

Tuberculosis of the joints and bone: two case reports

M. De Maria, M. Ceccarelli, V. Cama, I. Paolucci, F. Bellissimo

Department of Clinical and Experimental Medicine, Unit of Infectious Diseases, University of Messina, Messina, Italy

ABSTRACT:

- **Background:** The clinical signs and symptoms of tuberculosis (TB) usually reflect the site of infection. In addition to specific symptoms, constitutional and nonspecific signs and symptoms, such as fever, anorexia, weight loss, malaise and fatigue, can be found. We report two cases of extrapulmonary TB involving the osteoarticular system, observed between 2014 and 2016, showing the importance of taking into account TB as a possible cause of disease even when atypical lesions are observed far away from the lungs.
- **Keywords:** Tuberculosis, Joint, Bone, Extrapulmonary, Case report.

INTRODUCTION

Tuberculosis (TB) is one of the most frequent causes of death from infectious diseases¹⁻¹¹. The World Health Organization (WHO) estimated that in 2015 the incidence was 9.6 million new TB cases/year worldwide, with a mortality of 1.5 million/year³. WHO also reported that more than two billion people worldwide are infected with TB, without any signs of the disease: this circumstance is defined as “Latent TB Infection” (LTBI).

One out of 10 individuals with LTBI develops active TB in his/her lifetime³.

Risk factors for acquiring TB include age (children under 5 years and adolescents become infected more easily than adults), and conditions associated with immune deficiency (e.g.: HIV infection or immunosuppressant drugs).

It is possible to identify two main events that outline the medical history of TB: primary TB, which is characterized by the formation of the primary lesion (a caseous nodule in the infection site) with satellite adenopathy (primary complex), which can evolve towards latency or progression; and secondary TB, caused by the reactivation of a latent lesion or by a new infection, characterized by the formation of caverns within the caseous nodule. Whether it is a primary TB or a secondary one, it can follow two different evolutions, healing or

hematic dissemination, with the consequential spread of the disease^{1,2}.

From the clinical point of view TB is divided into:

- Pulmonary TB (primary or post-primary);
- Generalized or miliary TB;
- Extrapulmonary TB.

Before HIV pandemia, extrapulmonary TB constituted between 15 and 20% of all cases of TB. Among the HIV-infected patients, extrapulmonary TB prevalence is higher than 50%. Patients with extrapulmonary TB show symptoms and signs which depend on the organ involved. In addition to specific symptoms, they can also show constitutional and non-specific signs and symptoms, such as fever, anorexia, weight loss, malaise and fatigue^{1,2}. The most common anatomical sites are the lymph nodes, the central nervous system, the osteoarticular system, the genitourinary tract and the gastrointestinal system. Serous membranes (e.g.: pleura, pericardium, peritoneum), adrenal glands and eyes are less commonly affected. If primary TB occurs in childhood, bacteria can spread to vertebrae and epiphysis, still vascularized, of the long bones. However, in adults the involvement of the joint capsule can lead to a mono-articular arthritis that mainly affects wrist, hand and elbow, as well as the spine. When vertebrae are affected, extrapulmonary TB is called “Pott’s disease”: in its typical course, it affects two vertebrae, while the disc between them is compressed by the caseous lesion.

Early diagnosis of extrapulmonary TB is critical to prevent structural damage^{1,2}. Radiological examinations (Computed Tomography (CT) or Magnetic Resonance Imaging (MRI)) are critical, although^{1,2,9-11} biopsy is essential to identify with certainty *Mycobacterium (M.) tuberculosis* involvement. While antibiotic treatment can be enough for less extensive disease, more severe cases may require surgery.

CASE REPORTS

We report two cases of extrapulmonary TB involving the osteoarticular system, observed between 2014 and 2016, at the Infectious Diseases Department of the University Hospital “Policlinico G. Martino” in Messina.

Clinical Case A

A 22-year-old Italian female patient went to the emergency department reporting pain in the dorsal region, low-grade fever and fatigue. Her medical history was characterized by close contacts with people affected by pulmonary TB and an uncertain adherence to the prescribed prophylaxis with isoniazid. She also reported that some months before the admittance she was affected by a fistulous abscess lesion in the dorsal region, for which she was treated with surgical drainage and unspecified antibiotic therapy.

Chest CT scan showed the presence of pleural effusion on the left lung that extended from the apex to the base with a lobulated aspect. A massive abscess (10 cm in diameter) packed the manubrium and the upper third of the sternal body, causing osteolysis. The abscess extended to the anterior-superior mediastinum, where a purulent collection of about 48 x 17 mm, located between the sternum and the neck vessels, could be observed. The presence of a multifocal thickening of the lung parenchyma was described in the apical lobe of the right lung. Multiple lesions with characteristics of “tree-in-bud” were identified in the whole left lung. Chest CT scan documented the presence of a pathological process characterized by some osteolytic lesions between chest and abdomen, corresponding to the last dorsal vertebrae: D12 (part of the soma, lamina, transverse process and pedicle), D11 (part of the soma and peduncle) and the transverse processes of D10 and L1. These formations encompassed the right psoas and iliopsoas muscles and extended from the right para-spinal muscles to the subcutaneous soft tissue. Another abscess, with an elongated morphology of about 8 x 5 cm, was observed between the large and the medium right buttock muscles. The MRI of the spine confirmed the CT scan result.

Two drainages were placed, one endo-pleural and one in the sternal abscess, and samples of the drainage material, together with material from the wound in the lumbar region, were sent for microbiological exams, including cultures for common bacteria and mycobacteria, as well as Ziehl–Neelsen staining for Koch bacillus. In addition, an ultrasound-guided aspiration of the pre-trochanteric right abscess was performed. Laboratory tests showed no abnormalities and HIV test was negative.

The search for mycobacteria on the lumbar wound swab tested positive for many acid-fast resistant bacilli, while mycobacteria could not be found in the material withdrawn from the chest drainages. The biopsy on the para-spinal tissues showed the presence of necrosis, with epithelioid cells, lymphoid elements, multinucleated giant cells (Langerhans type), compatible with TB. At first, the patient had to stay in the supine position in bed; then, she was given a rigid brace with axillary supports to allow deambulation. The patient started anti-TB treatment with Isoniazid, Rifampin, Pyrazinamide, Ethambutol and Moxifloxacin, but she was lost to follow-up and her current clinical conditions are unknown.

Clinical Case B

A Russian female patient, aged 42, was referred to our clinic after the occasional radiological finding of small round opacities in the lungs. At the time of admission, the patient had no history of fever, sweats or weight loss. However, she complained of intense left knee pain. The affected joint appeared flushed, with soft tissue swelling that extended to the leg and a small lateral nodule. The patient declared to be taking methotrexate and sulfasalazine for rheumatoid arthritis, and isoniazid and pyridoxine since March 2014, as a prophylaxis for LTBI.

Blood tests showed only a slight increase in C-Reactive Protein (3.5 mg/dl) and anemia (Hemoglobin: 10.2 g). HIV test was negative. A partially excavated oval nodule (26 x 15 mm), which moderate post-contrast enhancement, was found in the apex of the lower right lobe at the chest CT scan. This nodule connected with the adjacent pleura. Similar lesions were found at the right apical lobe and in the left lung. Bacteriological and culture tests for mycobacteria on sputum and synovial fluid were performed, with positive results.

Anti-tubercular treatment with Isoniazid, Rifampin, Pyrazinamide and Ethambutol and an analgesic therapy were started. After having received the results of the antibiogram, showing resistance to Isoniazid, Rifampin and Ethambutol, treatment was changed. She began a second-line regimen with Amikacin, Linezolid, Terizidone, Moxifloxacin and Pyrazinamide, for two years totally. She successfully completed one year of treatment with five drugs; then, Amikacin was stopped. She is currently on treatment with four drugs and, at the end of the antibiotic therapy, she will have surgery to implant a knee prosthesis.

DISCUSSION

Despite being a curable disease, TB remains a major public health problem worldwide and one of the diseases with higher mortality. Extrapulmonary TB may have different presentations, some differing substantially from the classic lung localization.

It is often difficult to promptly diagnose extrapulmonary TB. Of importance, diagnostic delay, often linked to non-specific symptoms, can have a significant impact on disease progression, favoring the spread of TB to other organs or the impairment of organs already affected by TB.

These case-reports show the importance of taking into consideration a possible TB etiology even when lesions are observed far away from the lungs.

It also shows that the increasing use of immunosuppressive drugs, a potential cause LTBI reactivation, is a factor that needs to be taken into great consideration in the context of clinical practice.

TB should always be considered in the differential diagnosis, and TB screening should be implemented through information campaigns for healthcare personnel.

CONFLICT OF INTERESTS:

The Authors declare that they have no conflict of interests.

REFERENCES

1. Bennett JE, Dolin R, Blaser MJ. In: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8th Edition, Saunders, Elsevier, 2014.
2. Dennis Kasper, Anthony Fauci, Stephen Hauser, Dan Longo, J. Larry Jameson, Joseph Loscalzo. Harrison's Principles of Internal Medicine, 19th ed. Tuberculosis. Chapter 202, 2015.
3. http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf
4. Seddon JA, Graham SM. Childhood TB: can the End TB Strategy deliver? *Trans R Soc Trop Med Hyg* 2016; 110: 155-157.
5. Kunii O, Yassin MA, Wandwalo E. Investing to end epidemics: the role of the Global Fund to control TB by 2030. *Trans R Soc Trop Med Hyg* 2016; 110: 153-154.
6. Prasad A, Ross A, Rosenberg P, Dye C. A world of cities and the end of TB. *Trans R Soc Trop Med Hyg* 2016; 110: 151-152.
7. Lönnroth K, Raviglione M. The WHO's new End TB Strategy in the post-2015 era of the Sustainable Development Goals. *Trans R Soc Trop Med Hyg* 2016; 110: 148-150.
8. Lee JY. Diagnosis and treatment of extrapulmonary tuberculosis. *Tuberc Respir Dis (Seoul)* 2015; 78: 47-55.
9. Debi U, Ravisankar V, Prasad KK, Sinha SK, Sharma AK. Abdominal tuberculosis of the gastrointestinal tract: revisited. *World J Gastroenterol* 2014; 20: 14831-14840.
10. Kulchavenya E. Extrapulmonary tuberculosis: are statistical reports accurate? *Ther Adv Infect Dis* 2014; 2: 61-70.
11. Willemsen I, Mooij M, van der Wiel M, Bogaers D, van der Bijl M, Savelkoul P, Kluytmans J. Highly resistant microorganisms in a teaching hospital: The role of horizontal spread in a setting of endemicity. *Infect Control Hosp Epidemiol* 2008; 29: 1110-1117.