Revision shoulder arthroplasty with positive intraoperative cultures: The value of preoperative studies and intraoperative histology

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Currently, there are no reported results of patients without overt infection who had a positive intraoperative culture during revision shoulder arthroplasty. We therefore reviewed the intraoperative and preoperative investigations as well as the postoperative course of these patients who had positive intraoperative cultures. We reviewed the results of 75 shoulders without overt infection that underwent revision shoulder arthroplasty at our institution between January 1, 1974 and December 31, 2002 who had positive intraoperative cultures. Preoperatively, the results of 67 (93%) of 72 white-blood-cell counts were negative, 64 (91%) of 70 polymorphonuclear percentage distributions were negative, and 36 (86%) of 42 samples of erythrocyte sedimentation rate were negative. C-reactive protein concentration was measured in 16 patients, of which 12 (75%) had negative results. Results of intraoperative histologic evaluations were negative in 67 (92%) of 73 patients. The most common pathogen cultured was Propionibacterium acnes *in 45 of 75, followed by* Staphylococcus epidermidis *in 10 of 75. Another operation was necessary in 10 (13%) of 75 shoulders to decrease pain or improve function. The mean time to re-revision was 2.5 years. The data from this study suggest that there are no good preoperative or intraoperative investigations to detect who will have a positive intraoperative culture at the time of revision shoulder arthroplasty. (J Shoulder Elbow Surg 2006;15: 402-406.)*

Shoulder arthroplasty has become an excellent treatment option for various shoulder disorders. Greater understanding of the biomechanics of shoulder function in conjunction with better prosthetic design has led to decreasing complications associated with shoulder arthroplasty. As with other joint replacement procedures, however, infection has remained one of the most devastating complications requiring revision surgery. The prevalence of deep periprosthetic infection involving shoulder arthroplasty is reported to be between 0% and 3.9% for unconstrained shoulder arthroplasties and 0% and 15.4% for constrained arthroplasties.[3,4,11,12] The rates of subclinical infection are less well known and studied as are the treatment options and outcomes of patients with indolent infections. With an aging population that will need an increasing number of arthroplasties, methods to prevent, diagnose, and treat this complication are important to help reduce the impact of an unrecognized infection that may ultimately lead to failure.

Recent reports have detailed infections with shoulder arthroplasty, but there still is little information available to guide clinical decision-making with respect to patients who have had a shoulder arthroplasty that may have subclinical infection. Suggestions for treatment of the infected shoulder arthroplasty include antibiotic suppression, débridement with prosthesis retention, direct prosthetic exchange, delayed reimplantation, resection arthroplasty, arthrodesis, and amputation.[2,4,8,11,12] Most of those options, however, pertain to deep periprosthetic infections that can be clinically diagnosed. The purpose of this study was to determine the usefulness of preoperative and intraoperative laboratory studies in predicting which patients without overt clinical signs of infection would have positive intraoperative cultures and to classify the fate of these patients based on postoperative treatment.

MATERIALS AND METHODS

Between 1974 and 2002, 389 patients underwent revision shoulder arthroplasty (439 surgeries) at the Mayo Clinic. A retrospective analysis was performed on 85 patients who had at least one positive intraoperative culture after revision shoulder arthroplasty. The patients were identified with the use of a computerized database that con-

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tained the files of all who have had joint arthroplasty surgery since 1969. Eleven patients (12 shoulders) were excluded because they had clinically overt signs of infection either preoperatively or at the time of surgery. These signs included having a sinus that communicated directly with the joint and had been actively draining, rapid clinical deterioration due to sepsis, or the observation of purulence at the time of surgery. The study evaluated 74 patients and 75 shoulders. The mean age of the patients at the time of revision was 59.5 years (range, 27-79 years). There were 50 men and 24 women. The cultures were taken from 48 right and 27 left shoulders.

The indications for the initial shoulder arthroplasty were osteoarthrosis in 34 shoulders, traumatic arthritis in 20, rheumatoid arthritis in 8, rotator cuff arthropathy in 7, chronic shoulder instability in 2, acute fracture in 2, other inflammatory arthropathies in 1, and parosteal osteogenic sarcoma in 1 shoulder. Ten patients (10 shoulders) had previous revision surgery before the index revision without having positive culture results. The mean time to the revision procedure was 2.9 years from the previous one (range, 76 days-12.6 years). At the time of review, 10 patients had died. The mean follow-up time for all patients was 5 years (range, 1 day-18.6 years).

Ten patients (10 shoulders) required re-revision for persistent pain or loss of function. The mean age of these patients was 57.2 years (range, 45-75 years). There were 7 men and 3 women. Seven of the shoulders were on the right side, and 3 were on the left. The original indications for arthroplasty of these shoulders were traumatic arthritis in 4 shoulders, osteoarthrosis in 3, rheumatoid arthritis in 1, rotator cuff arthropathy in 1, and chronic dislocation in 1. The mean time between the original revision, with positive cultures, and the re-revision was 2.5 years.

This retrospective review showed that the patients had a variety of preoperative and intraoperative investigations to determine the presence or absence of infection (Table I). Each patient's history and physical examination findings before revision were also reviewed. Recorded data included any local or systemic sign of infection at the time of evaluation, including fever, malaise, increasing pain, or other infectious sites such as pneumonia; recent procedures performed (including dental work), use of immunosuppressants, and the level of surgeon's suspicion for latent infection. The physical examination documented drainage at the site of the previous incision, swelling, erythema, tenderness to palpation, pain with motion, stiffness, and weakness.

Preoperative investigations to determine the presence of infection included a white-blood-cell count in 72 patients, percentage of polymorphonuclear cells in 70 patients, measurement of erythrocyte sedimentation rate in 42 patients, and C-reactive protein level in 16 patients. Preoperative radiographs were examined for 54 patients. A shoulder arthrogram/shoulder aspiration was reviewed in 11 patients, and in 15 patients, a tagged leukocyte bone scan. Intraoperative investigations included culture of periprosthetic tissue and histologic evaluation of frozen sections from intraoperative samples of periprosthetic tissue. A positive result (suggestive of infection) or a negative result (not suggestive of infection) was defined for each investigation.

Table I Preoperative/intraoperative positive investigation results

	Total (%)	Re-revision (%)
Preoperative history		
Malaise	0/75 (0)	0/7 (0)
Fever	0/75 (0)	0/7 (0)
Increasing pain	63/75 (84)	7/7 (100)
Infection elsewhere	8/75 (10.67)	0/7 (0)
Use of immunosuppressants	9/75 (12)	0/7 (0)
History of recent procedure	2/75 (2.67)	0/7 (0)
Preoperative laboratory studies		
WBC	5/72 (6.6)	0/7 (0)
PMN	7/70 (10)	0/7 (0)
ESR	6/42 (14)	0/6 (0)
CRP	4/16 (25)	0/5 (0)
Preoperative physical exam		
Swelling	3/72 (4)	0/7 (0)
Erythema	1/74 (1.33)	0/7 (0)
Drainage	0/75 (0)	0/7 (0)
Intraoperative studies		
Histology	6/73 Positive (8.2)	0/7 Positive (0)
Final pathology	7/73 Positive (9.59)	0/7 Positive (0)

WBC, White blood cells; *PMN,* polymorphonuclear cells; *ESR,* erythrocyte sedimentation rate; CRP, C-reactive protein.

Preoperative investigations

The current standard practice in revision surgery is to preoperatively draw blood samples for evaluation of certain indices that may be helpful in ruling out infection. For our study, we looked at the samples of white-blood-cell count, erythrocyte sedimentation rate, percentage of polymorphonuclear cells, and C-reactive protein that were drawn within 2 weeks of surgery. The white-blood-cell count was considered to be elevated when it was more than 11.0 $\times$ 10^9/L. The number of polymorphonuclear cells was considered increased (a so-called left shift) when more than 80% of the total white-blood-cell count consisted of granulocytes. For the purposes of this analysis, an erythrocyte sedimentation rate of more than 22 mm/h and a C-reactive protein level of more than 1 dl/L were considered suggestive of infection and deemed a positive result. No values of either of these markers of inflammation were excluded, so results from patients with connective tissue disease or active disease elsewhere may have been falsely positive.

Preoperative radiographs are typically obtained before all revision arthroplasty procedures. Criteria for this study deemed suggestive for infection on x-ray film included complete lucent lines around the components, osteolysis, bone erosion, a shift of the components, or a combination of these. Two senior authors of this study reviewed the radiographs. A preoperative aspiration was obtained in those patients suspected of having a chronic occult infection. These aspirations were considered positive (suggestive of infection) if the Gram stain of the sample was positive for bacteria or if any culture was positive. Also, in certain patients suspected of having latent infection, it is becoming common practice to obtain a white-cell-tagged bone scan. In this retrospective study, 6 patients had a technetium scan and 9 had an indium scan. The results were read by the radiology staff at our institution and by the lead surgeon, and were interpreted as positive, equivocal, or negative for infection.

Intraoperative investigations

Two studies are typically performed during a revision joint arthroplasty. A biopsy specimen from the synovial surface that appears most inflamed is usually sent for histologic evaluation of frozen sections and for Gram-staining of the tissue sample. With use of the criteria of Mirra et al,[6] a result of the frozen section was considered positive when any single high-power field contained at least 5 stromal neutrophils. Intravascular neutrophils embedded within a surface fibrinous exudate or necrotic tissues were not considered positive. The frozen tissue was submitted for preparation of permanent paraffin-embedded sections. Hematoxylin and eosin-stained slides of these specimens were examined with use of the same criteria that were used for examination of the slides for frozen section. The authors compared the readings of both specimens performed by the pathology staff.

Intraoperative samples are also sent for Gram-staining and culture. For this study, only 1 culture had to be positive for the shoulder to be included. Further, 1 positive of a maximum of 6 cultures taken was still determined to meet the criteria for inclusion. A Gram stain was considered to have a true-positive result if the organism that was seen was consistent with the organism grown on culture.

RESULTS

This section is divided into two parts: the original patient population and the re-revision arthroplasty patients.

Preoperative clinic history and physical examination

No patients complained of any positive constitutional symptoms such as fever, malaise, or drainage. Two patients had a recent dental procedure before the revision. Ten patients mentioned recent infection elsewhere, of which 9 were respiratory and 1 a urinary tract infection. All were treated with 5 to 7 days of oral antibiotics prescribed by their primary care giver. Nine patients were currently taking immunosuppressants, predominantly for rheumatoid arthritis. Diabetes mellitus had been previously diagnosed in 7.

A small percentage of the patients was found to be tender to palpation around the joint (14 patients), had swelling or an effusion (3 patients), or had erythema locally (1 patient). As stated before, no drainage or sinus tracts were found on physical exam. The final aspect of the clinic visit before surgery involved the surgeon's suspicion of subacute infection. In only 6 patients was there a high concern for infection; otherwise, 29 patients had a low index, and in 40 cases, no mention of concern for infection was documented.

Preoperative and intraoperative investigations

The preoperative leukocyte count in 72 shoulders averaged 7.9×10^3 (range, 3.0×10^3-13.0×10^3). It was elevated to more than 11.0×10^3 in 5 patients (6.6%). The mean polymorphonuclear percentage (70 shoulders) was 64.7% (range, 22.2%-89.6%). This laboratory value was positive in 6 shoulders. The mean erythrocyte sedimentation rate (42 shoulders) was 12.4 mm/h (range, 0-66 mm/h), and was elevated in 6. C-reactive protein level was determined in 16 patients (average, 0.695 mg/dL; range, 0.04 to 3.2 mg/dL), and 4 were positive.

Fifty-four preoperative radiographs were reviewed. Both the glenoid and humerus were evaluated for complete lucent lines, osteolysis, bone erosion, and shift of the components. Thirty-three of the 54 radiographs were of total shoulder arthroplasties (TSAs), and 21 were of hemiarthroplasties. Fourteen of the 33 TSAs had complete lucent lines around the glenoid. Six of those glenoids also had mild erosion or shift, and 2 radiographs had evidence of osteolysis. Three radiographs had evidence of complete lucent lines about the humerus, and 7 had no osteolysis. Two radiographs had signs of humeral erosion, and none of the humeral components had shifted.

Before revision surgery, 11 shoulders underwent aspiration and arthrography was performed. Four of the 11 arthrograms were read as being positive for synovitis. All of the Gram stains were negative. Organisms were isolated on cultures of one aspirate. Bone scans were performed on 15 patients (6 technetium, 9 indium). Two technetium scans and 1 indium scan were probable for infection. Histologic evaluation was performed at the time of the revision in 73 patients. Six were originally read as being positive for acute inflammation, and 1 was changed to being positive a day later after review by a senior pathologist.

Of the 75 culture-positive shoulders, 71 (95%) had only one bacteriologic agent represented and 4 (5%) were polymicrobial. Forty-five shoulders (60%) were positive for *Propionibacterium acnes,* 10 (13%) for *Staphylococcus epidermis,* 7 (9%) for a general *Staphylococcus* species, and 2 each were positive for *Streptococcus viridans* and *Pseudomonas* (5% total). *Veillonella, Bacillus, Corynebacterium, Aspergillus, Alcaligenes* species, and *Proteus mirabilis* were each cultured from one shoulder. An average of 2.2 cultures were taken per operation and an average of 1.3 of those were positive. Of the 45 shoulders cultured with *P acnes*, 27 had more than one culture taken, and 13 of those had more than one culture return positive. For the 10 shoulders with culture-positive *S epidermis*, 9 had more than 1 culture taken and 2 of those had more than 1 culture grow the above species. The average first detection of growth was at 4.6 days. This is largely reflected in *P acnes* having an average of 5.1 days for first day of growth.

TREATMENT

After detection of the positive intraoperative cultures, a variety of treatment was used. Most of the patients (54 of 75) were only treated with the standard 2 to 3 doses of intravenous postoperative antibiotics; no antibiotic therapy was received afterward. Fourteen patients underwent some form of intravenous antibiotics in addition to routine postoperative dosing; the average duration of this treatment was 3 weeks (range, 1-6 weeks). Only one of these patients did not receive some form of oral antibiotic therapy afterward. The type and duration of the oral agents varied and is not completely known for all of the 13 patients. Likewise, 7 patients were started directly on oral antibiotic therapy after the positive cultures, but the type used and the duration specified also varied and was not completely documented in all cases.

The diagnosis of infection was classified as acute, subacute, or late on the basis of previous studies related to infection after elbow arthroplasty.[13,14] One of the 75 shoulders that had a revision arthroplasty had more than one preoperative study that was indicative of infection. This patient had the original arthroplasty performed for rheumatoid arthritis and was still using immunosuppressive medication for control of the inflammatory arthritis at the time of the revision. The time to the revision was 5 years, and this was, therefore, classified as a late infection. The laboratory markers, as suspected, were not overwhelmingly positive but positive nonetheless. The erythrocyte sedimentation rate was 25, and the white-blood-cell count was 11.1×10^9. The patient also had a frozen section positive for acute inflammation. Treatment was with an exchange arthroplasty, followed by the standard 48 hours of postoperative antibiotics. The culture was positive for *P acnes*. Suppressive antibiotic therapy was not instituted, and the patient has not required another revision procedure.

Re-revision arthroplasty

Ten (13.3%) of 75 patients eventually underwent a second revision procedure after having positive cultures from the first revision arthroplasty. The indications for this procedure were persistent pain in 7 patients, recurrent instability in 1, dislocation in 1, and presumed infection in 1. The mean time to the second revision was 2.5 years. The probability of survival of implants in patients in this series was 87% at 2 years, 87% at 5 years, and 84% at 10 years. Seven of the 10 patients also had positive intraoperative cultures. Five (71%) of the 7 were *P acnes*. One was *S epidermis* and one a nonspecified *Staphylococcus* species. An average of 3.2 culture specimens were taken during the procedure, and of those with positive cultures, an average of 2.3 were positive for some organism. The average time to the first detection of growth was 4.1 days.

DISCUSSION

Infection after TSA revision represents a potentially devastating complication. Fortunately, the occurrence of infection in the shoulder after arthroplasty or open rotator cuff repair is uncommon, with an incidence of approximately 0.5% to 3.9% for arthroplasty and 0.27% to 1.7% for the latter.[3,7,11,12] Little information exists characterizing indolent infections after total shoulder procedures, and the successful management of a patient with an infected TSA continues to be major challenge, with little published information to guide management and decision-making.

Major risk factors for infection developing after joint arthroplasty are diabetes mellitus, chronic diseases, acute infections other than at the location of the joint, and medical procedures performed after the arthroplasty.[11] In this study, a large percentage had at least 1 risk factor for infection, which was present in 36 of 75 patients. However, because of the retrospective analysis and lack of full information on all the patients, it was difficult to determine a difference in outcome comparing patients with and without risk factors for infection.

All of the preoperative and intraoperative tests discussed previously were not performed on each patient. To meet the minimum requirements for inclusion in this study, the patients only needed 1 positive culture taken during surgery and not have an overt infection of the shoulder in question, as previously discussed. No single laboratory value was deemed sufficient to diagnose any shoulder as being infected. A final diagnosis of subclinical infection for this study was determined from criteria established by Spangehl et al.[10] Their article outlined criteria for preoperative examinations, needing at least 3 positive results. The tests include erythrocyte sedimentation rate, C-reactive protein, preoperative aspiration, frozen section, and intraoperative culture. By our study inclusion criteria, every patient had a positive intraoperative culture and, therefore, needed at least 2 more positive tests for a diagnosis of infection (only 1 shoulder met that criteria).

Most of the shoulders (45 of 75) had cultures positive for *P acnes*. In publications on infection after shoulder surgery, *P acnes* has been documented as one of the top three offending agents along with p *S epidermidis* and *S aureus*.[7,11] Settecerri et al[9] reported 5 of 16 patients with deep infection after rotator cuff surgery grew *Propionibacterium*, followed by *S epidermidis* and *S aureus* at 4 each. In this study, *Propionibacterium* species were detected after an average of 5.1 days of growth, and that was always

in a broth medium. It is clear that this organism cannot be simply ignored as a contaminant.

P acnes is an anaerobic, gram-positive, bacilli that does not form spores.[5] It is considered to be a dominant anaerobic organism isolated from normal skin flora, especially in lipid-rich areas such as existing hair follicles and sebaceous glands in the axilla.[1] Descriptions of this organism as the cause of musculoskeletal infections have been limited, especially since almost all blood isolates are detected after prolonged incubation of blood cultures.[1] Because most of the bacteria cultures that were positive in this study are present in the normal skin flora, careful preparation and draping can theoretically help to prevent contamination. There continues to be no consensus regarding the routine shaving of axillary hair, but given the principles just discussed, it is highly recommended and is currently a standard part of preoperative preparation at this institution.

The presentation of our patients was similar in some ways with other studies of patients with infection of the glenohumeral joint. Most patients had initial clinical symptoms of pain with active and passive motion, weakness, and stiffness; however, virtually none of the patients had systemic signs or symptoms of infection. Most of the preoperative laboratory data proved not to be extremely useful. Only 5 (7%) of 72 patients had a positive white-blood-cell count. Spangehl et al[10] found only 7 (20%) of 35 patients who had positive white-blood-cell counts when they had a periprosthetic hip infection. Analysis of both sets of data shows that the white-blood-cell count rarely aids in the diagnosis of infection. By the same token, the percentage of polymorphonuclear cells was rarely elevated (9%) and was not helpful in the determination of possible infection.

The erythrocyte sedimentation rate and the level of C-reactive protein are nonspecific markers of inflammation. Both may be elevated in association with inflammatory, infectious, or neoplastic processes. Spangehl et al[10] demonstrated that with a careful history, the sensitivity and specificity of these studies can approach more than .80 for erythrocyte sedimentation rate and .90 for C-reactive protein. This study did not calculate the sensitivity and specificity of laboratory values, but our data do reflect more usefulness of these studies than white-blood-cell count or polymorphonuclear percentage; however, only 14% of the erythrocyte sedimentation rate and 25% of the C-reactive protein values obtained were positive for infection. Overall, therefore, no specific preoperative blood test is very useful in the determination of indolent infection after TSA.

The current recommendations for treatment of infected TSA include antibiotic suppression, débridement with prosthesis retention, direct exchange, delayed reimplantation, resection arthroplasty, arthrodesis, and amputation.[4,11,12] Those recommendations exist for those patients with clear periprosthetic infection with either supporting laboratory data, physical examination evidence, such as sinus tract existence with drainage, or purulence found at the time of surgery. Very few of these features were found in the 75 patients of this study. One (1.3%) could have been declared to have infection by preoperative studies; however, even that data were clouded because the patient had rheumatoid arthritis and was taking immunosuppressants. Only 10 (13%) of 75 patients required another surgery, and 48 of the remaining 65 (74%) were treated with very short doses of standard postoperative intravenous antibiotics and had no known treatment after that. The other 17 patients (16% of patient population) were treated with some form of either antibiotic suppression preceded by intravenous antibiotics or suppressive therapy alone. The treatment of indolent infection after shoulder arthroplasty is unclear, and further studies are needed to delineate the importance of surgical treatment and the intensity of antibiotic therapy necessary.

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