

CASE REPORT

Knee Tuberculosis: A Challenge in Diagnosis and Treatment

Muhammad Wafiuddin^{1*}, Ahmad Faizal Roslan¹, Ahmad Hafiz Zulkifly²

¹ Surgical-Based Department,
Faculty of Medicine and Health Sciences,
Universiti Malaysia Sabah, Kota Kinabalu,
Sabah, Malaysia

² Department of Orthopaedic,
Traumatology and Rehabilitation,
Kulliyyah of Medicine,
International Islamic University Malaysia,
Kuantan, Pahang, Malaysia

*Corresponding author's email:
drwafi1986@gmail.com

Received: 28 February 2020

Accepted: 19 November 2020

Keywords: *knee tuberculosis, tuberculosis (TB), fixed flexion deformity, total knee replacement*

ABSTRACT

Tuberculosis (TB) is an ancient disease dated back from ancient Greece time. Once rare in developed countries, now it has re-emerged due to immigration and secondary immunodeficiency. A 27-year-old lady had left knee pain for the past 4 years, went for knee diagnostic arthroscopy procedure, and diagnosed as pigmented villonodular synovitis (PVNS) of the left knee. Despite regular analgesics and physiotherapy, patient symptoms worsen. Two years after the initial treatment, the patient went for a further workout and diagnosed as knee tuberculosis, commenced on anti-TB treatment, the patient still left complicated with a stiff knee and fixed flexion deformity. Identification of knee tuberculosis during the initial phase is crucial as late diagnosis and treatment will leave the patient with debilitating complications.

INTRODUCTION

Tuberculosis (TB) forms tissue-damaging immune responses by infecting a person. The infection can disseminate via lymphatic or blood system to lymph nodes and other organs (Hunter, 2018). Bone and joint TB often showed more severe osteolytic lesions and a higher recurrent rate.

TB has a bimodal age distribution, where usually it affects the young (25 to 34 years) and elderly (36 to 60 years) (Al-Ghafli et al., 2019; Procopie et al., 2017). Male is affected more than female by gender and might be

influenced by the deterioration of immune status, due to environmental, social as well as genetic factors (Al-Ghafli et al., 2019).

The suggestive laboratory tests involve full blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), haemoglobin, and synovial fluid culture. The relevant radiological examination includes chest radiograph, diseased bone or joint radiograph, computed tomography (CT) scan, or magnetic resonance imaging (MRI). Surgical treatment and anti-tuberculosis drug therapy appear beneficial in treating these diseases (Qian et al., 2018). TB of the joint is a rare condition accounting for 1 – 3% of all TB cases, with hip as the most common followed by knee TB (Nguyen et al., 2020).

The patient might develop symptoms such as local pain, tenderness and limited range of motion. Systemic TB symptoms may be present in an osteoarticular TB patient. Sinus and discharge might appear in late-stage disease (Procopie et al., 2017). The mainstay therapy for osteoarticular TB is multidrug therapy (MDT) that includes ethambutol, isoniazid, rifampicin and pyrazinamide for 6 to 9 months (Pandita et al., 2020). Debridement, biopsy, synovectomy or arthrodesis are common surgical adjuncts along with chemotherapy and have specific indications tailored to the specific need of the patient (Dhillon et al., 2017).

CASE PRESENTATION

A 27-year-old Malay student presented with a sudden onset of acute left knee pain and swelling after a massage session. The pain was aching in nature and does not radiate elsewhere. She was still able to ambulate after the incident. She denied a history of

trauma, knee overuse, or sport-related injury before. She denies any fever cough or night sweats. She does not have any TB contact but works with foreign workers. She did not seek medical treatment for one year until she became debilitated from the knee pain. Early MRI findings showed the left knee synovium was swollen and gross in appearance. She underwent the first arthroscopic debridement of the left knee and tissue sample was taken and sent for histopathological examination. Results showed non-caseating granulomas. She subsequently did CT thorax and patchy consolidation found at both apical and right anterior segments of the upper lobes with axillary lymph nodes enlargement of 1.5 cm. At the same time, she was investigated for connective tissue disease, but all investigation turned out to be negative. Her sputum acid-fast bacilli (AFB) and Mantoux test were negative. She was treated for pigmented villonodular synovitis. Despite multiple arthroscopic debridements, the patient still experienced pain and need to walk with walking aid. MRI of the left knee was done again after a year and the features were suggestive of synovitis. She went for physiotherapy and took regular analgesics, but symptoms did not get well.

Two years after the initial treatment, she came to our clinic patient. She complained the pain was on and off, moderate in intensity but did not require analgesia and debilitated to ambulate properly. On examination, she was a moderate build woman, not septic looking, and walked using crutches. She walked with a short limb gait by tiptoeing on the affected side (Figure 1). On inspection, there was a small punctum with serous discharge over the lateral distal thigh. There is no tenderness on palpation, no swelling and she got a limited extension of the knee by 10 degrees and flexion by 90 degrees.



Figure 1 Left limb is shortened with flexion of the knee and equinus of the ankle

She subsequently went for left knee arthroscopy washout, right knee wound debridement and biopsy of bone and tissue. Immediately after the procedure, we started her on anti-TB treatment which comprises of intensive phase (ethambutol, isoniazid, rifampicin and pyrazinamide) for 2 months and maintenance phase (isoniazid and rifampicin) of anti-TB for 8 months. The culture was taken from her bone and thigh tissue; acid-fast stain and culture came back as positive.

After one year of anti-TB treatment, the pain subsided but the knee range of motion keep reducing despite regular physiotherapy session. Examination revealed fixed flexion deformity of 30 degrees with ankylosed knee where now the patella is non-mobile (Figure 2), and the patient had to walk using crutches and short limb gait. The X-ray finding was consistent with an active chronic infection of the knee joint and surrounding bone (Figures 3 and 4).



Figure 2 A 30°-fixed-flexion deformity of the left knee, note the extensive scar on the lateral aspect of the thigh from the previous operation

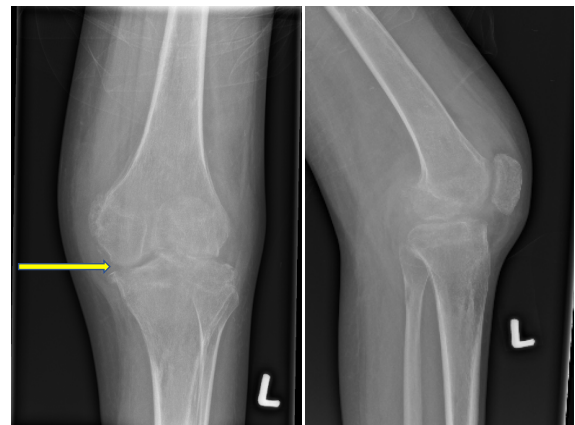


Figure 3 Knee X-ray upon presentation at our centre show joint space loss with the sclerosed distal femur and tibia bone (yellow arrow)



Figure 4 Repeated left knee X-ray after anti-TB treatment showed an ankylosed knee with radiolucency of the distal femoral lateral condyle (yellow arrow)

Since her admission to our centre and subsequent follow-up, her C-reactive protein and erythrocyte sedimentation rate were taken. However, the yielded result was insignificant. Currently, the patient knee is complicated by stiffness and MRI was done for pre-operative evaluation. MRI showed features of TB osteomyelitis and fibrotic tissue surrounding the joint (Figures 5 and 6). Currently, she is planned for total knee replacement once the infection resolved.



Figure 5 A 1.4 × 1.5 cm well-defined heterogeneous lesion at posterior medial femoral condyles (yellow arrow). Post-contrast study confirms cortical defect at the posteromedial area that communicates with the lesion.

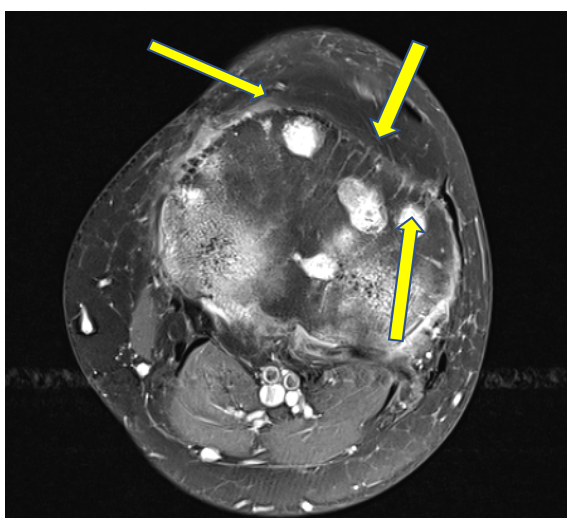


Figure 6 Yellow arrows show multiple large subchondral cysts seen at the left tibial plateau that directly communicates with joint space

DISCUSSION

Tuberculosis always mimics another type of disease and possesses a challenge to diagnose. It is not common in developed countries, once well controlled by vaccination programmes, immigration of foreign workers and low immunodeficiency status contribute to the resurgence of the disease. The incidence of extra-skeletal TB involving the knee is 8% from a total of 15 – 20% of extra-pulmonary tuberculosis cases (Pang et al., 2019).

From primary pulmonary infection, tuberculous bacilli will spread through lymph nodes and then spread via the haematogenous route to the extra-pulmonary organ. In mono-articular tuberculosis the haematogenous spread through synovial blood vessels. Once the bacilli reach the joint there will be persistent congestion and thickening of the synovial membrane and reactive joint effusion and in a later stage, it will cause marginal bone erosion and cartilage destruction (Rodriguez-Takeuchi et al., 2019). A total of 70% of extra-pulmonary TB is not associated with a primary lung infection (Pigrau-serrallach & Rodríguez-Pardo, 2013), as in our patient, she developed a primary lung lesion raising the suspicion of tuberculosis infection.

Our patient did not show any typical clinical manifestation of tuberculosis. During her first visit to our clinic, erythrocyte sedimentation rate and C-reactive protein were not significantly raised. No pulmonary signs and symptoms, no weight loss and she is a normal-built lady. This lack of systemic manifestation possesses a challenge in diagnosing her with tuberculosis. Her laboratory test such as sputum AFB and Mantoux test was negative. Definitive tissue diagnosis, e.g. biopsy with a demonstration of AFB is the gold standard in establishing the diagnosis as systemic and lung evidence involvement might not always present in the case of extra-pulmonary TB (Jetley et al., 2017). As in our patient, we proceeded with tissue

and bone biopsy and the result is positive with tuberculosis infection.

Biopsy for extra-pulmonary TB itself has shown a success rate of 65.2% (Bae et al., 2015). After the sample has been taken a polymerase chain reaction method, it has 80 – 85% sensitivity to confirm the diagnosis (Kivihya-Ndugga et al., 2004).

A plain X-ray would show periarticular osteoporosis, peripherally located osseous erosion and gradual diminution of the joint space or called as a Phemister's triad. Other radiographic features include joint effusion and osteolytic bone destruction. Occasionally, wedge-shaped areas of necrosis may be present on both sides of the affected joint. Bone sclerosis and periostitis occur late in the disease. The end-stage of tuberculous arthritis is characterized by severe joint destruction and, eventually, sclerosis and fibrous ankylosis when the active infectious stage has slowly extinguished. In contrast to pyogenic arthritis, the development of bone ankylosis is uncommon in tuberculous arthritis and when present, is more likely to be secondary to prior surgical intervention. A CT scan is particularly useful for evaluating the degree of bone destruction, sequestrum formation (although rare), and surrounding soft tissue extension (Vanhoenacker et al., 2009).

In MRI, synovial proliferation due to tuberculous arthritis is typically hypointense on T2 images which may be a very helpful sign for differentiating tuberculous arthritis from other proliferative synovial arthropathies. This relatively low signal intensity may be due to the presence of haemorrhage, inflammatory debris, fibrosis, and caseation necrosis (Suh et al., 1996).

Options for treatment once the diagnosis is confirmed must involve anti-TB chemotherapy, but surgery may be indicated to improve symptoms and quality of life in patients affected by joint infection. Treatment

for TB in the first instance revolves around four reserved drugs: isoniazid, rifampicin, pyrazinamide and ethambutol. Unlike pulmonary TB, the treatment for bone and joint disease is a lengthier process, often requiring twelve to eighteen months of chemotherapy. Surgical management options include debridement, synovectomy, arthrodesis and amputation, and success has been shown with primary joint arthroplasty (Leclere et al., 2009).

Yadav et al. (2015) reported a successful single-stage total knee arthroplasty (TKA) using posterior stabilizing implant during early stages of infection, where the patient is disease-free after one year of chemotherapy (Yadav et al., 2015). Habaxi et al. (2014) reported 10 successes of TKA inactive tuberculosis of the knee where at 2 years there is no dislocation, aseptic loosening of fracture of a prosthesis with one case having a recurrence of knee TB (Habaxi et al., 2014).

It is possible to do TKA in an active TB infection primarily due to inability of *Mycobacterium* to form a biofilm. *Mycobacterium* aggregates but showed an inability to adhere to a surface (Adetunji et al., 2014). In our patient, she completed anti-TB therapy for one year but her MRI finding still showed evidence of active infection, increasing the suspicion of resistant TB. Latest culture result showed active TB infection and no evidence of resistant TB. In this patient, it is safe to prolong anti-TB treatment until the ESR level is below 40 mm/h before implanting total knee replacement (Habaxi et al., 2014).

CONCLUSION

Knee TB is a rare disease, and a high index of suspicion is needed to diagnose the disease. Its latency and dormant nature render it difficult to diagnose. For now, this patient is planned for TKA to restore her joint mobility and function of life.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

CONSENTS

Written informed consent was obtained from the patient to publish the case with its related pictures. A copy of the written consent is available for review by the Chief Editor.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the patient for her permission to use her clinical history and findings.

REFERENCES

- Adetunji, V., Kehinde, A., Bolatito, O., & Chen, J. (2014). Biofilms formed by *Mycobacterium tuberculosis* on cement, ceramic, and stainless steel surfaces and their controls. *Journal of Food Protection*, 77 (4), 599 – 604. <https://doi.org/10.4315/0362-028XJFP-13-232>
- Al-Ghafli, H., Varghese, B., Enani, M., Alrajhi, A., Al Johani, S., Albarrak, A., Althawadi, S., Elkizzi, N., & Al Hajoj, S. (2019). Demographic risk factors for extra-pulmonary tuberculosis among adolescents and adults in Saudi Arabia. *PloS One*, 14 (3), e0213846. <https://doi.org/10.1371/journal.pone.0213846>
- Bae, K. M., Lim, S., Kim, H. H., Lee, W. J., Yun, N. R., Kim, C., & Kim, D. (2015). The relevance of biopsy in tuberculosis patients without human immunodeficiency virus infection. *The American Journal of Tropical Medicine and Hygiene*, 92 (3), 636 – 640. <https://doi.org/10.4269/ajtmh.14-0656>
- Dhillon, M. S., Agashe, V., & Patil, S. D. (2017). Role of surgery in management of osteo-articular tuberculosis of the foot and ankle. *The Open Orthopaedics Journal*, 11 (Suppl-4, M4), 633 – 650. <https://doi.org/10.2174/1874325001711010633>
- Habaxi, K. K., Wang, L., Miao, X. G., Alimasi, W. Q. K., Zhao, X. B., Su, J. G., & Yuan, H. (2014). Total knee arthroplasty treatment of active tuberculosis of the knee: A review of 10 cases. *European Review for Medical and Pharmacological Sciences*, 18 (23), 3587 – 3592. PMID: 25535127
- Hunter, R. L. (2018). The pathogenesis of tuberculosis: The early infiltrate of post-primary (adult pulmonary) tuberculosis: A Distinct Disease Entity. *Frontiers in Immunology*, 9. <https://doi.org/10.3389/fimmu.2018.02108>
- Jetley, S., Jairajpuri, Z. S., Pujani, M., & Khan, S. (2017). Tuberculosis 'The Great Imitator': A usual disease with unusual presentations. *Indian Journal of Tuberculosis*, 64, 54 – 59. <https://doi.org/10.1016/j.ijtb.2016.01.001>
- Kivihya-Ndugga, L., van Cleeff, M., Juma, E., Kimwomi, J., Githui, W., Oskam, L., Schuitema, A., van Soolingen, D., Nganga, L., Kibuga, D., Odhiambo, J., & Klatser, P. (2004). Comparison of PCR with the routine procedure for diagnosis of tuberculosis in a population with high prevalences of tuberculosis and human immunodeficiency virus. *Journal of Clinical Microbiology*, 42 (3), 1012 – 1015. <https://doi.org/10.1128/jcm.42.3.1012-1015.2004>
- Leclere, L. E., Sechriest, V. F. 2nd, Holley, K. G., & Tsukayama, D. T. (2009). Tuberculous arthritis of the knee treated with two-stage total knee arthroplasty. A case report. *The Journal of Bone and Joint Surgery*, 91 (1), 186 – 191. <https://doi.org/10.2106/JBJS.G.01421>
- Nguyen, T., Hung, K., Duong, T. B., & Binh, T. P. (2020). Case report tuberculous arthritis of the knee with rice body formation: A report of a rare case. *Case Reports in Orthopedics*, Article ID: 6369781. <https://doi.org/10.1155/2020/6369781>
- Pandita, A., Madhuripan, N., Pandita, S., & Hurtado, R. M. (2020). Challenges and controversies in the treatment of spinal tuberculosis. *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*, 19, 100151. <https://doi.org/10.1016/j.jctube.2020.100151>
- Pang, Y., An, J., Shu, W., Huo, F., Chu, N., Gao, M., Qin, S., Huang, H., Chen, X., & Xu, S. (2019). Epidemiology of extrapulmonary tuberculosis among inpatients, China, 2008-2017. *Emerging Infectious Diseases*, 25 (3), 457 – 464. <https://doi.org/10.3201/eid2503.180572>

- Pigrau-Serrallach, C., & Rodríguez-Pardo, D. (2013). Bone and joint tuberculosis. *European Spine Journal*, 22 (Suppl 4), 556 – 566. <https://doi.org/10.1007/s00586-012-2331-y>
- Procopie, I., Popescu, E. L., Huplea, V., Pleșea, R. M., Ghelase, Ș. M., Stoica, G. A., Mureșan, R. F., Onțică, V., Pleșea, I. E., & Anușca, D. N. (2017). Osteoarticular tuberculosis – brief review of clinical morphological and therapeutic profiles. *Current Health Sciences Journal*, 43 (3), 171 – 190. <https://doi.org/10.12865/CHSJ.43.03.01>
- Qian, Y., Han, Q., Liu, W., Yuan, W. E., & Fan, C. (2018). Characteristics and management of bone and joint tuberculosis in native and migrant population in Shanghai during 2011 to 2015. *BMC Infectious Diseases*, 18 (1), 543. <https://doi.org/10.1186/s12879-018-3456-3>
- Rodríguez-Takeuchi, S. Y., Renjifo, M. E., & Medina, F. J. (2019). Extrapulmonary tuberculosis: Pathophysiology and imaging findings. *RadioGraphics*, 39 (7), 2023 – 2037. <https://doi.org/10.1148/rg.2019190109>
- Vanhoenacker, F. M., Sanghvi, D. A., & De Backer, A. I., (2009). Imaging features of extraaxial musculoskeletal tuberculosis. *Indian Journal of Radiology and Imaging*, 19 (3), 176 – 186. <https://doi.org/10.4103/0971-3026.54873>
- Yadav, S., Yadav, C. S., Kumar, N., & Kumar, A. (2015). Total knee arthroplasty in a case of tuberculosis knee in healing stage: Is it safe? *Journal of Postgraduate Medicine, Education and Research*, 49 (3), 139 – 142. <https://doi.org/10.5005/jp-journals-10028-1163>

