CASE REPORT

De novo *Propionibacterium acnes* septic arthritisThomas Crowhurst,¹ Joanna Tieu,¹ Shaun Fowler,² Simon Burnet¹¹Department of Rheumatology, The Queen Elizabeth Hospital, Adelaide, South Australia, Australia²Fowler Simmons Radiology, Adelaide, South Australia, Australia**Correspondence to**
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SUMMARY

We report the third identifiable case of septic arthritis due to *Propionibacterium acnes* arising in the absence of prior surgical intervention. This anaerobic Gram-positive bacillus is now recognised as an important cause of postoperative infections, typically presenting in an indolent fashion some months after surgery. Reports of de novo septic arthritis due to *P. acnes* are exceedingly rare. Our case adds to the literature and significantly broadens the reported pathogenic potential of the organism, which in this instance has caused rapid and serious joint destruction.

BACKGROUND

Propionibacterium acnes is an aerotolerant anaerobic Gram-positive bacillus long considered a normal human skin commensal; however, its pathogenicity is increasingly recognised.¹ Cohort studies indicate *P. acnes* infections most commonly arise following orthopaedic surgery and neurosurgery, especially with implanted devices.^{2–6} Such infections tend to present in a subacute or insidious chronic manner. Postoperative *P. acnes* infections may be increasing.⁵ De novo *P. acnes* septic arthritis appears to be exceedingly rare, with only two cases identifiable in the English language literature.^{3, 7} We report a third such case in which this organism, in contrast with previous reports, has caused aggressive joint destruction.

CASE PRESENTATION

We report a case of a 42-year-old right-handed man from rural Australia who presented with acute right wrist pain and swelling. He was an avid golfer. His only medical history was childhood asthma and a vasectomy 3 months earlier. He took no medications and had no allergies. He had no personal history of crystal arthropathy, psoriasis or nephrolithiasis. He consumed five standard drinks of alcohol on most days and denied tobacco or illicit drug use. There was no relevant family history.

The patient was woken with severe right wrist pain. The wrist became stiff and markedly swollen over hours. There was no preceding trauma. He denied fevers, sweats, rigors or other focal infective symptoms. There was no other arthralgia. He denied prior episodes. There was no bite/sting. He had no recent exposure to natural waterways or livestock/pets. He had never been overseas. There was no history of tuberculosis exposure. There was no history to suggest immunodeficiency.

He presented to his general practitioner who initially treated empirically for gout with colchicine with no benefit. Plain radiography at this time was normal. He was twice referred for

ultrasound-guided aspiration, but this was not attempted as no joint fluid could be identified. Given persistence of these symptoms for 1 month, the patient was referred to a rheumatologist.

At the time of rheumatologist examination, there was marked synovitis of the right wrist with flexor and extensor tenosynovitis. Wrist flexion and extension were limited to only 10° with preserved neurovascular function. The remainder of the examination was unremarkable.

INVESTIGATIONS

Investigations at this time revealed mild leucocytosis ($11.1 \times 10^9/L$) with mild neutrophilia ($8.77 \times 10^9/L$), normal urate (0.44 mmol/L), normal calcium (2.29 mmol/L), normal renal function (creatinine 76 $\mu\text{mol/L}$) and a C reactive protein (CRP) of 170 mg/L with an erythrocyte sedimentation rate (ESR) of 70 mm/hour. Serum procalcitonin was not measured. Multiple blood cultures were negative. Rheumatoid factor, anticyclic citrullinated peptide and antinuclear antibodies were not detected. Hepatitis B, hepatitis C and HIV serology was negative.

Blind aspiration of the wrist joint was attempted at initial rheumatology review but was technically difficult. Analysis revealed calcium pyrophosphate dihydrate crystals, not deemed causative/contributory, and scant growth of *Staphylococcus epidermidis*, considered a contaminant. Oral prednisolone 20 mg daily was started. Ultrasound via a specialist radiologist demonstrated marked synovitis of the radiocarpal and ulnocarpal joints with prominent, thickened and markedly hyperaemic synovium. Ultrasound-guided aspiration performed at this time (5 weeks after symptom onset and 1 week after the initial blind aspiration) yielded erythrocytes and did not identify crystals, bacteria or leucocytes.

Seven weeks after symptom onset and 3 weeks after rheumatology consultation, with continued oral prednisolone 20 mg daily, there had been a significant reduction in inflammatory markers although synovitis persisted with only modest clinical improvement. The prednisolone was increased to 50 mg daily. MRI along with repeat plain radiography was then performed. This revealed a dramatic inflammatory process characterised by a rapid and progressive destructive arthropathy (figures 1 and 2). The clinical picture was of right wrist septic arthritis and the patient was admitted to facilitate surgical washout and synovial biopsy. Prednisolone was weaned to cessation at this time.

Inpatient investigation included multiple blood cultures with mycobacterial and fungal cultures, tuberculosis interferon- γ release assay, Q fever

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Figure 1 MRI of the right wrist revealing diffuse loss of the articular cartilage of the radiocarpal, distal radioulnar and midcarpal joints; diffuse marrow oedema through distal radius and carpus with evidence of bone erosion involving articular surfaces in all three compartments; diffuse postgadolinium enhancement of the synovium and peri-articular soft tissues in all three compartments and some involvement of the carpometacarpal joints two through five; full thickness defect in the scapholunate ligament and likely lunotriquetral ligament; inflammation of the extensor compartment two and four tendon sheaths but no significant flexor tenosynovitis; and no soft tissue calcification.

serology, iron studies, caeruloplasmin and copper level; all were normal and the patient remained afebrile. There was no lymphopaenia. Peripheral flow cytometry and immunoglobulins were normal. Plain radiographs of the contralateral wrist and both knees were normal with no evidence of chondrocalcinosis, and plain chest radiography was normal.

The patient proceeded to right wrist wash-out, synovial debridement and biopsy ~9 weeks after symptom onset and 5 weeks after the initial blind aspiration. Intraoperatively florid synovitis without effusion was seen. Histopathology of multiple biopsies noted surface synovium in some fragments, focal surface fibrin, no inflammatory infiltrate, no crystals, no acid

fast bacilli or fungal elements and no rheumatoid-like features. Subsequently prolonged incubation of two separate culture broths returned *P. acnes* and no other organisms.

DIFFERENTIAL DIAGNOSIS

De novo *P. acnes* infection was determined to be the cause of the rapidly progressive and destructive arthritis here. The clinical features and trajectory were felt to be entirely consistent with an infective process, the radiology strongly supported the clinical diagnosis of septic arthritis, the two separate broth culture results provided convincing microbiological data and finally the patient had a compelling response to treatment for *P. acnes* septic arthritis.

Uric acid and calcium pyrophosphate dihydrate crystal arthropathy were considered unlikely for a number of reasons. Monosodium urate crystals were not identified on any joint aspirate, effectively excluding gout, and the finding of calcium pyrophosphate dihydrate crystals on the first blind aspirate was considered a false positive; the severity of the presentation was felt inconsistent with acute calcium pyrophosphate dihydrate crystal deposition disease, identification of such crystals has a notable false-positive rate, the patient did not respond to treatment as expected for this condition and calcium pyrophosphate dihydrate crystals were not identified by subsequent ultrasound-guided and open synovial samples.⁸ Furthermore, review of all imaging from the case by a specialist musculoskeletal radiologist noted no features of gout such as punched-out erosions or tophi nor any features of calcium pyrophosphate dihydrate deposition disease such as chondrocalcinosis. The osteopaenia on plain films in addition to the diffuse and rapid chondral loss identified on MRI were felt to be inconsistent with crystal arthropathy of any form.

The scant growth of *S. epidermidis* from the first blind aspirate was considered to be contaminant; this organism is a common contaminant and was not detected in the other two synovial samples, both of which were taken before initiation of antibiotic therapy. Extended incubation of the initial two percutaneous synovial samples was not performed as this does not form part of standard laboratory procedures for such samples; local protocol is for 5-day culture of such specimens in contrast with 14-day cultures that are performed on surgical specimens. This provides an explanation for why *P. acnes* was identified only following the open biopsy.

Figure 2 Correlative plain radiography demonstrating diffuse periarticular osteopaenia of the carpus, distal radius and ulna plus bone erosion and complete loss of joint space.

An alternative possibility is that the initial presentation was one of an acute calcium pyrophosphate dihydrate crystal arthropathy with *P. acnes* being iatrogenically introduced by one of the initial percutaneous synovial fluid aspirates. This is significantly less likely for two additional reasons over and above the aforementioned points that the patient failed to respond to sufficient treatment for crystal arthropathy and that there were no radiographic features supporting a diagnosis of acute calcium pyrophosphate dihydrate crystal arthropathy. First, given the symptoms and signs reached maximal intensity very early in the disease course, it is evident that the process reached its destructive zenith well before any event that could have introduced *P. acnes*. Second, given this clinical trajectory, the relatively short interval between the percutaneous synovial fluid aspirates and MRI compared with the significantly longer overall disease duration would strongly argue that the infective process driving the joint destruction was present from symptom onset; the hypothesis that *P. acnes* was introduced by one of the percutaneous synovial fluid aspirates and subsequently caused such aggressive joint destruction in a maximum of 3 weeks is inconsistent with the clinical course.

There was no clinical, serological or radiological evidence of an incipient autoimmune disorder initially or at follow-up at 8 months.

TREATMENT

The patient was started on benzylpenicillin continuously via peripherally inserted central catheter at 10.8 g per day for 6 weeks followed by 3 months of amoxicillin 400 mg orally three times per day.

OUTCOME AND FOLLOW-UP

Follow-up during and at completion revealed ongoing symptomatic and clinical improvement, with reduced pain and synovitis with normal inflammatory markers. Eight months after presentation, the patient had no synovitis but was receiving occupational therapy for residual poor wrist range of movement.

DISCUSSION

Tebruegge *et al*³ analysed 49 patients with *P. acnes* infections. Neurosurgical patients represented the majority (28 cases) followed by orthopaedic patients (15 cases). Most (>93%) had preceding surgery and implanted material was infected in 59% and 80% of neurosurgical and orthopaedic patients, respectively. Neurosurgical patients presented at a median of 7.5 weeks postoperatively or after trauma (range 3–244 weeks) whereas for orthopaedic patients the median was 5 weeks (range 2.0–78 weeks). Both groups of patients tended to present without fever. Only two patients in this cohort had a *P. acnes* infection arise de novo in the absence of surgery; one with talocrural septic arthritis, though no other details were reported, and the other with thoracic empyema. Greater than 93% of all patients were cured through removal of implanted material and/or antibiotics.

Titécát *et al*⁵ examined trends in osteoarticular infections across a decade. *Propionibacterium acnes* was responsible for 5.8% of infections, becoming more common across the period. It is unclear whether any infections were de novo. Walter *et al*⁴ retrospectively audited 3144 patients with bone/joint infections over a 3-year period and found 103 were due to anaerobic organisms, with data presented for 61 of these patients. *Propionibacterium acnes* was responsible for 20 of these infections; all were postoperative and generally occurred late

(>6 months postintervention). Walter *et al* collected data for 16 of these cases to 24 months, noting complete cure in all.

Kanafani *et al*⁶ conducted a case–control review of 40 patients with postoperative *P. acnes* joint infections. The shoulder was the most common joint affected (75% of cases) followed by the hip (13%) and knee (8%). The infections tended to be indolent, presenting a median of 210 days postoperatively, although 24% manifested <1 month postoperatively and were aggressive. The two key risk factors were male gender (75% in cases vs 46% in controls) and history of surgery on same joint prior to index operation (43.6% in cases vs 7.5% in controls).

We identify one other report of de novo *P. acnes* septic arthritis excluding that by Tebruegge *et al*³. Yocum *et al*⁷ describe a 71-year-old man with sequential polyarthritis affecting his hands then the left hip, knee and ankle over 2 weeks. He was consistently afebrile. Synovial fluid predominantly cultured *P. acnes*; however, some sites harboured polymicrobial infections. One blood culture was positive for *P. acnes* but all others were negative. No radiological information is provided. The patient responded to clindamycin.

Kooijmans-Coutinho *et al*⁹ report two cases of *P. acnes* septic arthritis in patients with rheumatoid arthritis after intra-articular injection/arthrocentesis. Both presented with acute synovitis within days, with *P. acnes* detected by synovial fluid cultures, and both responded well to antibiotics. Radiographs demonstrated no bone erosion/joint space narrowing. One patient was afebrile while the other had low-grade fever. Bertin *et al* report a case of a 70-year-old woman with rheumatoid arthritis who developed monoarthritis of the knee 1 month after intra-articular steroid, with synovial fluid cultures growing *P. acnes* and the patient responding well with antibiotics.¹⁰ No radiographic information was provided.

There are few reports of other non-joint de novo *P. acnes* infections occurring in non-surgical settings. Burnham *et al*¹¹ summarise nine cases of meningitis secondary to this organism without preceding surgery. Acute and indolent presentations were equally represented. Acute presentations were characterised by classic meningism, whereas indolent presentations commonly involved headache and altered consciousness progressing over weeks to months. Consistent with apyrexial presentations in *P. acnes* bone and joint infections, all six adult presentations with de novo meningitis due to this organism demonstrated an absence of fever. All patients demonstrated response to treatment and the majority (7 of 9) had no residual deficits; one patient with prior stroke, advanced age (72 years) and underlying chronic lymphocytic leukaemia had residual neurologic deficits, while the index patient had complete microbiological response to vancomycin then ceftriaxone but developed leptomeningeal carcinomatosis secondary to malignant melanoma and entered hospice care.

The present case adds to the two other reported instances of de novo septic arthritis due to *P. acnes*. A general pattern in the literature is that infection with this organism in the postprocedure setting tends to present in a relatively indolent subacute or chronic manner. Our case reveals de novo *P. acnes* septic arthritis can cause rapid joint destruction over weeks. *Propionibacterium acnes* infection also appears to occur in the absence of fever, even in the context of a rapidly progressive and destructive septic arthritis. We suggest clinicians and laboratories remain cognisant of the potential for *P. acnes* to cause bone and joint infections after procedures (including simple arthrocentesis) and, rarely, for this seemingly indolent anaerobe to cause fulminant and destructive septic arthritis.

Learning points

- ▶ *Propionibacterium acnes* appears to be an increasingly common cause of postoperative septic arthritis, producing a typically insidious and indolent course without fever.
- ▶ *Propionibacterium acnes* can, in rare cases, cause rapidly progressive and destructive septic arthritis including as a de novo infection.
- ▶ Clinicians and laboratories should remain cognisant of the potential for this fastidious anaerobic organism, once considered a benign human skin commensal, to cause serious bone and joint infections.

Contributors TC contributed to conception and design of study and report; primary responsibility for drafting article; reviewed final article; agreed to be accountable for article content. JT contributed to conception and design of study and report; primary responsibility for reviewing drafted article in exhaustive detail; reviewed final article; agreed to be accountable for article content. SF contributed to conception and design of study and report; secondary responsibility for drafting article; reviewed final article; primary responsibility for image review and analysis; agreed to be accountable for article content. SB primary responsibility for conception and design of study and report; primary responsibility for data collection; secondary responsibility for drafting article; reviewed final article; agreed to be accountable for article content.

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