissue biopsy culture at a mean of 11.2 ± 8.9 weeks (range, 3.4 to 29.3 weeks) after the arthroscopic biopsy. The cement spacer was created according to a previously described technique\textsuperscript{22} with use of a 44-mm humeral head mold, 40 g of bone cement (Simplex P; Stryker, Kalamazoo, Michigan), 2.4 g of tobramycin, 1 g of vancomycin, and a 3.5-mm stainless-steel limited-contact dynamic compression plate (LC-DCP; Synthes, West Chester, Pennsylvania) bent to 135°. Once the antibiotic cement had cured and bound to the plate, the custom prosthesis was implanted into the proximal aspect of the humerus. All patients were treated with intravenous antibiotics for six weeks postoperatively under the direction of the infectious disease team on the basis of the bacterial sensitivity.

The spacer was subsequently removed in all eight patients during the second stage of the revision procedure (which involved reverse TSA in five, TSA in one, glenohumeral arthrodesis in one, and resection arthroplasty in one). Overall, eleven patients underwent a single-stage revision procedure (reverse TSA in six, TSA in three, glenohumeral arthrodesis in one, and resection arthroplasty in one). The one patient with a positive arthroscopic tissue biopsy culture who did not undergo placement of an antibiotic spacer underwent a single-stage revision from a TSA to a reverse TSA for glenoid loosening. In that patient, the positive growth of \textit{P. acnes} from the arthroscopic tissue biopsy was considered a contaminant because of the lack of laboratory and radiographic evidence of infection in addition to the negative result of the arthroscopic tissue culture. Nevertheless, \textit{P. acnes} was eventually identified from tissue obtained at the time of the revision. At twenty-five months of follow-up, the patient had not undergone any additional shoulder surgery and rated pain at rest as 0/10. She did report activity-related pain in the shoulder and an SSV of 60% as a consequence of the pain, but there was no clinical suspicion of a chronic periprosthetic shoulder infection and no additional surgery was planned.
loosening and one-stage reconstruction is not technically feasible.

The cost of an additional surgical intervention must be evaluated in relation to the potential clinical benefit to determine the value of the procedure. We routinely perform two-stage revisions for chronic infection in prosthetic shoulders, but the ideal treatment of periprosthetic shoulder infection is unclear.12,24-29.

Fuerst et al. compared the accuracy of preoperative knee aspiration with that of arthroscopic biopsy in patients undergoing exchange total knee arthroplasty for infection, utilizing culture of intraoperatively obtained tissue as the gold standard. The authors found that arthroscopic biopsy had superior sensitivity and negative predictive value compared with aspiration.20 The results of the present study involving shoulder arthroplasty are consistent with those findings. Schneeberger et al. reported the results of arthroscopic shoulder biopsies in nine non-arthroplasty patients. In that study, the authors routinely filtered the solid material obtained from the arthroscopic shaver during all arthroscopic revision procedures involving the shoulder. Although they studied a non-arthroplasty population, their results are similar to those of the present study in that nearly all patients with positive cultures had nearly normal preoperative laboratory markers of infection and fluoroscopically guided aspiration had low sensitivity (12.5%).

P. acnes is the most common cause of indolent infection following shoulder arthroplasty8,9, and the results of our study support that finding. It is interesting to note that no organism other than P. acnes was isolated in six of the seven patients diagnosed with infection. This aspect of the study is inconsistent with the results of previous studies demonstrating that other strains of bacteria, specifically Staphylococcus aureus and coagulase-negative Staphylococcus, are also commonly identified in periprosthetic shoulder infections.9,10. This could be explained by selection bias resulting from the retrospective nature of the present study and the fact that P. acnes is notoriously more indolent than other bacterial strains.

Because of the difficulty in diagnosing P. acnes infection by means of routine serum laboratory analysis and aspiration, the “surprise” intraoperative culture is a familiar concept to many surgeons performing revision shoulder arthroplasty.9,11. This situation often occurs when the surgeon has a low index of suspicion for infection after reviewing the recommended laboratory work and imaging prior to proceeding with revision shoulder arthroplasty but intraoperative cultures are positive later, often days to weeks after the surgery has been performed. The normal preoperative laboratory markers of infection in the population in the present study demonstrate how such laboratory values can be misleading in chronic periprosthetic shoulder infections. Our results are similar to those in prior studies demonstrating the insensitivity of preoperative laboratory markers of infection and glenohumeral aspiration for diagnosing occult periprosthetic shoulder infections.9,10,17 Intraoperative frozen sections can also be unreliable in the setting of revision shoulder arthroplasty.17 The treatment of patients with unexpected positive intraoperative cultures during revision shoulder arthroplasty remains controversial.9,11, However, the goal of arthroscopic biopsy prior to revision shoulder arthroplasty is to avoid this situation and provide a more sensitive tool in the armamentarium of the revision shoulder arthroplasty surgeon to more accurately manage patients with a potential infection of the shoulder.

This study has several limitations. In particular, the small study population and retrospective design limit the general application of the results. As previously stated, the study is prone to selection bias, and the nineteen patients who underwent arthroscopic biopsy may not truly represent the entire population of patients undergoing an evaluation for a periprosthetic shoulder infection. The population in this study did not include all patients undergoing revision who had positive cultures or confirmed infection. In addition, the tissue obtained at the time of revision surgery was held for a minimum of only seven days. It is possible that P. acnes would have been cultured from some of the patients with a negative open biopsy culture if that culture had been held longer.11 As a result, the sensitivity of the arthroscopic biopsy procedure is likely less than the 100% demonstrated in this study.

In conclusion, periprosthetic shoulder infections can be difficult to diagnose by routine methods. P. acnes is notoriously indolent and can often be present in patients with normal laboratory markers for infection and a negative culture following fluoroscopically guided glenohumeral aspiration. The results of this study support our hypothesis that evaluation of possible periprosthetic shoulder arthroplasty infection by culture of arthroscopically obtained tissue is a more reliable method than fluoroscopically guided aspiration and culture. Arthroscopic biopsy is a useful tool in the armamentarium of the revision shoulder arthroplasty surgeon to manage patients with potential infection involving the shoulder prosthesis.

Appendix

Tables showing the results of the patient work-ups and a comparison of the arthroscopic biopsy and aspiration culture results with those of the intraoperative biopsies are available with the online version of this article as a data supplement at jbjs.org.
References