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Case Report

Knee tuberculosis: an overlooked clinical entity

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Abstract

Introduction: The most common anatomic sites affected by extrapulmonary tuberculosis are lymph nodes, pleura, bones, and joints, urogenital tract, and meninges. Tuberculous arthritis is difficult to diagnose early because of its atypical insidious clinical manifestations and non-specific imaging findings.

Case report: A 59-year-old male presented with progressive swelling in his left knee for over two months. The patient was initially misdiagnosed with pigmented villonodular synovitis (PVNS) and had undergone total knee arthroplasty (TKA) two years ago, however, the TKA did not completely alleviate his symptoms. Comprehensive radiological and laboratory assessments, including X-rays, magnetic resonance imaging and computed tomography scans, and an interferon-γ release assay (IGRA), pointed towards a diagnosis of tuberculous knee arthritis. Definitive diagnosis was established through the detection of *Mycobacterium tuberculosis* (MTB) DNA in the synovial fluid via polymerase chain reaction (PCR) and a positive IGRA result.

Conclusions: The case underscores the importance of considering MTB infection in the differential diagnosis of chronic unilateral knee arthritis, especially given the atypical clinical manifestations and imaging findings that can mimic other conditions like PVNS.

Key words: knee; tuberculosis; pigmented villonodular synovitis; polymerase chain reaction.

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Introduction

Extra-pulmonary tuberculosis accounts for more than a third of all tuberculosis cases in China [1]. Skeletal tuberculosis manifestation contributed almost a third of the total extra-pulmonary symptoms [2]. Tuberculosis of the knee is the third most common site of skeletal tuberculosis after the spine and hip [3,4]. Extra-pulmonary tuberculosis has been recognized as a disease with many mimicry clinical manifestations that often lead to being misdiagnosed [5].

Tuberculous arthritis is often manifested as bacterial septic arthritis, crystal arthropathy, systemic rheumatic disease (such as rheumatoid arthritis), osteoarthritis, and malignancy [6]. Poncet disease, a reactive polyarthritis associated with extra-articular tuberculosis disease, should also be considered if several joints are involved and the patient has evidence of nonerosive arthritis [7]. Tuberculous arthritis can cause synovitis and joint destruction. Synovial thickening, joint effusions, juxta-articular osteopenia, peripheral osseous erosions, and gradual joint space narrowing on magnetic resonance imaging (MRI) or computed tomography (CT) are suggestive of joint tuberculosis [8].

Tuberculous arthritis of the knee joint may mimic pigmented villonodular synovitis (PVNS) [4]. PVNS is a benign proliferative disorder that affects synovial lined joints, bursa, and tendon sheaths. PVNS can also result in synovial hyperplasia and joint destruction [9,10]. Both tuberculous arthritis and PVNS in the knee joint of young, otherwise healthy-appearing individuals may present as monoarticular involvement with painful swelling of extended duration and limited motion [4]. In addition, both conditions can show synovial proliferation, reactive bone marrow edema, and cortical erosion on MRI [11]. It is to be noted that the mainstays of treatment for tuberculous arthritis and PVNS are totally different, since the treatment of tuberculous arthritis is mainly conservative rather than complete surgical resection of the diseased tissue as in PVNS. The present study describes a patient with tuberculosis of the knee, in whom the diagnosis was delayed because of lack of familiarity with the disease.

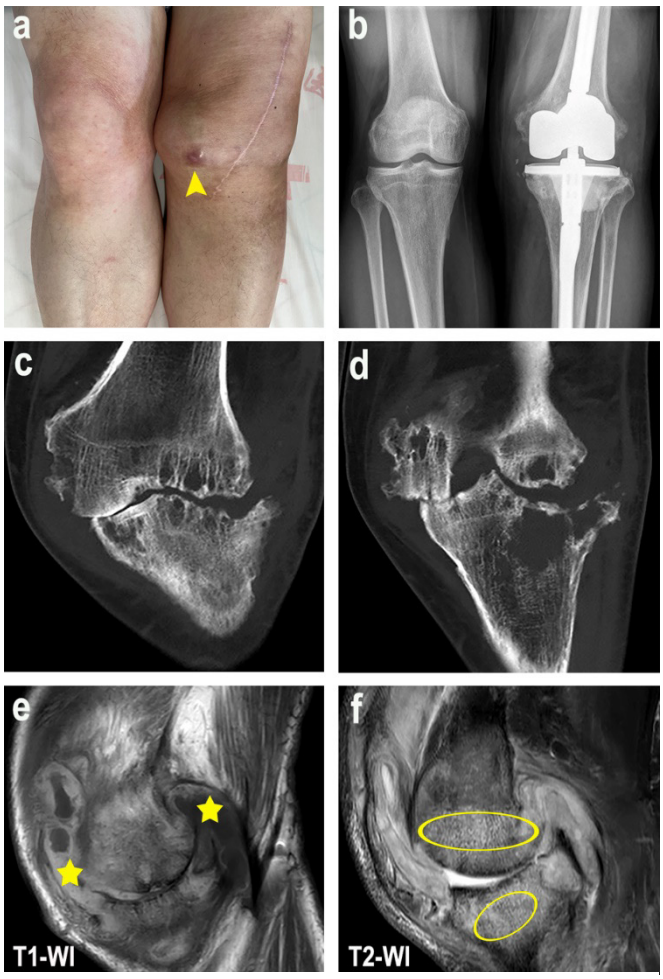
Case Report

A 59-year-old male patient presented with progressive swelling in his left knee joint for over two months. He was usually in good health. He neither drank nor smoked. Before this admission, he had taken levofloxacin orally for one week. Initial examination revealed moderate swelling of the left knee joint, with mild heating, but with no definite redness (Figure 1a). He had no cough, fever, night sweats or lower back pain. Complete blood count, liver function tests, antinuclear antibody, rheumatoid factor, anti-citrullinated peptide antibody; and tests for syphilis, human immunodeficiency virus, human cytomegalovirus, and Epstein-Barr virus were all normal. The HLA-B27 was negative. His erythrocyte sedimentation rate (ESR) level was normal, but high sensitive C-reactive protein (hs-CRP) and serum amyloid a protein (SAAP) were slightly elevated (hs-CRP 4.65 mg/L, reference range < 3 mg/L; SAAP 15.7 mg/L, reference range < 10 mg/L). The interferon-γ release assay (IGRA) specific for the *Mycobacterium tuberculosis* (MTB) was positive (2.66 IU/mL, reference range < 0.35 IU/mL). The diagnostic arthrocentesis revealed light bloody colored synovial fluid containing 10.9×10^9/L leukocyte cells, with 86% being neutrophil cells. Sodium urate crystal was not detected.

Sixteen years ago, he was diagnosed as having PVNS based on the intermittent swelling of left knee and synovial hyperplasia detected by MRI. Two years ago, he underwent total knee arthroplasty (TKA). This provided major improvement in symptoms but arthritic symptoms did not subside completely.

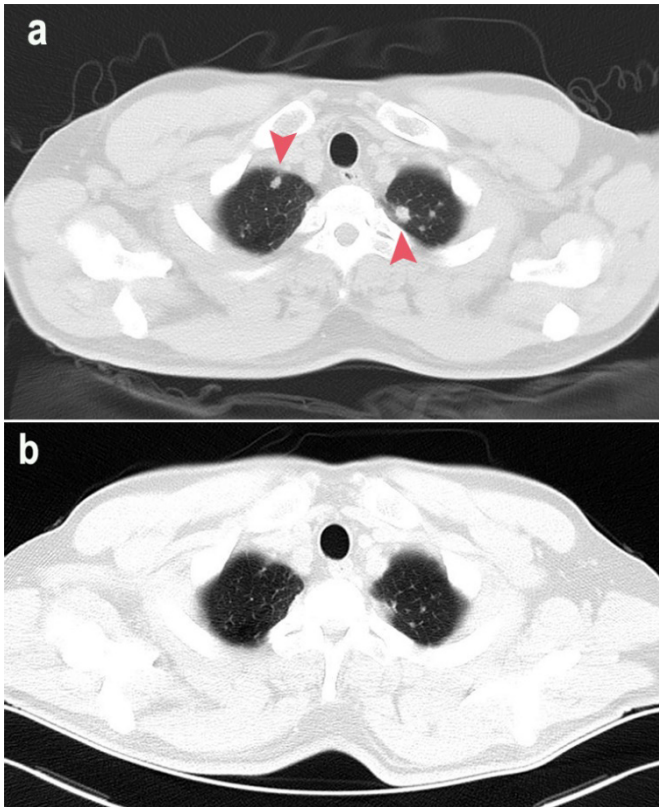
We carefully and comprehensively reviewed his radiologic images. Post-TKA X-ray showed periarticular osteopenia and cortical erosions in distal femur and tibial plateau of the left knee joint (Figure 1b). Prior to the arthroplasty, the CT showed massive bone destruction and disappearance of the medial space in the left knee joint (Figure 1c-d), and MRI showed evident synovial hyperplasia on T1-weighted sequence and bone marrow edema on T2-weighted fat saturation

Figure 1. Appearance, X-ray, computed tomography (CT), and magnetic resonance image (MRI) of the knee.



(a) sinus tract formation (arrow); **(b)** postoperative X-ray; **(c-d)** CT; **(e-f)** T1-weighted MRI sequence showing evident synovial hyperplasia (asterisk) and T2-weighted fat saturation sequence showing bone marrow edema (circle) prior to the arthroplasty.

Figure 2. Chest computed tomography **(a)** prior to knee arthroplasty; pulmonary nodules in both lungs (arrowheads); **(b)** after admission: one week after treatment with levofloxacin.

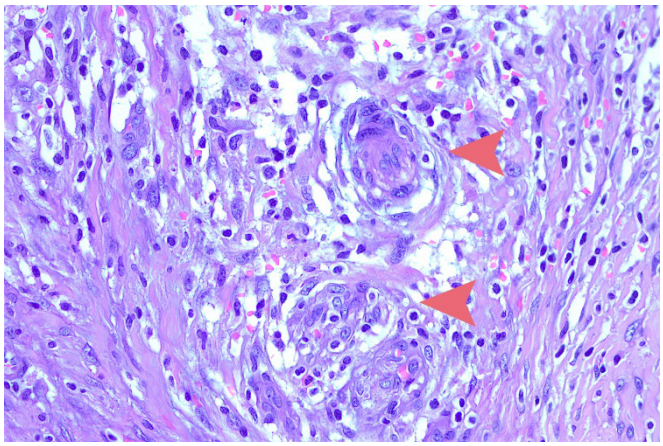


sequence (Figure 1e-f). It is to be noted that specific manifestations of PVNS, including multiple nodular mass, especially in the posterior joint space and low signal intensity indicating hemosiderin deposits, were not observed on the MRI. Perioperative chest CT showed multiple pulmonary nodules in the bilateral apex of lung (Figure 2a); and interestingly, the chest CT taken after this admission showed that they significantly reduced in size (Figure 2b).

The results of the patient's high sensitivity to levofloxacin and positive IGRA strongly suggested a diagnosis of tuberculous knee arthritis. We further reviewed the postoperative histopathologic images. The inflamed synovial specimen showed epithelioid histiocytosis, multinuclear giant cell reaction, and granulomatous nodules formation. However, the caseating necrosis caused by the MTB infection was not observed (Figure 3c). In addition, villiform synovial proliferation, or pigmented multinucleated giant cells with hemosiderin-laden macrophages, were not observed either (Figure 3c).

Nevertheless, diagnostic arthrocentesis was done twice on different days. The synovial fluid was repeatedly sent for bacterial culture and quantitative fluorescence polymerase chain reaction (PCR) tests. The PCR confirmed presence of MTB DNA in two samples of synovial fluid (Figure 4). Meanwhile, the gene sequence of MTB from another sample of synovial fluid was also detected by next-generation sequencing (NGS). The diagnosis of tuberculous knee arthritis was finally made based on the results of PCR and positive IGRA. Pending culture results, quadruple anti-tuberculosis treatment was initially prescribed. One of the three samples of synovial fluid cultured eventually tested positive for MTB. This result further supported the diagnosis of tuberculous knee arthritis. The patient completed a six-month course of anti-tuberculous treatment without any complications; and during the last follow-up, he had no swelling in his left knee.

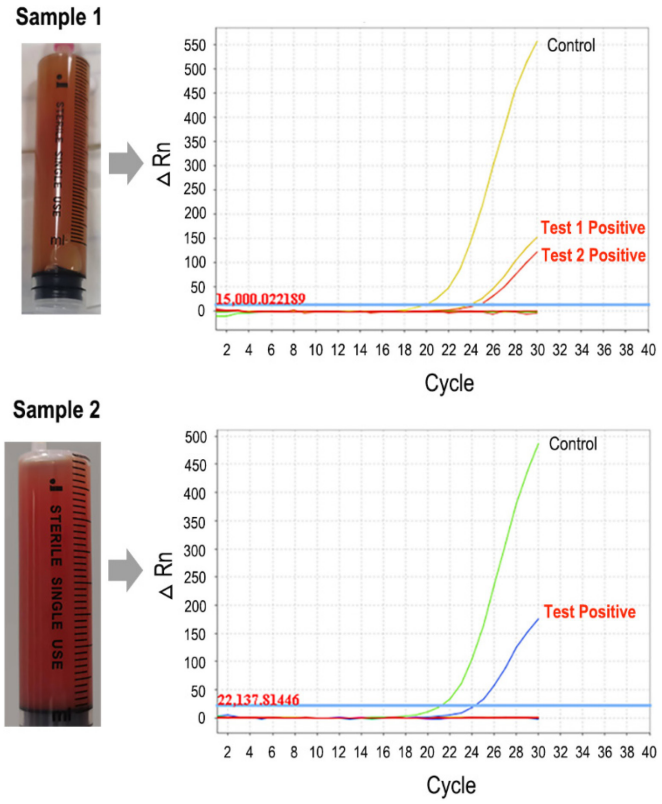
Figure 3. Pathological analysis: granulomatous nodules formation (arrowheads).



Discussion

We have described a case of tuberculosis affecting the lung and the left knee. PVNS complicated the diagnosis of tuberculous arthritis. The primary lesson from the present case report is that the physicians did not take MTB infection into consideration when confronted with a patient presenting with chronic unilateral knee arthritis of unknown origin. There were several reasons accounting for the misdiagnosis of MTB infection. First, tuberculous arthritis in an immunocompetent patient is especially rare. Second, knee joint involvement is a relatively rare manifestation of extrapulmonary tuberculosis [4,12]. Third, tuberculous arthritis has atypical insidious clinical manifestations and non-specific imaging findings [13]. The clinical and radiologic findings in joint tuberculosis and PVNS are occasionally similar [4]. Fourth, the

Figure 4. Quantitative fluorescence polymerase chain reaction (PCR).



Samples 1 and 2 are synovial fluid obtained on different days. The horizontal axis represents the amplification cycles, and the vertical axis represents the intensity of fluorescence.

pathological results of some cases had no caseous necrosis.

MRI results indicated that both tuberculous arthritis and PVNS can show synovial proliferation and cortical erosion. However, PVNS is characterized by extra-articular spread of nodular masses into the popliteus tendon sheath and the posterior aspect of the posterior cruciate ligament [14]. Clumps of hemosiderin deposits showed a low signal intensity on T1 and T2 weighted images, which was the most indicative feature of PVNS. The hemosiderin deposits were not observed in the MRI of the present case.

A definitive diagnosis of MTB was made by positive culture results. Confirmation of MTB by positive culture often takes 3-6 weeks, while the MTB PCR testing can help to speed up the decision-making process involved in the diagnosis of tuberculosis [15,16]. The sensitivity ranged between 42% and 93% in culture positive specimens [16,17]. Li *et al.* reported that the sensitivity of PCR applied to synovial fluid was 57.7%, which is lower than the sensitivity for sputum (81.0%) or pleural fluid (64.2%) samples [18]. In the present case, MTB derived from the synovial fluid was detected by PCR.

The role of surgery in treating tuberculous arthritis is still somewhat controversial. As mentioned before, the treatment of tuberculous arthritis is mainly conservative. The present case underwent TKA probably due to being misdiagnosed with PVNS. Arthroscopy is increasingly used for diagnostic and surgical management of tuberculous arthritis [4]. Surgical removal of the involved joint, which is followed by post-operative anti-tuberculous therapy, provide positive outcomes in patients with knee tuberculosis [19]. TKA is considered as the primary treatment of knee tuberculosis with a lower rate of recurrence [8,19]. However, the consensus about surgical timing, prosthesis selection, and timing for starting anti-tubercular therapy has not been established yet [19].

Conclusions

The objective of this case was to emphasize the importance of early diagnosis of tuberculous arthritis, so that treatment can be implemented in order to avoid progressive destruction of the joint. Rheumatologists should pay close attention to clinical suspicion of tuberculous arthritis in the differential diagnosis of monoarthritis. In addition, PCR analysis of the synovial fluid may help speed up the diagnosis.

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Informed consent

Informed consent was obtained from the patient.

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