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Review Article

Periprosthetic Infections of the Shoulder: Current Concepts

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Abstract

Although rare, periprosthetic infection of the shoulder is a serious event resulting in inferior clinical outcomes. Infections about the shoulder present unique diagnostic challenges owing to the relative high frequency of lower virulent organisms which often have subtle and modest clinical presentations and diagnostic findings. Success of treatment depends on micro-organism identification, appropriate surgical procedures and appropriate antibiotic therapy. Early periprosthetic shoulder infection can be treated with debridement and exchange of modular components, while chronic PSI requires a one-stage or two-stage revision procedure. Indications for a one-stage revision procedure are evolving but have demonstrated promising results in initial studies. Two-stage revision procedures are more common and demonstrate favorable survival rates. Resection arthroplasty remains an option for lower-demand patients or recalcitrant infection. The surgeons should understand the diagnostic and treatment strategies that are most likely to have the most favorable outcome for patients with a periprosthetic shoulder infection.

INTRODUCTION

Prosthetic joint infection (PJI), although relatively rare, is a serious complication of shoulder arthroplasty as it typically results in additional procedures and substantially worse functional outcomes for patients. When shoulder PJI does occur, there is a high incidence of relatively slow growing and low virulence causative organism which leads to challenges in both diagnosis and widely agreed upon optimal treatment strategies. As the number of shoulder arthroplasties continues to rise worldwide, surgeons should be familiar with the current concepts regarding diagnosis and treatment of PJI of the shoulder.

INCIDENCE, PRESENTATION AND TREATMENT

PJI is the most common reason for revision shoulder arthroplasty predicated by pain, stiffness, or implant loosening. (1) An incidence of slightly over 1% has been reported and can be higher (3.8%) in situations of reverse shoulder arthroplasty.(2-4) When considering those shoulders that have been revised due to ongoing shoulder pain and stiffness, one series reported PJI present in more than half of the shoulders that were revised.(5) Because of such reports which show some correlation between poor functioning arthroplasties and the detection of infection, some have advocated that a painful and stiff prosthetic shoulder should be viewed as a possible infection until proven otherwise. This of course can represent an oversimplified approach to what often can be a multitude of subtle factors that can lead to suboptimal functioning of a non-infected prosthetic shoulder (e.g. prosthetic sizing, implant positioning, soft tissue imbalance and so on). Nevertheless, the prudent surgeon should always be considering the possibility of infection so as to not neglect the possibility of indolent infection and therefore pursue the appropriate diagnostic workup steps appropriately.

Several organisms have been associated with shoulder PJI including Staphylococcal and Enterococcal species. The most common pathogen isolated in shoulder PJI is however Cutibacterium acnes. Reports indicate approximately 30%-70% of shoulder PJI are due to C. acnes [formally referred to as Propionibacterium acnes). (1,5,6) This gram-positive anaerobe is a normal skin inhabitant of the subcutaneous layer and has high concentrations in the axillae.(7–9) It is believed that during surgical procedures it can be introduced into the wound and thus progress into a PJI. Typically, it is a slow-growing and a lower virulence organism when compared to other PJI culprits such as Staphylococcal strains. As such, it can be difficult to isolate, may manifest in nonspecific clinical findings such as generalized shoulder pain and stiffness and require prolonged incubation in the laboratory to demonstrate positive cultures. Furthermore, many patients with PJI caused by C. acnes can have normal laboratory results typically used to screen for infection due to the relatively low inflammatory response. Clear and consistent guidelines for the process of definitively establishing a shoulder PJI have therefore been challenging to date.

Diagnostic Workup

When a shoulder arthroplasty presents with obvious signs of infection such as substantial erythema and swelling, prolonged

wound drainage or even a sinus tract, the surgeon should immediately recognize the need for aggressive treatment of the suspected infection. In these cases, serum markers such as white blood cell count (WBC), C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) are typically elevated substantially as one would expect in a clinically obvious infection with an obvious inflammatory reaction. However, because of the frequency of C. acnes in shoulder PJI the clinical presentation can be notoriously subtle in many circumstances thus leading to challenges during diagnostic work up.

As mentioned previously, patients presenting with a clinically obvious shoulder PJI (e.g. draining fistula) present the surgeon with limited diagnostic challenges. The treatment of such instances are discussed further below and should follow the basic principles of PJI of other locations such as hip or knee. This includes implant removal when beyond 6 weeks after index procedure, aggressive debridement, antibiotic therapy (typically a combination of temporary antibiotic-eluding cement spacers and IV therapy) followed by reimplantation when the infection shows objective evidence of having been eradicated.

The more challenging scenarios however are in those patients when the clinical signs of infection are less obvious and present with relatively nonspecific findings such as shoulder pain and stiffness and perhaps evidence of implant loosening or radiolucencies on radiographs.

Although imaging methods are nonspecific tests for PJI they do play a role. Radiographic evidence of loosening or radiolucent lines within the initial three years following the index procedure should be considered suspicious for infection.(10) More advanced studies such as CT or MRI are typically less helpful in the establishment of infection but may play a role in surgical planning.

The surgeon should at least entertain the suspicion of infection in a patient presenting with pain, stiffness and radiographic changes when no other obvious cause is identifiable. The initial workup should include laboratory tests that should not be used in isolation but instead as one part of a diagnostic assessment.

Laboratory Tests

Sedimentation Rate (ESR) should be utilized as they are serum markers for inflammation. Importantly however, both CRP and ESR measurements can demonstrate normal results despite the presence of infection. This is especially true when the organism is C. acnes (low virulence and slow growing). At least one study found CRP values elevated in only 72% of periprosthetic shoulder infections.(10)

Several other laboratory tests have been investigated for their utility. These include serum IL-6 levels, and assessment of the synovial fluid for alpha-defensin or leukocyte esterase. IL-6 has shown some promise with respect to specificity but has had various results regarding sensitivity and like other serum tests should be used only as part of an overall diagnostic picture.(11)

Obtaining synovial fluid from an aspiration offers the potential for several tests. A synovial fluid cell count greater than 2000/μl and/or more than 70% of polymorph nuclear leucocytes is considered indicative of a PJI.(10)

The leucocyte esterase strip test in another nonspecific test of the synovial fluid. The assay is an enzymatic test originally designed for use in urinalysis and estimates the leukocyte count in urine by using the amount of intracellular leukocyte esterase as a surrogate. This test has the advantage of being easily performed in the office setting with results quickly available.

For total knee and hip arthroplasties, the sensitivity of detecting PJI has been demonstrated between 69% and 81% and the specificity between 93% and 100%.(12,13) However, the results have been less favorable for shoulder-related screenings with sensitivity and specificity as 50% and 87% respectively.(14) This may be due to a higher incidence of lower virulent pathogens as the causative agent leading to a lesser inflammatory response. (12)

More recently, testing the synovial fluid for alpha-defensin has been investigated as additional diagnostic option. Different than CRP, the alpha-defensin immunoassay is specific to leukocyte activity triggered by bacteria and not a generalized marker of inflammation. (11,15–18) The laboratory-based ELISA test has shown high levels of sensitivity and specificity in recent studies (92% and 100%, respectively). A lateral flow version of the assay has been developed to allow more practical usage in the clinic or intraoperative settings as it can return a result within minutes. However, the sensitivity and specificity of the lateral flow test has to date been inferior (54% and 96%, respectively) to the laboratory test leading some to conclude that it should not be used for screening, but instead as a confirmatory test for PJI. (19–22) Although the test itself does not identify the causative organism, more recent data along with further advances suggest that the alpha-defensin test may play an increasingly important role in the detection of PJI.

Microbiological Data

Of course, culture results that are positive from a joint aspirate are also indicative of infection and can provide an example of a specific test that can be obtained from synovial fluid. That said, in some cases shoulder joint aspirates yield little, if any, diagnostic fluid and subsequent cultures, when possible, are prone to the same challenges of producing results with slow-growing organisms.(23–25)

Providing a higher diagnostic yield than joint aspiration fluid, culture and histological analysis of periprosthetic tissue via biopsy provides a further direct and specific diagnostic option. (26–29) Due to the aforementioned challenges of culturing shoulder infectious agents, 5 samples from various regions of the shoulder, including the synovial tissues, are recommended to be harvested for culture. This can be done via arthroscopic techniques. Samples can also be taken for histological analysis with the threshold of positivity being 5 or more identified polymorphonuclear leukocytes per high-power field.

When cultures are initiated, it is important to recognize that C. acnes typically slow growth requires prolonged incubation periods in many cases. At least 14 days is recommended for tissue or synovial fluid samples for this anaerobe. Reports have shown that some PJI with C. acnes did not show positive culture results until after the second week. (1, 5, 30–33) Adding to the challenge is that prolonged incubation times increase the

risk of contaminants arising within the sample thus potentially obscuring the value of the results with potential false positives. (34,35)

It is important to endeavor to identify the causative organism to allow for the most appropriate treatment. Although broad-spectrum antibiotics may be appropriate in many circumstances, for resistant strains of Staphylococcus sp., for instance, broad-spectrum antibiotics are insufficient. It is therefore is helpful to obtain a precise identification of the organism's resistance pattern to tailor systemic antibiotic therapy appropriately. This information will also be helpful in determining if a one-stage revision arthroplasty may be suitable as with more virulent pathogens that strategy may be inappropriate. (28,36)

Additional laboratory tests are under current investigation such as PCR-based test which could detect hard to find bacterial presence due to the test's ability to amplify nucleotide traces. (37) In time, such techniques may prove greater practical utility for the surgeon in the diagnostic phase.

Synthesis of Data

In 2018, the Musculoskeletal Infection Society updated its previously proposed criteria for defining PJI of the shoulder. (38) Review of literature as well as consensus agreement was used to compose a method to help stratify the probability of PJI and therefore 1) help standardize definitions and approaches to diagnosis and 2) provide decision-making assistance to the treating surgeon. The presence of one major criterion indicates high degree of confidence ("Definite PJI") of infection and is considered diagnostic of a shoulder PJI. (Table 1)

Additionally, a weighted scoring system was proposed to grade the likelihood of infection when a major criterion is absent. The minor criteria were identified in (Table 2). Likelihood of infection is graded from "probably PJI", "possible PJI" and "unlikely PJI" and stratified according to final score. (Table 3) Such a methodology to the organization of the data helps provide a therapeutic framework and guidance to treatment.

TREATMENT STRATEGIES

Presentation in the Acute Setting

Importance has been placed on the timing of infection after the index procedure. In the acute or immediate postoperative time frame, treatment can follow guidelines consistent with PJI of the hip and knee. This includes aggressive debridement of all periprosthetic soft tissues including a synovectomy. Additionally, all easily exchangeable or modular prosthetic components (e.g. inlay components, modular glenosphere) should be replaced with new, sterile implants after a thorough irrigation with antiseptic fluids. Given that an organism is typically not identified at the time of this procedure, tissue cultures are important as well as the initiation of empiric antibiotic therapy. This should be continued until pathogen identification is established and can then be adjusted accordingly. Multiple antibiotic therapeutic strategies for this situation have been described previously. (39–44) Serial clinical follow up combined with monitoring of normalization of inflammatory markers (CRP and ESR) can help provide insight into effectiveness of treatment.

Presentation in the Late Setting

When a PJI presents beyond the acute stage, irrigation and debridement alone have poor results due to the frequent presence of biofilm around the periprosthetic tissues which inhibit success

Table 1:

Meeting one of the following criteria is diagnostic of periprosthetic shoulder infection = Definite PJI
A sinus tract communicating with the prosthesis is present
Gross intra-articular purulence
Two positive cultures with phenotypically-identical virulent organisms

Table 2:

Minor criteria for the definition of shoulder PJI	Weight
Unexpected wound drainage	4
Single positive tissue culture (virulent organism)	3
Single positive tissue culture (low-virulence organism)	1
Second positive tissue culture (identical low-virulence organism)	3
Humeral loosening	3
Positive frozen section (5 PMN in at least 5 high-power fields)	3
Positive pre-operative aspirate culture (low or high-virulence)	3
Elevated synovial neutrophil percentage (>80%)*	2
Elevated Synovial WBC count (>3,000 cells / μL)*	2
Elevated ESR (>30 mm/hr)*	2
Elevated CRP (>10 mg/L)*	2
Elevated synovial alpha-defensin	2
Cloudy fluid	2

ESR: Erythrocyte Sedimentation Rate; CRP=C-Reactive Protein; PMN: Polymorphoneuclear Leukocyte; WBC: White Blood Cell; μL: Microliter
*beyond six weeks from recent surgery

Table 3:	
Weighted values for all positive tests performed	
Score Total	**Result**
6 or greater with identified organism	probable PJI
6 or greater without identified organism	possible PJI
6 or less	
• single positive culture virulent organism	possible PJI
• two positive cultures non-virulent organism	possible PJI
• negative cultures or only single positive culture for low virulent organism	unlikely PJI

with such tactics alone. For this reason, some investigators have now advocated the threshold of acute infection to be 6 weeks or less so as to minimize the chance of biofilm establishing itself in the periprosthetic region. (44,45) Removal of the implants and all foreign material combined with aggressive debridement is required. The surgeon has the option to consider a one-stage revision or proceed to a two-stage approach. The criteria for appropriateness of one-stage revision are evolving and have several factors to consider. The major advantage of a one-stage revision is that only one surgical procedure is performed. However, with more virulent organisms (e.g. methicillin resistant Staph. aureus) a one-stage approach is not optimal. Ideally, the offending pathogen has already been identified through the preoperative workup and thus allows both the risk stratification and appropriate antibiotic therapy to be considered to warrant a one-stage revision.

One-stage Revision

In the setting of a PJI with a relatively low virulent organism such as C. acnes combined with appropriately aggressive debridement and postoperative antibiotic therapy, one-stage revisions have demonstrated comparable functional outcomes with two-stage revisions. Although it is ideal to have an identified organism prior to the time of surgery, a common scenario is when some evidence of infection exists (pain, stiffness, modest laboratory values and perhaps radiographic findings) but without a culture-positive pathogen. In this setting, the surgeon can consider a one-stage revision procedure if the suspicion of infection is sufficiently high. Several tissue samples for culture may be obtained at that time. Following surgery, the patient is maintained on empiric oral antibiotic therapy until culture results have returned in 14-21days. If the culture results return positive, antibiotic therapy can be adjusted accordingly and should include intravenous therapy for 6-12 weeks. In the largest series reported, 35 patients underwent one-stage revision arthroplasty for infection. With a mean follow-up of 4.7 years, 90% demonstrated no recurrence of infection. Other reports demonstrated no recurrence of infection following one-stage revision. (23,46,47) In all of the reports, the authors stress the need for aggressive debridement of periprosthetic soft tissues and appropriate postoperative antibiotic therapy.

Two-stage Revision

Two-stage revision surgery is by far the most common technique for treating PJI of the shoulder. This also involves complete removal of foreign materials along with aggressive debridement of soft tissues but also typically utilizes an antibiotic-laden methylmethacrylate spacer. The spacer allows for the elution of a high concentration antibiotics to the local environment and a focus of articulation at the glenohumeral joint to allow a semblance of functional activity and maintenance of soft tissue length and relationships for subsequent final implant placement after the infection has been eradicated.(48–50) A high concentration of antibiotics can be placed in the spacer to allow for much higher local concentrations of antibiotics (and therefore efficacy) than would be possible through intravenous therapy alone.

Following the initial debridement and placement of the spacer, intravenous antibiotics are administered and tailored to the specific sensitivities of the pathogen. Achieving survival rates of 100% has been reported by several authors. (51–54) Following a shoulder PJI and the subsequent surgical treatments, the rotator cuff is typically in a very poor functional state and the glenoid may have substantial bony defects such that implant stability from the screw fixation afforded by a reverse arthroplasty baseplate may be warranted. As such, revision of the shoulder to a reverse shoulder arthroplasty platform is typically indicated.

Resection Arthroplasty

Explantation of an infected shoulder arthroplasty without further reconstruction can be considered a viable option in select patients. Functional outcomes of a resection arthroplasty may be less predictable.(55–59). (55–57,59) However, patients with a relatively poor health status or with sufficiently low functional demands may represent candidates for this procedure. In some cases, these patients have undergone multiple prior surgeries, are wishing to avoid further procedures that have extended rehabilitation times and still may have relatively high risks of poor outcomes.

The primary goal for resection arthroplasty is pain relief. These patients typically have low functional demands and, in some cases, cognitive deficits. Deep infections around the shoulder that have been recalcitrant to all reasonable treatments are often an indication for resection arthroplasty and should be considered a salvage procedure. The objective is therefore to provide a straightforward procedure that results in the improvement of pain and allows the patient to avoid complex treatments or rehabilitation regimens postoperatively.

Several series have been reported results of resection arthroplasty in this setting. Pain was reduced in one series 10 of 11 patients having a resection arthroplasty for failed

shoulder arthroplasty despite also having very limited shoulder function.(60) In a different investigation, 6 of 7 patients resulted in substantial or near complete pain relief after resection arthroplasty despite limited functional results of that shoulder. (58) In yet another study, 7 patients were reviewed in in which all of the patients had sufficient function to perform basic activities of daily living and also had improvements in comfort allowing them to conclude that resection arthroplasty was an option in select patients who are otherwise poor candidates for other reconstructive efforts.(55)

SUMMARY

Periprosthetic infection of the shoulder is a vexing problem which is made even more challenging by the difficulties identifying a pathogen and the evolving treatment options. Recent attempts to quantify the probability of infection affords some clarification and allows the surgeon to apply a methodology to the diagnostic picture. One-stage revision is possible, especially if the organism is identified pre-operatively to allow for appropriate planning, risk stratification and specific antibiotic tailoring. Although additional future studies will help clarify which therapeutic strategies are most indicated for each clinical scenario, adherence to the basic tenants of surgical management (early debridement of affected tissues and focused antibiotic therapy) will undoubtedly remain important.

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