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# Tuberculous bursitis of the wrist after anti-TNFalpha treatment: a case report

**Case Report**

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**Abstract:** In this report, we describe a case of tuberculous bursitis-osteomyelitis of the wrist, in an elderly patient with rheumatoid arthritis and anti-TNFalpha (anti-Tumor Necrosis Factor alpha) treatment.

**Keywords:** *Tuberculous • Bursitis • Tumor necrosis factor*



## Abbreviations

BCG - Bacille Calmette-Guerin
HIV - Human Immunodeficiency Virus
HRCT - High Resolution Computing Tomography
LTBI - Latent Tuberculosis Infection
MRI - Magnetic Resonance Imaging
PCR - Polymerase Chain Reaction
TNF - Tumor Necrosis Factor
TST - Tuberculin Skin Test

## 1. Introduction

TNFalpha is an essential cytokine in the control and containment of intracellular pathogens. It stimulates the formation and maintenance of granulomas that physically contain infection. The introduction of the anti-TNFalpha agents into clinical practice has been associated with increased incidence of infections, especially mycobacterial infections and those involving other intracellular pathogens [1]. We present a case of isolated tuberculous bursitis-osteomyelitis of the wrist, in an elderly patient with rheumatoid arthritis, treated with anti-TNFalpha agents.

## 2. Case Report

A seventy- four year old man presented to our hospital with a soft tissue mass in the dorsal aspect of the right wrist, which had been gradually increasing over the course of four months. He did not mention any recent trauma in the region. The patient had a past medical history of rheumatoid arthritis and was treated with methotrexate 10mg/week, methylprednisolone 4 mg/day, Etanrecept 50mg/week for 1 year and after interruption of Etanrecept he continued with Adalimumab 80mg/week for the last two months. Before the anti-TNFalpha treatment a tuberculin skin test (TST) was negative and chest-x-ray was normal. There was no overt tuberculosis in his medical or family history.

Upon physical examination of the patient, there was a soft tissue mass in the dorsal aspect of the right wrist, (Figure 1) .The range of motion of this right wrist was limited and no neurological deficit was observed. Fever had never been reported. The serum C-reactive protein levels were 8.81mg/dl (normal range from 0-5mg/dl), but all other laboratory findings were normal, while tuberculin skin test was positive with 17 mm-induration, and the interferon gamma release assay-QuantiFERON-Tb-Gold (QFT-G, Cellestis Limited, Carnegie, Victoria,

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**Figure 1.** Enlarged bursa in the dorsal aspect of patient right wrist.

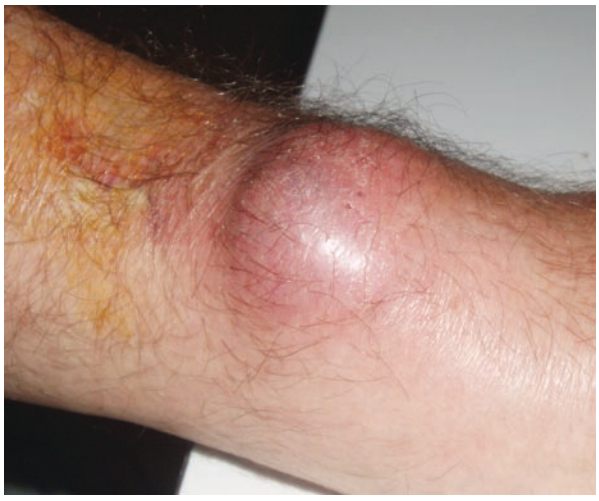
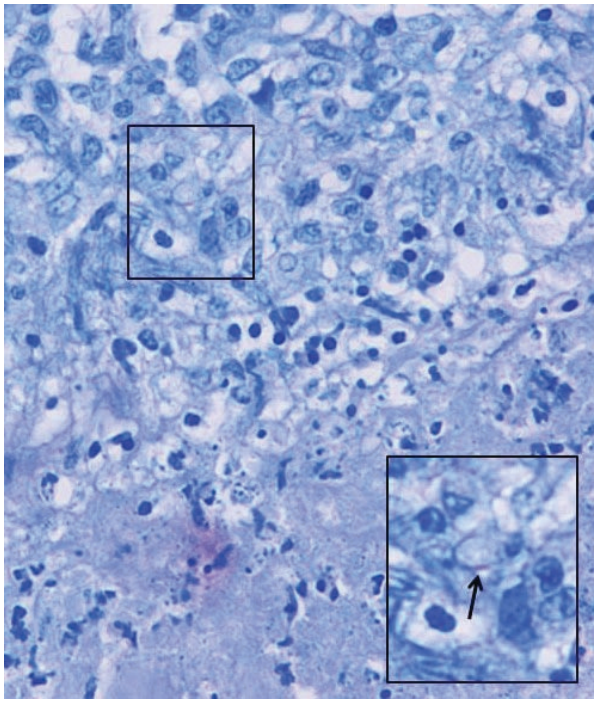


**Figure 2.** Mycobacterium tuberculosis bacterium (arrow). Acid-fast Ziehl-Neelsen stain: magnification X 400.



Australia) was positive for Mycobacterium tuberculosis infection. Needle aspiration of the mass revealed high viscosity fluid with extremely low level of glucose 1mg/dl, without crystals of uric acid, Gram-stain and culture were negative, Ziehl-Neelsen, PCR (Polymerase Chain Reaction) and culture for mycobacterium tuberculosis were negative, while it was not possible to count cells. Examination for hepatitis B, C and HIV were negative. MRI (Magnetic Resonance Imaging) of the right wrist revealed abscess in the left site of ulnae and pathological density signal was detected furthermore in distal part of ulnae and metacarpal bones, which was compatible with osteomyelitis. Chest HRCT (HRCT: High Resolution Computing Tomography) was negative for active pulmonary infection; the culture from sputum was negative for Mycobacterium tuberculosis, just us the PCR from gastric fluids. Surgical excision of the lesion was performed, and revealed an enlarged bursa with large amount of necrotic tissue and small fluid collection. Histologically, granulomas with central caseous necrosis were present in the bursa tissue, and Ziehl-Neelsen was positive for mycobacteria (Figure 2). PCR from paraffin embedded-formalin fixed tissue of infected bursa was negative for genetic material both Mycobacterium tuberculosis and nontuberculous mycobacteria.

Our patient was treated with isoniazid (300mg/day), rifampicin (600mg/day), and pyrazinamide (30mg/kg/day). After five months of follow-up, the patient had no major problems and the range of movement in his wrist was almost normal.

## 3. Discussion

Unlike tubercular disease in immunocompetent individuals, tuberculosis infection associated with TNF blockade frequently presents with extrapulmonary manifestations and disseminated disease. The unusual manifestations of tuberculosis in this group of patients may have made the diagnosis uncertain and delays in the diagnosis may have contributed to morbidity and mortality [2].

Our patient had negative TST and normal chest X-ray in his screening for LTBI (Latent Tuberculosis Infection) before the initiation of the anti-TNF, but negative TST results should be interpreted with caution in any patient who is immunosuppressed by drugs or autoimmune disease. Such persons are more likely to have false negative TST results and accordingly, a number of tuberculosis cases have occurred in individuals who had negative TST results before starting anti-TNF therapy [3]. Chest radiographs are not useful in screening for LTBI, as most latently infected individuals have normal chest radiographs [4]. The condition in our patient arose two months after the switch from etanrecept to adalimumab that may suggest reactivation of old infection. Etanrecept sheds approximately 50% of soluble and 90% of transmembrane TNF within 10 minutes of binding, and the incidence of tuberculosis seems to be lower than other anti-TNF agents [5].

Negative PCR for mycobacteria from the infected bursa and positive Ziehl-Neelsen with granuloma formation increase the diagnostic dilemma between Mycobacterium tuberculosis and other nontuberculous

mycobacteria and intracellular pathogens such us Nocardia, especially now that we have reports of increase incidence of nontuberculous mycobacterial infections in patients who receive anti-TNF therapy [6].

Non diagnostic PCR in our case was most likely the result of the use of paraffin and formalin in bursa tissue [7]. The positivity of interferon-gamma release assay which has higher sensitivity than TST in the detection of active disease [8], and the use of synthetic peptides that simulating peptides specific to Mycobacterium tuberculosis which are not shared by BCG vaccine or nontuberculous mycobacteria [9], strongly suggest the Mycobacterium tuberculosis infection in our case. Furthermore after five months follow-up patient had marked clinical and radiological improvement without use of clarithromycin and only with antituberculous treatment.

Tuberculous bursitis is a very rare condition that was reported in only approximately 1% of the cases of musculoskeletal tuberculosis. When present, most frequently it involves the trochanteric and subdeltoid bursa [10]. Rheumatoid arthritis is a common cause of bursitis but in chronic immunosuppressed patients especially if they are treated with anti-TNFalpha the presence of chronic bursitis may suggest mycobacterial disease. The use of CT scan or MRI, coupled with aspiration or biopsy, should lead to early recognition of musculoskeletal tuberculosis.

A successful outcome depends on the use of the optimum regimen of chemotherapy, for adequate period. The time of necessary treatment according to WHO guidelines in rifampicin-based treatment is 6-9 months [11]. Furthermore surgical removal of infected tissue in some cases may be useful to improve the efficacy of chemotherapy.

In conclusion, chronic bursitis in immunosuppressed patients especially if they are treated with anti-TNFa may suggest tuberculosis.

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