



# Tuberculosis Infection in the Upper Limb: Case Series and Review of the Literature

## *Manifestaciones de tuberculosis en el miembro superior: Serie de casos y revisión de la literatura*

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### Abstract

**Objective** To evaluate the outcomes of three cases of patients with history of autoimmune disorders presenting with bone, joint, and synovial involvement due to tuberculosis (TB) in the upper limb.

**Materials and Methods** A retrospective and descriptive case series.

**Results** Patients with clinical signs of infection of insidious course, who did not respond to the broad-spectrum antibiotic treatment or debridement, were diagnosed with osteoarticular TB through tools such as polymerase chain reaction (PCR) testing, and the diagnosis was confirmed through mycobacterial culture. The clinical signs of infection resolved with the tetraconjugate antibiotic therapy for tuberculosis; however, patients with bone involvement presented movement limitation sequelae due to joint destruction.

**Conclusion** Osteomuscular TB in the upper limb is uncommon, and it must be suspected in the presence of local signs of infection in patients with negative cultures for common bacteria that do not respond to antibiotic treatments and repeated local debridements.

### Keywords

- ▶ tuberculosis
- ▶ osteoarticular
- ▶ wrist
- ▶ elbow
- ▶ tenosynovitis

### Resumen

**Objetivo** Evaluar los desenlaces de tres casos de tuberculosis musculoesquelética en el miembro superior en pacientes con antecedentes de enfermedades autoinmunes que presentaban compromiso óseo, articular y sinovial en el miembro superior.

**Materiales y Métodos** Estudio descriptivo y retrospectivo tipo serie de casos.

**Resultados** Pacientes con signos clínicos de infección de curso insidioso, sin respuesta al tratamiento antibiótico de amplio espectro y con pobre respuesta a los desbridamientos quirúrgicos fueron diagnosticados por medio de herramientas como

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la prueba de reacción en cadena de la polimerasa (*polymerase chain reaction*, PCR, en inglés) y recibieron diagnóstico confirmatorio por cultivo de micobacterias. Los signos clínicos de infección resolvieron con la terapia antibiótica tetraconjugada para tuberculosis; sin embargo, los pacientes con compromiso óseo presentaron secuelas de limitación para el movimiento por la destrucción articular.

#### Palabras clave

- ▶ tuberculosis
- ▶ osteoarticular
- ▶ carpo
- ▶ codo
- ▶ tenosinovitis

**Conclusión** La tuberculosis osteomuscular en el miembro superior es infrecuente, y se debe sospechar ante la presencia de signos locales de infección con cultivos negativos para gérmenes comunes que no respondan a tratamientos antibióticos y a desbridamientos locales repetidos, en particular en pacientes con inmunosupresión.

**Nivel de evidencia:** IV

## Introduction

Tuberculosis (TB) is still a common infectious pathology, given that its incidence has been increasing due to different population phenomena such as migration, pharmacological immunosuppression, and its association with infection by the human immunodeficiency virus (HIV). Despite the advances in the pharmacological treatment and strict case monitoring and control measures, extrapulmonary manifestations of the disease are still evident. Osteomuscular involvement due to TB is rare and, if it occurs, it affects load-bearing areas of the axial or appendicular skeleton, such as the vertebrae, knee or hip.<sup>1-3</sup> In particular, TB in the wrist and hand is very unusual, representing 1 to 3% of the cases of musculoskeletal TB. The most common presentation of TB in the hand is tuberculous tenosynovitis.<sup>4</sup> Bone involvement of the carpus or elbow due to TB is rare, and tetraconjugate pharmacological management is still the mainstay of treatment.

## Materials and Methods

We herein present a descriptive observational case series study of three patients with compromised upper limb, hand, wrist, and elbow due to TB. The study was approved by the Research and Ethics Committee of the institution in which it was conducted.

## Description of the Cases

### Case 1

A 72-year-old woman presented with pain, swelling, and warmth in her left wrist. Her medical history included a diagnosis of systemic lupus erythematosus, treated with methotrexate for 5 years, in addition to previous systemic corticosteroid therapy. The physical examination revealed inflammatory changes in the wrist, limited finger flexion, and an area of resistance on the back of the wrist at the level of the fifth and sixth extensor compartments. The initial laboratory tests did not show a significant elevation in acute phase reactants. Further studies, including a simple X-ray, revealed marked soft tissue swelling, diffuse osteopenia with a reduction in the size of the carpal bones, and erosion of the

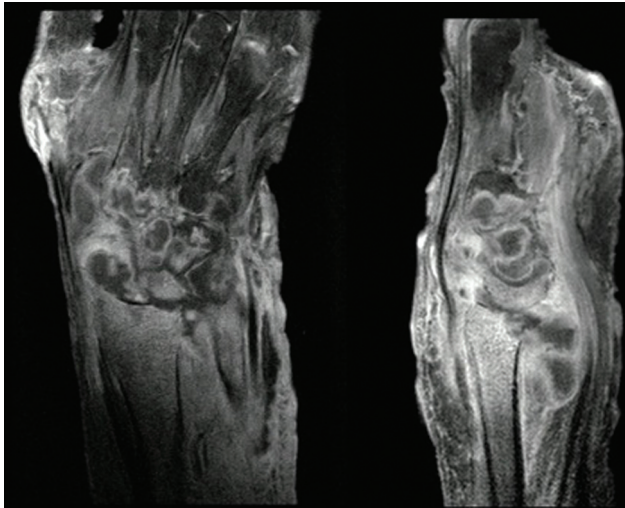
cortical bone in the carpal area and the articular surface of the radius (→ Fig. 1).

On magnetic resonance imaging (MRI), the distal radius and ulna, as well as the bones of the first row of the carpus, presented a high intensity in the short tau inversion recovery (STIR) sequence and an enhancement with the contrast medium, findings suggestive of osteomyelitis. Additionally, there were metaphyseal collections in the distal radius and ulna, thickened synovium, tenosynovitis of the flexor tendons, and cellulitis (→ Fig. 2).

Given these findings, surgical debridement with sequestrectomy of the carpal bones was performed on four occasions. The results of intraoperative cultures in the secretion and bone were negative for common aerobic and anaerobic bacteria. Empirical antibiotic coverage was started with first-generation cephalosporin, which was modified to trimethoprim sulfamethoxazole. Given the slow progression due to persistent local signs of infection and considering the history



**Fig. 1** Radiograph in anteroposterior (AP) and lateral views of the wrist showing diffuse osteopenia, erosion, and destruction of the cortical bone in the carpal bones and distal radius and ulna.



**Fig. 2** Contrast-enhanced magnetic resonance imaging (MRI) scans in coronal and sagittal cuts revealing diffuse enhancement in the carpal bones, collections, extensive cellulitis, and flexor tenosynovitis.



**Fig. 3** Clinical image 7 months after the surgical procedure, following 6 months of the tetraconjugate antibiotic treatment.

of chronic immunosuppression associated with the treatment of an autoimmune condition, an osteomuscular TB infection was suspected. Cultures and polymerase chain reaction (PCR) for *M. tuberculosis* were requested on a sample of the carpal bones, which tested positive. Following TB management protocols, tetraconjugate antibiotic therapy was initiated, leading to clinical improvement of the patient. The pathology study confirmed a pseudogranulomatous inflammation with areas of necrosis, and the culture reported multisensitive *M. tuberculosis*. The patient completed 6 months of the tetraconjugate antibiotic therapy, presenting complete resolution of the local inflammation (→ Fig. 3) and pain. One year after the diagnosis, there was still a limitation in completing the range of motion of the wrist, reaching a flexion of 20 degrees and an extension of 10 degrees.

### Case 2

A 61-year-old woman presented with pain, intermittent fever, and a 1-cm ulcer on the lateral aspect of the proximal



**Fig. 4** Radiographs of the elbow showing osteolysis of the articular surfaces, abundant joint fluid, and soft tissue edema around the joint.

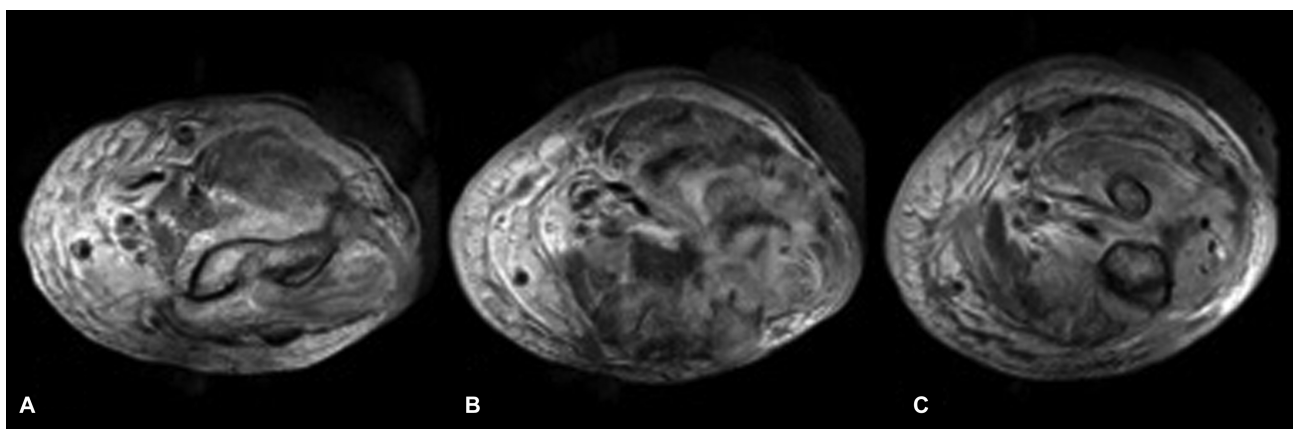
third of her forearm, with purulent discharge for 3 months. She had a history of rheumatoid arthritis and osteoporosis managed with methotrexate, deflazacort, and denosumab. The initial laboratory tests showed leukocytosis, neutrophilia, and positive acute-phase reactants. An X-ray of the elbow (→ Fig. 4) revealed osteolysis of the articular surfaces of the humerus, olecranon, and radius, with bone structure impaction and marked deformity, as well as signs of increased joint fluid and soft tissue edema.

The patient presented an unfavorable clinical course, with persistent hypotension that required vasopressor support in the intensive care unit. An arthrotomy of the left elbow was performed, as well as sequestrectomy and debridement of the proximal radius on 3 occasions, intraoperative cultures, and empirical coverage with cefepime and vancomycin. The intraoperative cultures reported methicillin-resistant *Staphylococcus aureus* and *Streptococcus pyogenes*. The PCR test for TB was negative. The MRI scan with gadolinium revealed an extensive joint inflammatory process of the elbow with thickening and a decrease in signal intensity in the T1 sequences of the bone marrow of the distal humerus and the proximal radius and ulna associated with diffuse cartilage loss, in addition to the reduction in the width of the joint space and sclerosis of the articular surfaces (→ Fig. 5).

Saucerization with intramedullary reaming was then performed, and a biopsy of synovial tissue was taken, which revealed granulomatous disease with central necrosis and few acid-fast bacilli. According to the concept of pulmonology and infectious disease, tetraconjugate antibiotics were started. One month later, there was an improvement in pain and in the initial inflammatory signs.

### Case 3

A 48-year-old man with a history of dermatomyositis presented with pain on the ulnar side of his left wrist and inflammatory changes, including swelling and erythema in the middle and proximal phalanges of the little finger, associated with pain, suggestive of infectious tenosynovitis.



**Fig. 5** Gadolinium-enhanced MRI scan of the left elbow. Distal humerus cut (A), elbow joint cut (B), and proximal radius and ulna cut (C). The images show extensive inflammatory process of the elbow joint with osteomyelitis of the proximal humerus, radius, and ulna, myositis, synovitis, and cellulitis, without associated collections, degenerative changes in the humeroradial and humeroulnar joints due to inflammatory arthropathy, subcutaneous rheumatoid nodules, and postoperative changes on the lateral aspect of the elbow.



**Fig. 6** Contrast-enhanced MRI scan of the hand showing increased signal intensity in the bone marrow at the base of the proximal phalanx of the little finger (A) and altered signal intensity in the capitate bone, with signs of bone marrow edema indicated by increased signal in the T2 sequence (B).

The initial laboratory tests did not show a significant elevation of acute-phase reactants, and X-ray images did not reveal any abnormalities.

The patient underwent two procedures for drainage of the collections in the synovial sheath of the left little finger flexors, with negative intraoperative cultures. Given his associated comorbidities, treatment with vancomycin and meropenem was initiated. Despite the antibiotic therapy, the patient continued to experience intermittent fever and local inflammatory changes. Additional studies, including a Doppler ultrasound of the left upper limb, revealed extensive superficial thrombosis of the cephalic vein and a distal collection in the distal third of the forearm. An MRI scan of the wrist (►Fig. 6) showed a multiseptated collection in the soft tissues of the dorsal region of the distal third of the forearm and signs suggestive of osteomyelitis of the capitate

bone. Based on these findings and on the unfavorable clinical progression, drainage and debridement of the reported collection were performed. Cultures, PCR for tuberculosis, and pathology studies were requested for samples from the forearm collection, as well as synovial tissue samples from the little finger and capitate bone. These results were positive, leading to the initiation of the tetraconjugate antibiotic therapy (►Fig. 7).

## Discussion

It is estimated that up to 25% of the world's population has latent TB disease. According to the World Health Organization (WHO), the annual incidence of active disease is estimated at 10 million people, and 95% of these cases occur in developing countries. In Colombia, 16 thousand cases were





**Fig. 7** Comparative photograph of the hands 3 months after the diagnosis of *M. tuberculosis* in the capitate bone of the left hand.

reported in 2019.<sup>1</sup> Extrapulmonary TB occurs in 20 to 40% of the cases, and, of these, between 10 and 20% manifest as musculoskeletal TB.<sup>2</sup> At this level, the most frequently affected site is the spine (in 50–60% of the cases), followed by joints such as the hip, knee and the foot/ankle.<sup>2</sup> At the level of the elbow, hand and wrist, TB is very rare, with a presentation that may range from 1 to 8%<sup>2</sup> or 1 to 4%,<sup>3</sup> depending on the series.

Osteomuscular TB can present as cutaneous TB, tuberculous tenosynovitis, bursitis, osteomyelitis, or hypersensitivity reactions.<sup>4</sup> Among these, tuberculous tenosynovitis is the most common, with a typical insidious course, with pain and limited mobility. In the initial or hygromatous phase, there is an exudate without tendon involvement. The second phase, or serofibrinous phase, is characterized by caseous material in the tendon sheath. Finally, in the fungoid phase, the caseous material extends to form a cold abscess, potentially leading to tendon ruptures. It can present as a palmar ganglion with initially painless swelling both distal and proximal to the carpal tunnel, or, less commonly, with the classic signs of Kanavel tetrad in cases of isolated digital involvement.<sup>4,5</sup>

The musculoskeletal involvement of TB is commonly caused by hematogenous dissemination; however, it can occur due to drainage of adjacent lymph nodes or contiguous infectious foci. Although infrequent, lesions due to direct inoculation can occur,<sup>6</sup> and their manifestation is usually localized and monoarticular.

Joint involvement is usually from proximal to distal, progressing through stages ranging from synovitis to joint collapse and destruction with ankylosis.<sup>3,6</sup>

Arthritis and tuberculous osteomyelitis are usually unifocal and simultaneous, because the bacillus invades the terminal portion of the arteries, causing endarteritis, bone destruction at the level of the epiphysis, and drainage of the joint space.<sup>2</sup> Imaging findings in osteomyelitis can range from cystic lesions, honeycomb pattern, infiltrative patterns with areas of osteolysis or sclerosis, or the image of “spina ventosa”, described as a fusiform expansion at the level of tubular bones such as the metacarpals or phalanges.<sup>4</sup> In the case of the elbow, the imaging finding may present in

Phemister triad, which includes juxta-articular osteopenia, decreased joint space, and bone erosion.<sup>7,8</sup>

Tuberculous osteoarthritis in the wrist is rare, particularly when involving osteomyelitis of the carpal bones. Prakash and Mehtani<sup>9</sup> reported satisfactory functional outcomes in pediatric patients treated solely with antibiotic therapy. Regarding tuberculous tenosynovitis, Kabakas et al.<sup>10</sup> concluded that only biopsy and targeted antibiotic therapy are necessary to control this infection, deeming tenosynovectomy unnecessary, as regression of lesions was observed in 12 patients treated under this approach. Cases of osteomyelitis involving the carpal bones are often diagnosed late and, as reported by Manas et al.,<sup>11</sup> typically result in lytic lesions, with destruction and collapse of the carpus, with symptom improvement following oral antibiotic treatment.<sup>12–15</sup>

Osteoarticular TB in the elbow is unusual, with few case reports in the last 10 years presenting as chronic edema in the elbow, pain, and, sometimes, fistulas.<sup>8,16–19</sup> Most cases have been diagnosed by culture and biopsy. The authors report<sup>16–19</sup> improvement in pain and edema with the use of the tetraconjugate antibiotic therapy. Only one case reported by Yazıcı et al.<sup>20</sup> required surgical debridement due to persistence of symptoms with the antibiotic management. Agarwal and Rastogi<sup>18</sup> reported satisfactory outcomes in pediatric patients treated solely with antibiotic therapy; however, they reported a correlation regarding late diagnosis and the extent and severity of joint involvement with loss of full extension of the elbow, despite treatment.

The diagnosis of this disease is usually late, after multiple surgical interventions such as sequestrectomies or debridements and empirical antibiotic coverage for pyogenic osteomyelitis with poor response. Due to the low diagnostic suspicion and low incidence, this diagnosis should be kept in mind to avoid futile treatments for the patient, such as the use of systemic corticosteroids, which worsen the course and severity of the disease.<sup>21</sup>

Due to the long latency of diagnosis and culture results, symptoms often worsen the patient’s condition. Therefore, the use of nucleic acid amplification tests by PCR has

represented a significant advance in obtaining more accurate and timely diagnoses of extrapulmonary TB. For musculoskeletal TB, according to a meta-analysis by Shen et al.,<sup>22</sup> the PCR test is highly sensitive and specific (81% and 83% respectively) for the diagnosis of the disease.<sup>22</sup> Other series<sup>23</sup> describe the histopathological report as the gold standard, with a specificity of 93.7% in a period of 24 hours, enabling the early start of the treatment. Antituberculosis management with tetraconjugate (rifampicin, isoniazid, pyrazinamide, and ethambutol) is usually sufficient; however, sometimes surgical management can be beneficial, with the aim of reducing or avoiding sequelae.<sup>4,6,7</sup>

It is important to highlight that the cases herein reported share the association of musculoskeletal TB with collagen diseases. Osteoarticular TB is more common in patients with pathologies such as systemic lupus erythematosus<sup>24</sup> due to the alteration in cellular immunity as well as the treatments to control it.<sup>25</sup> The association between active TB and autoimmune pathologies has been studied, linking *M. tuberculosis* with the development of autoimmunity and the proliferation of auto-antibodies and auto-reactive T lymphocytes.<sup>26,27</sup> Although the use of biological medications and high and prolonged doses of systemic corticosteroids can explain the immunosuppression that predisposes to TB infection, other mechanisms could explain the association between these diseases and the development of extrapulmonary TB. Some authors<sup>28</sup> propose that *M. tuberculosis* can induce the formation of antibodies or that it shares lipid antigens with human cells, inducing autoimmune responses.

Thus, taking into account the cases herein presented, we consider that, in patients with a history of autoimmune diseases who present osteoarticular infections of an atypical course, without elevation of acute-phase reactants and without response to the usual antibiotic treatments or repeated surgical debridements, it is pertinent to suspect TB infection. This infection can lead to joint destruction, with the functional limitation that this entails. Therefore, a biopsy with a PCR test for *M. tuberculosis* should be taken early, to enable an early diagnosis for a timely start of the tetraconjugate antibiotic therapy, also requesting cultures and a histopathological study to confirm the diagnosis.

## Conclusion

Musculoskeletal TB in the upper limb is rare; however, it should be suspected in the presence of local infection signs with negative cultures for common pathogens that do not respond to antibiotic treatments and repeated local debridements, especially in patients with any form of immunosuppression. Early diagnosis using molecular tests and targeted antibiotic treatment against tuberculosis improves the disease prognosis by reducing the functional limitations caused by joint collapse.

### Ethical Considerations

The project was approved by the Research and Ethics Committee of Hospital Universitario San Ignacio (approval

no. 02/2021). Patient data privacy was respected, as well as the principles of the Declaration of Helsinki.

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### Conflict of interests

The authors have no conflict of interests to declare.

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