Need for anti-tuberculosis treatment in patients with latent tuberculosis infection who undergo arthroplasty: a case report

Bingqiang Ren[1], Xuepeng Bai[2], Huawu Zhang[1], Lixin Sun[3], Lei Fang[1], Bo Liu[1], Dong Wang[1]

[1]Department of Joint Surgery, Shandong Second Provincial General Hospital, Jinan, China; [2]Department of Thoracic Surgery, Shandong Provincial Chest Hospital, Jinan, China; [3]Department of Medical Imaging, Shandong Second Provincial General Hospital, Jinan, China

Contributions: (I) Conception and design: D Wang, B Ren; (II) Administrative support: H Zhang, D Wang; (III) Provision of study materials or patients: D Wang, B Ren, X Bai, L Sun; (IV) Collection and assembly of data: D Wang, B Ren, L Fang, B Liu; (V) Data analysis and interpretation: D Wang, B Ren, X Bai; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Dong Wang. Department of Joint Surgery, Shandong Second Provincial General Hospital, 4 Duan Xing Xi Lu Road, Huaiyin District, Jinan, Shandong 250022, China. Email: greatwangdong@126.com.

Background: It is currently estimated that about 1/3 of the global population is infected with mycobacterium tuberculosis (TB), and about 90% of those infected have asymptomatic latent infections. It has been reported that 85–90% of newly diagnosed active TB cases evolve from patients with latent tuberculosis infection (LTBI). In approximately 5–10% of patients, LTBI progresses to active TB during their lifetime. The number of artificial arthroplasty procedures performed is increasing. The vast majority of people undergoing arthroplasty are aged 60 years and older. Aging and surgical trauma can reduce the ability of the body to fight infection, which can also promote the recurrence of old or dormant TB infections. TB has been reported to reoccur in LTBI patients after arthroplasty who do not receive anti-TB treatment. This article reports the case of an elderly female patient with LTBI and knee osteoarthritis who underwent total knee arthroplasty and achieved good clinical results with anti-TB drug treatment. There is a lack of guidelines for the treatment of patients with LTBI undergoing artificial arthroplasty. This article attempts to provide a time-based treatment approach to reduce the recurrence of LTBI based on a literature review.

Case Description: Based on a detailed history, a physical examination, and ancillary examinations, this 71-year-old female patient was found to have no active TB; however, after a positive ɣ-interferon release assay (IGRA) for TB infection, she was diagnosed with LTBI. She underwent artificial knee arthroplasty to treat osteoarthritis of the right knee. Anti-TB drugs were administered 2 weeks after the surgery, and good clinical results were achieved at the 53-month post-operative follow-up with no recurrence of TB.

Conclusions: Patients with LTBI who undergo artificial arthroplasty require anti-TB treatment to reduce the risk of TB recurrence.

Keywords: Latent tuberculosis infection (LTBI); artificial arthroplasty; anti-tuberculosis therapy; case report

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Introduction

Tuberculosis (TB) is one of the leading causes of death globally (1). In 2018, there was an estimated 10 million new TB cases globally, and 1.2 million [human immunodeficiency virus (HIV) negative] TB deaths and 251,000 (HIV positive) TB deaths (1). Mycobacterium TB infections affect about 1/3 of the world's population (2). The number of TB cases in China accounts for 9% of the world's total, and with 1,300,000 new cases every year, China is 1 of 30 countries with a high TB burden (2). Based on the state of the disease, TB is divided into latent tuberculosis infection (LTBI), active TB, and non-active TB. About a 1/4 of the global population is infected with latent TB (3). LTBI refers to a special state in which the host has sustained an immune response with mycobacterium TB antigens after infection with mycobacterium TB, but there is no evidence of clinically active TB. LTBI can progress to active TB.

About 90% of those infected with mycobacterium TB have asymptomatic latent infections (2). It has been reported that 85–90% of newly diagnosed active TB cases evolve from patients with LTBI (4). The ɣ-interferon release assay (IGRA), which detects ɣ-interferon production in T lymphocytes stimulated by specific antigens of mycobacterium TB, has many advantages. A study suggest that IGRA has high specificity, good reproducibility, and is not affected by swelling and allergic reactions in the diagnosis of mycobacterium TB infection (5). IGRA is recommended by the World Health Organization (WHO) for the detection of LTBI (2). T-SPOT.TB is a test for IGRA that directly counts the T cells that release ɣ-interferon. T-SPOT.TB is the 4th IGRA approved by the Food Drug Administration. At present, a diagnosis of LTBI does not depend on the pathogen and clinical manifestations of mycobacterium TB, but on the cellular immune response status of specific antigens of mycobacterium TB (6). The diagnosis of LTBI is based on positive IGRA results.

Artificial arthroplasty has achieved great success in the 20th century. With improvements in living standards and economic conditions, the number of artificial arthroplasty procedures performed is also increasing. It is estimated that as many as 1 million hip arthroplasties are performed worldwide each year, and that this number is increasing (7,8). In the United States (US), 700,000 knee arthroplasties are performed annually, and this number is increasing worldwide (9). The vast majority of people undergoing arthroplasty are aged 60 years and older (10,11). In the United Kingdom, the average age of patients undergoing hip arthroplasty is 69 years, and 68% of hip arthroplasty patients are older than 65 years (10,11). In Australia, 64% of patients undergoing hip arthroplasty are older than 65 years, and the median age of knee arthroplasty patients is 60 years (12,13).

Arthroplasty patients represent a special population. Arthroplasty patients are hospitalized for a long time, may be unable to adapt to the hospital environment, and are subject to mental and surgical stress, all of which can lead to significant increases in the incidence of TB infection (14). At the same time, aging and surgical trauma can reduce the ability of the body to fight infection, which can also promote the recurrence of old or dormant TB infections (14).

At present, reports on the diagnosis and treatment of patients with LTBI who undergo arthroplasty and the clinical effects of anti-TB treatments are rare. This article reviews the clinical results of the diagnosis, treatment, management, and anti-TB treatment of 1 patient with LTBI who underwent artificial arthroplasty at the Department of Joint Surgery of Shandong Second Provincial General Hospital. We present the following case in accordance with the CARE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5830/rc).

Case presentation

This article reports the case of a female patient, who was born in 1946, and who had continued to reside in her place of birth. In 2018, at the age of 71 years, the patient had experienced right knee pain for >10 years and responded poorly to non-surgical treatment. The patient had no history of medical disease, and no history of, or exposure to, TB. Additionally, the patient had no cough or sputum, no hypothermia or night sweats, and no other general conditions, such as abnormal wasting.

On examination of the right knee joint, no erythema and no sinus tracts or scarring were observed. However, the patient had pressure pain in the joint space, and joint mobility with 5 degrees of extension and 100 degrees of flexion. The results of the other physical examinations were negative. The Hospital for Special Surgery (HSS) score for the knee joint was 52.

Imaging showed a 20-degree valgus deformity of the right lower extremity, the narrowing of the lateral joint space, and osteoarthritic changes in the 3 interventricular spaces (*Figure 1*). Computed tomography (CT) of the chest showed no calcification, fibrous scar, or pleural effusion.

The patient underwent a positive T-SPOT test and was diagnosed with LTBI and osteoarthritis of the right knee (Kellgren-Lawrence, IV) based on the patient's symptoms, signs and ancillary examinations; however, the patient had no clinical signs of active TB. After discussion and gaining the patient's consent, a posterior stabilized cemented artificial total knee arthroplasty was performed in May 2018 (P.F.C; DePuy Orthopedics, Warsaw). Intraoperatively, the joint fluid was clear, with mild synovial hyperplasia and synovial edema. The patient's post-operative synovial pathology results showed non-specific inflammatory changes. The imaging findings showed a good prosthesis position and force line (*Figure 2*). The patient took rifampicin (450 mg) once a day on an empty stomach and isoniazid (300 mg) once a day on an empty stomach 2 weeks after the operation for 3 months. The patient recovered

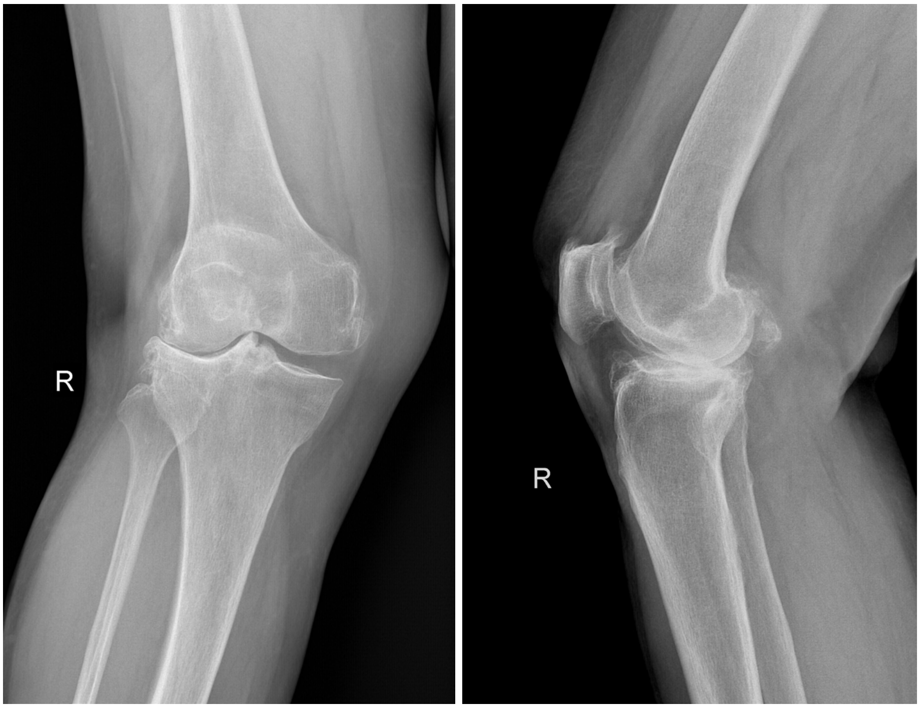

Figure 1 Pre-operative anteroposterior and lateral radiographs showing tricompartmental osteoarthritis with valgus deformity. R, right.

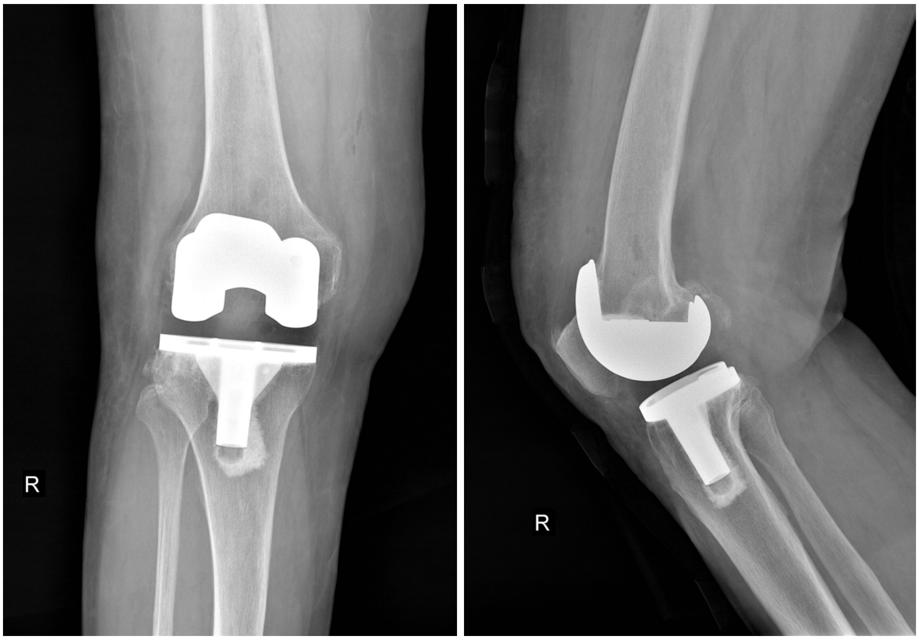

Figure 2 Immediate post-operative anteroposterior and lateral radiographs showing the implant after knee arthroplasty. R, right.

satisfactorily and returned to normal life 3 months after the surgery. 'I am very satisfied with the results of this procedure,' the patient said 3 months after surgery.

During the follow-up period, attention was paid to the clinical manifestations of the patient (e.g., whether there was pain or swelling, the range of motion, and the HHS

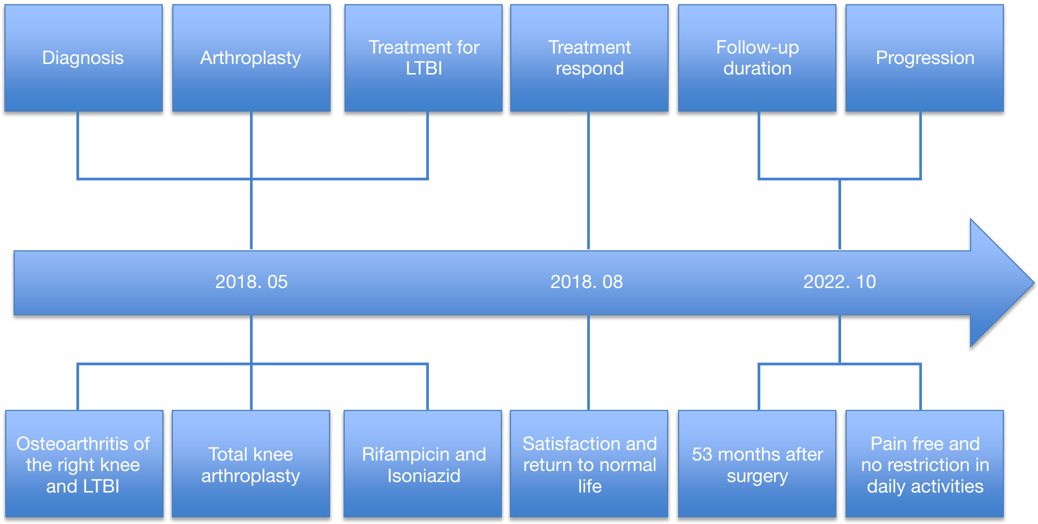

Figure 3 Timeline of interventions and outcomes. LTBI, latent tuberculosis infection.

score). The post-operative follow-up continued to October 2022, 53 months after the surgery (*Figure 3*). At which time, the patient was pain-free, with a mobility of 5 degrees of extension and 120 degrees of flexion, a HSS score of 94, and no restriction in her daily activities.

The work was approved by the ethics committee of Shandong Second Provincial General Hospital (No. XYK20211002). All procedures performed in this study were in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Globally, LTBI occurs in about 1/4 of the world's population. In approximately 5–10% of patients, LTBI progresses to active TB during their lifetime; the progression to active TB is related to the immune status of the host (15). One of the mechanisms of TB is the blood-borne transmission of LTBI through unidentified focal sites, in which infected monocytes migrate from the granuloma to inflammatory sites (16). The WHO recommends the preventive treatment of LTBI for people who are likely to progress to active TB and for those who would benefit from preventive treatment (2).

In 2020, the National Association of TB Control and the United States Centers for Disease Control and Prevention established treatment guidelines for LTBI. The guidelines contain 3 versions of a preferred scheme and 2 alternative treatment options that are suitable for LTBI patients sensitive to isoniazid and rifampicin (17). The drugs in the preferred regimen have good tolerability and efficacy, require a short treatment time, and have high treatment completion rates. The preferred protocols are as follows: (I) isoniazid and rifapentine once a week for 3 months. The potential disadvantages of this regimen are that the drugs are relatively expensive and may require multiple medications associated with systemic drug reactions or influenza-like syndromes; (II) Rifampicin once a day for 4 months; and (III) Rifampicin and isoniazid once a day for 3 months.

There is an alternative for patients with LTBI who cannot receive the preferred regimen, such as patients with drug intolerance or drug interactions; that is, isoniazid once daily for 6 or 9 months. In the selection of treatment regimens, shorter treatment regimens are preferred, which have good tolerability, high treatment completion rates, and are effective in the treatment of patients with LTBI. The WHO recommends: isoniazid once daily for 6 or 9 months, rifapentine plus isoniazid once a week for 3 months, isoniazid rifampicin daily for 3–4 months, or rifampicin daily for 3–4 months (2). From the safety point of view, 3–4 months of rifampicin and 3 months of rifapentine plus isoniazid had lower hepatotoxicity and higher completion rates.

TB has been reported to reoccur in LTBI patients after arthroplasty who do not receive anti-TB treatment.

Hattrup *et al.* reported the case of a 78-year-old patient who underwent shoulder arthroplasty for humeral head necrosis and developed a post-operative TB infection of shoulder (18). The patient's father and sister had developed TB as children, and the patient tested positive for tuberculin at that time but had no history, or clinical or imaging findings indicating TB. Reyes *et al.* reported the case of a patient with LTBI complicated by systemic lupus erythematosus and Sjogren's syndrome who underwent right total hip arthroplasty without anti-TB treatment (19). During the operation, TB was found in the hip joint, and the patient was diagnosed with a TB infection. McCullough *et al.* reported a case of TB infection after a right total hip arthroplasty in a LTBI patient who had not received anti-TB therapy (20).

Harwin *et al.* reported the case of a 60-year-old patient with LTBI who underwent total knee arthroplasty (21). The patient had come into contact with a TB patient some 25 years ago and received anti-TB treatment for 1 year despite having no positive TB test results and no clinical manifestations of active TB at that time; however, a TB infection occurred after the artificial knee arthroplasty. This patient developed TB infection after anti-TB treatment and the TB infection was thought to be related to the patient's rheumatoid arthritis.

Due to the lack of diagnosis and treatment guidelines for artificial arthroplasty in patients with LTBI, this patient was given anti-TB drugs for 2 weeks after the operation. The follow-up period was 53 months, the clinical effect was good, and the patient returned to self-care. No prosthesis loosening, osteolysis, or TB recurrence was observed.

This study had its limitations. First, it was a retrospective study with a short follow-up period. Since a diagnosis of LTBI cannot be used to determine whether the TB disease is active, LTBI needs to be combined with clinical manifestations, such as a low fever, night sweats, wasting, and weakness, and imaging tests, such as a chest X-ray or chest CT, to exclude active TB disease. However, a literature search revealed that reports on patients with LTBI who had to undergo arthroplasty were rare. To date, this is the first report of a patient with LTBI who had to undergo arthroplasty.

Anti-TB treatment should be administered to patients with LTBI who have to undergo artificial arthroplasty.

Conclusions

Patients with LTBI who undergo artificial arthroplasty require anti-TB treatment to reduce the risk of TB recurrence.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-5830/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5830/coif). All authors report that this work was supported by the Projects of Medical and Health Technology Development Program in Shandong Province (grant No. 202104070644). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The work was approved by the ethics committee of Shandong Second Provincial General Hospital (No. XYK20211002). All procedures performed in this study were in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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