Clinical Case Report

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Skipped multifocal extensive spinal tuberculosis involving the whole spine

A case report and literature review

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Abstract

Rationale: Skipped multifocal extensive spinal tuberculosis (TB) involving the whole spine is very rare. So far, only 3 cases have been reported.

Patient concerns: We report a rare case of skipped multifocal extensive TB involving the whole spine of a 33-year-old Chinese male. The patient had been asymptomatic until his symptom was significantly aggravated, which caused him to have difficulty in walking and sleeping. The whole spinal computed tomography (CT) scan showed multifocal worm-eaten and osteolytic bony destruction spread over noncontiguous multilevel vertebral involvement in cervical, thoracic, lumbar, and sacral. In addition, the patient presented with low back pain, progressive fever, night sweats, and weight loss. An open biopsy was undergone indicating granulomatous inflammation after thorough radiographic examinations and laboratory investigations, which to our knowledge have been rarely reported by the published medical reference literature.

Dignoses: It was initially diagnosed as lymphoma, multiple myeloma, or a metastatic disease by the radiologist. Final pathology confirmed it as an atypical form of spinal TB, which is extremely rare.

Interventions: The patient with no progressive severe neurological symptoms, spinal deformity, or a huge abscess was put on a combination of anti-TB treatment and discharged in an improved state to continue medication for a total of 12 months.

Outcomes: This article is a case report, no outcomes.

Lessons: Multifocal extensive spinal TB involving the whole spine is rarely reported in the literature, which presents with atypical presentations and imaging features. It is noticeable that the possibility of TB is considered for any skip lesions involving the spine cautiously. Meanwhile, careful physical examination, trials of anti-TB treatment, and using the whole spine MRI routinely also play an important role in the diagnosis and treatment of this disease.

Abbreviations: CT = computed tomography, MRI = magnetic resonance imaging, TB = tuberculosis.

Keywords: atypical lesion, diagnosis, noncontiguous multisegment, skip lesion, spinal tuberculosis, treatment

1. Introduction

Multifocal extensive spinal tuberculosis (TB), belonging to an atypical form of spinal TB, is also known as multiple levels noncontiguous vertebral TB that is rare but insidious symptoms, insufficiently emphasized and diagnostic delays that may exhibit a higher risk of causing permanent neurological deficit and kyphotic deformity compared to the rest of atypical spinal TB.[1–3] Historically, the incidence of noncontiguous spinal TB has ranged from 1.1% to 16.3%, but recently this rate has tended to increase to 71.4% by using whole magnetic resonance imaging (MRI) routinely, indicating that TB may affect the spine at multiple noncontiguous sites more frequently than thought previously.[1,4–6] In 2000 and 2014, Yalniz and Thammaroj et al[7] reported a series of atypical tuberculous spondylitis with an incidence of 2.1% to 5%, including isolated posterior element involvement, solitary vertebral body destruction, skip lesions, extradural lesions without bony involvement, destructive lesions of the sacrum with a pelvic mass, a vertebral osteomyelitis form, and bony destruction with intramedullary involvement.[2,7] According to a retrospective survey conducted by Thammaroj and Kitkhuandee, the skip lesions type was the most common atypical pattern in their series. By new definition, the skip lesions were separate lesions in at least 2 vertebrae regardless of the location on the spine.[7] To date, there are a few cases reported with noncontiguous multiple tuberculous spondylitis in some published medical literature, and most of the reported cases have lesions only on 2 or 3 levels.[8–10] However, skipped multifocal extensive spinal TB involving all spinal levels is reported as rare.

The treatment principles for patients with atypical spinal TB are similar to typical cases.[4,6] Overwhelmingly, early recognition and treatment are therefore necessary to minimize spinal deformity and permanent neurological deficit. Normative chemotherapy is essential

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for sterilizing the lesions and preventing recurrence. Meanwhile, surgery is an efficient treatment for patients with spinal TB that manifests as kyphotic deformity, neurological deficit, or a huge abscess and postoperative nutritional support is also important.[1,4,11,12] Polley and Dunn[1] stated that those patients with skip lesions are more prone to develop neurological complications than the rest cases indicating a high incidence of surgical intervention. Identification of noncontiguous vertebral TB, symptomatic or not, however, is important because it can influence the decision of surgical intervention, the number of levels instrumented and may dictate the need for bracing of levels not surgically treated.[4,8,13]

To the best of our knowledge, there have been few reports in the English literature of a case of noncontiguous multisegment tuberculous spondylosis involving the whole spine (cervical, thoracic, lumbar, and sacral segments) with paravertebral and epidural abscess but with preserved intervertebral discs, which caused none of any symptoms of spinal cord compression and kyphotic deformity.[6,8,11] Here, we present such a case without any surgical intervention. The patient underwent an open biopsy and anti-TB trial treatment, discharged in an improved state to continue medication for a total of 12 months. Also, we review the relevant literature on multifocal extensive spinal TB involving the whole spine to discuss this form of atypical TB regarding for clinical features and treatment (Table 1). The patient and his parents gave informed consent for the submission of this case study for publication.

2. Case report

2.1. Clinical history

A 33-year-old man presented with a 6-month history of insidious low back pain intermittently. Twenty days before admission to our hospital, his back pain was significantly aggravated, which caused him to have difficulty in walking and sleeping. He denied the history of systemic disease and trauma. Recently, the pain severely affected his life and work especially when movements. There was no history of exposure to TB, including his family. The patient had systemic TB symptoms and signs including night sweats and decreased appetite with weight loss and progressive low-grade fever. He admitted a history of smoking, alcohol consumption without drug abuse. Physical examination demonstrated there was no visible or palpable spinal deformity, but definite tenderness could be elicited over the spinous processes of the extensive lower thoracic vertebrae. Neurologic examination represented no specific findings including that his reflexes of knee and ankle were normal. Subsequently, muscle strength and tension of lower limbs were also normal, and the straight leg raise test was negative in bilateral lower limbs. No other positive findings were found on physical examination. Laboratory investigations revealed red blood cells count, hemoglobin level, and white blood cells count were all within a normal range in spite of high erythrocyte sedimentation rate (ESR, 48 mm/hour), high C-reactive protein (66.9 mg/L). TB antibody and purified protein in derivate of tuberculin (PPD) test and human immune deficiency viral infection (HIV) were negative, but the TB spot (T-Spot) test was positive. Besides, the result of bone marrow puncture and serum protein electrophoresis (SPE) were all negative. Other laboratory tests were within reference range.

2.2. Imaging examinations

During the hospitalization, the patient underwent thorough radiographic examinations.

Routine image analysis demonstrated normal chest X-ray and abdominal ultrasound evidenced normal findings. A thoracolumbar spine X-ray was unremarkable. Whereas further computed tomographic of whole spine images surprizing us, indicated multifocal diffuse lesions located in cervical, thoracic, lumbar, and sacral vertebrae showing multiple level worm-eaten and osteolytic bony destruction, including C5, T1-T5, T7-T12, L1-L5, and S1 (Fig. 1). At the bodies of C5, T1, T2, T4-T5 (spinous processes and adjacent ribs), T8-T11, L1-L5, and S1 vertebrae, osteolytic bone lesions were noted along with the similar lesions at the transverse process of T7 (neural arch), T11-T12 (spinous processes, neural arch, and adjacent ribs), L1, and L4. Intervertebral discs spared. There was a paravertebral mass at the T9-T10 level (Fig. 2). On whole spinal magnetic resonance imaging (MRI) examination, there were heterogeneous mixed high-intensity changes at C3, C5, T1-T5, T7-T12, L1-L5, and S1 segments on T2 weighted images and decreased signal intensity on T1 weighted images. Besides, the epidural abscess at the

Table 1

Summary of reported cases of skipped multifocal extensive spinal tuberculosis involving the whole spine (cervical, thoracic, lumbar, and sacral vertebrae).

References	Ethnicity	Year of study	Presentation	Sites of tuberculosis disease	Treatment	Outcome
Emel et al[6]	Turkey	2006	Neck and low back pain, dysphagia, swelling on left preauricular region, reduced lower limb power	C2–C4, C3/4 discitis, T1, T2, T12, and L3, T12 collapse, T11/12 paravertebral mass, T7, T8, T9, L1, L2, L5, S1, and S2 small abscesses	Operative T10–L1 anterior drainage, debridement, fusion, and instrumentation, T8–T9–L2–L3 posterior instrumentation	No complications, mobile
Thawani et al[10]	America	2011	Back pain, weight loss, fatigue, anorexia, decreased mobility	C5, T6, T8 and adjoining posterior ribs, L5, S1, S2, intervertebral discs spared	Operative decompression of C5, L5, S1	No complications, mobile
Wang et al[8]	China	2015	Neck and back pain, numbness and weakness of 4 limbs	C3–C6, T2–T5, T11–T12, L1, L3, L5, S1, and S2. C3–C6 and T2–T5 paraspinal abscess. C3–C6 epidural abscess	Nonoperative antituberculosis therapy for 12 mo	No complications, significant improvement of the neural function of limbs, mobile
Present report	China	2017	Low back pain	C5, T1–T5, T7–T12, L1–L5, and S1. T9–T10 paraspinal abscess and T7, T12 epidural abscess. Intervertebral discs spared	Nonoperative antitubercular trial therapy for 2 mo and quadruple antitubercular therapy for 10 mo	No complications, mobile

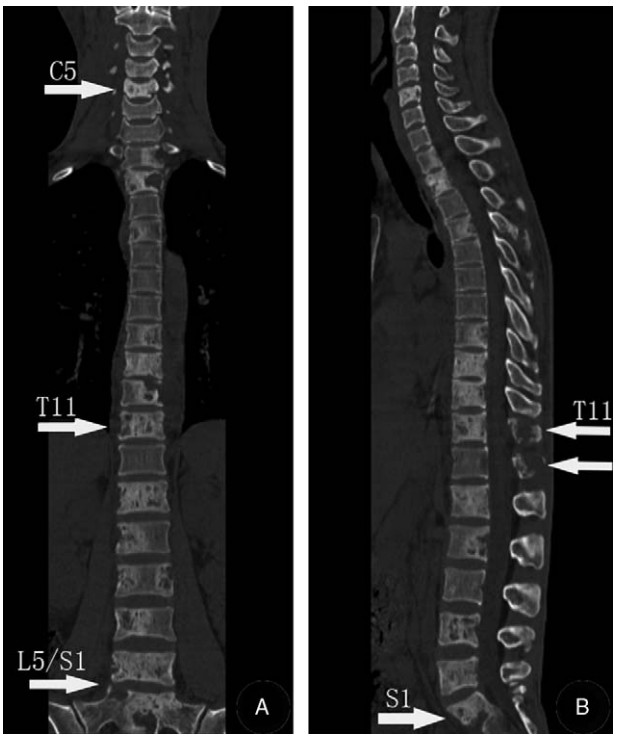

Figure 1. Computed tomographic images of the entire spine. Coronal (A) and sagittal (B) images showed that worm-eaten and osteolytic bony destruction spread over noncontiguous multilevel vertebral involvement in cervical, thoracic, lumbar, and sacral, with the similar lesions at the posterior elements. And there was no evidence of the obvious collapse of the adjacent vertebral body.

posterior of the spinal canal at T7 and T12 compressed the dural sac distinctly and a fusiform paraspinal abscess located at T9-T10 without obvious collapse of the adjacent vertebral body (Fig. 3).

2.3. Management

According to the constitutional symptoms of TB and all imaging and laboratory findings of this patient in our department, we hold a multidisciplinary conference including oncologists, radiologists, and orthopedists. Eventually, differential diagnoses such as lymphoma, multiple myeloma, and metastatic disease were suspected. Considering the risk of spinal cord compression and pathologic fracture, which may cause progressive severe neurological symptoms and deformity, could happen at any time. An open biopsy rather than computed tomography (CT)-guided needle biopsy was conducted by our experienced surgeon at the T11 level to make a clear diagnosis. Intraoperatively, we located at the spinous process of T11, then resected the partial lesion of the right transverse process. The excised specimen resembled a kind of cheese with necrosis material.

Pathological examination indicated a chronic granulomatous inflammation with abundant caseous necrosis, considering tuberculous inflammation (Fig. 4). And, negative microscopy for acid-fast bacilli from the specimen. However, in some cases, it was difficult to distinguish the lesions caused by *Mycobacterium tuberculosis* from other bacterial granulomas that may be still misdiagnosed. Meanwhile, we acquired the consent from the patient and his family to start on anti-TB trial chemotherapy, including rifampicin (450 mg/day), isoniazid (300 mg/day), ethambutol (750 mg/day), pyrazinamide (750 mg/day), and levofloxacin (500 mg/day), paying attention to nutrition supplement at the same time. The treatment turned out to be successful based on the lab test results, showing his ESR is reduced to 18 mm/hour, CRP to 11.3 mg/L, and significant improvement of systemic TB symptoms within 8 weeks of starting antitubercular trial therapy. Then the final diagnosis was an unusual presentation of skipped multifocal extensive spinal TB. As a consequence, we switched to a standard anti-TB chemotherapy without levofloxacin for a total duration of 12 months. Furthermore, the patient had achieved complete recovery without any complications. At 18-month follow-up, all the worm-eaten and osteolytic bony lesions were healed apparently, showing the disappearance of paravertebral and epidural abscess, and there was no evidence of recurrence on CT scan (Figs. 5 and 6).

3. Discussion

Spinal TB continues to be regarded as a serious threat to human health worldwide, according to latest reports, Asia and Africa still have a high prevalence of spinal TB. But, due to the increasing incidence of immigration, diabetes, human immunodeficiency virus (HIV) infection, and new drug-resistant strains, TB is becoming a major public health threat in industrialized countries, that is, Europe and the United States, and if overlooked it might lead to significant neurologic complications and kyphotic deformity.[5,14] Multinational and multicenter studies showed TB is the most common cause of vertebral body infection

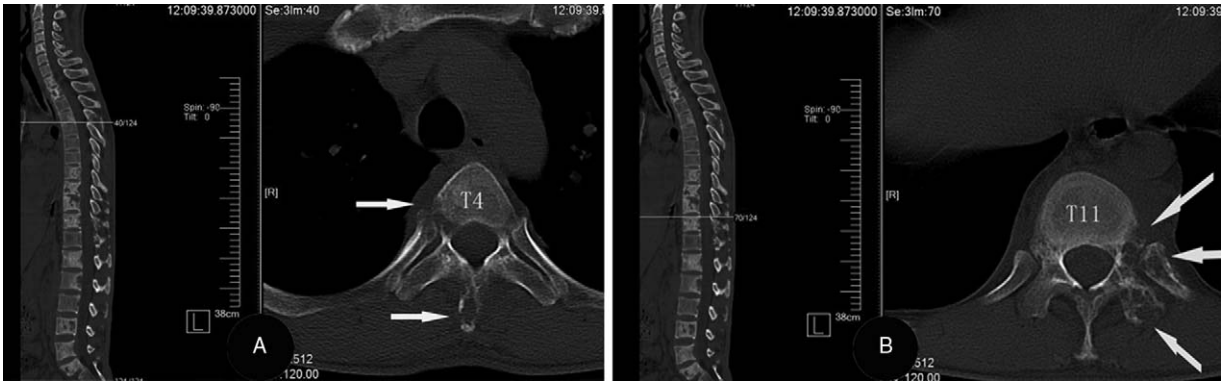

Figure 2. Computed tomographic images of T4 and T11 segments revealed that osteolytic lesions are located at the joins of the vertebrae, adjacent ribs, and the posterior elements (neural arch and spinous processes) with the paraspinal soft tissue edema.

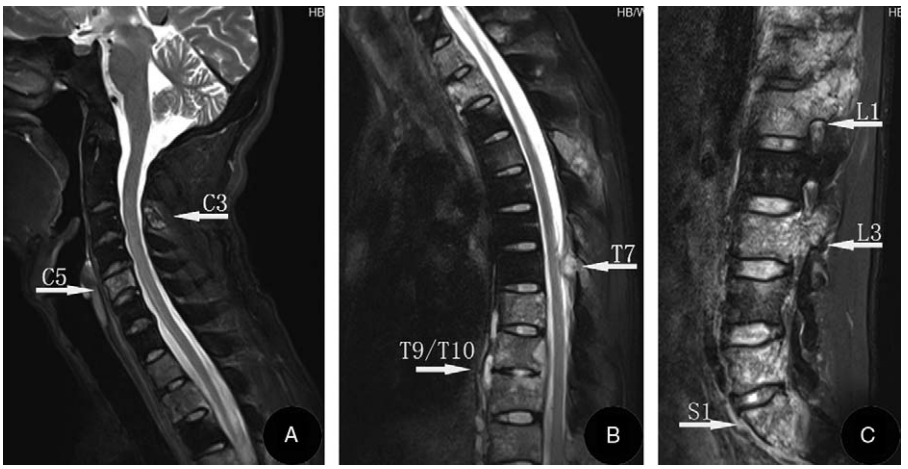

Figure 3. Magnetic resonance imaging (MRI) of the entire spine. Sagittal (A–C) T2-weighted image images STIR showed that heterogeneous mixed high-intensity changes at C3, C5, T1–T5, T7–T12, L1–L5, and S1 segments. Sagittal T2W image STIR showed hyperintensity of L1 and L3 vertebral body with associated heterogeneous signal extending anteriorly into the posterior region. There was also fusiform paraspinal abscess involving the T9/T10 level and small epidural abscess at the posterior of the spinal canal at T7. The disc spaces and height of vertebrae are relatively preserved.

affecting the spine in 3% to 5% of patients, and spinal TB is also known as Pott disease. Spinal TB (Pott disease) is the most common as well as the most dangerous form of musculoskeletal TB and accounts for 1% of all TB cases, and 50% to 60% of osseous TB.[2,13,15,16] Thoraco-lumbar junction is most commonly affected in tuberculous spondylitis, but a study undertaken by Kaila et al[5] showed more number of multiple level noncontiguous cases were seen involving the lumbar spine, followed by the thoracic spine. The typical presentation of spinal TB involves systemic TB symptoms and imaging presentations including multiple contiguous spinal vertebral bodies and their intervertebral discs without the involvement of the posterior elements, which could be easily recognized and diagnosed.[2,3,17] Over the past 20 years, with the rapid development of computer technology and computer graphics contributing to a great improvement of medical imaging, more and more atypical spinal TB without typical clinical and imaging features above were detected and classified by scholars. In a study of 184 patients, Yalniz et al (2000)[2] reported a low incidence of atypical spinal TB cases (2.1%), including skip vertebral lesions, isolated spinous process lesion, and neural arch lesions, and afterwards, other researchers reported related researches. According to the review of the published medical literature, Thammaroj et al (2014) stated the incidence of reported atypical or unusual spinal TB was to 2.1% to 5% of all spinal TB cases, and the skip lesions type was the most common atypical pattern in their series, which is similar to the research of Kaila and Polley.[1,5,7] The reported incidence of skip lesions in centers that do not perform routine whole spine MRI is 1.1% and 10% using a combination of regional radiography, CT, and MRI, and 16.3% using bone scan scintigraphy before commencing anti-TB therapy.[5,7] Recent studies showed the incidence of multiple levels noncontiguous vertebral TB was 71.4%, and this is higher than previously quoted when the whole spine MRI is not undertaken routinely for those patients suspected TB infection. The reasons for the high incidence of the noncontiguous disease is unclear. It may well be due to the high prevalence of TB in the community with delayed presentation of a few months before the diagnosis is made or TB may affect the spine at multiple noncontiguous sites more frequently than thought previously.[11,14,17,18] It is described this form of spinal TB showing a higher incidence in areas with high prevalence of TB, and it is reported to be a manifestation of HIV infection, multidrug resistant TB (MDR-TB), or chronicity.[6]

To date, there are several cases of noncontiguous spinal TB, and the skip lesions were mainly separate lesions in at least 2 or 3 vertebrae regardless of the location on the spine. In 2001,

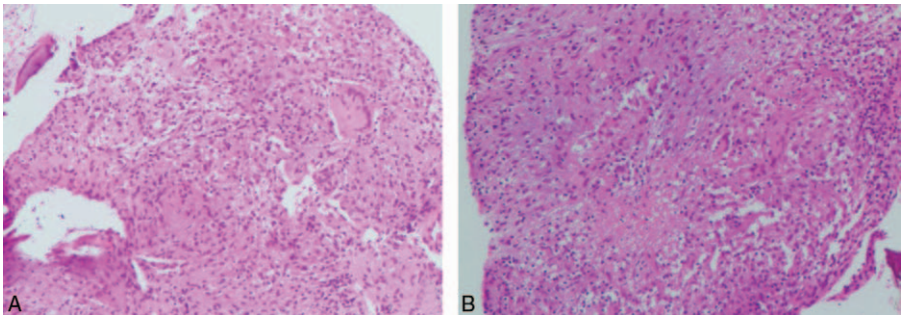

Figure 4. Histopathology photomicrographs of the excised specimen. (A) Low power view showed epitheloid granulomata (H&E, original magnification ×40). (B) (H&E, original magnification ×100) showed abundant caseous necrosis with multinucleated giant cells, considering tuberculous infection.

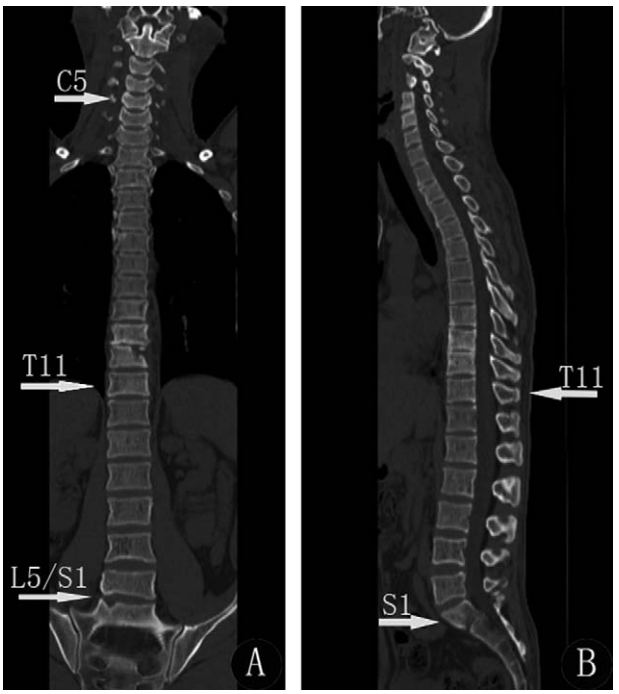

Figure 5. Computed tomographic images of the entire spine at 18-month follow-up. Coronal (A) and sagittal (B) showed that all the worm-eaten and osteolytic lesions of bone destroy were healed apparently including the vertebral bodies and posterior elements. And there was no evidence of recurrence.

Turgut[19] presented a case report of multifocal extensive spinal TB involving cervical, thoracic, and lumbar vertebrae described as the first such report in English language literature. However, extensive skip lesions involvement of all spinal levels is extremely rare. To the best our knowledge, there have only been 3 reported cases of this whole spinal TB (Table 1). Emel et al[6] (2006) reported 1 case with multifocal spinal TB involving almost all spinal levels and acknowledged that noncontiguous spinal is not a "fulminant" type of TB. Based on our study and previously reported cases, we summarize the reason for low incidence with this multifocal spinal TB involving all spine. First, Nowadays presentation of tuberculous spondylitis is variable and atypical, and a large proportion (40%) of the affected noncontiguous sites may also be asymptomatic.[1,7] Kaila et al (2007)[5] currently suggested performing whole spine MRI on all patients with suspected spinal infection to aid detection of multiple level noncontiguous TB. If we underestimate, such asymptomatic lesions may progress initially undetected to cause long-term morbidity. Second, both clinicians and radiologists seemed impatient with radiographic presentations, especially, many lesions overlooked on X-ray once 1 obvious lesion is identified.[14,20] Third, the lack of careful physical examination and experience. Some patients may be misdiagnosed as a metastatic tumor or lymphoma, or the imaging findings are not compatible with physical examination, delaying the diagnosis and treatment. Ultimately, these patients may suffer a high risk of death and deformity, which may be reported in current literature. However, as such lesions may not be asymptomatic and overlooked at presentations, whole body bone scan or MRI spine may enable early detection and institution of treatment to reduce morbidity.

Currently, MRI is widely used examination and differentiation methods for spinal TB and other spinal disorders in the clinic, owing to the sensitivity (100%) and specificity (88.2%) for the diagnosis of spinal TB. It, in particular, has a high sensitivity and specificity for the early diagnosis of vertebral lesions and is, therefore, the imaging technique of choice in spinal involvement, which is superior to other radiologic methods in revealing the extent of the disease and soft tissue involvement.[5,7,17] Vertebral involvement without disc destruction is the most commonly reported atypical form of spinal TB. Sivalingam and Kumar[17] acknowledged that multiple level skip lesions were seen in 14 cases (23.7%) without the involvement of intervertebral discs. The infection typically commences at the superior or inferior vertebral end-plates anteriorly then extends by subligamentous extension over multiple vertebral segments.[5] MRI showed subligamentous abscess and abnormal signal involving multiple vertebral segments with preserved discs.[7] These features are consistent with our presented case. In addition, Momjian and George[21] demonstrated that this form of multiple levels noncontiguous vertebral TB is associated with more frequent extraspinal skeletal involvement. Presentation of noncontiguous multiple spinal TB without the involvement of intervertebral disc resembles that of a neoplastic disease, lymphoma, or multiple myeloma. There are numerous similarities in the imaging and clinical manifestations between noncontiguous vertebral TB, a neoplastic disease, lymphoma, and multiple myeloma; however, differentiation requires the presence of a combination of general

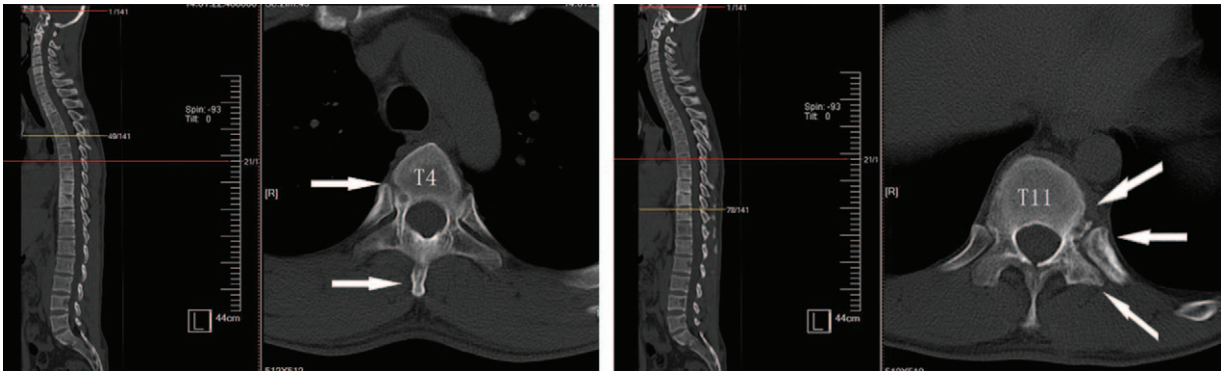

Figure 6. Computed tomographic images of T4 and T11 segments at 18-month follow-up. Compared to Fig. 2, the imaging revealed that osteolytic lesions are healed apparently at the joins of the vertebrae, adjacent ribs, and the posterior elements (neural arch and spinous processes) without the paraspinal soft tissue edema.

symptoms, laboratory test results, appropriate radiological results, and the physician's experience.[17,22,23] The appearance of vertebral lymphoma at MRI can be nonspecific. However, lesions showing bone marrow replacement and a surrounding soft-tissue mass without large areas of cortical bone destruction suggest lymphoma. And on MRI, lymphomatous infiltration appears as focal or diffuse vertebral lesions, mostly high or variable T2 signal in the vertebral and paraspinal lesions, a high signal on STIR sequence and low T1 signal with diffuse heterogeneous enhancement. The specific features of lymphoma indicated paraspinal masses with a vertebral lesion, but no extensive cortical bone destruction.[21] In neoplastic involvement of the spine, the disc spaces are usually spared, and paravertebral masses are not seen except when solid extraosseous soft tissue component is associated with destructed vertebral bodies.[17,18,22] Jung et al[24] suggested that thin and smooth enhancement of abscess wall and a well defined paraspinal abnormal signal is more in favor of tubercular abscess compared with neoplasm. A study of Khattry et al[20] reported a case of tuberculous spondylitis in an adolescent was misdiagnosed as a neoplastic disease, due to multiple skip lesions involving vertebral bodies and pedicles with sparing of the intervertebral discs. They stated that the skip multifocal spine lesions with disc sparing and absence of paravertebral lesion favors a neoplastic lesion while the presence of paravertebral lesion/collection favors the possibility of a tuberculous pathology. As for a metastatic disease, the spine is the most frequent site for bony metastases. Approximately 12% of patients with cancer present with spinal metastases, which often occur in middle-aged and elderly patients, and the major sites of spinal lesions are the lower thoracic and upper lumbar regions as similar as spinal TB.[23,25] The imaging features of spinal metastases included that the posterior elements of the vertebral bodies, pedicles, and lamina are involved, and a rim of bright T2 signal around the lesions; a halo sign frequently. The intervertebral discs are preserved. Besides, spinal metastases usually showed low T1 signal and high signal in T2 and STIR sequences and are brightly diffusely enhancing in postcontrast T1 fat saturation sequences. Sclerotic lesions are of low signal in all sequences.[20–23] However, Sinan et al[26] reported that 10% of their tuberculous spondylitis cases having isolated posterior arch involvement. In 2011, Zheng et al[23] reported a case of spinal metastasis whose imaging presentation is similar to TB. Differentiating tuberculous spondylitis from these conditions is very important since the line of management completely differs, and also early intervention helps in minimizing the residual spinal deformity and permanent neurological deficits.

The treatment principles of multifocal extensive spinal TB are similar to typical spinal TB deriving from the experience in treating contiguous spinal TB.[1,4,13] In the early days, the reported cases in the literature were with multiple spinal tuberculous involvements except one who required surgical treatment. The higher operation percentage of the multilevel spinal TB is possibly due to "fulminant" behavior of the disease in those patients and a higher incidence of central nervous system involvement.[2,6] It is reported that patients with atypical spinal TB, as having skip lesions or posterior element involvement, are more prone to develop neurological complications and can be attributed to delayed diagnosis.[5,10,27] Indications for surgery were the presence of definitive spinal cord compression with a deteriorating neurological condition, persistent neurological deficits despite anti-TB treatment, the vertebral destruction that led to spinal instability, severe kyphotic deformity, and large paravertebral or retropharyngeal abscess.[4,15,16] Polley and (2009)[1] reported that there was a higher incidence of neurology in the noncontiguous group (75%) compared to the rest of our group (58.5%). Shi et al[12] adopted complete debridement, deformity correction, graft fusion, and internal fixation for patients with noncontiguous multifocal spinal TB. A total of 29 cases achieved satisfactory deformity correction and the correction angle loss, having a significant recovery from kyphosis and neurologic symptoms. Huang et al[27] presented a retrospective study in 23 cases of multiple noncontiguous spinal TB, which all received surgical intervention and indicated a great outcome at the follow-up without any major complications. Wang et al[4] described that surgical intervention only focuses on the responsible level is less invasive and can achieve satisfactory clinical and radiographic outcomes. Momjian and George[21] also thought the treatment principles for atypical spinal TB were similar to those for typical TB. For patients with noncontiguous multiple level spinal TB, however, not all the segments require surgery. In patients without neurologic deficit, medical therapy is the treatment of choice, and surgical intervention may be needed in relatively few cases. Shen et al[11] reported a case of atypical, multilevel, and noncontiguous tuberculous spondylitis that affected the vertebrae of thoracic, lumbar, and sacrum without surgical indication, such as spinal instability or nerve damage. The patient was treated conservatively with anti-TB drugs, and the treatment was turned out to be successful at 1-year follow-up. In cases with central nervous system involvement, medical therapy is the first choice again but, when indicated, a combination of medical and surgical treatment yielded the best results. Diagnosis and treatment at early stages would resolve the neurological deficits without operation in about 40% of cases. Nearly 60% of patients would require to be operatively decompressed without jeopardizing mechanical stability. But in reported studies varied between purely medical and a combination of chemotherapy and surgery, all reported with a good outcome.[4,11,13,15,18,27]

4. Conclusions

Noncontiguous multiple tuberculous spondylitis is not uncommon, and most of the reported cases have lesions only on 2 or 3 levels. To the best of our knowledge, multifocal extensive spinal TB involving the whole spine is rarely reported in the literature, which may be presented as asymptomatic and have a higher incidence of neurological complications. It is noticeable that the possibility of TB is considered for any skip lesions involving the spine cautiously. Meanwhile, careful physical examination, trials of anti-TB treatment, and using the whole spine MRI routinely also play an important role in early diagnosis and treatment of this disease.

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