Osteoarticular tuberculosis (TB) accounts for 1–5% of all TB cases and 10–18% of those with extrapulmonary infection. Diagnosis is difficult, because the lungs are rarely involved and there are no specific signs or symptoms. The purpose of this study was to assess the frequency and clinical and laboratory findings in osteoarticular TB in two referral hospitals in Tehran, Iran. The hospital dataset of patients admitted with osteoarticular TB during 2003–2005 was reviewed. Patients’ demographic data, clinical presentation and radiological and pathological findings were analysed. Weight loss (50%), fever (36%) and night sweats (38.5%) were the most common constitutional symptoms. Knee, ankle, hip and shoulder joints were the most frequent sites for TB arthritis. In osteomyelitis, long and short bones were equally affected. In TB spondylitis, the lumbar (22.7%) and thoracic (50%) vertebrae were the most commonly involved sites. The most frequently reported complications were sphincter disorder (39.1%), paraplegia (28.9%) and kyphosis (19.3%). TB osteomyelitis must always be borne in mind in countries where TB has high prevalence.

Keywords: Extrapulmonary tuberculosis, Iran, osteoarticular tuberculosis, spondylitis, tuberculosis

Introduction

Tuberculosis (TB) is one of the most important infectious diseases, causing two million to three million deaths annually worldwide. About 20% of patients with active TB have extrapulmonary involvement [1]. Osteoarticular TB accounts for 1–5% of total TB cases and 10–18% of extrapulmonary TB cases [2]. About 19 million to 38 million people suffer from different forms of osteoarticular TB, including spinal TB, arthritis with synovial disease, osteomyelitis, and soft tissue diseases [1].

Confirming the diagnosis of osteoarticular TB is difficult, because there are no specific clinical manifestations and the lungs are not simultaneously involved in most cases. Thus, many patients are misdiagnosed as having other osteoarticular diseases, such as brucellosis, tumour metastases, and rheumatoid arthritis. This delay in diagnosis leads to complications such as joint destruction, spondylitis, and even paralysis [2,3].
culture or pathology in one or more samples (bone biopsy or synovial biopsy) and compatible imaging reports (simple X-ray, computed tomography scan or magnetic resonance imaging).

Age, sex, nationality, clinical manifestations, the time interval between onset of symptoms and diagnosis, the synchronization of pulmonary and extrapulmonary TB, and radiological and pathological findings were recorded. Patients were categorized as having arthritis, spondylitis or osteomyelitis on the basis of radiological presentations and anatomical site.

Data were entered into an SPSS datasheet (version 11.5), and a descriptive analysis was performed. We used an independent two-sample t-test to compare mean differences. Quantitative results are shown as mean ± standard deviation or number (%) if necessary. All statistical calculations were performed with SPSS v. 13. p-Values <0.05 were considered to be significant.

Results

Following review of records of 135 patients diagnosed as having osteoarticular TB, 36 cases with appropriate data were eligible to enter the study. The male/female ratio was 1.12, with the age ranging from 12 to 83 years. The time between the onset of symptoms and final diagnosis was 1–108 months. Table 1 outlines the demographic data of the studied cases. There were 22 patients with TB spondylitis (61.1%), eight with TB arthritis (22.2%), and five with TB osteomyelitis (13.9%). One patient had simultaneous arthritis and osteomyelitis. Just over one-quarter of patients had concurrent pulmonary symptoms. Table 2 shows the patient data according to the type of involvement.

The most frequent general manifestations were pain (90%), weight loss (51.9%), night sweats (38.5%), and fever (35.6%).

The most frequently affected joints were knee (44.4%), hip (22.2%) and ankle (33.3%) joints. Long bones (femur and tibia) and short bones (calcaneus and toes) were equally affected (4.4% each) in TB osteomyelitis. Fistulae were reported in 14% of osteoarticular cases.

In TB spondylitis, the lumbar (22.7%) and thoracic (50%) vertebrae were the most frequently involved sites. Multiple-level skip lesions (combinations) were seen in five cases (22.7%). All of the cases except one were reported to have simultaneous involvement of two or more vertebrae. The most common complications in patients with spondylitis were paraplegia (68%), anal sphincter disorder (41%), and kyphosis (22.7%).

Blood leukocyte counts fell within the normal range in most cases (74.8%). The mean haemoglobin concentration and erythrocyte sedimentation rate (ESR) were 12.1 ± 1.9 g/dL and 57.0 ± 35.7 mm/h, respectively. Articular fluid analysis revealed inflammation and lowered sugar along with an average of 5303 ± 3750 cells/mm³ in the two patients with TB arthritis.

Purified protein derivative (PPD) skin test findings were positive in 16 of 29 patients (41.5%) for whom this test was reported: six cases had arthritis, eight spondylitis, and two osteomyelitis.

Radiological findings suggestive of spondylitis (narrowing of the intervertebral cavity, anterior collapse, wedge-shaped deformity of the vertebra, disk involvement, or paravertebral abscess) were noted in 67.4% of the patients. The most frequent findings in these patients were disk destruction (53.3%), paravertebral abscess (29.6%), wedge formation (19.3%), and cold abscess (3%). Radiological findings consistent with arthritis, including osteoporosis adjacent to joints, osteopathic ero-

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<th>TABLE 1. Demographic information of 36 patients with osteoarticular tuberculosis in the present study</th>
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<th>TABLE 2. Demographic information of 36 patients with osteoarticular tuberculosis in the present study (please note that all percentages are calculated within each disease subgroup)</th>
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sions, and reduction of synovial space, were reported in 20.7% of cases. The formation of new subperiosteal bone and lytic lesions suggestive of osteomyelitis were seen in 8.1% of cases.

Chest radiographic evidence of previous pulmonary TB or compatible changes were reported in 31.1% of patients. Pathological findings supportive of TB (granuloma and caseous necrosis) were reported in 31 patients (86.1%). There were positive tissue cultures in two patients with spondylitis (5%), a positive smear from a paravertebral abscess in one patient (2%), and a positive PCR finding of the synovial fluid and smear in one patient (2%). No synovial fluid culture was positive tissue cultures in two patients with spondylitis (5%), a positive smear of synovial fluid in one patient (2%), a positive smear from a paravertebral abscess in one patient (2%), and a positive PCR finding of the synovial fluid and smear in one patient (2%). No synovial fluid culture was positive for TB arthritis, whereas the synovial fluid smear and synovial tissue culture were positive in 33.3% and 40% of patients, respectively.

Finally, we compared the patients with definite (n = 36) and indefinite diagnoses (n = 99). Independent-samples t-test suggested no significant difference between these groups in demographic characteristics, clinical manifestations, site and type of disease (arthritis, osteomyelitis, and spondylitis), complications, radiological and pathological findings, synovial fluid smear and culture, and concurrent pulmonary TB. Paraplegia (P 0.056) and anal sphincter dysfunction (P 0.057) were more frequent in the group with indefinite diagnosis, but this difference did not quite reach statistical significance.

Discussion

Osteoarticular TB emerges following the haematogenous spread of TB bacilli or the direct spread of TB from an adjacent infectious focus. The most common age for osteoarticular TB has been different in various studies. A retrospective study in Nigeria found that osteoarticular TB was most prevalent during the second and third decades (mean age: 27.3 years) [6]; however, a similar study from Iran (1971–1995) reported the first and second decades to be most commonly affected, and the study of Houshian et al. in Denmark found that the most common age was over 60 years [5,7]. In the present study, the mean age of the patients was 39.94 ± 21.58 years.

Osteoarticular TB usually presents as chronic monoarticular arthritis in joints supporting the weight of the body (vertebrae, hip, and knee); however, few oligoarticular or polyarticular cases have been reported [1,8]. In several studies, pain was the most common sign of osteomyelitis, accompanied by visible inflammation, limited range of motion, and cold abscess formation. General malaise, back pain, vertebral tenderness, neurological signs, abscess formation, kyphosis and fistulae were present in subsequent stages [1,9]. Similarly, pain, weight loss and night sweats were the most common manifestations in the patients of the present study.

In our study, the mean time interval between disease onset and diagnosis or referral for complications was 12.94 months (range: 1–108 months). Ruiz et al. [1] reported a 12.3 ± 14.2-month interval, which was much shorter than that of our study.

Generally, osteoarticular sites, particularly the vertebral column, are most commonly involved [1,9,10]. The metacarpal and metatarsal bones are usually involved in TB osteomyelitis, and lower thoracic and upper lumbar vertebrae are involved in adult TB spondylitis. The most frequent osteoarticular manifestations in our study were thoracic (50%) and lumbar (23%) spondylitis. It is notable that paravertebral abscess was reported in 29.6% of the cases. In a study in Iran (1971–1995), the vertebral column was the most commonly involved site (40.88%), followed by the knee (26.10%) and hip (15.27%). The thoracic, lumbar and thoracolumbar vertebrae were the most common sites of vertebral infection [5]. Another study conducted in Iran between 1993 and 1995 reported similar results but with more frequent involvement of L3 and L4 vertebrae [3].

In published studies, the ESR, as an inflammatory index, is always high in osteoarticular TB. The mean ESR was 84.5 mm/h in the Malaysia study and 48 mm/h in the Iranian study conducted between 1971 and 1995 [5,11]. In the present study, the mean ESR was 55.71 ± 33.9 mm/h.

Radiological images can also contribute to the suspicion or confirmation of TB. Wedge-shaped necrotic areas are commonly seen on both sides of affected joints. Bone sclerosis and periostitis occur in late stages, and severe joint destruction occurs commonly at the end-stages. In the present study, radiological evidence of involvement of more than one vertebra was reported in 95% of cases, and multiple-level skip lesions (combinations) were seen in five cases (22.7%). These were higher rates than reported by Dharmalingam (12.1% of cases) [11].

In a study in Malaysia during 1994–1998, paradiskal inflammation was the most prevalent damage (47% of the cases) [11]. Paravertebral abscess, reduction of disk height and vertebral fusion were reported in 40.9%, 27.3% and 13.6% of patients, respectively [12]. Paraspinal abscess were found in 80% of the radiographs in a study in Saudi Arabia [9]. In the present study, disk destruction was observed in eight of the 23 patients (40%) with TB spondylitis, and paravertebral abscess was reported in 13 patients (59.1%). Concurrent pulmonary TB existed in 28.7% of the cases, and this was evident in 33.3% of the chest radiographs. This is a much lower frequency than in many other studies, which report rates <66% [11].
The PPD skin test was positive in 41.5% of the cases in the present study; this rate is lower than those in similar studies [2,5]. This finding is in contrast to the higher expected prevalence of PPD positivity in countries such as Iran, where bacille Calmette–Guérin vaccination is routinely administered at early ages; and the disease is endemic.

The PPD test was positive in 77% of the cases in a study performed in Iran [5]. In a similar 10-year study in Nigeria, a positive PPD test was reported in 66.6% of cases [6], whereas a New Jersey study in the USA found a positive rate of 41% [13]. The lower positivity rate for PPD testing in our study may have been due to patient malnutrition and/or poor performance of the test; in some cases, the interns in charge were seen injecting PPD subcutaneously instead of intradermally.

Although the diagnosis of osteoarticular TB is confirmed by culture and pathological findings, cultures are time-consuming, and pathological and tissue biopsies are usually used for confirming the diagnoses [14]. It is notable that positive cultures are reported in <80% of cases, even in the best centres [15,16]. Obviously, this rate is much lower than in Iran. Despite the endemic nature of osteoarticular TB, more rapid diagnostic methods such as PCR or rapid culture methods such as BACTEC are not yet available in many medical centres in Iran. Therefore, pathological findings, as well as the existence of granuloma and caseous necrosis, are still used for diagnosing extrapulmonary TB in Iran. This may be an explanation for the absence of significant differences between clinical characteristics seen in definite and indefinite diagnoses of extrapulmonary TB in this study.

Non-specific manifestations of this disease and the ineffectiveness of diagnostic tests such as the PPD result in a delay in referral to specialist physicians. It is therefore essential that physicians remember to include osteoarticular TB in the differential diagnoses of long-term backache and arthritis in countries such as Iran, where TB has a high prevalence.

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Transparency Declaration

The authors have no conflicts of interest to declare.

References