

DISSEMINATED REFRACTARY TUBERCULOSIS WITH BICEPS TENDON INVOLVEMENT IN AN IMMUNOCOMPETENT PATIENT

Marcelo dos Reis Oliveira¹, Márcio Schiefer², Marcos Britto da Silva³, César Fontenelle⁴, Yonder Archanjo Ching-San Júnior⁵, José Sérgio Franco⁶

ABSTRACT

Objective: The authors report a rare case of disseminated tuberculosis which had compromised the long head of biceps tendon and shoulder joint, during standard drug therapy. **Methods:** On a first sight, the accurate diagnosis wasn't accomplished and the patient had been treated with physiotherapy for rotator cuff tear. However, the patient presented with a fast growing mass in anterior region of the proximal third of the arm, complaining of pain increase. Aspirative puncture of the mass revealed a yellow

fluid and the laboratorial analysis confirmed infection by *M. Tuberculosis*. The patient was treated with surgical debridement and his drug therapy was changed. **Results:** Resolution of infectious status and complete shoulder function restoration was succeeded. **Conclusion:** Due to its high prevalence in Brazil, tuberculosis must always be considered as a possible cause of inflammatory joint disease, even in immunocompetent patients.

Keywords - Tuberculosis osteoarticular; Shoulder; Rotator cuff; Infection

INTRODUCTION

For centuries, tuberculosis has afflicted humanity⁽¹⁾ and has been considered the leading cause of death from a single infectious agent in adults worldwide, according to the WHO⁽²⁾. Brazil is 14th among 23 countries accounting for 80% of all cases worldwide. Sources from the Ministry of Health estimate the prevalence in the country to be 58 cases per 100,000 inhabitants, with about 50 million infected, and 111,000 new cases and 6,000 deaths per year⁽³⁾.

The incidence of infection with *Mycobacterium tuberculosis* is increasing in both developed countries and developing countries, due to the following

factors: increasing numbers of immunocompromised patients, drug resistance, aging populations, and occupational exposure of healthcare professionals⁽⁴⁾. However, osteoarticular involvement is uncommon and occurs in less than 5% of all forms of tuberculosis⁽⁵⁾. Bone involvement is predominant and the spine is the region that is most frequently affected⁽⁶⁾. Joint involvement is even less common, and 50 to 73% occurs in the load-bearing joints, such as the hips and the knees⁽⁷⁻⁹⁾. The shoulder is rarely involved^(6,7).

We report a case of disseminated tuberculosis in an immunocompetent patient with musculoskeletal involvement, involving the shoulder joint, mainly the biceps tendon sheath.

1 – Resident, Orthopedics and Traumatology, Hospital Universitário Clementino Fraga Filho (HUCFF), Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil.

2 – Member, Shoulder and Elbow Group, HUCFF-UFRJ. Orthopedist, National Institute of Traumatology and Orthopedics (INTO, Instituto Nacional de Traumatologia e Ortopedia), Rio de Janeiro, Brazil.

3 – Medical Assistant, HUCFF-UFRJ (Shoulder and Elbow Group). Master in Orthopedics and Traumatology, UFRJ, Rio de Janeiro, Brazil.

4 – Clinic Head and Medical Residence Program Coordinator, Traumatology and Orthopedics Clinic, HUCFF-UFRJ. Master in Orthopedics and Traumatology, UFRJ, Rio de Janeiro, Brazil.

5 – Resident (R2) in Orthopedics and Traumatology, Hospital Universitário Clementino Fraga Filho (HUCFF), Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil.

6 – Head, Department of Orthopedics and Traumatology, School of Medicine, UFRJ. Associate Professor, School of Medicine, UFRJ, Rio de Janeiro, Brazil.

Study conducted at the Traumatology and Orthopedics Clinic, HUCFF-UFRJ, Rio de Janeiro, RJ, Brazil.

Correspondence: Av Afrânio de Melo Franco, 141/110, Rio de Janeiro, RJ. CEP: 22430-060. Tel: (21) 2274-3244; telephone/fax: (21) 2274-2561.

E-mail: marcioschiefer@hotmail.com

We declare no conflict of interest in this article

CASE REPORT

JVS, male, age 41, mason, White, born in Paraíba, resident of Rio de Janeiro, visited the orthopedic outpatient clinic at the Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro (HUCFF-UFRJ), on the 47th day of treatment for disseminated tuberculosis (pleural and liver involvement) with RHZ (rifampicin, isoniazid, and pyrazinamide), complaining of right shoulder pain for about a year after trauma from falling from standing height. The pain was initially mild and intermittent, localized in the anterior region of the right shoulder and did not limit his daily activities. About 20 days prior to the assessment, the intensity of pain increased and became constant, worsening at night and limiting daily activities.

On physical examination, active elevation was 110°, active external rotation was 60° and active internal rotation was at the fourth lumbar vertebra. Reported diffuse pain with mobilization. He had a visible mass in the anterior medial third of the right arm, without signs of inflammation. On palpation, it was mobile, soft and had well-defined limits. The Neer⁽¹⁰⁾, Yocum⁽¹¹⁾, and Hawkins⁽¹²⁾ tests were positive; the O'Brien test⁽¹³⁾ and acromioclavicular compression were painless; the Speed⁽¹⁴⁾ and Yergason⁽¹⁵⁾ tests were negative; he complained of pain on palpation of the intertubercular groove. The maneuvers to assess the integrity of the rotator cuff were hampered by severe pain.

At the time, he brought a report of a shoulder ultrasonography performed at another institution, which described "slight irregularity of the articular bone surface, complete rupture of the rotator cuff, thickening and heterogeneity of the rotator cuff compatible with tendinosis, presence of thick liquid with the sheath of the long head tendon of the biceps and the subdeltoid bursa. Hemorrhagic bursitis? Synovial proliferation".

At the time, the clinical diagnosis at the outpatient clinic was of rotator cuff injury with associated tendinopathy of the biceps. MRI was requested and the patient was referred to physical therapy.

After 15 days, the patient came to the emergency room of HUCFF, reporting worsening of symptoms and an increase of tumor volume in the anterior region of the arm associated with the appearance of localized heat and erythema (Figure 1). He was febrile (38.8°C) and had completed the 2nd month of RHZ. Immediately, laboratory and image exams were performed upon suspicion of infection.

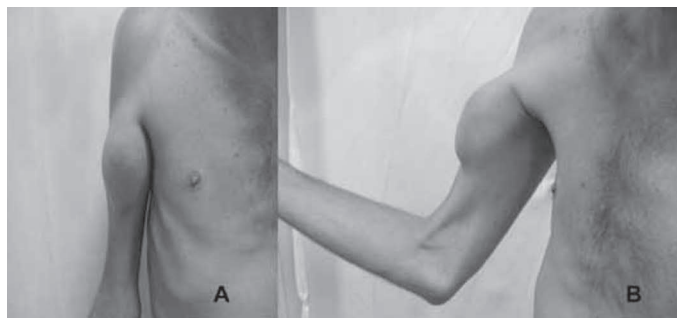


Figure 1 – Front (A) and side (B) photographs showing a large mass in the anterior region of the proximal third of the right arm.

Lab: leukocytes 5.960/mm³ (normal differential count), hemoglobin 11.8 g/dL, hematocrit 36.4%, platelets 249.000/mm³, ESR 80mm in one hour, albumin 3.6 g/dL, total protein 6.5 g/dL, transferrin 202.3 mg/dL. Moreover, HIV serology was negative and he was reactive to the tuberculin test (10mm).

Shoulder ultrasonography showed collection of ill-defined contours and thick heterogeneous content located in the anterior portion of the biceps involving the long and short tendons measuring approximately 10 x 7 x 4 cm. That collection was insinuating superiorly. There was similar content in the subcoracoid and subacromial/subdeltoid bursa and glenohumeral space. The supraspinal tendon was thickened by tendinosis. The rest of the rotator cuff was without changes.

Radiographic study was complemented by simple radiographs and magnetic resonance imaging. The radiographs did not reveal additional relevant information. In contrast, magnetic resonance imaging revealed the presence of predominantly hypointense lesions on T1 and hyperintense in the other sequences, localized in the meta-epiphyseal region of the humerus and glenoid, in addition to large joint effusion and synovial thickening; it also showed voluminous anterior collection in the proximal third of the arm, in close relation with the biceps tendon (Figure 2).

The collection involving the biceps tendons was punctured percutaneously, immediately before the surgical procedure, under surgical antisepsis with iodine alcohol solution (Figure 3). The test for acid-fast bacilli (AFB) by the Ziehl-Neelsen method was positive.

The patient was then submitted to surgery under brachial plexus block, in the supine position. A deltopectoral incision was made, extending distally over the mass. A large amount of purulent discharge with clots emerged

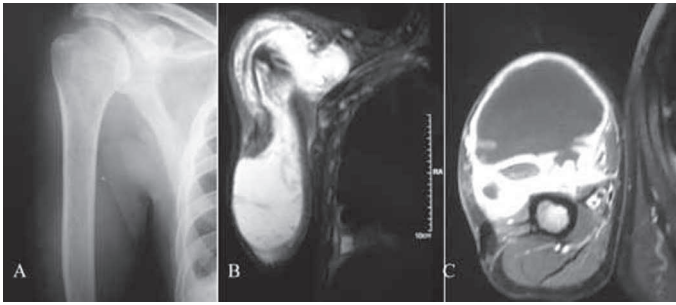


Figure 2 – Imaging tests. (A) Anteroposterior plain radiograph of the shoulder and proximal half of the left humerus, showing only an increase in the volume of soft tissue. (B) Coronal oblique slice magnetic resonance image of the shoulder and upper half of the right arm, T2-weighted fat-suppressed, revealing voluminous collection in the proximal region of the arm, following the long portion of the biceps proximally. (C) T1-weighted axial slice magnetic resonance image of the proximal region of the right arm showing large collection in its anterior region.



Figure 3 – Photograph showing the performance of fine needle aspiration of the mass, which revealed heterogeneous, thick, and yellowish liquid content. The smear of the liquid using Ziehl-Neelsen staining confirmed the presence of acid-fast bacilli (AFB).

(Figure 4) after opening the bicipital sheath. On inspection during surgery, this was found to be the main focus of infection. Drainage of pus was performed, debridement of devitalized tissue and abundant washing of structures, including the shoulder joint with saline. The wound was closed with simple stitches and the patient was closely monitored during the postoperative period. He was discharged after five days.

The material was sent for histopathology, cytopathology, smear microscopy (Ziehl-Neelsen method), and culture for mycobacteria in Lovestein-Jansen medium and for common germs. Histopathological examination revealed “acute and chronic nonspecific inflammation” and the cytopathological exam showed

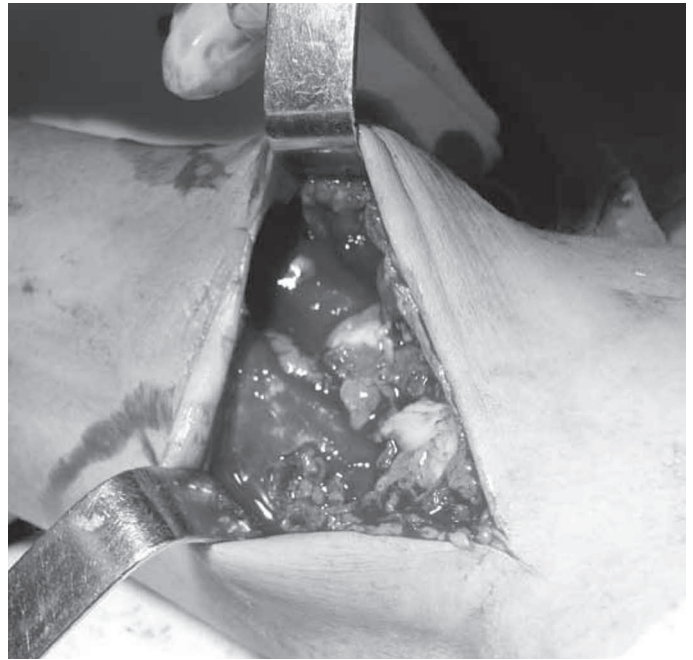


Figure 4 – Photograph obtained during surgery, after draining the collection showing infectious material on the coracobrachialis and biceps muscles, with moderate tissue damage. The patient underwent rigorous debridement and thorough washing of the wound.

“synovial hyperplasia and cellular necrosis”. The cultures were negative. The diagnosis was confirmed by positive AFB smear.

Due to daily fever persisting in the 3rd month of treatment with RHZ, besides presenting the disseminated form of tuberculosis (pleural, musculoskeletal, and liver), we chose to optimize therapy by adding ethambutol and amikacin to the regimen and removing pyrazinamide. He remained in use of four drugs for three months when amikacin was then removed from the regimen. He remained under treatment with rifampicin, isoniazid, and ethambutol until the completion of 12 months of treatment.

He evolved to complete resolution of pain and complete functional improvement of the right shoulder. In addition, there was also complete regression of the pleural effusion and the success of therapeutic regimens more clearly confirmed the previous diagnosis of tuberculosis. There was no recurrence of swelling at the wound site, and other signs of local infection were no longer observed. At the moment, with 24 months of follow-up, he complains of mild discomfort in the right shoulder only upon great exertion and its function is graded as good (33 points) according to the UCLA scale⁽¹⁶⁾ (Figure 5). Radiography from the last consultation shows no changes.



Figure 5 – (A, B and C): Photographs of the patient showing good final clinical results after 24 months of outpatient treatment.

DISCUSSION

Musculoskeletal involvement is uncommon in tuberculosis and occurs in less than 5% of cases⁽⁵⁾. Of these, most cases have bone tuberculosis and only a small number of patients have joint tuberculosis; muscle and/or tendon involvement is even more rare, accounting for 1% of the cases of musculoskeletal tuberculosis^(5,8,17). Joint involvement occurs predominantly in the load-bearing joints, while the involvement of the shoulder joint occurs in only about 2% of cases of joint tuberculosis⁽²⁾. The relative rarity of joint tuberculosis, in particular, in the shoulder, is one of the factors that contributes to the usual delay in the diagnosis of the condition. Moreover, the signs and symptoms are nonspecific and often drawn out clinically, evolving gradually over several months^(7,8,18-23). The time between the onset of symptoms and initiation of treatment may extend to one year^(8,17). Although our first diagnostic impression of the injury in the outpatient clinic was rotator cuff injury associated with tendinopathy of the biceps, in our case, the diagnosis was made easier because the patient was undergoing drug treatment of extrapulmonary tuberculosis (pleural and liver) and returned spontaneously to the hospital, and came to the emergency room 15 days later with a large mass in the proximal region of the right arm. Additional exams are of great value in the confirmation of the diagnosis, since the clinical features are nonspecific. Laboratory tests are usually normal except for ESR, which is usually high^(22,24). As in our case, most patients are positive in the tuberculin test (purified protein derivative – PPD)⁽¹⁷⁾, although this test has little value, especially in areas of high prevalence of tuberculosis^(4,23). Among the imaging tests, MRI

is the gold standard⁽²⁵⁾ and it was useful in our case in revealing musculoskeletal signs compatible with tuberculosis. Gahlaut et al.⁽²⁶⁾ call attention to the difficulty in the diagnosis of extrapulmonary tuberculosis and suggest that it be confirmed by the presence of one of the following criteria: 1 – positive culture for *M. tuberculosis*, 2 – demonstration of AFB in a smear, 3 – biopsy material containing caseous granuloma typical of a tuberculosis infection. The combination of various diagnostic modalities is important for the detection of musculoskeletal tuberculosis⁽⁸⁾, and this was essential in our case, in which the cultures were negative, histopathological and cytopathological exams were inconclusive and only the smear was positive.

In our case, there was bone (in the proximal humerus), joint, and tendon involvement, according to the evaluation of the magnetic resonance imaging and the surgical findings. The intra-articular situation of the long portion of the brachial biceps promotes their involvement in cases of aseptic or septic arthritis of the shoulder. However, in this case, the inspection during surgery showed the biceps tendon sheath at the level of the intertubercular groove to be the main focus of infection. The occurrence of extrapulmonary tuberculosis seems to result from the reactivation of latent foci after a primary infection⁽²⁷⁾. Most joint forms occur due to extension of the focus from adjacent bone, although direct hematogenous infection of the synovial membrane can also occur⁽²⁴⁾. The involvement of tendons also seems to occur most likely due to contiguity⁽¹⁸⁾. Bickel et al.⁽¹⁸⁾ proposed that tuberculous tenosynovitis originates from the primary involvement of bone, and subsequent tendon involvement; the initial focus

is then cured and the disease would localize only in the tendon. While we recognize through the review of pathogenic mechanisms of extrapulmonary tuberculosis that the primary involvement of the biceps tendon is unlikely, there is no way to confirm in this case whether the osteoarticular infection preceded the tendon involvement or vice versa. In fact, no case of isolated bicipital tendinitis tuberculosis was found during the literature review done in the preparation of this report, although many authors have reported other atypical locations^(19,20,28,29,31-34). Only one third of patients with musculoskeletal tuberculosis have a history of pulmonary disease⁽⁴⁾, although the presence of findings consistent with previous tuberculosis is common in imaging studies (chest radiography and computed tomography)^(7,23). Our patient, although he denied a history of pulmonary disease, revealed cicatricial changes in the apex of the right lung in CT scans, consistent with previous pulmonary tuberculosis.

The occurrence of extrapulmonary, including musculoskeletal, tuberculosis, is more common in immunocompromised patients. In immunocompetent individuals, extrapulmonary tuberculosis accounts for 15-20% of all forms of tuberculosis, while in immunocompromised individuals, extrapulmonary tuberculosis accounts for 50% of cases. This is another peculiarity of this case: it is of an immunocompetent patient with disseminated tuberculosis which also failed to be treated by standard drug treatment.

The incidence of multidrug-resistant tuberculosis (MDR-TB) has increased; it is estimated that 3% of all new cases are multidrug resistant⁽³⁶⁾. However, by definition, MDR-TB is one in which *in vitro* tests show resistance to at least rifampicin and isoniazid. It is pointed out in the second Brazilian Tuberculosis Consensus⁽³⁾ that a retreatment regimen lasting 12 months should be proposed for patients who experience failure of the standard RHZ regimen, regardless of sensitivity testing. Similarly, the World Health

Organization proposes the adoption of the failure of standard treatment in places where sensitivity tests are not available⁽³⁵⁾. In cases of confirmed multidrug resistance, alternative drug treatment should last up to 18 months^(3,36). In our case, sensitivity testing of the material obtained from the collection in the synovial sheath of the biceps was not possible, as Koch's bacillus was not isolated in culture. However, pleural fluid culture performed at the beginning of evolution two months before the onset of symptoms on the right shoulder revealed *M. tuberculosis* sensitive to first-line drugs. In this case, acquired resistance may have occurred, as it is much more common than primary resistance⁽³⁾, or simply non-adherence to treatment; the latter possibility was vehemently denied by the patient. In fact, due to the failure of the initial treatment, our patient underwent the retreatment regimen for 12 months, with complete resolution of the disseminated infection.

The treatment of musculoskeletal tuberculosis is essentially clinical (drugs) and its duration should be extended to 12 months. Early diagnosis and treatment promote complete or nearly complete recovery of joint function in about 95% of cases⁽²³⁾. According to Erdem et al.⁽²³⁾, surgical treatment of musculoskeletal tuberculosis should be indicated in cases of persistent symptoms after four months of chemotherapy. However, in our case, surgical treatment was necessary due to the presence of a large collection of infectious content in the right arm, with a rapid increase in volume over a short period of time (Figure 1).

Finally, the importance of this report is to highlight the growing presence of musculoskeletal tuberculosis and call the attention of orthopedists to performing this diagnosis. Due to its high prevalence in Brazil, tuberculosis should always be considered in the differential diagnosis of cases of chronic and progressive involvement of the joints, bones, muscles, tendons, and bursae, even in immunocompetent individuals.

REFERENCES

1. Mohan A, Sharma SK. Epidemiology. In: Sharma SK, Mohan A. Tuberculosis. New Delhi: Jaypee Brothers Medical Publishers; 2001. p.14-29.
2. World Health Organization. Global tuberculosis control e surveillance, planning, financing. WHO report 2005 [WHO/HTM/TB/2005.349].
3. Sociedade Brasileira de Pneumologia e Tisiologia. II Consenso Brasileiro de Tuberculose 2004. Disponível em: (http://www.sbpt.org.br/downloads/arquivos/cons_tuberculose_2004.pdf)
4. Watts HG, Lifeso RM. Current concepts review. Tuberculosis of bones and joints. *J Bone Joint Surg.* 1996;78(2):288-98.
5. Yao DC, Sartoris DJ. Musculoskeletal tuberculosis. *Radiol Clin North Am.* 1995;33(4):679-89.
6. Malaviya AN, Kotwal PP. Arthritis associated with tuberculosis. *Best Pract Res Clin Rheumatol.* 2003;17(2):319-43.
7. Al-Saleh S, Al-Arfaj A, Naddaf H, Haddad Q, Memish Z. Tuberculous arthritis:

- a review of 27 cases. *Ann Saudi Med.* 1998;18(4):368-9.
8. Garrido G, Gomez-Reino J, Fernandez-Dapica P, Palenque E, Prieto S. A review of peripheral tuberculous arthritis. *Semin Arthritis Rheum.* 1988;18(2):142-9.
 9. Halsey JP, Reeback JS, Barnes CG. A decade of skeletal tuberculosis. *Ann Rheum Dis.* 1982;41(1):7-10.
 10. Neer CS 2nd. Anterior acromioplasty for the chronic impingement syndrome in the shoulder: a preliminary report. *J Bone Joint Surg Am.* 1972;54(1):41-50.
 11. Yocum LA. Assessing the shoulder. History, physical examination, differential diagnosis and special tests used. *Clin Sports Med.* 1983;2(2):281-9
 12. Hawkins RJ, Kennedy JC. Impingement syndrome in athletes. *Am J Sports Med.* 1980;8(3):151-8.
 13. O'Brien SJ, Pagnani MJ, Fealy S, McGlynn SR, Wilson JB. The active compression test: a new and effective test for diagnosing labral tears and acromioclavicular joint abnormality. *Am J Sports Med.* 1998;26(5):610-3.
 14. Crenshaw AH, Kilgore WE. Surgical treatment of bicipital tenosynovitis. *J Bone Joint Surg Am.* 1966;48(8):1496-502.
 15. Yergason RM. Supination sign. *J Bone Joint Surg* 1931;13:1:60.
 16. Ellman H, Hunker G, Bayer M: Repair of the rotator cuff: end-result study of factors influencing reconstruction. *J Bone Joint Surg Am.* 1986;68(8):1136-44.
 17. Albornoz MA, Mezgarzede M, Neumann CH, Myers AR. Granulomatous tenosynovitis: a rare musculoskeletal manifestation of tuberculosis. *Clin Rheumatol.* 1998;17(2):166-9.
 18. Bickel WH, Kimbrough RF, Dahlin DC. Tubercular tenosynovitis. *JAMA.* 1953; 151(1):31-5.
 19. Abdelwahab IF, Kenan S, Hermann G, Klein MJ, Lewis MM. Tuberculous Peroneal Tenosynovitis. A case report. *J Bone Joint Surg.* 1993;75(11):1687-1690.
 20. Adams R, Jones G, Marble HC. Tuberculous tenosynovitis. *N Engl J Med.* 1940;223:706-8.
 21. Hortas C, Ferreira JL, Galdo B, Arasa FJ, Barbazán C, Mera AJ, et al. Tuberculosis and arthritis of peripheral joints with previous inflammatory rheumatic disease. *Br J Rheum.* 1988;27(1):65-7.
 22. Aboudola S, Sienko A, Carey RB, Johnson S. Tuberculous Tenosynovitis. *Hum Pathol.* 2004;35(8):1044-1046.
 23. Erdem H, Baylan O, Simsek I, Dinc A, Pay S, Kocaoglu M. Delayed diagnosis of tuberculous arthritis. *Jpn J Infect Dis.* 2005;58(6):373-5.
 24. Kapukaya A, Subasi M, Bukte Y, Gur A, Tuzuner T, Kilinc N. Tuberculosis of the shoulder joint. *Rev Rhum.* 2006;73:263-8.
 25. De Vuyst D, Vanhoenacker F, Gielen J, Bernaerts A, De Schepper AM. Imaging features of musculoskeletal tuberculosis. *Eur Radiol.* 2003;13(8):1809-19.
 26. Gahlaut DS, Nath K, Sikka KK, Singh KN, Samuel KC. Generalized skeletal muscle tuberculosis. *J Indian Med Assoc.* 1973;61(2):92-4.
 27. Sharma SK, Mohan A. Extrapulmonary tuberculosis. *Indian J Med Res.* 2004;120(4):316-53.
 28. Goldberg I, Avidor I. Isolated tuberculous tenosynovitis of the Achilles tendon. A case report. *Clin Orthop Relat Res.* 1985;(194):185-8.
 29. Varshney MK, Trikha V, Gupta V. Isolated tuberculosis of Achilles tendon. *Joint Bone Spine.* 2007;74(1):103-6.
 30. Trikha V, Gupta V. Isolated tuberculous abscess in biceps brachii muscle of a young male.. *J Infect.* 2002;44(4):265-6.
 31. Nishida J, Furumachi K, Ehara S, Satoh T, Okada K, Shimamura T. Tuberculous bicipitoradial bursitis: a case report. *Skeletal Radiol.* 2007;36(5):445-8.
 32. Jira M, Qacif H, Sekkach Y, El Qatni M, Elouennass M, Ghafir D. Ténosynovite tuberculeuse: une localisation rare. *Rev Med Interne.* 2007;28(1):56-8.
 33. Learch TJ, Hsiao NM. Tuberculous infection of the gracilis muscle and tendon clinically mimicking deep venous thrombosis: sonographic findings. *Skeletal Radiol.* 1999;28(8):457-9.
 34. Holder SF, Hopson CN, Vonkuster LC. Tuberculous arthritis of the elbow presenting as chronic bursitis of the olecranon. A case report. *J Bone Joint Surg.* 1985;67(7):1127-9.
 35. Crofton J, Chaulet P, Maher D, Grosset J, Harris W, Horne N, et al. Guidelines for the management of drug-resistant tuberculosis. WHO/TB/96.210 Rev1. Geneva:World Health Organization; 1997.
 36. Sharma SK, Mohan A. Multidrug-resistant tuberculosis Indian. *J Med Res.* 2004;120:354-76.