



Periprosthetic tuberculosis of the knee joint treated with antituberculosis drugs: a case report

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We report a 55-year old man with periprosthetic tuberculosis infection following a total knee arthroplasty surgery performed during an active tuberculosis infection. The patient was conservatively treated with anti-tuberculosis drugs and retention of prosthesis. There was no recurrence during an 18-month follow-up period. Tuberculosis arthritis should be considered in the differential diagnosis in patients with osteoarthritis requiring replacement surgery. Conservative treatment with antituberculosis drugs may be an option in periprosthetic tuberculosis infections without loosening.

Key words: Antituberculosis drugs; knee joint; periprosthetic infection; tuberculosis arthritis.

Tuberculosis (TB) is frequently seen in developing countries, but with increasing prevalence of HIV and drug-resistant bacteriae it is becoming increasingly common in developing countries.^[1] Increase in pulmonary tuberculosis leads to an increase in musculoskeletal system involvement. Hereby, we see increasingly more patients with tuberculosis in our orthopaedic practice.^[2]

Due to the lack of specific findings, the diagnosis of TB synovitis is not straightforward.^[3] Once this rare cause of secondary osteoarthritis is overlooked, a replacement surgery may be performed in a would-be aseptic arthritic joint. It has been shown that in cases with previous TB arthritis, infection may be activated following knee and hip arthroplasty.^[4] Periprosthetic tuberculosis infection may also arise with hematogenous spread of the bacteriae.^[5] It is more difficult to diagnose TB infection in the joint after arthroplasty.^[3,6] When diagnosis is confirmed, treatment options range from

wide debridement to two-phase revision surgery in conjunction with medical treatment.^[2]

In this manuscript, we report a 55-year old man with periprosthetic tuberculosis infection following a total knee arthroplasty surgery performed during an active tuberculosis infection. The patient was conservatively treated with anti-tuberculosis drugs and retention of prosthesis.

Case report

A 55-years-old man referred to our outpatient clinic with pain, redness, swelling and movement restriction in left knee. The history of the patient revealed that 20 days ago, total knee replacement was performed in another medical center. Patient had admitted to the hospital with symptoms of pain in his left knee worsening during previous year and with the addition of symptoms like swelling, local warmth and restriction of movement. In

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the Orthopaedics Department, patient was diagnosed as osteoarthritis and cemented total knee replacement was performed. During surgery, biopsy was performed due to suspicious synovial pathology. Pathology report revealed chronic granulomatous inflammation and formation of granuloma. Fifteen days after surgery, upon recurrence of symptoms like pain, swelling and redness in the knee, patient referred to Infectious Diseases Department. Pain was less intense compared to pre-surgery but redness and swelling developed again and increased progressively. Before surgery, arthrocentesis was performed several times for swelling but no microbiological and biochemical evaluation was carried out. Fever, night sweats, anorexia and weight loss were present before surgery and gradually increased afterwards.

Examination of the patient revealed anterior longitudinal incision scarring on left knee and severe effusion plus redness and local warmth around the knee. Knee flexion was at 90 degrees and extension was full. Upon these findings, arthrocentesis was performed and around 120 ml fluid was aspirated. Fluid had a dark yellow, slightly viscous and opaque appearance and contained particles. Evaluation of aspiration fluid revealed cell count as $36,000/\text{mm}^3$ (88% lymphocyte). Culture was performed from aspiration fluid and histological evaluation was requested. Brucella plate and tube agglutination tests of aspiration fluid were negative. Rapid bacteriological cultures revealed no growth. Ziehl-Neelsen staining showed acid resistant bacteriae (ARB). Adenosine deaminase level was measured as 166 U/L (N: 0-40) in synovial fluid. Patient had no BCG vaccination scar on left shoulder. Laboratory findings were as follows: complete blood count; leucocyte $9870/\text{mm}^3$, hematocrit 39.3%, hemoglobin 13.2 g/dl, platelets $602,000/\text{mm}^3$, erythrocyte sedimentation rate (ESR) 79 mm/h, CRP: 1.69 mg/dl (reference interval: 0.1-0.5). Biochemical values were within normal limits. Serum rose bengal and brucella tube agglutination tests were negative. Lung X-rays were normal. Knee X-ray revealed no signs of loosening of prosthesis. Tuberculin skin test (PPD) was 25 mm. There was no special finding in personal or family history. Patient was diagnosed to have arthritis due to tuberculosis 20 days after surgery. After 4 weeks following knee aspiration, *M. tuberculosis* was determined in sinovial fluid culture and diagnosis was confirmed. Because there were no signs of loosening, surgical intervention was ruled out and anti-TB medical treatment was initiated. During first 2 months, 4 major drugs (isoniazide, rifampicin, ethambutol and pyrazinamide) were given. Treatment continued with isoniazide and rifampicin for 10 months. Patient completely recovered both clinically and according to laboratory values; treatment was continued for 2 additional months to complete to one year and discontinued.

After medical treatment, knee examination at six and eighteen months revealed full extension and flexion at 120 degrees. Signs of pain and swelling were completely relieved. Patient had no pain during knee movements and weight-bearing. There were no signs of prosthesis loosening in direct X-rays.

Discussion

Tuberculosis is an infection seen all around the world, though more prevalent in developing countries. According to World Health Organization data, 8.9-9.9 million newly diagnosed TB cases were reported worldwide in 2008.^[7]

The most frequent form of extra-pulmonary TB is TB lymphadenitis (43.2%); bone-joint involvement constitutes 10.9% of the cases.^[8] In Turkey, TB is endemic and TB morbidity rate in 2007 is reported as 25.2 in 100,000. According to 2009 report of Ministry of Health Tuberculosis Control Department, rates of extra-pulmonary TB cases between 2005 and 2007 in Turkey are determined as 27%, 28.2%, and 30.5%, respectively.^[9]

Knee joint tuberculosis is the third frequent osteoarticular TB form, following spinal and hip joint involvements.^[10] It is difficult to diagnose osteoarticular TB involvement in knee.^[11] It generally involves one joint and systemic symptoms like fever and weight loss or pulmonary involvement are not common.^[12] Our patient was residing in an endemic area for TB. Her complaints were present for many years.

Vigilance and suspicion is essential in the diagnosis of bone and joint TB. Even though imaging techniques may increase suspicions, diagnosis should be confirmed with histopathological and microbiological evaluations. Radiological changes develop slowly and are not specific to the disease. Cold abscess or fistula formation may be seen.^[13] Tuberculin skin test (PPD) may help in determining the diagnosis in developed countries where BCG vaccination is not performed as a routine.^[14] Our patient did not have BCG vaccination and PPD test revealed a positive result.

In TB arthritis patients, ESR is generally high. Nevertheless, ESR usually increases after surgical intervention and has a limited value.^[2] Our patient had surgery and ESR was high. It has been reported in several articles that the disease has an insidious onset, presents with various clinic manifestations and as in our case, diagnosis may be delayed after arthroplasty.^[15]

To confirm the diagnosis, synovial tissue sampling and TB culture should be performed. During direct examination of synovial fluid, ARB can be detected in only 20-40% of the cases but there is significant growth in 80% of the cultures.^[14] Growth is seen in 4

to 6 weeks of the culture but in some cases, ARB may be seen under direct microscope with Ziehl-Neelsen staining.^[1] In a three-case series of Marmor et al.,^[2] ARB evaluation of sinovial fluid was always negative and diagnosis was confirmed by culture. In our case, ARB positivity in sinovial fluid assisted in early diagnosis. As a result, treatment was initiated shortly after prosthetic surgery. Growth of *M. tuberculosis* in culture confirmed the diagnosis.

In the recent years, there is a number of TB arthritis cases developing after replacement surgery.^[2,4] In the literature, cases diagnosed years after prosthetic surgery were also reported.^[5] In our case, we think that diagnosis of osteoarthritis and replacement surgery was performed without completing a meticulous diagnostic workup. First, we suspected that the patient may have TB or brucellosis infection, based on the report indicating the chronic granulomatous inflammation and granuloma formation as a result of pathology. Brucellosis Wright agglutination test was found to be negative. Especially in cases with mild clinical symptoms, where the routine bacterial and anaerobe cultures are negative, and in joint infections that are non-responsive to antibiotic treatment, diagnosis of TB should be ruled out.^[16] The long lasting symptoms after arthroplasty suggested joint TB.

The diagnosis of periprosthetic tuberculosis is often delayed when the history of TB is not known. However, the perioperative macroscopic findings were observed and recorded. Synovial hypertrophy, severe inflammation, discoloring in joint liquid, and generalized cartilage wear should alert the surgeon to make a tissue sampling for pathological analysis.^[17,18]

Periprosthetic TB-arthritis may be successfully treated with removal of prosthesis and anti-TB therapy.^[14] In cases diagnosed before any joint cartilage damage, long-

term anti-TB therapy may control the disease and prevent replacement surgery.^[19] In cases with severe cartilage damage arthrodesis or arthroplasty may be recommended only after the eradication of the infection with medical treatment.^[4] On the other hand, TB may recur after arthroplasty. It has been reported that re-activation of TB after arthroplasty is more frequent in the knee joint (27%) than the hip joint (6%).^[20] Eskola et al. reported that a long time period between primary TB treatment and arthroplasty effects success in surgery and in their patient series, this duration is 30 years on average.^[4]

With early diagnosis, prosthesis can be preserved and treatment is possible solely with debridement and medical therapy. Marmor et al.^[2] diagnosed TB in 5th, 6th and 9th months in three patients after knee arthroplasty; the only patient who was treated with medical therapy was the one diagnosed at 5th month. In the remaining two patients, surgical removal of prosthesis and two-stage revision surgery was required, in conjunction with medical treatment.

An anti-TB therapy with 4 major drugs (isoniazid, rifampicin, ethambutol and pyrazinamide) is recommended for 2 months in developing countries, whereas in developed countries, 3 drugs (isoniazid, rifampicin and pyrazinamide) is regarded as sufficient. In the maintenance phase, isoniazid and rifampicin is recommended.^[4] In joint TB, treatment duration of 12 months is recommended.^[21] In the case of delayed prosthesis TB case reported by Neogi et al.,^[5] treatment was extended to 18 months. In another case similar to our patient reported by Lee et al.,^[19] treatment was extended to 12 months. In our case, quadruple anti-TB drugs for 2 months in the initial phase and dual drug treatment for 10 months in the maintenance phase was administered.

Table 1 shows the data of the previous reports on periprosthetic TB infections after replacement surgery.

Table 1. The data of the previous reports on late onset periprosthetic tuberculosis after replacement surgery.

Author	Age/sex	Time elapsed	Anti-tubercular drugs & duration (months)	Treatment	Followup	Outcome
Bryan et al. 1980 ^[20]	72/F	8 years	I,E,R (24)	Arthrodesis	3 years	Good
Zeiger et al. 1984 ^[21]	40/F	4 years	NS	Resection arthroplasty	NS	NS
Wolfgang 1985 ^[11]	62/M	1 years	I,R (24)	Staged exchange	12 months	Good
Tokumoto et al. 1995 ^[22]	71/F	1.7 years	I,E (18)	Debridement	8 years	Good
Lusk et al. 1995 ^[23]	75/F	15 years	I,E,P (6)	Resection arthroplasty	6 months	Died
Spinner et al. 1996 ^[24]	70/F	6 years	I,E,P (9)	Debridement	2.5 years	Good
Marmor et al. 2004 ^[2]	77/F	4 months	I,E,P (8)	Debridement	18 months	Good
Marmor et al. 2004 ^[2]	66/M	2 months	I,R,P (6)	Revision arthroplasty	5 years	Good
Marmor et al. 2004 ^[2]	65/F	3 months	I,R,P (6)	Revision arthroplasty	7 years	Good
Khater et al. 2007 ^[25]	75/F	3 months	I,E (18), R,P (BY)	Resection arthroplasty	NS	NS
Neogi et al. 2009 ^[5]	73/F	14 years	I,R (12), E,P (4)	Medication only	3 years	Good
Current case	55/M	3 years	I,R (12), E,P (2)	Medication only	1.5 years	Good

E: Ethambutol, I: Isoniazid, P: Pyrazinamide, R: Rifampicin, S: Streptomycin, NS: not specified.

In conclusion, due to the lack of pathognomonic signs, the diagnosis of TB arthritis is not straightforward and often delayed. In an osteoarthritic patient with TB history, a generalized cartilage damage, and synovial inflammation TB arthritis should be considered in the differential diagnosis. Also, in periprosthetic infections, TB should be considered in differential diagnosis and diagnosis should not be delayed. In cases diagnosed early with no signs of prosthetic loosening, anti-TB therapy may control the disease.

Conflicts of Interest: No conflicts declared.

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