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CASE SERIES

Diagnostic Challenges in Patients with Osteoarticular Tuberculosis in Mexico: Case Series

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ABSTRACT

Introduction: Osteoarticular tuberculosis poses a significant diagnostic and therapeutic challenge in developing countries, where the absence of molecular tools demands reliance on clinical suspicion and histopathological findings for diagnoses. Here, we present a compilation of case studies on osteoarticular tuberculosis for academic reference and support to aid primary care physicians in providing the best possible patient care.

Methods: Retrospective analysis of cases diagnosed with osteoarticular tuberculosis through biopsy from 2010 to 2020 at a Mexican Traumatology and Orthopedics Hospital, examined using descriptive statistics.

Results: Thirty-three patients were registered: 23 men (70%) and 10 women (30%). The most affected regions included the spine in 28 cases (84%), the hip in 3 (9%), and the elbow and sternoclavicular joints in 1 case each. The main clinical manifestations were paravertebral abscesses in 16 patients (48%), discitis in 12 (36%) and arthritis in 5 (15%), while the primary associated diseases were immunosuppression in 8 cases (24%), 2 cases with hepatitis (6%) and 3 with hypertension (9%).

Discussion: Tuberculosis is endemic in Mexico, similar to other developing countries, with numerous reported cases of osteoarticular tuberculosis. This study highlights the importance of using alternative diagnostic tools when molecular tests and cultures are not accessible to general practitioners and orthopedic physicians who treat patients with clinical suspicion of osteoarticular tuberculosis.

Introduction

In 1993, the World Health Organisation recognised that tuberculosis infects one-third of the world's population, with most cases occurring in developing countries.[1] Globally, Mexico has been considered an endemic country for tuberculosis; in 2015, approximately 20,561 new cases were diagnosed, with the highest prevalence in the northern border states of the country.[2-4]

According to the World Health Organisation, extrapulmonary infections correspond to 15% of the diagnosed world population, while osteoarticular tuberculosis represents 3%–5%. In Mexico, 18.5% of new tuberculosis cases corresponded to extrapulmonary tuberculosis and 11.3% to osteoarticular tuberculosis.[2] It is important to highlight that the reported cases of tuberculosis and extrapulmonary tuberculosis and its occurrence fluctuate in regions worldwide. As a result, varied methodologies for the diagnosis are necessary in different geographical regions.[5]

Although osteoarticular tuberculosis causes 450 cases annually in Mexico, scientific data on this subject is practically non-existent. This finding represents a significant challenge for first-level physicians in its diagnosis, mainly due to the limitation of molecular diagnostic tools for this type of tuberculosis, making empirical treatment a common practice based on clinical and imaging findings.[6]

This approach in endemic regions relies on the assumption of enhanced clinical expertise resulting from a high patient volume, the ready accessibility of imaging tools such as radiographies, tomography and magnetic resonance imaging (MRI) linked to limited laboratory resources as Polymerase Chain Reaction (PCR), and delayed culture and drug sensitivity outcomes. In this way, in Mexico as in other countries, clinical experience and tomography and RMI, are the only ways to diagnose extrapulmonary tuberculosis and the therapeutic test is commonly used to confirm the diagnosis.[7]

The study aims to describe the primary manifestations of osteoarticular tuberculosis in patients treated at a High Specialty Traumatology and Orthopedics Hospital in Monterrey, Mexico, during the last 10 years. Additionally, we sought to demonstrate the need to use alternative diagnostic and treatment tools for patients with osteoarticular tuberculosis in countries with limited access to molecular diagnostic tools.

Methods

A retrospective, cross-sectional, and descriptive study was carried out from October to November 2020 at the Traumatology and Orthopaedics High Specialty Medical Unit No. 21 in Monterrey, Mexico, where patients entitled to the Mexican Social Security Institute of five northeastern states of Mexico (Tamaulipas, Nuevo León, Coahuila, San Luis Potosí and Zacatecas) receive health attention.

A census study aimed to examine the clinical records of patients diagnosed with osteoarticular tuberculosis between 2010 and 2020. Patients with a clinical diagnosis of osteoarticular tuberculosis and who presented histopathological data compatible with this disease were included, according to the World Health Organisation diagnostic criteria for tuberculosis, which mention: a) presumptive tuberculosis when there is clinical suspicion of the disease, b) clinically confirmed tuberculosis when there is clinical evidence of tuberculosis and treatment is decided based on clinical diagnosis and finally, c) bacteriologically confirmed tuberculosis when the presence of the bacillus is confirmed by smear, culture or rapid test (WRD such as Xpert MTB/RIF).[8]

In this study, eligibility for osteoarticular tuberculosis cases was contingent upon the presence of clinical data on tuberculous disease and meeting at least three of the following criteria: mononuclear infiltrate, epithelioid cells, giant cells, granuloma formation, caseous necrosis, and positive Ziehl–Neelsen staining. The finding of stained bacilli was not taken as the primary standard since most biopsies were taken from tissue with significant damage and caseous necrosis, finding few or no bacilli in the affected area. We consider these cases clinically confirmed and not bacteriologically confirmed tuberculosis, as no sputum smears, cultures, or rapid tests were available.

The clinical records of 33 patients were recovered, of which 23 were male (70%) and 10 female (30%). Data were collected in an Excel database and grouped according to their characteristics using descriptive statistics. The variables included were the reason for consultation, lesion location, sex, age group, and presence of co-morbidities. The variable reason for the consultation was nominal qualitative; the variable at the injury site was nominal qualitative according to the affected site; gender was a dichotomous variable with the male: female scale. The age groups considered were 0–9, 10–29, 30–49, 50–69 and 70–89 years. The co-morbidity variable was initially qualitative binomial; first, with a yes/no question to suffer or have suffered diseases that compromise the immune

system, such as diabetes, infection by human immunodeficiency virus (HIV), hepatitis, and cancer. Additionally, the co-morbidity variable was included as a nominal qualitative variable.

All variables were measured according to the proportions of the presence of the variable against the total number of patients. The percentages were calculated by multiplying the proportions by 100. As this is a descriptive study, there are no hypothesis contrasts.

Results

Twenty-three males (70%) and 10 females (30%) were registered. Additionally, 45% of the cases were in the age group between 30 and 49 years, followed by seven patients (21%) aged between 60 and 69 years. The average age was 44.21 ± 6.45 years. The age range was between 1 and 78 years. Associated diseases occurred in 13 of the patients (40%); among them, 8 patients had immunosuppression (24%), 6 had diabetes (18%), 2 had HIV (6%), another 3 patients had arterial hypertension (9%) and 2 more had hepatitis (6%). It is important to note that 20 patients (60%) did not present any associated disease, and only 10 patients (30%) of the total mentioned had suffered from pulmonary tuberculosis.

The primary location of osteoarticular tuberculosis cases was in the spine (Pott's disease) in 28 cases (85%; Figure 1), of which the thoracic spine was affected in 22 patients (67%) and the lumbar spine in 6 (18%). Furthermore, three cases involved damage to the coxofemoral region (9%), one to the elbow (3%), and another to the sternoclavicular joint (3%). Among the main clinical manifestations, abscesses were found in the spine in 16 cases (48%; 14 vertebral [42%] and 2 in the hip bone [6%]), as well as discitis and vertebral osteomyelitis in 12 cases (36%) and arthritis in 5 patients (15%), of which 3 (9%) had hip arthritis, elbow arthritis (3%) and finally sternoclavicular joint arthritis (3%).

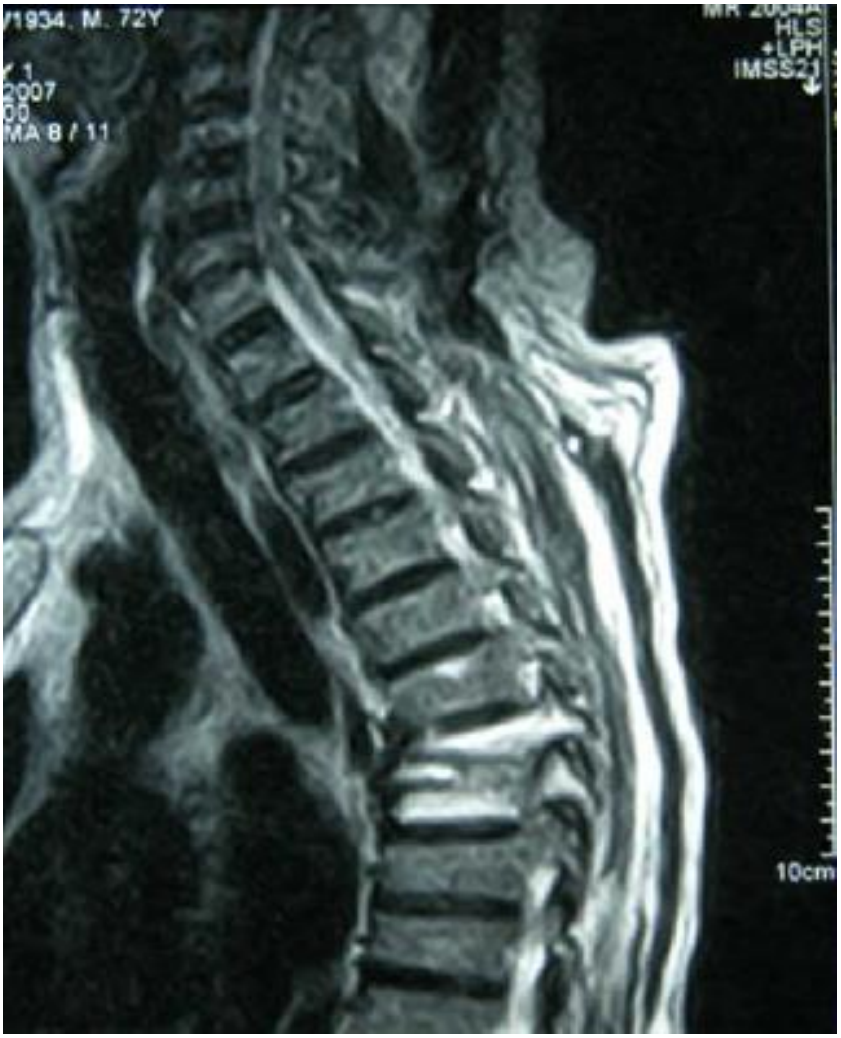

Figure 1. Lateral view magnetic resonance imaging of a 72-year-old male patient with osteoarticular tuberculosis at T8-T9.

All cases received medical treatment, as shown in Table 1. Epidemiological specialists from the Mexican Social Security Institute's Traumatology and Orthopaedics High Specialty Medical Unit No. 21 conducted the patient follow-up. Patients underwent a bone tissue biopsy for diagnosis, processing it with Ziehl–Neelsen staining: each tissue sample of each patient was cut with a thickness of 1 mm on a microtome, fixed with 10% formaldehyde solution 10%, deparaffinised and hydrated with xylol, and subsequently stained with fuchsin, bleached, contrasted with methylene blue, washed with distilled water and finally dehydrated to be seen under the microscope. Additionally, some patients received specialised surgical treatment according to the location of the lesions: spinal instability in 17 patients (51%), paravertebral abscess drainage in 16 (48%) of them, and arthrotomy and joint drainage in five more patients (15%). After medical (Table 1) and surgical treatment, all patients showed improvement without any casualties.

Table 1. First-line anti-tuberculosis drugs of the Official Mexican Standard for the Prevention and Control of Tuberculosis (NOM-006-SSA2-2013).

DRUG	PRESENTATION	DOSE	
		Pediatric (daily dose mg/kg)	Adults (daily dose)
Isoniazid	100 mg (tablet)	15–300 mg	300 mg
Rifampicin	300 mg (capsule) 100 mg / 5ml (syrup)	15–600 mg	600 mg
Pyrazinamide	500 mg (tablet)	25–40 mg up to 2 g	2 g
Ethambutol	400 mg (tablet)	15–30 mg up to 1.2 g	1.2 g

Discussion

Although Mexico is considered an endemic area for tuberculosis[8], there are thousands of cases of pulmonary tuberculosis and many cases of osteoarticular tuberculosis. However, the lack of molecular diagnostic tools leads to underreporting of cases of osteoarticular tuberculosis. For this reason, we focus on the importance of using alternative diagnostic tools in countries with limited access to molecular diagnosis. Thus, this will enable first-contact physicians to use other instruments along with clinical suspicion to offer a fitting diagnosis and treatment for these patients.

After decades of decreasing the incidence of tuberculosis, in recent years, an increase in the number of cases has been observed, mainly due to poverty, forced displacement of the population, and the HIV epidemic.[9] Currently, the presence of osteoarticular tuberculosis is not limited by the conditions of the patient's immune system or by the socioeconomic stratum to which they belong. Thus, the clinical suspicion of osteoarticular tuberculosis should not be limited to immunocompromised patients or those of low socioeconomic status.

In Mexico, as in other countries, the prevalence of tuberculosis is higher in men than in women.[5] Regarding osteoarticular tuberculosis, the World Health Organisation and other authors do not mention that it occurs more frequently in any given sex.[10] However, some reports have found a higher prevalence in women[11]. In contrast, others report a higher predisposition in men for osteoarticular tuberculosis and women to lymphatic tuberculosis.[12] Consistent with the data reported for pulmonary tuberculosis in Mexico, our findings showed a marked trend in males.[2]

Osteoarticular tuberculosis can appear in any age group. However, it occurs predominantly in people with predisposing factors such as immunosuppression and low socioeconomic status.[13-15] A higher osteoarticular tuberculosis prevalence has been associated with patients with HIV, hepatitis, cancer, and other autoimmune diseases.[15-17] However, other diseases, such as diabetes, predispose to tuberculosis, but not osteoarticular tuberculosis.[18-19] In this study, co-morbidities were present in 40% of patients and immunosuppression in 8 cases (24%): 6 cases (18%) with diabetes, 2 cases (6%) with HIV and 2 cases (6%) with C hepatitis.

Conversely, although tuberculosis is considered a more frequent infection in adults over 50 years of age, osteoarticular tuberculosis reports show a greater predisposition in young people.[10,21-23] In this series, 15 patients (45.5%) were between 30 and 49 years, with another peak of 7 patients (27%) after 60 years, demonstrating that osteoarticular disease is more frequent in young adults and is consistent with previous findings.

Osteoarticular tuberculosis affects the spinal joints most frequently, more than 50% of the time, but it can also occur in the pelvis, femur, hip, and tibia.[24-26] In this study, damage to the load-bearing joints occurred in 93% of cases, affecting the spine in 28 patients (84%) and the hip in 3 more (9%).

There is evidence of a growing trend in the incidence of osteoarticular tuberculosis worldwide.[13,27-28] One potential factor contributing to this global increase is the presence of *Mycobacterium bovis* as the primary causal agent, which exhibits unique transmission mechanisms that make it remarkably resilient to typical antibiotic treatments.[29-31] From this research, it can be inferred that osteoarticular tuberculosis is often under-reported and underdiagnosed due to the lack of diagnostic tools to confirm the presence of mycobacteria bacteriologically.[32]

According to the World Health Organisation parameters, the diagnostic criteria for tuberculosis in patients treated at the Mexican Social Security Institute's Traumatology and Orthopedics High Specialty Medical Unit No. 21 is clinically confirmed since, in most cases, there is no bacteriological confirmation in patients biological samples.[33-34] This finding is considered a limitation of diagnostic confirmation. However, therapeutic success in these patients is considered one of the main contributions to this investigation.

Furthermore, first-contact physicians should consider the possibility of osteoarticular tuberculosis in patients who have or do not have pulmonary tuberculosis, with spinal injuries and with or without weight loss, since in most cases, a delay of up to 4 months could occur in making the diagnosis.[35] Thus, it is crucial to obtain a thorough medical history of patients and begin treatment promptly after establishing a clinical diagnosis, in addition to monitoring patients with pulmonary tuberculosis consistently and those who have co-morbidities such as HIV, diabetes, or hepatitis C. In this series of cases, osteoarticular tuberculosis occurred in up to 60% of the patients in presumably healthy people without predisposing to risk factors or associated diseases. Thus, it is crucial for first-contact physicians to conduct a comprehensive clinical assessment, always considering the potential diagnosis of osteoarticular tuberculosis.

Conclusion

Osteoarticular tuberculosis is a clinical form of tuberculosis, often present in Mexico, and it is common in young men with and without a history of pulmonary tuberculosis, where the most common site of involvement is the spine in the thoracic region. In these patients, the main co-morbidities were immunosuppression, diabetes, HIV infection, and C hepatitis virus infection. The diagnosis was clinically confirmed with support from histopathological data but without bacteriological confirmation, and antifungal therapy satisfactorily resolved all cases.

Osteoarticular tuberculosis treatment based on clinical confirmation supported by histopathological findings appears sufficient and appropriate to Mexico's economic and infrastructural conditions. However, the time to diagnosis can be improved by training primary care physicians to promptly detect the disease, avoiding the loss of time and economic resources with imaging studies and repeated antimicrobial treatments.

Conflicts of Interest Statement

The authors report no conflicts of interest associated with this publication.

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