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Case report

Unmasking tuberculous arthritis in a prosthetic joint: Diagnostic and therapeutic challenges

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ABSTRACT

An 85-year-old woman with a history of total knee replacements for osteoarthritis in the past, presented with left knee swelling and pain that persisted for 14 months. An initial diagnosis of synovial cyst was made, and she underwent multiple aspirations and symptomatic treatments without improvement. Repeat arthrocentesis showed a WBC of 56,000/μL with 61 % neutrophils and 34 % lymphocytes. Synovial fluid bacterial and fungal cultures were negative. The acid-fast bacilli (AFB) culture revealed the Mycobacterium tuberculosis complex and was confirmed by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) Mass Spectrometry. This case highlights the challenges of diagnosing tuberculous prosthetic joint infection in an elderly individual with knee pain.

Introduction

Knee replacement surgeries are among the most common orthopedic procedures in the United States. The number of total hip and total knee arthroplasty procedures in the United States has shown a consistent upward trend over time, and this growth is expected to persist in the future. [1,2] Prosthetic joint infection (PJI) is one of the most significant complications following the implantation of a prosthesis. [3] The United States experienced a nearly twofold rise in infections among hip and knee arthroplasties between 1990 and 2004, with the incidence of PJI ranging from 2 % to 10 % among all recipients. [1,4] Infections that occur early (less than three months after surgery) or delayed (3–24 months after surgery) are typically acquired during implantation. Conversely, late infections (more than 24 months after surgery) are primarily acquired through the dissemination of microorganisms via hematogenous seeding. [5]

The most common causative organisms of PJI are Coagulase-negative staphylococci, followed by Staphylococcus aureus, Enterococcus spp., Cutibacterium, and Enterobacterales. [6] An estimated 22 % of cases of PJI are culture-negative, with Mycobacterium tuberculosis (MTB) being a subset for which the incidence is unknown. [1,3] Delayed diagnosis or misdiagnosis of PJI caused by MTB is common due to nonspecific presentations and a lack of clinical suspicion. [7]

Case

An 85-year-old female with obesity who had a history of bilateral knee replacements presented with worsening swelling and pain in her left knee over 14 months. She had no trauma, fevers, chills, fatigue, night sweats, cough, shortness of breath, or weight changes.

Her medical history was significant for hypertension, diabetes mellitus, and atrial fibrillation. She had undergone total left and right knee replacements in 2015 and 2016 due to osteoarthritis. The patient immigrated to the United States from Puerto Rico at age 12.

On examination, her vital signs were normal, and her BMI was 31. Her physical exam was noncontributory except for a cystic mass palpated at the medial aspect of the left knee, with no signs of erythema, warmth, or tenderness. Her complete blood count and complete metabolic panel were within the normal limit.

She was seen by the orthopedist and underwent arthrocentesis, and the initial analysis of her synovial fluid showed a white cell count (WBC) of 3560/μL with 97 % neutrophils, but crystal analysis, gram stain, and bacterial culture were all negative. The left knee X-ray was unremarkable, and there were no signs of loosening the prosthesis. An MRI of the left knee done outpatient read “A large cystic mass measuring 6.9 cm anteroposterior by 4.2 cm transverse by 9.3 cm craniocaudal, originating from the medial component”. Despite multiple aspirations and symptomatic treatment for the presumptive diagnosis of a synovial cyst, her symptoms persisted. Subsequent arthrocentesis showed a

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significantly elevated WBC count of 56,000/μL with 61 % neutrophils and 34 % lymphocytes, glucose 2 mg/dl, total protein 4.8 gm/dl. Synovial fluid bacterial and fungal cultures were negative. However, synovial fluid alpha-defensin was positive, and the AFB culture revealed the presence of Mycobacterium tuberculosis complex, confirmed by real-time PCR and MALDI-TOF Mass Spectrometry.

The workup for pulmonary tuberculosis, including sputum for the Xpert MTB/RIF assay, AFB smear, and cultures, all yielded negative results. A chest CT scan showed no evidence of active pulmonary disease. A four-drug regimen, including isoniazid, rifampin, ethambutol, pyrazinamide, and vitamin B6, was initiated for the treatment of tuberculous prosthetic joint infection.

Discussion

This clinical case highlights the diagnostic complexities associated with tuberculous arthritis, particularly in patients with prosthetic joint implants. Pain is the most common symptom of prosthetic joint infections (PJIs), and patients usually exhibit local signs and symptoms such as severe pain, swelling, redness, warmth, and fever. Patients with tuberculosis (TB) tend to have a low body weight and experience a loss of appetite. However, the patient in question did not exhibit the typical profile characteristics. Diagnosing tuberculous PJI in this case was a challenge as there were no signs of acute inflammation in the left knee, no constitutional symptoms, and the patient's body mass index (BMI) was 31.

PJI is a severe joint infection typically diagnosed through the culture method. However, approximately 22 % of PJI cases are culture-negative, which can be due to several reasons, including non-infectious causes such as arthrofibrosis, aseptic loosening, avascular necrosis, central sensitization, and component malpositioning, as well as infectious causes. One of the infectious causes of culture-negative PJI is Mycobacterium tuberculosis (MTB), but its incidence rate is currently unknown.

Making a precise diagnosis and distinguishing between prosthetic joint infections (PJI) and non-infectious joint failure is crucial, as they require different treatment approaches. Identifying the causative organism in PJI is also essential for selecting the appropriate antimicrobial agents and surgical management strategies.

MTB can infect a prosthesis site either through hematogenous spread from a reactivated latent focus elsewhere in the body or by reactivating dormant bacteria in an individual previously exposed to the pathogen. [8] Unlike septic arthritis of native joints, prostheses act as foreign bodies and promote biofilm formation by several organisms, which create barriers against antimicrobial agents and evade the host immune systems. [9]

Notably, the patient in question did not demonstrate the typical characteristics of tuberculous periprosthetic joint infection (TB PJI), and knee fluid cultures for bacteria and fungus were negative. Nevertheless, the persistence of symptoms with a positive alpha defensin compelled the physician to request synovial fluid acid-fast bacilli (AFB) smears and cultures. In the initial year of the patients knee pain, she was managed by the patients orthopedist and infectious disease was not involved which led to delay in diagnosis. The definitive test for diagnosing TB PJI is AFB culture, as synovial fluid AFB smears can result in false negatives due to the low sensitivity of AFB smear microscopy on extrapulmonary samples, which are often paucibacillary. However, incorporating nucleic acid amplification testing (NAAT)/polymerase chain reaction (PCR) has facilitated more rapid identification of Mycobacterium tuberculosis in the synovial fluid aspirate or tissue sample. [10] Blood and urine cultures were not performed in our patient.

As there is currently no definitive consensus on the ideal medical or combined surgical management for TB PJI, clinicians typically make case-specific decisions in consultation with infectious diseases. One systematic review analyzed 51 publications of TB PJI and found that most cases were managed by debridement and/or joint removal. [11] Another study of 107 cases of TB PJI revealed that the duration of anti-mycobacterial therapy ranged from 6 months to 3 years, with longer courses in patients who did not undergo debridement or hardware removal. [6] However, a case series and literature review by Uhel et al. revealed that a significant number of patients with confirmed TB PJI had favorable outcomes without undergoing surgery. This suggests that prolonged antituberculosis treatment may serve as a potential cure for a considerable proportion of TB PJI cases. [12] Similar conclusions have been drawn by Von Keudell et al., showing that timely initiation of antituberculosis therapy could potentially facilitate the preservation of the implant. However, it might be necessary to continue with suppressive therapy as well. [13] In our patient, surgical revision was not considered as the patient was deemed a poor surgical candidate. There is no guidance in the literature on which course would have been more beneficial for our patient.

We performed a literature review from 2010 to the present and found 10 publications consisting of 11 patients with knee PJI due to MTB (Table 1). Only 4/11 (36.4 %) of patients were treated with antibiotics alone, with the majority requiring surgery for either debridement or joint revision. Unfortunately, the recurrence rates are not known with antibiotics vs antibiotics and surgery. The time of onset of infection after joint implantation was very variable, occurring immediately post-op and up to years after surgery. Most of the cases had delays in diagnosis, likely owing to the indolent course, nonspecific symptoms, and low index of

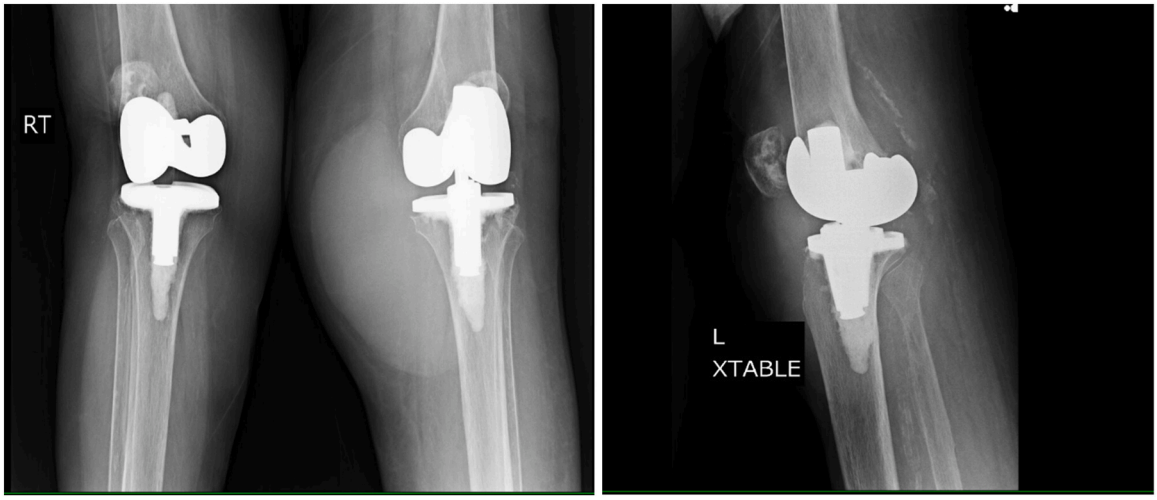

Fig. 1. Left AP view, Right lateral view of left knee. Large left knee effusion. S/p left knee arthroplasty with perihardware lucency.

Table 1
Published 14 cases of Knee PJI due to MTB from the year 2010 to the present.

Authors	Age	Number of patients	Time after joint implantation	Joint affected	Treatment employed	Time to Dx	Concurrent infections	Mycobacterium type
Elzein et al. [14]	73	1	2 years	Knee	Antibiotics and surgery	4 months	No	M. tuberculosis
Lara-Oya et al. [15]	77	1	3 years	Knee	Antibiotics and surgery	6 months	No	M. tuberculosis
Veloci et al. [16]	34, 62	2	8 months, immediately post-op	Knee, Knee	Antibiotics and surgery, antibiotics	3 years, 3 years	No, No	M. tuberculosis, M. tuberculosis
Wang et al. [17]	72	1	3 years	Knee	Antibiotics	2 months	No	M. tuberculosis
Tachi et al. [18]	67	1	1 year	Knee	Antibiotics and surgery	13 months	MSSA, S. dysgalactiae	M. tuberculosis
Von Keudell et al. [13]	84	1	5 months	Knee	Antibiotics	Weeks	No	M. tuberculosis
Barry et al. [19]	80	1	8 years	Knee	Antibiotics	6 months	No	M. tuberculosis
Harwin et al. [20]	60	1	7 months	Knee	Antibiotics and surgery	14 months	No	M. tuberculosis
Lee et al. [21]	79	1	2 months	Knee	Antibiotics and surgery	Unspecified	No	M. tuberculosis
Klein and Jacquette [22]	36	1	Immediately post-op	Knee	Antibiotics and surgery	12 months	No	M. tuberculosis

suspicion.

Currently, there are no standardized guidelines for treating TB PJI. Although joint revision surgery is often used in conjunction with antibiotics to control infection in PJI, it is still being determined whether it is necessary to treat TB PJI with surgery, as there are documented cases in the literature that have been successfully treated with anti-TB medications alone. [6,11–13] Additionally, the appropriate timing of surgery, the duration of anti-TB therapy, and the methods for monitoring the response to treatment are not yet well-defined. In our literature review, no definitive factors could be identified favouring antibiotics alone versus antibiotics and surgery.

The patient in question was initiated on a four-drug regimen consisting of rifabutin 300 mg daily, isoniazid 300 mg daily, pyrazinamide 1000 mg daily, ethambutol 800 mg daily, and pyridoxine 50 mg daily with no provision for joint revision. The patient was followed by the Department of Health and duration of therapy was for one year with the possibility of extension depending on clinical improvement.

Conclusion

Mycobacterium tuberculosis is an infrequent yet noteworthy cause of prosthetic joint infection following knee arthroplasty. It should be considered as a potential cause in culture-negative prosthetic joint infections, particularly in patients with a history of tuberculosis or relevant epidemiological risk factors. When patients with PJI do not respond to empirical antibiotic treatment and have negative synovial or tissue cultures for common bacteria, clinicians should contemplate the possibility of atypical pathogens, such as fungal or TB infections. Further research and awareness in diagnosing and managing such infections can contribute to better patient outcomes and informed decision-making for clinicians facing these challenging cases.

Ethical approval

Ethical approval not required

Consent

Written consent was obtained and can be presented upon request

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Author statement

Dr. Rahman and Dr. Randhawa contributed to writing the abstract, introduction, case presentation, discussion, and conclusion. Dr. Lin is the principal investigator and oversaw the process, was involved in revisions, and outlining important aspects of the case presentation.

CRediT authorship contribution statement

Asbah Rahman: Writing – original draft. **Yu Shia Lin:** Writing – original draft, Supervision. **Aastha Randhawa:** Writing – original draft.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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