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Nora Renz[1] · **Anna Rienmüller**[2] · **Olivier Borens**[3] · **Markus Scheibel**[1] · **Andrej Trampuz**[1]

[1] Center for Septic Surgery, Center for Musculoskeletal Surgery, Charité – University Medicine Berlin, Berlin, Germany

[2] Department of Orthopaedic Surgery, Medical University of Vienna in the General Hospital, Vienna, Austria

[3] Septic Surgical Unit, Department of Surgery and Anesthesiology, Lausanne University Hospital, Lausanne, Switzerland

Shoulder periprosthetic joint infection caused by *Propionibacterium acnes*

A retrospective cohort study

Introduction

Propionibacterium spp. is a facultative anaerobic Gram-positive bacterium, which is commonly found in the pilosebaceous follicles of the human skin, oral cavity, conjunctiva, respiratory and intestinal tract, and external ear canal [1]. Although it is often considered nonpathogenic, *Propionibacterium* spp. can cause severe infections including endocarditis, meningitis, brain abscess, endophthalmitis, conjunctivitis, and osteomyelitis or spondylodiscitis [2]. *Propionibacterium* spp. was also isolated in atherosclerotic lesions and several inflammatory conditions, but its pathogenetic role in these clinical situations is less clear.

The capability of forming a biofilm on the surface of medical devices is a predisposing factor for infection, especially in relation to artificial heart valves, ventriculoperitoneal shunts, joint prostheses, spinal hardware, and fracture-fixation devices [3]. However, perioperative antibiotic prophylaxis, new implant designs, and an improvement of surgical techniques and the operating room environment have considerably reduced the risk of intraoperative infection [4]. The frequency of periprosthetic joint infection (PJI) continuously increases as the number of implanted prostheses and indwelling time rise. In addition, improved diagnostic procedures, such as sonication of the removed prosthesis, inoculation in blood culture bottles, and molecular diagnostics, have improved the detection rate [3, 5–9].

Propionibacterium acnes PJI typically causes chronic infection manifesting several months after surgery, rarely in the early postoperative course [10–13]. Data on *P. acnes* shoulder PJI are limited, predominantly originating from case reports or smaller case series. We therefore performed a retrospective cohort study investigating the epidemiology, clinical characteristics, diagnostic pathway, treatment, and outcome of patients with shoulder PJI caused by *P. acnes*.

Patients and methods

Hospital setting. The study was conducted at two university institutions, a primary and a tertiary health-care center. They are major providers of medical care, together serving about 2 million inhabitants. The study was approved by the local Ethics Committees.

Study population. From 1 January 2010 through 31 December 2015, consecutive episodes of *P. acnes* shoulder PJI were included. Episodes of PJI were identified using the microbiology database and the infectious diseases consultation list. Each episode was evaluated by an orthopedic surgeon and infectious diseases specialist according to predefined criteria (see next section).

Definitions. PJI was diagnosed when at least one of the following criteria was present [3, 14]: (1) visible purulence of a preoperative aspirate or intraoperative periprosthetic tissue (as determined by the surgeon); (2) presence of a sinus tract communicating with the prosthesis; (3) acute inflammation in intraoperative permanent tissue sections at histopathology (as determined by the pathologist); (4) microbial growth in preoperative joint aspirate, at least two intraoperative periprosthetic tissue samples, or sonication fluid of the removed implant (>50 CFU/ml); (5) synovial fluid with >2,000 leukocytes/µl or >70 % granulocytes. Time to infection was defined as the interval from arthroplasty (or last surgical intervention of prosthesis) to the diagnosis of PJI. According to the time of manifestation, PJIs were classified in early (<3 months after surgery), delayed (3–24 months after surgery), and late (>24 months after surgery) infections.

Data collection. Hospital charts were reviewed with a standardized case-report form to retrieve demographic, clinical, and laboratory data. The following data were extracted: age, sex, underlying joint condition, prosthesis type, date of primary implantation, microbiology findings, histology findings, antimicro-

Tab. 1 Demographics and prosthesis characteristics

Characteristic	Patients ($n = 20$)
Age, median (range) – years	65 (54–77)
Male gender	15 (75 %)
Length of hospital stay, median (range) – days	42 (10–246)
Reasons for primary arthroplasty	
Osteoarthritis	9 (45 %)
Trauma	7 (35 %)
Cuff tear arthropathy	2 (10 %)
Rheumatoid arthritis	1 (5 %)
Osteonecrosis	1 (5 %)
Arthroplasty type	
Primary prosthesis	11 (55 %)
Revision prosthesis	4 (45 %)
Time from prosthesis implantation to diagnosis of PJI, median (range) – months	34 (2–60)
Preoperative diagnosis	
Confirmed PJI with *Propionibacterium* spp.	4 (20 %)
Confirmed PJI with unknown or other pathogen[a]	6 (30 %)
Suspected PJI	4 (20 %)
Aseptic loosening	6 (30 %)
Clinical signs and symptoms	
Shoulder pain	18 (90 %)
Local signs of inflammation (swelling or erythema)	12 (60 %)
Fever (>38 °C)	3 (15 %)
Sinus tract	3 (15 %)
Pseudoparalysis	2 (10 %)
Presentation of patients in relation after surgery	
Early (<3 months after arthroplasty)	3 (15 %)
Delayed (3–24 months after arthroplasty)	6 (30 %)
Late (>24 months after arthroplasty)	11 (55 %)
Radiological loosening of the prosthesis	14 (70 %)

Data are no. (%) of episodes, unless otherwise indicated

[a] Co-infection with coagulase-negative staphylococci was found in four patients, including *Staphylococcus epidermidis* ($n = 3$) and *S. hominis* ($n = 1$)

Tab. 2 Laboratory and microbiological characteristics

Characteristic	Patients ($n = 20$)
Preoperative serum C-reactive protein	
<10 mg/l	13 (65 %)
10–50 mg/l	6 (35 %)
>50 mg/l	2 (5 %)
Leukocyte count and differential in joint aspirate	
Leukocyte >2,000/µl	9/10 (90 %)
Granulocytes >70 %	10/10 (100 %)
Growth of *Propionibacterium* in samples	
Preoperative joint aspirate	4/12 (33 %)
Intraoperative periprosthetic tissue	12/20 (60 %)
Sonication fluid from removed prosthesis	16/18 (89 %)

Data are no. (%) of episodes, unless otherwise indicated

bial and surgical therapy, and treatment outcome at follow-up. We assessed radiological images at the time of diagnosis for signs of loosening (defined as a line zone greater than 1 mm on one or both components).

Results

Demographics and prosthesis characteristics. The demographic and prosthesis characteristics of 20 episodes of *Propionibacterium* shoulder PJI are shown in Tab. 1. The median age at time of PJI diagnosis was 65 years (range, 54–77 years). The median time from implantation to diagnosis of PJI was 34 months (range, 2–60 months). The diagnosis of PJI was preoperatively confirmed in 50 % of patients and suspected in 20 %; in 30 %, PJI was not considered before surgery. In nine patients (45 %), a previous revision was performed on the index shoulder prosthesis (four septic revisions, five presumed aseptic revisions). The shoulder pain was the primary clinical sign (90 %), followed by local signs of inflammation (60 %), whereas sinus tracts (15 %) and fever (10 %) were less common. Most patients (55 %) presented more than 24 months after arthroplasty, followed by delayed presentation during the period of 3–24 months after arthroplasty (30 % of patients). Radiological loosening was present in 14 patients (70 %).

The laboratory and microbiological results are shown in Tab. 2.

The preoperative C-reactive protein (CRP) value was normal (<10 mg/l) in 13 patients (65 %). Among ten patients in whom aspiration of the joint fluid was performed, leukocyte count was increased by >2,000 leukocytes/µl in nine patients (90 %) and granulocytes were increased by >70 % in all patients.

P. acnes was detected in preoperative joint aspirate in four of 12 patients (33 %) in whom the joint was punctured. Intraoperative tissue samples revealed the pathogen in 60 % and sonication of the prosthesis in 89 %. In four patients (20 %), co-infection with coagulase-negative staphylococci was present.

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N. Renz · A. Rienmüller · O. Borens · M. Scheibel · A. Trampuz

Shoulder periprosthetic joint infection caused by *Propionibacterium acnes* . A retrospective cohort study

Abstract

Background. *Propionibacterium acnes* is increasingly recognized as an important cause of shoulder periprosthetic joint infection (PJI). We performed a retrospective cohort study of *P. acnes* shoulder PJI to analyze the clinical, diagnostic, and treatment characteristics.
Methods. Patients diagnosed with shoulder PJI caused by *P. acnes* were retrospectively analyzed in two university hospitals. Patient data were retrieved through chart review. The outcome was evaluated at patient follow-up visits.
Results. The study included 20 patients with shoulder PJI (median age, 65 years; range, 54–77 years); 75 % were males. The median time from prosthesis implantation to diagnosis of PJI was 34 months (range, 2–60 months). Most PJI (55 %) were diagnosed >24 months after arthroplasty, followed by delayed manifestation 3–24 months after arthroplasty in 30 %. The diagnosis of PJI was preoperatively confirmed in 50 % of patients and suspected in 20 %. Persistent pain was present in 90 %, local signs of inflammation in 60 %, and radiological signs of loosening in 70 % of patients. *P. acnes* was cultured in joint aspirate in 33 %, periprosthetic tissue in 60 %, and sonication fluid in 89 % of patients. In four patients, coinfection with coagulase-negative staphylococci was found. One-stage prosthesis exchange was performed in four patients (20 %) and two-stage exchange in 15 patients (75 %); in one patient the prosthesis was not re-implanted. After a median follow-up of 26 months (range, 12–47 months), 18 patients (90 %) showed no signs or symptoms of infection.
Conclusion. *P. acnes* PJI typically manifested several years after implantation. In 30 % of patients, PJI was not suspected before surgery. In patients with persistent pain or prosthesis loosening, low-grade PJI should be excluded, including infection caused by *P. acnes*.

Keywords

Propionibacterium acnes · Shoulder · Periprosthetic joint infection · Biofilm · Arthroplasty

Periprothetische Schultergelenkinfekte verursacht durch *Propionibacterium acnes* . Eine retrospektive Kohortenstudie

Zusammenfassung

Hintergrund. *Propionibacterium acnes* wird zunehmend als wichtiges verursachendes Pathogen von Endoprotheseninfektionen des Schultergelenks erkannt. In dieser retrospektiven Kohortenstudie wurden klinische, diagnostische und therapeutische Charakteristika von Schulter-Endoprotheseninfektionen verursacht durch *P. acnes* analysiert.
Methoden. Patienten mit Schulter-EPI und Nachweis von *P. acnes* wurden in zwei Universitätskliniken analysiert. Die Daten wurden aus Patientenakten extrahiert. Der Behandlungserfolg wurde mittels klinischen Nachkontrolluntersuchungen erhoben.
Ergebnisse. In die Studie waren zwanzig Patienten (medianes Alter 65 Jahre; Zeitspanne 54–77 Jahre) mit Schulter-Endoprotheseninfektionen einbezogen, 75 % waren männlichen Geschlechts. Im Durchschnitt lagen 34 Monate zwischen Primärimplantation und Diagnosestellung (Zeitspanne 2–60 Monate). Die meisten Endoprotheseninfektionen (55 %) wurden >24 Monate nach Primärversorgung diagnostiziert, bei 30 % der Patienten nach 3–24 Monaten. Die Diagnose wurde präoperativ in 50 % der Fälle bestätigt und in 20 % der Fälle vermutet. Bei 90 % waren persistierende Schmerzen vorhanden, 60 % zeigten lokale Entzündungszeichen und bei 70 % wurde eine radiologische Lockerung festgestellt. *P. acnes* wurde bei 33 % im Gelenkpunktat, bei 60 % im periprothetischen Gewebe und bei 89 % der Patienten in der Sonikationsflüssigkeit nachgewiesen. Bei 4 Patienten (20 %) zeigte sich eine Koinfektion mit koagulase-negativen Staphylokokken. 4 Patienten (20 %) wurden mit einem einzeitigen Endoprothesenwechsel behandelt, bei 15 Patienten (75 %) wurde ein zweizeitiger Wechsel durchgeführt. Ein Patient hat die Reimplantation einer Endoprothese verweigert und der Spacer verblieb im Gelenk. Nach einem medianen Follow-up von 26 Monaten (Zeitspanne 12–47 Monate) zeigten 18 Patienten (90 %) keine Infektzeichen oder -symptome.
Schlussfolgerung. *P. acnes* Endoprotheseninfektionen treten typischerweise einige Jahre nach Primärversorgung auf. Bei 30 % der Patienten wurde vor der Operation keine Infektion vermutet. Bei Patienten mit persistierenden Schmerzen oder Frühlockerung der Endoprothese sollte eine Low-grade-Infektion ausgeschlossen werden, einschließlich durch *P. acnes* verursachte Infektionen.

Schlüsselwörter

Propionibacterium acnes · Schulter · Endoprotheseninfektion · Biofilm · Endoprothetik

Surgical and antimicrobial treatment. All 20 patients underwent surgical intervention (Tab. 3). In four patients (20 %), a one-stage exchange was performed, for whom the pathogen was known preoperatively through joint aspiration (n = 2) or during previous revision surgery for suspected aseptic loosening (n = 2). In most patients, a two-stage exchange was performed (n = 15, 75 %) with spacer implantation in the prosthesis-free interval. A short interval of 2–3 weeks until re-implantation was performed in five patients (25 %), whereas a long interval of 6–11 weeks was followed for ten patients (50 %). Temporary spacers of bone cement were impregnated with vancomycin (2 g per 40 g of polymethylmethacrylate). One patient refused re-implantation surgery and the spacer remained in place. Antimicrobial treatment included intravenous treatment for at least 1 week, followed by oral treatment for a planned total duration of 12 weeks.

Outcome evaluation. Patients were evaluated at regular follow-up visits with a median follow-up time of 26 months (range, 6–47 months). Evaluation of clin-

Tab. 3 Treatment and outcome

Characteristic	Patients (n = 20)
Surgical treatment	
One-stage exchange	4 (20 %)
Two-stage exchange – short interval (<6 weeks)	5 (25 %)
Two-stage exchange – long interval (≥ 6 weeks)	10 (50 %)
Removal of implant and permanent spacer implantation	1 (5 %)
Antimicrobial treatment, median (range) – days	
Duration of total therapy	85 (10–110)
Duration of initial intravenous therapy	18 (7–25)
Treatment outcome evaluation	
Follow-up time, median (range) – months	26 (6–47)
Infection-free status at follow-up[a]	18 (90 %)

Data are no. (%) of episodes, unless otherwise indicated
[a]One of 18 patients refused re-implantation of the prosthesis and retained the spacer. At follow-up 17 months after explantation this patient was infection-free

ical signs and symptoms of infection, CRP values, and x-ray analysis was performed 3–6 months after termination of antimicrobial treatment. At last follow-up, 18 patients (90 %) showed no signs or symptoms of infection. One patient refused re-implantation of the prosthesis and retained the spacer. At follow-up 17 months after explantation this patient was infection-free.

Discussion

While growth of *P. acnes* was previously often considered contamination, its pathogenic role was revealed in the past decade [2]. Improved diagnostic tests, higher awareness of possible PJI, and a better understanding of the pathogenesis in PJI have increased the detection of *P. acnes* PJI, especially after shoulder arthroplasty [12]. The slow growth rate and low virulence of *P. acnes* are the reason for delayed clinical presentation of infection [10]. The typical latency period from prosthesis implantation until clinical manifestation ranges from 1 to 3 years, but can extend to 10 years or more after implantation [15]. In the present study, the median latency between implantation and clinical manifestation of PJI was 2.8 years (34 months) and the longest period was 5 years. However, many patients probably had nonspecific signs and symptoms several months before diagnosing the PJI, such as chronic shoulder pain or decreased mobility. In the present study, in 30 % of patients PJI was not suspected preoperatively because of subtle clinical symptoms. This finding underlines the importance of the low threshold of differentiating "normal" postoperative pain or limited function from low-grade PJI [3].

For the correct diagnosis of chronic PJI, joint aspiration should be performed, although arthrocentesis may be difficult in shoulder joints. In synovial fluid, the leukocyte count and differential should be determined and the specimen sent for microbiological examination [4, 9, 16]. In *P. acnes* PJI, synovial fluid cultures are often false negative, as this facultative anaerobic pathogen is difficult to culture, requiring anaerobic culture media and prolonged incubation time (10–14 days) [2]. Owing to the slow replication rate and adherence to the implant surface, microbiological detection is challenging and contributes to the false-negative preoperative cultures, thus causing delay in the diagnosis of infection [2]. In four patients in our study (27 %), PJI was only confirmed by sonication of the implant and could not be diagnosed in preoperative joint aspirate or intraoperative periprosthetic tissue. Tunney et al. [17] demonstrated, that by using tissue cultures most PJI were missed, in particular *P. acnes*, which were only found by sonication of the removed prosthesis. Several other investigators confirmed the added value of sonication in the diagnosis of PJI [5, 6, 18].

Positive culture with isolation of low-virulent skin flora may be misinterpreted as contamination if the diagnostic work-up is not performed properly and does not include corresponding histopathological examination and cell count. Therefore, a meticulous diagnostic sampling of tissue and synovial fluid, which allows for confirmation of inflammation, is crucial in interpreting the microbiological results.

In PJI with *P. acnes*, CRP and blood leukocyte count are often normal and therefore do not allow exclusion of the PJI [3]. In our study, CRP levels were normal in the majority of patients (80 %).

Almost half of the patients in our study (40 %) had undergone at least one previous revision surgery for nonspecific symptoms (with partial or complete exchange of the prosthesis) before diagnosis of *P. acnes* PJI. Even if *P. acnes* was not found during previous revisions, the symptoms may have already been caused by this pathogen. In other studies, previous revision has been found to be a risk factor for PJI with *P. acnes* [19, 20].

Owing to its broad antimicrobial susceptibility, including rifampin as biofilm-effective antibiotic, *P. acnes*-caused PJI can be treated with a one-stage revision (absence of a sinus tract provided) or a two-stage revision with a short interval (2–3 weeks) [4].

In summary, *P. acnes* PJI typically manifests months to years after implantation and the infection is often not suspected before surgery. In patients with persistent pain or prosthesis loosening, low-grade PJI should be excluded, in particular infection caused by *P. acnes*. Only a complete diagnostic work-up with histopathological examination and joint aspiration with determination of cell count and differential allow for the discrimination between infection and contamination of this skin-resident organism.

Conclusion

- **Prosthetic shoulder infections caused by *P. acnes* often show a subtle clinical presentation due to the low-virulence of the organism, which causes delay or missing of the diagnosis.**

- **Owing to the slow replication rate and adherence to the implant surface, as well as the need for specific culture media and incubation time, microbiological detection is challenging and contributes to the false-negative preoperative cultures.**
- **Only a complete diagnostic work-up with histopathological examination and joint aspiration with determination of cell count and differential allow for the discrimination between infection and contamination of this skin-resident organism.**
- **Because of its broad susceptibility including rifampin as biofilm-effective antimicrobial agent and rare formation of sinus tracts, *P. acnes*-caused PJI can be treated with a one-stage revision or a two-stage revision with a short interval, depending on the bone and soft tissue condition.**

Corresponding address

Dr. N. Renz
Center for Septic Surgery, Center for Musculoskeletal Surgery, Charité – University Medicine Berlin
Charitéplatz 1, 10117 Berlin, Germany
nora.renz@charite.de

Compliance with ethical guidelines

Conflict of interest. N. Renz, A. Rienmüller, O. Borens, M. Scheibel, and A. Trampuz state that there are no conflicts of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975 (in its most recently amended version).

References

1. Grice EA, Segre JA (2011) The skin microbiome. Nat Rev Microbiol 9(4):244–253
2. Portillo ME, Corvec S, Borens O, Trampuz A (2013) Propionibacterium acnes: an underestimated pathogen in implant-associated infections. Biomed Res Int 2013:804391
3. Corvec S, Portillo ME, Pasticci BM, Borens O, Trampuz A (2012) Epidemiology and new developments in the diagnosis of prosthetic joint infection. Int J Artif Organs 35(10):923–934
4. Zimmerli W, Trampuz A, Ochsner PE (2004) Prosthetic-joint infections. N Engl J Med 351(16):1645–1654
5. Trampuz A, Piper KE, Jacobson MJ, Hanssen AD, Unni KK, Osmon DR et al (2007) Sonication of removed hip and knee prostheses for diagnosis of infection. N Engl J Med 357(7):654–663
6. Portillo ME, Salvado M, Trampuz A, Siverio A, Alier A, Sorli L et al (2015) Improved diagnosis of orthopedic implant-associated infection by inoculation of sonication fluid into blood culture bottles. J Clin Microbiol 53(5):1622–1627
7. Portillo ME, Salvado M, Sorli L, Alier A, Martinez S, Trampuz A et al (2012) Multiplex PCR of sonication fluid accurately differentiates between prosthetic joint infection and aseptic failure. J Infect 65(6):541–548
8. Achermann Y, Vogt M, Leunig M, Wust J, Trampuz A (2010) Improved diagnosis of periprosthetic joint infection by multiplex PCR of sonication fluid from removed implants. J Clin Microbiol 48(4):1208–1214
9. Piper KE, Jacobson MJ, Cofield RH, Sperling JW, Sanchez-Sotelo J, Osmon DR et al (2009) Microbiologic diagnosis of prosthetic shoulder infection by use of implant sonication. J Clin Microbiol 47(6):1878–1884
10. Dodson CC, Craig EV, Cordasco FA, Dines DM, Dines JS, Dicarlo E et al (2010) Propionibacterium acnes infection after shoulder arthroplasty: a diagnostic challenge. J Shoulder Elbow Surg 19(2):303–307
11. Kanafani ZA, Sexton DJ, Pien BC, Varkey J, Basmania C, Kaye KS (2009) Postoperative joint infections due to Propionibacterium species: a case-control study. Clin Infect Dis 49(7):1083–1085
12. Mook WR, Garrigues GE (2014) Diagnosis and management of periprosthetic shoulder infections. J Bone Joint Surg Am 96(11):956–965
13. Rienmüller A, Borens O (2016) *Propionibacterium* prosthetic joint infection: experience from a retrospective database analysis. Eur J Orthop Surg Traumatol 26(4):429–434
14. Trampuz A, Perka C, Borens O (2013) Prosthetic joint infection: new developments in diagnosis and treatment. Dtsch Med Wochenschr 138(31–32):1571–1573
15. Mook WR, Klement MR, Green CL, Hazen KC, Garrigues GE (2015) The incidence of propionibacterium acnes in open shoulder surgery: A controlled diagnostic study. J Bone Joint Surg Am 97(12):957–963
16. Trampuz A, Zimmerli W (2005) Prosthetic joint infections: update in diagnosis and treatment. Swiss Med Wkly 135(17–18):243–251
17. Tunney MM, Patrick S, Curran MD, Ramage G, Hanna D, Nixon JR et al (1999) Detection of prosthetic hip infection at revision arthroplasty by immunofluorescence microscopy and PCR amplification of the bacterial 16S rRNA gene. J Clin Microbiol 37(10):3281–3290
18. Janz V, Wassilew GI, Kribus M, Trampuz A, Perka C (2015) Improved identification of polymicrobial infection in total knee arthroplasty through sonicate fluid cultures. Arch Orthop Trauma Surg 135(10):1453–1457
19. Zappe B, Graf S, Ochsner PE, Zimmerli W, Sendi P (2008) Propionibacterium spp. in prosthetic joint infections: a diagnostic challenge. Arch Orthop Trauma Surg 128(10):1039–1046
20. Sperling JW, Cofield RH, Torchia ME, Hanssen AD (2003) Infection after shoulder instability surgery. Clin Orthop Relat Res 414:61–64