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Case Report

Role of QuantiFERON TB Gold Test for Diagnosis of Tuberculosis Infection in Prosthetic Knee Joint: A Case Report

Norliyana M, Nor Hamdan MY (✉), Rizal AR

Department of Orthopaedic, Faculty of Medicine, Universiti Kebangsaan Malaysia. Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia.

Abstract

Mycobacterium tuberculosis (MTB) is a rare cause of prosthetic joint infection. The diagnosis is challenging especially in cases of latent tuberculosis. QuantiFERON-TB Gold (QFT®) is an interferon-gamma relative assay (IGRA) which is highly specific and sensitive for detection of MTB infection. We report a case of 76-year-old lady diagnosed with tuberculous prosthetic joint infection following total knee replacement. Histological examination of abnormal synovial tissue taken intraoperatively reveals chronic granulomatous lesion and raised suspicion of tuberculous infection in otherwise asymptomatic patient. The tuberculin skin test, MTB acid-fast stain and tuberculosis polymerase chain reaction were negative. The diagnosis dilemma was solved with positive result of QuantiFERON TB Gold Test. The patient was treated with anti-tuberculous drug without any surgical intervention. At five months follow-up, patient was clinically well with no symptoms and signs of infection.

Keywords: Interferon-gamma, latent tuberculosis, mycobacterium tuberculosis, total knee replacement, tuberculosis

Correspondence:

Nor Hamdan Mohamad Yahaya. Department of Orthopaedic, Faculty of Medicine, Universiti Kebangsaan Malaysia. Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: +603-91455555 Fax: +603-91456640 E-mail:drhamdan@ppukm.ukm.edu.my

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Introduction

Tuberculosis prosthetic joint infection commonly involves the hips and knees and may results from hematogenous spread or local reactivation of dormant nidus of tuberculosis in response to tissue trauma (1,2). The infection can occur during the surgery and the entire lifespan of the implant. Early infection (less than 3 months post-operative) and delayed-onset (3 to 24 months post-operative) usually occurred during surgery (1). Late infection (more than 24 months) are commonly acquired by haematogenous route (1). Barbari et al restrospectively reviewed 2116 cases of prosthetic joint infection (PJI) over 22 years and only 7 (0.3%) were tuberculous infection (3). The risk of reactivation of latent tuberculosis is higher in total knee arthroplasty (27%) than total hip arthroplasty (6%) (3).

The diagnosis of tuberculous prosthetic joint infection is based on detection of MTB in acid-fast stain and cultures. Histological findings of granuloma support the diagnosis of TB infection but it is nonspecific (1). QuantiFERON-TB Gold (QFT®) is an interferon-gamma relative assay (IGRA) newly developed as an alternative to tuberculin skin test. It is a whole blood test that employs synthetic M. tuberculosis proteins, culture filtrate protein-10 and early secretory antigenic target-6 as specific antigen (4). The cell-mediated immune response will react by secreting cytokine, interferon gamma (IFN-y) when the infected blood is exposed with the M. tuberculosis-specific antigen in QFT. The concentration of IFN-y is measured using a sensitive ELISA. QFT is highly specific and sensitive test with a positive result is strongly predictive of true infection with MTB. This test gives faster results on the same day as compared to TST and MTB culture.

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A 76-year-old lady had right knee pain for 3 years duration. The pain became progressively worse and limits her ambulation prompting her to seek medical treatment. Diagnosis of right knee osteoarthritis was made and confirmed with radiographs of the right knee consistent with features of osteoarthritis (Fig. 1). She was counselled for right total knee replacement (TKR).

Prior to the planned TKR, she developed right knee pain and swelling. Clinical examination revealed a warm knee with range of motion of 0 to 30°. Aspiration of the right knee was attempted but revealed a dry tap. Blood laboratory investigations showed total white cell count was 5.3x 109/L and C-reactive protein (CRP) was 3.14mg/dl (normal range is <5mg/dl). Her operation was postponed and she was investigated for inflammatory arthritis. Uric acid level, rheumatoid factor and anti-cyclic citrullinated peptide were within normal range. She was given analgesics to relief the pain. A month later, the knee swelling resolved and repeated CRP was 2.17mg/dl. She was planned for right total knee arthroplasty one month after her initial operation date.

Patient underwent combined spinal epidural and intravenous prophylactic antibiotic (Ceftriaxone 2g) was administered during induction. She was in placed supine position with tourniquet applied over her right thigh. Approach to the knee joint was via medial parapatellar. Intraoperative findings were reddish brown inflamed synovium at suprapatellar area (Fig. 2) and the bone appeared normal. Our intraoperative diagnosis at that time was pigmented villonodular synovitis. The synovium was excised completely. Femoral and tibia were cut and prepared as per standard TKR procedure. Implants used were posterior stabilised Zimmer® Gender Solutions™ NexGen® High-Flex femoral component size D, tibial component size 2 with 12mm insert. A drain was inserted intraoperatively and wound closure was with subcuticular technique using absorbable suture. Postoperative was uneventful and patient was discharged at day five.

The histopathological result of the synovium was chronic granulomatous inflammation and tuberculosis infection cannot be excluded. The Ziehl-Neelson, para-aminosalicylic acid (PAS) and Groccot shows absence of acid fast bacilli and fungal element respectively. The culture and sensitivity test showed no growth at 72 hours. The tuberculosis polymerase chain reaction (TB PCR) of the synovium was also negative for Mycobacterium Tuberculosis DNA. The

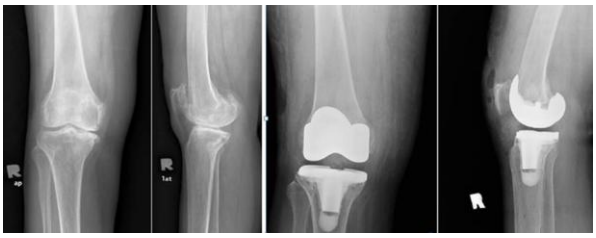

Figure 1: Radiograph of right knee before and after total knee arthroplasty.

Figure 2: Brownish red hypertrophied synovium at suprapatellar (arrow).

patient also tested negative for HIV and syphilis. However, interferon gamma release assays (IGRAs) QuantiFERON®-TB Gold (QFT-G) test from the patient's blood sample was positive. Chest radiograph and sputum examinations were unremarkable. The erythrocyte sedimentation rate was elevated, 89mm/hr and the subcutaneous tuberculin test (Mantoux test) was negative.

The patient was re-admitted at three weeks post-operation for initiation of anti-tuberculous drugs for right knee tuberculosis infection. She was started with oral Akurit 4 (rifampicin 150 mg, isoniazide 75 mg, pyrazinamide 400 mg, ethambutol 275 mg) three tablets daily and Pyridoxine 10mg daily for induction phase. At five months post-operation, she was ambulating well with no symptoms and signs of tuberculosis infection.

Discussion

The diagnosis of osteoarticular TB by identification of MTB is difficult. MTB cultures are positive in 60-80% of cases, positive acid-fast stains of joint fluid in 20-25% of cases and histological examinations are nonspecific (1). The detection of MTB, the bacteria which causes tuberculosis was dependent on tuberculin skin test (TST). TST results may affected

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by previous vaccination with Bacillus Calmette–Guérin (BCG) and error in measuring the size of induration (5).

In comparison with tuberculin skin test, QuantiFERON®-TB Gold (QFT-G) is reported to have higher sensitivity and specificity for detecting tuberculosis and unaffected by previous exposure to atypical mycobacterium and prior BCG vaccination (6,7). Abdel-Samea et al. conducted a comparative study between QFT-G and TST in diagnosis of Mycobacterium tuberculosis infection (6). They reported that QFT-G showed 100% sensitivity and 100% specificity, while tuberculin test sensitivity is 94.7% and specificity is 80% (6).

In another study among 50 cases of active pulmonary tuberculosis, the sensitivity of QFT-G and TST were reported as 80% and 28% respectively (7). Ak et al. conducted a study comparing the positivity of QFT-G and TST in 44 cases of pulmonary tuberculosis and 21 cases of extrapulmonary tuberculosis. They reported 75% positivity of QFT-G and 68.2% positivity of TST in active pulmonary tuberculosis patient, while in cases of extra-pulmonary tuberculosis the positivity was 76.2% and 62% respectively (8).

In this case, the patient had no symptoms of pulmonary tuberculosis and, sputum tests and chest radiograph were normal. Although she had history of knee swelling and raised CRP one month prior to operation, the knee arthrocentesis was dry. Therefore, she was treated as acute exacerbation of osteoarthritis and latent tuberculosis infection was not expected. Intraoperatively, the impression of pigmented villonodular synovitis was made based on findings of brownish red hypertrophied synovium. We proceeded with the joint replacement after excision of hypertrophied synovium. The only positive results that support the diagnosis of tuberculosis joint infection were histopathological examination of granuloma and positive QFT.

It is possible this patient had latent tuberculosis infection as she is asymptomatic. In latent tuberculosis infection (LTBI), the MTB survives in the body in a dormant state. The person is not contagious and does not experience any symptoms. The lifetime risk for developing active TB is about 5-10% (1). Detection and treatment of LTBI is important to prevent reactivation to active disease especially in people with compromised immune systems.

We decided to treat this patient with oral Akurit 4, a combination of rifampicin, isoniazid, ethambutol, and pyrazinamide for induction phase and followed by maintenance phase to complete 12 months duration of treatment. The patient did not underwent knee washout or removal of implants based on evidence of literatures that reported good results with appropriate treatment without the need for prosthesis removal (1,3,9,10).

Furui in 2015 reported positive intraoperative synovial fluid culture and tissue biopsy in a total knee arthroplasty patient. Anti-tuberculosis therapy was started and there was no evidence of loosening in radiograph at 7-month follow-up (10). Another case of tuberculosis PJI after two months post-operation was successfully treated with anti-tuberculosis drugs for 12 months only without evidence of recurrence (9). Asymptomatic patient with tuberculous septic arthritis confirmed at the time of surgery or in early postoperative period can be treated with anti-tuberculosis therapy for 12-18 months with retention of implant (3,9). In cases of late onset MTB prosthetic joint infection, removal of implant and infected tissue, followed by long term anti-TB drugs are recommended (1,11).

Another factor that favors retention of implant in early tuberculous infection is the biological characteristics of MTB that differs from other bacteria. MTB has lower tendency of adherence to metal surfaces thus are less likely to develop biofilm (12). This feature makes MTB susceptible to anti-tuberculous drugs and retention of implant in early tuberculous prosthetic joint infection feasible. Based on this knowledge, arthroplasty in advanced tuberculous arthritis would not increase the risk of tuberculosis reactivation in patient with adequate debridement and post-operative anti-tuberculous therapy (13).

Conclusion

Tuberculous prosthetic joint infection is rare and the diagnosis is challenging especially in latent TB cases. Interferon gamma release assays (IGRAs) known as QuantiFERON®-TB Gold (QFT-G) is a reliable test to identify latent TB infection and early treatment can be initiated. QFT-G is a specific and sensitive test for detecting tuberculosis and unaffected by previous exposure to atypical mycobacterium and prior BCG vaccination. The management of tuberculous prosthetic joint infection depends on the stage of infection and the outcome is good.

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