Spinal and Bone Tuberculosis

Jonathan Bull and Veronica White

Introduction

Tuberculosis of the skeleton, TB osteomyelitis, makes up a small but significant proportion of TB cases. Evidence of TB affecting the bone has been found in skeletons at many archaeological sites including in Egyptian mummies [1–4].

Diagnosis can be difficult and often occurs late in the patient's presentation, but the disease can cause significant morbidity due to these delays and the location of the pathology. Patients with spinal disease may be left with significant post treatment pain or neurology, paraplegic or even tetraplegic, depending on the site of the infection. Those with TB of the joints or long bones can be left with deformity, chronic pain or loss of range of movements.

Incidence

In 2018 it was estimated that there were ten million cases of TB worldwide, of which seven million were notified to national TB programmes; only 15% of these cases were reported as extra pulmonary, ranging from 8 to 24% depending on the region; it is well recognised that this is due to under reporting as well as under diagnosis [4, 5]. The true incidence of TB osteomyelitis in developing countries is therefore likely to be similar if not more than European cases, particularly with HIV co-infection [3, 4]. Active infection occurs in patients of all ages.

In England in 2018, 5–6% of TB cases were in the skeleton of which 3–4% were in the spine giving a total of 147 cases of spinal TB and 90 non-spinal bony cases [5].

J. Bull · V. White (✉)
Barts Health NHS Trust, The Royal London Hospital, London, UK
e-mail: jonathan.bull1@nhs.net; veronica.white6@nhs.net

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The majority of patients were born in high risk countries and are likely to have acquired their primary TB infection in earlier life [2, 4, 6–8]. Whilst the number of cases was not enormous, morbidity from TB osteomyelitis can be considerable as outlined above.

Aetiology

The TB bacillus is thought to reach the bones via the blood stream with haematological seeding, via rich vascular plexuses, including Batson's paravertebral venous plexus, that supply the spinal vertebrae [2]. Non-tuberculous mycobacterial infection is much less common, and is associated with previous injury or surgery, such as joint arthroplasty [3]. There has recently been a series of cases of Mycobacterium Chimera reported post cardiac surgery which has been found to be due to contamination of cardiopulmonary bypass heater-cooler units [9]. Mycobacterium bovis infection has been reported after intravesical Bacilli Calmette Guérin (BCG) therapy and is also thought to be spread via the venous network that links the spine and the pelvis [3, 10–12]. Multi-drug resistant tuberculosis (MDR TB) can also affect any skeletal site and requires treatment with the same complex medication as pulmonary MDR TB disease.

Spinal Tuberculosis

In the UK, Percival Pott first described spinal TB in 1779 and his name, Pott's disease, is still used to describe the infection) [1, 2, 13]. This is not to be confused with either Pott's fracture or Pott's puffy tumour which are a complex fracture of the ankle and osteomyelitis of the frontal bone of the skull respectively [14, 15].

Presentation of spinal TB can be insidious, and is often, at least initially, misdiagnosed with outcomes being variable, and despite good antibiotic and sometimes surgical treatment, can lead to long term disability.

Spinal TB tends to affect the vertebral bodies which have a rich vascular supply, skipping the intervertebral discs and radiology showing disc sparing. Frequently it affects more than one vertebra and if it is in adjacent vertebrae it may then involve the intervertebral disc. It occurs at any level and can be multi-level but most commonly affects the thoracic and lumbar spine. It is therefore important to image the whole of the spine at the time of diagnosis as lesions may be non-contiguous. Vertebral involvement and infection can lead to bony destruction and vertebral collapse which causes the typical anterior wedge fracture and wedging synonymous with Pott's disease (Fig. 1) [2, 4, 13]. Gibbus formation and kyphosis may also

Fig. 1 MRI scan of thoracic spine showing gross destruction of thoracic spine with wedge fractures, a paraspinal abscess causing marked impingement on the spinal canal and cord compression

occur and can cause spinal cord compression and paraplegia. TB also affects the sacroiliac joints where it can present as a unilateral osteomyelitis [3].

Skeletal TB does not occur in isolation; in a third cases of active TB can be found elsewhere in the body. TB infection in the spine tends to travel along the subcostal neurovascular bundle or in the venous drainage from the vertebrae, hence further foci of infection are often found in the ribs, or the psoas or iliacus muscles, with a third of cases also have associated unilateral or bilateral psoas abscess(es). A chest x-ray is mandatory, but is often normal despite the lungs being the primary focus of infection [2, 7, 16].

Occasionally patients present in outpatients with, for example, pulmonary or lymph node TB and a gibbus will be found on examination; these patients need to be investigated urgently for spinal TB [1].

Presentation of Spinal TB

Most but not all patients with spinal TB present with back pain. About 50% of patients will present with neurology such as lower limb weakness, paraesthesia, and rarely bowel or bladder symptoms; 50% will also have at least one systemic symptoms of fever, night sweats and/or weight loss [2, 4, 8].

The difficultly in making the diagnosis arises due to back pain being a very common presentation in primary care. However, both patient and doctor often forget to acknowledge the presence of systemic symptoms, which can help in making a diagnosis.

Patient characteristics can be helpful, for example, born or lived in a high incidence area of TB, but this is not always the case and often TB exposure will have been many years if not decades before presentation.

Incidental diagnosis on a CT or MRI scan organised for other symptoms such as abdominal pain is a common presentation. Occasionally patients with, for example, pulmonary TB will be diagnosed and started on treatment, only to develop either back pain or a superficial paraspinal abscess on TB treatment. It is only at this stage that both patient and clinician are concerned about the spine and urgent investigations should be organised.

Disease in the cervical spine can present with neck and shoulder pain, brachial plexus or radiculopathic symptoms. Patients can present via the Ear, Nose and Throat specialists with dysphasia, hoarseness and dysphagia due to formation of a retropharyngeal abscess (Fig. 2). If there is spinal cord compression at the cervical spine level patients may complain of weakness and numbness of the upper and lower limbs, progressing to tetraplegia. If there is any concern about the stability of the cervical spine then the patient should be placed in a hard cervical orthosis (Fig. 3).

Thoracic spine disease commonly presents with back pain, but also radicular pain radiating anteriorly in a band like distribution to the chest wall; some patients

Fig. 2 MRI scan of cervical spine with evidence of a large retropharyngeal abscess, prevertebral collection and destruction of the odontoid peg; the patient presented with neck pain and nasal speech. The abscess was drained surgically, the patient placed in a halo brace and treated for TB. He made a full neurological recovery

Fig. 3 Cervical orthosis or hard collar

will complain of epigastric pain which on investigation is due to referred pain. Cord compression can lead to lower limb symptoms and can lead to paraplegia (Figs. 4 and 5).

Patients with lumbo-sacral disease complain of lower back pain and difficult sitting and rising from a chair. Sacroiliac joint infection can limit walking and present with hip or buttock pain potentially leading to superficial skin abscesses. Occasionally cauda equina syndrome can be as a consequence of TB and documentation of bowel or bladder symptoms is essential.

Both thoracic and lumbar disease can be associated with a tracking of infection through the subcutaneous tissues and abscess formation on the skin, which can sometimes be the first sign of the disease. This can track to the skin surface can lead to discharging sinuses (Fig. 6).

Infection at any of these sites can initially be asymptomatic, particularly when limited to the vertebrae themselves; however, there is often formation paraspinal abscesses, or cold abscess, which if they are adjacent to the spinal cord, can cause signs and symptoms of upper or lower limb neurology and paraplegia, or if invading the nerve root, radicular pain [1–3, 8].

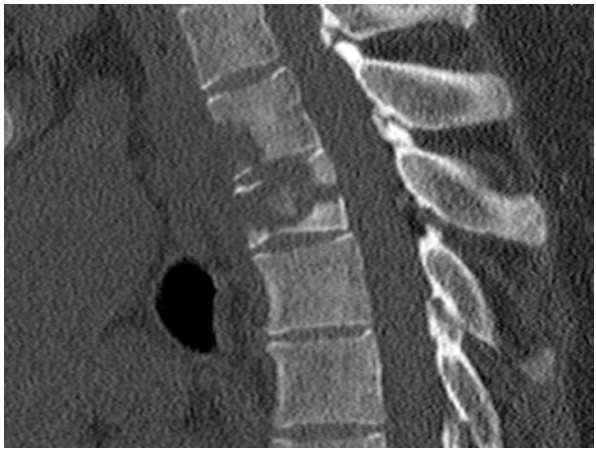

Fig. 4 31 year-old man who presented with intrascapular pain; CT scan shows anterior lesions at T3 and T4 (T4 is starting to develop a classical anterior wedge fracture)

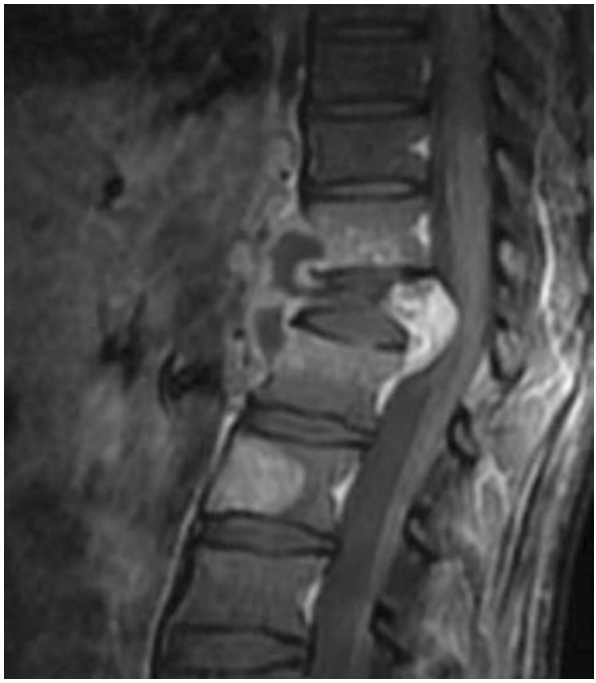

Fig. 5 23 year-old woman presented acutely with weakness, numbness, pain and needles in lower limbs; MRI scan shows complete destruction of T12 associated with an epidural and prevertebral collection

Investigation of Spinal TB

MRI scans are now the imaging modality of choice and show areas of infection and bone destruction in affected areas. T1-weighted images show a low signal and T2 weighted images a bright one. CT scans are useful when looking at the structure of the bone and bony stability. Bone scans or skeletal scintigraphy assess bone

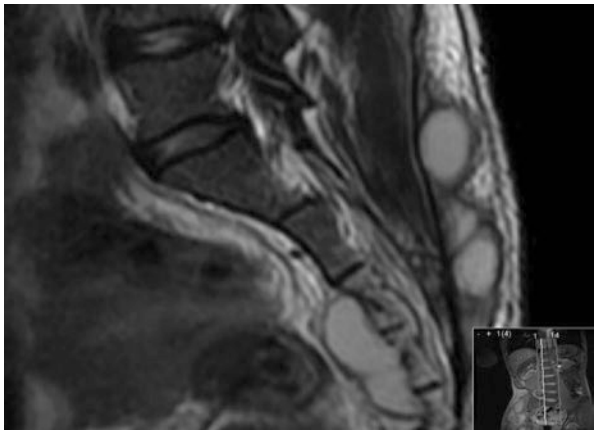

Fig. 6 40 year-old man presenting with lower back pain and a fluctuant abscess over his left gluteal region. MRI shows a presacral collection and multi loculated abscess in subcutaneous tissues

metabolism so can be used to assess whether there is an area of high bone turnover that can occur with bacterial infection, TB or metastases; PET-CT scans can similarly be used to look for evidence of multifocal infection [1, 3, 13].

Depending on the site of disease, radiological biopsy should be carried out to send samples for histopathology, standard microbiology (MC&S), and acid-fast bacilli (AFB). This can be done by CT guided biopsy or US scan guided biopsy, depending on the site of disease. Occasionally open surgical biopsy is necessary, either due to the difficult site of pathology or as part of surgical intervention to stabilise the spine. Microbiology samples can include solid tissue and/or pus and should be sent in a pathology pot dry or in saline solution; the microbiology teams are unable to process samples sent in formalin as this kills any bacteria.

Histology samples may show classic caseating granuloma, although bone biopsies are often difficult to process in the laboratory as they need to be decalcified first. Standard microbiology may reveal bacterial infection such as staphylococcus, particularly in patients who are immunocompromised. Occasionally spinal lesions diagnosed as metastatic cancer on imaging only, are then found on biopsy to be due to TB.

A chest x-ray should always be undertaken on presentation to rule out active infectious pulmonary TB and if there are any concerns about lung infection the patient should be appropriately isolated whilst in hospital and sputum samples sent (see below).

Standard blood tests should be undertaken but are generally unhelpful at confirming a diagnosis: patients who have been unwell for some time may have a normochromic, normocytic anaemia due to underlying infection or other pathology. The ESR is often raised in bony disease, but a normal result does not rule out infection. Similarly, a negative tuberculin skin test or IGRA (interferon gamma release assay—T-spot or Quantiferon) should not steer the physician or surgeon away from the diagnosis when there is a high clinical and radiological suspicion given the insufficiently high sensitivity of these tests. If patients present with multifocal lesions an immunological profile is useful to rule out a primary or acquired immunological defect.

Differential Diagnosis

Alternative diagnoses include secondary metastatic cancers, primary malignancy being much less common, and staphylococcus osteomyelitis, as outlined above; non-tuberculous mycobacterium infection does occur, particularly in patients who are immunosuppressed, for example post chemotherapy or HIV co-infection.

Presentation of Bone and Joint TB

Bone TB tends to occur in the larger joints such as the hip or knee and presents as a monoarthritis (Fig. 7). Rarely it presents as a trochanteric bursitis. Symptoms include joint pain swelling and loss of function, and is often misdiagnosed as being caused by another cause of monoarthritis. It is most commonly caused by haematogenous spread, but sometimes as the results of previous penetrating or non-penetrating trauma, instrumentation or joint replacement. Systemic symptoms are less common in bony TB which makes it more difficult to diagnose [3, 4, 17–19].

If the long bones are affected, the bone medulla tends to be infected first, unless the infection is the results of trauma or previous instrumentation. As the infection spreads, it can breach the bony cortex and spread along the subcutaneous fissure,

Fig. 7 MRI scan of knee joint. Whilst there is no obvious underlying osteomyelitis of the bone, there is an inflammatory arthropathy associated with a complex massive synovial thickening with joint fluid. Biopsy of the synovium showed granulomas and synovial fluid grew MTB (courtesy of Dr. Susan Cross)

and lead to subcutaneous collections. Therefore, bony TB can be associated with a chronic overlying a discharging sinus and when cutaneous TB is diagnosed in this way, care should be taken to assess the underlying skeleton, preferably with MRI imaging, to ensure that this is not an underlying associated osteomyelitis (Fig. 8).

Tuberculous dactylitis tends to occur in children and effects the tubular bones of the hands or feet [19].

TB rarely occurs in prosthetic joints sometimes many years after the original replacement. These patients may require surgical debridement and resection arthroplasty as well as standard TB therapy [3].

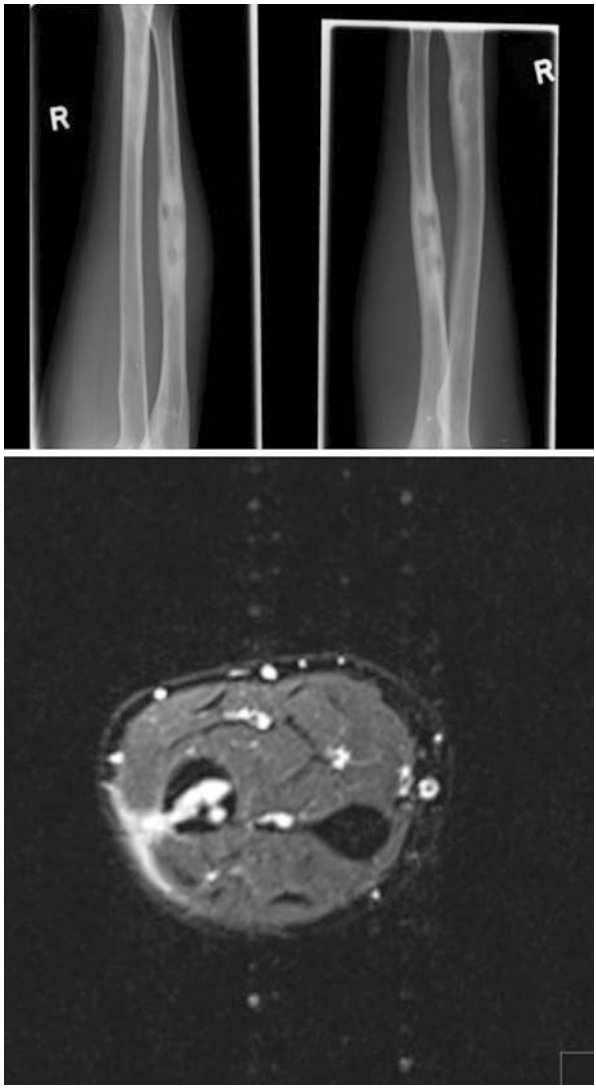

Fig. 8 Plain x-ray and MRI of right ulnar: x-ray shows mid shaft osteomyelitis with bony sclerosis and expansion. The MRI shows cross sectional imaging with breaching of the cortex and infection tracking through the subcutaneous tissues (courtesy of Dr. Susan Cross)

TB is occasional found in the sternum, often incidentally after a CT scan of the chest to investigate the underlying parenchymal disease and can occur after sternotomy following cardiac surgery [4, 20]. Active infection is also seen in the cranium and mastoids; when patients present with subcutaneous lesions the skull vault or face, underlying TB osteomyelitis should be ruled out with appropriate imaging.

Investigation of Bone and Joint TB

Plain x-ray can initially be helpful, but only if they are abnormal, and tends to show soft tissue swelling, followed by osteopenia, periosteal bone thickening and periarticular bone destruction. TB can also affect the tendon sheaths. However, it is not unusual for plain films to look completely normal, only to find multiple abnormalities on MRI (Fig. 9). Biopsies can be of the bone or synovium, which can be done under radiological guidance and synovial fluid can also be sent for MC&S and AFB, as well as cytology [4, 13]. Blood tests are as outlined above.

Differential Diagnosis

Rheumatoid arthritis, pyogenic infection, often cause by *Staphylococcus aureus*, brucellosis, actinomycosis, candidiasis, histoplasmosis and fungal infection can all mimic TB infection in the bone. Benign and malignant tumours such as enchondromas, giant cell tumours and malignant metastases [4, 19] can also imitate TB.

Isolation Precautions

Most cases of spine and bone TB are not infectious. However, when patients present, whether it be to an outpatient clinic or for admission to hospital, a chest x-ray should be one of the first investigations to be undertaken once any concern about neurological compromise is stabilised. The majority of patients will have a normal chest x-ray, but where there is doubt or obvious signs of pulmonary TB, patients should be isolated in a side room with appropriate infection control precautions. Sputum should be sent urgently for AFB and the patient kept in isolation until three negative sputa are processed. If there is concern about drug resistant TB, the patient should be isolated in a negative pressure facility.

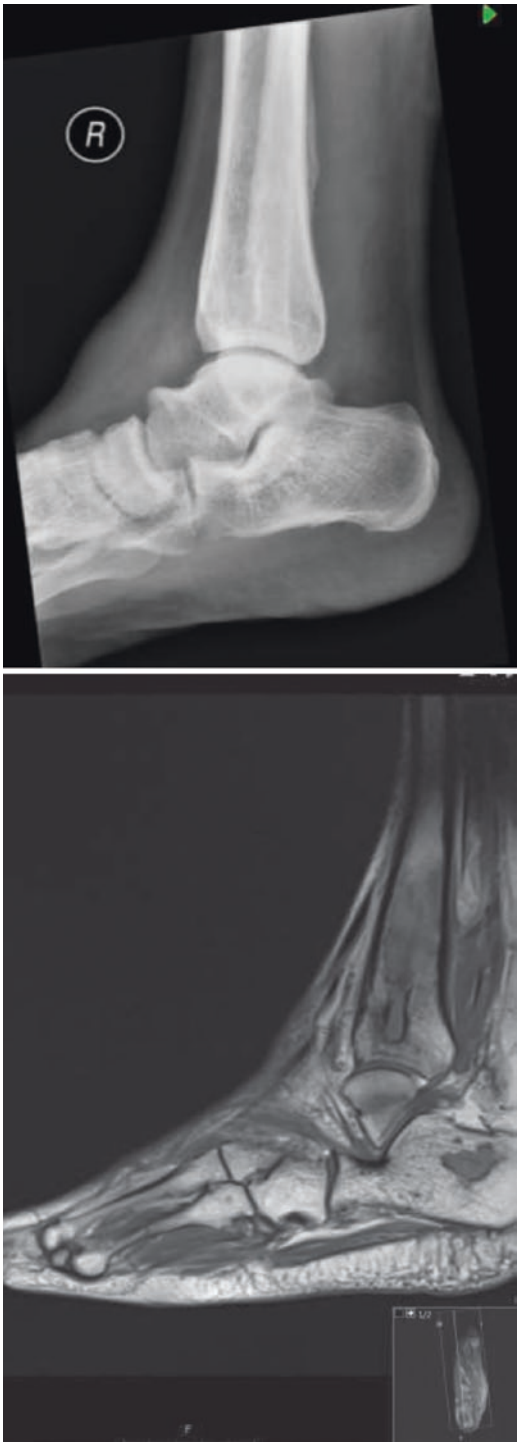

Fig. 9 Plain x-ray and MRI of the same patient's foot: the plain x-ray appears normal but the MRI shows florid changes in distal tibia and calcaneum—the sensitivity is much better on MRI for osteomyelitis and plain x-rays should not be trusted when the index of clinical suspicion is high (courtesy of Dr. Susan Cross)

Non-tuberculous Mycobacterium (NTM) and Multi Drug Resistant TB (MDR TB)

Osteomyelitis due to other members of the mycobacterium family is rare. NTM is more common in patients who are immunocompromised, after trauma or instrumentation. Depending on the organism, drug treatment can be more complex and prolonged and should be undertaken by expert in looking after non-tuberculous mycobacterium. MDR TB occurs in the bone at the same rate is pulmonary disease i.e. about 1–2% of patients and should be managed in a designated MDR TB centre [3, 10].

NTM can be found in replacement joints following surgery. Treatment may also require debridement of the affect area and removal of the prosthesis. Mycobacterium chimera has recent been found to cause infection in some patients post cardiac bypass surgery and can also affect the sternum [9].

Poncet's Disease

This refers to a painful polyarthropathy which can predate the diagnosis of active tuberculosis by many months. Also described as 'tuberculous rheumatism' it is thought to be caused by extra articular tuberculosis, most commonly active pulmonary TB, and is a reactive arthritis rather than being due to direct infection of the joints. It differs from active joint TB, which tends to be a monoarthritis, in that it affects many joints, x-rays tend to be normal and aspiration of the joints shows a sterile arthritis. It is thought to be caused by an immunological reaction. The symptoms settle once the underlying TB infection is treated [4, 19, 21, 22].

Treatment of TB Osteomyelitis

Both the British, American and WHO guidelines on management of TB recommend 6 months treatment for spinal and bone TB [23–25]. However, many specialists treat spinal TB for 9–12 months, sometimes times longer, partly due to concerns about multi-level spinal involvement and also involvement of the central nervous system, particularly when there is evidence of infection that is directly involving the spinal cord [1]. Length of treatment can also be influenced by the greater availability of MRI scans: clinicians use them to monitor progress, and when the site of infection still appears to be active, there is a tendency to continue TB treatment. What is unclear is at which point the infection resolves and the imaging is simply showing residual inflammation that will settle over time. Treatment should be guided by symptoms rather than imaging appearances.

Particularly with spinal TB, patients should be warned that once they start treatment, they should urgently report any changes in neurological symptoms. Similar to lymph node TB, encapsulated TB infection in the spine tends to enlarge at the start of TB treatment. Particularly if the infection is close to a nerve root or is part of a para spinal abscess adjacent to the spinal cord, a very small increase in size of a TB abscess can lead to progressive neurology and even lead to paraplegia which, if not addressed urgently, can lead to permanent disability. If patients are in hospital at the beginning of treatment, they should be told to report any new symptoms and examined neurologically on a daily basis; outpatients should be instructed to present to the nearest Emergency department if concerned about new neurology.

There are no clear guidelines on the use of steroids in spinal or bony disease and they should not be used routinely [13]. Steroids are rarely used in the treatment of bone TB. However, in spinal disease where there are neurological symptoms on presentation with spinal disease or when there is concern that an enclosed lesion close to important neurological structures such as the spinal cord with impending spinal cord compression, steroids may be started concomitantly with TB treatment using either iv or oral dexamethasone or oral prednisolone. Again, there is no specific guidance on the length of course, and the dose of steroids generally has to be doubled when rifampicin is used in the treatment regime. The authors would recommend a decreasing dose over an 8–12 week period. Treatment with steroids is more complex in patients with HIV who develop immune reconstitution syndrome (IRIS).

The side effects of steroids must be considered. Common effects include increased appetite and weight gain, acne and skin striae, osteopenia and osteoporosis. Patients should always be considered for bisphosphonates. Some patients develop psychological side effects including depression and/or hypomania. Clinicians should also consider a 9 am cortisol 2 weeks after finishing a prolonged course of steroids to ensure that there is not prolonged adrenal suppression. Very occasional patients can develop avascular necrosis of the hip as a result of high dose steroid use.

A well recognised side effects of treatment with isoniazid is a peripheral neuropathy, often presenting in a glove or stocking distribution. In patients with spinal disease it can be difficult to conclude whether new neurological is due to drug side effects or worsening burden of infection.

Non-pharmacological Treatment

Typically, it is possible to manage patients with spinal TB in a spinal brace, in part to manage their pain and to prevent or diminish the chance of progressive deformity. The risk of the deformity not only being cosmetic but also with a risk of long-term pain. Braces can be used for lesions in all locations in the spine and images of cervical and thoraco-lumbar orthoses are illustrated (Figs. 3 and 10).

Occasionally large joints may require temporary support with a brace; in generally however, the patients should be encouraged to exercise and mobilise both to use

Fig. 10 Thoraco-lumbar orthosis or TLSO brace

the joint and encourage muscle strength in the surrounding structures. Physiotherapy and hydrotherapy can be helpful in some patients and patients with healing spinal infection should be encourage to attend Pilates classes and swim at least twice a week.

Diet and weight can also be important: any patient who has become immobile for whatever reason, and particularly if they have been given a course of steroids, tend to gain weight which puts further stress on the affected spine or joint. We also recommend the measurement of Vitamin D levels and appropriate replacement when needed.

Surgical Intervention

Different approaches to the surgical management of spinal TB are, to some extent, based on geography. This is particularly pertinent in developing countries with access to health resources can be limited and is coincident with patients travelling longer distances for their care. In such situations, the luxury of regular reviews of

patients is not practical and a single definitive single treatment such as surgery is undertaken [26, 27]. Surgical intervention with debridement and instrumentation will reduce the burden on the patient and facilitates with an early return to their home where TB chemotherapy can be continued without recourse to prolonged surgical follow up.

In developed countries it is possible to regularly review patients and potentially run a more conservative approach with TB chemotherapy using spinal orthosis and regular imaging to assess for the development of deformity. If the patient is not managing in terms of pain or signs and symptoms progress then timely surgical intervention can be undertaken.

Indications for surgery are progressive deformity and pain that cannot be managed with a brace and analgesia alone [28]. In patients that have neurological deficit that is progressing then surgery is indicated although it can be possible to manage a stable deficit with conservative treatment and this may improve as the patient responds to TB chemotherapy.

Deformity (gibbus) may well need correction as it can lead to long term pain in spite of TB typically resulting in fusion across the affected segments [28, 29]. Timing of surgery can be complex; experience in resource limited environments suggests that even early surgery with instrumentation when the patient has had only a very short course of treatment does not typically result in persistent infection. This is in the context of extensive surgical debridement.

In general TB of the spine without neurological deficit can be managed conservatively. Where surgery is considered a multidisciplinary approach can be helpful to ensure all options are explored (Fig. 11).

The majority of long bone or joint TB is treated conservatively with antituberculous therapy. However, infection may lead to bony destruction and deformity which may require debridement, joint replacement or reconstruction, the latter being generally recommended once TB treatment has been completed. However, surgery can take place if necessary whilst the patient is on treatment. Mycobacterial infection in prosthetic joints may require early debridement and removal of the prostheses which is replaced whilst on treatment or once the infection is completely cleared.

Outcomes and Long-Term Morbidity

The outcome of spinal TB is partially dependent on the original site of the disease, the degree of neurological involvement on presentation, any delay in diagnosis, as well as success of treatment and motivation of the patient to engage in exercise programmes. Aiding long term recovery can at least in the first instance be about managing expectations. All patients should be warned at the beginning of treatment that they may experience long term mild to moderate back pain, similar to many patients with mechanic back pain who have not had the burden of an infective episode. As outlined above, physiotherapy and an incremental increase exercise can

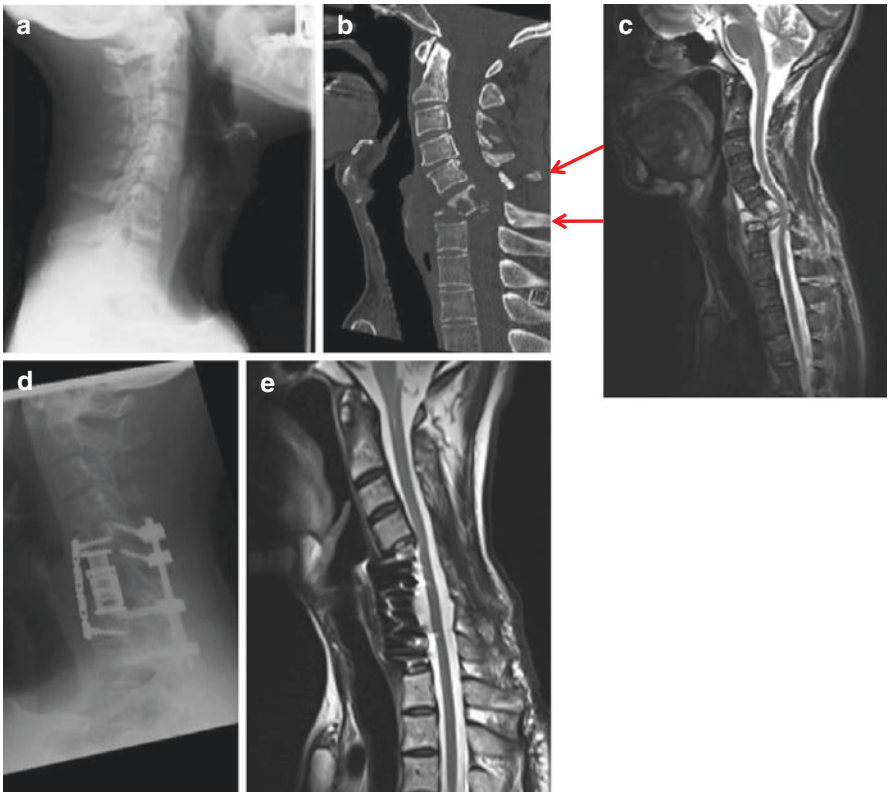

Fig. 11 48 year-old man with 9 months of neck pain who had initially presented to his emergency department 4 months previously with the same neck pain (**a**) he was discharged with a diagnosis of degenerate spondylosis. Represented with worsened neck pain CT (**b**) and MRI (**c**) show complete destruction of C7 vertebral body and partial destruction of C6 (note the two red arrows pointing to the spinous processes of C6 and C7) with retrolisthesis and canal compromise without neurological deficit. He was initially fitted with a HALO brace and started on TB Chemotherapy. After 2 weeks of treatment when it was felt that the disease burden had been reduced he underwent an anterior and posterior fixation where the deformity was corrected. [Post OP x ray (**d**) and MRI (**e**)]

often be the key to a successful pain-free recovery and should be discussed from the initiation of treatment.

At least half of patients with spinal disease can be expected to make a complete recovery, with or without intermittent back pain. Others may be left with long term neurological sequelae such as foot drop, bladder instability, radicular pain or paraesthesia. At worse a very small percentage of patients may be left with either paraplegia or tetraplegia as a result of TB infection. Patients with long bone and joint TB can be left with bony deformities, limitation of movements and chronic pain.

Patients with long bone and joint TB can be left with bony deformities and limitation of movements; joint infection may lead to bony destruction and deformity

and which may require debridement, joint replacement or reconstruction in the future, which are general recommended once TB treatment has been completed. However, surgery can take place if necessary whilst the patient is on treatment.

Some patients continue to require multidisciplinary care with neurorehabilitation, pain specialists, physiotherapy, occupational therapy and spinal or orthopaedic specialists.

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