



# Enfermedades Infecciosas y Microbiología Clínica

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## Scientific letter

### Tuberculosis on joint prosthesis as a form of presentation of miliary tuberculosis



#### *Tuberculosis sobre prótesis articular como forma de presentación de una tuberculosis miliar*

Joint tuberculosis is a rare form of infection among the causes of musculoskeletal and extrapulmonary tuberculosis. Diagnosis and treatment can be complicated, especially in elderly patients. The case we present is evidence of this.

This was the case of an 82-year-old woman with a history of myasthenia gravis treated with 10 mg of prednisone and pyridostigmine who underwent bilateral hip replacement surgery in 2018 (due to avascular necrosis) and 2020.

She initially consulted due to constitutional syndrome with weight loss of 10 kg in a year, along with low back pain and a two-month history of disabling bilateral coxalgia. Initial blood tests revealed slightly elevated LDH levels of 284 U/l, haemoglobin of 10.3 g/dl with normal mean corpuscular volume and C-reactive protein of 146 mg/dl. A chest X-ray was performed, which revealed a bilateral miliary pattern, as well as a Mantoux test, which was negative. On admission, the general condition of the patient was good, despite exhibiting a low-grade fever of 37.3°C. With one of the initial diagnostic suspicions being giant cell arteritis/polymyalgia rheumatica, a positron emission tomography-computed tomography (PET-CT) scan was first requested (Fig. 1), which revealed pathological uptake suggestive of granulomatous involvement (lymphadenopathy in multiple territories, lung with miliary pattern, lumbar vertebrae and both hips).

Since the Mantoux test can produce false negatives in multiple scenarios, some of which were present in our case (disseminated tuberculosis, chronic treatment with corticosteroids, or old age), an interferon gamma release assay (IGRA) test, smear microscopies and PCR were requested on *Mycobacterium tuberculosis-complex* in sputum, all three being positive (our microbiology laboratory did not inform us about the quantification of the smear microscopy). Subsequently, a hip puncture was performed, obtaining positive joint fluid smear microscopies, confirmed with culture, as well as in sputum, leading to the diagnosis of miliary tuberculosis with pulmonary, lymph node and osteoarticular involvement. To complete the study, HIV serology was requested and was negative. We did not obtain data on previous vaccination against tuberculosis. A study of resistance to tuberculostatics was carried out, with susceptibility to all first-line drugs. Treatment was started with isoniazid, rifampicin, pyrazinamide and ethambutol, which had to be discontinued due to gastrointestinal and hepatic toxicity, finally carrying out induction treatment for two months with isoniazid, ethambutol, linezolid and levofloxacin, subsequently continuing with isoniazid and ethambutol.

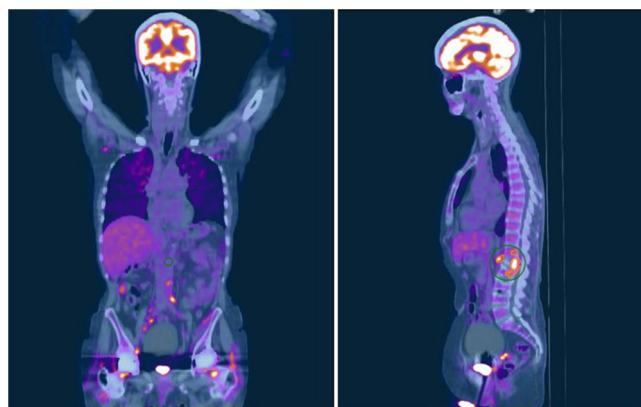


Figure 1. PET-CT coronal and sagittal slices, respectively.

One month after the start of medical treatment, resolution of the fluid collection of the left iliacus muscle was confirmed by computerised axial tomography (CT). Three months later, a chest X-ray was performed, with disappearance of the pulmonary miliary pattern. The smear microscopies and the sputum culture for mycobacteria were repeated, all of which were negative, and cure was confirmed after completing the induction treatment.

Musculoskeletal tuberculosis occurs in 10%–35% of cases of extrapulmonary tuberculosis.<sup>1</sup> Active disease can develop immediately after contagion, or, more commonly, as reactivation. Risk factors are immunodeficiencies and multiple comorbidities, especially the use of corticosteroids and immunomodulators. The route to infection of the bone is normally haematogenous, although cases of contiguous infection have also been described, via the lymphatic system or by percutaneous inoculation, as occurs in joint prosthesis surgery and osteosynthesis.<sup>2</sup>

When tuberculosis infects prosthetic joints, it typically manifests with pain, synovitis and occasionally drainage from the affected joint. Latent infections can lead to the formation of abscesses, or to a constitutional syndrome with anorexia, weight loss, asthenia and night sweats, as in our case.

For diagnosis, elevation of acute phase reactants, CT, nuclear magnetic resonance or the increasingly used PET-CT can be helpful. Definitive diagnosis will be by culturing the biopsy in mycobacterial media and identifying acid-and alcohol-fast bacilli in smear microscopy.<sup>3</sup>

Neither the best therapeutic pharmacological regimen nor its duration for this form of tuberculosis have been clearly established, since it is such a rare entity. Surgical management for infections of joint prostheses is hotly debated, since the ability to adhere and form biofilm is lower than that of other bacteria that cause infections of this type.<sup>4</sup>

This case is of interest due to its rarity, since it is a tuberculosis infection on a hip joint prosthesis, for which our patient had also

undergone surgery shortly before the onset of the clinical signs and symptoms. In the literature, the description of this type of infection is limited to very small case series, with the largest of them having 13 patients.<sup>4</sup>

The most common and probable aetiopathogenic mechanism is the reactivation of a latent tuberculosis infection or post-primary tuberculosis with haematogenous spread to the joints and lymph nodes in relation to immunosuppression by corticosteroids. However, trauma surgery could have been the cause of the local reactivation of tuberculosis due to the rupture of granulomas with subsequent dissemination to the lung.

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Raquel Moya Megías<sup>a,\*</sup>, Concepción Fernández Roldán<sup>b</sup>,  
Judith Constán Rodríguez<sup>b</sup>, María Rosario Javier Martínez<sup>b</sup>

<sup>a</sup> Servicio de Medicina Interna, Hospital Universitario Virgen de las Nieves, Granada, Spain

<sup>b</sup> Unidad de Enfermedades Infecciosas, Hospital Universitario Virgen de las Nieves, Granada, Spain

\* Corresponding author.

E-mail address: [raquelmoyamegias@gmail.com](mailto:raquelmoyamegias@gmail.com) (R. Moya Megías).

<https://doi.org/10.1016/j.eimce.2023.04.013>

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## Infectious spondylodiscitis by *Serratia marcescens*: A diagnostic challenge



### Espondilodiscitis infecciosa por *Serratia marcescens*: un reto diagnóstico

Infectious spondylodiscitis (ISD) is aetiologically classified as pyogenic/bacterial, granulomatous (tuberculous, brucellar and fungal) or parasitic.<sup>1</sup> The most common route of dissemination in bacterial ISD is haematogenous, it is usually monomicrobial and is preferentially located at the lumbar level (58%).<sup>2</sup> Its incidence is increasing due to the greater number of susceptible patients: advanced age, spinal surgery, immunosuppression and use of intravascular and urinary devices.<sup>3</sup> There is a significant delay in its diagnosis due to the non-specificity of the symptoms, often with low back pain as the only symptom.

We present a case of ISD due to *Serratia marcescens* as a complication of a nosocomial urinary infection in a patient with a catheter.

A 76-year-old hypertensive woman on diet therapy suffered an acute ischaemic stroke during her holiday in another autonomous community and was admitted to the nearest referral hospital. One month after admission, during her hospital stay, she presented with bacteraemia of urinary origin (bladder catheter user) due to *S. marcescens* isolated in urine and blood cultures. We do not know which antibiotic therapy she received or its duration.

She was transferred to a neurological rehabilitation centre in our community. Thirty days later, she again presented with bacteraemia due to *S. marcescens* of unknown origin. Endocarditis was ruled out by transthoracic and transoesophageal echocardiograms and she was treated with intravenous ertapenem for 14 days. After four months, she began to experience low back pain radiating to the left leg that did not subside with analgesic treatment. An MRI was performed with findings consistent with ISD (L5-S1). She was admitted to the infectious diseases department of our hospital for aetiological study and treatment. Three CT-guided biopsies were obtained, whose aerobic/anaerobic/prolonged culture in enrichment medium/mycobacteria and 16S rRNA gene PCR were negative. During admission, serial blood cultures were obtained with negative results.

After eight weeks on empirical broad-spectrum antibiotic therapy, which consisted of combined intravenous therapy of cefepime and daptomycin, she did not exhibit clinical improvement, and the MRI revealed radiological deterioration (Fig. 1). It was decided to perform an open surgical biopsy, and nine samples were sent to our microbiology service.

The direct aerobic/anaerobic culture was negative in the nine samples. Growth was observed after five days in the enrichment medium (BD BBL™ Thioglycollate Medium) in only 1/9 samples, which corresponded to a fragment of the L5-S1 disc. In the sub-culture, *S. marcescens* was isolated and identified by MALDI-TOF (Bruker® Daltonics). To rule out the possibility of contamination during sample collection and/or processing, the presence of this microorganism was confirmed using the FilmArray® BCID2 sepsis panel. This technique was performed on biopsy *in situ* after homogenisation with sterilised glass beads and saline solution subjected to vortex mixing. The strain was sensitive to piperacillin/tazobactam, cefepime, carbapenems, aminoglycosides and co-trimoxazole using the BD Phoenix™ M50 antibiogram sys-

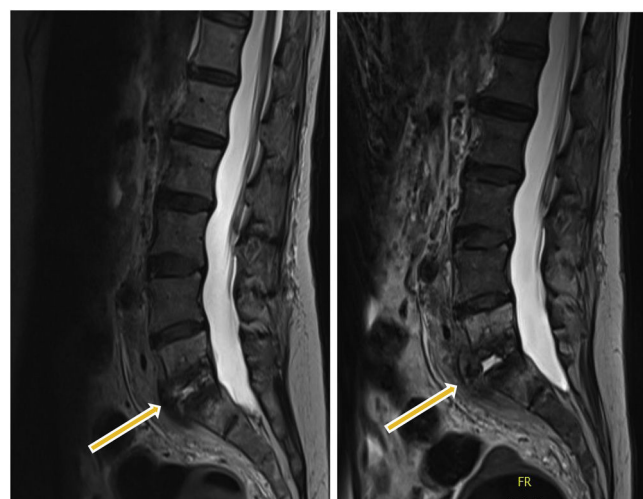


Fig. 1. MRI of the lumbosacral vertebra.