Three cases of misdiagnosed skeletal lytic lesions: the mimicry of tuberculosis

Introduction

In areas of low to medium prevalence of tuberculosis, unfamiliarity with the disease leads to delays in diagnosis or even misdiagnosis. Osteomyelitis or septic arthritis caused by *Mycobacterium tuberculosis* in adults commonly presents as a single lesion. The three cases of skeletal tuberculosis reported in this article presented as multifocal disease with bony lytic lesions in otherwise healthy patients in a British district general hospital.

These cases presented to different medical specialties, and were misdiagnosed as metastatic malignancy, osteoarthritis and rheumatoid arthritis. Delay in diagnosis allows the disease to progress, leading to bony destruction and possible neurological involvement that early intervention would have prevented. These case reports highlight the warning signs that should have alerted the clinicians earlier that this could be tuberculosis and outline how the delay in diagnosis has impacted their mobility.

Discussion

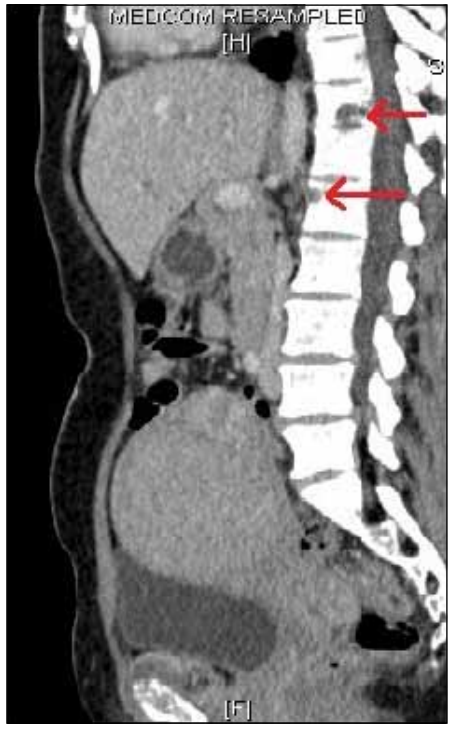
In 2010 there was a rise in extrapulmonary manifestations of tuberculosis, with 4.3% of all reported cases affecting the spine and 2.1% other bony sites (Health Protection Agency, 2011a,b). Tuberculosis affecting the musculoskeletal system is difficult to diagnose as the initial symptoms are non-specific. In 50% of cases there is no concurrent pulmonary infection or radiological evidence of the disease in the chest (Gardam and Lim, 2005; Franco-Paredes et al, 2006). Some cases of tuberculosis osteomyelitis or arthritis were initially treated as osteoarthritis (Gardam and Lim, 2005). It is thought that there is a delay of 16–19 months between initial symptoms and the diagnosis of skeletal tuberculosis, because of its indolent course and clinicians' limited experience (Yao and Sartoris, 1995; Watts and Lifeso, 1996; Gardam and Lim, 2005). Delay leads to destruction of bone and surrounding structures, and has lead to two of these patients becoming wheelchair bound.

M. tuberculosis is spread by the lymphohaematogenous route from the primary lung site, or by direct invasion from an already infected site (Fanning, 1999).

Figure 1. Expansile lytic lesion causing a pathological fracture of the pubic symphysis (green arrow).

Tuberculosis can cause spondylitis, osteomyelitis, septic arthritis and tenosynovitis. As vertebral bones have good vascular

Figure 2. Several lytic areas along the vertebrae (red arrow).



Case Report 1

A 55-year-old woman, who emigrated from China to the UK more than 25 years ago, was admitted with a 6-month history of abdominal, back and left hip pain, accompanied by weight loss. On examination there was a palpable hard mass arising from the pelvis. Her only abnormality on blood tests was that she had an erythrocyte sedimentation rate of 52 mm/hr. The computed tomography scan reported that there were lytic lesions in T11, and the inferior pubic rami with a fragmentary lesion in the left sacroiliac joint (*Figures 1* and *2*). There was also a large pelvic mass arising from the cervix. It was concluded from the computed tomography that she had a large pelvic malignancy with multiple bony metastases. Biopsy of the pelvic mass showed no malignant cells but the appearance was consistent of granulomatous endometritis. On microscopy acid-fast bacilli were present, and later culture was positive for *Mycobacterium tuberculosis*.

She started to complain of increased back pain and urinary retention 5 months into antituberculous treatment, and repeat magnetic resonance imaging showed a decrease in inflammation but loss of vertebral height in T11 and T12 causing angulation of the spine. She was given a back brace and continued her treatment for a course of 9 months. Her constitutional symptoms resolved and follow-up imaging showed no new lesions or progression of established lesions. However, she was left with a prominent kyphosis and spinal impingement, and underwent neurosurgical intervention. She is now wheelchair bound.

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supply, skeletal tuberculosis commonly affects the spine, followed by infective arthritis in weight-bearing joints, and then osteomyelitis affecting the extraspinal bones (Watts and Lifeso, 1996; Gardam and Lim, 2005). *M. tuberculosis* destroys surrounding tissue by spreading along ligaments or any path of less resistance, e.g. in vertebral disease, *M. tuberculosis* can cause spondylitis affecting many levels, such as in case 1.

Skeletal tuberculosis is an uncommon form of extrapulmonary tuberculosis, and the polyarticular presentation is even more uncommon, usually seen in areas of high tuberculosis prevalence and in the immunosuppressed (Muradali et al, 1993; Gardam and Lim, 2005). Most bony lesions in adults caused by tuberculosis are reported as fragmentary (Jain, 2010). The current cases all had more than one musculoskeletal lesion, mostly lytic, presenting in immunocompetent patients residing in areas of low tuberculosis prevalence. Similar cases have been reported but from countries where tuberculosis is endemic (Ali et al, 2004).

The course of tuberculosis is indolent with vague signs and symptoms, but certain 'red flags' in the history and imaging should make one consider the possibility of skeletal tuberculosis. The main symptoms in skeletal tuberculosis are pain, swelling and limitation of movement (Papadopoulos et al, 2003; Gardam and Lim, 2005). In some cases, the constitutional signs of tuberculosis such as weight loss and night sweats are not present (Papadopoulos et al, 2003).

A main risk factor for musculoskeletal tuberculosis seems to be if the patient was born in or is a descendant of those from countries with a high prevalence of tuberculosis. The Health Protection Agency (2011a,b) reports that 53% of non-UK born patients had extrapulmonary disease compared with 30% of UK born patients. Bone and joint tuberculosis is more common in women, and those over 65 years of age (Gardam and Lim, 2005). A study

Figure 3. Lytic lesions in the proximal phalynx of the right foot breaking through the cortex, and sclerosis around the first metatarsophalangeal joint.

Figure 4. Lateral view of the right first toe.

Case Report 2

A 74-year-old Indian immigrant presented with ascites and systemic lymphadenopathy. Lymph node biopsy showed presence of granulomata. Ascitic fluid culture had no growth of mycobacterium, but she was started on empirical antituberculous medication. She was lost to follow up and only received 3 months of treatment.

One year later she developed pain in her right first metatarsophalangeal joint. Radiograph of the right foot was reported to have changes of minor degeneration and was initially treated as osteoarthritis. She presented again 4 months later with pain over the right first metatarsophalangeal joint. X-ray of the right foot first phalanx showed evidence of sclerosis and multiple small lytic lesions (*Figures 3* and *4*). After multiple admissions with toe pain, she was referred to rheumatology. On X-ray of the right first metatarsophalangeal joint the lytic lesions had broken the cortex. Blood tests showed a mildly raised erythrocyte sedimentation rate of 32 mm/hr, positive rheumatoid factor, normal white cell count and a C-reactive protein level of 4 mmol/litre. Magnetic resonance imaging of the foot showed signal changes around the first metatarsophalangeal joint implying inflammation that was spreading through the phalynx, and multiple areas of high signal in the T2 images throughout the calcaneum. It was concluded that this was an erosive inflammatory arthropathy. She was treated with an intraarticular steroid injection. Four months later she developed a hot, swollen right first toe, and the plain radiograph revealed complete destruction of the first metatarsophalangeal joint (*Figure 5*). The joint aspirate grew *Mycobacterium tuberculosis*, and she was promptly started on a 6-month course of antituberculous medication.

Figure 5. Progression of the disease leading to complete destruction of the joint.

Case Report 3

The final case is of a 34-year-old woman of Indian origin, born in the UK. She was referred for orthopaedic review as a result of lower back pain for 3 months. She had no restriction to movement but was tender over her L5 spinal process. X-ray showed some loss of height at L5/S1 and she received physiotherapy.

She was re-referred 14 months later as the pain had worsened. On examination she was again tender over L5/S1. Magnetic resonance imaging was performed and the most striking feature was a collection involving the right psoas muscle and right hip joint. There were also areas of high signal in other surrounding muscles, right sacroiliac joint and vertebral ligaments. She revealed that she had night sweats but no weight loss, nor any known contact with tuberculosis. The collection was drained and did not culture any bacteria, including mycobacterium.

She was admitted with right hip swelling and pyrexia 2 months later. Plain radiograph of the hip showed widening of the joint space indicating an effusion, and severe destruction of the femoral head. Hip aspiration was performed which again was mycobacterium culture negative. All blood tests including white cell count were normal, except a mildly raised C-reactive protein level and a very high erythrocyte sedimentation rate of 113 mm/hr. The decision was made to start treatment for tuberculosis, regardless of no confirmed bacteriological evidence, as no other cause could be found. Magnetic resonance imaging at 6 months of treatment showed resolution of the psoas collection, her symptoms resolved and her erythrocyte sedimentation rate was normal, but she is currently using a wheelchair because of the destruction of her hip joint.

identifying the risk factors for extrapulmonary tuberculosis, in which the most common form was bone and joint tuberculosis, concluded immunosuppression, e.g. being HIV positive, was an independent risk factor (Yang et al, 2004).

Initial imaging during the investigation of musculoskeletal tuberculosis is the plain radiograph. If there is a suggestion of tuberculosis further imaging is required. When compared with computed tomography, magnetic resonance imaging offers greater diagnostic value showing early bony change and extent of disease.

In vertebral disease mycobacterium spread via the nutrient arterioles that end next to the anterior aspect of the vertebrae, causing anterior corner destruction but sparing the posterior aspect. Consequently the anterior portion collapses causing a wedge deformity in the spine called a gibbus (Gardam and Lim, 2005; Jain, 2010). Large paravertebral soft tissue shadows are visible and the intervertebral discs are seen as areas of high signal in T2 weighted magnetic resonance images. These have high sensitivity and specificity of 100% and 88.2% respectively for the diagnosis of tuberculosis spondylitis (Jain, 2010).

The gold standard for diagnosing tuberculosis is culture of aspirated fluid or tissue. This has a high false negative rate, and takes a long time, so samples should be viewed for acid-fast bacilli and also sent for histology (Fanning, 1999; Jain, 2010).

The National Institute for Health and Clinical Excellence (2011) recommends the standard regimen: 2 months of isoniazid, rifampicin, pyrazinamide and ethambutol, then reducing to isoniazid and rifampicin for a further 4 months. Similar to other case series, the current cases developed paradoxical lesions after starting treatment, perhaps because these lesions were present and asymptomatic at the start of treatment, or maybe because there was an immunological response. Regardless there is no need to change the medication if cultures show that the *M. tuberculosis* is sensitive to treatment (Muradali et al, 1993).

Conclusions

Multifocal skeletal tuberculosis, albeit uncommon, has been scarcely reported and is often misdiagnosed. In patients who have presented with unusual destructive bony lesions and whose ethnic origin is from a country with high prevalence of tuberculosis, one should have a low threshold for investigating for tuberculosis, as early treatment can prevent devastating consequences to their mobility. BJHM

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LEARNING POINTS

- Skeletal tuberculosis can present in various different forms; this article provides evidence of tuberculosis presenting with multiple bony lytic lesions.
- Multifocal tuberculosis can present in immunocompetent patients.
- Think tuberculosis in those whose musculoskeletal symptoms have not responded to initial management, especially in immigrants and their descendants.