

Extraspinal Osteoarticular Tuberculosis A Forgotten Entity?

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ABSTRACT

Tuberculosis affects a significant percentage of the world's population and is responsible for bone and joint infections particularly in the developing world. The problem has been compounded by the HIV/AIDS epidemic. Whereas tuberculous involvement of the spine is readily included in a list of differentials for destructive lesions of the spine, infection in other skeletal areas is often not considered. In endemic areas, physicians are aware of the clinical and radiological presentations of musculoskeletal tuberculosis. In non-endemic areas, this knowledge is often lacking. Diagnostic delay often results in increased morbidity and mortality. There is a need therefore to highlight extra-spinal osteoarticular tuberculosis as a real entity.

La Tuberculosis Osteoarticular Extraespinal ¿Una Entidad Olvidada?

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RESUMEN

La tuberculosis afecta a un porcentaje significativo de la población mundial, y es causa de infecciones en los huesos y las articulaciones, particularmente en los países en vías de desarrollo. El problema ha sido agravado por la epidemia del HIV/AIDS. Mientras que la tuberculosis vertebral suele incluirse con prontitud en la lista de diagnósticos diferenciales de las lesiones destructivas de la columna vertebral, la infección en otras áreas de la estructura ósea a menudo se pasa por alto. En las regiones endémicas, los médicos conocen las manifestaciones clínicas y radiológicas de la tuberculosis músculoesquelética. En las regiones no endémicas, este conocimiento está a menudo ausente. Con frecuencia, la demora en el diagnóstico trae como consecuencia una mayor morbilidad y mortalidad. Por lo tanto, se hace necesario prestar atención a la tuberculosis osteoarticular extraespinal como una entidad real.

West Indian Med J 2005; 54 (3): 202

INTRODUCTION

Tuberculosis affects a third of the world's population and each year there are about 20 million prevalent cases and 8 million new cases (1). Tuberculosis remains a major cause of bone and joint infection globally, particularly in the developing world (2). The developed world however has seen a resurgence in the incidence of skeletal tuberculosis. This increase has been attributed to the Acquired Immunode-

ficiency syndrome (AIDS), homelessness, a decline in tuberculosis control programmes, immigration and intravenous drug abuse (3–5).

Tuberculosis has been reported in every bone of the body (6). The spine and the hip are the most frequently involved sites with the vertebrae involved in about 50% of cases (7,8). Spinal tuberculosis is often considered as a differential in destructive lesions of the spine. By contrast, tuberculosis of other areas such as the foot and ankle are less common and are often detected at a much more advanced stage (9). Concomitant pulmonary involvement is unusual in cases of bony tuberculosis leading to further diagnostic delay (10–12). Osteoarticular tuberculosis usually represent secondary infection. In children, this has been reported to be

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related to Bacille-Calmette-Guerin (BCG) immunization (13, 14).

Four cases of extra-spinal osteoarticular tuberculosis, all of which were missed at the initial clinical presentation are presented. These cases illustrate different modes of presentations, the diagnostic difficulties and the different radiographic appearances associated with bony tuberculosis. Treatment options are also discussed.

CASE REPORTS

Case 1

A 27-year-old man presented to the orthopaedic clinic with a five month history of recurrent dislocation of the right shoulder. He had been seen privately and an arthrodesis proposed as the shoulder had been so badly destroyed. He had no fever, weight loss or night sweats. Examination revealed a large soft tissue swelling within the anterior shoulder. Radiographs showed destruction of both the humeral head and glenoid (Fig. 1). The diagnosis of a soft tissue sarcoma was entertained. He had a normal haemoglobin, white cell count and an erythrocyte sedimentation rate (ESR) of 23



Fig. 1: Radiograph of the shoulder joint showing Pnemister's triad of destruction on both articular surfaces, joint space narrowing and periarticular osteoporosis.

mm/hr (Westergren). A computed tomography (CT) scan showed destruction of the humeral head and glenoid. Biopsy of the humeral head revealed granulomatous inflammation not unlike tuberculosis. Ziehl-Neelsen (Z-N) stain demonstrated acid-fast bacilli. He was seronegative for HIV. He was treated with anti-tuberculous therapy. When last seen at nine months post commencement of treatment, he had mild pain at the extreme of movement of the joint.

Case 2

A 65-year-old Caucasian woman was referred with a history of pain in her left foot. Examination showed tenderness in the mid-tarsal joints. Radiographs were reported as degenerative changes in the talo-navicular joint. She was started on nonsteroidal anti-inflammatory medication and physiotherapy. When this failed to relieve her pain, she had steroid injection to the affected joint area. This increased the pain in her foot and she was prescribed insoles. As her symptoms continued unabated, she was referred to a foot specialist, six months after presentation. Repeat radiographs showed a cystic lesion in the talo-navicular joint area. There was also gross destructive changes in the first tarso-metatarsal joint (Fig. 2). The possibility of an infection was considered but not specifically mycobacterial. She was admitted for



Fig. 2: Radiograph of the foot (antero-posterior and oblique) showing a rheumatoid type destruction of the first, second and third tarso-metatarsal joints.

debridement and fusion of the joint. Chest radiographs showed 'fibrotic changes, no active pulmonary pathology'. Surgery had to be delayed because of von-Willibrandt's disease. Subsequently she developed fever, drowsiness and vomiting with symptoms and signs of pneumonia and became confused. Her foot had a large cystic swelling on the medial aspect in the talo-navicular joint. Chest radiographs showed features of miliary tuberculosis. Anti-tuberculous therapy was initiated. She did not respond to treatment; deteriorated and died eight days post admission and one year after her initial presentation. A post mortem examination showed evidence of mycobacterial infection in the lungs, spleen and vertebral bone marrow in addition to the foot. The kidneys, adrenals and ovaries were all normal.

Case 3

A 21-year-old male was seen in the orthopaedic clinic with a two-year history of pain in his left hip. He had sustained trauma to the left hip some three years prior to presentation. He reported no fever or cough. Examination revealed a wasted lower extremity. Radiographs showed destructive

changes in the roof of the acetabulum with joint space narrowing. His haemoglobin was normal as was his white cell count but with a lymphocytosis of 59%. Erythrocyte sedimentation rate was 42 mm/hr (Westergren). Chest radiographs were normal and a m99 Technetium methylenediphosphonate (MDP) bone scan showed increased uptake in the acetabulum, the ischium and the head and neck of the left femur. After a failed closed needle biopsy, an open biopsy was performed. Specimens were sent both for culture and histology. There was no growth from the culture but the histology showed granulomatous inflammation. Special stains for both mycobacteria and fungi were negative. He was started on anti-tuberculous therapy. Subsequently, he developed oral candidiasis which was appropriately treated. His HIV status was negative. Anti-tuberculous therapy was continued for 18 months. At his last follow-up, three years post infection, he had developed secondary osteoarthritis of the hip joint. The patient's cousin from the same district had been treated for spinal tuberculosis with paraplegia three months prior to his presentation.

Case 4

An 18-month-old child was admitted to hospital with a two-month history of swelling of the left thigh and a limp. She had no fever but there was malaise, anorexia, weight loss and night sweats. Her immunization was up-to-date and she had received her BCG vaccine at age ten days. Examination revealed a small-for-stated-age child who was afebrile with few inguinal adenopathy. Her chest and abdomen were normal. There was a swelling to the left thigh, which exhibited no features of infection. Radiographs showed a lytic lesion in the proximal femur, which had eroded the lateral cortex with periosteal new bone formation (Fig. 3). The differential diagnosis entertained included an osteosarcoma, neuroblas-



Fig. 3: Antero-posterior radiograph of pelvis showing cystic lesion of the proximal femur with breach of lateral cortex and extensive periosteal reaction.

toma or leukaemia. Investigations showed haemoglobin of 10gm/dl, white cell count $10.3 \times 10^3/\text{ul}$, platelets $552 \times 10^3/\text{ul}$ and an ESR of 70 mm/hr (Westergren). Abdominal ultrasound was normal. Mantoux test was positive. Moderately

increased uptake in all three phases of the m99Tc MDP bone scan was noted. At biopsy, a small amount of pus was found in the medullary cavity. Cultures showed no growth. She was seronegative for HIV and HTLV-1. Magnetic resonance imaging (MRI) was reported as an intramedullary tumour with soft tissue extension. Histology showed caseating granulomatous inflammation with acid-fast bacilli on Z-N stain. She was started on quadruple therapy which included streptomycin, rifampicin, isoniazid and pyrazinamide, and the bone protected in a hip spica. At one year post treatment, the bone had reconstituted itself and the periosteal reaction had settled. The child was walking with no limp or leg length discrepancy.

DISCUSSION

Osteoarticular tuberculosis constitutes 1–3% of extra-pulmonary cases and the spine and hip are the most commonly affected sites (7, 15). Involvement of the bones of the foot and ankle is rare and is detected at a more advanced stage (9). Several factors may contribute to the diagnostic delay. The lack of familiarity with the spectrum of bone lesions may be one such contributory factor (16). Physicians particularly in the developed world quite often do not consider tuberculous osteomyelitis at an early stage in the diagnostic work up of their patients. This has led to the delay in treatment with sometimes disastrous consequences (17). To compound the issue, tuberculosis is considered more of an immigrant population disease. This has led to the earlier diagnosis in the immigrant population of developed countries as compared to the indigenous populations. This seriously prejudiced the outcome in the indigenous group which often have marked joint destruction by the time treatment is started (12). Case 2 was seen in a developed country and illustrates this point very well. In endemic areas, tuberculosis is considered foremost and hence diagnosed earlier and appropriately treated. Younger physicians in Jamaica where tuberculosis is not considered endemic are unfamiliar with the spectrum of the osteoarticular disease and hence are likely to miss cases.

The first clinical symptom is often non-specific pain in and around the joints. This is often accompanied by swelling. These symptoms were the most common presenting complaints in Vohra's series and the duration of symptoms ranged from two to 39 months (3). Anorexia, weight loss and enlarged lymph nodes is seen in less than a third of the cases (3). Only in Case 4 were these documented. Eren *et al* (18) also noted fever in addition to loss of appetite and weight. Children usually present with localized pain, swelling and tenderness particularly in the lower limb, with difficulty in weight-bearing. Fluctuance and a discharging sinus are sometimes seen (2, 3).

A negative Mantoux test does not preclude a diagnosis of tuberculosis. The Mantoux test was positive in 70% of the children with cystic tuberculosis of bone presented by Rasool *et al* (16). In areas where BCG vaccination is routine, it may add to the confusion. Further, bony tuberculosis as a result of

Bacille-Calmette-Guerin (BCG) immunization has been reported (13, 14). It is most often seen in the first five years of life and the interval between vaccination and presentation may vary from five months to five years (13, 14).

The ESR by itself is not of much value in helping to make the diagnosis. In the cases presented by Vohra *et al* (3), 88%, had an elevated ESR, which ranged from 31–83 mm/hr (Westergren) whereas Rasool *et al* reported normal ESR in 40% of their patients (16). The C-reactive protein (CRP) was mentioned by Wang *et al* however in 22 of his 23 patients, the value was negative (4). For early detection and species identification of mycobacteria, enzyme linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) techniques are currently in wide use (19, 20).

Chest radiographs are of little help in diagnosing musculoskeletal tuberculosis as only a third of patients have a history of pulmonary disease (3). Rasool *et al* had only 15% with pulmonary tuberculosis (16). It is not until the disease is widespread that the chest radiograph becomes positive as was demonstrated by Case 2 where radiographs of the chest done two months before the patient died were reported as showing no evidence of active pulmonary disease.

The earliest radiographic features are often non-specific with erosion at the peripheral margins of a joint. This may mimic an arthritic process as seen in Cases 1 and 2. Peri-articular osteoporosis occurs as a result of disuse and may take some time to appear. Similarly, the joint space may be preserved until late in the disease because of the time taken for the destruction of the articular cartilage. Phemister's radiographic triad of periarticular osteoporosis, marginal erosion and joint space narrowing may not be present at the earliest presentation of the disease leading to diagnostic delay (9). In retrospect, the radiological features demonstrated in Case 1 represented a classic Phemister triad (Fig. 1).

In the foot, there are different radiographic features of tuberculosis as illustrated by Mittal *et al* (21). These patterns may be that of rheumatoid, cystic, subperiosteal scalloping, kissing (on either side of the joint) and *spina ventosa*. The latter is seen more often in children in the short tubular bones *eg* the metatarsals which are expansile, with bony destruction and periosteal thickening. Case 2 typified the rheumatoid type which involves the midfoot (Fig. 2). Here all the tarsal bones except the talus and the calcaneus may coalesce into a mass of bone not unlike the rheumatoid carpus.

Cystic tuberculosis is more commonly encountered in children than in adults and may either be solitary or multiple. The solitary cystic form is more common than the multiple cystic variety (2) which itself is uncommon. These cysts can occur anywhere in the skeleton. Typically, the lesions are radiolucent, round to oval and are situated in the peripheral skeleton near the metaphysis. The cystic lesions may extend to involve the cortex or may break through it as was evident in Case 4. The physis is no barrier to spread and lesions may extend to involve the epiphysis (22). The cyst-like appearance is due to variable marginal sclerosis (16). The differen-

tial diagnosis of these solitary cystic lesions should include bacterial or fungal infections, simple or aneurysmal bone cysts, cartilagenous tumours and osteoid osteomas (8, 11, 23, 24). In adults, common sites outside the spine for cystic tuberculosis include the skull, shoulder and pelvic girdles (22, 23).

Other imaging modalities are of limited value in the diagnosis of musculoskeletal tuberculosis. A MRI or CT scan may be of value in demonstrating lesions in and around bones long before they are evident on plain radiographs (3, 5). The CT scan is better than MRI in detecting cortical bone destruction and calcifications within soft tissue abscesses (5). The MRI scan can detect early joint effusions and soft tissue swelling. Neither is specific in making the diagnosis of tuberculosis.

Osteoarticular tuberculosis is pauci-bacillary and it is often difficult to demonstrate or culture the organism from these lesions even in endemic areas (21). Newton *et al* reported identifying by direct microscopy and/or culture, the tubercle bacillus in 75% of their patients (12). Vohra *et al* however cultured the organism in a third of cases (3). Mittal *et al* had a similar culture positive result (21). Despite adequate tissue sampling, no organisms were cultured in Cases 1, 3 and 4. Ziehl-Neelsen staining demonstrated acid-fast bacilli after granulomatous inflammation was seen on histology in Cases 1 and 4.

In endemic regions, where medical and laboratory facilities might be limited, the clinical, radiological appearance and elevated ESR are sufficient to diagnose tuberculosis and begin treatment (4, 12, 21). Biopsy is usually reserved for the non-responders or where resistant strains are common and additionally in areas where the disease is not prevalent (4). In non-endemic areas, the presence of granulomatous synovitis is sufficient grounds for treating a patient with full chemotherapy in the presence of negative culture (12). Despite culture and biopsy, no organism was demonstrated in Case 3. He was however treated as tuberculosis based on the above and also the fact that his cousin who lived in the same district and with whom he had close contact, had spinal tuberculosis.

Unlike pulmonary tuberculosis which can be treated with short course antituberculous therapy, musculoskeletal tuberculosis should be treated for 12 to 18 months (3, 4, 14). The drugs of choice comprise streptomycin, rifampicin, isoniazid, pyrazinamide and ethambutol. The initial quadruple therapy may include streptomycin intramuscular for two months following which rifampicin, isoniazid and pyrazinamide are continued for at least twelve months. Mittal *et al* (21) had a slightly different regimen. They started with quadruple therapy including pyrazinamide, isoniazid, rifampicin and ethambutol for two months followed by rifampicin and isoniazid for 16 months with follow-up liver function test and eye examination every three months. They reported good results without the necessity for surgery. Eren *et al* (18) also had good results with this regimen. No relapse was reported

by either Vohra *et al* (3) or Wang *et al* (14), who both treated their patients for 12 and from 9–18 months respectively.

There is consensus in the literature that surgery is an adjunct drug. Debridement and curettage is indicated for non-healing lesions, with resection of sequestered phalanx or metatarsal being rarely necessary (14, 16, 21). Wang *et al* reported complete healing of bony lesions with curettage and debridement alone (14). Similar results were quoted by Rasool *et al* (16).

The outcome is usually good if lesions are treated for nine to eighteen months (3, 14, 16); relapses being reported in cases of noncompliance (12). Death was reported by Newton *et al*, but neither the disease nor therapy was thought to be responsible. In Case 2, death occurred due to overwhelming miliary tuberculosis. Functional residual disability does occur especially in weight-bearing joints and is a direct result of diagnostic delay (12). Extraspinal osteoarticular tuberculosis does occur and can prove a diagnostic dilemma. With appropriate early treatment, the outcome is usually good. There ought to be an awareness of the various clinical and radiographic presentations if pitfalls are to be avoided.

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