



Musculoskeletal tuberculosis in Bradford – a 6-year review

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ABSTRACT

INTRODUCTION Tuberculosis (TB) remains the most common cause of death from infectious disease world-wide. In the UK, the incidence of TB has risen by 25% over the last 10 years; extrapulmonary diagnosis remains challenging and can be delayed. This study evaluates the epidemiology of musculoskeletal tuberculosis in a large multi-ethnic UK city.

PATIENTS AND METHODS A review of prospectively recorded data of incidence, anatomical site, ethnic distribution, treatment and drug resistance of musculoskeletal tuberculosis over a 6-year period was performed.

RESULTS From January 1999 to December 2004, there were 729 TB notifications; 61 cases (8.4%) had musculoskeletal involvement. Of the patients, 74% were immigrants from the Indian subcontinent; nearly 50% had spinal involvement; 24 patients underwent surgical intervention; 29 were subjected to either diagnostic or therapeutic radiological intervention; and resolution of symptoms was achieved in 59 out of 61 cases.

CONCLUSIONS This study highlights the high proportion of musculoskeletal TB in immigrant patients in an area with a relatively large at-risk population, but will also serve to alert physicians, in areas with smaller at-risk populations, of the possibility of musculoskeletal TB.

KEYWORDS

Drug resistance – Epidemiology – HIV – Musculoskeletal tuberculosis – Tuberculosis

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Tuberculosis (TB) remains the most common cause of death from infectious disease world-wide.¹ The World Health Organization (WHO) estimates there were 8.8 million new cases of TB in 2005, equating to 140 per 100,000 population,² and annual deaths are reported to reach 3 million.³

In the UK, tuberculosis has risen by 25% over the last 10 years and is still rising.⁴ In 2002, 6638 people were newly diagnosed (an incidence of 15 per 100,000 population) and around 350 people die, per annum, in the UK alone.⁴

Musculoskeletal tuberculosis accounts for around 10–15% of all TB notifications in the non-industrialised world.⁵ However, in the Western world, musculoskeletal TB tends to be uncommon and accounts for around only 1–2% of all cases of tuberculosis and about 10–15% of extrapulmonary TB.⁶ The spine is the most common site for osseous involvement, accounting for around 50% of cases,⁷ followed by the pelvis (12%), hip and femur (10%), knee and tibia (10%) ribs (7%) and multiple sites (3%).⁸

The diagnosis of extrapulmonary tuberculosis is often challenging and can be delayed. A positive chest radiograph, or positive skin tuberculin test, will support the diagnosis though it is not excluded by negative results.^{9–11} Concomitant pulmonary tuberculosis has been reported to be present in less than 30% of extrapulmonary TB cases.⁹

The purpose of this study was to evaluate the epidemiology of musculoskeletal tuberculosis by reviewing its incidence and treatment over a 6-year period in a large, multi-ethnic UK city. Bradford is known for its ethnic diversity and, particularly, for its high proportion of immigrants from areas with a high prevalence of TB. The 2001 census reported the population of Bradford to be 467,665; of these 101,624 (22%) were from ethnic minorities and predominantly from the Indian subcontinent. Nearly 16% of Bradford's population was from Pakistan alone, and the census also noted that 10% of Bradford's population were born outside of the UK.¹²

We aim to highlight the importance in confirmation of the diagnosis and subsequent surgical and chemotherapeutic management.

Patients and Methods

All patients diagnosed with TB in our institution are managed, either primarily or jointly, by dedicated respiratory physicians with an interest in tuberculosis. TB is a notifiable disease and data regarding diagnosis, anatomical site, ethnicity, treatment, drug resistance and outcome are recorded prospectively, for all patients (irrespective of site), by our Specialist Tuberculosis Nurse-Led team.

Review of these data was performed to assess the incidence, anatomical site, ethnic distribution, treatment and drug resistance of musculoskeletal tuberculosis over a 6-year period from 1999 to 2004, in our institution. Results were evaluated and compared to previously reported data for purposes of discussion.

Results

Demographics

In the 6 consecutive years, from January 1999 to December 2004, the total number of patients diagnosed with tuberculosis in Bradford was 729, equating to an annual incidence of around 26 per 100,000 population. Of these, 61 cases of musculoskeletal TB were identified though only 8 patients (13%) had concomitant pulmonary TB.

Thirty-five of the patients (57%) were male and the overall average age was 42 years (range, 13–79 years). The average age for white patients was 70 years (range, 57–77) compared to an average of 40 years (range, 13–79) for Asian sufferers.

Ethnic origin

Forty-five (73.8%) of the patients identified, in this study, were immigrants from the Indian subcontinent and a further 11

Table 1 Ethnic distribution of musculoskeletal TB presentations

Ethnicity	Patients (n)	Patients (%)
Indian sub-continent	45	73.8
<i>Pakistan</i>	36	59.0
<i>India</i>	8	13.2
<i>Bangladesh</i>	1	1.6
UK-born Asians	11	18.0
White	5	8.2

Table 2 Anatomical site of musculoskeletal TB

Anatomical site	Patients (n)	Patients (%)
Spine	29	47.6
<i>Cervical</i>	2	3.2
<i>Thoracic</i>	8	13.2
<i>Thoracic/lumbar</i>	4	6.6
<i>Lumbar</i>	10	16.4
<i>Not classified</i>	5	8.2
Humerus/elbow	6	9.8
Knee	5	8.2
Chest wall	5	8.2
Hip/femur	4	6.6
Pelvis/SIJ	4	6.6
Wrist	3	4.9
Fingers	2	3.4
Ankle	1	1.6

(18.0%) were UK-born Asians. Five patients (8.2%) were white and only a quarter of the patients diagnosed with musculoskeletal TB were born in the UK (Table 1).

Anatomical site

The spine was the most common anatomical site to be involved. Twenty-nine (48%) patients suffered with spinal disease; 10 patients had involvement of the lumbar spine, 8 the thoracic spine, 4 both thoracic and lumbar spine, a further 5 patients were not sub-classified and only 2 patients had involvement of the cervical spine.

The second most common site was the upper extremities: 11 patients (18%) were identified. In six, the humerus and elbow were affected, of whom 5 had elbow joint involvement. Three and two patients presented with wrist and finger involvement, respectively.

This was closely followed by knee; 5 patients (8%) were affected and of these 4 patients suffered joint sepsis. Similarly, 5 patients presented with chest wall tuberculosis (ribs and/or sternum) – these patients were managed jointly by the thoracic surgeons and respiratory physicians.

Four patients suffered with TB of the hip and femur, another 4 of the pelvis and sacro-iliac joint and the final patient presented with TB of the talo-navicular joint.¹⁵ In all, 13 patients suffered joint sepsis, with the knee joint most commonly involved (4 patients; Table 2).

Surgical intervention

All 13 patients who presented with infected joints underwent formal joint washout in the operating theatre and joint fluid was taken for microscopy, culture and

sensitivities. A further seven patients underwent incision and drainage of superficial abscesses: these were carried out by orthopaedic surgeons for limb lesions and thoracic surgeons for chest wall abscesses (five patients presented with superficial chest wall involvement).

Of the 29 patients with spinal involvement, only four required spinal surgery; all four patients had neurological compromise which resolved following surgical decompression and subsequent anti-tuberculous drug therapy. Two further patients with neurological compromise associated with spinal involvement underwent primary medical treatment as symptoms were long-standing and non-progressive. The neurological symptoms, in both of these patients, resolved following successful drug therapy.

In total, 29 patients underwent either diagnostic or therapeutic radiological aspiration under computerised tomography (CT) guidance. All specimens were sent for microscopy, culture and sensitivities.

Microbiology and drug resistance

Forty-two (69%) of patients had culture-positive specimens for *Mycobacterium* spp. and all but three patients were sensitive to first-line anti-tuberculous drug therapy; all patients with resistant strains had spinal involvement.

The first patient was a 20-year-old Pakistani girl who arrived in the UK just prior to the diagnosis of spinal TB; surgical decompression was performed and *Mycobacterium tuberculosis* was cultured from purulent fluid obtained intra-operatively which was resistant to both Isoniazid and Ethambutol. A successful clinical outcome was achieved with Rifampicin, Pyrazinamide, Ciprofloxacin, Clarithromycin and Prothionamide.

The other two patients were a 16-year-old Pakistani boy and a 79-year-old Pakistani male patient, who had resided in the UK for 14 and 55 years, respectively. Similarly, spinal TB was diagnosed and *M. tuberculosis* was cultured from a surgically obtained specimen; resistance was to Isoniazid only. Successful outcomes, in both patients, followed treatment with Rifampicin and Ethambutol for 1 year.

Risk factors

IMMUNOSUPPRESSION

No patients were diagnosed with HIV infection at either presentation or during patient follow-up.

EXPOSURE

Only nine patients were known to have had contacts with TB sufferers either in the UK or abroad. One patient was diagnosed following contact screening.

HEALTHCARE WORKERS

There were no healthcare workers diagnosed with musculoskeletal TB in the study period.

Outcome

Overall treatment outcome was excellent with complete resolution of symptoms achieved in 59 cases (92%) at 1-year follow-up (post treatment). Of the remaining two patients, one visited his native country (Pakistan) on two separate occasions during treatment, and compliance to treatment was questioned. Subsequent relapse required prolonged treatment for cure to be achieved. The other patient died during treatment secondary to unrelated comorbidity.

Discussion

In 1993, the WHO declared tuberculosis a global emergency as it continues to claim up to 3 million lives per annum.⁵ It is estimated that up to one-third of the world's population are harbouring latent infection with mycobacterium tuberculosis; although over 90% of cases are found in the non-industrialised world, there has been a re-emergence of TB in the industrialised world.¹ In terms of numbers, pulmonary TB has been by far the most contributory; however, concomitant rises in musculoskeletal TB have been reported.⁶

The resurgence of TB incidence, in developed countries, has been attributed to a rise in immunosuppressed patients (especially secondary to the HIV epidemic), multidrug-resistant strains of *Mycobacterium* spp., an ageing population, increased healthcare worker exposure and immigration.^{8,14}

This study highlights the high proportion of musculoskeletal TB in immigrant patients, the majority of whom are originally from the Indian subcontinent where TB prevalence is high. Houshain *et al.*¹⁵ has reported similar findings of increased pulmonary and extrapulmonary TB secondary to immigration and it has also been shown that clinical presentation of TB varies with ethnicity.¹⁶ Many parts of the UK have been subjected to diverse changes in immigration over the past decade; therefore, it is likely that these areas will also see a resurgence in TB.

The MRC report on TB notifications in 1983 highlighted a 51 times increase in extrapulmonary TB in patients from the Indian subcontinent than Caucasian patients.¹⁷ This was first reported in Bradford by Nicholson in 1974;¹⁸ he noted an overall annual incidence (of bone and joint TB) of about 10 per 100,000 population, though for the Asian population this reached 280 per 100,000 in 1961–1965. However, the paper is now only of historical value as it predates the emergence of HIV; there is no current data available on TB prevalence in areas with large Asian populations.

The overall annual incidence of TB in Bradford is currently around 26 per 100,000 population – accounting for about 2% of the UK's tuberculosis burden – with nearly three-quarters of affected patients arriving from outside the UK. The relatively low incidence of TB within the white population of Bradford tended to affect older patients than

immigrant sufferers. Thus supporting theories of the re-emergence being, in part, due to an ageing indigenous population as well as immigration from endemic areas.

There are numerous reports highlighting the susceptibility of HIV-positive patients to re-activation of tuberculous infection and that HIV-positive patients are more likely to progress to active disease than immunocompetent individuals.^{19,20} However, there were no known cases of HIV infection in our cohort of patients at either presentation or during subsequent clinical follow-up. Nevertheless, routine HIV testing for patients suffering with TB is not carried out at our institution currently. Similarly, no healthcare workers were identified with tuberculous infection.

Only two patients in our series were infected with drug-resistant strains of *M. tuberculosis* (one with resistance to Isoniazid and Ethambutol, the other Isoniazid alone). Isolated Isoniazid resistance in Bradford has been reported in 3.8% of all *M. tuberculosis* TB presentations, over the 10-year period from 1995–2005.²¹ However, multidrug-resistant strains account for less than 1% of all TB notifications in Bradford.

The commonest anatomically involved site was the spine (29 of 61 patients; 48%) which correlates well with other series that report spinal involvement in about 50% of patients.^{7,8,14,22} Interestingly, we noted a higher proportion of upper limb TB than previously reported;⁸ 11 patients (18%) were affected.

Tuberculous infection of joints follows either direct invasion from an adjacent area of tuberculous osteomyelitis or from haematogenous spread. Typically joint involvement is monoarticular, primarily affecting the large weight-bearing ones such as hip and knee. Oligoarticular or polyarticular patterns are unusual, ranging from 5–15% of cases, only occasionally with small joint involvement, and more often in those who are immunosuppressed.⁶ The triad of juxta-articular osteoporosis, peripherally located osseous erosions and gradual narrowing of the joint space is known as the Phemister triad and is characteristic of tuberculous arthritis (though this can be mimicked in rheumatoid arthritis and fungal disease).¹⁰ If untreated, the eventual result of TB infection of a joint is fibrous ankylosis.¹¹ Thirteen patients presented with joint involvement, all of whom received formal joint washouts in conjunction with chemotherapy (that was overseen by our respiratory team) as part of their overall management.

The delays in recognising and diagnosing TB have been well documented.⁹ This may, in part, be due to patients giving vague histories, perhaps complicated by misleading stories of unrelated trauma, and also that concomitant pulmonary involvement is not always present. Of our cohort, 87% did not show any signs or symptoms of pulmonary disease, whereas previously pulmonary involvement has been reported to be undetectable in around half of cases.²⁵

Once diagnosis has been confirmed, anti-tuberculous treatment is instituted and subsequent management is overseen, in our institution, by respiratory physicians with a special interest in TB. The treatment of TB is curative regardless of site (so long as the organism remains sensitive to drug therapy) though outcome will depend on compliance with the prescribed treatment regimens.²⁴

This study highlights the importance of increased clinical suspicion of musculoskeletal TB. In areas with relatively large at-risk populations, this may already be present. However, in areas with smaller at-risk populations, a similar proportion of cases would be expected and clinical vigilance is, therefore, required to alert physicians of the possibility of musculoskeletal TB.

Conclusions

The diagnosis of musculoskeletal tuberculous infection remains a challenge to clinicians and requires a high index of suspicion. Prompt diagnosis and treatment of skeletal TB are important to prevent serious bone and joint destruction and neurological compromise in spinal TB. Management should be undertaken jointly by orthopaedic surgeons and respiratory physicians.

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