Review
Spinal tuberculosis: A review

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Spinal tuberculosis is a destructive form of tuberculosis. It accounts for approximately half of all cases of musculoskeletal tuberculosis. Spinal tuberculosis is more common in children and young adults. The incidence of spinal tuberculosis is increasing in developed nations. Genetic susceptibility to spinal tuberculosis has recently been demonstrated. Characteristically, there is destruction of the intervertebral disk space and the adjacent vertebral bodies, collapse of the spinal elements, and anterior wedging leading to kyphosis and gibbus formation. The thoracic region of vertebral column is most frequently affected. Formation of a 'cold' abscess around the lesion is another characteristic feature. The incidence of multi-level noncontiguous vertebral tuberculosis occurs more frequently than previously recognized. Common clinical manifestations include constitutional symptoms, back pain, spinal tenderness, paraplegia, and spinal deformities. For the diagnosis of spinal tuberculosis magnetic resonance imaging is more sensitive imaging technique than x-ray and more specific than computed tomography. Magnetic resonance imaging frequently demonstrates involvement of the vertebral bodies on either side of the disk, disk destruction, cold abscess, vertebral collapse, and presence of vertebral column deformities. Neuroimaging-guided needle biopsy from the affected site in the center of the vertebral body is the gold standard technique for early histopathological diagnosis. Antituberculous treatment remains the cornerstone of treatment. Surgery may be required in selected cases, e.g. large abscess formation, severe kyphosis, an evolving neurological deficit, or lack of response to medical treatment. With early diagnosis and early treatment, prognosis is generally good.

Keywords: Tuberculosis, Myelopathy, Spinal cord, Antituberculous treatment, Cold abscess, *Mycobacterium tuberculosis*

Introduction

Spinal tuberculosis is a frequently encountered extrapulmonary form of the disease. In developed nations, most cases of spinal tuberculosis are seen primarily in immigrants from endemic countries. Because the epidemic of human immunodeficiency virus (HIV) infection caused resurgence in all forms of tuberculosis, increased awareness about spinal tuberculosis is necessary. Despite its common occurrence and the high frequency of long-term morbidity, there are no straightforward guidelines for the diagnosis and treatment of spinal tuberculosis. Early diagnosis and prompt treatment is necessary to prevent permanent neurological disability and to minimize spinal deformity.[1,2]

Spinal tuberculosis is one of the oldest diseases known to mankind and has been found in Egyptian mummies dating back to 3400 BC.[3] The disease is popularly known as Pott's spine. The name traces back its origin from the description of tuberculous infection of the spine by Sir Percival Pott in his monograph in 1779.[4] The majority of his patients were infants and young children. The classic destruction of the disk space and the adjacent vertebral bodies, destruction of other spinal elements, severe and progressive kyphosis subsequently became known as Pott's disease. Currently, the term 'Pott's disease/Pott's spine' describes tuberculous infection of the spine and the term 'Pott's paraplegia' describes paraplegia resulting from tuberculosis of the spine.

This review focuses on the various aspects of spinal tuberculosis. An extensive review of the literature published in English was carried out using the PubMed and Google Scholar databases. The search terms included tuberculosis, skeletal tuberculosis, spinal tuberculosis, Pott's disease, Pott's paraplegia, and central nervous system tuberculosis.

Epidemiology

Tuberculosis is a disease of poverty that affects mostly young adults in their most productive years. The risk of developing tuberculosis is estimated to be 20–37

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times greater in people co-infected with HIV than among those without HIV infection. In 2009, approximately 1.2 million new tuberculosis cases were reported among people living with HIV; 90% of these cases were concentrated in the African and South East Asian regions. The highest number of tuberculosis-related deaths were in Africa.[5,6] Although multidrug-resistant tuberculosis is not common in spinal disease, there have been a few recent case reports.[7]

The exact incidence and prevalence of spinal tuberculosis in most parts of the world are not known. In countries with a high burden of pulmonary tuberculosis, the incidence is expected to be proportionately high. Approximately 10% of patients with extrapulmonary tuberculosis have skeletal involvement. The spine is the most common skeletal site affected, followed by the hip and knee. Spinal tuberculosis accounts for almost 50% cases of skeletal tuberculosis.[8]

Spinal tuberculosis is uncommon in the western world. Most of the patients with spinal tuberculosis in developed countries are immigrants from countries where tuberculosis is endemic. A study evaluated the epidemiology of musculoskeletal tuberculosis in United Kingdom and a review of data of musculoskeletal tuberculosis over a 6-year period was performed. From 1999 to 2004, there were 729 patients with tuberculosis. Approximately 8% (61) cases had musculoskeletal involvement; nearly 50% of these patients had spinal involvement. The majority (74%) of patients was immigrants from the Indian subcontinent.[9] In France, in a hospital-based survey, the overall incidence of vertebral osteomyelitis was estimated at 2.4/100 000. In 2002–2003, 1422 and 1425 patients were classified as definite (64%), probable (24%), and possible (12%) vertebral osteomyelitis. The main infectious agents reported were *Staphylococcus* spp. (38%) and *Mycobacterium tuberculosis* (31%).[10] In endemic countries, spinal tuberculosis is more common in children and younger adults, while the disease affects the adult population in developed Western and Middle East countries.[9,11]

Spinal tuberculosis in HIV-infected persons
Tuberculosis is the most common HIV-related opportunistic infection worldwide.[12] In a Nigerian study, the records of 1320 HIV-infected patients were reviewed. One-hundred and thirty eight (10%) patients were coinfected with tuberculosis. Fifty (36%) coinfected patients had some type of extrapulmonary tuberculosis; 15 had both pulmonary tuberculosis and extrapulmonary tuberculosis. Among the 35 patients with extrapulmonary tuberculosis, 14% patients had spinal tuberculosis.[13] A study from South Africa, evaluated 525 medical records of all patients seen for spinal conditions, of which 104 (20%) had spinal tuberculosis. About 90% of patients with spinal tuberculosis were African and 10% from other races. The incidence of spinal tuberculosis was approximately 1 and 3 per 100 000 for Africans and other races, respectively. All the patients had a history of pulmonary tuberculosis. In this study, 28% patients were HIV-positive.[14]

Multi-level noncontiguous vertebral tuberculosis
Multi-level noncontiguous spinal tuberculosis is an atypical form of spinal tuberculosis that affects two noncontiguous vertebrae without destruction of the adjacent vertebral bodies and intervertebral disks. So far, there have been a few recent case reports with involvement of two or more noncontiguous vertebrae. However, in one study, the incidence of multi-level noncontiguous vertebral tuberculosis was observed as high as 71% and a large proportion of the patients with affected noncontiguous vertebral sites were asymptomatic. In this retrospective analysis, patients were included if spinal infection was identified by whole spine magnetic resonance imaging (MRI) and confirmed as tuberculosis by a combination of histology and microbiology.[15] In another study, authors identified 16 cases of noncontiguous spinal tuberculosis from a single surgeon series of 98 patients. Most noncontiguous lesions were evident on plain radiology and noncontiguous tuberculosis was not associated with HIV infection, multidrug-resistant tuberculosis or with chronicity of the disease.[16]

Pathogenesis and pathology
Predisposing factors for tuberculosis include poverty, overcrowding, illiteracy, malnutrition, alcoholism, drug abuse, diabetes mellitus, immunosuppressive treatment, and HIV infection. These are also predisposing factors for spinal tuberculosis as well.[17] In Iran, older age, male gender, chronic peritoneal dialysis, imprisonment, and previous tuberculous infection were identified as risk factors for tuberculous spondylitis.[18] Genetic susceptibility to spinal tuberculosis has recently been demonstrated. A group of workers investigated the association between the FokI polymorphism in the vitamin-D receptor gene and spinal tuberculosis in a Chinese population and this gene was found to be associated with susceptibility to spinal tuberculosis.[19]

Spinal involvement is usually a result of hematogenous spread of *M. tuberculosis* into the dense vasculature of cancellous bone of the vertebral bodies. The primary infection site is either a pulmonary lesion or an infection of the genitourinary system.[20–22] Spread occurs

either via the arterial or the venous route. An arterial arcade, in the subchondral region of each vertebra, is derived from anterior and posterior spinal arteries; this arcade form a rich vascular plexus. This vascular plexus facilitates hematogenous spread of the infection in the paradiskal regions. Batson's paravertebral venous plexus in the vertebra is a valve-less system that allows free flow of blood in both directions depending upon the pressure generated by the intra-abdominal and intrathoracic cavities following strenuous activities like coughing. Spread of the infection via the intraosseous venous system may be responsible for central vertebral body lesions. In patients with noncontiguous vertebral tuberculosis, again it is the vertebral venous system that spreads the infection to multiple vertebrae.

Spinal tuberculosis is initially apparent in the anterior inferior portion of the vertebral body. Later on it spreads into the central part of the body or disk. Paradiskal, anterior, and central lesions are the common types of vertebral involvement. In the central lesion, the disk is not involved, and collapse of the vertebral body produces vertebra plana. Vertebra plana indicates complete compression of the vertebral body. In younger patients, the disk is primarily involved because it is more vascularized. In old age, the disk is not primarily involved because of its age-related avascularity. In spinal tuberculosis, there is involvement of more than one vertebra because its segmental arteries bifurcate to supply two adjacent vertebrae. Spread of the disease beneath the anterior or posterior longitudinal ligaments involves multiple contiguous vertebrae. A lack of proteolytic enzymes in mycobacterial infections (in comparison with pyogenic infections) has been suggested as the cause of the of the subligamentous spread of infection.[1,2,8,17,23–26]

In spinal tuberculosis, characteristically, there is destruction of the intervertebral disk space and the adjacent vertebral bodies, collapse of the spinal elements, and anterior wedging leading to the characteristic angulation and gibbus (palpable deformity because of involvement of multiple vertebrae) formation. The upper lumbar and lower thoracic spine are most frequently involved sites. More than one vertebra is typically affected, and the vertebral body is more frequently affected than the posterior arch.[27] Distortion of spinal column leads to spinal deformities (Table 1).

Paraplegia is the most devastating complication of spinal tuberculosis. Hodgson, in his classical paper on Pott's paraplegia, classified paraplegia into two groups according to the activity of the tuberculous infection. These two groups were paraplegia of active disease

Table 1   Mechanisms of paraplegia/tetraplegia in spinal tuberculosis

Causes of neurological involvement	
Early-onset paraplegia	
Mechanical pressure	Mechanical pressure by tuberculous debris, sequestrem of bone or disk, abscess, subluxation and dislocations, concertina collapse, and internal gibbus
Tuberculous granuloma	Tuberculoma in extradural, intradural, or intramedullary regions
Tuberculous myelitis	Uncommon. May involve spinal cord parenchyma
Spinal artery thrombosis	Infective thrombosis of anterior spinal artery
Tuberculous arachnoiditis	Meningeal inflammation and fibrosis
Late-onset paraplegia	
Transection of spinal cord by bony bridge	Transverse ridge of bone produced by severe kyphosis
Fibrosis of dura (pachymeningitis)	Formation of tough, fibrous membrane encircling the cord

(early-onset paraplegia) and paraplegia of healed disease (late-onset paraplegia).

Early-onset paraplegia develops in the active stage of spinal tuberculosis and requires active treatment. This type of paraplegia has a better prognosis and is frequently seen in adults with Pott's spine. In these patients, paraplegia is caused by formation of debris, pus, and granulation tissue due to destruction of bone and intervertebral disk. Destruction of the anterior vertebral column leads to subluxation and subsequent dislocation of the spine. Concertina collapse (compression fracture without involvement of the intervertebral disk) may occur because of extensive tuberculous destruction. Concertina collapse bulges into the parenchyma of the spinal cord. Intrinsic factors cause meningomyelitis by direct involvement of spinal cord, surrounding meninges and roots or by involvement of blood vessels supplying the spinal cord. In addition, some rarer causes of paraplegia include infective thrombosis of arteries supplying the spinal cord and nonosseous intramedullary or extramedullary tuberculoma of the spinal cord (Table 1). Late-onset paraplegia is a neurological complication that develops after a variable period in a patient with healed tuberculosis. Late-onset paraplegia may develop two to three decades after active infection. It is often associated with marked spinal deformities.[28]

Clinical features

The characteristic clinical features of spinal tuberculosis include local pain, local tenderness, stiffness and spasm of the muscles, a cold abscess, gibbus, and a prominent

spinal deformity. The cold abscess slowly develops when tuberculous infection extends to adjacent ligaments and soft tissues. Cold abscess is characterized by lack of pain and other signs of inflammation (Fig. 1).

The progression of spinal tuberculosis is slow and insidious. The total duration of the illness varies from few months to few years, with average disease duration ranging from 4 to 11 months. Usually, patients seek advice only when there is severe pain, marked deformity, or neurological symptoms.[29–31]

Constitutional symptoms are present in approximately 20–30% of cases of osteoarticular tuberculosis. The classical constitutional features of tuberculosis indicating presence of an active disease are malaise, loss of weight and appetite, night sweats, evening rise in temperature, generalized body aches, and fatigue.

Back pain is the most frequent symptom of spinal tuberculosis. The intensity of pain varies from constant mild dull aching to severe disabling. Pain is typically localized to the site of involvement and is most common in the thoracic region. The pain may be aggravated by spinal motion, coughing, and weight bearing, because of advanced disk disruption and spinal instability, nerve root compression, or pathological fracture.

Chronic back pain as the only symptom was observed in 61% of cases of spinal tuberculosis.[32,33]

Neurologic deficits are common with involvement of thoracic and cervical regions. Left untreated, early neurologic involvement may progress to complete paraplegia or tetraplegia. Paraplegia may occur at any time and during any stage of the vertebral disease. The reported incidence of neurological deficit in spinal tuberculosis varies from 23 to 76%.[30] The level of spinal cord involvement determines the extent of neurological manifestations. In cervical spinal tuberculosis, patients manifest with symptoms of cord or root compression. The earliest signs are pain, weakness, and numbness of the upper and lower extremities, eventually progressing to tetraplegia. If the thoracic or lumbar spine is involved, upper extremity function remains normal while lower-extremity symptoms progress over time eventually leading to paraplegia.[20] Patients with cauda equina compression due to lumbar and sacral vertebral damage have weakness, numbness, and pain, but have decreased or absent reflexes among the affected muscle groups. This is in contrast to the hyperreflexia seen with spinal cord compression along with bladder involvement (cauda-equina syndrome).
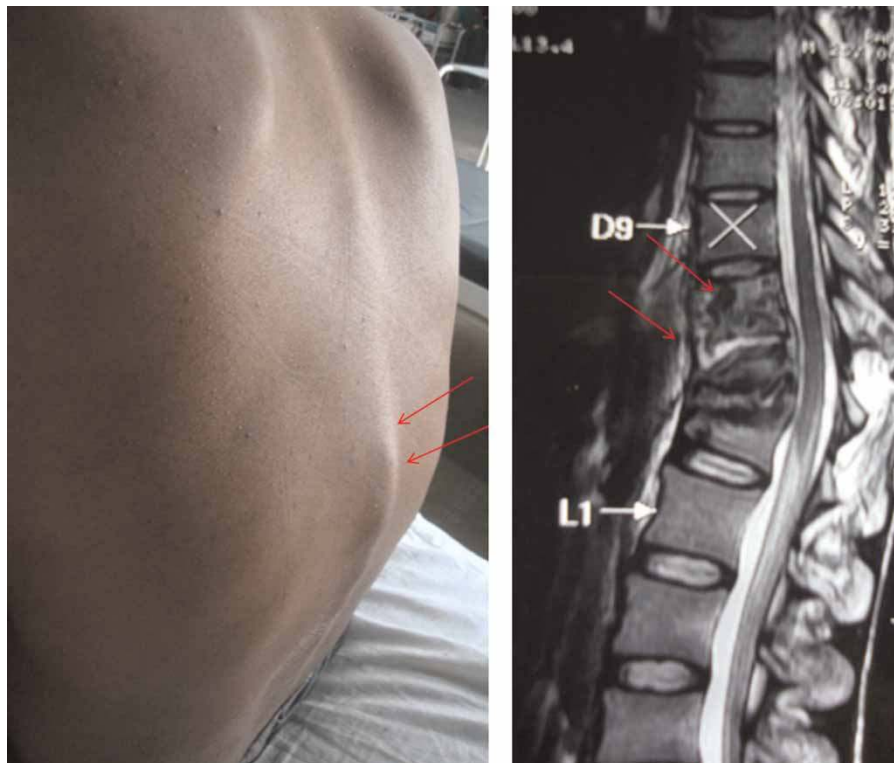

Figure 1 'Gibbus formation' in the thoraco-lumbar region of a patient with spinal tuberculosis (left). The magnetic resonance shows spinal tuberculosis at T10–T12. Spinal tuberculosis causes the destruction, collapse of vertebrae, and angulation of vertebral column (right).

Formation of a cold abscess around the vertebral lesion is another characteristic feature of spinal tuberculosis. Abscess formation is common and can grow to a very large size. The site of cold abscess depends on the region of the vertebral column affected. In the cervical region, the pus accumulates behind prevertebral fascia to form a retropharyngeal abscess (Fig. 2). The abscess may track down to the mediastinum to enter into the trachea, esophagus, or the pleural cavity. Retropharyngeal abscess can produce considerable pressure effects such as dysphagia, respiratory distress, or hoarseness of voice. In the thoracic spine, the cold abscess usually presents as a fusiform or bulbous paravertebral swellings and may produce posterior mediastinal lumps (Fig. 3). The cold abscesses formed at lumbar vertebrae most commonly present as a swelling in the groin and thigh. Abscess can descend down beneath the inguinal ligament to appear on the medial aspect of thigh. Pus collection can follow the blood vessels to
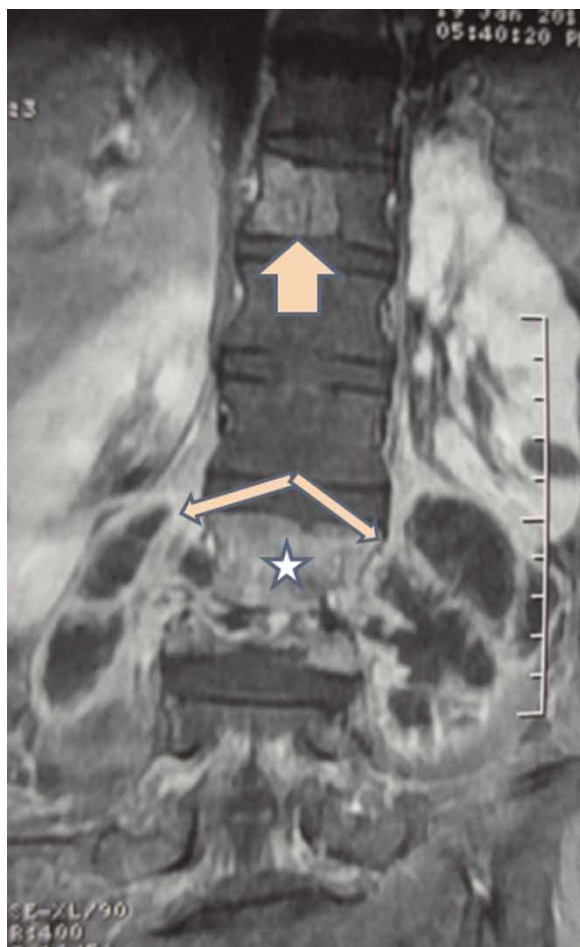

Figure 2   T1-weighted image of an MRI scan shows a bilateral paravertebral abscess with destruction of lumbar vertebrae as well as the intervertebral disks.

form an abscess in gluteal region if it follows femoral or gluteal vessels, respectively.[1,17]

Spinal deformity is a hallmark feature of spinal tuberculosis. Type of spinal deformity depends on the location of the tuberculous vertebral lesion. Kyphosis, the most common spinal deformity, occurs with lesions involving thoracic vertebrae. The severity of the kyphosis depends on the number of vertebrae involved. An increase in kyphotic deformity by 10° or more may be seen in up to 20% of cases, even after the treatment. Atlanto-axial tuberculosis may present as torticollis.[8,34]

Diagnosis
Diagnosis of spinal tuberculosis depends on presence of characteristic clinical and neuroimaging findings. Etiological confirmation requires the demonstration of acid-fast bacilli on microscopy or culture of material obtained following biopsy the lesion. Polymerase chain reaction is also an effective method for bacteriological diagnosis of tuberculosis. Screening of the whole spine should be done to look for noncontiguous vertebral lesions.

Imaging
Conventional radiographs give a good overview; computed tomography (CT) visualizes the disko-vertebral lesions and paravertebral abscesses, while MRI is useful in determining the spread of the disease to the soft tissues and to determine the extent of spinal cord involvement.[35]

Plain radiographs
In resource-poor countries, vertebral radiography still remains the cornerstone of spinal imaging. It often provides enough information for diagnosis and treatment of spinal tuberculosis. The plain radiograph described changes consistent with tuberculosis spine in up to 99% of cases.[29,36–38] The characteristic radiographic findings include rarefaction of the vertebral end plates, loss of disk height, osseous destruction, new-bone formation and soft-tissue abscess. Often, multiple vertebrae are involved and late fusion or collapse of vertebrae is not uncommon[39] (Table 2).

Tuberculous cold abscesses may also be seen on plain radiographs as soft tissue shadows adjacent to the spine. In cervical spine, increase in prevertebral soft tissue space is a reliable radiological parameter suggesting inflammatory pathology (retropharyngeal abscess).[40] Widening of the superior mediastinum in antero-posterior x-ray and increased prevertebral soft tissue shadow with anterior convexity of tracheal shadow in lateral x-rays of the upper dorsal spine are strong
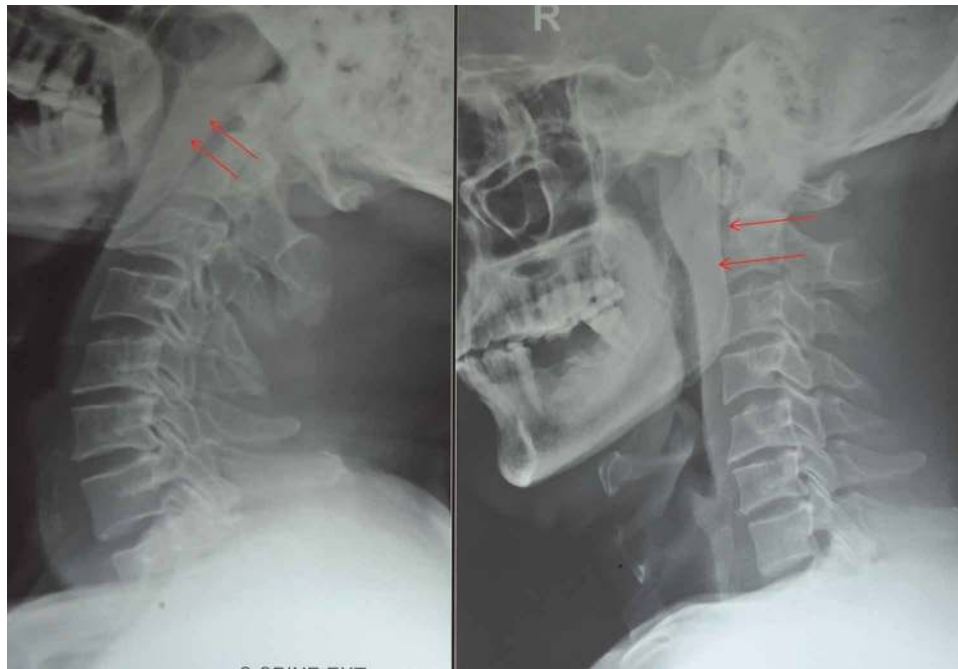
Figure 3   X-rays of cervical region showing retropharyngeal abscess.

Table 2   Various types of vertebral involvement in spinal tuberculosis

Type of involvement	Mechanisms of involvement	Radiological appearances
Paradiskal	Spread of disease via the arteries	Involves adjacent margins of two consecutive vertebrae. The intervening disk space is reduced
Central	Spread of infection along Batson's plexus of veins	Involves central portion of a single vertebra; proximal and distal disk spaces intact
Anterior marginal	Abscess extension beneath the anterior longitudinal ligament and the periosteum	Begins as destructive lesion in one of the anterior margins of the body of a vertebra, minimally involving the disk space but sparing the vertebrae on either side
Skipped lesions	Spread of infection along Batson's plexus of veins	circumferentially involvement of two noncontiguous vertebral levels without destruction of the adjacent vertebral bodies and intervertebral disks
Posterior	Spread via the posterior external venous plexus of vertebral veins or direct spread	Involves posterior arch without involvement of vertebral body
Synovial	Hematogenous spread through subsynovial vessels	Involves synovial membrane of atlanto-axial and atlanto-occipital joints

indicators of the disease in the underlying vertebrae. Dorsal and lumbar spine abscesses are seen as paravertebral soft tissue shadows. The presence of calcification within the abscess is virtually diagnostic of spinal tuberculosis. Such calcifications are formed because of the lack of proteolytic enzymes in *M. tuberculosis*.[41]

Certain vertebral sites where it is difficult to appreciate bony changes on conventional x ray are craniovertebral junction and cervico-dorsal junction.[40] The main disadvantage is that radiographs generally remain normal in the early stages of the disease. Approximately one-third of calcium must be lost from a particular area for osteolysis to be appreciated radiographically.[42] It is also difficult to assess spinal cord compression, soft tissue involvement, abscesses and extent of disease on plain x-rays. On the contrary, by the time disease is apparent on x-rays, the patient has already reached an advanced stage of illness with, with the majority having vertebral collapse and neurological deficits.

Concomitant pulmonary tuberculosis is frequent in patients with spinal tuberculosis. From 50 and 75% of patients with osteoarticular tuberculosis and up to 67% of patients with spinal tuberculosis have an associated primary lung focus or have a reported history of pulmonary tuberculosis.[22,43] In a series of 60 patients with miliary tuberculosis and neurological complications, 3 patients had Pott's paraplegia[44] (Fig. 4).
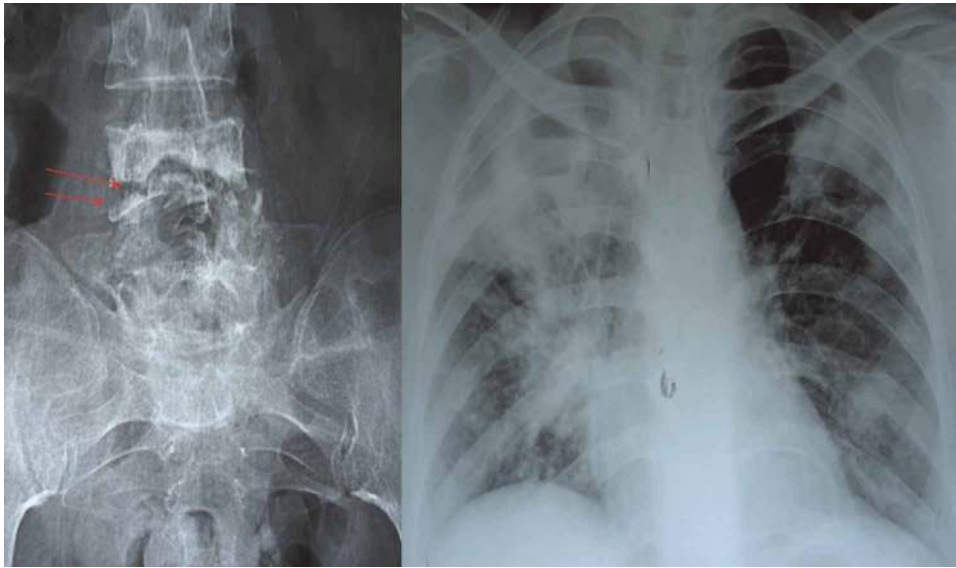
Figure 4   X-ray of sacral region of spine shows destruction of vertebrae which is suggestive of spinal tuberculosis (left). X-ray chest of same patient which shows presence of extensive pulmonary tuberculosis (right).

Computed tomography

CT demonstrates abnormalities earlier than plain radiography. The pattern of bone destruction may be fragmentary in 47% of the cases; osteolytic in 34%, localized and sclerotic in 10%, and subperiosteal in 30% cases.[45] Other findings include soft tissue involvement and paraspinal tissue abscess. CT is of great value in the demonstration of any calcification within the cold abscess or visualizing epidural lesions containing bone fragments. CT is of the greatest value in the delineation of encroachment of the spinal canal by posterior extension of inflammatory tissue, bone or disk material, and in the CT-guided biopsy.[38,46]

Magnetic resonance imaging

MRI is the neuroimaging of choice for spinal tuberculosis. MRI is more sensitive than x-ray and more specific than CT in the diagnosis of spinal tuberculosis. MRI allows for the rapid determination of the mechanism for neurologic involvement.[23,25,47,48]

MRI readily demonstrates involvement of the vertebral bodies, disk destruction, cold abscess, vertebral collapse, and spinal deformities. In the early stages, however, only disk degeneration with alteration of bone marrow signal intensity of vertebra is seen, which may not be sufficiently diagnostic of spinal tuberculosis. Abscess formation and collection and expansion of granulation tissue adjacent to the vertebral body is highly suggestive of spinal tuberculosis. MRI is also useful in detecting intramedullary or extramedullary tuberculoma, spinal cord cavitation, spinal cord edema, and possibly unsuspected noncontiguous lesions of the spine.[23,25,36,49] The subligamentous spread of a paraspinal mass and the involvement of multiple contiguous bones and intramedullary spinal changes can be very well demonstrated by MRI[50] (Table 2) (Figs. 1, 2 and 5).

The posterior spinal element, specifically the pedicle involvement, is generally not a characteristic feature of spinal tuberculosis. In a study, pedicle involvement was noted in unusually high (65%) number of patients. In this study the highest involvement was at the thoracic level. The mean vertebral body, disk collapse, prevertebral abscess, and kyphosis were more severe in the pedicle-involved group.[51] There is no pathognomonic finding on MRI that reliably distinguishes tuberculosis from other spinal infections or from a possible neoplasm.[47,48]

Bone scan

There are no pathognomonic scintigraphic features of spinal tuberculosis. Infection usually causes a hot spot, but avascular bone fragments may produce a cold spot. Bone scan is, however, helpful in differentiating from metastatic lesions, which usually show uptake of radioactive substance at multiple sites. The technetium 99 m bone scan was negative in 35% of an series of patients with Pott's spine.[52,53] In another study, the pattern of uptake similar to metastatic disease was seen in 63% of the patients of Pott's spine.[39] Gallium scintigraphic scans were also negative in most of the patients with active tuberculosis of the spine.[53]

Figure 5 X-ray of cervical region which shows spinal tuberculosis of cervical six to seven vertebrae and a retropharyngeal abscess (left). T1-weighted image of an MRI of same patient, which shows destruction of C6–C7 vertebrae.

Cytological and microbiological confirmation

Etiological confirmation can be made either by demonstration of acid-fast bacilli on pathological specimen or histological evidence of a tubercle or the mere presence of epithelioid cells on the biopsy material.[54]

Neuroimaging guided-needle biopsy from the affected site is the gold standard technique for the early histopathological diagnosis of spinal tuberculosis.[38] CT-guided needle biopsy usually yields sufficient material either from the spine itself or from an adjacent abscess. Open biopsy of the spine is usually performed when either closed techniques have proved insufficient or other procedures, such as decompression and possibly arthrodesis, are planned. In an Indian study, fine needle aspiration biopsy done under CT guidance was successful in diagnosing spinal tuberculosis in 34 out of 38 patients.[55] Surgery may be required in up to 10% of cases to establish the etiological diagnosis.[33] Material obtained from biopsy should be submitted for cytologic, histologic, and bacteriologic studies. Smear positivity for acid-fast bacilli may be seen in up to 52% of cases and culture positivity in about 83% of cases.[56] However, as with respiratory tuberculosis, culture is not the gold standard for diagnosing spinal tuberculosis because mycobacterial bacilli are not readily detected from extrapulmonary sites.[57]

Histologic studies confirm the diagnosis of spinal tuberculosis in approximately 60% of patients. The most common cytological findings observed are epithelioid cell granulomas (90%), granular necrotic background (83%), and lymphocytic infiltration (76%). Scattered multinucleated and Langhans' giant cells may be seen in up to 56% of cases.[58–61] False-negative results of biopsy are common and, therefore, diagnosis of spinal tuberculosis must be made on ground of clinical manifestations and radiology when bacteriology proves negative.[62]

Polymerase chain reaction and other immunological tests

Conventional microbiological methods like Ziehl–Neelsen staining for acid-fast bacilli and culture of *M. tuberculosis* on Lowenstein Jensen media have low sensitivity and specificity.[53,63] In addition, culturing *M. tuberculosis* is time consuming, taking 6–8 weeks for the growth to appear.[64] So, mostly, the diagnosis of tuberculosis depends on histological evidence. Polymerase chain reaction has shown very promising results for the early and rapid diagnosis of the disease. This technique is able to detect as few as 10–50 tubercle bacilli in various clinical samples.[65] This test offers better accuracy than a smear and can be performed at greater speed than cultures.[66] Various studies have reported sensitivity of polymerase chain reaction ranging from 61 to 90% and a specificity of 80–90%.[67–71]

The QuantiFERON-TB Gold assay detects cell-mediated inflammatory responses in vitro to tuberculosis infection by measuring interferon-gamma harvested in plasma from whole blood incubated with the *M. tuberculosis*-specific antigens. In a study, 70 consecutive patients with vertebral collapse underwent a battery of investigations including the QuantiFERON assay. The patients were classified as having tuberculosis on the basis of positive smear or culture, a biopsy consistent with tuberculosis, or a therapeutic response to antituberculosis chemotherapy. Tuberculosis was diagnosed in 51 patients, and 19 had vertebral collapse that was attributable to other causes. In this study, sensitivity was estimated as 84% and specificity was 95%.[72]

Other tests

Erythrocyte sedimentation rate (ESR) is generally raised many folds in the majority of patients with spinal tuberculosis. ESR declines to normal or near normal when the active tuberculous lesion is controlled. In pyogenic infection, leucocytosis parallels with raised ESR, while in patients with spinal tuberculosis, there is markedly elevated ESR with a normal white blood cell count.[73]

Differential diagnosis

Spinal tuberculosis should be considered in the differential diagnosis of chronic back pain (with or without constitutional, neurological, or musculoskeletal manifestations) and in young persons. The spinal tuberculosis should also be considered in immigrant patients of chronic back pain coming from endemic countries.[33] Several spinal diseases need be differentiated from spinal tuberculosis. Common differential diagnosis includes pyogenic spondylitis, brucellar spondylitis, sarcoidosis, metastasis, multiple myeloma, and lymphoma (Table 3).

The characteristic imaging characteristics of vertebral tuberculosis include extensive paraspinal soft tissue shadows, thoracic region involvement, well-defined paraspinal abnormal signal, subligamentous spread, and presence of spinal deformities.[74] In brucellar spondylitis, the lumbar vertebrae are the most frequently affected followed by thoracic and cervical segments of the vertebral column. The differentiating imaging characteristics of brucellar spondylitis include disk space involvement, minimal paraspinal soft tissue shadow, and absence of gibbus deformity. A pyogenic infection of vertebrae is found more often in the lumbar and cervical regions. Pyogenic spondylitis does not involve the vertebrae, posterior arch and spinous process, and often there is no gibbus deformity. Intervertebral disk destruction is more frequent in pyogenic spondylitis.[74–76] Sarcoidosis can produce multifocal lesions of vertebrae and disks, along with paraspinal masses that appear identical to tuberculosis[77,78] (Table 4). Osteoporotic vertebral involvement is more common in thoracic regions. Osteoporotic vertebral lesions do not involve the pedicle or have contour abnormalities.

In patients with metastatic spinal cord involvement, the intervertebral disk height is usually preserved, but this may be affected in lymphoma and multiple myeloma. The vertebral end-plates are also distinct and usually regular. The posterior vertebral segments are more extensively affected early on. It is difficult to differentiate spinal tuberculosis from a metastatic

Table 3 Diagnosis of spinal tuberculosis: summary points

1. X-ray, CT, or MRI of the spine should be performed in all patients
2. Spinal MRI determines extent and nature of the bony destructions as well as soft tissue involvement (including spinal cord)
3. Screening of whole spine should be done to look for skipped lesions
4. All patients should have a chest x-ray to detect coexisting pulmonary tuberculosis
5. Advantages and disadvantages of both biopsy and needle aspiration should be discussed with the patient, with the aim of obtaining adequate material for diagnosis
6. Material obtained from the site of disease by needle biopsy or open surgery should be submitted for microbiology, histology, and culture
7. Appropriate treatment regimen should be started without waiting for culture results
8. Clinicians should consider spinal tuberculosis even if histology and rapid diagnostic tests are negative, but clinical suspicion is strong
9. The appropriate drug regimen should be continued even if subsequent culture results are negative

Table 4 Differential diagnosis of vertebral involvement because of pyogenic, tuberculous, brucellar or metastatic diseases

	Pyogenic	Tuberculous	Brucellar	Metastatic
Duration of illness (in months)	2-3	3-6	2-6	<2
Usual age of presentation	Any age	Children and young adults	Middle-aged	Middle-aged and elderly
Anatomical location	Lumbar	Lumbo-thoracic	Lumbar	Thoracic
Vertebral and other structures involved	Vertebral bodies and the intervening disk, minimal soft tissue involvement	Vertebral bodies and the intervening disk, extensive soft tissue involvement (cold abscess)	Vertebral bodies and the intervening disk, minimal paraspinal soft tissue involvement, sacroiliitis	Posterior wall of the vertebral body (60%), pedicles and lamina (50%)
Common predisposing factors	Systemic illnesses like diabetes mellitus	Exposure to tuberculous infection	Ingestion of unpasteurized milk	Presence of systemic malignancy
Common clinical features	Fever and marked back pain, myelopathy	Fever, malaise and weight loss, backache, myelopathy	Fever, malaise, weight loss, backache	Bone pain at night, backache, back pain followed by radicular pain, myelopathy
Laboratory features				
Leukocytosis	Present	Absent	Present	Absent
Raised ESR	Raised	Raised	Raised	Not raised
C-reactive protein	Raised	May be raised	May be raised	Not raised
Neuroimaging (salient features)	Destruction of vertebral bodies and disc spaces, marked enhancement of the lesion, epidural abscess	Destruction of vertebral bodies and disc spaces, rim enhancement of the soft-tissue masses	Intact vertebral architecture despite diffuse vertebral osteomyelitis	Low signal intensity on T1-weighted images, hypersignal on T2-weighted images and heterogeneous enhancement

disease on MRI if there is prominent central body tuberculosis and epidural tuberculous granuloma without osseous involvement.[30] In elderly patients with vertebral damage, metastatic disease of the spine should always be considered (Table 4).

Treatment

In patients with spinal tuberculosis, antituberculous treatment should be started as early as possible. Antituberculous treatment often needs to be instituted empirically, much before an etiological diagnosis is established. In resource-poor countries, etiological diagnoses may not be established at all. In patients with established complications of spinal tuberculosis, surgery may also be required. Sequelae like kyphosis require surgical intervention.[79,80]

Almost all antituberculous drugs penetrate well into tuberculous vertebral lesions. The distribution of antituberculosis drugs such as rifampin, isoniazid, and pyrazinamide was evaluated in affected vertebral tissues of spinal tuberculosis. In patients without vertebral sclerotic wall around the tuberculous foci, the isoniazid concentrations in foci were of bactericidal levels. Levels of rifampin and pyrazinamide in foci corresponded to the minimal inhibitory concentrations of each drug, respectively. The sclerotic bone of affected vertebra played a role in blocking the antituberculosis drug's penetration. In another study, three drugs resulted in an effective bactericidal concentration level in osseous tissues around the foci of spinal tuberculosis except for the 4 mm of osseous tissue surrounding the sclerotic wall. The results suggested that osseous tissues within 4 mm surrounding the sclerotic wall should be removed during the surgery.[81,82]

Antituberculous treatment

Various studies have shown that the majority (82–95%) patients of spinal tuberculosis respond very well to medical treatment. The treatment response is apparent in form of pain relief, decrease in neurological deficit, and even correction of spinal deformity.[58–60,79,80] Patients with potentially dangerous craniovertebral junction tuberculosis also respond satisfactorily to medical treatment.[83] Patients with medically resistant spinal tuberculosis need careful reassessment of the differential diagnosis before surgery is planned surgery.[59,84]

Therapeutic regimen

The total duration of treatment and numbers of drugs needed for adequate treatment have always been subject to controversy.[84] World Health Organization (WHO) recommends a category-based treatment for

tuberculosis. Spinal tuberculosis falls under category-1 of the WHO treatment category. The category-1 antituberculosis treatment regimen is divided into two phases: an intensive (initial) phase and a continuation phase. In the 2-month intensive phase, antituberculous therapy includes a combination of four first-line drugs: isoniazid, rifampicin, streptomycin, and pyrazinamide. In the continuation phase, two drugs (isoniazid and rifampicin) are given for 4 months. Because of the serious risk of disability and mortality and because of difficulties of assessing treatment response, WHO recommends 9 months of treatment for tuberculosis of bones or joints.[85] The American Thoracic Society recommends 6 months of chemotherapy for spinal tuberculosis in adults and 12 months in children.[86] The British Thoracic Society recommends 6 months of daily treatment with rifampicin and isoniazid, supplemented in the initial 2 months with pyrazinamide and either ethambutol or streptomycin (the 6-month four-drug regimen), irrespective of age.[87] Although 6 months of treatment is considered sufficient, many experts still prefer a durations of 12–24 months or until radiological or pathological evidence of regression of disease occurs.[30,33,88,89] To avoid poor compliance, directly observed treatment and short-course regimens may be administered.[90] There is no definite role for corticosteroids in spinal tuberculosis except in cases of spinal arachnoiditis or nonosseous spinal tuberculosis.[57,91]

Supportive measures

General supportive measures, together with prolonged recumbency and rest, formed the basis of treatment for a patient with tuberculosis of the spine before the era of antituberculous chemotherapy. Sanatorium care was formerly the avenue of treatment for patients with pulmonary and bone tuberculosis. Today, the majority of patients with bone tuberculosis are treated with ambulatory care without prolonged recumbency and rest. Although cast or brace immobilization was a classic form of treatment, it was found to be inefficient and has generally been abandoned.[10]

Surgery

There is controversy about the precise role of surgery in the management of spinal tuberculosis. This difference of opinion goes back to 1960 when Hodgson and Stock advocated surgical treatment, and Konstam and colleagues advocated conservative treatment.[92–94] However, many experts feel that neither all cases of tuberculosis of spine should be treated conservatively, nor do all cases require surgery. Approximately 40% of the cases of tuberculosis of the spine with paraplegia

show recovery with antituberculous treatment, rest, and/or traction. Tuli, in 1975, proposed a 'middle-path regimen' for treatment of spinal tuberculosis. It advocates conservative treatment with multi-drug chemotherapy and surgery reserved for specific indications.[95]

The Medical Research Council of the United Kingdom, on the basis of results of some hallmark studies, had shown that antituberculous treatment alone can be effective, with a resolution of neurological sequelae and prevention of substantial progression of kyphosis. A Cochrane Database Review assessing the role of routine surgery in addition to chemotherapy in spinal tuberculosis also concluded that evidence was insufficient for the routine use of surgery. There were no statistically significant differences for any of the outcome measures: kyphosis angle, neurological deficit (none went on to develop this), bony fusion, absence of spinal tuberculosis, death from any cause, activity level regained, change of allocated treatment, or bone loss.[58] The guidelines published by the Royal College of Physicians noted that there was no additional advantage of routinely carrying out anterior spinal fusion over standard chemotherapy.[57]

A randomized trial performed primarily among ambulatory patients by the Medical Research Council Working Party on Tuberculosis of the Spine demonstrated no additional benefit of surgical debridement or radical operation (resection of the spinal focus and bone grafting) in combination with chemotherapy compared with chemotherapy alone. Myelopathy with or without functional impairment most often responds to chemotherapy.[96] In two Medical Research Council studies conducted in Korea, 24 of 30 patients in one study and 74 of 85 patients in an earlier study had complete resolution of myelopathy or complete functional recovery when treated medically.[97,98]

In some circumstances, however, surgery appears to be beneficial and may be indicated.[97,98] Potential benefits of surgery were less kyphosis, immediate relief of compressed neural tissue, quicker relief of pain, higher percentage of bony fusion, quicker bony fusion, less relapse, earlier return to previous activities, and less bone loss. It may also prevent late neurological problems due to kyphosis of the spine if fusion has not occurred.[32,99] One expert suggested that indications for surgery were pan-vertebral lesions, refractory disease, severe kyphosis, an evolving neurological deficit, and clinical deterioration or lack of clinical improvement.[100,101]

Two types of surgical procedures are performed. One is debridement of the infected material. In this form of

Table 5 Indications of surgery in spinal tuberculosis

Indications for surgery in patients without neurological complications	Indications for surgery in patients with neurological complications
Progressive bone destruction in spite of ATT	New or worsening neural complications or lack of improvement with conservative treatment
Failure to respond to conservative therapy	Paraplegia of rapid onset or severe paraplegia
Evacuation of paravertebral abscess when it has increased in size despite medical treatment	Late-onset paraplegia
Uncertainty of diagnosis, for biopsy	Neural arch disease
Mechanical reasons: spinal instability caused by destruction or collapse, destruction of two or more vertebrae, kyphosis	Painful paraplegia in elderly patients
Prevention of severe kyphosis in young children with extensive dorsal lesions	Spinal tumor syndrome (epidural spinal tuberculoma without osseous involvement)
Large paraspinal abscess	

ATT, antituberculous treatment.

surgery no attempt is made to stabilize the spine. The other procedure is debridement with stabilization of the spine (spinal reconstruction). This is a more extensive procedure and the reconstructions are performed with bone grafts. Stabilization may also be done using artificial materials like steel, carbon fiber, or titanium[58] (Table 5).

Treatment of spinal tuberculosis in HIV infection

Treatment of tuberculosis in patients with HIV infection follows the same principles as treatment of uninfected patients. Spinal tuberculosis in HIV-infected patients can also be satisfactorily treated with good clinical outcome irrespective of HIV status and treatment with antiretroviral therapy.[102,103] However, there are several important differences between patients with and without HIV infection. These differences include the potential for drug interactions, especially between the rifamycins and antiretroviral agents, paradoxical reactions that may be interpreted as clinical worsening, and the potential for the development of acquired resistance to rifamycins when treated with highly intermittent therapy. Major orthopedic surgery in HIV-positive patients has potential for increased risk for sepsis.[104]

Management of complications

Measures that are helpful in minimizing the increase in kyphosis include recumbency in the early active stage of the disease and prolonged protection of the spine with suitable braces in later stages. Most experts believe that kyphosis greater than 30° is likely to generate back pain and may deteriorate further, and hence, requires surgical correction.[105–107] Aspiration or surgical drainage was carried out for some patients with large cold abscesses because it was thought to improve the patient's general condition, and prevent rapid progression of the abscess along the spine. This has been

shown to be ineffective, however, and surgical drainage of a cold abscess alone is no longer recommended.[23] Abscesses usually resolve with medical therapy as antituberculosis drugs penetrate very well.[108,109]

Prognosis

Prognosis is generally good in patients without neurological deficit and deformity. Various studies show that 82–95% cases respond to medical treatment alone in the form of pain relief, improving neurological deficit, and correction of spinal deformity.[23,108] In a recently published study among patients with neurologic deficit, significant recovery occurred in 92%, with 74% improving from nonambulatory to ambulatory status. This study included 82 patients; 52% of patients presented in a nonambulatory state, 21% had mild neurologic deficits, and 27% had intact neurological function.[110] In a study from an endemic country, the majority (79 patients, 61%) of patients had severe motor and sensory impairment. Imaging revealed multiple vertebral involvements in 90 patients (80%). All patients were managed using antituberculous treatment; however, 33 patients required operative treatment as well. Marked clinical improvement was seen in 91 patients (70%) within 6 months of treatment.[111]

In Korea, a retrospective study examined the treatment outcome in patients with spinal tuberculosis. A total of 116 patients with spinal tuberculosis were analyzed. Forty-seven patients (35%) had severe symptoms. Radical surgery was carried out in 84 (62%) patients. Twenty patients were treated with short-term chemotherapy, while 96 underwent long-term antituberculous treatment. At the end of chemotherapy, 94 patients had achieved a favorable status and 22 an unfavorable one. Age and radical surgery were significantly related to a favorable outcome by logistic analysis.[112] Patients with craniovertebral junction tuberculosis can

be managed conservatively regardless of the extent of bony destruction and the majority have satisfactory outcome.[113] In a retrospective study of 71 patients, 11 patients underwent early surgery. Five (8%) patients required delayed surgery for reducible atlantoaxial dissociation. The remaining 82% patients were effectively managed conservatively.[114]

Conclusion

The prognosis for spinal tuberculosis is improved by early diagnosis and rapid intervention. A high degree of clinical suspicion is required if patients present with chronic back pain, even in the absence of neurological symptoms and signs. Medical treatment is generally effective. Surgical intervention is necessary in advanced cases with marked bony involvement, abscess formation, or paraplegia. Spinal tuberculosis affects young people, so efforts should be made for its effective prevention. Controlling the spread of tuberculosis is only way available to prevent spinal tuberculosis.

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