CLINICAL RESEARCH

Propionobacter acnes Infection as an Occult Cause of Postoperative Shoulder Pain

A Case Series

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Abstract

Background Infections after shoulder surgery are potentially devastating complications. Propionibacterium acnes is recognized as a causal agent in shoulder infections. The clinical presentation is usually insidious and nonspecific, but a P. acnes infection could be an occult cause of postoperative shoulder pain.

Questions/purposes What are the clinical and microbiologic characteristics of a postsurgical P. acnes shoulder infection and how should it be addressed?

Patients and Methods Ten patients with an average age of 57 years presented with P. acnes postsurgical shoulder infection. Clinical infection signs and surgical history were assessed and joint aspirates and tissue biopsy specimens were obtained. Diagnosis was confirmed by microbiologic cultures.

Results At the time of confirmation of the diagnosis, clinical signs of infection were absent. C-reactive protein and erythrocyte sedimentation rates were inconsistently elevated. Cultures took a mean 7 days to confirm organism growth. The average time from surgery to diagnosis of infection was 1.8 years (range, 0.07–8.0 years). All patients underwent irrigation and débridement and were treated with antibiotics for 6 weeks.

Conclusions P. acnes shoulder infections should be considered as a cause for persistent, unexplained shoulder pain. Shoulder aspirations and tissue samples should be obtained. Surgical débridement and intravenous antibiotics are necessary treatment modalities.

Level of Evidence Level IV, Prognostic study. See the Guidelines for Authors for a complete description of levels of evidence.

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Introduction

Infection after shoulder surgery is a potentially devastating complication. The incidence of infection after rotator cuff repair ranges between 0.27% to 1.9% [3, 18, 27, 28, 37], whereas the incidence after shoulder arthroplasty ranges from 0% and 15.4% [9, 11, 38, 41, 44]. Infections after proximal humerus fractures are less common [4, 29, 32, 40, 46].

P. acnes is being recognized as a causal agent in shoulder infections with increasing frequency [3, 7, 14, 18, 33, 35, 37, 39, 45]. This nonspore-forming microaerophilic bacillus has a low level of virulence but has been established as a pathogen in endocarditis [30, 42], meningitis [5, 43], arthritis [23], osteomyelitis [1, 31] and spondylitis [10, 13]. It has been described as the infectious etiology in 16% of prosthetic shoulder infections [38] and in 21% of revision shoulder arthroplasties [22]. In another series, P. acnes was the major etiology of postoperative septic arthritis, comprising 56% of shoulder infections [26]. Herrera et al. [18] in 2002 reported the incidence of deep infection after open rotator cuff repair to be 0.27% to 1.7%. Athwal et al. [3] found an incidence of 0.43% after different techniques of rotator cuff reconstructions. P. acnes was reported as the most common infecting organism in both studies.

In contrast, reports of P. acnes in lower-extremity infections, including prosthetic joint infections or after arthroscopy, are rare [8, 25, 31, 38]. This is likely because P. acnes is predominant in the pilosebaceous follicles [34] that are most prevalent in the head, neck, and thorax. P. acnes is a dominant anaerobic bacteria isolated from the healthy skin in moist areas such as the axilla. This is another reason why the shoulder is thought to have a propensity for infections with this type of microorganism [14].

Because it is difficult to detect, the actual number of P. acnes shoulder infections probably has been underestimated. P. acnes is a fastidious organism, requiring prolonged growth duration and anaerobic conditions to grow in culture. When isolated, it often is disregarded as a contaminant owing to its presence as a commensal of upper-body skin sites. Furthermore, the clinical presentation of P. acnes is usually insidious and nonspecific.

Patients present without the typical signs of infection such as fever or local inflammatory reaction and invariably have normal leukocyte counts (WBCs) [22].

To increase our awareness of the potential of P. acnes infection as an occult cause of postoperative shoulder pain, we investigated a series of patients diagnosed with postsurgical P. acnes shoulder infections to answer the following questions: (1) What characterizes a P. acnes infection of the shoulder, in clinical presentation and quantification of laboratory markers? (2) How are the microbiologic diagnosis and analysis best obtained? (3) How should this infection be treated and what clinical results of therapy can be expected?

Patients and Methods

We retrospectively reviewed all patients diagnosed with postsurgical deep P. acnes shoulder infections at our clinic between June 2006 and November 2007. Inclusion criteria required culture-positive specimens obtained deep to the deltoid in patients with symptoms of pain, prosthetic dysfunction, or joint sepsis. Patients with superficial wound infections involving the skin or subcutaneous tissue were excluded. We identified 10 patients, including two women and eight men, with P. acnes shoulder infections. The mean age of the patients was 57.8 years (range, 24–81 years) (Table 1). Their average followup was 1.7 years (range, 3 months to 2.5 years). The research protocol was reviewed and approved by the local institutional review board.

For the purpose of this study, a deep shoulder infection was defined as a positive bacterial culture from specimens obtained deep to the deltoid muscle. A symptomatic infection was defined as any one of the following symptoms was present: pain, prosthetic dysfunction (decreased ROM or joint instability), swelling, drainage, fever, leukocytosis, elevated inflammatory markers, or purulence in the joint. The index operation was defined as the last operation that preceded the diagnosis of infection.

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Table 1. Demographics of included patients

Characteristic	Value
Number of patients	10
Male/female	8/2
Mean age (years)	57.8
Index operation performed at other facility	6/10
Index operation	
RTC repair	4/10
ORIF humerus fracture	1/10
TSA	5/10

RTC = rotator cuff; ORIF = open reduction and internal fixation; TSA = total shoulder arthroplasty.

A successful outcome was defined as eradication of infection and elimination of pain and joint dysfunction.

The index operation was arthroscopic rotator cuff repair in four patients, open reduction and internal fixation (ORIF) for a proximal humerus fracture in one patient, and shoulder arthroplasty in five patients. Four patients had infections developed from after surgery at our facility and six sought treatment from us for ongoing shoulder problems after having the index procedure at an outside facility. Medical comorbidities that may have been contributing factors included Type II diabetes in two individuals and hepatitis C in one.

Comprehensive histories and physical examinations were obtained from all patients. Pain (location, duration, and character), swelling, appearance (erythema or lack thereof), and ROM were assessed for each patient. All underwent screening laboratory studies including WBC, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). From these clinical data, the following data elements were abstracted: demographics; description of index operation, facility, and timing of index procedure in relation to definitive diagnosis of infection; medical comorbidities; duration of infection symptoms; chief complaint and description of symptoms at time of presentation in our clinic; physical examination findings; operative findings at time of initial débridement; laboratory findings; treatment regimen; and timing and clinical outcome at last followup.

All culture specimens were obtained before administration of any prophylactic or therapeutic antibiotic therapy. Before surgery, all the shoulders were aspirated. Nine of the 10 shoulders were aspirated under flouroscopic guidance to ensure accurate needle placement. One patient underwent aspiration in the outpatient office but this patient had a massive rotator cuff tear with a contiguous subacromial and intraarticular space. Most of the time, no fluid was obtained. In all suspected cases that had a negative aspiration, the joint was lavaged with saline before making an incision, and the lavage fluid then was sent for culture. Joint aspirates or lavage samples and a minimum of two deep tissue samples (preferably three to five) were collected during the operation, including joint capsule, synovial lining, bone, or granulation tissue. An average of three biopsy specimens (range, 1–6 specimens) were taken from each shoulder to address the possible problem of false-negative specimens as much as possible. After tissue biopsies, antibiotic therapy was instituted intraoperatively with empiric prophylactic antibiotics (typically a first-generation cephalosporin) and then was modified under the guidance of an infectious diseases expert to a therapeutic regimen when the cultures turned positive. Patient specimens were processed immediately after their arrival at the laboratory, under sterile conditions in a laminar flow hood

for aerobic and anaerobic culture. For aerobic culture, specimens were cultured on trypticase-soy agar containing 5% sheep blood (Remel, Lenexa, KS, USA), chocolate agar (Remel), and MacConkey agar (Remel). Cultures were incubated at 36°C under standard aerobic conditions. For anaerobic culture, Brucella media (Anaerobe Systems, Morgan Hill, CA, USA) were inoculated and cultured at 36°C in an anaerobic chamber. Media were checked daily (aerobes) or every other day (anaerobes) for bacterial growth. For tissue samples, thioglycolate broth (Remel) also was inoculated and incubated in aerobic and anaerobic conditions. Clouded broth was Gram stained and subcultured onto appropriate agar plates. Cultures were discontinued and declared negative if no growth was visible at 3 days for aerobes. As there was a high suspicion of the possibility of P. acnes, prolonged testing was requested for anaerobes. Orthopaedic specimens always were requested to be held for 14 days. Positive colony growth was identified by standard microbiologic procedures [19]. Pinpoint yellow- or buff-colored colony growth in anaerobic conditions was subjected to aerotolerance testing. A positive aerotolerance test combined with a Gram stain morphology showing pleomorphic gram-positive rods was subjected to anaerobic catalase and indole testing, and identification of P. acnes was confirmed using the RapID™ ANA II Identification System (Remel). Isolates confirmed as P. acnes were subjected to β-lactamase testing.

The diagnosis of P. acnes infection was made with a mean of three tissue biopsy specimens (capsule tissue, bone, subacromial tissue) and a minimum of one biopsy specimen on which the P. acnes organism grew. Pain and functional outcomes were measured using the American Shoulder and Elbow Surgeon (ASES) score (scale 0–100), which has been validated for common shoulder disorders such as rotator cuff disorders, instability, and osteoarthritis. In addition, patients rated their daily pain on a 1 to 10 scale with 1 being no pain and 10 being worst pain. Patients were asked to rate how satisfied they were with their treatment outcome on a 10-point scale, with 1 being very unsatisfied and 10 being very satisfied.

All patients underwent a minimum of one surgical débridement. Four of the five patients with shoulder prostheses underwent removal of their implants with insertion of a antibiotic coated cement spacer. This subset had an average of three surgical débridements. All but one patient had reimplantation of a new prosthesis. Patients who had an infection after rotator cuff arthroscopy underwent a mean of one surgical débridement and the suture anchors were removed, whereas the patient with the ORIF of a proximal humerus fracture required only one débridement and hardware removal in the same setting; the fracture was not yet completely healed. In the subset of patients who had undergone prior rotator cuff surgery, there were no

obvious recurrent tears. In all 10 of these patients, the definitive diagnosis of P. acnes infection was not known at the time of surgery. At the time of the initial débridement (seven were performed open, three performed arthroscopically), all tissue specimens sent for immediate intraoperative Gram stain were negative. Penicillin VK was prescribed for three patients and intravenous ampicillin-sulbactam was prescribed for nine patients. All patients received antibiotics for a minimum of 6 weeks. None of the 10 patients had a β-lactamase-producing strain of P. acnes. Patient treatment outcomes with a minimum 1 year followup are reported for seven of the 10 patients. Subjective followup was obtained through mail.

Results

The most consistent complaint of all patients was persistent shoulder pain (Table 2). Only one patient had symptoms of fever, swelling, and active wound drainage (this was a subacute case diagnosed 4 weeks after arthroscopic rotator cuff repair). For the nine patients who had pain as their primary complaint, swelling around the shoulder was found in one additional patient; three patients also had decreased ROM or stiffness; and one patient had erythema. Despite prolonged symptoms of pain, with a mean duration of symptoms of 3 months (range, 1–9 months), the mean time from the index surgery to diagnosis of infection was 1.8 years (range, 26 days to 8 years).

The preoperative WBCs in these 10 patients were normal (normal range, $5 \times 10^3/mm^3$ to $10 \times 10^3/mm^3$), and ESR and CRP (normal range, 1–25 mm/hour and < 10 mg/dL, respectively) were not consistently elevated. The WBC averaged $6.8 \times 10^3/mm^3$ (range, 4.8–$10.4 \times 10^3/mm^3$). The average CRP was 9.1 (range, < 3–31 mg/dL). The CRP was elevated above normal limits in two of 10 patients (average, 26; range, 21–31 mg/dL). The ESR averaged 6.9 mm/hour (range, 1–10 mm/hour) in eight patients within normal limits; the average ESR for two patients with elevated levels was 29 mm/hour (range, 19–39 mm/hour). P. acnes took an average of 7 days (range, 5–13 days) to grow on the cultures of all 10 patients. P. acnes grew on only five of 10 lavage or aspiration samples.

All but three patients remained pain-free at clinical followup (Table 2). One patient initially did well and then had increased pain development. This patient progressed to another surgery and had positive cultures of P. acnes. This could be considered a failure of our treatment as opposed to a new infection. The two other patients reporting continued pain had the lowest satisfaction with surgical outcomes scores. The average postoperative ASES score for patients with more than 1-year followup (eight patients) was 78 points. Overall, the average patient satisfaction score with surgical outcomes in patients who did not progress to another surgery was 7 of 10 points. Four of the five patients who had arthroplasties maintained their ROM, with one patient electing not to have prosthesis reimplantation.

Discussion

Infections after shoulder surgery are a potentially devastating complication. P. acnes is recognized as a causal agent in shoulder infections. The clinical presentation is usually insidious and nonspecific, but a P. acnes infection could be an occult cause of postoperative shoulder pain. To increase the awareness of P. acnes infection as a cause of postoperative shoulder pain, we attempted to answer the following questions: What characterizes a P. acnes infection of the shoulder from clinical and microbiologic perspectives? How should this infection be treated and what outcome can be expected?

This study has several limitations inherent in retrospective reviews of charts and laboratory results. It is a small case series, representing a conglomerate of shoulder infections at a referral sports medicine clinic, which could result in selection bias. Patient treatment outcomes are encouraging, yet the study's sample size and lack of specific followup makes it difficult to make specific recommendations. This report nevertheless is intended to alert orthopaedic surgeons that patients can present with subclinical infections after shoulder surgery and it may take prolonged anaerobic culture of up to 14 days to identify this slow-growing fastidious bacterium. Although there is a risk that we included patients who had P. acnes contamination in our cohort, the clinical improvement after surgical débridement and antibiotic therapy makes us believe the possibility of false-positives was less likely.

Insidious protracted pain was the most frequent presentation of infection attributable to P. acnes. The nonspecific clinical findings and P. acnes' indolent nature have posed challenges to others in diagnosing a P. acnes infection after shoulder surgery [22]. Only one patient (10%) in our patient population had wound drainage and fever. Assessment of a comparable patient selection after total shoulder arthroplasty found none presented with fever [19]. However, Athwal et al. [3] noticed wound drainage in 72% and erythema in 64% of the patients. This discrepancy might be attributable to different bacteria, as organisms other than P. acnes grew on 19 of 39 specimens [3]. The standard laboratory data often are negative or nonspecific. As in previous studies [3, 14], ESR and CRP levels have not been reliable indicators for infection.

Patients were diagnosed an average of 1.8 years after their index operations, with symptomatic complaints

Table 2. Individual patient data

Patient	Gender	Age at surgery (years)	Time from index surgery from prior procedure (days)	Duration of symptoms (months)	CRP at baseline (mg/dL)	ESR at baseline (mm/hour)	Comorbidities	Index procedure	Number of prior surgical procedures	Follow-up (years)	Subjective satisfaction	ASES score at final followup (0–100 scale)
1	Male	69	973	3	8	8	Prehypertension hepatitis	Hemiarthroplasty	1	102 days (clinic note)		Incomplete ASES scores (< 1-year followup)
2	Male	64	43	1.25	21	39	None	Arthroscopic rotator cuff repair	0 2 cortisone injections	2.3	Yes, very satisfied	100 points (27-point ↑)
3	Male	66	2790	1	4	7	None	Reverse TSA	5	2.3	Yes, very satisfied	90 points (no preoperative score)
4	Male	63	966	1	< 3	5	Diabetes	TSA, possible septic joint	2	2.2	No, very unsatisfied	48 points (3-point ↑)
5	Male	46	90	None	< 3	1	Hypertension	Revision arthroscopic rotator cuff repair	3	2.2	No, surgery elsewhere	Incomplete ASES scores
6	Male	57	26	2	31	19	None	TSA	0	2.5	Yes, very satisfied	90 points (53-point ↑)
7	Male	24	120	9	9	10	Diabetes	Suspected septic joint capsular release	3	2.3	Yes, very satisfied	100 points (85-point ↑)
8	Male	81	550	12	8	8	None	Arthroscopic rotator cuff repair	1	1.3 (clinic note)	Patient requested physical therapy for continued pain	8 points preoperative, incomplete postoperative score
9	Female	53	98	None	< 3	8	None	ORIF of proximal humerus fracture	0	1.6	No, very unsatisfied	38 points (6-point ↑)
10	Female	51	900	5	< 3	8	None	Failed hemiarthroplasty with rotator cuff repair	6	157 days (clinic note)		32 points preoperative (< 1-year followup)

CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; ASES = American Shoulder and Elbow Surgeon; TSA = total shoulder arthroplasty; ORIF = open reduction and internal fixation; ↑ = increase.

averaging 3 months. This is similar to the report by Zeller et al. [45], who classified the majority of infections in their series as late chronic infections as opposed to acute postoperative infections. One patient in our study presented 8 years after the index operation. It was unclear whether the infection was indolent for those years or acquired secondarily.

Previously reported risk factors associated with P. acnes infections were male gender, first surgery of the day, and increased duration of the surgical procedure [11]. Acute outbreak of P. acnes was decreased by improved ventilation systems and cleaning of the operating room [11]. Although the majority of our patients were men, it is unlikely the ventilation systems or cleaning played a role as most infections in our patients developed at outside institutions and procedures are performed in high-efficiency particulate air-filtered rooms.

P. acnes required prolonged incubation in the laboratory to detect growth, 5 to 13 days; similar ranges are supported by other studies [21, 26, 36]. In most clinical laboratories in the United States, conventional cultures are held only for 5 days [19]. Based on our findings and those of others, we recommend cultures be held for at least 14 days [18]. Furthermore, similar to others [15, 21], we found intraoperative Gram stains unhelpful in diagnosing P. acnes infection. At the time of the initial débridement, all specimens sent for intraoperative Gram stain in our series were negative. There are recent reports on PCR in combination with sequencing of 16S rDNA [16] and multiplex PCR of sonification fluid in detecting periprosthetic P. acnes joint infections [2] in patients who had false-negative P. acnes cultures. A limitation of this testing technique is the time it takes to confirm a diagnosis; the results come in too late to help in the clinical diagnosis. Poor bacterial DNA extraction properties also may limit sensitivity of the test, along with possible cross-contamination from the patient's or staff's skin. Molecular testing may be useful in the future to confirm the presence of P. acnes, but it was not available to us at the time of this study.

P. acnes often is susceptible to penicillin, tetracyclines, chloramphenicol, erythromycin, and vancomycin, but resistance is increasing. Sixty percent of isolates are resistant to at least one antibiotic, likely owing to widespread antibiotic use for acne vulgaris [12, 33]. Information on resistance is gleaned mainly from cases of acne vulgaris, so correlations with the much less common systemic infections are unclear. In our series, none of the isolates possessed a β-lactamase, suggesting good susceptibilities to penicillin and its derivatives. Therefore, penicillin G, 2 mU intravenously every 4 hours or via continuous infusion, was the most focused therapy for serious deep infections [23]. Other β-lactam antibiotics also have been used successfully for serious infection [20]. Alternative agents, if susceptible, may include clindamycin, vancomycin, or a combination therapy with vancomycin and doxycycline [17, 24]. Unlike other anaerobes, most P. acnes are resistant to metronidazole [42]. Combination therapy of rifampin and amoxicillin [10] and rifampin with either penicillin or linezolid [6] also have been reported successful for treatment of P. acnes shoulder prosthesis infections. There are no clear data on prosthesis retention; thus, removal of foreign bodies or a two-stage joint arthroplasty for arthroplasty infections should be considered in difficult cases.

Infection by P. acnes is a potentially devastating complication after shoulder surgery. Nonspecific complaints of pain and stiffness were the most common findings, whereas the typical clinical signs of infection usually are absent. As this is an indolent type of infection, the normal laboratory indicators of sepsis are unreliable. Coupled with difficulty in growing P. acnes in culture, this makes the diagnosis of a P. acnes infection easy to miss. Given the incidence, better awareness of the problem and possibly a change in prophylaxis might be considered in the future. Although it is possible to eliminate infections of P. acnes with surgical débridement and appropriate antibiotics, patients should be counseled on potential permanent functional limitations of their shoulder.

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