OSTEOARTICULAR TUBERCULOSIS: HOW OFTEN IS IT MISSED?

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Abstract. This study was carried out to analyze the clinical presentations and outcomes of osteoarticular tuberculosis (OAT) at a university hospital in AlKhobar, Saudi Arabia. A prospective observational study was carried out between 1 January 1998 and 31 December 2007. Patients demographic characteristics were recorded, including age, gender, nationality, clinical manifestation, delay in diagnosis, laboratory results, findings on imaging studies, histological and bacteriological studies of biopsy specimens, treatment modalities, surgical interventions and final outcomes. Fifty-two patients were diagnosed with OAT during the study period. The majority were males (64%), about half were below age 30 years. The mean age at diagnosis was 33 years. There were 32 Saudis (64%), and 18 non-Saudis (36%). Pyrexia, loss of appetite and night sweats were the presenting symptoms in 44, 38 and 36%, respectively. The average time from onset of symptoms to diagnosis was 185 days (7-730 days). On admission, the average erythrocyte sedimentation rate (ESR) was 68 mm/h (4-142). A Mantoux test was performed, in 48 patients the results were positive. The vertebral column was the site of infection in 88% of patients. All patients were managed with standard antituberculous therapy. Forty-two patients (84%) had a favorable outcome.

INTRODUCTION

Tuberculosis (TB) is a major global public health problem leading to morbidity and mortality (Dye *et al*, 1999). Pulmonary tuberculosis is the most common form of the disease and spreads easily among close contacts. However, extrapulmonary organs may be infected. Osteoarticular tuberculosis (OAT) represents between 3 and 5% of all cases of tuberculosis, and between 10 and 15% of extrapulmonary cases (Meier, 1994). Primary OAT has been reported to occur without a history of contacts with TB patients (Vergara-Amador, 2007). OAT can lead to disablility with secondary arthritis, paraplegia and quadriplegia if the diagnosis is not made early and treated appropriately (Resnick and Niwayama, 1988; Zevallos and Justman, 2003). The diagnosis is often delayed due to a low degree of suspicion regarding the disease and the insidious nature of the clinical and radiological presentations (Ellis *et al*, 1993; Al-Saleh *et al*, 1998; Batra *et al*, 2007).

We report here the presentation of OAT cases during the past decade at our teaching hospital, the length of delay in diagnosis and the procedures involved in the diagnosis and the outcomes.

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MATERIALS AND METHODS

We carried out an observational prospective study. The study hospital, King Fahd hospital, is a 475-bed tertiary level care university Hospital in eastern Saudi Arabia. The study was carried out between 1 January 1998 and 31 December 2007. The diagnosis of osteoarticular tuberculosis was based on one or more of the following: a culture positive for *Mycobacterium tuberculosis*, a biopsy showing granulomas with caseating necrosis, or a strong clinical suspicion (concomitant pulmonary tuberculosis or extrapulmonary tuberculosis, and typical imaging studies). The following information was recorded: demographic characteristics including age, gender, nationality, risk factors; clinical manifestations including pain, decline in general health, fever, and neurological abnormalities; laboratory test results including erythrocyte sedimentation rate (ESR), human immunodeficiency virus (HIV) status, white blood cell count (WBC), alkaline phosphatase; findings from imaging studies including plain radiographs, computed tomography (CT), and magnetic resonance imaging (MRI); results from histological and bacteriological studies of biopsy specimens; treatment modalities and duration; surgical interventions and final outcomes.

A favorable outcome was defined as no relapse or functional disability, an unfavorable outcome was defined as a relapse of symptoms due to poor compliance in treatment requiring second-line treatment or eventually responding to treatment.

RESULTS

During the study period 489 patients were admitted with a diagnosis of tuberculous infection. Fifty-two patients were diagnosed with OAT. The demographic data is given in Table 1. The majority of cases were males (61.5%), half of them were below the age of 30 years. The mean age at diagnosis was 33 years (range: 13 to 78). There were 32 Saudis (64%) and 18 non-Saudis (36%). The presenting symptoms are given in Table 2. Thirteen patients presented with paraplegia and quadreplegia. Low-grade fever and night sweats were the most common presenting symptoms, at 42.3% and 38.5%, respectively. Pain was the presenting symptom in 44 patients. The duration of symptoms was from 7 days to 2 years. Nine patients (18%) had a chronic underlying disease (diabetes in 8 patients, and sickle cell anemia in 1 patient). None of the patients were infected with human immunodefi-

Table 1
Demographic data regarding 52 patients with osteoarticular tuberculosis.

Variable	Number (%)
Male	32 (61.5)
Female	20 (38.5)
Age	
13-25	9
26-44	24
45-64	15
65 and above	4

Table 2
Presenting symptoms typical for tuberculous infection in 52 patients.

Symptoms	No. (%)
Fever	22 (42.3)
Night sweats	20 (38.5)
Loss of appetite	19 (36.5)
Neurological deficit	12 (23.1)
Quadreplegia	2 (3.8)
Paraplegia	11 (21.1)

ciency virus. A cutaneous sinus or ulcer was observed in 2 patients (4%). The vertebral column was the most common site of infection in 76.9% of patients (Table 3), the thoracic spine was involved in half the patients.

The average time from onset of symptoms to the diagnosis of OAT was 185 days (7-730 days). On an average, the patient presented 2.9 times (range 1-6) to the hospital with their symptoms before diagnosis, 47 (94%) sought medical advice at least once. On admission, the average erythrocyte sedimentation rate (ESR) was 68 mm/h (4-142), in 96% of patients the ESR was elevated. A Mantoux skin test was performed, 48 patients (43%) had positive test of 10 mm or more. Disc space narrowing was the most frequent radiological finding on plain radiograph (Fig 1). Computerized tomography and magnetic resonance imaging showed bony destruction and spinal and paraspinal abscesses (Fig 2). In patients with severe spinal tuberculosis adjunctive surgical therapy was required in 50%. Forty-six patients underwent biopsies of suspected lesions, either as a primary procedure or secondary to a definitive surgical procedure. Positive histology was found in 32 lesions (70%),

Table 3
Site of osteoarticular infection.

Location	Frequency (%)
Cervical spine	5 (9.6)
Thoracic spine	21 (40.4)
Lumbo-sacral spine	14 (26.9)
Combination (skip)	4 (7.7)
Sacroiliac joint	3 (5.8)
Sternoclavicular joint	3 (5.8)
Knee joint	1 (1.9)
Hip joint	1 (1.9)

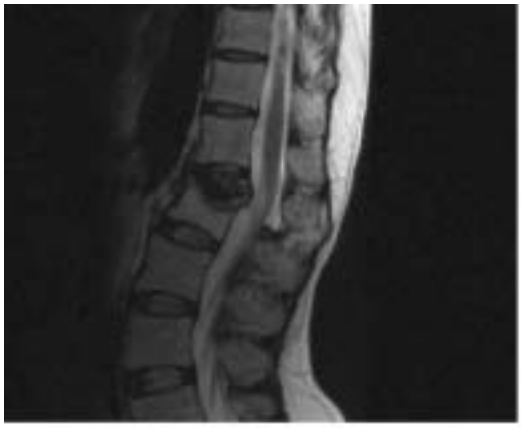

Fig 1–MRI of the lumbar spine showing collapse of the body with narrowing of the spinal canal.

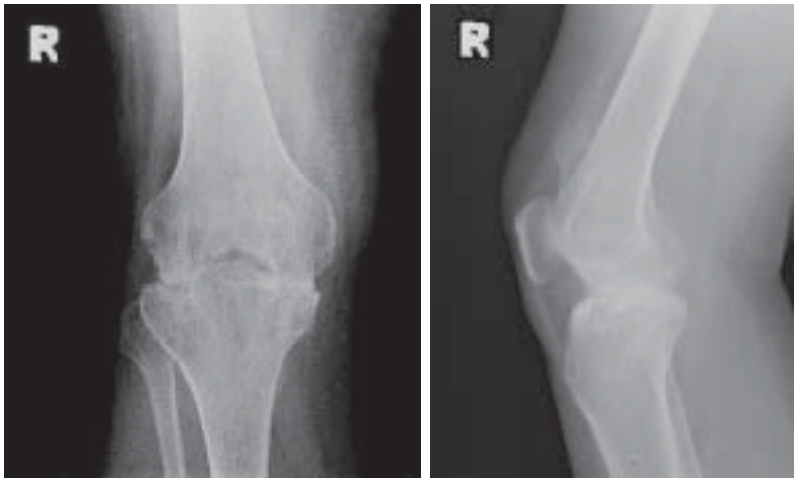

Fig 2–Radiograph of the right knee showing bony ankylosis.

whereas microbiological examinations (mycobacterial cultures and Ziehl-Neelsen stains) were positive in 19 lesions (41%). In the other four patients, tuberculosis was confirmed from other sites (2 from the lungs, one each from lymph nodes and a breast). All patients were managed with standard antituberculous therapy consisting of isoniazid, rifampin, pyrazinamide, and ethambutol during the initial 8-week phase followed by isoniazid and rifampin during the continuation phase.

One patient died after surgery due to acute myocardial infarction. Two patients were lost to follow-up after 3 months of treatment. Forty-two patients (84%) had a favorable outcome, three patients had mild residual neurological deficits and two patients had an unfavorable outcome due to poor compliance with treatment, requiring second line treatment, and eventually responding to treatment.

DISCUSSION

This study shows OAT is common among people living in eastern Saudi Arabia. It represents 10% of all tuberculosis cases diagnosed between 1998 and 2007. This is higher than the average 3-5% reported in the literature (Meier, 1994). Our patients were younger, the vertebral column was the most common site of involvement. The mean age the patients in our study was 33 years, whereas in western countries, patients with OAT are much older (Perronne *et al*, 1994; Alotham *et al*, 2001). Sandher *et al* (2007) reported 44% of patients studied had the spine as the site of infection, lower than in our study (88%). This suggests that patients in Saudi Arabia suffer more from spinal tuberculosis than from other osteoarticular sites. Physicians should have a strong index of suspicion for the diagnosis of tuberculous spondylitis, when patients present with common symptoms such as pain, fever and night sweats to avoid morbidity such as paraplegia or quadriplegia.

The incidence of OAT in some countries has changed remarkably over the years. One study from the United Kingdom (Sandher *et al*, 2007) reported 79 cases in one district in 8 years (9.8 cases/year), Mateo *et al* (2007) reported the incidence of OAT at a university hospital of 53 cases in 22 years (2.4 cases/year). In our study the incidence was 51 cases in 11 years (4.6 cases/year).

Pain in the affected area was the most common symptom (Tuli, 2002); 88% of patients had pain as the presenting symptom. Fifty percent of patients presented with fever, weight loss, night sweats and loss of appetite.

The average erythrocyte sedimentation rate was 68 mm/h, 4% of patients had a normal ESR. Patients presenting with typical symptoms and an elevated ESR should have the diagnosis of OAT considered. In patients with spinal tuberculosis, fine-needle aspiration and percutaneous vertebral biopsy gave an early diagnosis. This agrees with a report that early diagnosis of spinal tuberculosis can be made by obtaining material for biopsy (Pertuiset *et al*, 1999). The median time from onset of symptoms to diagnosis in our study was 185 days, which is better than that reported by Mariconda *et al* (2007) of 216.6 days and that reported by Mateo *et al* (2007) of 240 days. The most important factor in delayed diagnosis was delay by the physician, resulting in multiple visits to a healthcare provider for the same illness. The majority of patients had more than 1 physician visit before diagnosis. Morbidity from tuberculosis is influenced by the time from onset of symptoms until start of treatment (Rodger *et al*, 2003).

The mainstay of treatment for OAT is appropriate antimicrobial therapy. The

American Thoracic Society recommends 6 to 9 months of therapy for patients with drug-sensitive disease (CDC, 2003). All patients in our study were given a minimum of 9 months of anti-tuberculous treatment and monitored closely by an infectious disease unit. Medical therapy alone was given in 25 cases (50%) and in another 25 patients (50%) additional surgical therapy was added, including open biopsy, arthrotomy and joint debridement.

Delay in diagnosis causes delay in treatment allowing the disease to spread more easily. Socio-economic status and lack of education are factors which influence the delay in presentation by the patients. Lack of awareness by physicians adds to further delay. Huong *et al* (2007) rightfully suggested that education of private health care providers should help reduce the delay in the diagnosis of tuberculosis. We believe education of people in general in endemic areas will help in early diagnosis. A comprehensive strategy needs to be developed to reduce the delay in diagnosis so that early appropriate treatment can be given.

In conclusion, our study demonstrates that OAT is not uncommon in young men and women living in Saudi Arabia. Despite the endemicity of tuberculosis, there is often a delay in diagnosis. The non-specific clinical manifestations of the disease and lack of awareness of physicians, contributes to delay in diagnosis, resulting in increased morbidity and permanent disability.

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