Published in final edited form as:

Arthritis Care Res (Hoboken). 2020 March ; 72(3): 293–300. doi:10.1002/acr.24082.

An 80-Year-Old Man With Fevers, Altered Mental Status, and Joint Effusions

Naomi Serling-Boyd, Zachary Wallace, Jana Jarolimova, Sheila Arvikar, Eli M. Miloslavsky
Massachusetts General Hospital, Boston

CASE PRESENTATION

Chief symptoms

An 80-year-old man presented with fevers, altered mental status, weakness, and pain in both legs.

History of present illness

An 80-year-old man with atrial fibrillation, hypertension, osteoarthritis status post bilateral total shoulder arthroplasty and right hip arthroplasty, a recent diagnosis of dementia, and monoclonal gammopathy of undetermined significance (MGUS) was admitted with fever, joint pain, and weakness. Prior to his first admission for these symptoms, he had been living independently at home with his wife and exercised multiple times weekly. Two months prior to the current hospitalization, he was admitted to another hospital (first admission) for acute functional decline with leg weakness that had developed over the course of approximately 2 weeks, altered mental status with episodes of confusion, and fever to 102.2°F. He noted shoulder and knee pain that was worse with movement. On physical examination, he was fully alert and oriented and was noted to have 4/5 strength with hip flexion, as well as 4/5 strength with shoulder abduction bilaterally. No spinal tenderness was noted on examination. He was able to ambulate with assistance. An evaluation for infections included blood cultures (negative after 5 days), a normal lumbar puncture result (1 nucleated cell per microliter, normal protein), normal urinalysis findings, chest radiography without any focal consolidation or other acute findings, and negative Lyme serologies. Serum procalcitonin was elevated at 0.29 ng/ml (normal range 0.00–0.08). Other laboratory values can be found in Table 1. Computed tomography (CT) of his chest, abdomen, and pelvis did not reveal any acute process or lymphadenopathy. Transthoracic echocardiogram (TTE) revealed dilated right and left atria, a left ventricular ejection fraction of 65%, and no evidence of

Address correspondence to Naomi Serling-Boyd, MD, Massachusetts General Hospital, 55 Fruit Street, Bulfinch 165, Boston, MA, 02114. nserling-boyd@mgh.harvard.edu.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Serling-Boyd had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Serling-Boyd.

Acquisition of data. Serling-Boyd, Wallace, Jarolimova, Arvikar, Miloslavsky.

Analysis and interpretation of data. Serling-Boyd, Wallace, Jarolimova, Arvikar, Miloslavsky.

No potential conflicts of interest relevant to this article were reported.

vegetations. He was seen by the infectious disease service and started doxycycline treatment for a presumed tick-borne infection, resulting in mild improvement in his mental status. He was discharged with home health services, with plans to complete a 2-week course of doxycycline.

After completing the doxycycline course, he was readmitted (second admission) with fevers (to 102.5°F on admission) and recurrent altered mental status. He was noted to have an effusion of the left prosthetic shoulder joint. Orthopedic surgery service was consulted and aspirated his left shoulder, which showed 3,205 nucleated cells per microliter with 71% neutrophils, 21% lymphocytes, and 8% macrophages; fluid was negative for crystals, and joint fluid culture was negative. Additional evaluation included a normal creatine phosphokinase and rheumatoid factor (RF) finding, as well as negative results for anti-cyclic citrullinated peptide (CCP), anti-Jo-1, myositis panel, antinuclear antibody (ANA), anti-double-stranded DNA, anti-Ro, anti-La, anti-Sm, anti-U1 RNP, and Lyme antibody screen. He was treated with a 1-month course of doxycycline for a possible indolent prosthetic joint infection.

The patient was then readmitted (third admission) to the same hospital for altered mental status, joint pain, and fevers (to 101°F). He reported left hip pain as well as myalgias throughout his entire upper body without any reported morning stiffness. His temperature was 100.5°F on admission and he was hemodynamically stable. His erythrocyte sedimentation rate (ESR) was 45 mm/hour (normal range 0–13) and C-reactive protein (CRP) level was 99.8 mg/liter (normal range 0–8). Polymyalgia rheumatica (PMR) was considered, and he was started on prednisone 60 mg daily with significant improvement in his symptoms the following day. He received prednisone 60 mg daily for 2 days, followed by 40 mg daily for 2 days. His family reported that his symptoms started to worsen again while taking prednisone 40 mg daily. He was discharged with a dosage of prednisone 30 mg daily with a plan to decrease to 20 mg daily in 1 week. Three weeks later, while taking prednisone 20 mg daily, he presented to this hospital (current admission) with leg and shoulder pain, weakness, fever of 102°F, and worsening confusion and agitation. He endorsed weakness and pain in both legs and pointed to his right shoulder to indicate pain as well. His family reported new urinary and fecal incontinence as well as possible back pain.

Medical, social, and family history

The patient's past medical history was notable for atrial fibrillation, hypertension, dementia, and monoclonal gammopathy of undetermined significance. His surgical history included a sigmoid resection for perforated diverticulitis (13 years prior to presentation) as well as bilateral total shoulder arthroplasty (8 and 10 years prior to presentation) and a right hip arthroplasty (13 years prior to presentation), all performed for primary osteoarthritis. He had been seen by the hematology department for evaluation of MGUS and was not noted to have any evidence of end-organ damage. As part of this evaluation, he underwent a fat pad biopsy, which was negative for amyloidosis. He previously smoked for 20 years and quit almost 40 years prior to presentation. He also had a history of alcohol use disorder but had been abstinent for the past 2 years. He lived at home with his wife and had been previously independent. He denied any recent travel and denied having any pets or animal exposures.

His family history was notable for heart disease and cancer in multiple relatives, as well as a niece with rheumatoid arthritis (RA).

Medications

At the time of this current admission, the patient's medications included prednisone, aspirin, atovaquone, lisinopril, omeprazole, quetiapine, thiamine, naproxen, polyethylene glycol, senna, calcium carbonate–vitamin D3, melatonin, and nystatin powder.

Review of systems

Further review of systems revealed a new oral ulcer on the patient's inner lip as well as recent-onset urinary incontinence without dysuria in the setting of recent confusion. The patient and his family denied that he had had any recent change in weight, headaches, visual changes, watery eyes, dry eyes, dry mouth, rhinorrhea, jaw claudication, chest pain, shortness of breath, acid reflux, nausea, vomiting, diarrhea, paresthesias, rashes, or Raynaud's phenomenon.

Physical examination

Physical examination revealed a blood pressure of 137/78 mm Hg, heart rate of 80 beats per minute, respiratory rate of 16 breaths per minute, temperature of 98°F, and oxygen saturation of 99% on room air. He was an elderly gentleman who was mildly confused, although pleasant and cooperative. His head and neck examination was notable for an aphthous oral ulcer on the inside edge of his front lip, as well as areas of white and yellow plaque on his inner cheeks and posterior oropharynx. He had poor dentition. His heart rate was irregularly irregular; there were no audible murmurs. The patient was breathing comfortably, and his lungs were clear to auscultation. His musculoskeletal examination was notable for decreased right shoulder abduction to approximately 80 degrees, with warmth, tenderness, and a palpable glenohumeral effusion. He had bony hypertrophy of his metacarpophalangeal joints, as well as his proximal and distal interphalangeal joints. He had pain with internal rotation of his right hip, though no pain with range of motion of his left hip. His right knee had mild warmth and a small effusion appreciated. Range of motion of his knees was normal bilaterally. His other joints had no evidence of deformity, tenderness, warmth, erythema, or effusion. His neurologic examination was somewhat limited due to poor cooperation. He was alert and oriented to name, although did not know the year or location. He was conversant, yet intermittently agitated and speaking nonsensically. Gait was not assessed due to his pain and altered mental status. His strength was 4/5 with bilateral hip flexion and shoulder abduction, 4/5 with ankle flexion and extension, and hand grip was 5/5. He had no clonus, and reflexes were 2+ at the bilateral knees. Spinal tenderness was difficult to assess due to the patient's mental status. He was moaning at times, and it was unclear if this was due to pain. Examination of his skin was unremarkable; there were no sinus tracts, rashes, or other notable lesions.

Laboratory and radiographic evaluation

A complete blood count revealed an elevated white blood count at $12.1/\text{mm}^3$ (normal 4.5–11), hemoglobin of 12.8 gm/dl (normal range 13.5–17.5), and elevated platelets of $420/\text{mm}^3$

(normal range 150–400) (Table 1). His white blood count differential revealed 86.3% neutrophils, 6.4% lymphocytes, 4.1% monocytes, 0.1 % eosinophils, 0.2% basophils, and 2.9% immature granulocytes. His metabolic panel was notable for normal renal function with a creatinine of 0.7 mg/dl (normal range 0.6–1.5). Serum calcium was 8.5 mg/dl (normal 8.5–10.5). Serum albumin was 2.2 gm/dl (normal range 3.3–5.0). Uric acid was 2.4 mg/dl (normal 3.6–8.5). ESR was elevated at 52 mm/hour (normal range 0–13), and CRP level was elevated at 91.3 mg/liter (normal range 0–8). IgG level was 1,637 mg/dl (normal range 614–1,295), IgA level was 518 mg/dl (normal range 69–309), and IgM level was 72 mg/dl (normal range 53–334), and serum protein electrophoresis revealed an abnormal 0.26 gm/dl IgG lambda M component band in the gamma region, as well as 2 IgG kappa M components of 0.19 gm/dl and 0.09 gm/dl in the gamma region. Serum kappa free light chains were mildly elevated at 35.3 mg/liter (normal range 3.3–19.4) and serum lambda free light chains were mildly elevated at 35.6 mg/liter (normal range 5.7–26.3), though the kappa-to-lambda ratio was normal at 0.99 (normal range 0.3–1.7). The urinalysis findings were negative, without evidence of blood or protein, and urine culture grew few (1,000 to <10,000) gram-negative rods. Blood cultures were initially negative. See Table 1 for laboratory values during this admission as well as prior admissions.

Radiographs of his shoulders revealed bilateral total shoulder prosthesis with high-grade subluxation of the glenoid component superiorly, likely a result of loosening, as well as severe degenerative changes of the glenoid bilaterally. Radiograph of his right knee showed severe medial tibiofemoral compartment predominant degenerative changes as well as chondrocalcinosis and trace joint effusion. CT findings of his chest were unremarkable.

The right knee arthrocentesis revealed 7,433 nucleated cells per microliter with 68% neutrophils, 26% lymphocytes, and 6% monocytes. Crystal analysis results were positive for calcium pyrophosphate crystals, some of which were intracellular. Gram stain and culture results were negative at 5 days. The right shoulder arthrocentesis revealed 29,500 total nucleated cells per microliter with 85% neutrophils, 11% lymphocytes, and 3% monocytes, as well as calcium pyrophosphate crystals, none of which were noted to be intracellular.

CASE SUMMARY

An 80-year-old man with a history of atrial fibrillation, hypertension, dementia, and monoclonal gammopathy of undetermined significance presented with an oligoarticular inflammatory arthritis as well as recent fevers and urinary and fecal incontinence in the setting of a prednisone taper prescribed for a diagnosis of PMR. Physical examination was notable for a confused man with diffuse pain as well as multiple joint effusions involving native and prosthetic joints. Laboratory evaluation revealed mild leukocytosis and thrombocytosis, elevated inflammatory markers, and hyponatremia. Synovial fluid from his right knee and right shoulder revealed inflammatory fluid with neutrophilic predominance and calcium pyrophosphate crystals, with a negative gram stain and culture at 5 days.

DIFFERENTIAL DIAGNOSIS

Fever with oligoarticular joint effusions involving prosthetic as well as native joints raised concern for infectious etiologies, although gram stain and culture findings from the patient's synovial fluid were negative after 5 days. We will focus on the differential diagnosis of oligoarticular arthritis in this patient.

Inflammatory arthritis.

Seronegative spondyloarthritis as well as RA could be considerations in this patient. Five conditions (psoriatic arthritis, reactive arthritis, irritable bowel disease (IBD)-associated arthritis, ankylosing spondylitis, and undifferentiated spondyloarthropathy) comprise the seronegative spondyloarthropathies. Each of these conditions can present with peripheral arthritis, with psoriatic arthritis often presenting as an asymmetric oligoarthritis in 70% of patients, reactive arthritis often involving the large joints of the lower extremities, and enteropathic arthritis presenting either as an asymmetric oligoarticular arthritis or a symmetric polyarticular arthritis of the small joints (1). However, our patient had no personal history or evidence of psoriasis on examination, no history of IBD, and no known preceding gastrointestinal or genitourinary infections. The patient did possibly endorse low back pain, although this was difficult to assess by history. Ankylosing spondylitis can involve the hips, shoulders, and sternoclavicular joints, among others, although it generally presents before age 40 years, and the patient did not endorse a longstanding history of back pain, making this less likely (1). Reactive arthritis would be considered less likely given the lack of an apparent preceding infection (although in many cases a preceding infection is not apparent), absence of ocular symptoms or pyuria, and the distribution of joints, which tends to favor the lower extremities, although can include the upper extremities. Reactive arthritis would remain a diagnosis of exclusion after evaluation of other etiologies in this case. Fever is rarely part of the presentation of spondyloarthropathy, although in cases with fever and seronegative spondyloarthropathy, Whipple's disease is one consideration to keep on the differential (2). RA can present at an older age; classically it presents as a symmetric polyarthritis of the smaller joints and involves the hands. However, it can present as an asymmetric oligoarticular arthritis or even as a PMR-like presentation. However, the predominance of large joints points away from RA (3). Additionally, RA rarely causes high fevers, and the patient's test results were negative for both RF and CCP, which makes RA less likely.

Systemic rheumatologic disease.

Other systemic rheumatologic diseases such as lupus, vasculitis, myositis, adult-onset Still's disease (AOSD), or sarcoidosis can present with polyarthralgias or polyarticular arthritis. However, this patient had no evidence of extraarticular systemic disease. In this patient, an ANA test result was negative, which makes lupus less likely. The patient had a normal creatine kinase (CK) level and a negative myositis panel, which made myositis less likely, and his pain and weakness seemed to be more articular rather than muscular. He had no other cutaneous or other stigmata of vasculitis, and no rash to suggest AOSD. He had no hypercalcemia, hilar lymphadenopathy, erythema nodosum, or other findings to suggest sarcoidosis.

PMR.

PMR presents with pain and stiffness of the shoulders and hips, generally in a symmetric distribution. Estimates of the prevalence of clinically detectable synovitis in patients with PMR vary widely, from almost none to more than two-thirds of patients (3). One study of PMR and temporal arteritis patients showed that of the patients who had peripheral arthritis, 34% had a monoarthritis, 62.3% had an oligoarthritis, and 3.8% had a polyarthritis at the time of diagnosis (4). Joint involvement during the disease course included most commonly the knee (55.6% of cases), metacarpophalangeal joints (46.3% of cases), and wrist (42.6% of cases) (4). In this study, no patients had hip or shoulder involvement by frank arthritis (4). Synovial fluid white cell differentials can be lymphocytic predominant; in one study, more than half of the synovial fluid analysis results showed a predominance of mononuclear cells (3). PMR can also be a source of fevers, with one study showing that PMR was responsible for 4 of 31 cases of fever of unknown origin in elderly patients and was responsible for several cases of fever lasting more than 3 months (5). Although this patient had a diagnosis of PMR, as supported by elevated inflammatory markers that improved with steroids, the oligoarticular nature of his joint effusions, the failure to respond to prednisone at 20 mg daily, and the involvement of both his shoulder and hip joints made it less likely that he had a peripheral arthritis associated with PMR.

Crystalline arthritis.

While the patient had no prior history of either gout or pseudogout, the analyses of synovial fluid from his right knee and shoulder revealed calcium pyrophosphate crystals. Given this positive result of crystals from 2 joints, we considered the possibility that the entirety of his presentation was due to oligoarticular calcium pyrophosphate dihydrate crystal (CPPD) arthritis (i.e., pseudogout) since it can cause fevers (6). The most commonly involved joint in pseudogout is the knee, followed by the wrist, shoulder, and ankle (7). This patient's urinary and fecal incontinence raised concern for a process involving the spine as well. Although rare, pseudogout can affect the spine; one autopsy study of more than 1,000 spinal specimens from patients with CPPD arthritis showed that crystals can accumulate in a variety of locations in the vertebral column, including the intervertebral disks, median atlantoaxial articulations, intraspinal and extraspinal ligaments, and apophyseal and sacroiliac joints (8). Pseudogout has also been known to present with mass-like involvement of the spine that can be mistaken for tumors and has been reported as a cause of cauda equina syndrome (9). However, crystal-induced arthritis after arthroplasty is rare, with only several dozen cases reported. When it does occur, it is attributed to crystal deposition in the remaining synovial membrane or in the neosynovium that can develop around the prosthetic joint (10). Given the protracted course of this patient's presentation and the fact that his initial left shoulder aspiration was negative for crystals, we thought that pseudogout was an unlikely explanation for his entire illness, although we could not rule out a contribution of pseudogout to his clinical presentation.

Septic arthritis.

There was a high concern for infection given fevers and oligoarticular inflammatory arthritis involving prosthetic joints. Risk factors for septic arthritis include older age, such that being

age >80 years is associated with a 3.5-fold higher likelihood of septic arthritis in a patient presenting with arthritis (11). In addition, the presence of either a hip or knee prosthesis is associated with 3-fold higher likelihood of septic arthritis (11). Risk factors for infection after arthroplasty include obesity, malnutrition, diabetes mellitus, RA, smoking, alcohol, older age, bacterial colonization, and immunosuppression, among others (12). This patient had risk factors for septic arthritis, but we generally associate bacterial septic arthritis with a higher synovial white cell count. Moreover, his synovial fluid cultures were negative, although these are positive in only about 60% of patients with nongonococcal septic arthritis of prosthetic joints; the gram stain is even less sensitive, with organisms seen in only half of cases (12). The patient had previously received a course of doxycycline, which could have further reduced the sensitivity of the gram stain and culture, although he had not been taking antibiotics during the time period immediately preceding his admission. It is relevant to note that joint infections caused by atypical or fastidious organisms, such as the *Mycoplasma* species, mycobacteria, or fungi can be even more difficult to diagnose based on synovial fluid cultures.

CLINICAL COURSE

Given the patient's fecal and urinary incontinence, magnetic resonance imaging (MRI) of the lumbar spine was performed and revealed T2 hyperintensity in the L4–L5 disc space with associated end plate edema, suggestive of discitis and/or osteomyelitis (Figure 1). MRI also demonstrated a multiloculated posterior epidural collection adjacent to the right L4–L5 facet joint that could have been reflective of an epidural abscess or a synovial cyst. An MRI of the pelvis revealed edema throughout the distal right psoas and iliacus muscles with a fluid collection that was concerning for abscess. MRI of the patient's brain showed some nonspecific chronic white matter disease and was negative for any acute lesions.

Six days after aspiration of the patient's right knee, the mycobacterial culture grew a rapidly growing nontuberculous mycobacterial species, eventually speciated to *Mycobacterium abscessus* complex. Aspirations from the right shoulder, right hip, and left shoulder also grew *M abscessus*, as did blood cultures (after 7 days) and a biopsy of the L4–L5 disk. A diagnosis of disseminated *M abscessus* infection was made. Explantation of the affected joints was thought to be too morbid given the number of joints involved, so the patient underwent arthroscopic lavage of his right shoulder and right knee. However, without joint explantation, curative treatment was thought to not be possible given the disseminated nature of the infection. He was initially treated with an empiric regimen of linezolid, imipenem, and azithromycin while awaiting sensitivities. This regimen was transitioned to tigecycline, imipenem, and azithromycin once final sensitivity data revealed that his strain was sensitive to macrolides, with a plan for an indefinite duration of therapy given the disseminated nature of the infection. Prednisone was tapered off over 4 weeks. After discharge, the patient initially improved, with resolution of his fevers and improvement in his joint pain. However, he continued to have severe debility at home as well as subjective toxicity to oral and intravenous antibiotic therapy, thereby limiting his quality of life. Thus, approximately 3 months after hospital discharge the decision was made to discontinue antibiotics and transition him to hospice care.

DISCUSSION

Mycobacteria are a genus of *Actinobacteria* and include more than 190 different species. The Greek prefix myco means fungus and refers to the way in which they grow. They are often divided into *Mycobacterium tuberculosis* complex, mycobacteria causing leprosy, and nontuberculous mycobacteria (13). They are not identified on Gram stain and can be difficult to detect. Nontuberculous mycobacteria are ubiquitous in the environment, often present in water and food sources, and are notoriously difficult to treat (13, 14). Ninety percent of nontuberculous mycobacterial infections involve the pulmonary system, and the remainder involve the lymph nodes, skin, soft tissue, bones, and less frequently the eye or nervous system (13). Septic arthritis, including prosthetic joint infections, due to mycobacteria has been described as well. In general, these infections occur more commonly in patients who are immunosuppressed, although there are reports of an increasing prevalence of cases in apparently immunocompetent patients as well (15). There is also increasing appreciation of the role of inherited and acquired defects in the host immune response, particularly the T helper cell type (Th1) pathway, in susceptibility to nontuberculous mycobacterial infection, especially among younger patients (16). One study of 31 cases of vertebral osteomyelitis caused by nontuberculous mycobacteria revealed that only 51.5% had some degree of underlying immunosuppression (17). Prior to his prednisone use, our patient did not have any known risk factors for mycobacterial infection.

M abscessus is a rapidly growing nontuberculous mycobacteria (RGM) (14). RGM are defined by growth in culture within 7 days, which is slower than most bacteria, though faster than slow growing mycobacteria or *M tuberculosis* (13). They exist ubiquitously in the environment with increasing incidence for unclear reasons, although it has been postulated that environmental factors could be contributing (18). The clinical disease spectrum ranges from skin and soft tissue infections to surgical wound infections, catheter-related sepsis, pulmonary infections, and prosthetic joint infections (14, 19). There have been multiple cases of wound infections by *M abscessus* in patients who have received cosmetic surgery, particularly in Latin American countries (20). One case series refers to “lipotourists,” where US or other residents travel abroad to undergo cosmetic surgery for fat removal; proposed reasons for infection include environmental contamination of the water systems, surgical instruments, medications, or antiseptic solutions (21). Regarding joint involvement, one study reported a cohort of patients with nontuberculous mycobacteria involving large joints, all of which were prosthetic, in contrast to infections involving small joints that occurred in the absence of prostheses (19). Infections are more likely to disseminate in immunocompromised patients, but dissemination has been reported in immunocompetent patients (14, 15, 18).

Septic arthritis from *M abscessus* results from direct inoculation or hematogenous dissemination. One study showed that the average synovial white blood cell count in patients with mycobacterial septic arthritis was approximately 30,000 nucleated cells/microliter (22). The synovial fluid count in this patient was remarkably low for septic arthritis, which likely contributed to the initial low suspicion for infection. His preceding treatment with doxycycline may have decreased synovial fluid cell counts and the sensitivity of culture.

Disseminated infection, as in this case, is associated with a high risk for morbidity and mortality. Disseminated infection is defined by involvement of more than 1 organ system, more than 2 groups of lymph nodes, or positive blood cultures (14). Moreover, immunosuppressive medications, such as the prednisone administered in this case, have also been associated with higher mortality (14).

Morbidity and mortality are particularly high *M abscessus* infections because treatment approaches are challenging, and as there is a lack of randomized controlled trial data, treatment is often based on expert opinion. Surgical treatment with resection of the prosthesis is often required along with prolonged courses of multi-drug antimycobacterial therapy for curative treatment (23). Regarding medical therapy, RGM are associated with inducible macrolide resistance as well as multiple intrinsic and extrinsic drug-resistance mechanisms. As such, susceptibility testing and use of multiple concurrent antibiotics are always required. It is recommended that RGM be tested for susceptibility to amikacin, cefoxitin, ciprofloxacin, clarithromycin, doxycycline, imipenem, linezolid, moxifloxacin, trimethoprim-sulfamethoxazole, and tobramycin (13).

Further complicating this patient's management was the involvement of prosthetic joints. In general, prosthetic joint infections (PJI) are estimated to complicate approximately 1% of primary hip and knee arthroplasties (23). In addition to immunosuppression, as in this case, other risk factors for PJI include obesity, diabetes mellitus, and RA (23). The most common clinical manifestations include pain (the most common symptom), joint swelling or effusion, fever, drainage, or the presence of a sinus tract (which in some criteria is considered to be definitive evidence of prosthetic joint infection) (23). Loosening of the components of the prosthesis or periprosthetic lucency on imaging can be suggestive of infection as well (23). Synovial fluid aspiration is critical in any suspected case of PJI; however, cell counts are generally much lower than in native joint infection. The sensitivity of a synovial fluid leukocyte count of >1,700 cells/microliter or a differential of >65% neutrophils was considered to be 94% and 97%, respectively (24). The most common organisms include *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, *Streptococcus* species, aerobic gram-negative bacilli, and less commonly *Enterococcus* species, anaerobic bacteria, or polymicrobial (23). Nontuberculous mycobacteria are an extremely rare cause of PJI; these are only described in small case series and reports, and *M abscessus* is an even more rare cause (23). In general, PJI often require a combination of medical therapy (e.g., antibiotics) and revision surgery, but this approach is best determined in consultation with orthopedic surgeons as well as infectious disease specialists (24). There are no specific management recommendations for *Mycobacterial* prosthetic joint infections.

It is likely that the entirety of this patient's presentation was due to *M abscessus*. While a crystalline arthritis was considered as a potential cause of his presentation, especially before synovial fluid cultures grew RGM, it was thought to be an unlikely explanation for the entirety of his presentation. We cannot rule out the possibility that pseudogout contributed to some of his pain and swelling.

Multiple studies have evaluated the frequency of concomitant crystal arthritis and septic arthritis. Studies have found rates ranging from 1.5 to 5% of patients with crystalline

arthritis who also have concomitant infection (25,26). One study found that the mean synovial white blood count in patients with concomitant crystalline and septic arthritis was 113,000 (95% confidence interval 72,700–153,200), although much lower values have been reported as well (25). Multiple mechanisms have been postulated regarding why this coexistence occurs. It has been suggested that crystalline arthritis may predispose patients to joint-space infection. In another report by Gordon et al, septic arthritis preceded the appearance of calcium pyrophosphate crystals in the joint fluid, suggesting that infection leads to shedding of crystals from the cartilage and synovium into the joint space. Subsequently, in a rat model, they demonstrated release of crystals after injection of pyogenic bacteria (27). Although infrequent, if infection is suspected, this suspicion should not be eliminated by the discovery of crystals in the joint fluid.

Ultimately, it is unclear whether this patient initially had a single joint affected by RGM and prednisone subsequently led to dissemination of the infection, or whether it had begun to disseminate prior to the initiation of prednisone. This case highlights the need for high clinical suspicion of infection in patients with prosthetic joints, even in the setting of a positive crystal analysis and awareness of mycobacteria as potential pathogens.

FINAL DIAGNOSIS

Oligoarticular mycobacterial septic arthritis with disseminated *M abscessus* infection with concomitant crystalline arthritis.

REFERENCES

1. Duba A, Mathew S. The seronegative spondyloarthropathies. *Prim Care Clin Off Pr* 2018;45:271–87.
2. Várölgöyi C, Bubán T, Szakáll S, Hargitai Z, Galuska L, Jeney C, et al. Fever of unknown origin with seronegative spondyloarthropathy: an atypical manifestation of Whipple's disease. *Ann Rheum Dis* 2002;61:377–8. [PubMed: 11874851]
3. Chou C, Schumacher R. Clinical and pathologic studies of synovitis in polymyalgia rheumatica. *Arthritis Rheum* 1984;27:1107–17. [PubMed: 6487395]
4. Gran J, Myklebust G. The incidence and clinical characteristics of peripheral arthritis in polymyalgia rheumatica and temporal arteritis: a prospective study of 231 cases. *Rheumatology (Oxford)* 2000;39:283–7. [PubMed: 10788536]
5. Iikuni Y, Okada J, Kondo H, Kashiwazaki S. Current fever of unknown origin 1982–1992. *Intern Med* 1994;33:67–73. [PubMed: 8019044]
6. Bone D, Bennett R. Pseudogout mimicking systemic disease. *JAMA* 1981;246:1438–40. [PubMed: 7265449]
7. Cassetta M, Gorevic P. Gout and pseudogout in the geriatric patient. *Geriatrics* 2004;59:25–30.
8. Resnick D, Pineda C. Vertebral involvement in calcium pyrophosphate dihydrate crystal deposition disease. *Radiology* 1984; 153: 55–60. [PubMed: 6089266]
9. Lee J, Cho K, Kim E. Cauda equina syndrome caused by pseudogout involving the lumbar intervertebral disc. *J Korean Med Sci* 2012;27:1591–4. [PubMed: 23255864]
10. Yahia SA, Zeller V, Desplaces N, Chazeraïn P, Lhotellier L, Marmor S, et al. Crystal-induced arthritis after arthroplasty: 7 cases. *Jt Bone Spine* 2016;83:559–62.
11. Margaretten M, Kohlwe S, Moore D, Bent S. Does this adult patient have septic arthritis? *JAMA* 2007;297:1478–88. [PubMed: 17405973]
12. Nair R, Schweizer M, Singh N. Septic arthritis and prosthetic joint infections in older adults. *Infect Dis Clin N Am* 2017;31:715–29.

13. Koh W. Nontuberculous mycobacteria: overview [review], *Microbiol Spectr* 2017;5.
14. Fukui S, Sekiya N, Takizawa Y, Morioka H, Kato H, Aono A, et al. Disseminated *Mycobacterium abscessus* infection following septic arthritis. *Medicine (Baltimore)* 2015;94:e861. [PubMed: 26020393]
15. Piersimoni C, Scarparo C. Extrapulmonary infections associated with nontuberculous *Mycobacteria* in immunocompetent persons. *Emerg Infect Dis* 2009;15:1351–8. [PubMed: 19788801]
16. Wu U-I, Holland SM. Host susceptibility to non-tuberculous mycobacterial infections. *Lancet Infect Dis* 2015;15:968–80. [PubMed: 26049967]
17. Petitjean G, Fluckiger U, Scharen S, Laifer G. Vertebral osteomyelitis caused by non-tuberculous mycobacteria. *Clin Microbiol Infect* 2004;10:951–3. [PubMed: 15521995]
18. Stout J, Koh W-J, Yew W. Update on pulmonary disease due to nontuberculous mycobacteria. *Int J Infect Dis* 2016;45:123–34. [PubMed: 26976549]
19. Hsiao C, Cheng A, Huang Y, Liao C, Hsueh P. Clinical and pathological characteristics of mycobacterial tenosynovitis and arthritis. *Infection* 2013;41:457–64. [PubMed: 23335268]
20. Maurer F, Castelberg C, von Braun A, Wolfensberger A, Bloemberg G, Bottger E, et al. Postsurgical wound infections due to rapidly growing mycobacteria in Swiss medical tourists following cosmetic surgery in Latin America between 2012 and 2014. *Euro Surveill* 2014;19.
21. Furuya EY, Paez A, Srinivasan A, Cooksey R, Augenbraun M, Baron M, et al. Outbreak of *Mycobacterium abscessus* wound infections among “Lipotourists” from the United States who underwent abdominoplasty in the Dominican Republic. *Clin Infect Dis* 2008;46:1181–8. [PubMed: 18444853]
22. Shu C, Wang J, Yu C, Lee L. Mycobacterial arthritis of large joints. *Ann Rheum Dis* 2009;68:1504–5. [PubMed: 19674984]
23. Tande A, Patel R. Prosthetic joint infection. *Clin Microbiol Rev* 2014;27:302–45. [PubMed: 24696437]
24. Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2013;56:1–25. [PubMed: 23230301]
25. Shah K, Spear J, Nathanson L, McCauley J, Edlow J. Does the presence of crystal arthritis rule out septic arthritis? *J Emerg Med* 2007;32:23–6. [PubMed: 17239729]
26. Papanicolas L, Hakendorf P, Gordon D. Concomitant septic arthritis in crystal monoarthritis. *J Rheumatol* 2012;39:157–60. [PubMed: 22133623]
27. Gordon T, Reid C, Rozenbils M, Ahern M. Crystal shedding in septic arthritis: case reports and in vivo evidence in an animal model. *Aust N Z J Med* 1986;16:336–40. [PubMed: 3465309]

Figure 1. Magnetic resonance image of the lumbar spine. STIR imaging demonstrates signal abnormality in the L4–L5 disc space (white arrow) with associated end plate edema and cortical bone loss suggestive of discitis and osteomyelitis. The image also shows a multiloculated posterior epidural collection (blue arrow) adjacent to the right L4–L5 facet joint, concerning for an epidural abscess.

Table 1.

Laboratory evaluation results at each hospital admission *

Laboratory test	First admission	Second admission	Third admission	Current admission	Normal range
WBC, cells/mm ³	10,96	7.9	6.8	12.1	4.5–11
WBC differential, %					
Neutrophils	82.5	60.3	81.4	86.3	NS
Lymphocytes	10.7	21.9	8.4	6.4	NS
Monocytes	5	16.1	9.4	4.1	NS
Eosinophils	0	0.5	0	0.1	NS
Basophils	0.9	0.6	0.4	0.2	NS
Immature granulocytes	0.9	0.6	0.4	2.9	NS
Hemoglobin, gm/dl	14.8	13.2	12.5	12.8	13.5–17.5
Platelets, cells/mm ³	262	415	406	420	150–400
Creatinine, mg/dl	0.85	0.85	0.64	0.69	0.6–1.5
ESR, mm/hour	30	51	45	52	0–13
CRP, mg/liter	120.7	105.7	99.8	91.3	0–8
Uric acid, mg/dl	2.4	3.4	3.0	2.4	3.6–8.5
Synovial fluid WBC, cells/mm ³	NA	3,205 (LS)	NA	29,500 (RS), 7,433 (RK)	<200
Synovial fluid WBC differential, %					
Neutrophils	NA	71	NA	85 (shoulder), 68 (knee)	NS
Lymphocytes	NA	21	NA	11 (shoulder), 26 (knee)	NS
Monocytes	NA	0	NA	3 (shoulder), 6 (knee)	NS
Macrophages	NA	8	NA	1 (shoulder), 0 (knee)	NS
Synovial fluid crystals	NA	Negative (LS)	NA	Calcium pyrophosphate (RS and RK)	Negative

* WBC = white blood cell; NS = no specific reference range; NA = not applicable; LS = left shoulder; RS = right shoulder; RK = right knee.