# Association of tibial osteomyelitis and pneumonitis due to miliary tuberculosis in a patient with systemic lupus erythematosus

Vitor Emer Egypto Rosa[1], Daniel Martin[1], André Marun Lyrio[2], Maria Aparecida Barone Teixeira[3], José Roberto Provenza[4]

## ABSTRACT

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease, which has great prevalence and uncommon manifestations of opportunistic infectious diseases, mainly due to the multiple abnormalities of the immune system and the immunosuppressive effect of the medications used in its treatment. Patients whit SLE have an increased incidence of tuberculosis, and osteoarticular involvement occurs in 1%–3% of the cases, manifesting as pain, reduction in mobility, and increased osteoarticular volume. The radiographic findings are often nonspecific. Magnetic resonance imaging (MRI) is an useful test to define the severity of bone involvement; however, the etiological diagnosis can only be established by use of synovial fluid or bone cultures or the histological study of the affected areas. Due to the lack of specificity of the findings, there is usually a mean diagnosis delay of 11 months. We report the case of a female patient with SLE and predisposing factors for tuberculosis infection/reactivation. The MRI was important to define bone involvement, and the etiological diagnosis was established by use of bone biopsy. The patient also had lung involvement due to miliary tuberculosis, shown on plain chest radiography and CT scan and confirmed on culture of *Mycobacterium tuberculosis* in the sputum. There was a 1.5-month delay in beginning therapy, which is considered a short time when compared to the reports in the literature. In conclusion, bone tuberculosis, although rare, should always be remembered as a differential diagnosis of patients with SLE and osteomyelitis, mainly those with history of pulmonary tuberculosis.

**Keywords:** osteomyelitis, tuberculosis, systemic lupus erythematosus, osteoarticular tuberculosis.



## INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder, which has great prevalence and uncommon manifestations of opportunistic infectious diseases, mainly because of the multiple abnormalities of the immune system and the immunosuppressive effect of the medications used in its treatment.[1–5] Patients whit SLE have an increased incidence of tuberculosis, approximately seven times that of the general population, and the osteoarticular involvement occurs in 1%–3% of the cases, affecting mainly the spine and long bones, and, less commonly, the peripheral joints.[1]

Risk factors and mechanisms of that involvement are uncertain, but the association between infection and previous osteoarticular inflammation has been described, with an apparent predilection of the *Mycobacterium tuberculosis* for those areas through its previous phagocytosis by macrophages.[1,6]

The disease usually manifests with pain, decreased mobility, and increased osteoarticular volume. The radiographic findings usually lack specificity. Magnetic resonance imaging (MRI) is useful to define the severity of bone involvement and to identify the extra-articular extension of the disease. However, etiological diagnosis can only be established by use of synovial fluid or bone cultures or the histological study

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Departments of Internal Medicine and Rheumatology, Medical School of the Pontifícia Universidade Católica de Campinas – PUC-Campinas.
1. Resident Physician of the Department of Internal Medicine – PUC-Campinas
2. Resident Physician of the Department of Rheumatology – PUC-Campinas
3. Full Professor of the Department of Internal Medicine – PUC-Campinas
4. Full Professor of the Department of Rheumatology – PUC-Campinas
*Correspondence to:* Vitor Emer Egypto Rosa. Rua Jorge Neme, O-405 – Jardim Alvorada. CEP: 17280-000. Pederneiras, SP, Brasil. E-mail: vitoremer@yahoo.com.br

of the sites affected.[7] Changes on lung radiography occur in about 50% of the patients with osteoarticular tuberculosis; disease activity in osteoarticular areas, however, is unusual, and the association of osteoarticular tuberculosis and miliary tuberculosis has been reported in 10% of the cases.[7]

Due to the lack of specific findings, the diagnosis is usually delayed (on average 11 months), which significantly contributes to increase morbidity and mortality in those patients.[1]

The interest in the reported case is due to the diagnostic approach to tuberculosis – a highly prevalent pathology among us – in a female patient with SLE, a disease that predisposes to tuberculosis and can mimic the osteoarticular and lung involvement of tuberculosis. Therefore, this case report is an alert to that association.

## CASE REPORT

The patient APSC is a catholic 44-year-old housewife, born in the state of Paraná, coming from the city of Santo Antônio do Jardim, state of Minas Gerais. She reported lung tuberculosis treated 35 years before, and being first diagnosed with cutaneous lupus 20 years before, for which she underwent treatment with prednisone (40 mg/day) and chloroquine (250 mg/day). She reported resolution of her clinical condition and discontinuation of those drugs ten years before.

One month ago, she observed a progressive increase of volume in her right leg, close to her right knee, with local pain and heat, in addition to low evening fever, which led to resuming the treatment with prednisone (40 mg/day) and chloroquine (250 mg/day). Her evolution was slow and progressive until an abscess was diagnosed in the area. As the patient did not improve after drainage of the abscess and antibiotic therapy with amoxicillin-clavulanate for seven days, she was hospitalized due to sepsis. On physical examination, a 6×6-cm abscess in the anterior and proximal region of the right tibia was evidenced, accompanied by hyperemia and increased local temperature. It drained a large quantity of a brownish-yellow secretion through a 1-cm micropuncture. Areas of alopecia on the scalp with diameters of up to 4 cm were observed. Lung examination showed only "Velcro-like" crackles in both bases.

At that moment, the patient met criteria for disease activity and had systemic lupus involvement as follows: oral ulcers; photosensitivity; hemolytic anemia (hemoglobin: 10.6 g/dL and positive direct Coombs test); thrombocytopenia (74,000/mm$^3$); homogeneous ANA (1:1280); positive anti-DNA antibody (1:20); lymphocytopenia (362/mm$^3$); C4 consumption = 0.7 mg/dL (9–36 mg/dL); positive lupus anticoagulant antibody (2.54); and positive anticardiolipin IgM (11.2). For investigating bone infection, plain knee radiography was requested, and resulted normal. Radiography was supplemented by MRI, which evidenced bone marrow edema in the tibia consistent, through clinical correlation, with an infectious process.

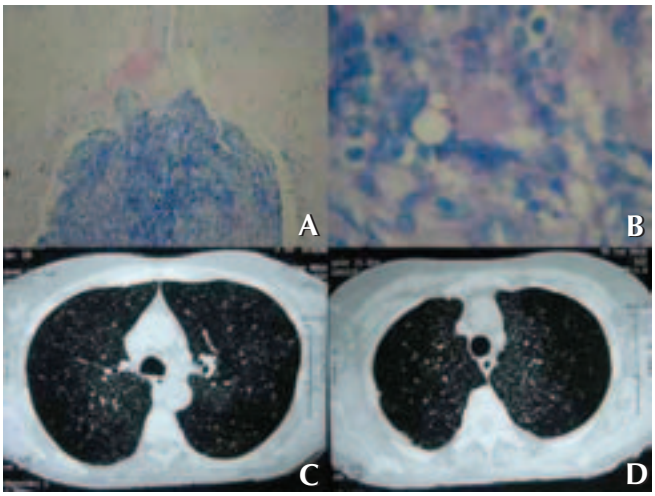


**Figure 1**
**(A)** Photomicrography (PMG) showing bone trabecula and caseous necrosis area. Original magnification x40, Ziehl-Neelsen staining. **(B)** PMG confirming the presence of *M. tuberculosis*. Original magnification x1,000, Ziehl-Neelsen staining. (**C** and **D**) Chest CT scan showing reticulo-micronodular interstitial lung infiltrate.

The patient underwent surgery, but no secretion was found during the procedure, only fragile bone structure. The histopathological study of the bone fragment demonstrated caseous necrosis granuloma, and the Ziehl-Neelsen staining confirmed the presence of *M. tuberculosis* (Figure 1 A and B). The plain chest radiography showed a reticulo-micronodular interstitial lung infiltrate, which was confirmed on chest CT scan (Figure 1 C and D). Sputum bacilloscopy was negative. Bronchoscopy with bronchoalveolar lavage was then performed, and the culture was positive for *M. tuberculosis*.

The patient was treated with oxacillin for 35 days because of the growth of oxacillin-sensible *Staphylococcus aureus* in biopsy culture specimen from the tibial abscess (secondary infection). In addition, the patient also received the quadruple regimen for tuberculosis (isoniazid, pyrazinamide, rifampicin and ethambutol) after diagnostic confirmation, on the 14$^{th}$ day of hospitalization. She also had her prednisone dosage increased to 60 mg/day, aiming at stopping the systemic manifestations of SLE, mainly thrombocytopenia. The outpatient clinic follow-up showed a good evolution, with weight gain and control of the tuberculosis and systemic manifestations of

SLE, except for thrombocytopenia. After four months of treatment, the reduction in the prednisone dose to 40 mg/day was initiated, and the use of the therapeutic regimen for tuberculosis was programmed for at least one year.

## DISCUSSION

Prevalence of tuberculosis in lupus patients is described as 3.6%–11.6% of the cases.[2] Hodkinson et al.[1] have reported an osteoarticular involvement in 32.1% of their patients with extrapulmonary disease, 10% of whom showed miliary tuberculosis, similarly to the present case.[1] Mok et al.[5] have reported osteomyelitis in 8.3% of those patients, with a recurrence rate of infection by *M. tuberculosis* of 1.66%, regardless of prophylaxis with isoniazid, and, differently from the present case, lung tuberculosis did not recur as extrapulmonary disease.[5] Wu et al.,[6] in their series of 11 lupus patients with osteomyelitis, have found *M. tuberculosis* as the etiological agent in 9.09% of the cases.

Our patient had the following predisposing factors for tuberculosis infection/reactivation: chronic use of prednisone and SLE activity (pancytopenia, C4 reduction and positive anti-DNA antibody).[2–5] As reported in the literature, MRI was important only to define the bone involvement not evidenced on plain radiography, and the etiological diagnosis was established by use of bone biopsy.[7]

The nonspecific clinical and imaging findings, from the etiological point of view, delayed the beginning of therapy by 1.5-month, a short period compared to that in the literature (11 months, on average).[1] That can be justified by the strong suspicion of a *M. tuberculosis* infection due to our patient's history of previous tuberculosis infection and the changes found on her lung imaging. In addition, the concomitant *S. aureus* infection corroborates the hypothesis of the *M. tuberculosis* tropism for previously injured sites,[1,6] indicating that, in SLE patients, that etiology should be investigated even in the presence of a previously isolated agent from culture. Some authors[1] state that macrophages that phagocytize *M. tuberculosis* at the primary site of infection (usually lungs) migrate by use of chemotaxis to the injured site, justifying such tropism.[1]

In conclusion, bone tuberculosis, although rare, should always be considered as a differential diagnosis in SLE patients with osteomyelitis. In addition, tibial MRI supported the indication for the invasive treatment of the region, and the strong clinical suspicion led to time reduction between symptom onset, diagnosis and suitable therapy.

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