

Native joint *Propionibacterium* septic arthritis

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Abstract

Propionibacterium species are associated with normal skin flora and cultures may be dismissed as contaminants. They are increasingly recognized as a cause of septic arthritis following shoulder arthroplasty and arthrotomy. We identified three cases of *Propionibacterium* septic arthritis in native joints mimicking atypical osteoarthritis and review the literature, clinical course, and treatment of 18 cases. Two cases of *Propionibacterium* *acnes* in native knee joints and one in a sternoclavicular joint are described. A literature search for *Propionibacterium* septic arthritis was performed. Clinical course, treatment, and outcome are reviewed for all cases. Our three cases were combined with 15 cases from the literature. Fourteen cases showed few signs of acute infection, slow culture growth, and delayed diagnosis. In 3 cases an early culture was dismissed as a contaminant. Six cases were reported as caused by recent arthrocentesis. Fifteen cases were cured with antibiotics, although 5 of these 15 also required surgical intervention. Two patients were diagnosed while undergoing surgery for osteoarthritis. Four patients required arthroplasty and two of our patients will require arthroplasty for good functional results. *Propionibacterium* as a cause of septic arthritis in native joints demonstrates few signs of acute infection, presents with prolonged course, and is often misdiagnosed or unsuspected. Anaerobic growth may be delayed or missed altogether, and outcomes are consequently poor. Consider *Propionibacterium* septic arthritis in atypical osteoarthritis prior to arthroplasty.

Introduction

Propionibacterium species are anaerobes associated with normal skin flora, and cultures may be dismissed as contaminants. They are a less virulent but now well recognized cause of infection following shoulder surgery; and infection of orthopedic hardware, vertebral osteomyelitis, endovascular devices, and cerebrospinal shunts. The course is indolent, often without typical signs or symptoms of infection. Delayed anaerobic growth may contribute to falsely negative cultures, late diagnosis, and poor outcomes. Delayed recognition of *Propionibacterium* septic arthritis following shoulder arthroplasty has been well documented,¹ but native joint septic arthritis may be under recognized, undiagnosed, and consequently falsely attributed to orthopedic surgery.

Materials and Methods

We present three cases of *Propionibacterium acnes* septic arthritis in native joints, which exemplify chronic and atypical characteristics. The two septic knee joints were falsely considered to represent osteoarthritis. We did a search of the literature using PubMed citation septic arthritis *Propionibacterium* for cases, and Clinical Key citation *Propionibacterium* for case series. Fifteen cases laid out in Table 1 alongside our case numbers 1-3 demonstrate similar presentations and outcomes (see supplemental references for cases reviewed from the literature).

Case Report #1

A 56 year-old healthy male with moderate osteoarthritis of his right knee noted swelling and pain in the knee after a night out with friends. Four years prior he had repair of his right knee anterior cruciate ligament, without residual hardware or staples. He suspected minor trauma superimposed on his osteoarthritis and nursed the knee over 4 months. He presented to Arthritis Clinic with a large knee effusion for consideration of steroid injection. Arthrocentesis yielded 60cc of mildly inflammatory and bloody synovial fluid. Analysis revealed no crystals, many old RBCs, 2169 cells (30% neutrophils, 40% macrophages, 30% lymphocytes). Culture became positive on the 5th day with *P. acnes* which was considered to be a skin contaminant; given the long duration of symptoms, low cell count, and minimal pain. No steroid injections were given, and he was referred for arthroscopy to assess for polyvillonodular synovitis

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(PVNS), other synovial tumor, and extent of osteoarthritis. Synovial biopsies were negative for PVNS, and cultures again grew *P. acnes*. The diagnosis of septic arthritis was confirmed by synovial pathology and he received 6 weeks of IV ceftriaxone and arthrocentesis with negative cultures. He suffered residual painful ambulation and post infectious synovitis with recurrent sterile effusions. He will require future total joint arthroplasty, if cultures remain negative and post infectious synovitis subsides.

Case Report #2

A 44 year-old healthy male presented with tricompartment osteoarthritis. In 2001 he sustained a patellar rupture that was repaired primarily. He subsequently had a revision of the repair with xenograft. He had persistent knee pain and was treated with hyaluronate derivatives, cortisone injections, and multiple knee arthroscopies. He presented to the Orthopedic Surgery clinic with a joint effusion in August 2014 to pursue knee arthroplasty. At surgery in December 2014 the synovium was noted to be discolored with bloody, brown tinged synovial fluid and yellow-brown colored cartilage with irregularities, fissuring, and full-thickness loss. Synovial samples were taken and the knee was irrigated and closed without arthroplasty. Intra-operative syn-

ovial fluid cultures were negative, but synovial tissue culture became positive on the 7th day with *P. acnes*. He was started on Ceftriaxone and returned to the operating room for a synovectomy. He completed a 6-week course of Ceftriaxone with cure, but prior poor functional status has not improved.

Case Report #3

A 60 year-old male with medical comorbidities including obesity, alcohol abuse, and cirrhosis developed pain and swelling at the left sternoclavicular joint in September 2014, while working as a mason, without skin break or direct trauma. He was prescribed prednisone and cyclobenzaprine, but a week later developed fever and was admitted to hospital and given a short course of antibiotics for possible pneumonia. CXR was suspicious for a lung nodule. CT and PET scan showed a metabolically active lung mass adjacent to the sternoclavicular joint and manubrium. He left the hospital without complete evaluation. In November 2014 a follow-up CT scan noted improvement in lung findings, but progressive erosion of the SC joint. In February 2015 he returned to the admitting hospital where a CT guided biopsy revealed mild fibrosis and lymphoplasmacytic infiltrate, and culture grew *P. acnes* from thyoglycolate broth only. He remained afebrile; CRP was 10.3. Given the chronic course and possibility of skin contamination, a surgical biopsy was performed and confirmed *P. acnes* osteomyelitis with 3 of 4 positive tissue cultures. He was treated with 6 weeks of IV ceftriaxone followed by 3 weeks of PO moxifloxacin, with improvement in pain, swelling, and function.

Results

Insidious presenting courses occurred in 14 cases, most with predisposing trauma or arthritis, frequently osteoarthritis (OA). There were 4 acute presentations (cases 9, 10, 11, 12), all with likely unrecognized insidious courses. Case 9 presented with a hand abscess, acute *Propionibacterium* sepsis, and likely concomitant seeding of an osteoarthritic knee joint. This case was one of 3 polymicrobial infections (noted by μ). In the other two polymicrobial cases, multiple organisms were isolated following prolonged presenting symptoms (cases 7 and 8). Case 10 was diagnosed as acute crystal proven calcium pyrophosphate wrist arthritis, but progressed slowly over 9 weeks before a synovectomy with multiple cultures grew *Propionibacterium*. Case 11 had

Table 1. *Propionibacterium* septic arthritis in native joints.

Case	Age/Sex	Site	Risk	Duration	Prior surgery	Hardware	Treatment	Outcome	Function
1	56M	Knee ^s	OA	4 months	ACL repair	None	Ceftriaxone arthroscopy	Cure	Poor
2	44M	Knee, culture of synovial Bx	OA	? months	Patellar tendon repair	None	Ceftriaxone Synovectomy	Cure	Poor
3	60M	Sternoclavicular ^s	OA	6 months	None	None	Ceftriaxone Moxifloxacin	Cure	Good
4	71M	Shoulder ^s	OA	chronic	Recurrent	None dislocations	Clindamycin	Failure Arthroplasty	Good: two stage arthroplasty, cure
5	65F	Hip	Trauma	6 months	Fracture ORIF	Pin failed-removed	Methicillin Girdelston	Cure	Good arthroplasty
6	27M	Sternomanubrial joint, neck abscess	Reactive arthritis, steroid acne	3 months	None	None	Penicillin	Cure	Good
7	71M	Elbow ^μ	Trauma	years	Bone resection	None	Clindamycin arthrolyomy	Cure	Poor
8	50M	Elbow ^μ	Burns osteomyelitis	years	Bone resection	None	Vancomycin more bone resection	Failure epithelioid sarcoma	Poor
9	71M	Knee ^μ	Hand abscess, sepsis	2 weeks	None	None	Clindamycin	Cure	Good
10	42M	Wrist* synovial Bx	CPPD (1 day)	9 weeks	None	None	Penicillin	Cure	Poor
11	10M	Ankle*	JIA, many ankle steroid injections	4 days ? longer	Synovectomy	None	Penicillin clindamycin	Cure, chronic bone necrosis	Poor
12	52F	Knee*	RA	3 days	None	None	Penicillin	Cure	Good
13	28F	Knee*	RA	4 months	None	None	Clindamycin	Cure	Good
14	70F	Knee* culture of Synovial Bx	RA	1 month	None	None	Pristinamycin	Cure Gentamicin	Good
15	17F	Shoulder	Arthritis, acne HLA-B-27+	17 months	None	None	Amoxicillin Rifampicin	Cure erosion	Poor
16	78F	Hip*	OA, sepsis; lymphoma	6 months	None	None, bone resection	Cefazolin	Antibiotic spacer, Rifampin	Good: two stage cure arthroplasty
17	46M	Elbow	Abrasion	5 months	None	None	Amoxicillin	Cure	Good, arthroplasty
18	51M	Knee	Acne vulgaris	14 months	None	None	Azithromycin	Failure	Poor, sepho rx

*Arthrocentesis associated; ^μInitial culture discounted as contaminant; ^μMultiple organisms isolated.

underlying Juvenile Inflammatory Arthritis (JIA) and case 12 had underlying Rheumatoid Arthritis (RA). These two short presentations may have ignored longer courses attributed to the underlying inflammatory arthritis. The most common predisposing condition for *Propionibacterium* septic arthritis was underlying arthritis, and only one patient (case 16) was immunocompromised, with underlying lymphoma.

Propionibacterium can be difficult to grow, and when cultures are positive skin contamination complicates interpretation. In at least three cases an earlier culture was positive for *Propionibacterium* and was dismissed as a contaminant (noted by §). *Propionibacterium* are common skin flora; it is difficult to discern true infection from skin contamination. In our 3 cases, cultures took 5 days to 7 days for growth. All cases grew *P. acnes* except one which was *P. avidum*. Species known to cause deep infection include *P. acnes*, *P. avidum*, and *P. propionicum*. Since many laboratories do not speciate *Propionibacterium*, a request for speciation might help distinguish colonization from true infection.

Multiple cultures have been required when this organism is sought following septic shoulder arthroplasty.² Cases 2, 10 and 14 grew only from synovial biopsy cultures; synovial fluid cultures were negative. Several cases were not suspected and discovered at surgery (cases 2, 4, 5, 7). Case 17 is unique in that after a synovial fluid culture grew *P. acnes*, a stored frozen synovial biopsy specimen from 4 months earlier was retrospectively cultured anaerobically and also grew *P. acnes*. This case documents at least a four month course of septic arthritis, diagnosed as reactive arthritis and eventually treated as SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis) with poor outcome.

Although arthrocentesis associated septic arthritis is very rare, 6 cases were reported as possibly caused by recent arthrocentesis (noted by *). These cases do not report concurrent cultures from incident arthrocentesis. Since *Propionibacterium* are known to colonize normal skin, it is possible the organism was introduced by injection. Shoulders have been shown to harbor more *Propionibacterium* seated in anaerobic deep sweat glands and hair follicles than other anatomic locations,³ accounting for septic complication following shoulder arthroplasty.⁴ However, joint infection following arthrocentesis or injection varies between 0.007% and 0.037%.^{5,6} Given the rarity of needle induced septic arthritis, it is more likely the 6 cases thought to be arthrocentesis associated were actually previously infected cases of insidious onset septic

arthritis, true to the nature of *Propionibacterium* arthritis and misdiagnosed as various chronic arthritides.

All cases were cured of infection, except one complicated by adjacent epithelioid sarcoma (case 8), and one that failed to respond but was not recultured (case 18). *Propionibacterium* is susceptible to most antibiotics, with the notable exception of metronidazole.⁷ All patients received at least six weeks of appropriate antibiotics. Four patients required arthroplasty, and two of our patients will require arthroplasty to achieve good functional outcome. Outcomes in other patients were often complicated or poorly functional.

Two patients were diagnosed while undergoing surgery for OA. In our case number 2, arthroplasty was deferred. In case number 4, shoulder arthroplasty was performed, but failed and required subsequent two stage revision arthroplasty. Case 5 was also diagnosed from cultures taken during hip arthroplasty; ORIF of an intracapsular fracture failed with hip subluxation. Cure required prosthesis removal, Girdelstone fixation, antibiotics and eventual second stage arthroplasty. Six additional patients (cases 7, 8, 10, 11, 15, 18) had poor functional outcomes; one patient had bone necrosis, another had severe joint erosion, one required arthrotomy with debridement, one required synovectomy with poor wrist function, another required bone resection, and case 18 failed azithromycin and was treated as SAPHO syndrome. One patient (case 6) suffered necrosis of the sternomanubrial joint, of little functional consequence. The patient with acute septic arthritis due to hand abscess and sepsis had good functional outcome of the secondary knee infection. Three patients with RA (cases 12, 13, 14) underwent relatively early diagnostic arthrocentesis for monoarticular arthritis and had good outcomes. *Propionibacterium* arthritis was curable in this series; but gradual onset, few hallmarks of acute infection, and delayed diagnosis often resulted in poor function.

Discussion and Conclusions

Propionibacteria are anaerobes of low virulence and part of our normal flora; but isolates at sterile sites, positive Gram stain, pure growth of *Propionibacterium* species *acne*, and indolent monoarticular arthritis in native joints may all indicate true infection. Arthrocentesis and culture including anaerobic broth should be considered for joints with chronic inflammatory arthritis prior to steroid injection or joint arthroplasty. The shoulder is heavily colonized with *Propionibacterium*.³ Infection after joint

arthroplasty or rotator cuff surgery in a native joint may be due to *Propionibacterium*. Shoulder osteoarthritis is rare, because shoulders are non-weight bearing joints; this diagnosis particularly merits arthrocentesis with anaerobic culture prior to arthroplasty.

Propionibacteria form biofilms and truly septic joints need to be cleared of infection prior to insertion of hardware. Cases 4 and 5, where arthroplasties were retained, both failed cure with antibiotics alone. *Propionibacterium* septic prosthetic joints may benefit from two stage revision arthroplasty (case 4), as debridement with retention or one stage arthroplasty is likely to fail secondary to biofilms.

Cultures taken at surgery can be interpreted as infection or as contamination. Two studies cultured shoulders at multiple sites in the operating room just prior to total shoulder arthroplasty utilizing anaerobic thioglycolate broth held for at least 14 days; 41.8% and 56% had at least one culture positive for *P. acnes*.^{4,8} Another perioperative culture study grew *P. acnes* in just 3.1% of patients, but did not use thioglycolate broth for their anaerobic culture, perioperative antibiotics were given prior to culture, and shoulders were not considered infected by histopathology.⁹ Early septic arthritis following shoulder arthroplasty occurs in less than 1%, so are these culture positive preoperative shoulder joints infected or just colonized? The first study treated all culture positive joints with one month of oral antibiotics following arthroplasty. Mook *et al.*¹⁰ tried to determine the rate of deep meticulous culture growth from patients undergoing open surgery of the glenohumeral joint. In patients without prior surgery, 18% had at least one positive culture, 93% of which grew *P. acnes*. None were considered infected, but an accompanying editorial reviewed other studies and concluded the management of painful shoulder arthroplasty remains highly variable.¹¹

SAPHO syndrome represents a constellation of synovitis, acne, palmo-plantar pustulosis, hyperostosis, and osteitis. The well-known association with *P. acnes* is exemplified by a study confirming 14 of 21 patients with culture positive needle biopsies of osteitis lesions, and their response to antibiotics.¹² Previously considered a form of reactive arthritis, could SAPHO represent insidious *Propionibacterium* infection, or autoimmunity initiated by such infection? Diagnosis of atypical osteoarthritis syndromes, such as Milwaukee Shoulder, SAPHO syndrome, and Chronic Recurrent Multifocal Osteitis (CRMO)¹³ should all be reconsidered in this context.

References

1. Kanafani ZA, Sexton DJ, Pien BC, et al. Postoperative joint infections due to *Propionibacterium* species: a case-control study. *Clin Infect Dis* 2009;49:1083-5.
2. Dodson CC, Craig EV, Cordasco FA, et al. *Propionibacterium acnes* infection after shoulder arthroplasty: a diagnostic challenge. *J Shoulder Elbow Surg* 2010;19:303-7.
3. Patel A, Calfee RP, Plante M, et al. *Propionibacterium acnes* colonization of the human shoulder. *J Shoulder Elbow Surg* 2009;18:897-902.
4. Levy PY, Fenollar F, Stein A, et al. *Propionibacterium acnes* postoperative shoulder arthritis: an emerging clinical entity. *Clin Infect Dis* 2008;46:1884-6.
5. Geirsson AJ, Statkevicius S, Vikingsson A. Septic arthritis in Iceland 1990-2002: increasing incidence due to iatrogenic infections. *Ann Rheum Dis* 2008;67:638-43.
6. Hollander J. Intra-articular corticosteroid therapy in arthritis. *MD State Med J* 1969;19:62.
7. Roberts SA, Shore KP, Paviour SD, et al. Antimicrobial susceptibility of anaerobic bacteria in New Zealand: 1999-2003. *J Antimicrob Chemother* 2006;57:992-8.
8. Sethi PM, Sabetta JR, Stueck SJ, et al. Presence of *Propionibacterium acnes* in primary shoulder arthroscopy: results of aspiration and tissue cultures. *J Shoulder Elbow Surg* 2015;24:796-803.
9. Maccioni CB, Woodbridge AB, Balestro JC, et al. Low rate of *Propionibacterium acnes* in arthritic shoulders undergoing primary total shoulder replacement surgery using a strict specimen collection technique. *J Shoulder Elbow Surg* 2015;24:1206-11.
10. Mook WR, Klement MR, Green CL, et al. The incidence of *Propionibacterium acnes* in open shoulder surgery: a controlled diagnostic study. *J Bone Joint Surg Am* 2015;97:957-63.
11. Hasan SS, Ricchetti ET. When is a positive culture in shoulder surgery not an infection? *J Bone Joint Surg Am* 2015;97:e51.
12. Assmann G, Kueck O, Kirchhoff T, et al. Efficacy of antibiotic therapy for SAPHO syndrome is lost after its discontinuation: an interventional study. *Arthritis Res Ther* 2009;11:R140.
13. Wipff J, Costantino F, Lemelle I, et al. A large national cohort of French patients with chronic recurrent multifocal osteitis. *Arthritis Rheumatol* 2015;67:1128-37.