CASE REPORT

Total knee prosthesis infected with *Mycobacterium tuberculosis*Fatehi E Elzein,¹ Mohammed Haris,² Saad S Alolayan,¹ Nisreen Al Sherbini²

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SUMMARY

Mycobacterium tuberculosis (MTB) infection of a prosthetic joint is rarely reported in developed countries.¹ Typically, MTB infection involves the hips or knees, and the infection can occur secondary to crushing and degradation of the granuloma during surgery or, less commonly, from distant foci spreading through the blood. In the present case, MTB infection likely resulted from haematogenous spread since multiple hot spots suggestive of MTB infection were noted in other sites. Early diagnosis allows for antitubercular therapy with retention of the prosthesis, while late diagnosis frequently results in removal and reimplantation of the joint. To avoid major surgery, a high index of suspicion is required to diagnose prosthetic joint tuberculosis.

BACKGROUND

Bone and joint infections constitute 10%–11% of extrapulmonary tuberculosis (EPTB) cases, which account for 1%–3% of all tuberculosis (TB) cases.² Prosthetic joint (PJ) TB is extremely rare, with only 30 cases reported in the literature. A series of seven patients with mycobacterial tuberculous PJ infection (PJI) was identified in one centre over a 22-year period. Interestingly, patients who received a total knee arthroplasty were more affected (27%) than those with a total hip arthroplasty (6%).³ However, the number is too small to reach a conclusion.

Identification of EPTB of the joints is often problematic as EPTB may be overlooked. Less than half of patients with TB have a TB treatment history, and fewer than 30% have abnormal chest X-ray to raise the suspicion of TB arthritis.⁴ In addition, absence of the associated systemic symptoms adds to the difficulty in diagnosing TB; consequently, (PJ) TB is likely to be discovered late with an expected adverse outcome.

Diagnosis of TB is generally confirmed by identification of TB bacilli in culture or by using molecular techniques like PCR. In one study, it was found that synovial histopathology and culture was positive in 73% and 55% of patients, respectively. In contrast, synovial fluid culture was positive in only 18% of patients.⁵ This underscores the value of combining different diagnostic modalities to establish a TB diagnosis. Molecular testing, though not employed in the synovial specimens of our patient, can aid in the diagnosis of TB. The Genexpert test speeds the diagnosis pending the culture result of

mycobacteria and predicts isoniazid (INH)/rifampicin resistance early in the course of treatment.

Optimal surgical treatment for *Mycobacterium tuberculosis* (MTB) PJI is still controversial. One-stage and two-stage exchange arthroplasty, debridement with retention of the prosthesis and medical management have all been used for PJ management. Early diagnosis allows for medical treatment and retention of the prosthesis. However, only a few cases have been diagnosed within 3 months of surgery.⁶ This is frequently due to a combination of a low index of suspicion, masking owing to a simultaneous bacterial infection, or low yield of smears and culture for acid-fast bacillus. Coinfection, making the diagnosis of TB difficult, is reported among MTB prosthetic infection cases, with *Staphylococcal* species being the most common coinfecting organism.⁷ Late diagnosis leads to tubercular osteomyelitis, which induces severe bone damage with poor functional results. In a series of patients, all individuals who had bony damage or radiolucent changes of the total knee replacement underwent removal of the implant. However, patients without these changes on imaging attained a good outcome and retained the prosthesis with or without debridement.¹

Herein, we describe a rare case of TB of the PJ diagnosed in a region of moderate TB prevalence. PJ TB could be under-reported; to improve the prognosis in such patients, physicians, especially those in endemic areas, should maintain a high index of suspicion for early diagnosis of TB. Accordingly, there is a clear need to remind physicians to consider and pursue a potential diagnosis of TB.

CASE PRESENTATION

A 73-year-old man was admitted to the hospital 14 months following bilateral total knee replacement. His surgery was complicated by the left knee wound's dehiscence, which required 6 weeks of antibiotics treatment; after this, he remained symptom free for 1 year. His current complaints included 3 months of left knee pain, swelling, blood and pus discharge, fever and restriction of movement. There was no significant improvement despite three sessions of incision and drainage and 6 weeks of antibiotics. He is not known diabetic, but he is on regular treatment for hypertension and hyperlipidaemia. There is a strong history of animal contact including sheep and camels. Examination revealed a swollen, tender, hot left knee with a pus-discharging sinus. Both the erythrocyte sedimentation

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Figure 1 PA and lateral plain radiograph of the (L) knee joint showing the prosthesis with soft tissue swelling in addition to knee joint effusion. PA, postero-anterior.

rate and C reactive protein levels were high at 73 mm/hour and 88 mg/L, respectively. Plain radiograph showed findings suggestive of chronic superimposed left knee joint infection. There is soft tissue swelling with (L) knee effusion and fragmentation of the patella. There was also new bone formation from the posteromedial aspect of the left knee (figure 1). A three-phase bone scan displayed increased activity around the left knee prosthesis extending to the lower third of the left femur. Incidentally noted was a focal increased tracer uptake anteriorly in the fifth and seventh right ribs (figure 2A,B). Similarly, a white cell count scan revealed abnormal increased white cell count uptake in the region of the left knee. In correlation with the bone scan results, these features were suggestive of infected left knee prosthesis (figure 3A). Furthermore, the observed changes had significantly regressed on a follow-up (figure 3B). The patient underwent left knee revision with debridement and an insert change and augmentation of quadriceps muscles. Blood, knee aspirate, pus and eight cultures from different sites of the joint including bone, cement, synovium and intramedullary canal were all negative for bacteria. Blood, synovial fluid cultures and serology for brucella were negative. Three weeks following revision, the joint aspirate grew MTB. A culture taken 2 months at a previous hospital was also positive for a fully sensitive MTB. He denied weight loss,

Figure 2 (A and B) Increased activity around the left knee prosthesis extending to the lower third of the left femur. (C) A focal increased tracer uptake in fifth and seventh ribs anteriorly.

Figure 3 A white cell count scan revealed abnormal increased white cell count uptake in the region of the left knee before (A) and following treatment (B).

night sweats and history or contact with patients with TB. The chest radiograph was normal; a sputum smear, PCR and culture for MTB were negative. He was started on isoniazid 300 mg, pyrazinamide 2 g and rifampicin 600 mg for 2 months and then isoniazid and rifampicin once daily for a total of 1 year. He tolerated the medications well, with a decline of C reactive protein to 14 g/L and erythrocyte sedimentation rate to 8 mm/hour.

DIFFERENTIAL DIAGNOSIS

1. Multidrug-resistant bacterial PJI
2. Brucella PJI (since the patient is from an endemic area)
3. TB PJI.

TREATMENT

1. Isoniazid 300 mg
2. Rifampicin 600 mg
3. Ethambutol 1.2 g
4. Pyrazinamide 2 g
5. Pyridoxine 40 mg.

All five medications were given once daily for 2 months, then followed by isoniazid, rifampicin and pyridoxine for 10 months. Ethambutol was discontinued earlier on confirmation of mycobacteria sensitivity.

OUTCOME AND FOLLOW-UP

Six months following treatment, the erythrocyte sedimentation rate dropped to 8 mm/hour and CRP regressed to 40 mg/L.

DISCUSSION

Older age, prior joint surgery and underlying comorbid medical conditions predispose individuals to TB of the PJs.¹ Similar to that of other patients reported in the literature, presentation of TB in this patient was chronic, with an onset several months after arthroplasty, leading to sinus formation. Nevertheless, the presence of fever was unusual. Overall, systemic symptoms classically seen with other MTB infections, such as fever, anorexia or weight loss, are uncommon in TB-related PJI.³

Bone scans are non-specific and should not be routinely used to diagnose PJI. However, the abnormal bone scan in this patient, coupled with high uptake in the ,which improved on treatment, was highly suggestive of infection. In general bone scan, leucocyte-labelled scans and MRI are not routinely done. When scan are requested, the combination of technetium-labelled scan and white cell count scan give a better sensitivity and specificity.⁸ The presence of hot spots on the white cell count scan seen in the ribs and shoulder of our patient were interesting and possibly signified multiple sites of infection. However, this was difficult to confirm in the absence of biopsy findings. Multifocal TB, though rare, has previously been reported in immunocompetent patients.⁹

One-third of patients with prosthetic knee infection have simultaneous TB infection in distal areas. Therefore, infection in other foci should be suspected when TB infection is confirmed in total knee arthroplasty. In contrast to Staphylococcal infection, MTB rarely results in significant biofilm formation, owing to its poor adherence to metal.¹⁰ Electron microscopy has demonstrated *Staphylococcus epidermidis* colonisation on a wide surface area of experimental prostheses, but few MTB-infected cells were scattered on the prosthesis. Hence, MTB is associated with limited biofilm formation and poor attachment to the prosthesis. This may allow for medical treatment of PJI with MTB that permits retention of the prosthesis. Moreover, studies on biofilm and quorum sensing revealed the presence of cyclic dimeric guanosine monophosphate in mycobacteria. This molecule mediates quorum sensing associated with increasing tolerance to antimicrobials.¹¹ Although investigational studies of MTB confirmed that high doses of rifampicin were highly effective in the clearance of MTB embedded within the biofilm, some mycobacteria outlive this treatment. Consequently, a prolonged course of treatment may be crucial.¹² In the future, drugs that target or inhibit biofilm formation could substantially shorten TB treatment in addition to retention of the prosthesis. Currently, the duration of anti-TB medication is variable. In general, a minimum duration of 9–12 months is recommended. Our patient had MTB that was fully sensitive, and he received treatment for a total of 12 months.

Data on prosthetic TB infection from endemic areas are sparse. At present, the number of prostheses in the developing

world, where TB is still prevalent, is increasing. There are currently no guidelines to encourage screening for latent TB prior to joint surgery. Pursuing early diagnosis of TB remains the most important tool to improve the outcomes for these high-cost, demanding surgeries.

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Contributors FEE wrote the manuscript and shared the treatment of the patient. MH was the resident following the patient in hospital and shared in collecting the literature. SSA is an orthopaedic surgeon who looked after the patient and revised the surgical part in the case reporting. NAS is the infectious diseases consultant who followed the patient and reviewed the manuscript.

Competing interests None declared.

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Learning points

- ▶ Tuberculosis infection of prosthetic joints is rare in comparison with other bacterial infections but can cause substantial morbidity when it arises. A high index of suspicion is needed, especially in culture-negative infections.
- ▶ Copathogens such as *Staphylococcus aureus* and *Enterococcus faecalis* can occur, leading to confusion and interference with a correct diagnosis.
- ▶ Rifampicin used as antibiofilm in staphylococcal infection can lead to rifampicin resistance in an overlooked tuberculosis-infected prosthetic joint infection (PJI). Combination of specific antistaphylococcus therapy and rifampicin is standard treatment of staphylococcal PJI.
- ▶ Early diagnosis is associated with successful medical treatment and retention of the prosthesis.
- ▶ The antituberculosis drug combination and duration of treatment can be similar to native joint and bone infection.

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