










Case Report

## Osteoarticular Tuberculosis Mimicking Ewing's Sarcoma in an Infant

### *Ewing Sarkomunu Taklit Eden Osteoartiküler Tüberküloz Tanılı İnfant*

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#### ABSTRACT

Osteoarticular tuberculosis (TB) of the bone is a rare form of TB, accounting for 1-5% of all extra-pulmonary TB cases worldwide. An otherwise healthy 11-month-old girl complained of swelling on her right wrist and avoidance of using it. She had no history of trauma, fever, weight loss, or other systemic symptoms. A mass on the dorsolateral side of the right wrist, measuring about 4x5cm, was found. In magnetic resonance imaging results, it was reported that there was a mass lesion of lytic character (Ewing's sarcoma) with periost reaction. Excisional biopsy was performed; non-necrotizing granuloma was found. Mycobacteriological culture could not be performed since the tissue specimen was formalin-fixed and paraffin-embedded. The biopsy material obtained from the bone has no fresh tissue; the M. TB complex was determined upon mycobacteriological molecular examination of the tissue specimen on the waxed block. Therapy lasted for nine months. TB of the bone should be among the differential diagnoses even in the absence of pulmonary involvement and constitutional symptoms of TB. For diagnosis, it is essential to culture for the mycobacterial subtype by tissue biopsy and confirms the culture material by PCR.

**Keywords:** Bone tumor, mycobacterium tuberculosis complex, pcr, paraffin-embedded

#### ÖZET

Kemiğin osteoartiküler tüberkülozu (TB), dünyadaki tüm akciğer dışı TB vakalarının %1-5'ini oluşturur ve özellikle pediatrik vakalarda, nadir görülen bir TB formudur. 11 aylık bir kız olgu sağ el bileğinde şüpheli kırık öyküsü nedeniyle dış merkezden sevk edildi. Hastanın sağ el bileğinde şişlik ve sağ ön kol ve elini kullanmaktan kaçınma mevcuttu. Travma, ateş, kilo kaybı öyküsü yoktu. Olgunun fizik bakışında sağ el bileği dorsolateralinde yaklaşık 4x5cm boyutlarında kitle saptandı. Diğer sistem bakışı olağandı. Laboratuvar testinde lökosit sayısı 9600 hücre/mm<sup>3</sup>, hemoglobin düzeyi 9,6 gr/dL, trombosit sayısı 396 000 hücre/mm<sup>3</sup>, C-reaktif protein 4,3 mg/L, eritrosit sedimentasyon hızı (ESH) 45 mm/saat saptandı. Manyetik rezonans görüntüleme sonucunda; kemikte belirgin genişlemeye neden olan periost reaksiyonlu litik karakterde kitle lezyonu (Ewing sarkomu) olduğu bildirildi. Yapılan eksizyonel biyopsi sonucunda; nekrotizan olmayan granülom

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bulundu. Doku örneği formalinle fikse ve parafine gömüldüğü için mikobakteriyolojik kültür yapılamadı. Kemikten alınan biyopsi materyalinde taze doku olmadığı için parafinli blok üzerindeki doku örneğinin mikobakteriyolojik moleküler incelemesi sonucunda *M. tuberculosis* kompleksi belirlendi. Akciğer grafisi normaldi. Osteoartiküler tüberküloz tanısı için izoniazid, rifampin, pirazinamid ve etambutol ile tedavileri başlandı. Kemik TB'ü, özellikle TB'un endemik olduğu ülkelerde, akciğer tutulumu ve TB'un yapısal semptomları olmasa bile ayırıcı tanılar arasında yer almalıdır. Tanı için doku biyopsisi ile mikobakteriyel alt tip için kültür yapmak ve kültür materyalini moleküler yöntemlerle doğrulamak çok önemlidir.

**Keywords:** Kemik tümörü, *mycobacterium tuberculosis* kompleksi, PCR, parafine gömülü

## INTRODUCTION

Tuberculosis (TB) is a disease caused by *Mycobacterium tuberculosis* complex bacillus and is often transmitted through inhalation. All tissues can be affected, but organ involvement is usually divided as pulmonary (85-90%) and extra-pulmonary disease (10-15%) (1).

Osteoarticular TB of the bone is an infrequent form, which accounts for approximately 1-5% of all extra-pulmonary TB cases worldwide, especially in pediatric cases (1,2). It may affect any joints but most commonly affect the spine (Pott's disease), weight-bearing joints and characteristically monoarticular (1). The symptoms and clinical manifestations mimic other conditions, such as bone tumors. Hence, careful diagnosis is required. Herein we presented an 11-month old case that demonstrated that clinicians should pay particular attention to the possibility of TB as the cause of monoarthritis even when pulmonary involvement is not documented.

## Case Report

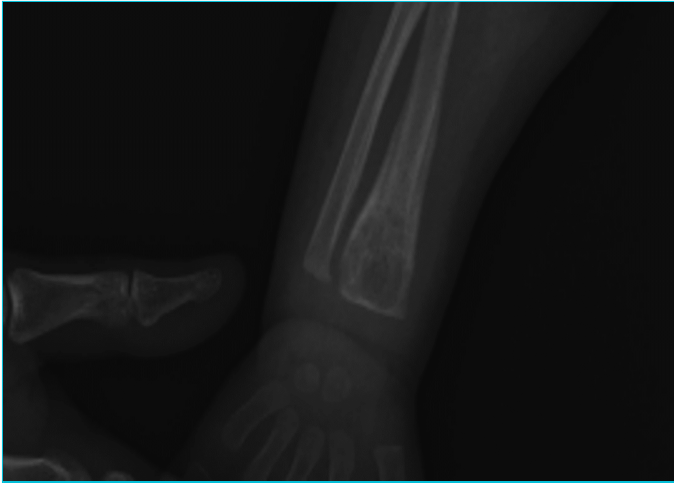
An otherwise healthy 11-month-old girl was referred from an external center with a suspect bone fracture on her right wrist. The patient complained of swelling on the right wrist and avoidance of using it. After two weeks, a lump on her right wrist was getting bigger. She had no history of trauma, fever, weight loss, or other systemic symptoms. In family history, two uncles of her mother and one of her aunts had a history of TB many years ago. The patient showed good general condition and vital signs within the normal limit on physical examination. We found a mass on the dorsolateral side of the right wrist, measuring about 4x5cm. The mass was supple, well bordered, the same color as the

patient's skin, and tender. The range of motion of the right wrist was limited. The remaining findings of the examination were normal.

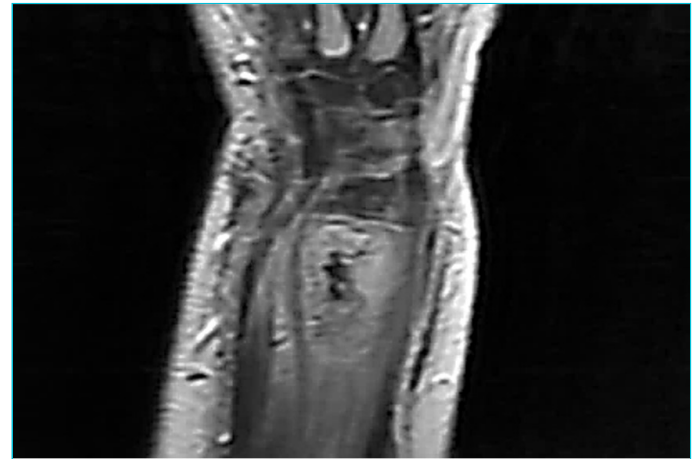


**Figure 1.** Slightly hyperemic 4x5 cm swelling on the right forearm near the patient's wrist.

The laboratory test revealed a leukocyte count of 9600 cells/mm<sup>3</sup>, a hemoglobin level of 9.6 gr/dL, platelet count of 396 000 cells/mm<sup>3</sup>, C-reactive protein was 4.3 mg/L, erythrocyte sedimentation rate (ESR) was elevated 45 mm/hour. Anti-HIV, hepatitis B and C, Brucella and Salmonella serologies were all negative. In magnetic resonance imaging result, it was reported that there was a mass lesion (Ewing's Sarcoma?) of lytic character with periost reaction causing noticeable expansion on the bone at right radius distal thought to present malign characteristics.



**Figure 2.** A lytic mass lesion with periosteal reaction was found on the X-ray in the distal right radius.



**Figure 3.** View of the right forearm in the second week of treatment.

Upon the excisional biopsy performed on the case, mostly CD3, partially CD20 positive lymphocytes, CD38 positive plasma cells and CD68 positive histiocytes partly forming non-necrotizing granuloma and capillary proliferation were found; no malignant cells could be observed, and granulomatous inflammation was considered according to these findings. It was learnt that no bacillus was present in the acid-resistant staining (ARS) performed on the tissue. The patient was then referred to our clinic for revealed the etiology of granulomatous inflammation on the wrist. Since the biopsy material obtained from the bone has no fresh tissue, the *M. TB complex* was determined upon mycobacteriology molecular examination of the tissue specimen on the waxed block (Xpert MTB/RIF ultra-real-time PCR system). Mycobacteriological culture could not be performed since the tissue specimen was formalin-fixed and paraffin-embedded. The size of induration was 7 mm in the tuberculin skin test performed. No bacillus was determined in fasting gastric fluids obtained from the case in the ARS performed. TB PCR was negative and no mycobacteriology culture reproduction was determined. Chest radiography was normal. The lymphocyte panel was normal. There was no genetic predisposition to mycobacterial infection from the resulting genetic panel. Therapy was initiated with isoniazid, rifampin, pyrazinamide, and ethambutol to diagnose osteoarticular TB. Ethambutol was stopped after two months and the treatments lasted for nine months. A significant regression in the bone lesions was observed during the 9-month follow-up. The consent of the patient's parents was obtained for this study.

## DISCUSSION

Osteoarticular TB in children usually manifests as chronic progressive monoarthritis, often affecting large joints, such as the spine and weight-bearing joints; the wrist is less commonly affected (1). Poor socioeconomic conditions are an important risk factor (3). TB may destroy any tissue and lead to extensive loss of joint function. In children, this can be catastrophic because of the growing articular cartilage, leading to progressive deformities. As in our patient, some cases have been misdiagnosed due to ignorance, insidious and nonspecific clinical symptoms, and uncharacteristic imaging findings. Therefore, it is crucial not to delay diagnosis, especially in endemic regions.

Children with osteoarticular TB usually had contact with a patient with TB in the past. In some studies, it was found that there was contact with a patient with TB in 25% to 36% of cases (1,4). In our case, three close relatives had a history of pulmonary TB disease before the patient was born.

In the literature, wrist involvement has been reported in up to 10% of patients with osteoarticular TB (4). A common feature of TB of the wrist is a delay in diagnosis and the persistence of stiffness and pain after treatment (5). Involvement of other organs, especially the lungs, may be detected at the time of diagnosis. In our patient, no organ involvement was detected other than the wrist. In a study with osteoarticular TB, almost 30% of patients had TB in other body parts (4).

Although it is challenging to detect the tubercle bacillus in culture, the definitive diagnosis of osteoarticular TB is generally made by culture of the tubercle bacillus from body fluids and biopsy material. Because of the paraffin-embedded tissue sample, we were unable

to detect the tubercle bacillus in culture, but we were able to detect the tubercle bacillus by real-time PCR. There are studies demonstrating the diagnostic effect of real-time PCR in osteoarticular TB (6,7). Sharma et al. (6) studied 80 patients with suspected osteoarticular TB. They found that real-time PCR for TB was positive in 66 (82.5%) of the 80 patients, while culture was positive in three patients and microscopy in one patient. Another study also supports that all patients with joint and bone TB had positive real-time PCR results for the diagnosis of TB (7).

In younger children, cases of vaccine-associated TB have been reported in populations vaccinated with bacillus Calmette-Guerin (BCG) (8). Between 1998 and 2014, 71 cases of osteomyelitis associated with *M. bovis* were reported in Taiwan (8). Symptoms of these cases generally began seven to 14 months after vaccination, and 81% of cases involved the extremities. The positivity rate of culture for *M. bovis* was 70%, and the positivity rate of the real-time PCR test was 93.3%. Montagnan et al. (9) reported the case of a 2-year-old who presented with swelling of the left knee. Polymerase chain reaction and culture were used to detect *M. TB* complex in the surgical specimen. The child had no relatives with a history of TB. Molecular tests performed on the specimen using primers for *M. bovis* were positive. Although our patient's close relatives had a history of TB due to *M. tuberculosis*, there was also a possibility of TB due to *M. bovis*. Because the tissue sample was formalin-fixed and paraffin-embedded, a biopsy sample could not be valuable for *M. bovis* in this regard. In our center, there was no specific PCR kit for *M. bovis*, so PCR could not differentiate between *M. TB* and *M. bovis*.

Osteoarticular TB has many common clinical and radiological features that mimic Ewing's sarcoma, Langerhans cell histiocytosis, infections, such as fungi, brucellosis, and sarcoidosis (1,10). Typical radiographic findings of TB osteomyelitis, usually not found in pyogenic osteomyelitis, including translucent components, infiltration, and focal erosions. In TB osteomyelitis, sclerosis is absent and there are fewer sequestrum and periosteal reactions (11). In our patient's MRI findings, the mass showed radiological lytic features and extension with periosteal reaction. It was suspected to be Ewing's sarcoma, after which an excisional biopsy was performed and revealed a non-necrotizing granuloma.

In conclusion, TB of the bone should be among the differential diagnoses, especially in countries where TB is endemic, even in the absence of pulmonary involvement and constitutional symptoms of TB. For diagnosis, it is critical to culture for the mycobacterial subtype by tissue biopsy and confirms the culture material by PCR.

#### Conflict of Interest / Çıkar Çatışması

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