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 arthroscopy. 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 osteoarthritides. 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 (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-
Results

A 60-year-old male with medical conditions including obesity, aortic valve disease, and hepatitis C (cases 7 and 10) presented with a 7th day with Propionibacterium acnes. He was started on a 7-day course of Ceftriaxone and on a follow-up CT a week later developed pain and was admitted to hospital. He left the hospital without complete evaluation. In November 2014 a follow-up CT scan noted improvement in lung findings, but progressive improvement in lung findings, but progressive improvement in lung findings. In February 2015 he returned to the urology department. He was prescribed prednisone and antibiotics for possible pneumococcal infection. The case was one with a manubrium. He left the hospital without complete evaluation.

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

| Case | Age/Sex | Site                                      | Risk                        | Duration | Prior surgery | Hardware                  | Treatment                        | Outcome       | Function  |
|------|---------|-------------------------------------------|-----------------------------|----------|---------------|---------------------------|----------------------------------|---------------|----------|
| 1    | 56M     | Knee§                                     | OA                          | 4 months | ACL repair    | None                      | Ceftriaxone arthroscopy           | Cure          | Poor      |
| 2    | 44M     | Knee, culture of synovial Bx              | OA                          | 7 months | Patellar tendon repair | None                      | Cure                           | Poor          |
| 3    | 60M     | Sternoclavicular§                         | OA                          | 6 months | None          | None                      | Cure                           | Good          |
| 4    | 71M     | Shoulder§                                 | OA                          | Chronic  | Recurrent     | None                      | Cure                           | Good          |
| 5    | 65F     | Hip                                       | Trauma                      | 6 months | Fracture ORIF | Pin failed removed         | Methicillin                   | Cure          | Good      |
| 6    | 27M     | Sternomastoidal joint, neck abscess       | Reactive arthritis, steroid | 3 months | None          | None                      | Penicillin                     | Cure          | Good      |
| 7    | 71M     | Elbow                                     | Trauma                      | Years    | None          | None                      | Clindamycin                     | Cure          | Poor      |
| 8    | 50M     | Elbow                                     | Burns osteomyelitis         | Years    | Bone resection| None                      | Vancomycin more bone resection  | Failure epithelioid sarcoma     | Poor          |
| 9    | 71M     | Knee                                      | 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    | 4 days   | None          | None                      | Penicillin clindamycin           | Cure, chronic  | Poor      |
| 12   | 52F     | Knee*                                     | RA                          | 3 days   | None          | None                      | Penicillin                      | Cure          | Good      |
| 13   | 23F     | Knee*                                     | RA                          | 4 months | None          | None                      | Clindamycin                     | Cure          | Good      |
| 14   | 70F     | Knee* culture of Synovial Bx              | RA                          | 1 month  | None          | None                      | Pristinamycin                   | Good          |
| 15   | 17F     | Shoulder                                  | Arthritis, acet. HLA-B 27*  | 17 months| None          | None                      | Amoxicillin clindamycin          | Cure erosion    | Poor      |
| 16   | 78F     | Hip*                                      | OA, sepsis; lymphoma        | 6 months | None          | None                      | Cefadroxil                      | Good two stage | Poor      |
| 17   | 46M     | Elbow                                     | Abrasion                    | 5 months | None          | None                      | Amoxicillin                     | Cure, arthroplasty | Good, arthroplasty |
| 18   | 51M     | Knee                                      | Acne vulgaris               | 14 months| None          | None                      | Clindamycin                     | Cure          | Poor      |

*Arthritis associated; §Initial culture discounted as contaminant; *Multiple 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 immune-compromised, 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 arthroplasty 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 sternomandibular 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 monoarthritis 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 acnes, 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.8,9 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 mucitic 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.
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