■ REVIEW ARTICLE

Tuberculosis of the spine

A FRESH LOOK AT AN OLD DISEASE

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The dismal outcome of tuberculosis of the spine in the pre-antibiotic era has improved significantly because of the use of potent antitubercular drugs, modern diagnostic aids and advances in surgical management. MRI allows the diagnosis of a tuberculous lesion, with a sensitivity of 100% and specificity of 88%, well before deformity develops. Neurological deficit and deformity are the worst complications of spinal tuberculosis. Patients treated conservatively show an increase in deformity of about 15°. In children, a kyphosis continues to increase with growth even after the lesion has healed. Tuberculosis of the spine is a medical disease which is not primarily treated surgically, but operation is required to prevent and treat the complications. Panvertebral lesions, therapeutically refractory disease, severe kyphosis, a developing neurological deficit, lack of improvement or deterioration are indications for surgery. Patients who present with a kyphosis of 60° or more, or one which is likely to progress, require anterior decompression, posterior shortening, posterior instrumented stabilisation and anterior and posterior bone grafting in the active stage of the disease. Late-onset paraplegia is best prevented rather than treated. The awareness and suspicion of an atypical presentation of spinal tuberculosis should be high in order to obtain a good outcome. Therapeutically refractory cases of tuberculosis of the spine are increasing in association with the presence of HIV and multidrug-resistant tuberculosis.

Tuberculosis of the spine, if not treated adequately, may cause serious sequelae. Potent antitubercular drugs, modern diagnostic aids and advances in the surgical management have improved the outcome, but certain issues remain. These include the importance of early diagnosis in order to prevent and, if necessary, to treat kyphotic deformity, the principles of treating uncomplicated and complicated cases, the diagnosis and management of atypical presentations, the management of the sequelae of severe kyphotic deformity and the emergence of multidrug resistance.

Spinal tuberculosis is indolent and slow-growing and can be diagnosed both clinically and radiologically in endemic regions.[1,2] However, the lesions are best seen by MRI rather than by radiography.[3] The low signal on T1-weighted images and the bright signal on T2-weighted images in affected vertebral bodies, the relative preservation of the disc, the presence of a septate pre- and paravertebral or intra-osseous abscess with a subligamentous extension and breaching of the epidural space, (Fig. 1) are all characteristically seen on MRI.[4-6] The imaging features, with high sensitivity and specificity are disruption of the end-plate, 100% and 81.4% respectively, paravertebral soft-tissue shadow (96.8%, 85.3%) and a high signal intensity of the intervertebral disc on the T2-weighted image (80.6%, 82.4%). The overall sensitivity and specificity for diagnosis are 100% and 88.2%, respectively.[6] A well-defined abnormal paravertebral signal and a smooth-walled abscess are seen in 90% of tuberculous lesions, but not in a pyogenic vertebral abscess.[7,8] A pattern of bone destruction with relative preservation of the disc and heterogenous enhancement may differentiate spondylitic tuberculosis from pyogenic discitis, which may show perdiscal bone destruction and homogenous enhancement.[7] The presence of an abscess and bone fragments differentiate spinal tuberculosis from neoplasia and if there is doubt an image-guided biopsy is indicated.[9]

An MR scan will detect a tubercular lesion before it can be seen on a plain radiograph.[10-12] Multiple level tubercular lesions in the spine are observed in 16.3% to 71.4% of cases when an MRI study of the whole spine is performed.[13-15] The diffuse hyperintense signal on the T2-weighted and the hypointense appearance on the T1-weighted images are suggestive of liquid extradural compression. Caseous

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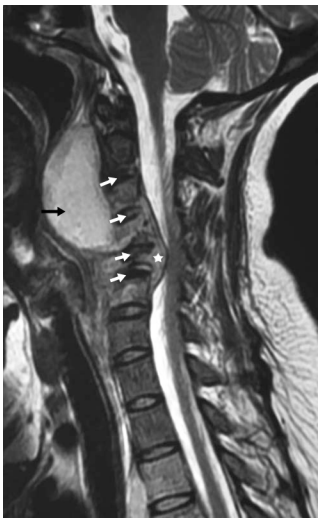

Fig. 1a

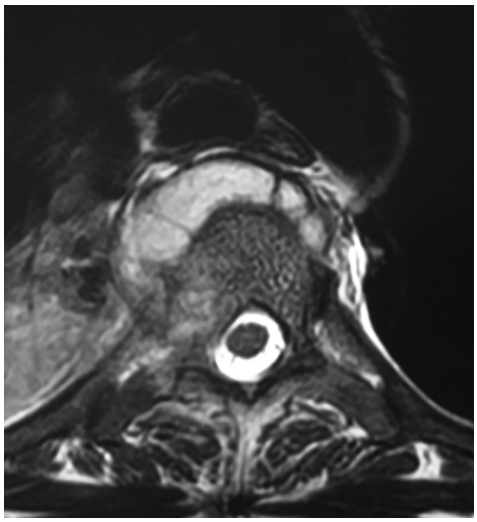

Fig. 1b

Figure 1a – A T2-weighted mid-sagittal MR scan of cervical spinal TB showing disease in vertebral bodies adjacent to the preserved intervertebral disc spaces (white arrows), subligamentous formation of an abscess (black arrow) and epidural involvement (star). Figure 1b – A T2-weighted axial MR scan of the same patient showing a septate pre- and paravertebral abscess and an intra-osseous abscess suggestive of a tubercular lesion.

tissue shows hyperintensity and granulation tissue heterogenous hyperintensity on T1- and T2-weighted images. The changes in the spinal cord may be interpreted as oedema of the cord, myelomalacia, atrophy of the cord and syringomyelia.[16] Oedema of the cord is compatible with good neurological recovery following treatment, while myelomalacia, accompanied by a severe neurological deficit may show incomplete recovery.[16] Mild atrophy of the cord is observed even when there is a successful neurological outcome. Moderate to severe atrophy, with or without syringohydromyelia, is seen in late-onset paraplegia.[16]

CT will delineate bone destruction earlier. Lesions of less than 1.5 cm are better appreciated than on plain radiography, but it is less accurate in defining the epidural extension of the disease. The bone destruction observed is either fragmentary (47%), osteolytic (33%) subperiosteal (10%) or localised and sclerotic (10%). Granulation tissue is seen as a high attenuation lesion and an abscess or caseous tissue as of low attenuation. Bone destruction with the shadow of a paravertebral abscess showing bone expansion with heterotopic bone or calcification is considered to be a sign of a tuberculous lesion.[17,18]

Relative lymphocytosis, a low level of haemoglobin and a raised ESR are found in active tubercular disease. The mantoux test is non-diagnostic in an endemic region and may be negative in an immunodeficient state. The sensitivity of staining for acid-fast bacilli may vary from 25% to 75%. Culture of acid-fast bacilli requires a long incubation period of four to six weeks, although Bactec radiometric culture takes less than two weeks.[19] The serological tests are non-diagnostic in lesions with a low level of bacilli. The immunoglobulin (Ig) G and IgM titres show significant differences between the initiation of treatment and at three months later, but do not correlate with the stage, the recovery of the disease or the duration of antituberculous treatment.[20,21] The polymerase chain reaction is an efficient and rapid method of diagnosis and can differentiate between typical and atypical mycobacteria. It analyses the expression of genes, even from the single cell. A positive result from a polymerase chain reaction is not a substitute for culture and is not indicative of the activity of the disease, since it does not differentiate live from dead micro-organisms and has been obtained from an 'ancient' sample of bone tissue.[20,22]

A CT/fluoroscopic-guided fine-needle aspiration cytology biopsy is diagnostic for spinal lesions in between 88.5% and 96.4% of cases.[23,24] In a series of 29 cases in which adequate tissue could be procured, cytological findings of epitheloid granulomas (89.7%), a granular necrotic background (82.8%) and lymphocytic infiltration (75.9%) were observed. The smear for acid-fast bacilli was positive in 51.7% and culture could be obtained in 82.8% of untreated cases.[23-25] Culture, staining for acid-fast bacilli and histopathology are not capable of ascertaining the diagnosis in all cases, hence tissue from a biopsy should always be subjected to staining, culture and sensitivity, a polymerase chain reaction and histopathological examination.

The neurological deficit in tuberculosis of the spine

The worst complications of tuberculosis of the spine are para- or tetraplegia, hemiplegia or monoplegia.[26,27] Paraplegia with active disease may be caused by mechanical pressure on the spinal cord by an abscess, granulation tissue, tubercular debris and caseous tissue, or by mechanical instability produced by pathological subluxation or

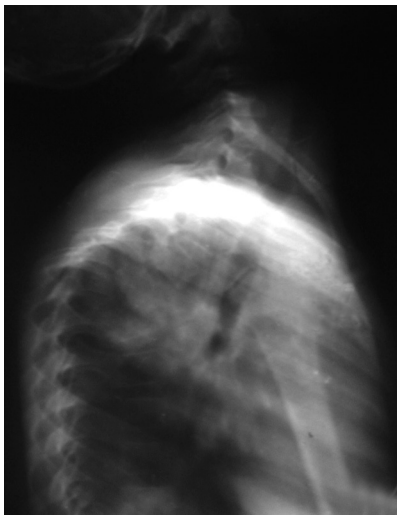

Fig. 2a

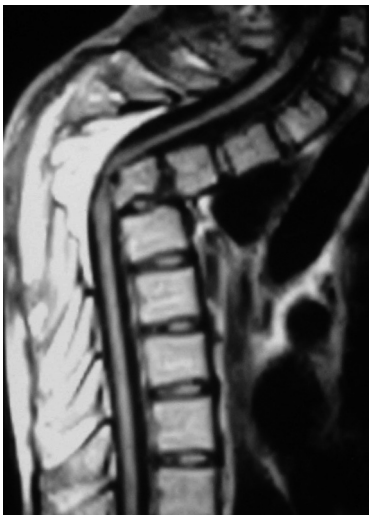

Fig. 2b

Figure 2a – Plain lateral radiograph of the upper dorsal spine obtained in 1987 in a boy then aged five years showing disease in four vertebrae with kyphosis. He was treated by chemotherapy. He was asymptomatic for 16 years and then began to show a neurological deficit. By 2007 he had a severe deficit. Figure 2b – A T1-weighted image mid-sagittal MR scan of the same patient, taken in 2007, showing a healed lesion of the upper dorsal spine with severe kyphosis. The internal salient is indenting the spinal cord which shows severe atrophy.

dislocation. Oedema of the spinal cord, myelomalacia or direct involvement of the meninges and cord by tubercular infection and inflammation, infective thrombosis or endarteritis of spinal vessels may also lead to neural loss. Epidural involvement is observed in over 80% of cases without clinical evidence of a neurological deficit.[6] Encroachment of the canal of up to 76% is compatible with an intact neural state. In the presence of mechanical instability the patient may develop neurological deficit at a lesser canal encroachment.[28]

Paraplegia with healed disease (Fig. 2) may occur when the initial lesion has healed with a residual severe deformity ten to 20 years before. It is produced by stretching the spinal cord over an internal anterior bony projection, producing gliosis. MRI shows severe atrophy of the cord and/or syringohydromyelia, or constricting scarring of and around the dura.[16,27] Reactivation of the disease is found in 30% to 40% of cases on exploration.[29] Symptomatic severe stenosis of the lumbar canal and ossification of the ligamentum flavum adjacent to severe kyphosis may produce an incomplete neurological deficit.[30,31]

Spinal deformity

The development of kyphosis is the rule rather than the exception. Patients treated conservatively have a mean increase in deformity of 15° and in between 3% and 5% the final deformity is > 60°.[32,33] After anterior decompression and bone grafting kyphosis continues to increase for six months.[34] Slippage and breakage of the graft, with consequent progression of the kyphosis and neurological deficit, are more frequent when the graft spans two disc levels.[35,36] In children the kyphosis continues to increase even after healing of the lesion. The growth potential of vertebral bodies may be destroyed by the disease, surgical resection and debridement or by the effect of biomechanical forces on the growth plate of both the fusion mass and the vertebral segment within the kyphotic region.[37] Progression of the kyphosis is found to be worst when anterior resection and fusion alone are performed. It is least when both anterior and posterior fusion is undertaken or with anterior debridement alone, when some growth potential is preserved.[38] The unabated growth of the posterior column may also add to the progression, but in their study Upadhyay et al[39] did not notice any evidence of disproportionate growth of the posterior spine.

Rajasekaran[40,41] observed continued progression of the deformity during the quiescent phase until the growth was complete in 40% of his patients, while 43% had spontaneous improvement and 17% showed no change. The progression of deformity was either of an angular kyphosis or by a buckling collapse.[41] The status of the posterior column and the type of stabilisation undertaken were the main factors determining deformity.

The vertebrae can restabilise when there is a large contact area on the distal vertebrae (type-A restabilisation), usually seen when the vertebral body is partially destroyed or in the lumbar region. When vertebral destruction is severe, with marked loss of vertebral height, and the patient already has a moderate kyphosis, one or both facets may sublux or dislocate, with the proximal vertebra stabilising with point contact on the distal (type-B restabilisation). The compressive force produces suppression of growth

resulting in a deformity of between 40° and 60°. The remaining part of the vertebral body may grow as a wedge. Type-C restabilisation occurs when there is severe destruction of the anterior column. The dislocation of both facets leads to a buckling collapse. The proximal vertebral body may rotate through 90° with its anterior border resting on the distal vertebra. The horizontal vertebrae are spared gravitational forces and hence grow longer, adding to the kyphosis. Buckling collapse is likely to occur in children younger than seven years of age with three or more vertebral bodies affected in the dorsal or dorsolumbar spine. Signs of a 'spine at risk' include retropulsion, subluxation, lateral translation or toppling.[40-42]

Other complications include a large retropharyngeal abscess producing problems with swallowing and hoarseness. Tubercular arteritis and a pseudo-aneurysm in association with an adjacent lesion has also been described.[43] The local instability and angular kyphotic deformity accelerate the degeneration of involved segments and ossification of the ligamentum flavum is likely to develop in response to the repetitive stimulus of excessive wear.[30,31] The spinal cord may undergo intrinsic changes to produce late-onset paraplegia. Patients develop painful costopelvic impingement and a reduced vital capacity, resulting in respiratory compromise.[2,21]

Principles of treatment

Before the advent of antibiotics only 25% of patients achieved healing when treated in a sanatorium. The remainder died from military disease.[21] Later treatment, such as posterior spinal fusion without curettage of the diseased bone, gave disappointing results.[21] The introduction of antibiotics allowed bacterial control of the disease and healing, but with a residual kyphosis. With improvements in imaging and diagnostics, better operating-theatre facilities, the introduction of intensive-care units and the use of modern spinal instrumentation, healing may be achieved with minimal or no spinal deformity.[44,45]

Tuberculosis of the spine without a deficit. The choice of treatment of uncomplicated tuberculosis of the spine was at one time controversial. The divergent philosophies of management by radical surgery or by ambulant chemotherapy were resolved by the multicentre trial organised by the Medical Research Council (MRC) of the United Kingdom. Conservative treatment involving the use of two or three antituberculous drugs with bedrest or ambulant chemotherapy, the radical clearance of a lesion and the Hong Kong method of anterior debridement and fusion or anterior debridement alone, gave similar long-term results with no late relapse or late-onset paraplegia.[46] The only advantage of the radical operation was less late deformity compared with debridement.[46] The cure rate for conservative treatment and for the Hong Kong method was 85% and 89.9%, respectively. Tuberculosis of the spine is a medical disease and should be treated with antituberculous drugs, rest and mobilisation with a suitable orthosis.[47-50] Surgery is indicated if the diagnosis is uncertain, for a panvertebral lesion, a potentially unstable spine which should be stabilised, for refractory disease, in an adult with kyphosis of 60° or more and in children when the kyphosis is likely to progress with growth.[27]

Antitubercular drugs are found in pus and granulation tissues at well above the minimum inhibitory concentration.[51-53] Isoniazid, rifampicin and pyrazinamide have been found above minimum inhibitory concentration in foci outside the sclerotic wall, and at undetected levels in foci inside the sclerotic wall.[54] Sclerotic bone seems to play an important role in blocking the penetration of antituberculous drugs into the disease focus.[54]

A daily dosage regime and an intermittent short course as described below, are currently the treatment of choice. *In vitro* exposure of tubercle bacilli to antituberculous drugs is followed by a lag period of several days before growth begins again. Hence maintenance of a continuous inhibitory concentration of the drug is not necessary to kill or to inhibit growth of *Mycobacterium tuberculosis*.[55-57] The most popular protocol is to use rifampicin, isoniazid, ethambutol and pyrazinamide for an initial two months followed by a maintenance phase of rifampicin and isoniazid for six, nine, 12 or 18 months. It was found that antituberculous therapy for six or nine months, with surgical excision of the lesion and bone grafting, produced clinical and radiological results comparable to those at 18 months.[58,59] Even in the presence of paraplegia, a combination of surgery when indicated and a short course of drug treatment for nine months was effective[60] if given under supervision. Recurrence after a short-course regime has also been described. Five of eight patients who had a six-month regime relapsed, while none of 30 patients, who had treatment for nine months or longer, did.[61]

The radiological evidence of healing lags behind by three months. In the absence of reliable serological and immunological markers of healing, the 'healed status' is achieved if there is clinical and radiological evidence of healing with no recurrence after two years. Short-course regimes after surgery and ambulant chemotherapy have both given encouraging results. Since the MRC trial failed to resolve the issue of the duration of drug treatment for spinal disease, a well-planned and executed randomised, control trial is needed to establish this.

Tuberculosis of the spine with a neurological deficit. The best treatment of spinal tuberculosis with paraplegia is to prevent the development of the paraplegia.[27,62] The objective is to decompress the spinal cord by conservative treatment and/or surgery, to stabilise the spine if needed and to respond appropriately to direct involvement of the spinal cord and meninges. Surgical treatment is practised worldwide even for a minimal grade of neurological deficit. Tuli[62] observed neurological recovery in 30% to 40% of patients having drug treatment and rest for four to six weeks while waiting for surgery or being made fit for it. However, waiting for a few weeks under these circumstances is clearly not

justified.[62] The patients in whom MRI shows a relatively preserved cord with evidence of myelitis or oedema and a predominantly fluid collection in the extradural space, respond well to conservative treatment if mechanical compression is the only cause of the neurological deficit.[16,27,63] Early surgical decompression is indicated when MRI shows that the extradural compression is due to granulation tissue or caseous tissue, with little fluid component compressing the spinal cord, and with features of oedema of the cord, myelitis or myelomalacia. The indications for surgical decompression with or without stabilisation are development, no improvement or worsening of neural deficit after conservative treatment,[16,27] the acute onset of a severe grade of paraplegia and paraplegia with involvement of the neural arch, or panvertebral involvement with or without pathological subluxation or dislocation.[27,63]

Instrumented stabilisation. Instrumented stabilisation can safely be performed in a tubercular infected bed.[64] In most reported series this was done in patients with a mild initial kyphosis of 30° to 35° in order to prevent further deterioration.[63] The indications for instrumented stabilisation are panvertebral disease, long segment disease in which the bone graft after anterior decompression is more than the length of two vertebral bodies[65] or when correction of a kyphosis is contemplated.[35,66] The span of anterior instrumentation in long segment disease requires a wider exposure. Posterior instrumentation, such as the use of a Hartshill implant, can take purchase in healthy vertebrae one segment above and below.[35] Pedicle screw fixation can also be used.

Correction of kyphosis in active disease. This is indicated when the patient presents with a severe kyphosis of ≥ 60°, or if the kyphosis is likely to heal with this amount of deformity. This will occur if three or more vertebrae are involved with a loss of 1.5 or more vertebral bodies in the dorsal or dorsolumbar spine.[6,44,66,67] Children younger than seven years of age, with three or more affected vertebral bodies in the dorsal or dorsolumbar spine and two or more 'at-risk signs', are likely to have progression of the kyphosis with growth and should undergo correction.[40-42]

At operation, anterior decompression or corpectomy, shortening of the posterior column, posterior instrumented stabilisation, grafting of the anterior gap and posterior fusion are performed in a sequential manner in a single stage.[66] During the procedure the spinal cord should be kept under vision in case it should become elongated. Correction of the kyphosis can be done by:

a) a single-stage transpedicular approach;[68-71]

b) two-stage anterior decompression and bone grafting followed by correction of the kyphosis and posterior instrumentation[72,73] or

c) a single-stage correction by an extrapleural anterolateral approach.[35,44,66]

The soft tissue on the lateral wall of the pedicle and vertebral body should be removed by blunt dissection and elevated on both sides by a single-stage transpedicular approach. The cancellous bone and granulation tissue should be curetted until the residual bony cortex remains. A dorsal closing-wedge osteotomy is undertaken. Before performing decompression and closing the wedge osteotomy the pedicle screws should be placed in the proximal and distal vertebral bodies, or Hartshill segmented spinal instrumentation undertaken later. During closure the thecal sac should be constantly kept under vision to avoid compromise of the cord.[68-71]

Correction of the kyphosis can be achieved by anterior decompression through a transthoracic transpleural or retroperitoneal approach with grafting of the gap, followed by posterior instrumentation through a midline posterior approach at the same time or two to three weeks later. Moon et al[72] initially performed posterior instrumentation followed by an anterior procedure in two stages in their early cases, but later did both in the same operation. The correction achieved was from 37° to 15°, finally healing at 18°.[72] Louw[73] performed transthoracic anterior decompression and vascularised rib grafting during the same procedure, or two weeks later, by shortening of the posterior column with a multilevel posterior osteotomy, instrumentation and fusion. The overall length of the anterior column was not altered and the kyphosis was corrected by an anterior graft acting as a pivot. The mean pre-operative kyphosis of 56° was corrected to 27°, which healed at 30°.

The anterior and posterior columns of the vertebral body can be exposed by an extrapleural anterolateral approach in the lateral position to correct a kyphosis (Fig. 3).[35,44,66] The thoracic cavity and diaphragm are not violated, thus pulmonary morbidity is avoided. The lateral position reduces the risk of a neural deficit and obviates the need for temporary stabilisation.

The cervical and lumbar kyphosis should be corrected at a lesser degree. Lumbar kyphosis is best corrected by a pedicle subtraction osteotomy. However, for cervical kyphosis (Fig. 4) it may be necessary to resort to cervical traction followed by anterior decompression, bridging the gap by a bone graft and anterior instrumented stabilisation using a plate.

Healed kyphosis and late onset paraplegia. Correction of a kyphosis in a patient with poor pulmonary function is a difficult procedure with a high risk of neurological injury. Yau et al[74] described a multistage procedure with spinal osteotomy and halopelvic distraction with an anterior and posterior fusion. The mean pre-operative kyphosis of 115.5° was corrected to 87.2° with three deaths in 29 patients. The authors concluded that this was a relatively small reward for such a major undertaking. Moon[75] believed that cosmetic correction of a long-standing severe healed kyphosis should not be performed. Such corrective surgery may be undertaken in severe deformity with recurrent disease and when paraplegia or death from chest complications is imminent. Recently, correction of a healed kyphosis of the lower dorsal and dorsolumbar spine by transpedicular subtraction osteotomy has been described.[76]

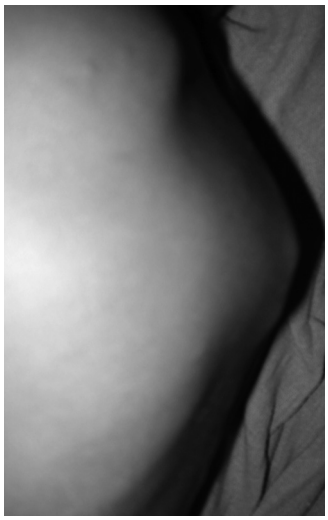

Fig. 3a

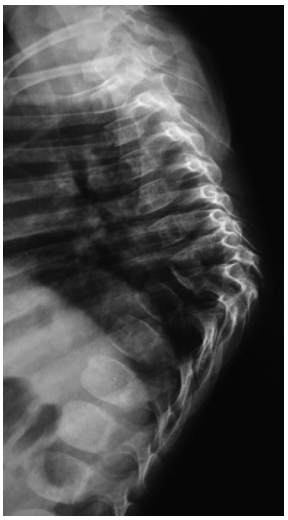

Fig. 3b

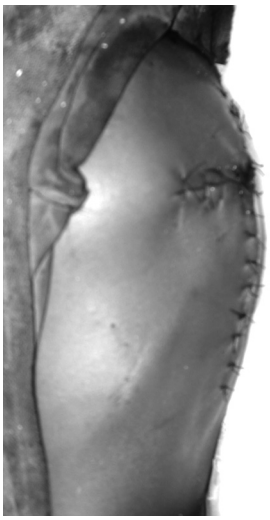

Fig. 3c

Figure 3a – A clinical photograph of a child aged three years with spinal tuberculosis showing a severe kyphotic deformity of the thoracic spine. Figure 3b – A plain lateral radiograph of the dorsal spine of the same patient showing involvement of D7 to D10 with severe kyphosis. This kyphosis will grow with growth of the child even after healing of the disease, hence correction is indicated. Figure 3c – A clinical photograph of the same patient showing good correction of the kyphosis achieved by an extrapleural anterolateral approach.

A mean pre-operative kyphosis of 58.8° was corrected to 17.9° with no major intra-operative complications. Anterior decompression and fusion are advocated in all such cases.[77,78] The internal bony prominence may be removed by a transthoracic transpleural approach. The extrapleural anterolateral approach allows direct exposure of this without jeopardising the already compromised pulmonary function.[78] The spinal cord has very little physiological, neural and vascular reserve, hence the high risk of neurological deterioration. The internal kyphectomy allows the spinal cord to transpose anteriorly. The response to anterior decompression is faster, better and safer in patients with a reactivation of tubercular disease,[78] while with healed disease decompression is technically more difficult and recovery less satisfactory.[79] Neurological deterioration, transient or permanent, and cerebrospinal fluid fistulae have been described and the patient should be warned before the surgery about the possibility of complications.[79] Internal kyphectomy is still worth performing in moderate and severe paraplegia since even mild sensory recovery may improve the quality of life.

Atypical spinal tuberculosis

The typical paradiscal tubercular lesion is well-described, easily recognised and treated[80,81] Atypical spinal tuberculosis is defined as compressive myelopathy with no visible or palpable spinal deformity and without the radiological appearance of a typical vertebral lesion.[80-83] Such lesions are relatively uncommon, mimic low-grade pyogenic infection, brucella and sickle-cell spondylitis, hydatid disease, lymphoma and malignant deposits and are difficult to diagnose and treat in the early stages with more chance of neurological complications.[80,81] Atypical lesions may present as an intraspinal tubercular granuloma, involvement of the neural arch, compressive myelopathy in single vertebral disease, a concertina collapse of a vertebra or a sclerotic vertebra with bridging of the intervertebral body.

Granulomatous lesions of the epidural, intradural, or intramedullary spaces present as a compressive myelopathy, the spinal tumour syndrome, without obvious radiological signs.[84,85] An extradural lesion may not have bony destruction or there may be a small lesion of a vertebral body not discernible on radiographs. MRI will demonstrate the lesion. Operation is the treatment of choice in order to procure tissue for histological diagnosis and to decompress the spinal cord. A laminectomy is required for an extradural extraosseous granuloma, but if the vertebral body is diseased, anterior or anterolateral decompression is indicated. Usually an extradural granuloma shows good neurological recovery after surgery.[84,85] Laminectomy is the operation of choice for a subdural granuloma. The dura is opened where it is tense. These patients also show good recovery. An intramedullary granuloma presents with a painless, compressive myelopathy with a past history of tuberculosis. The differential diagnosis includes solid tumours of the spinal cord and cysticercosis. Gadolinium-enhanced MRI is the investigation of choice. An intramedullary tuberculoma, if suspected on MRI, may resolve with antituberculous therapy and close observation of the neurological status.[86,87] Surgical decompression and myelotomy are indicated in order to decompress the spinal cord and to ascertain the diagnosis if the neurological status

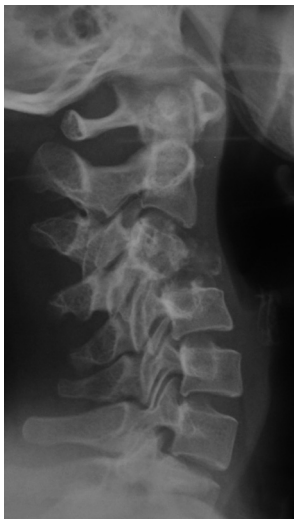

Fig. 4a

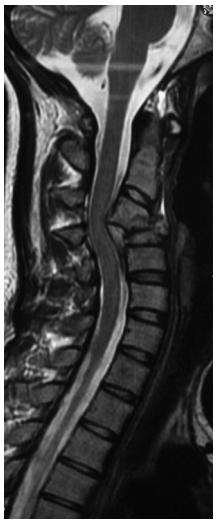

Fig. 4b

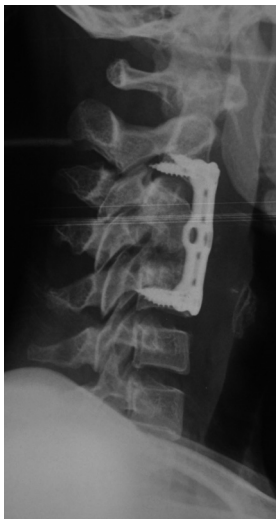

Fig. 4b

Figure 4a – A plain lateral radiograph of the cervical spine of 21-year-old woman showing destruction of C3-4 with loss of anterior body height and kyphosis of the upper cervical spine. Figure 4b – A T2-weighted mid-sagittal MR scan showing complete loss of the vertebral body of C4 and cervical kyphosis with the posterior border of C3 indenting the spinal cord. The patient had no neurological deficit. Figure 4c – A plain lateral radiograph of the cervical spine after anterior decompression, interbody grafting between C3 and C5 and plating. The kyphosis has been corrected.

deteriorates. Tubercular granuloma should be considered in the differential diagnosis of spinal tumour syndrome in zones endemic for tuberculosis.[86,87] Between 2% and 10% of all tubercular spines have a sole lesion in the posterior elements,[2,83] with a higher incidence of paraplegia.[82,83] It may affect the spinous process, the laminae, pedicles, apophyseal joints and transverse processes, with involvement of the pedicle being the most common. Plain radiography does not demonstrate these lesions, but the absence of a pedicular shadow in the anteroposterior view is suggestive of a pedicular lesion.[80] CT and MRI can clearly delineate such lesions. Fine-needle aspiration cytology is a useful diagnostic investigation. Chemotherapy is indicated in cases with no neurological deficit and a laminectomy in those with signs of neurological involvement.[81]

Tuberculous infection can start in the centre of the vertebral body which will be weakened by permeation with granulation tissue and may show concentric collapse.[81] Plain radiography may show collapse of the body with preservation of the adjacent disc space. MRI usually differentiates tuberculous disease from other pathologies and will show inflammatory changes in adjacent vertebrae. CT-guided biopsy is indicated for tissue diagnosis.[82,88]

Multidrug-resistant tuberculosis

This occurs when the organism develops resistance to rifampicin and isoniazid while resistance to any other drug is described as 'other drug resistance'.[89] The survival rate at five years for a patient with multidrug-resistant tuberculosis is 50%, similar to that of a patient with spinal tuberculosis in the pre-antibiotic era. Between 60% and 90% of HIV-positive cases have extrapulmonary tuberculosis.[90] Multidrug-resistant tuberculosis has developed because of erratic drug ingestion, monotherapy, suboptimal drug dosages, and inadequate duration of non-adherence to the drug treatment.[89]

If there has been no clinical improvement after adequate chemotherapy for three months and there is persistent growth of *Mycobacterium* from the sputum, development of multidrug-resistant pulmonary tuberculosis must be suspected. Since spinal tuberculosis is a paucibacillary disease and there is difficulty in procuring repeated samples of tissue from which to isolate the organism, the clinical criteria for suspicion of multidrug-resistant tuberculosis must be defined. Before resistance is demonstrated on culture and sensitivity, it is prudent to label suspected patients as 'therapeutically refractory cases'. Suspicion may be raised by a lack of clinical or radiological improvement, by the appearance of a new lesion or a cold abscess or by an increase in bone destruction after chemotherapy for three to five months.

The dose and duration of antituberculous drugs taken in the past should be listed. Early surgery is indicated to ascertain the diagnosis, identify the organism, perform culture and sensitivity tests and to reduce the bacterial load. Conventional bacteriological microscopy and cultures have limited sensitivity, specificity and a delayed diagnosis. Culture in Bactec radioactive liquid medium and genotypic analysis involving amplification by polymerase chain reaction followed by post-amplification analysis of mutation, have reduced the turnaround time to days rather than weeks or months.[91-93] The conventional assay must still be performed. Drugs for multidrug-resistant tuberculosis are

toxic, expensive, and are taken for a longer period of time. Therefore this condition is better prevented than treated. A minimum of four and preferably six bacteriocidal drugs should be used. A single drug should never be added to a failing regime and all drugs should be used for 24 months or longer. The adverse drug reactions and hepatic side-effects should be monitored diligently.

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References

1. **Jain AK, Kumar S, Tuli SM.** Tuberculosis of spine (C1 to D4). *Spinal Cord* 1999;37:362-9.
2. **Tuli SM.** *Tuberculosis of the skeletal system.* Second ed. New Delhi, India: Jaypee Brothers Medical Publishers, 1997.
3. **Griffith JF, Kumta SM, Leung PC, et al.** Imaging of musculoskeletal tuberculosis: a new look at an old disease. *Clin Orthop* 2002;398:32-9.
4. **Sharief HS, Clark DC, Aabed MY, et al.** Granulomation spinal infections: MR imaging. *Radiology* 1990;177:101-7.
5. **Andronikou S, Jadwat S, Douis H.** Patterns of disease on MRI in 53 children with tuberculous spondylitis and the role of gadolinium. *Pediatr Radiol* 2002;32:798-805.
6. **Danchaivijitr N, Temram S, Thepmongkhol K, Chiewvit P.** Diagnostic accuracy of MR imaging in tuberculous spondylitis. *J Med Assoc Thai* 2007;90:1581-9.
7. **Chang MC, Wu HT, Lee CH, Liu CL, Chen TH.** Tuberculous spondylitis and pyogenic spondylitis: comparative magnetic resonance imaging feature. *Spine* 2006;31:782-8.
8. **Jung NY, Jee WH, Ha KY, Park CK, Byun JY.** Discrimination of tuberculous spondylitis from pyogenic spondylitis on MRI. *AJR Am J Roentgenol* 2004;182:1405-10.
9. **Gupta RK, Agarwal P, Rastogi H, et al.** Problems in distinguishing spinal tuberculosis from neoplasia on MRI. *Neuradiology* 1996;38(Suppl 1):97-104.
10. **Desai SS.** Early diagnosis of spinal tuberculosis by MRI. *J Bone Joint Surg [Br]* 1994;76-B:863-9.
11. **Akman S, Sirvanci M, Talu U, Gogus A, Hamzaoglu A.** Magnetic resonance imaging of tuberculous spondylitis. *Orthopedics* 2003;26:69-73.
12. **Jain AK, Jena AN, Dhammi IK, Kumar S.** Fate of intervertebral disc space in paradiscal tuberculous lesions. *Indian J Orthop* 1999;33:90-4.
13. **Deng YW, Lu GH, Wang B, et al.** One stage posterior vertebral column resection for the treatment of throciclumbar tuberculosis with kyphotic deformity. *Zhang Nan Da Xue Bao Yi Xue Ban* 2008;33:865-70 (in Chinese).
14. **Polley P, Dunn R.** Noncontiguous spinal tuberculosis: incidence and management. *Eur Spine J* 2009;18:1096-101.
15. **Kaila R, Malhi AM, Mahmood B, Saifuddin A.** The incidence of multiple level noncontiguous vertebral tuberculosis detected using whole spine MRI. *J Spinal Disord Tech* 2007;20:78-81.
16. **Jain AK, Jena A, Dhammi IK.** Correlation of clinical course with magnetic resonance imaging in tuberculous myelopathy. *Neural India* 2000;48:132-9.
17. **Jain R, Sawhney S, Berry M.** Computed tomography of vertebral tuberculosis: patterns of bone destruction. *Clin Radiol* 1993;47:196-9.
18. **Sinan T, Al-Khawari H, Ismail M, Ben-Nakhi A, Sheikh M.** Spinal tuberculosis: CT and MRI feature. *Ann Saudi Med* 2004;24:437-41.
19. **Negi SS, Khan SF, Gupta S, et al.** Comparison of the conventional diagnostic modalities, baltec culure and polymerase chain reaction test for diagnosis of tuberculosis. *Indian J Med Microbiol* 2005;23:29-33.
20. **Jain AK, Jena SK, Singh M, et al.** Evaluation of clinico-radiological, bacteriological, serological, molecular and histological diagnosis of osteoarticular tuberculosis. *Indian J Orthop* 2008;42:173-7.
21. **Tuli SM.** Tuberculosis of the spine: a historical review. *Clin Orthop* 2007;460:29-38.
22. **Zink AR, Grabner W, Nerlich AG.** Molecular identification of human tuberculosis in recent and historic bone tissue samples: the role of molecular techniques for the study of historic tuberculosis. *Am J Phys Anthropol* 2005;126:32-47.
23. **Kang M, Gupta S, Khandelwal N, et al.** CT-guided fine-needle aspiration biopsy of spinal lesions. *Acta Radiol* 1999;40:474-8.
24. **Mondal A, Misra DK.** CT-guided needle aspiration cytology (FNAC) of 112 vertebral lesions. *Indian J Pathol Microbiol* 1994;37:255-61.
25. **Francis IM, Das DK, Luthra UK, et al.** Value of radiologically guided fine needle aspiration cytology (FNAC) in the diagnosis of spinal tuberculosis: a study of 29 cases. *Cytopathology* 1999;10:390-401.
26. **Dhammi IK, Singh S, Jain AK.** Hemiplegic/monoplegic presentation of cervical spine (C1-C2) tuberculosis. *Eur Spine J* 2001;10:540-4.
27. **Jain AK.** Treatment of tuberculosis of the spine with neurologic complications. *Clin Orthop* 2002;398:75-84.
28. **Jain AK, Aggarwal A, Mehrotra G.** Correlation of canal encroachment with neurological deficit in tuberculosis of the spine. *Int Orthop* 1999;23:85-6.
29. **Hsu LC, Cheng CL, Leong JC.** Pott's paraplegia of late onset: the course of compression and results after anterior decompression. *J Bone Joint Surg [Br]* 1988;70-B:534-8.
30. **Luk KD, Krishna M.** Spinal stenosis above a healed tuberculosis kyphosis: a case report. *Spine* 1996;21:1098-101.
31. **Chen Y, Lu XH, Yang LL, Chen DY.** Ossification of ligamentum flavum related to thoracic kyphosis after tuberculosis: case report and review of the literature. *Spine* 2009;34:41-4.
32. **Guven O.** Severe kyphotic deformity in tuberculosis of the spine. *Int Orthop* 1996;20:271.
33. **Rajasekaran S, Shanmugasundaram TK.** Prediction of the angle of gibbus deformity in tuberculosis of the spine. *J Bone Joint Surg [Am]* 1987;69-A:503-9.
34. **Upadhyay SS, Saji MJ, Sell P, Sell B, Hsu LC.** Spinal deformity after childhood surgery for tuberculosis of the spine: a comparison of radical surgery and debridement. *J Bone Joint Surg [Br]* 1994;76-B:91-8.
35. **Jain AK, Dhammi IK, Prashad B, Sinha S, Mishra P.** Simultaneous anterior decompression and posterior instrumentation of the tuberculous spine using an anterolateral extrapleural approach. *J Bone Joint Surg [Br]* 2008;90-B:1477-81.
36. **Rajasekaran S, Soundarapandian S.** Progression of kyphosis in tuberculosis of the spine treated by anterior arthrodesis. *J Bone Joint Surg [Am]* 1989;71-A:1314-23.
37. **Upadhyay SS, Saji MJ, Sell P, Hsu LC, Yau AC.** The effect of age on the change in deformity after anterior debridement surgery for tuberculosis of the spine. *Spine* 1996;21:2356-62.
38. **Schulitz KP, Kothe R, Leong JC, Wehling P.** Growth changes of solidly fused kyphotic bloc after surgery for tuberculosis: comparison of four procedures. *Spine* 1997;22:1150-5.
39. **Upadhyay SS, Saji MJ, Sell P, Yau AC.** The effect of age on the change in deformity after radical resection and anterior arthrodesis for tuberculosis of the spine. *J Bone Joint Surg [Am]* 1994;76-A:701-8.
40. **Rajasekaran S.** The problem of deformity in spinal tuberculosis. *Clin Orthop* 2002;398:85-92.
41. **Rajasekaran S.** Buckling collapse of the spine in childhood spinal tuberculosis. *Clin Orthop* 2007;460:86-92.
42. **Rajasekaran S.** The natural history of post-tubercular kyphosis in children: radiological signs which predict late increase in deformity. *J Bone Joint Surg [Br]* 2001;83-B:954-62.
43. **Jain AK, Chauhan RS, Dhammi IK, Maheshwari AV, Ray R.** Tubercular pseudoaneurysm of aorta: a rare association with vertebral tuberculosis. *Spine J* 2007;7:249-53.
44. **Jain AK, Dhammi IK, Jain S, Mishra P.** Kyphosis in spinal tuberculosis: prevention and correction. *Indian J Orthop* 2010;44:127-36.
45. **Jain AK.** Tuberculosis of the spine. *Clin Orthop* 2007;460:2-3.
46. **No authors listed.** A 15-year assessment of controlled trials of the management of tuberculosis of the spine in Korea and Hong Kong: thirteenth report of the Medical Research Council Working Party on Tuberculosis of the Spine. *J Bone Joint Surg [Br]* 1998;80-B:456-62.
47. **Jutte PC, Van Loenhout-Rooyackers JH.** Routine surgery in addition to chemotherapy for treating spinal tuberculosis. *Cochrane Database Syst Rev* 2006;1:CD004532.
48. **Nene A, Bhojraj S.** Results of nonsurgical treatment of thoracic spinal tuberculosis in adults. *Spine J* 2005;5:79-84.
49. **Tuli SM.** Results of treatment of spinal tuberculosis by "middle-path" regime. *J Bone Joint Surg [Br]* 1975;57-B:13-23.
50. **Kotil K, Alan MS, Bilge T.** Medical management of Pott disease in the thoracic and lumbar spine: a prospective clinical study. *J Neurosurg Spine* 2007;6:222-8.
51. **Tuli SM, Kumar K, Sen PC.** Penetration of antitubercular drugs in clinical osteoarticular tibercular lesions. *Acta Orthop Scand* 1977;48:362-8.
52. **Wu Q, Duan L, Lin Y.** Comparison of three antituberculous drugs in serum and cold abscesses of patients with spinal tuberculosis. *Zhonghua Jie He He Hu Xi Za Zhi* 1998;21:617-19 (in Chinese).
53. **Kumar K.** The penetration of drugs into the lesions of spinal tuberculosis. *Int Orthop* 1992;16:67-8.
54. **Ge Z, Wang Z, Wei M.** Measurement of the concentration of three antituberculosis drugs in the focus of spinal tuberculosis. *Eur Spine J* 2008;17:1482-7.
55. **Dickinson JM, Mitchison DA.** In vitro studies on the choice of drugs for intermittent chemotherapy of tuberculosis. *Tubercle* 1966;47:370-80.
56. **Dickinson JM, Ellard GA, Mitchison DA.** Suitability of isoniazid and ethambutol for intermittent administration in the treatment of tuberculosis. *Tubercle* 1968;49:351-66.

57. Dickinson JM, Mitchison DA. Suitability of rifampicin for intermittent administration in the treatment of tuberculosis. *Tubercle* 1970;51:82-94.

58. Upadhyay SS, Saji MJ, Yau AC. Duration of antituberculosis chemotherapy in conjunction with radical surgery in the management of spinal tuberculosis. *Spine* 1996;21:1898-903.

59. Parthasarathy R, Sriram K, Santha T, et al. Short-course chemotherapy for tuberculosis of the spine: a comparison between ambulant treatment and radical surgery: ten year report. *J Bone Joint Surg [Br]* 1999;81-B:464-71.

60. Rajeswari R, Balasubramanian R, Venkatesan P, et al. Short-course chemotherapy in the treatment of Pott's paraplegia: report on five year follow-up. *Int J Tuberc Lung Dis* 1997;1:152-8.

61. Ramachandran S, Clifton IJ, Collyns TA, Watson JP, Pearson SB. The treatment of spinal tuberculosis: a retrospective study. *Int J Tuberc Lung Dis* 2005;9:541-4.

62. Tuli SM. Treatment of neurological complications in tuberculosis of the spine. *J Bone Joint Surg [Am]* 1969;51-A:680-92.

63. Jain AK, Dhammi IK. Tuberculosis of the spine: a review. *Clin Orthop* 2007;460:39-49.

64. Oga M, Arizono T, Takasita M, Sugioka Y. Evaluation of the risk of instrumentation as a foreign body in spinal tuberculosis: clinical and biologic study. *Spine* 1993;18:1890-4.

65. Rajasekran S, Soundarapandian S. Progression of kyphosis in tuberculosis of the spine treated by anterior arthrodesis. *J Bone Joint Surg [Am]* 1989;71-A:1314-23.

66. Jain AK, Maheshwari AV, Jena S. Kyphus correction in spinal tuberculosis. *Clin Orthop* 2007;460:117-23.

67. Jain AK, Aggarwal PK, Arora A, Singh S. Behaviour of the kyphotic angle in spinal tuberculosis. *Int Orthop* 2004;28:110-14.

68. Laheri VJ, Badhe NP, Dewnany GT. Single stage decompression, anterior interbody fusion and posterior instrumentation for tuberculous kyphosis of the dorso-lumbar spine. *Spinal Cord* 2001;39:429-36.

69. Lee SH, Sung JK, Park YM. Single-stage transpedicular decompression and posterior instrumentation in treatment of thoracic and throracolumbar spinal tuberculosis: a retrospective case series. *J Spinal Disord Tech* 2006;19:595-602.

70. Gokce A, Ozturkmen Y, Mutlu S, Caniklioglu M. Spinal osteotomy: correcting sagittal balance in tuberculous spondylitis. *J Spinal Disord Tech* 2008;21:484-8.

71. Bezer M, Kucukdurmaz F, Guven O. Transpedicular decancellation osteotomy in the treatment of posttuberculous kyphosis. *J Spinal Disord Tech* 2007;20:209-15.

72. Moon MSW, Woo YK, Lee KS, et al. Posterior instrumentation and anterior interbody fusion for tuberculous kyphosis of dorsal and lumbar spines. *Spine* 1995;20:1910-16.

73. Louw JA. Spinal tuberculosis with neurological deficit: treatment with anterior vascularised rib grafts, posterior osteotomies and fusion. *J Bone Joint Surg [Br]* 1990;72-B:686-93.

74. Yau AC, Hsu LC, O'Brien JP, Hodgson AR. Tuberculous kyphosis: correction with spinal osteotomy, halo-pelvic distraction, and anterior and posterior fusion. *J Bone Joint Surg [Am]* 1974;56-A:1419-34.

75. Moon MS. Tuberculosis of the spine: controversies and a new challenge. *Spine* 1997;22:1791-7.

76. Kalra KP, Dhar SB, Shetty G, Dhariwal Q. Pedicle subtraction osteotomy for rigid post-tuberculous kyphosis. *J Bone Joint Surg [Br]* 2006;88-B:925-7.

77. Rajeswari R, Ranjani R, Santha T, Sriram K, Prabhakar R. Late onset paraplegia: a sequela to Pott's disease: a report on imaging, prevention and management. *Int J Tuberc Lung Dis* 1997;1:468-73.

78. Bilsel N, Aydingöz O, Hanci M, Erdogan F. Late onset Pott's paraplegia. *Spinal Cord* 2000;38:669-74.

79. Wong YW, Leong JC, Luk KD. Direct internal kyphectomy for severe angular tuberculous kyphosis. *Clin Orthop* 2007;460:124-9.

80. Jain AK, Sethi A, Sethi R, Kumar S. Atypical presentation of spinal tuberculosis. *Indian J Orthop* 1997;31:164-70.

81. Pande KC, Babhulkar SS. Atypical spinal tuberculosis. *Clin Orthop* 2002;398:67-74.

82. Naim-ur-Rahman. Atypical forms of spinal tuberculosis. *J Bone Joint Surg [Br]* 1980;62-B:162-5.

83. Babhulkar SS, Tayade WB, Babhulkar SK. Atypical spinal tuberculosis. *J Bone Joint Surg [Br]* 1984;66-B:239-42.

84. Kumar S, Jan AK, Dhammi IK, Aggarwal AN. Treatment of intraspinal tuberculoma. *Clin Orthop* 2007;460:62-6.

85. Jain AK, Singh S, Sinha S, Dhammi IK, Kumar S. Intraspinal tubercular granuloma: an analysis of 17 cases. *Indian J Orthop* 2003;37:182-5.

86. Dhammi K, Jain AK, Buxi TB. Non-operative management of an intramedullary tuberculoma. *Trop Doct* 2002;32:44-5.

87. Jena A, Banerji AK, Tripathi RP, et al. Demonstration of intramedullary tuberculomas by magnetic resonance imaging: a report of two cases. *Br J Radiol* 1991;64:555-7.

88. Pande KC, Pande SK, Babhulkar SS. Concentric collapse of the vertebral body: an atypical form of spinal tuberculosis. *Neurol Inf Epidemiol* 1997;2:225-7.

89. Loddenkemper R, Sagebiel D, Brende A. Strategies against multidrug-resistant tuberculosis. *Eur Respir J* 2002;36(Suppl):66-77.

90. Waters DA. Surgery for tuberculosis before and after human immunodeficiency virus infection: a tropical perspective. *Br J Surg* 1997;84:8-14.

91. Victor TC, Lee H, Cho SN, et al. Molecular detection of early appearance of drug resistance during Mycobacterium tuberculosis infection. *Clin Chem Lab Med* 2002;40:876-81.

92. Garcia de Viedma D, de Sol Diaz Infantes M, Lasala F, et al. New real-time PCR able to detect in a single tube multiple rifampin resistance mutations and high-level isoniazid resistance mutations in Mycobacterium tuberculosis. *J Clin Microbiol* 2002;40:988-95.

93. Palomino JC. Molecular detection, identification and drug resistance detection in Mycobacterium tuberculosis. *FEMS Immunol Med Microbiol* 2009;56:103-11.