

Osteoarticular tuberculosis in paediatrics: A review of 20 years of cases in a tertiary hospital[☆]



Tuberculosis osteoarticular en la edad pediátrica, revisión de casos en 20 años en un hospital terciario

Dear Editor:

Tuberculosis (TB) is one of the most prevalent infectious diseases worldwide. Paediatric patients are at significantly higher risk than adults of progressing to tuberculosis disease and developing disseminated and extrapulmonary forms of TB. In addition, in recent years we have witnessed an emergence of multidrug-resistant (MDR) strains of *Mycobacterium tuberculosis* (MTB) in Spain, especially in immigrants from highly endemic countries.^{1–3} Extrapulmonary forms of TB, and osteoarticular TB in particular, pose a considerable diagnostic challenge on account of their insidious course and atypical manifestations.^{4,5} Osteoarticular TB amounts to approximately 1–5% of all cases of paediatric TB, and to 10–17% of extrapulmonary TB cases.^{1,4} However, few case series have been published on this form in the literature, and most of these studies were conducted in highly endemic countries.

The aim of our study was to define the characteristics of paediatric osteoarticular TB in Spain. We made a retrospective review of cases of osteoarticular TB diagnosed in patients aged less than 14 years in the Hospital Universitario La Paz over a period of 20 years (January 1996–December 2015). We collected epidemiologic, clinical, radiologic, microbiologic, treatment and outcome data. We considered that skin tuberculin tests were positive when the induration was 5 mm or greater at 48–72 h from the intradermal injection of 2 units of RT-23 tuberculin in 0.1 mL solution (Statens Serum Institut; Copenhagen, Denmark). We entered and analysed the data in Excel (Microsoft; Redmond, USA).

We identified 213 cases of children with confirmed TB, of which 11 (5.2%) presented with osteoarticular involvement. This presentation was the third most frequent following pulmonary TB (132 cases, 62%) and tuberculous lymphadenitis (41 cases, 19%). Of the 11 patients with osteoarticular involvement, 4 (36.4%) received a diagnosis of spinal TB (3 dorsal, 1 lumbar); 5 (45.4%) of articular TB (2 in the knee, 1 in the hip, 1 in the ankle, and 1 with polyarticular TB with hip, knee and shoulder involvement); and 2 (18.2%) of isolated osteomyelitis (1 in the femur, 1 in the mastoid process). Five cases (45%) presented with concomitant pulmonary involvement. The male to female ratio was 1.2:1, and the mean age at diagnosis was 5.3 ± 3.6 years. The median delay in diagnosis was 12 months (range, 2 weeks–3

years). The most frequent reason that led to suspicion of TB was the presence of characteristic findings on magnetic resonance (bone destruction with cold abscesses or synovial hypertrophy) in children of immigrants from countries with a high TB burden (9 patients, 82%). All the patients were immunocompetent. The investigation of contacts identified the index case in 4 patients (36.4%) and relatives with latent tuberculosis infection in 5, and was negative in 2.

The most frequent presenting symptom was functional impairment (64%) accompanied by pain in 45% of cases, and fever in 36% of cases. All patients had a positive tuberculin skin test. The presence of *M. tuberculosis* was confirmed in 82% (9/11): 2 in joint fluid (PCR and culture) and 7 in a synovial, bone or perilesional abscess biopsy specimens (1 by culture, 6 by PCR and culture), with the additional detection of growth in the gastric aspirate culture of 2 of these patients. The most frequent radiologic findings were bone destruction (82%), cold abscesses (36%) and synovial hypertrophy (27%). Two strains of MDR-MBT were isolated, both in children born in Spain but with index cases from highly endemic countries: one patient had travelled to China and stayed with a grandfather that had TB; the other one was living with a Moroccan man that died of the disease.

The duration of treatment ranged from 9 to 12 months, except in patients with MDR strains, who were treated for 24 months. One boy needed to switch treatments due to acute drug-induced liver failure. Forty-five percent of patients required surgical intervention (3 to drain the lesion, 2 to stabilise the joint). Forty-five percent developed sequelae in the long term: 3 patients developed kyphosis, 1 leg-length inequality and 1 limited mobility.

In our case series, paediatric osteoarticular TB was the third most frequent form of disease presentation, which was similar to what has been described in the literature.¹ We would like to highlight the diagnostic delay and the high percentage of children that required surgical intervention and had sequelae in our study. These findings underscore the importance of including tuberculosis disease in the differential diagnosis of osteoarticular lesions with a slow course, accompanied by pain or with prolonged functional impairment, even in the absence of fever, and especially in immigrant children or children in contact with immigrants from highly endemic countries.¹ Furthermore, the prevalence of MDR-MBT is higher in these patients, so it is essential that adequate samples are collected to take advantage of the available molecular diagnostic techniques for the early detection of drug resistances.

References

1. Santiago B, Blázquez-Gamero D, Baquero-Artigao F, Ruiz-Contreras J, Bellón JM, Muñoz-Fernández MA, et al. Pediatric extrapulmonary tuberculosis: clinical spectrum, risk factors and diagnostic challenges in a low prevalence region. *Pediatr Infect Dis J.* 2016;35:1175–81.
2. Del Rosal T, Baquero-Artigao F, García-Miguel MJ, Méndez-Echevarría A, López G, Aracil FJ, et al. Impact of immigration on pulmonary tuberculosis in Spanish children: a three-decade review. *Pediatr Infect Dis J.* 2010;29:648–51.
3. Santiago B, Baquero-Artigao F, Mejías A, Blázquez D, Jiménez MS, Mellado-Peña MJ. Pediatric drug-resistant tuberculosis in Madrid: family matters. *Pediatr Infect Dis J.* 2014;33:345–50.

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4. Enache SD, Pleșea IE, Anușca D, Zaharia B, Pop OT. Osteoarticular tuberculosis—a ten years case review. *Rom J Morphol Embryol.* 2005;46:67–72.
5. Eisen S, Honywood L, Shingadia D, Novelli V. Spinal tuberculosis in children. *Arch Dis Child.* 2012;97:724–9.

María José Pérez Durán^{a,*}, Bárbara Moreno Sanz-Gadea^a,
Teresa del Rosal Raves^b, María José Mellado Peña^b,
Fernando Baquero-Artigao^b

^a Hospital Universitario La Paz, Madrid, Spain

^b Servicio de Pediatría-Enfermedades infecciosas y Tropicales, Hospital Universitario La Paz, Madrid, Spain

* Corresponding author.

E-mail address: mjopduran@gmail.com (M.J. Pérez Durán).
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Description of an isoniazid-resistant tuberculosis outbreak in a block of apartments[☆]



Descripción de un brote de tuberculosis resistente a isoniácida en una comunidad de vecinos

Dear Editor:

Drug resistance is an additional difficulty in the diagnosis and treatment of tuberculosis (TB). A rate of isoniazid (H) resistance of up to 9.6% has been reported in children in Spain.¹ We present data on an outbreak of isoniazid-resistant TB, with emphasis on contact tracing and the diagnostic and treatment characteristics of paediatric cases.

The index case was a man aged 39 years with active laryngeal TB and pulmonary cavitation that cared for children in an apartment block. He was isolated in the hospital from the moment of diagnosis and treated with H, rifampicin (R), pyrazinamide (Z) and ethambutol (E). Seven weeks later, resistance to H was confirmed (S315T mutation in the *katG* gene), so H was discontinued and streptomycin (S) and moxifloxacin added to the regimen. The patient suffered a tendon rupture that led to discontinuation of moxifloxacin, and eventually completed 12 months of treatment.

The contact tracing involved performance of a tuberculin skin test (TST) that was repeated 2 months later in individuals with indurations of less than 5 mm. Children aged up to 14 years underwent a QuantiFERON[®] test (Cellestis, Victoria, Australia) and chest radiograph (CXR). Contacts with a TST induration of 5 mm or greater and normal CXR underwent ultrasound examination of the mediastinum to assess for potential lymphadenopathies not visible in CXR. Lymph nodes greater than 1 cm considered abnormal.

The investigation comprehended 16 adults and 15 children. None of the contacts were immigrants or had been vaccinated with BCG. Six children had indurations of 0 mm (Table 1) and were treated with H for primary chemopro-

phylaxis until the second TST, and this was negative in all of them.

Eight children with an induration of 5 mm or greater and a normal chest CXR received a diagnosis of latent tuberculosis infection (LTBI) and started HR treatment until resistance to H became known, eventually completing 6 months of R (6 R). One of them presented with subcarinal adenopathies of 2.3 cm in diameter on mediastinal ultrasound examination, but received a diagnosis of and treatment for LTBI per this study protocol. This patient remained asymptomatic and the lymphadenopathy was no longer visible on ultrasound after 4 months of treatment. One girl developed asymptomatic hypertransaminasaemia, which resolved with the discontinuation of treatment followed by its gradual reintroduction. One adolescent did not adhere to treatment repeatedly, and eventually completed 5 R.

The QuantiFERON[®] test was negative in children without infection and positive in children with LTBI, except for 1 girl aged 8 years with an induration of 17 mm in the TST and close contact with the index case.

One boy aged 4 years with an induration of 20 mm and adenopathies on CXR received a diagnosis of tuberculosis disease (TBD) and started treatment with HRZE. His samples were negative, and after H resistance in the source case became known, completed 6 RZE. He was followed up at the clinic one year after he finished the treatment.

Of the adults that were investigated, 10 had a positive result in the initial TST and 1 more had a positive result in the second test. All had normal CXR, received a diagnosis of LTBI and were treated with a 4 R regimen.

The rate of isoniazid resistance in Spain is greater than 4%, so induction treatment of TBD should include 4 drugs unless it is known that the strain is sensitive to H.² The recommended regimens for isoniazid resistant TB are 6–9 RZE, 2 RZES/7 RE or 2 RZE/7–10 RE, with the possible addition of a quinolone the first 2 months.^{3,4} The boy with TBD in our study started treatment with 4 drugs and only completed 6 months of RZE, since Z was used throughout the treatment and due to the low bacillary population in the patient.

In our unit, we use the 3 HR regimen for LTBI, which shortens the duration of treatment, improves adherence and covers the possibility of H resistance from the beginning of treatment. Cases with documented resistance to H require a 4–6 R regimen.^{3,5}

Six children were treated ineffectively with H for primary prophylaxis, as the resistance to H was unknown at the time, but fortunately the results of the second TST were negative in all.

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