1 **Tuberculosis of the elbow: A rare form of presentation of extrapulmonary tuberculosis.**

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12 Osteoarticular tuberculosis (OTB) remains a major diagnostic and management
13 challenge. Globally, OTB accounts for 2.2–4.7% of all tuberculosis cases in Europe and
14 the USA (1). The most frequent form of OTB is tuberculous spondylitis or Pott's
15 disease, followed by osteomyelitis (2). Tuberculous (TB) arthritis, less frequent, mainly
16 affects large weight bearing joints, such as the hip and knee, being the elbow
17 exceptionally affected.

18 We present a case of a 53-year-old Spanish man who was admitted to the
19 emergency department with a 12 years history of pain and swelling of his right elbow
20 which had worsened over the last six months. He denied previous injury and had no
21 underlying disease. He had received corticosteroid infiltrations, last time two months
22 before consulting. Physical examination revealed inflammation of the posterolateral
23 region of the right elbow with associated distal paraesthesia, wrist drop and complete
24 inability to extend the wrist and move the fingers.

25 On admission, he was afebrile and acute-phase reactants were slightly elevated.
26 The chest X-ray was completely normal. The ultrasound image of the elbow showed

discrete articular effusion and thickening of the articular capsule with hairy and nodular projections. Magnetic resonance imaging showed bone destruction with severe subchondral erosions. Under suspicion of pigmented villonodular synovitis, a biopsy was performed for anatomopathological study, which reported chronic synovitis with necrotizing granulomas and no hemosiderin or malignancy features. *Mycobacterium tuberculosis* (MTB) DNA was detected without mutations in the genes associated with resistance to first and second line antituberculous drugs (ANYPLEXTM II MTB Detection/MDR/XDR, Seegene). Ziehl-Neelsen stain of the biopsy was positive. Latent tuberculous infection was confirmed with both the tuberculin skin test and the IFN- γ release assay (Quantiferon-TB Gold[®]). Treatment with isoniazid (INH), rifampicin (RIF), ethambutol (EMB) and pyrazinamide (PZA) was started for four months and reduced to INH and RIF for 14 months. After 10 days of treatment, the patient reported a transitory increase of the pain and swelling followed by drainage of semi-liquid caseous material, concordant with fistulization, through the puncture site of the elbow. By then, the liquid medium culture (BD MGIT 960) of the biopsy was positive (10 days). Growth on the solid medium (Löwestein-Jensen) was observed after 14 days of incubation. Isolated non-chromogenic mycobacteria were identified as *M. tuberculosis* by PCR and reverse hybridization (GenoType MTBC, HAIN Lifescience). Susceptibility to first line anti-TB drugs was confirmed by culture in Middlebrook (BD MGIT 960). Whole Genome Sequencing (WGS) of the *M. tuberculosis* strain (Nextera XT protocol and Illumina MiSeq platform) showed no resistance-related mutations and was identified as Lineage 4.10/PGG3, one of the most recently described sublineages within the globally distributed Lineage 4 (3).

The patient progresses favorably a year after treatment completion, with decreased inflammation, resolution of the fistula and recovery of the elbow motility

with complete flexion and extension of the right wrist.

OTB follows a progressive course of several months, developing fistulous paths from the cartilage to the skin surface when the infection is advanced. Fever or systemic symptoms are infrequent. Acute-phase reactants are often raised, but levels are lower than those seen in pyogenic vertebral infections (1). Differential diagnosis includes other subacute or chronic infections such as those caused by *Brucella* spp., *Burkholderia pseudomalle* or *Candida* spp. (4), together with local or adjacent tissue tumors. Imaging tests are nonspecific but can help to delimit the extent of soft-tissue and bone affection. Anatomopathological examination of the biopsy of the injury might reveal the presence of granulomas. Given the lack of specificity of the manifestations, clinical suspicion is difficult, and the diagnosis is often delayed with subsequent prolonged therapy needed in some cases (5). After suspicion, MTB growth in conventional culture media takes at least one week in liquid broth and more than two weeks in solid medium (6). Recently developed molecular techniques might accelerate the detection of MTB, with sensitivity in extrapulmonary samples over 75% (7).

In summary, we describe a very rare case of TB arthritis in a Spanish patient with no documented previous history of tuberculosis. Since delay in both early diagnosis and adequate treatment of this condition is associated with high morbidity and risk of severe complications, TB must be considered as part of the differential diagnosis of osteoarticular illness in non-endemic regions.

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