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Non-purulent low-grade infection as cause of pain following shoulder surgery: preliminary results

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Abstract Low-grade infection was systematically searched for in all revision shoulder surgeries by harvesting tissue samples. Ten consecutive patients were identified with a non-purulent low-grade infection of the shoulder. All of these patients suffered from pain and eight were stiff. Preoperative aspiration in eight patients yielded bacterial growth in only one case. Serum C-reactive protein levels were normal in seven out of 10 cases. *Propionibacterium acnes* was identified in seven, coagulase-negative *Staphylococcus* in two and *Staphylococcus saccharolyticus* in one case. The delay between harvesting the tissue samples and detection of bacterial growth averaged eight days (range, 2–17). After debridement and antibiotic treatment for a mean of 4.5 months, tissue samples were repeatedly harvested in nine patients due to persistent pain. The infection was microbiologically eradicated in six out of nine cases that had a repeated biopsy. However, nine out of 10 patients continued to suffer from moderate to severe pain. Low-grade infection of the shoulder can be a cause of persistent pain and stiffness. The results of antibiotic treatment are disappointing. Further studies are necessary to analyse this difficult pathology.

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Introduction

Various causes may lead to painful failures after shoulder surgery. Infection is one and needs to be ruled out in patients who present with pain and/or decreased range of motion after shoulder surgery. Purulent infections of the shoulder have been described [1–9]. Scarce data exist about non-purulent, non-draining, low-grade infections of the shoulder.

The purpose of this report is to describe our experience with 10 patients who presented with pain after shoulder surgery and who had synovial tissue cultures harvested at the time of revision surgery that were positive for bacteria with low pathogenicity.

Materials and methods

Patients

Since 2001, tissue samples have been regularly harvested to search for low-grade infection during all shoulder revision surgeries. Ten consecutive patients were identified between June 2001 and December 2002 with a low-grade infection of the shoulder joint following shoulder surgery. Three had been operated on at our institution and seven elsewhere. Patients with prior shoulder replacement were excluded from this study.

There were nine males and one female with a median age at the time of the index operation of 50 years (32–59). In nine cases the dominant arm was involved. Six patients were smokers (mean 18 cigarettes per day, range 10–30). One patient suffered from type II diabetes mellitus. No other risk factors for infection were identified. All patients were off work due to symptoms related to their affected shoulder.

The revision surgery at which the low-grade infection was detected was defined as the index operation. Before index surgery, the patients had an average of two (one to five) prior procedures including open or arthroscopic rotator cuff repairs (6), acromioplasties (6), open reduction and internal fixation (1), stabilisation (1) or other procedures (6). The mean duration between the first prior operation and the index procedure was 10 months (5–24). The index procedures with harvesting of tissue samples were arthroscopic acromioplasties in five cases, arthroscopic capsulotomies in four cases, and open debridement and bone anchor removal in one case.

Before the index operation, all patients had a clinical examination with determination of the Constant-Murley score [10], laboratory studies (including C-reactive protein) and plain radiographs. Five patients had recently had a MR arthrography. Eight patients had a fluoroscopically guided aspiration of the glenohumeral joint for bacterial cultures before the index operation. This aspiration was performed by a radiologist at our institution. To perform this aspiration, a small amount of local anaesthetic (0.5–1.0 ml of Scandicain 2%, Mepivacain, AstraZeneca, Zug, Switzerland) was first administered intracutaneously and also before penetration of the joint capsule. Special care was taken to avoid injection of local anaesthetic into the joint. After aspiration of glenohumeral joint fluid, several millilitres of iopamidol contrast medium (Iopamiro 300, Bracco, Milan, Italy) was injected to ensure the correct intraarticular, glenohumeral position of the needle using fluoroscopy.

Detection and definition of low grade infection

Low-grade infection was determined by harvesting tissue samples at the index operation. In nine cases the samples for cultures were harvested by arthroscopy and in one case by open surgery. Two patients received 2 g of cefazolin (Kefzol, Eli Lilly, Vernier, Switzerland) intravenously half an hour before the index procedure. All other patients received no antibiotics preoperatively in order to avoid a negative influence on the detection of bacteria. On average, four tissue samples were harvested (two to seven). In most cases, two samples were obtained from the glenohumeral joint and two from the subacromial space. Arthroscopic harvesting of the samples was obtained with a shaver (5.0 mm full radius resector). One layer of 10×10 cm large sterile gauze placed at the outflow of the shaver (instead of the outflow tube) served as a filter, which allowed relatively large amounts of tissue probes to be collected. Synovium, capsule and/or subacromial bursa were harvested. The gauzes with the filtered tissue samples or the tissue probes from the open biopsies were placed into sterile containers and then sent to the Institute for Medical Microbiology of the University of Zurich of microbiological workup. Microorganisms were identified using standard methods. In particular, culture and identification of *Propionibacterium acnes* was performed as described by Jakab and coauthors [11]. The cultures were incubated for at least 10 days. Minimal inhibitory concentrations (MIC) of relevant antibiotics against identified bacteria were determined by standard E-test.

Low-grade infection of the shoulder joint was defined by the presence of at least two positive cultures identifying the same bacteria from the biopsies and the absence of pus and fistulas. If only one culture was positive, the result was arbitrarily interpreted as a contamination.

Follow-up

The data of this study were retrospectively collected from the charts. Nine out of 10 patients had a follow-up examination at our outpatient clinic after a mean of 18 months (9–40) after the index procedure with determination of the Constant-Murley score and plain radiographs. The degree of stiffness was estimated according to the notes in the chart. Stiffness was defined as mild for a passive limitation of the shoulder joint up to 25°, as moderate for 25–50º and as severe for more than 50º. One patient had a cardiac infarction two months after the index procedure. He refused further treatment. For this case, there was only a telephone follow-up nine months after the index procedure.

Statistical analysis

The relationship between discrete variables was determined using the Wilcoxon signed rank test.

Results

Clinical and radiological presentation before index procedure

The study population consisted of 10 patients with infected shoulder. Eight patients had undergone joint aspiration prior to the diagnosis of infection. The sample was positive in only one patient, yielding growth of coagulase-negative *Staphylococcus* (coagulase-negative S.).

Patient characteristics prior to the index procedure are shown in Table 1. All patients had painful shoulders and eight had mild to moderate stiffness. All patients were afebrile with normal leukocyte counts. C-reactive protein was normal in seven cases and mildly to moderately elevated in three patients (6, 7.5 and 33.4 mg/l).

Nine patients had no radiographic signs of arthrosis. One patient had a moderate arthrosis on the preoperative radiographs according to the classification of Samilson and Prieto [12]. There were five preoperative MR arthrographies that did not show signs of bacterial infection such as joint effusion, bone marrow oedema, cortical erosions, focal bone destruction or periostal reaction.

Findings at index procedure

The intraoperative findings during the index procedure showed synovitis in most patients (Table 2). In two patients, more than one bacterial species was cultured from one or more samples. *P. acnes* was the most commonly isolated pathogen (seven of 10 patients), while coagulase-negative S. was found in two patients, and *Staphylococcus saccharolyticus* in one case.

The inflammatory response in the involved joints was absent to minimal in most patients, as the samples contained no or few leukocytes. This microscopic finding was in contrast to the finding of synovitis in most patients.

Antibiotic treatment and clinical presentation at latest follow-up

In this series therapy of the low-grade infections mainly consisted of debridement and oral antibiotics (Tables 1 and 3). Antibiotic treatment was based on the MICs of different antibiotics for the identified pathogens. The following antibiotics were used: amoxicillin and clavulanic acid (Augmentin, GlaxoSmithKline, Münchenbuchsee, Switzerland), ciprofloxacin (Ciproxin, Bayer, Zurich, Switzerland), clindamycin (Dalacin C, Pfizer, Zurich, Switzerland), levofloxacin (Tavanic, Aventis Pharma, Zurich, Switzerland), rifampicin (Rimactan, Medika, Aesch, Switzerland) and teicoplanin (Targocid, Aventis Pharma, Zurich, Switzerland). The duration of antibiotic treatment varied between 3 and 36 weeks (Table 3). The antibiotics were administered orally except for teicoplanin (intravenous treatment). Due to persistent symptoms after completion of antibiotic therapy and in order to determine whether the infection was eradicated, a second arthroscopic biopsy was performed in all cases except for the patient with the cardiac infarction. In five of these patients the culture of the biopsies yielded growth of *P. acnes*. In a sixth patient coagulase-negative S. were identified. The patients with positive cultures underwent a second cycle of antibiotic treatment. However, the clinical results remained unsatisfactory (Tables 1 and 3). Additional cycles of antibiotic treatment with durations ranging between 13 and 30 weeks were administered following positive cultures of repeated biopsies in patients 1, 5 and 10. Despite these prolonged courses of treatment, cultures of a third set of biopsies were again positive and the clinical situation remained unchanged with persistent pain and decreased range of motion of the affected joint for two of these patients.

Overall, at latest follow-up, nine out of 10 patients had severe to moderate pain. Stiffness improved in one patient only. Subjectively, half of the patients felt a slight improvement of their symptoms, but only one described the condition of his shoulder as satisfactory whereas the other nine were not satisfied with the outcome.

One patient with persistent *P. acnes* infection was finally treated with a fusion of the shoulder due to severe pain despite a relatively intact joint (moderate chondromalacia). The fusion healed uneventfully. The patient's pain improved somewhat, especially at rest and at night, but the position of the fusion was not satisfactory. A corrective osteotomy was performed. The intraoperative cultures revealed coagulase-negative S. as well as *P. acnes*. After corrective osteotomy, the symptoms worsened to the level before fusion.

Complications

Several patients had gastrointestinal symptoms associated with oral antibiotic therapy, but no other adverse events were noted in the charts.

Discussion

In this report we describe 10 patients with chronic shoulder pain who meet standard microbiological criteria for the diagnosis of low-grade bacterial infection, namely the isolation of the same pathogen in at least two samples from a normally sterile site. However, the diagnosis of infection can be challenged by two aspects that do not fit the classical presentation of a bacterial infection. First, the patients did not present with typical clinical signs of infection (swelling, fever, pus, draining, etc.) and had only minimal

Table 1 Characteristics of the 10 patients prior to diagnostic surgery (index procedure) and at latest follow-up

Case number	Pain (Pre/f-up)	Active flexion (°) (Pre/f-up)	Stiffness (Pre/f-up)	Arthrosis (Pre/f-up)	Subjective assessment at f-up	Subjective result at f-up	Constant-Murley score (%) (Pre/f-up)
1	Sev/mod	80/50	Mod/na	None/na	Pain same/ ROM worse (fusion, see text)	Unsat	29/10
2	Sev/sev	120/80	Mod/mod	None/none	Same	Unsat	28/14
3	Sev/mod	150/160	Mild/none	None/none	Better	Sat	70/83
4	Sev/sev	75/na	Mild/na	None/none	Same	Unsat	18/na
5	Mod/mild	150/140	Mild/mild	None/none	Better	Unsat	60/na
6	Sev/mod	80/100	Mild/mild	None/none	Pain same/ ROM better	Unsat	24/49
7	Sev/sev	150/160	None/none	None/none	Better	Unsat	53/56
8	Mod/mod	80/90	Mod/mod	None/none	Better	Unsat	20/39
9	Mod/sev	110/100	None/none	None/none	Same	Unsat	60/33
10	Mod/sev	50/80	Mod/mod	Mod/mod	Same	Unsat	18/6
Mean		105/107*					38/36*

Pre/f-up before index procedure/at latest follow-up, *sev* severe, *mod* moderate, *ROM* range of motion, *Unsat* unsatisfactory, *Sat* satisfactory, *na* not available

*Difference not significant

Table 2 Intraoperative findings at index procedure and microbiological results at the time of diagnosis

Case number	Degree of synovitis	Bacterial species	Site of positive sampling	Number positive/ number of samples	Microscopy of samples	Quantification of growth
1	Severe	*P. acnes*	Glenohumeral	2/2	Few leukocytes	Isolated colonies
2	Marked	*P. acnes*	Glenohumeral	2/2	Few leukocytes	Isolated colonies
3	None	*S. saccharolyticus*	Glenohumeral	2/2	No leukocytes	Isolated colonies
4	Severe	Coagulase-negative S.	Glenohumeral	2/4	Few leukocytes	After enrichment only
5	Marked	*P. acnes*	Glenohumeral	2/2	Few leukocytes	After enrichment only
			Subacromial	2/2		
		S. saccharolyticus	Subacromial	1/4		
6	Mild	Coagulase-negative S.	Glenohumeral	2/2	Few leukocytes	Isolated colonies
			Subacromial	2/2		
7	Marked	*P. acnes*	Glenohumeral	2/2	Few leukocytes	Isolated colonies
			Subacromial	2/2 (in 1 sample also Peptostreptococcus)		
8	Marked	*P. acnes*	Glenohumeral	2/2	Few leukocytes	Isolated colonies
			Subacromial	2/2		
9	No information	*P. acnes*	Glenohumeral	1/2	Few leukocytes	Isolated colonies
			Subacromial	1/7		
10	No information	*P. acnes*	Glenohumeral	5/7; 1/7 viridans *Streptococcus* only	No to moderate amount of leukocytes (one sample)	Isolated colonies

P Propionibacterium, *S Staphylococcus*

to moderate intraarticular inflammation. Microscopy of tissue samples revealed no microorganisms on gram stain and no or only a few leukocytes. Second, the expected response to antibiotic treatment – eradication of the pathogen and clinical improvement – did essentially not occur. On the contrary, most patients continued to be symptomatic. These findings are, however, preliminary and definitely require further investigation.

Oral antibiotic treatment, which is considered to be appropriate by current standards, appears relatively inefficient as such low-grade infections, whether eradicated or not, seem to be associated with persistent clinical symptoms.

Table 3 Antibiotic treatment and microbiological outcome

Case number	1st antibiotic treatment course	Duration of treatment (weeks)	Culture result of 2nd biopsy (number positive/ total number of samples)	Microscopy of samples at 2nd biopsy	Antibiotic treatment after 2nd biopsy	Duration of 2nd antibiotic treatment (weeks)	Persistence of infection[a]	Subjective assessment at follow-up
1	Am+Cl	4	*P. acnes* (3/3)	No leukocytes	Am+Le	30	Yes	Pain better/ROM worse (fusion)
2	Am	8	*P. acnes* (3/4)	Few leukocytes	Am, then Le+Ri	4 (Am), 26 (Le+Ri)	No	Same
3	Tei	3	Negative (0/4)	Few leukocytes	No	No	No	Better
4	Ci+Ri	8	No biopsy	No biopsy	No	No	Unknown	Same
5	Ci+Ri	36	*P. acnes* (5/6)	Few leukocytes	Am	13	Yes	Better
6	Ci+Ri	24	*P. acnes* (1/4)	Few leukocytes	No	No	No	Pain same/ROM better
7	Am	24	Negative (0/4)	No leukocytes	No	No	No	Better
8	Am+Ri	24	Coag-neg S. (1/7)	Few leukocytes	No	No	No	Better
9	Am+Ri	4	Negative (0/4)	Few leukocytes	No	No	No	Same
10	Ci+Ri, then Am	3 (Ci+Ri), 26 (Am)	*P. acnes* (3/4)	Few leukocytes	Am+Ri	26	Yes	Same

Am amoxicillin and clavulanic acid (2–3 g/day), *Cl* clindamycin (1.8 g/day), *Le* levofloxacin (1 g/day), *Ri* rifampicin (0.9 g/day), *Tei* teicoplanin (0.4 g/day), *Ci* ciprofloxacin (1–1.5 g/day), *P* Propionibacterium, *Coag-neg S*. coagulase-negative *Staphylococcus*
[a]Persistence of infection shown at 3rd biopsy

Most of the infections in this study were caused by *P. acnes* and coagulase-negative S. These bacteria have been recognised as typical skin flora, located particularly in moist areas such as the axilla [13, 14]. In various studies, high rates of contamination with such bacteria during surgery have been identified probably because these bacteria are located deep within the skin, thus not being fully accessible to antiseptic solutions that are used preoperatively for skin preparation [15–17].

Infections with *P. acnes* such as endocarditis, meningitis, brain abscess, septic arthritis, osteomyelitis and implant-related infections have been described [11, 13, 18–29]. At the shoulder, several studies reported *P. acnes* infections, most of them with the typical symptoms of infection such as wound erythema, purulent drainage or chronic sinus tracts as well as systemic symptoms such as fever and elevated C-reactive protein levels [1, 2, 6, 8]. In contrast to these studies, in our study these typical local and systemic symptoms of infection (except of pain) were absent, making detection of *P. acnes* infection difficult [30–32].

The diagnosis of *P. acnes* infection and other low-grade infections in this series was only made if cultures of at least two tissue samples were positive. These slow-growing bacteria may require prolonged incubation. Therefore, the recommendation is to monitor cultures for at least 10 days before declaring a result as negative. Similar conclusions have previously been made by other authors [1, 33, 34].

One shoulder in the current series was infected by *S. saccharolyticus*. It is part of the typical skin flora [35, 36]. In a literature search we found only two reported cases of endocarditis and one case of spondylodiscitis [37–39].

Therapy of low-grade infections mainly consisted in this series of oral antibiotics for a duration of 3–36 weeks. As harvesting of the tissue samples was predominantly done by arthroscopic synovectomies and subacromial bursal resection including removal of foreign bodies such as sutures or anchors, debridement was considered also part of the treatment. In three out of 10 cases the infection persisted. Due to the small number of cases and the lack of a prospective, randomised study design, we cannot make a recommendation regarding a successful treatment protocol. In some reported series, debridement followed by intravenous or oral antibiotics resulted in clinical eradication of the infection in all cases [1–3, 6, 8]. Whether intravenous treatment would have changed the outcome in this study cannot be answered with the current data. Oral instead of intravenous antibiotic treatment was chosen because the MIC of the selected antibiotics were very low. Local tissue and intraarticular concentrations, although not measured, probably exceeded the MIC against the microorganisms by far. Another obvious advantage of oral treatment is the feasibility of prolonged treatment in the outpatient setting.

Limitations of this study are the retrospective study design and the small number of patients. Therefore, the findings of this study should be considered as preliminary, and further investigations are needed.

In conclusion, pain after shoulder surgery can be caused by low-grade infection without the typical symptoms of infection such as erythema, purulent draining or fever. The diagnosis can only be made by tissue harvesting for cultures and a prolonged incubation time of about 10 days. Risk factors for failure of treatment with persistence of bacteria despite prolonged courses of antibiotic therapy might need a prospective study design.

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