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Original Article

Tuberculous arthritis — a fourteen-year experience at a tertiary teaching hospital in Taiwan

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Background and Purpose: To characterize the clinical and microbiological features of tuberculous arthritis and to clarify the factors affecting treatment outcome.

Methods: We retrospectively reviewed 51 adult patients with a diagnosis of tuberculous arthritis at Chang Gung Memorial Hospital-Linkou over a 14-year period.

Results: There were 35 males and 16 females with a mean age of 58.9 years (range, 32 to 89 years). The mean duration of symptoms and signs before diagnosis was 25.4 months (range, 0.25 to 180 months). Joint pain (96.1%) and swelling (90.2%) were two major presentations. Forty five (88.2%) patients had monoarthritis. Knee (26.7%) was the most frequently involved one. Twenty six (51.0%) patients had roentgenologic evidence of pulmonary tuberculosis (TB). Forty three patients (84.3%) had positive TB culture of synovial fluid and/or tissue. Of which, 27 (63%) had positive acid-fast bacillus smear. Twenty five patients had sputum for mycobacterial smear and culture, and 17 of them had positive TB culture. Thirty six patients received post-treatment follow-up for 3 to 110 months. Among them, 8 had relapses and 28 had treatment success. Compared the relapse to the success, the former had a higher ratio of drug resistant strains (odds ratio, 7.8; 95% confidence interval, 1.025-59.337; p=0.047) and had a longer treatment duration (22.0 ± 4.4 vs 13.2 ± 4.1 months; p=0.001).

Conclusions: Tuberculous arthritis often occurred in elderly people with male predominance. Drug resistant strain may cause a relapse of tuberculous arthritis, which may result in longer treatment duration. Routine chest X-ray and sputum for mycobacterial smear and culture could be necessary to find concurrent pulmonary TB.

Key words: Antitubercular agents; Drug resistance, bacterial; Treatment outcome; Tuberculosis, osteoarticular pathology

Introduction

Tuberculous arthritis is a slowly progressive disease leading to joint destruction in the absence of adequate therapy [1]. Tuberculous bone and joint infections account for up to 35% of extrapulmonary tuberculosis (TB) and, overall, for almost 2% of all forms of TB [2, 3]. Spinal disease accounts for approximately one-half of patients with skeletal TB, followed by involvement of peripheral joints [4]. The diagnosis of tuberculous arthritis is mainly based on the demonstration of tubercle bacilli in synovial material or granulomatous inflammation with or without caseous necrosis in the synovium [1,5]. The most common presentation is chronic granulomatous monoarthritis [1,6-9]. Multifocal osteoarticular TB has been reported in 10-15% of cases in developing countries [6,10]. Joint pain and swelling are two major symptoms [1,4,8,10,11]. Weight-bearing joints are more frequently affected [1,8,9, 11]. The most commonly involved joints are the knee and hip [1]. Comorbid illness, impaired immunity, low socioeconomics, or history of TB may predispose to tuberculous arthritis [1,12].

Tuberculous arthritis can be mimicked by pyogenic, fungal or viral infection, non-tuberculous mycobacterial infection, or inflammatory arthritis [1,13]. Synovial specimens should be examined routinely, with microscopy, Gram stain, acid-fast stain, cultures and

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histology being used to confirm the diagnosis [1,3,4]. Radiographic changes may be late, and areas of disease could be clinically silent [14]. Both computed tomography (CT) and magnetic resonance imaging (MRI) are helpful in evaluating the disease and the outcome of treatment [4,14].

Antituberculous chemotherapy is the mainstay of tuberculous arthritis treatment. Surgical intervention is an adjunct to medical treatment and may help to promote early healing [4,5,15]. The treatment duration of tuberculous arthritis has varied widely [16]. Except for disseminated TB and tuberculous meningitis, the recommended treatment duration of extrapulmonary TB is 6 to 9 months according to American Thoracic Society (ATS) and Centers for Disease Control and Prevention (CDC; Atlanta, GA, USA) recommendations [17]. The duration of antituberculous chemotherapy could be extended to 18 or 24 months for multifocal osteoarticular TB because of the high rate of resistance of pathogens to chemotherapeutic agents and the typically impaired host immunity [6]. In order to delineate the clinical, laboratory, and microbiologic features that affect treatment outcome of tuberculous arthritis, we conducted a retrospective study at a tertiary teaching hospital over a 14-year period.

Methods

Study periods and patient selection

We reviewed the charts of all patients over 18 years old with a discharge diagnosis of tuberculous arthritis at Chang Gung Memorial Hospital-Linkou from January 1992 to December 2005. The diagnosis of tuberculous arthritis was made if at least one of the following criteria was met: (1) *Mycobacterium tuberculosis* isolated from synovial fluid or tissue biopsy specimen; (2) histology of synovial tissue demonstrating caseating granuloma or granulomatous inflammation with positive acid-fast bacillus (AFB) smear; and (3) evidence of synovial granuloma with positive TB culture of the specimen other than synovial fluid or tissue [1,5]. Multifocal osteoarticular TB was defined as osteoarticular lesions occurring simultaneously at two or more non-contiguous bones attributed to *M. tuberculosis* [14].

The following information from each case was collected: demographic data, underlying diseases, clinical features, mycobacterial smears and cultures, histology, blood tests, radiographic findings, treatment regimen and response, complications of antituberculous chemotherapy, and clinical outcomes.

Definition of relapse

'Relapse' was defined as the return of signs and symptoms of tuberculous arthritis when a patient had had a remission during treatment or after completion of treatment [17]. 'Treatment success' was defined as improvement in joint function, symptoms and signs without any evidence of relapse, and erythrocyte sedimentation rate in the normal range after completion of therapy. Patients were not enrolled in the analysis of post-treatment outcome if they died before the completion of treatment, were lost to follow-up or were still on treatment at the time of study data analysis.

Statistical analysis

Bivariate analysis was conducted to determine potential risk factors for relapse and success in the treatment of tuberculous arthritis. Categorical variables were compared using Fisher's exact test and a p value <0.05 was considered to be statistically significant. An odds ratio (OR) and 95% confidence interval (CI) were calculated to evaluate the strength of any association, as well as the precision of the estimate of the effect. Continuous variables were compared by Mann-Whitney U test and a p value of <0.05 was considered to be statistically significant. All statistical calculations were done using the Statistical Package for the Social Sciences for Windows (Version 12.0; SPSS, Chicago, IL, USA) software package.

Results

In total, 51 patients with articular TB were identified, including 35 males and 16 females, with a mean age of 58.9 years (range, 31 to 89 years). The demographic, clinical and laboratory characteristics are summarized in Table 1. Seventeen patients (33.3%) had previous local trauma and 19 (37.3%) had previous operation at the involved joints. Sixteen patients (31.4%) had received long-term corticosteroid therapy before diagnosis. Thirty three patients (64.7%) had comorbidities, including diabetes mellitus (15), previous pulmonary TB (5), chronic renal failure (5) [1 with hemodialysis, 4 without hemodialysis], chronic obstructive pulmonary disease (4), pneumoconiosis (3), rheumatoid arthritis (3), alcoholism (3), malignancy (3) [lung, esophagus and prostate gland, 1 each], poliomyelitis (3), mixed connective tissue disease (2), asthma (1), liver cirrhosis (1), heart transplant recipient on immunosuppressive therapy (1), and previous spinal TB (1). Fifteen patients (29.4%) had two or more comorbid diseases.

Table 1. Characteristics of patients with tuberculous arthritis (n = 51)

Variable	No. (%) or mean ± SD
Clinical characteristics	
Age (years; mean ± SD)	58.9 ± 11.2
Gender (male/female)	35/16
Duration of symptoms before diagnosis (months; mean ± SD)	25.4 ± 41.6
Clinical symptoms/signs	
Joint pain	49 (96.1)
Joint swelling	46 (90.2)
Periarticular abscess	27 (52.9)
Wound discharge	18 (35.3)
Fever	8 (15.7)
Weight loss	7 (13.7)
Draining sinus	6 (11.8)
Laboratory findings	
White blood cell count (/mm^3; mean ± SD)	8027.5 ± 2338.3
Hemoglobin (g/dL; mean ± SD)	11.8 ± 1.9
ESR (mm/h; mean ± SD)	57.3 ± 32.1

Abbreviations: SD = standard deviation; ESR = erythrocyte sedimentation rate

The duration of symptoms and signs before diagnosis of tuberculous arthritis ranged from 0.25 to 180 months (mean ± standard deviation [SD], 25.4 ± 41.6 months). Fourteen patients (27.5%) received blood tests for antibody to human immunodeficiency virus, and the results were all negative. Monoarthritis was seen in 45 patients (88.2%), with knee (12, 26.7%) the most common site. Six patients (11.8%) had multiple joints involvement. The affected joints were as follows: knees (n = 16), wrists (12), ankles (11), hips (10), shoulders (4), elbows (3), and tarsal-metatarsal joint (1). The spine was affected in 4 patients, with 5 sites of involvement, including 1 thoracic, 2 lumbar, and 1 cervical spine. The sternoclavicular junction and sacroiliac joint were involved in 1 patient each. Overall, weight-bearing joints comprised 62.3% of affected joints (Table 2).

The pathology of 48 patients with synovial biopsy demonstrated evidence of mycobacterial infection in 46 patients (95.8%). The histopathology was also relevant in 1 patient with tuberculous pleurisy, 2 with enlargement of regional lymph nodes (one cervical and one axillary) and 2 with TB of the spine.

M. tuberculosis was isolated from synovial fluid and/or tissue in 43 patients (84.3%), of which, 27 (63%) had positive AFB smear. Seventeen of 25 patients with sputum for mycobacterial smear and culture had positive culture for TB, of which 10 had positive AFB smear simultaneously. Two of the 17 patients with positive TB culture had no correlated radiographic evidence. Therefore, one-third of the 51 enrolled patients had active pulmonary TB. *M. tuberculosis* was isolated from spinal tissues in two patients and from pelvic abscess in 1. Positive AFB smear was seen in these 3 patients. Of 51 *M. tuberculosis* isolates from sputum, spinal tissue, pelvic abscess or synovial fluid/tissue, 46 (90.2%) were susceptible to all first-line antituberculous agents, such as isoniazid (INH), rifampicin (RIF), ethambutol (EMB), pyrazinamide (PZA) and streptomycin (SM). One (2.0%) was resistant to EMB, one resistant to PZA, one resistant to SM, one resistant to both INH and SM, and one resistant to INH, RIF, EMB, PZA and SM.

Joint abnormalities on radiographs included bony destruction (n = 9), bony fracture (7), osteoporotic change (6), osteolytic lesion (5), joint space narrowing (5), bony erosion (4), soft tissue swelling (3), osteonecrosis (1), and cystic lesions (1). The rest showed minimal joint abnormalities only. Chest X-ray was performed on all patients, and 26 (51.0%) had evidence of active or old pulmonary TB. Ten patients had CT examination, which

Table 2. Distribution of monoarthritis (n = 45)

Location	Total No. (%)
Shoulder	4 (8.9)
Sternoclavicular joint	1 (2.2)
Elbow	3 (6.7)
Wrist	9 (20.0)
Hip	8 (17.8)
Knee	12 (26.7)
Ankle	7 (15.6)
Foot	
Tarsal-metatarsal joint	1 (2.2)
Total	45 (100.0)

revealed osteolytic lesions, destructive bones, sinus tract or soft tissue masses in 9 cases, and was negative in 1. MRI was performed in 4 patients; 3 had arthritis with or without periarticular abscesses and 1 had a negative result.

Of the 51 patients, 47 (92.2%) received both medical treatment and surgical synovectomy, while 4 (7.8%) received medical treatment alone. All of these latter patients received a minimum of two antituberculous agents, such as INH (5 mg/kg/day), RIF (10 mg/kg/day), and EMB (15-25 mg/kg/day), with or without PZA (20-25 mg/kg/day). Thirty six patients (70.5%) had post-treatment follow-up, with a mean duration of 32.3 months (range, 3 to 110 months). Five patients were lost to follow-up before completion of treatment, including 3 after 2 months of treatment, 1 after 3 months of treatment, and 1 after 4 months of treatment. Five patients were still on treatment at the time of study data analysis, including 2 cases with multifocal arthritis. Five patients died before completion of treatment, including 2 for massive gastric ulcers bleeding with hypovolemic shock, 1 for concurrent methicillin-resistant *Staphylococcus aureus* pneumonia with respiratory failure, 1 for rhinocerebral mucormycosis, and 1 for *Salmonella enteritidis* B septicemia. No patient died of TB or complications of antituberculous chemotherapy.

Of these 36 patients, 8 had relapses and 28 had treatment success. All of the relapses happened after completion of antituberculous chemotherapy. The time after completion of antituberculous chemotherapy was 1 month in 1 patient, 4 months in 1 patient, 5 months in 1 patient, 6 months in 4 patients and 15 months in 1 patient. The mean (± SD) time of relapse was 6.1 ± 2.2 months after completion of treatment. The duration of antituberculous chemotherapy before relapse ranged from 12 to 18 months (mean ± SD, 15.0 ± 2.5 months). All patients received another course of antituberculous chemotherapy after relapse. The treatment duration in the 4 patients with multifocal tuberculous arthritis ranged from 19.5 to 36 months (mean ± SD, 25.6 ± 5.2 months), and two of them had relapse. In the 8 relapsed patients, 2 had multifocal arthritis and 6 had monoarthritis. Compared to the success cases, relapse cases had longer duration of antituberculous chemotherapy (mean ± SD, 22.0 ± 4.4 vs 13.2 ± 4.1 months; p=0.001) [Table 3].

Drug-resistant *M. tuberculosis* strains had been isolated from 3 of the relapse cases and 2 of the treatment success. There seemed to be a higher incidence of drug-resistant strains in relapse cases (OR, 7.8; 95% CI, 1.025-59.337; p=0.047).

Eleven patients (21.5%) had long-term corticosteroid use before diagnosis of tuberculous arthritis due to chronic obstructive pulmonary disease, asthma, pneumoconiosis, autoimmune disease, previous transplantation or joint pain. Concurrent corticosteroid use in addition to antituberculous treatment did not contribute to relapse or success (Table 3).

Table 3. Bivariate risk factors for relapse and success

Variable	Relapse (n = 8) No. (%)	Success (n = 28) No. (%)	OR (95% CI)	p^a
Duration of symptoms before diagnosis (months; mean ± SD)	38.1 ± 42.0	22.9 ± 21.5	-	0.924
Total treatment duration (months; mean ± SD)	22.0 ± 4.4	13.2 ± 4.1	-	0.001
TB-resistant strains	3/8 (37.5)	2/28 (7.1)	7.800 (1.025-59.337)	0.047
Concomitant disease				
Diabetes mellitus	2/8 (25.0)	6/28 (21.4)	1.222 (0.195-7.675)	1.000
Corticosteroid use	3/8 (37.5)	8/28 (28.6)	1.500 (0.288-7.807)	0.678
Pneumoconiosis	2/8 (25.0)	1/28 (3.6)	9.000 (0.697-116.220)	0.118
Rheumatologic disease[b]	1/8 (12.5)	3/28 (10.7)	1.190 (0.107-13.300)	1.000
Chronic airway disease[c]	0/8 (0.0)	3/28 (10.7)	0.521 (0.024-11.538)	1.000
Alcoholism	0/8 (0.0)	3/28 (10.7)	0.521 (0.024-11.538)	1.000
Liver cirrhosis	0/8 (0.0)	1/28 (3.6)	1.688 (0.052-55.067)	1.000
Organ transplant	0/8 (0.0)	1/28 (3.6)	1.688 (0.052-55.067)	1.000
Chronic renal failure	0/8 (0.0)	1/28 (3.6)	1.688 (0.052-55.067)	1.000
Previous pulmonary TB	0/8 (0.0)	3/28 (10.7)	0.521 (0.024-11.538)	1.000
Previous spinal TB	1/8 (12.5)	0/28 (0.0)	8.000 (0.243-263.443)	0.222
Poliomyelitis	0/8 (0.0)	2/28 (7.1)	0.813 (0.033-19.908)	1.000

Abbreviations: OR = odds ratio; CI = confidence interval; TB = tuberculosis

[a]Fisher's exact test for categorical variables and Mann-Whitney *U* test for continuous variables.

[b]Rheumatoid arthritis + mixed connective tissue disease.

[c]Asthma + chronic obstructive pulmonary disease.

Discussion

Tuberculous arthritis often presents as mild, slowly progressive, chronic worsening arthritis and patients with tuberculous arthritis often have nonspecific systemic and pulmonary symptoms, which lead to delay in diagnosis and treatment [14]. The differential diagnoses of tuberculous arthritis include septic arthritis, gout, pseudogout, Reiter's syndrome, rheumatoid arthritis, viral arthritis, and Lyme disease, each of which can present with acute involvement of one or a few joints. Tuberculous arthritis is usually monoarticular [1, 6-9] and primarily affects the weight-bearing joints, particularly knee and hip [1,8,9,11]. In this study, forty five patients (88.2%) presented with monoarthritis, and the knee was the most commonly involved joint (12, 26.7%). The total weight-bearing joints constituted 62.3% (Table 2).

The male-to-female ratio was 35:16. The mean age was 58.9 years. Male and elderly patients predominated. These results are similar to those of a previous report [1]. The mean duration of symptoms before diagnosis was 25.4 months. In contrast to other studies, the average duration before diagnosis was 16 to 19 months [12,18]. More than 90% of our patients had joint pain and swelling, a finding again consistent with Berney et al's data [1]. Only 13-15% of our patients had fever or weight loss, whereas the average from other reports is in the range 30-50% [8,19].

Granuloma was found in synovial tissue in 95.8% of patients. This is compatible with other reports (95-95.6%) [1,8]. *M. tuberculosis* had been isolated from synovial fluid and/or tissue in 84.3% of our patients, whereas previous data showed 94% [1]. Our lower positive culture rate may be due to treatment initiation before diagnostic procedures. Direct joint trauma may play a role in the pathogenesis of tuberculous arthritis [1,9], and a history of local trauma has been found in up to 30% to 50% of the patients [8,9,20,21]. Seventeen patients (33.3%) had a history of local trauma in this study. The primary focus of tuberculous arthritis in adults may be from a quiescent pulmonary or other extraosseous focus [1]. Skeletal TB with evidence of active intrathoracic TB was presented in 30-36% of patients [1,8]. Seventeen of our patients (33.3%) had evidence of active pulmonary TB based on positive TB culture of sputum. Moreover, 26 patients (51.0%) had active or old pulmonary TB on radiographs. The lungs may be the primary focus in these cases. A higher ratio of radiographic evidence for pulmonary TB was seen in this study than in previous studies [1,8]. Failure to find a primary pulmonary focus does not exclude tuberculous arthritis [6,14]. Therefore, sputum cultures for *M. tuberculosis* and radiographs of the chest should be done routinely when tuberculous arthritis is suspected.

There are no specific radiographic features that are pathognomonic of TB of other bones or joints. The common findings were joint involvement, including bony destruction, bony fracture, osteopenia, soft tissue swelling, joint space narrowing, cysts in bone adjacent to a joint, osteolytic lesions, and subchondral erosions involving both sides of the joint [1,4,14]. Radiographic changes may be late and areas of disease could be clinically silent [14]. CT scan and MRI are thought to be helpful for detecting and localizing lesions [4,14]. CT-guided percutaneous aspiration and biopsy could be used for obtaining tissue for diagnosis and drainage of abscesses [14].

Sixteen of the 51 patients (31.4%) had long-term corticosteroid use before diagnosis of tuberculous arthritis. Rheumatologic disease may confuse the diagnosis of tuberculous arthritis initially, due to the similar symptoms and signs. Prolonged corticosteroid use may play an important role in the development of tuberculous arthritis. Systemic, intra-articular, or oral corticosteroid therapy was often used for arthralgia prior to diagnosis of tuberculous arthritis, possibly masking the diagnosis. Corticosteroid treatment is a useful adjunct in treating some forms of extrapulmonary TB, specifically meningitis and pericarditis caused by drug-susceptible organisms [17,22,23], but is not recommended for bone and joint TB according to ATS and CDC recommendations [17]. Some human immunodeficiency virus-infected patients might be missed as blood tests for human immunodeficiency virus were not routine in our patients [1,24].

The incidence of multifocal osteoarticular TB is about 10-15% in developing countries [6,10] and 7-10% in the Indian population [6]. It was 11.8% in this study. Prolonged treatment, for up to 2 years, may be necessary for multifocal osteoarticular TB if patients have poor immune status [6]. The treatment duration of our patients with multifocal tuberculous arthritis ranged from 19.5 to 36 months, with a mean of 25.6 months, which is similar to a previous report [6]. ATS and CDC recommendations are for a shorter course of treatment for tuberculous arthritis, while extrapulmonary TB in children can be treated with the same regimens as pulmonary disease [17]. The mean duration of anti-tuberculous chemotherapy in our 36 patients available

for evaluation of follow-up was 15.1 months. Of them, 13 (36.1%) had less than 12 months of treatment, including 8 (22.2%) with a shorter course of treatment (≤9 months). No relapse occurred and no drug-resistant strains were found in these patients. Thus, if patients had tuberculous arthritis exclusively involving drug-sensitive strains and received adequate antituberculous chemotherapy, short-term therapy would be adequate. This is compatible with the ATS and CDC recommendations. The mean duration of medical treatment in the other 23 patients (63.9%) was 18.9 months (range, 13-36 months), including 8 relapsed patients treated for more than 12 months. Most patients relapsed within the first 6-12 months after completion of therapy [17]. The mean time of relapse in our cases was 6.1 months, despite relapsing patients having received an average of 15 months of treatment before relapse. Short-course antituberculous chemotherapy may be not suitable in these cases.

Patients with a relapse had a significantly longer duration of antituberculous chemotherapy, a higher incidence of drug-resistant strains, and a significantly lower success rate. Poor compliance to antituberculous agents might contribute to the emergence of drug-resistant strains. Direct observation of therapy may improve this problem [17]. Comorbid diseases did not contribute to a higher relapse rate, despite these diseases associated with impaired immunity requiring a longer duration of antituberculous chemotherapy. Poor treatment outcome has been associated with elderly patients, infection with drug-resistant strains, poorly cooperative patients with complicated course, and longer duration of symptoms before diagnosis [6].

Tuberculous arthritis is a disease of insidious onset, and its diagnosis requires a high index of suspicion, which remains a challenge to clinicians [25]. Once tuberculous arthritis is diagnosed, treatment should be initiated as soon as possible, and has the potential to achieve healing with near normal function in 90-95% of patients [7]. Early diagnosis and optimal treatment of tuberculous arthritis are fundamental requirements for the prevention of further bone and joint destruction.

References

1. Berney S, Goldstein M, Bishko F. Clinical and diagnostic features of tuberculous arthritis. Am J Med. 1972;53:36-42.
2. Rieder HL, Snider DE Jr, Cauthen GM. Extrapulmonary tuberculosis in the United States. Am Rev Respir Dis. 1990; 141:347-51.
3. Watts HG, Lifeso RM. Tuberculosis of bones and joints. J Bone Joint Surg Am. 1996;78:288-98.
4. Vohra R, Kang HS, Dogra S, Saggar RR, Sharma R. Tuberculous osteomyelitis. J Bone Joint Surg Br. 1997;79: 562-6.
5. Hoffman EB, Allin J, Campbell JA, Leisegang FM. Tuberculosis of the knee. Clin Orthop Relat Res. 2002;398: 100-6.
6. Kumar K, Saxena MB. Multifocal osteoarticular tuberculosis. Int Orthop. 1988;12:135-8.
7. Tuli SM. General principles of osteoarticular tuberculosis. Clin Orthop Relat Res. 2002;398:11-9.
8. Al-Saleh S, Al-Arfaj A, Naddaf H, Memish Z. Tuberculosis arthritis: a review of 27 cases. Ann Saudi Med. 1998;18: 368-9.
9. Garrido G, Gomez-Reino JJ, Fernández-Dapica P, Palenque E, Prieto S. A review of peripheral tuberculous arthritis. Semin Arthritis Rheum. 1988;18:142-9.
10. Lachenauer CS, Cosentino S, Wood RS, Yousefzadeh DK, McCarthy CA. Multifocal skeletal tuberculosis presenting as osteomyelitis of the jaw. Pediatr Infect Dis J. 1991;10: 940-4.
11. Newton P, Sharp J, Barnes KL. Bone and joint tuberculosis in Greater Manchester 1969-79. Ann Rheum Dis. 1982;41:1-6.
12. Enarson DA, Fujii M, Nakielna EM, Grzybowski S. Bone and joint tuberculosis: a continuing problem. Can Med Assoc J. 1979;120:139-45.
13. Weaver P, Lifeso RM. The radiological diagnosis of tuberculosis of the adult spine. Skeletal Radiol. 1984;12: 178-86.
14. Muradali D, Gold WL, Vellend H, Becker E. Multifocal osteoarticular tuberculosis: report of four cases and review of management. Clin Infect Dis. 1993;17:204-9.
15. Gardam M, Lim S. Mycobacterial osteomyelitis and arthritis. Infect Dis Clin North Am. 2005;19:819-30.
16. Pertuiset E, Beaudreuil J, Lioté F, Horusitzky A, Kemiche F, Richette P, et al. Spinal tuberculosis in adults. A study of 103 cases in a developed country, 1980-1994. Medicine (Baltimore). 1999;78:309-20.
17. American Thoracic Society; CDC; Infectious Diseases Society of America. Treatment of tuberculosis. MMWR Recomm Rep. 2003;52(RR-11):1-77.
18. Martini M, Quahes M. Bone and joint tuberculosis: a review of 652 cases. Orthopedics. 1988;2:861-6.
19. Hodgson SP, Ormerod LP. Ten-year experience of bone and joint tuberculosis in Blackburn 1978-1987. J R Coll Surg Edinb. 1990;35:259-62.
20. Davidson PT, Horowitz I. Skeletal tuberculosis. A review with patient presentations and discussion. Am J Med. 1970; 48:77-84.

21. Rasool MN, Govender S, Naidoo KS. Cystic tuberculosis of bone in children. J Bone Joint Surg Br. 1994;76:113-7.
22. Thwaites GE, Nguyen DB, Nguyen HD, Hoang TQ, Do TT, Nguyen TC, et al. Dexamethasone for the treatment of tuberculous meningitis in adolescents and adults. N Engl J Med. 2004;351:1741-51.
23. Yang CC, Lee MH, Liu JW, Leu HS. Diagnosis of tuberculous pericarditis and treatment without corticosteroids at a tertiary teaching hospital in Taiwan: a 14-year experience. J Microbiol Immunol Infect. 2005;38:47-52.
24. Kramer F, Modilevsky T, Waliany AR, Leedom JM, Barnes PF. Delayed diagnosis of tuberculosis in patients with human immunodeficiency virus infection. Am J Med. 1990;89:451-6.
25. Ong Y, Cheong PY, Low YP, Chong PY. Delayed diagnosis of tuberculosis presenting as small joint arthritis — a case report. Singapore Med J. 1998;39:177-9.

