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Utility of prerevision tissue biopsy sample to predict revision shoulder arthroplasty culture results in at-risk patients

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Background: The diagnosis of infection after shoulder arthroplasty can be challenging. The current study evaluated the utility of a prerevision biopsy sample in predicting positive cultures or a final diagnosis of infection in the setting of an "at-risk" failed shoulder arthroplasty.

Methods: The study reviewed 77 patients with no history of infection undergoing revision shoulder arthroplasty by a single surgeon between June 2010 and July 2015. All patients with a C-reactive protein and erythrocyte sedimentation rate within normal reference ranges and no fluid on aspirate, or an abnormal value for the erythrocyte sedimentation rate or C-reactive protein, or both, and no growth on aspirate, underwent a prerevision biopsy because they were considered "at-risk" for infection. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to evaluate the utility of biopsy specimens to predict positive cultures as well as a final determination of infection.

Results: A prerevision biopsy was performed in 17 patients with a failed arthroplasty. The sensitivity, specificity, PPV, and NPV, for a positive prerevision biopsy sample to predict a positive final culture were 0.75, 0.6, 0.82, and 0.5, respectively. The sensitivity, specificity, PPV, and NPV for an infection defined by a prerevision biopsy sample to predict an infection defined by the combined final revision and biopsy cultures were 0.9, 0.86, 0.9, and 0.86, respectively.

Conclusions: The ability for prerevision biopsy specimens of failed arthroplasties to predict the presence of bacteria at the time of revision surgery is high, although lower than previously reported. If biopsy results are used to define and predict a diagnosis of infection, the sensitivity, specificity, PPV, and NPV all significantly improve.

Level of evidence: Level III; Diagnostic Study

Keywords: Tissue biopsy; revision; shoulder arthroplasty; infection; cultures; arthroscopic

Sepsis and infection after shoulder arthroplasty is uncommon, with a reported rate of 1% to 2% for primary replacements and 3% to 4% for revision replacements.[1,10-12] Diagnosis of these relatively uncommon events can be extremely challenging. Most patients with chronically infected arthroplasties do not present with typical clinical signs of infection, except for pain. Numerous tests have been used in the setting of a painful arthroplasty before revision to aid in the diagnosis of infection, including blood work, aspiration, and various imaging studies such as plain radiographs and

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bone scans. Efforts have recently been made to determine other methods to identify infection in the setting of a painful arthroplasty, including serum interleukin 6 (IL-6), synovial IL-6, synovial α-defensin, and prerevision tissue biopsy samples.[2,6-9,14,15]

Complicating the problem even further is that one of the most common organisms resulting in infection is *Propionibacterium acnes*.[11,12] *P acnes* is extremely fastidious and often does not create a large inflammatory response.[1] Elevated inflammatory markers, such as white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), can aid in making the clinical diagnosis of infection, although these have been reported to be within normal reference ranges in 75% to 93% of patients with positive cultures at the time of revision arthroplasty.[4,13] Synovial fluid IL-6 and α-defensin have shown improved ability to predict infection in the setting of a painful arthroplasty compared with standard markers of inflammation.[6,7] Very limited data exist on the role of tissue biopsy cultures in evaluating a painful shoulder arthroplasty.[2,9,15]

The purpose of this study was to compare the results of prerevision shoulder biopsy cultures with final revision arthroplasty cultures to determine the ability of a positive prerevision biopsy culture to predict a positive final revision culture. The hypothesis is that prerevision biopsy cultures have a high sensitivity and specificity to predict final revision cultures. We also compared the ability of a prerevision diagnosis of infection based on the biopsy sample to accurately diagnosis a postrevision diagnosis of infection based on the combined results of the final revision and biopsy cultures.

Materials and methods

Medical records were retrospectively reviewed of all patients who underwent an arthroscopic or open biopsy of a painful shoulder arthroplasty by the primary surgeon (R.Z.T.) between June 2010 and July 2015. The current study focused on a select population of patients who underwent a surgical biopsy of a painful shoulder arthroplasty before definitive revision arthroplasty with component removal to determine whether the failure had an infectious etiology. Not all revision arthroplasties performed by the primary surgeon during the study period had a prerevision biopsy. An algorithm was followed to identify at-risk patients for infection, and these patients subsequently underwent a prerevision biopsy.

All patients with a painful arthroplasty underwent laboratory evaluation, including ESR and CRP, as well as a fluoroscopically guided intra-articular aspiration (cultures were held for 2 weeks). Patients were classified into 1 of 4 categories, and prerevision biopsy was performed according to the grouping: (1) gross purulence, drainage, fluctuance, a sinus tract or a positive aspirate (bacterial growth on culture), (2) ESR and CRP were normal and the aspiration had no growth, (3) results for ESR or the CRP, or both, were abnormal, with no growth on the aspiration, and (4) results for ESR and CRP were normal and no fluid was available on the aspirate.

Group 1 patients were considered infected; therefore, revision arthroplasty was performed consisting of explantation and placement of an antibiotic-impregnated cement hemiarthroplasty or a resection arthroplasty without performing a prerevision biopsy. Group 2 patients were considered at low risk for infection; therefore, revision arthroplasty was performed without performing a prerevision biopsy. Group 3 and 4 patients were considered "at-risk" for the presence of infection at definitive revision; therefore, prerevision biopsies were performed in these groups. The current study evaluates the patients treated in groups 3 and 4.

During the 5-year period, 17 prerevision biopsies were performed. A total of 77 revision arthroplasties were performed during the same period; therefore, only 22% of revisions also underwent a prerevision biopsy. All other revisions had normal results for ESR and CRP and a negative aspiration or were clinically infected with drainage, redness, or a sinus.

Biopsies were performed in an open or arthroscopic fashion. An open biopsy was performed in the setting of a known deficient rotator cuff (reverse total shoulder or anatomic arthroplasty with cuff deficiency). An open biopsy was performed using the proximal 3 cm of the prior deltopectoral incision for the biopsy. The proximal deltoid was retracted laterally, and the glenohumeral joint was entered lateral to the coracoid and conjoint tendon. An arthroscopic biopsy was performed for an anatomic arthroplasty with an intact rotator cuff. An arthroscopic biopsy was performed using a posterior portal for viewing and an anterior rotator cuff interval portal to retrieve intra-articular tissue. At least 2 and preferably 3 tissues samples were sent for Gram stain and culture, with cultures being held for 2 weeks.

Pathology specimens were not sent at the time of biopsy for the initial 4 patients evaluated during the course of this study. Starting in 2011, the addition of pathology to the biopsies became standard (remaining 13 patients in the series). Revision arthroplasty was performed at a minimum of 3 weeks after the biopsy to allow the skin incisions to fully heal.

The medical records were reviewed for demographic data, prebiopsy diagnosis, prebiopsy laboratory information (CRP, ESR), prebiopsy aspiration culture and Gram stain (if performed), biopsy specimen Gram stain and culture, and frozen section results from the biopsy sample (if performed). Final revision arthroplasty data were also obtained from the medical record, including the final revision arthroplasty procedure, Gram stain and cultures from the final revision sample, and final frozen section results from the final revision sample (if performed).

All cultures were assessed for aerobic and anaerobic bacteria held for 2 weeks with specific instructions to rule out *P acnes*. A minimum of 2 samples (3 samples for the final 15 patients) were taken for culture at the time of the biopsy and also at the time of revision arthroplasty. The biopsy samples were obtained from the glenohumeral joint during the arthroscopic and the open procedure in a random fashion. Samples for the revision cultures were obtained underneath the humeral implant or inside the humeral canal, surrounding the glenoid and underneath the glenoid component, if present.

Because the samples may be predisposed to contamination, we also used the definition of infection reported by Frangiamore et al[5] (Table I) to categorize patients. The only modification we made to the definition was that we substituted a positive culture for a positive aspirate culture in the "definite infection" group.[5] Diagnosis of "infection" is considered positive if patients are classified as having a "definite infection" or "probable infection."

"Definite infection" is defined as a positive ESR or CRP result and >1 positive culture (for biopsies —both obtained during the biopsy with the same bacteria; for revisions—both obtained during the revision with the same culture) or 1 positive revision culture and 1