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Case study

Skipped Multifocal Extensive Pott's Disease with Quadriplegia: A Rare Case Report and the Challenges of Management in our Environment

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ABSTRACT: Objective: We are reporting unanticipated noncontiguous multifocal Pott's disease involving the whole spine with quadriplegia. Therefore, the communique aimed to provide updated data on this critical atypical spinal TB and highlights the rarity and challenges of management in our environment.

Case presentation: The patient is a 62-year-old Cameroonian female farmer with recalcitrant back pain for two years until her symptom was significantly aggravated, causing her to have difficulty walking and standing. Besides, the patient presented with progressive fever, night sweats, and weight loss. Examination findings revealed gibbus at T7-11 vertebral spine. The bilateral upper and lower limbs' findings confirmed power grade zero, hypotonia, and hypo-reflexes, the sensation was diminished (Quadriplegia). The CT myelogram showed multifocal worm-eaten and osteolytic bony destruction, appearance which suggests noncontiguous multilevel vertebral involvement in cervical, thoracic, lumbar, and sacral spine. Gene Xpert MTB/RIF test was positive. Sputum stain for acid-fast bacilli yielded *Mycobacterial tuberculosis*. The initial diagnosis was multiple myeloma or metastatic disease by the GP, but the final pathology confirmed skipped multifocal extensive TB involving the whole spine with quadriplegia, -an atypical form of spinal TB, which is extremely rare. Subsequently, the patient was commenced on a combination of anti-TB therapy and discharged in an improved state to continue the medication for 12 months.

Conclusion: While assessing patients with spinal TB or Pott's disease, clinicians must recognize skipped multifocal extensive noncontiguous Pott's disease as a potential differential diagnosis; that is rarely reported in the published literature. Interestingly, physicians have a global resolve that early diagnosis yields excellent results in Pott's disease treatment. Finally, clinicians managing such cases should be well informed of the various limitations in such a resources-constrained environment like ours to reduce the risk of attendant morbidities and mortalities.

Keywords: Atypical lesion, Anti-TB treatment, Noncontiguous multisegment, Pott's disease, Skip lesion, Spinal tuberculosis

INTRODUCTION

Historically, typical features of spinal TB had been described in mummies from Egypt and Peru as far back as 5000BC. Besides, DNA typing from a vertebral lesion in a 12-year-old dating back to AD1000 identified *Mycobacterium tuberculosis* (Mbata *et al*., 2012; Mclain and Isada, 2004). "The disease has been described as 'Yakshama' in the oldest Indian medical treatises of Charaka Samhita and Sushruta Samhita, dating back to 1000 and 600 BC, respectively" (Rajasekaran *et al*., 2018; Taylor *et al*., 2007; Tuli, 2013).

"In 1779, Sir Percival Pott described tuberculous spondylitis and its clinical presentation of paraplegia in patients with kyphotic deformities in the European population. Subsequently, Spinal TB was named as Potts' disease (PD)" (Rajasekaran *et al*., 2018; Dobson, 1972). "Significant progress has been achieved in the 19th and 20th centuries, including i) the discovery of the causative agent, *Mycobacterium tuberculosis,* ii) development of Bacillus Calmette-Guerin (BCG) vaccine, iii) invention of chemotherapeutic agents, iv) advances in diagnostics, and v) improvement in surgical outcomes" (Rajasekaran *et al*., 2018; James, 2005). "PD is one form of extrapulmonary TB that is frequently encountered. This disease type is rare in a developed country but mainly identified in immigrants from endemic area," (Mahadewa, 2016; Roni and Irsal, 2015). Also, there is no reliable data about the incidence and prevalence of PD globally or nationally. However, in areas with a high TB burden, the incidence could be proportionately high since it is estimated that 10% of pulmonary TB will have skeletal involvement. The spine is the most common skeletal site affected, followed by the hip and knee. PD accounts for almost 50% of cases of skeletal TB (Mahadewa, 2016; Roni and Irsal, 2015). "The human immunodeficiency virus (HIV) pandemic caused TB resurgences globally, making increased awareness about PD crucial. Despite its predictably high occurrence and morbidity, there are no comprehensive guidelines for diagnosing or managing PD. However, it is generally agreed that early diagnosis and prompt management are crucial to prevent permanent deformity and neurological disability" (Mahadewa, 2016; Zuwanda and Raka, 2013).

Definition of terms

Atypical spinal tuberculosis

"Yalniz and Thammaroj *et al.,* in 2000 and 2014, Wu *et al*. (2018), Thammaroj *et al*. (2014) reported a series of atypical tuberculous spondylitis with an incidence rate of 5% - 2.1%. They are collectively remarked to include 1) Isolated posterior element involvement, 2) Solitary vertebral body destruction, 3) Skip lesions, 4) Extradural lesions without bony involvement, 5) Destructive lesions of the sacrum with a pelvic mass, 6) Vertebral osteomyelitis form, and 7) Bony destruction with intramedullary involvement" (Wu *et al*., 2018; Yalniz *et al*., 2000; Thammaroj *et al*., 2014). Interestingly, the skip lesions can be defined as separate lesions in at least two vertebrae regardless of their location (Wu *et al*., 2018; Yalniz *et al*., 2000; Thammaroj *et al*., 2014). To date, some works of literature submitted that there are a few cases reported with noncontiguous multiple tuberculous spondylitis worldwide; where there are estimated lesions in more than 2 or 3 vertebrae levels (Wu *et al*., 2018; Wang *et al*., 2015; Kim *et al*., 2014; Thawani *et al*., 2011).

Multifocal extensive spinal tuberculosis

"Multifocal extensive spinal TB, belonging to an atypical form of Skip-lesions spinal TB, is also known as multiple noncontiguous vertebral TB levels. However, skipped multifocal extensive spinal TB involving all spinal levels is reported as rare. This disease entity is not only rare but characterized by insidious symptoms, insufficiently emphasized, and diagnostic delays that could predispose the victims to a higher risk of permanent neurological deficit and kyphotic deformity compared to the rest of atypical spinal TB" (Wu *et al*., 2018; Yalniz *et al*., 2000; Polley and Dunn, 2009; Naimurrahman *et al*., 1999). Interestingly, "the incidence of noncontiguous spinal TB has ranged from 1.1% to 16.3%. Still, this rate has recently 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" (Wu *et al*., 2018; Polley and Dunn, 2009; Wang *et al*., 2017; Kaila *et al*., 2007; Emel *et al*., 2006). "According to a retrospective survey conducted by Thammaroj and Kitkhuandee, the skip lesions type was the most common atypical pattern in their series. The treatment principles for atypical spinal TB patients are similar to typical cases," (Wu *et al*., 2018; Polley and Dunn, 2009; Wang *et al*., 2017; Kaila *et al*., 2007; Emel *et al*., 2006).

Aim of the study

We are reporting unanticipated noncontiguous multifocal Pott's disease involving the whole spine with quadriplegia. Therefore, the communique aimed to provide updated data on this critical atypical spinal TB and highlights the rarity and challenges of management in our environment.

Case presentation

We report a 62-year-old female farmer who initially presented to a general practitioner (GP). She had a two-year history of the upper back and waist pain radiating to both thighs intermittently. Both symptoms were insidious in onset but persistently got worse. Subsequently, she developed progressive weakness of both upper and lower limbs of one-month duration. The GP made a diagnosis of Multiple Sclerosis and referred her to a Neurologist at another tertiary institution for presumed expert management. However, the patient and caregiver decided to present at a separate tertiary center for a second opinion before the Neurologist's scheduled visit. At the presentation, she had a fever, severe neck, mid-back, and waist pain, which recently prevented her daily routine farm duty. She equally experienced dwindling urinary and fecal incontinence. There was associated

history of night sweats, decreased appetite, and 10 kilograms weight-loss over the past few months. Besides, the patient had no history of cough or shortness of breath. There had been deterioration in her overall status and progressive limb weakness to complete quadriplegia. However, she denied any history of trauma or close contact with a person with tuberculosis or chronic cough before the onset of her quadriplegia. She is a known hypertensive and peptic ulcer disease patient; who was well controlled on Hydrochlorothiazide 25mg daily and Omeprazole 20mg daily. There was no background history of other medical illnesses, such as diabetes or HIV- infection. The family, social and past surgical history was not significant.

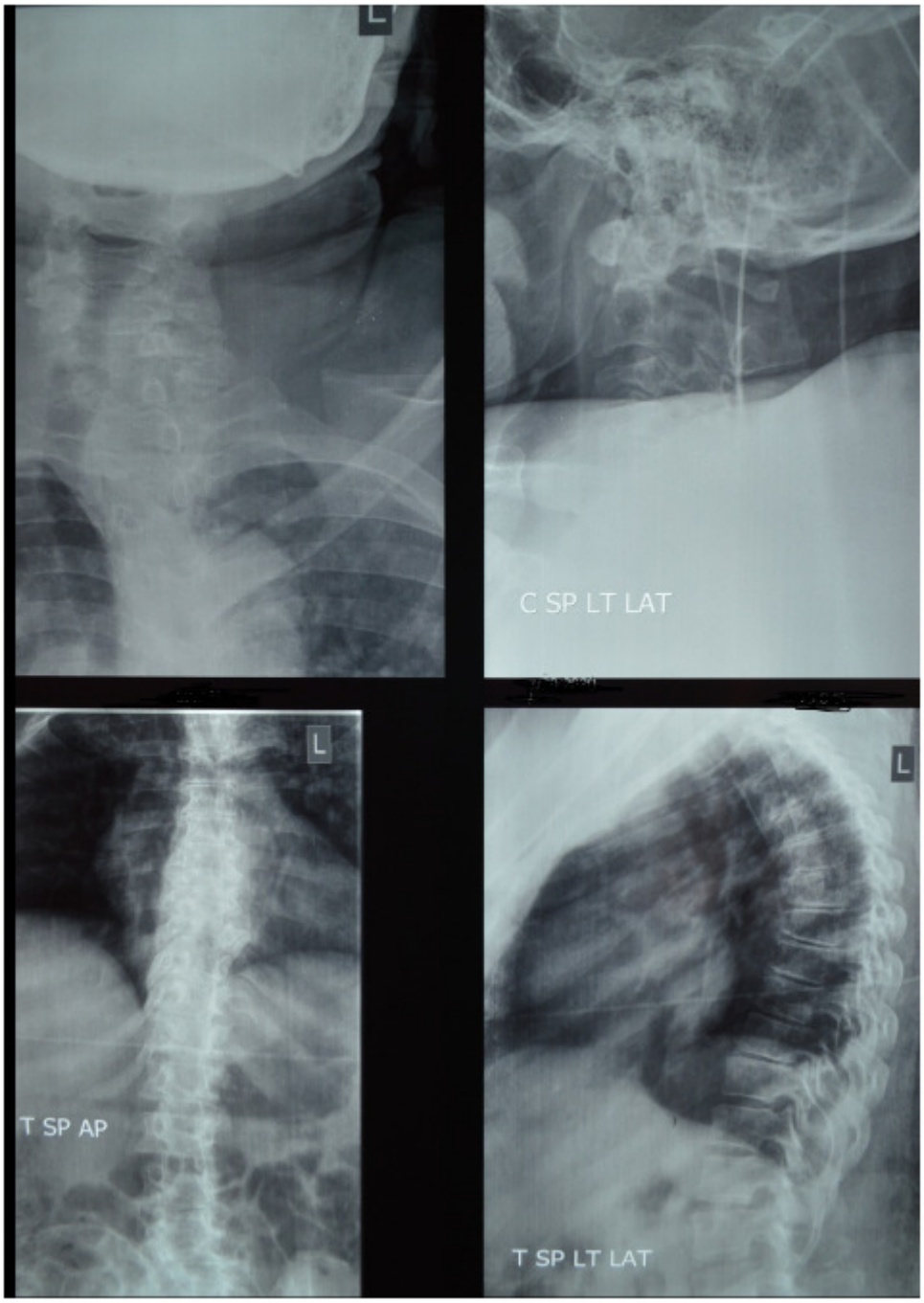
Physical examination findings revealed a chronically ill-looking middle-aged woman, conscious but lethargic. She was not pale, afebrile, not dyspneic, well oriented in time, place, and person. The blood pressure 120/78 mmHg; Pulse rate 88/min (regular, large volume, synchronous, no radio-femoral delay), respiratory rate 18/min, SPO2 100%, temperature 37.8°C, and jugular venous pressure (JVP) was not raised. Pulmonary examination revealed good air entry bilaterally, normal vesicular breathing, with no crepitation or wheezing. The cardiac study showed regular S1 and S2, with no added sound. The abdominal examination showed normal findings. Her musculoskeletal systems' examination findings revealed tenderness in the cervical, thoracic, and lumbar regions, gibbus at T7-11 vertebral spine. The neurological study showed the Glasgow coma scale (GCS) was 15/15. The cranial nerves examination was intact. The upper limbs' findings confirmed power grade zero, hypotonia, and hypo-reflexes, the sensation was diminished. Bilateral lower limb examination equally revealed power grade zero, hypotonia, and hypo-reflexes, the sensation was diminished.

The plain chest radiograph was essentially normal, and cervical radiograph showed degenerative changes with marginal osteophytes at C3, C4, and C5, C6. A Cervico-Thoracolumbosacral/pelvic radiograph showed characteristic features of disseminated Pott's disease (disseminated multilevel spondylodiscitis associated with multilevel cord myelopathy) (Figures 1-2). The abdominal ultrasound was virtually routine. Echocardiography showed ischemic heart disease, mild diastolic dysfunction, and normal systolic functions with an ejection fraction of 73%. Esophagogastroduodenoscopy (OGD) revealed pan –gastritis with positive H-pylori. CT myelogram- whole spine with contrast showed opinion features of disseminated Pott's disease (disseminated multilevel spondylodiscitis associated with multilevel cord myelopathy), characterized by worm-eaten and osteolytic bony lesions of C5-C7, T6-T10, and L4-S1 vertebral spine, as seen in (Figures 3-4).

A full blood count was done, which showed hemoglobin of 13.5g/dl, white blood cells (WBC) 3, 800, Westergreen-erythrocyte sedimentation rate (ESR) 98 mm in the first hour; with a high C-reactive protein (CRP) (62.6mg/L). TB antibody and purified protein in derivate of tuberculin (PPD) test and human immune deficiency viral infection (HIV) were negative, but the Gene Xpert MTB/RIF test was positive. Sputum stain for acid-fast bacilli yielded *Mycobacterial tuberculosis*. Serum electrolyte, urea, and creatinine were typical. Fasting blood glucose, lipid profile, and urinalysis were essentially normal, and urine culture yielded no organisms. We made a diagnosis of skipped multifocal extensive Pott's disease with quadriplegia. Meanwhile, we acquired the consent from the patient and his family to start on anti-TB chemotherapy, including rifampicin (450mg/day), isoniazid (300mg/day), ethambutol (750mg/day), and pyrazinamide (750mg/day), for two months; followed by INH and rifampicin for a further ten months. The patient was provided with a Philadelphia-type cervical corset was used for cervical immobilization and thoracolumbosacral orthoses for thoracolumbar immobilization. Also, she was kept on strict bed-rest for the initial period of two months. We equally ensured that the patient paid significant attention to nutritional supplements at the same time. The treatment turned out to be successful based on the laboratory test results, which showed that her ESR was reduced to 18mm/hour, CRP to 11.3mg/L, and significant improvement of systemic TB symptoms within eight weeks of starting anti-tubercular therapy. By the first month of the continuation phase of treatment, the right upper limb's strength was grossly 4, right lower limb 3+, left upper limb 3+, and left lower limb 3+. By the second month, her sphincteric functions had fully returned. By the 4th month of treatment, she was standing with support. She was discharged home in the 6th month as she was walking with a bilateral elbow crutch and continuing physiotherapy on an out-patient basis. Subsequent follow-up visits scheduled at monthly intervals for twelve months with a satisfactory outcome.

Epidemiology

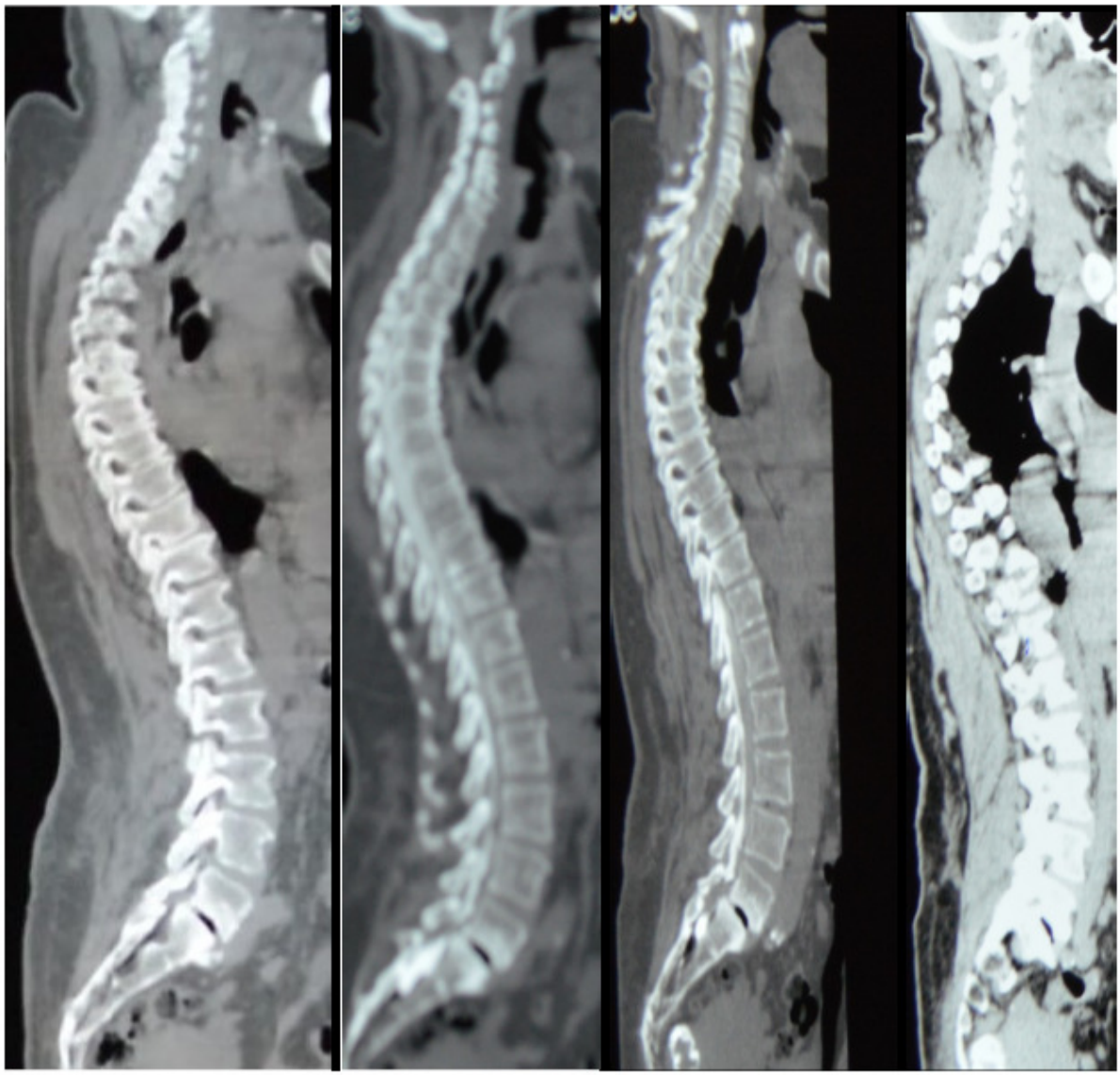
"In 2016, there was an estimated incidence of 10.4 million new TB cases as per the World Health Organization (WHO)," (Rajasekaran *et al*., 2018 WHO, 2016a). While the European region contributed only 3%, the South East Asian Region alone had 46.5% of the global TB burden (Rajasekaran *et al*., 2018; WHO, 2016b; WHO, 2016c). The deaths related to TB remained one of the top ten causes of death worldwide, despite the decline of TB deaths by 22% from 2000 to 2015 (Rajasekaran *et al*., 2018; WHO, 2016b; WHO, 2016c). PD continues to be regarded as a severe threat to human health worldwide. Some literature submitted that Asia and Africa still have a high prevalence of 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



Figures 1-2: Plain radiograph of whole spine.

The plain chest radiograph was essentially normal, and cervical radiograph showed degenerative changes with marginal osteophytes at C3, C4, and C5, C6. A Cervico-Thoracolumbosacral/pelvic radiograph showed opinion features of disseminated Pott's disease (disseminated multilevel spondylodiscitis associated with multilevel cord myelopathy).

threat in industrialized countries, that is, Europe and the United States. If overlooked, this situation might lead to significant neurologic complications and kyphotic deformity (Rajasekaran *et al*., 2018; Oettinger *et al*., 1999; International Organizations for Migration (IOM) (2015); WHO, 2020). "Multinational and multicenter studies showed TB is the most common cause of vertebral body infection affecting the spine in 3% to 5%. PD is the most common and most dangerous form of musculoskeletal TB. It accounts for 1% of all TB cases,



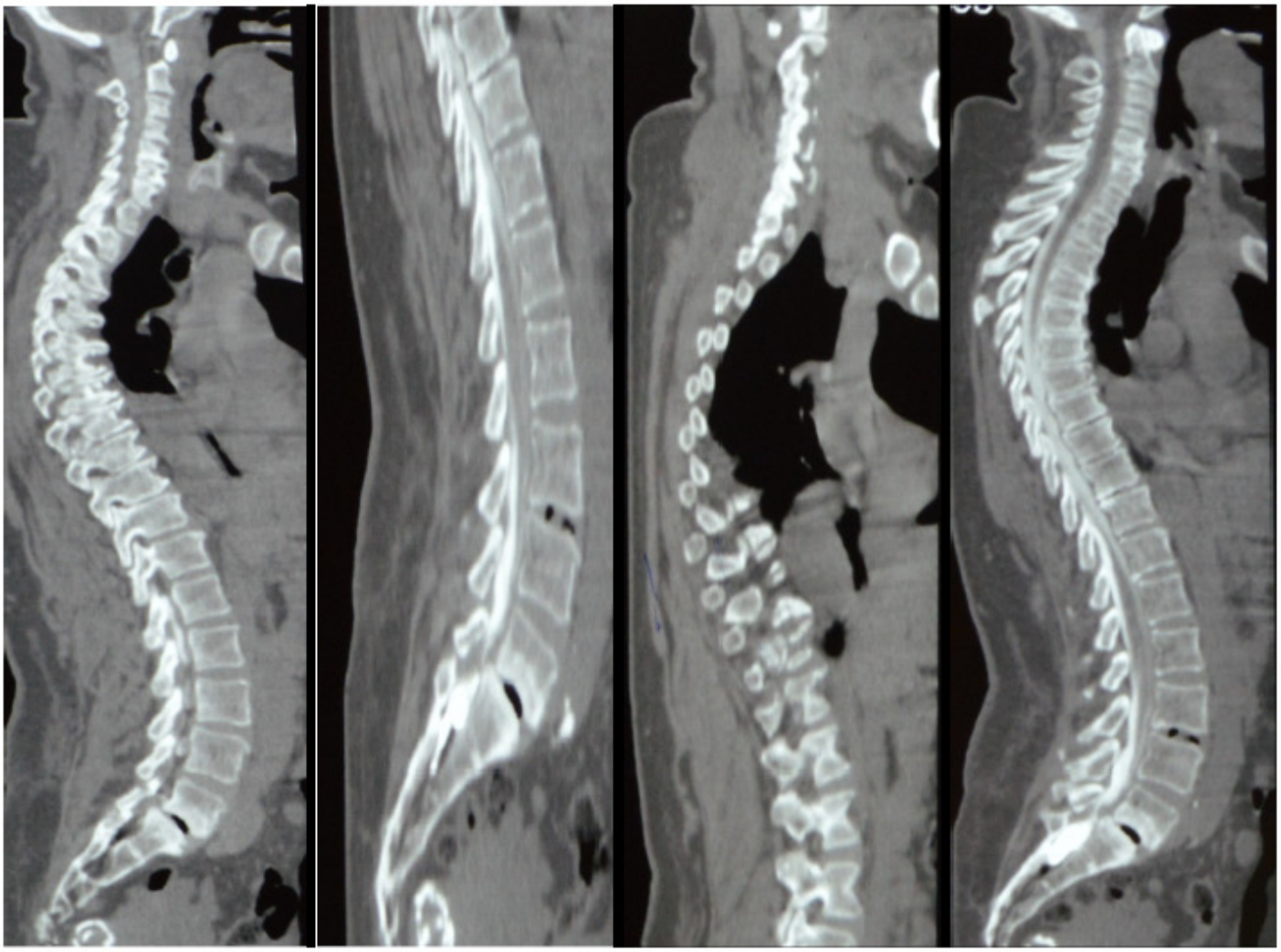
Figures 3: CT myelogram of whole spine.

CT myelogram- whole spine with contrast showed opinion features of disseminated Pott's disease (disseminated multilevel spondylodiscitis associated with multilevel cord myelopathy), characterized by worm-eaten and osteolytic bony lesions of C5-C7, T6-T10, and L4-S1 vertebral spine.

and 50% to 60% of osseous TB," (Rajasekaran *et al*., 2018; Tuli, 2013; WHO, 2015; Jain and Dhammi, 2007). Interestingly, "the HIV pandemic has led to the resurgence of TB, which invariably has had little impact on the epidemiology of PD. Meanwhile, in a large French study, none of the 82 cases of PD was HIV positive," (Mbata *et al*., 2012; Dass *et al*., 2002; Cotton *et al*., 1996). "Similarly, in other large longitudinal studies among HIV-infected patients, few were reported with PD even after long-term follow-up" (Mbata *et al*., 2012; Vassilopoulos *et al*., 1997; Munoz-Fernandez *et al*., 1991). To date, "there are a few cases reported with noncontiguous multiple tuberculous spondylitis in some published medical literature. Most of the reported cases have lesions only on 2 or 3 levels. However, skipped multifocal extensive spinal TB involving all spinal levels is reported as rare" (Wu *et al*., 2018; Wang *et al*., 2015; Kim *et al*., 2014; Thawani *et al*., 2001; Wang *et al*., 2017; Emel *et al*., 2006) as seen in (Table 1).

Pathophysiology of spinal TB

"The causative pathogen for TB is the *Mycobacterium tuberculosis* complex, which has around 60 species. The most common among the existing species is *Mycobacterium*



Figures 4: CT myelogram of whole spine.

CT myelogram- whole spine with contrast showed opinion features of disseminated Pott's disease (disseminated multilevel spondylodiscitis associated with multilevel cord myelopathy), characterized by worm-eaten and osteolytic bony lesions of C5-C7, T6-T10, and L4-S1 vertebral spine.

tuberculosis; others include *Mycobacterium bovis, Mycobacterium microti, and Mycobacterium africanum* are known to affect humans," (Rajasekaran *et al*., 2018; Huang *et al*., 2014). "It is a slow-growing fastidious, aerobic bacillus. The primary site of infections can be in the lungs, lymph nodes of the mediastinum, mesentery, gastrointestinal tract, genitourinary system, or other viscera. The bacillus tends to remain dormant for prolonged periods and multiplies every 15 to 20 hours in aerobic conditions whenever favorable. Spinal infection is always secondary and is caused by hematogenous dissemination of the bacillus from a primary focus" (Rajasekaran *et al*., 2018; Schirmer *et al*., 2010; Tuli, 1993). "Anatomically the intervertebral disc is an avascular structure. The 'paradiscal' arteries split on either side of the disc and reach the subchondral region of each disc's upper and lower endplates. This arterial supply of the vertebra favors subchondral bone involvement on either side of the disc, 'paradiscal,' which is the most common type observed," (Rajasekaran *et al*., 2018; Rasouli *et al*., 2012). "The other involvement patterns are 'central,' resulting in vertebral body loss, 'posterior,' when posterior appendicular structures are involved, and 'non-osseous abscess' formation. TB results in granulomatous inflammation characterized by lymphocytic infiltration and epithelioid cells, which may merge to form the classical Langhans-type giant cells and end up in caseation necrosis affected tissues forming a cold abscess. With the progressive destruction of the vertebral body, the spine's deformation causes kyphosis," (Rajasekaran *et al*., 2018; Rajasekaran *et al*., 2014; Jain, 2010).

Table 1: Summary of reported cases of skipped multifocal extensive spinal tuberculosis involving the whole SPINE (Wu et al., 2018; Thawani et al., 2011; Wang et al., 2017; Emel et al., 2006).

AUTHORS / YEAR OF STUDY	COUNTRY	PRESENTATION	SITES OF TUBERCULOSIS DISEASE	TREATMENT	OUTCOME	REFERENCES
Wu *et al.* (2018)	China	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 anti-TB trial therapy for 2 months and quadruple anti-TB therapy for 10 months	No complications, mobile	(Wu et al., 2018)
Thawani *et al.* (2011)	USA	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	(Thawani *et al.*, 2011)
Wang *et al.* (2015)	China	Neck and back pain, numbness and weakness of four 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 anti-TB therapy for 12 months	No complications, significant improvement of the neural function of limbs, mobile	(Wang *et al.*, 2017)
Emel *et al.* (2006)	Turkey	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	(Eme *et al.*, 2006l)
Present report	Cameroon	Neck and back pain, numbness and weakness of four limbs	C5, T6, T8 and adjoining posterior ribs, L5, S1, S2, intervertebral discs spared	Nonoperative anti-TB therapy for 12 months	No complications, significant improvement of the neural function of limbs, mobile	

Clinical presentations

Atypical Pott's disease

"The clinical picture of PD or spinal TB or is hugely variegated. PD usually is insidious in onset, and the disease progresses at a slow pace" (Rajasekaran *et al.*, 2018; Ansari *et al.*, 2013). "The diagnostic period, since the start of symptoms, may vary from 2 weeks to several years. The manifestation of PD depends on the severity and duration of the disease, site of the infection, and the presence of complications such as abscess, sinuses, deformity, and neurological deficit," (Rajasekaran *et al.*, 2018; Wibaux *et al.*, 2013). "In the standard clinical settings, PD can either be complicated or uncomplicated. In complicated PD, patients present with deformity, instability, and neurological deficit. Uncomplicated PD is one in which diagnosis is made before the development of such complications. Backache is the most common of all symptoms. It is primarily due to the bone's inflammation and rarely can be radicular during the active stage. Rest pain at the involved level is pathognomic, and the intensity is proportional to the amount of bone destruction and instability" (Rajasekaran *et al.*, 2018; Su *et al.*, 2010). "Constitutional symptoms such as loss of weight, loss of appetite, fever, and malaise are more frequently associated with PTB than PD," (Rajasekaran *et al.*, 2018; Hayes *et al.*, 1996).

Atypical Pott's disease

"Patients without the typical clinical features of axial pain, constitutional symptoms, kyphosis, or characteristic radiological features (paradiscal) are considered having atypical presentation" (Rajasekaran *et al.*, 2018; Babhulkar *et al.*, 1984). "Batson's paravertebral venous plexus plays a role in skip lesions of PD and is believed to be one cause for atypical presentations. Concentric vertebral collapse, isolated neural arch involvement, ivory vertebra, circumferential vertebral involvement, contiguous or skip vertebral

Table 2: Classification of neurological deficit (Jain and Kumar, 2013; Tuli, 1969, Jain and Kumar, 2013; Jain *et al*., 2005).

STAGES	CLINICAL PRESENTATIONS
Stage I	Patient unaware of neural deficit, Clinician detects plantar extensor and/or ankle clonus.
Stage II	The patient has spasticity with motor deficit but is a walker. The anticipated motor score in tetraparesis is between 60 and 100. In paraparesis, it is between 80 and 100. The sensory impairment is the lateral column.
Stage III	Bedridden spastic patient. Anticipated motor score for quadriplegic is 0–30, and for paraplegic it is 50–80. Sensory scoring is the same as in stage II.
Stage IV	Bedridden patient with severe sensory loss, and/or pressure sores. Anticipated motor score in tetraplegia is 0 and in paraplegia it is 50. There is impairment of both lateral and posterior column sensations.
Stage V	Same as stage IV and/or bladder and bowel involvement, and/or. Flexor spasms/flaccid tetraplegia/ paraplegia.

Table 3: Frankel classifications (Djientcheua *et al*., 2013).

GRADE	Description
A	Complete loss of motor and Sensory function below the lesion
B	Complete motor function loss. Sensory function present below the lesion
C	Residual motor function, That is un-usable
D	Subnormal motor function, That can be used
E	Normal

lesions, and multifocal osseous involvement are atypical radiographic patterns. Atypical clinical presentations such as prolapsed intervertebral disc, as reported by Pande and Babhulkar, isolated cold abscess without bony involvement, and intraspinal pure soft tissue granulomas occur," (Rajasekaran *et al*., 2018; Pande and Babhulkar, 2002). "Meningeal, neural, and perineural tissue involvement is rare, but easily identifiable in magnetic resonance imaging (MRI) and can cause features of compressive myelopathy without radiographic bony destruction" (Rajasekaran *et al*., 2018; Ahmadi *et al*., 1993).

Staging of neural deficit

"There is yet no consensus as per the International Classification System for neurological defects in PD. An ideal classification system should assess the quadriplegic/paraplegic patient's functional status and reflect cord compression severity. Classification suggested by Tuli and modified by Jain seems most rational, which classifies all cases of paraplegia and demonstrates the seriousness of cord compression as the score for sensory and the motor deficit is added" (Jain and Kumar, 2013; Tuli, 1969; Jain *et al*., 2005). "The neurological deficit could be categorized into five stages, as seen in (Table 2); Almost in 95 % of all cases, quadriplegia/paraplegia at the spinal cord level in tuberculosis could be classified" (Jain and Kumar, 2013; Tuli, 1969; Jain *et al*., 2005). However, "the lesions around the conus and cauda equina present with sphincter involvement very early in the disease process and have upper and lower motor neuron (UMN/LMN) mixed paraparesis/paraplegia with more sensory loss (bizarre neural deficit). Neural deficit association with intraspinal granulomas and atypical locations of the lesions may not always fit the classification," (Jain and Kumar, 2013; Tuli, 1969; Jain *et al*., 2005). "Besides, other authors have utilized the Frankel classification in which the patients were classified preoperatively and postoperatively for neurological deficits following PD, according to (Table 3)," (Djientcheua *et al*., 2013). "Frankel's classification limitation is that it does not classify the stage 1 neural deficit. The patient does not appreciate motor weakness. The patients only have a reflex abnormality, paraplegia with bladder and bowel involvement, paraplegia in flexion/ flaccid paraplegia, and paraplegia with flexor spasm" (Jain and Kumar, 2013; Tuli, 1969; Jain and Kumar, 2013; Jain *et al*., 2005). "In the ASIA scale, the severity of neural deficit, as reflected by score, depends on the level of involvement and cord compression severity at the involved level; The higher the spinal cord destruction level, the lower the accrued score" (Jain and Kumar, 2013; Tuli, 1969; Jain and Kumar, 2013; Jain *et al*., 2005).

Diagnostics of spinal TB

Molecular biology diagnostics

To date, state of the art diagnostic tools is being adopted for TB in general. Apart from indirect serological markers of inflammation, immunological tests have also been used with varied results (Mbata *et al*., 2012; Rajasekaran *et al*., 2018). "Growth of *Mycobacterium* species in culture specimens obtained from the infected tissue is the

single most confirmatory diagnostic test of PD and is considered the 'gold standard' approach. However, due to its very poor sensitivity, histopathological studies demonstrating classical granulomas and staining of smears to identify acid-fast bacilli (AFB) are considered as reference standards for all other diagnostic modalities" (Mbata *et al*., 2012; Rajasekaran *et al*., 2018;). Interestingly, "molecular diagnostics are frequently being used because of its rapidity and reliability; for instance, polymerase chain reaction (PCR) and other immune-typing tests apart from histopathological examination are variably utilized" (Rajasekaran *et al*., 2018; Rajasekaran *et al*., 2016). "BACTEC radiometric culture takes two weeks, less than the four weeks of incubation time in standard AFB culture techniques" (Rajasekaran *et al*., 2018; Cruciani *et al*., 2004). "Gene Xpert MTB/RIF test is a fully automated diagnostic test that yields results as early as 90 minutes and has a 95.6% sensitivity and specificity of 96.2%" (Rajasekaran *et al*., 2018; Maynard-Smith *et al*., 2014; Steingart *et al*., 2013). Also, "it aids in identifying resistance to rifampicin. In March 2017, the WHO recommended the use of a next-generation Xpert MTB/RIF assay, named Xpert MTB/RIF Ultra, as they found it, to have better detection rates of *Mycobacterium tuberculosis* in specimens with low numbers of bacilli, especially in smear-negative, culture-positive samples, in pediatric models and extrapulmonary specimens" (Rajasekaran *et al*., 2018; WHO, 2017). "The classical histological features of TB are the presence of caseation necrosis, epithelioid cell granuloma, and Langhans giant cells and have been reported in around 72% to 97%" (Rajasekaran *et al*., 2018; Lifeso *et al*., 1985; Alothman *et al*., 2001). Therefore, the diagnosis of PD is based on correlating clinical and classical imaging findings on Computed tomography (CT) scan or Magnetic resonance imaging (MRI) and is confirmed by both culture and sensitivity, Gene Xpert PCR test, or by histopathological evidence.

In a related development, "there was a recent new test released by the WHO. Determine™ TB LAM Ag test (LF-LAM) is a urine test for detecting LAM antigen, a lipopolysaccharide present in mycobacterial cell walls, which is released from metabolically active or degenerating bacterial cells. LAM appears to be present predominately in people with active TB disease," (WHO). "This recommendation also applies to HIV positive adult out-patients with signs and symptoms of pulmonary or extrapulmonary TB who have a CD4 cell count less than or equal to 100 cells/µL, or HIV positive patients who are seriously ill, regardless of CD4 count or with unknown CD4 count, based on the generalization of data from in-patients"(WHO). Besides, "the recommendation covers HIV positive children with signs and symptoms of TB (pulmonary and extrapulmonary) based on the conception of data from adults while acknowledging minimal data and concern regarding the LF-LAM assay's low specificity children. Therefore, given the low quality of evidence, it is vehemently submitted that LF-LAM should not be used as a screening test for TB," (WHO).

Imaging diagnostics

"Plain radiographs have no role in the early diagnosis of PD. Disc space narrowing and rarefaction of vertebral endplates can be identified as the disease progresses" (Rajasekaran *et al*., 2018; Dharmalingam, 2004). "Further destruction leading to kyphosis and instability can be made out only in late stages. It is useful in assessing coronal and sagittal alignment. Sixty percent to 70% of PD may have an active pulmonary lesion. Thus chest radiography is essential," (Rajasekaran *et al*., 2018; Dharmalingam, 2004). "CT scan demonstrates vertebral destruction well before plain radiographs. It is instrumental in identifying the extent of bony destruction, posterior column involvement, junctional pathologies, joint involvement, and regional stability," (4, Sinan *et al*., 2004). "Four types of destruction have been noticed in decreasing frequency: a) fragmentary, b) osteocytes, c) subperiosteal, and d) localized sclerotic lesion" (Rajasekaran *et al*., 2018; Jain *et al*., 1993). "CT is also of immense value in obtaining percutaneous CT-guided biopsy for establishing the diagnosis," (4, Adapon *et al*., 1981). "MRI has been the imaging modality of choice as it has been able to detect the earliest changes. Gadolinium-enhanced MRI further helps in differentiating TB from other causes of infective spondylodiscitis," (Rajasekaran *et al*., 2018; Kaila *et al*., 2007; de Souza *et al*., 2013). "The extent of soft tissue involvement, the spread of abscess, and neural compression are best visualized in MRI. Whole spine screening aids in identifying skip lesions. MRI is also of immense value in assessing the response to treatment," (Rajasekaran *et al*., 2018; Kaila *et al*., 2007). "Nuclear imaging by 18F-fluorodeoxyglucose (18F-FDG) labeled positron emission tomography (PET) scan helps in real-time assessment of disease activity, compared with CT and MRI, as 18F-FDG is known to accumulate in inflammatory cells such as neutrophils and activated macrophages at the site of inflammation" (Rajasekaran *et al*., 2018; Vorster *et al*., 2014). "However, none of the imaging options are reliable in distinguishing spinal infection and neoplasm, making histopathological examination mandatory to confirm the diagnosis or rule out neoplasm" (Rajasekaran *et al*., 2018; Rajasekaran *et al*., 2011).

Laboratory diagnostics

"Erythrocyte sedimentation rate (ESR) is a sensitive marker of infection and can be used to monitor therapeutic response, but its low specificity is a concern. Usually, in TB, ESR is >20 mm/ h and decreases as healing progresses. C- reactive protein (CRP) is more

specific for an acute infection than TB," (Rajasekaran *et al*., 2018; Guo *et al*., 2010; Rajasekaran *et al*., 2016). "Serological examination of IgM and IgG levels, which are high in active and chronic infective stages of TB, would not differentiate between active and healed disease or between natural infection and BCG vaccinated individuals; thus, they are not recommended" (Rajasekaran *et al*., 2018; Jain *et al*., 2008; Chen *et al*., 2016). "Though the WHO suggests using the Mantoux tuberculin skin test in low-income countries, it is of no diagnostic value in endemic areas. It may also be falsely negative in immunodeficient individuals. Hence, it is of some use only in latent TB. Two other tests used in latent TB are interferon-g (IFN-g) release assays and whole blood-based enzyme-linked immunosorbent assays, measuring the amount of IFN-g produced sequelae to *Mycobacterium tuberculosis* antigens" (Rajasekaran *et al*., 2018; Kumar *et al*., 2010). Though they are specific and differentiate between natural TB and BCG vaccination, these tests cannot distinguish between latent TB and active TB (Rajasekaran *et al*., 2018; Brodie *et al*., 2008; Lee, 2015). "The WHO has urged countries to ban inaccurate and unapproved blood tests instead of relying on accurate microbiological or molecular tests" (Rajasekaran *et al*., 2018; Ghanashyam, 2013). "The significance of tissue diagnosis is well established, and it would be ideal to subject tissue samples obtained to AFB staining, AFB culture, and aerobic culture along with antibiotic sensitivity testing by line probe assays" (Rajasekaran *et al*., 2018; Ghanashyam, 2013).

Management

"Spinal TB or PD can be managed either medically or surgically. Optimal prognosis and recovery are associated with treatment initiation at the earliest stage possible," (Dean *et al*. 2019; Garg and Somvanshi, 2011). "As a systemic infectious disease, medical management includes an aggressive, anti-tubercular, antimicrobial regimen and physical therapy and immobilization," (Dean *et al*. 2019; Garg and Somvanshi, 2011). "Some studies have shown that routine surgical treatment doesn't provide a long-term benefit to medical management. One randomized control trial by the Medical Research Council Working Party compared combined surgical and medical intervention to medical intervention alone. It studied 130 patients treated with isoniazid and amino-salicylate sodium (sodium PAS) with or without operative debridement within two months of the start of medical therapy" (Dean *et al*. 2019; Medical Research Council Working Party on Tuberculosis of the Spine, 1978), as seen in (Table 4) (Mahadewa, 2016; Mohammad *et al*., 2012). Another randomized controlled trial evaluated 201 patients treated with six months of isoniazid plus rifampicin with or without radical anterior resection with bone grafting (Dean *et al*., 2019; Parthasarathy *et al*.,1999). "Both studies' results at the five-year assessment revealed no added benefit of combined therapy over medical therapy alone. However, both of these studies excluded patients with advanced diseases. Surgical management is generally indicated for cases requiring tissue samples to establish a diagnosis, disease refractory to medical treatment, neurologic compromise, spinal instability, and deformity" (Dean *et al*. 2019; Jutte, 2006). "Several studies have been performed to try to define surgical candidacy more precisely. A prospective observational study by Rajasekaran. (2001) evaluated 61 children with PD who were treated with medical therapy for 15 years," (Dean *et al*. 2019; Rajasekaran, 2001). "It was found that unlike in adults, spinal deformity in children during the active phase of the disease progresses even after the completion of treatment, especially during growth. The final spinal deformity can be predicted by a scoring system based on the spinal radiographic signs. One possible conclusion of that research report is that children with a predicted absolute spinal deformity with kyphosis of 30-60 degrees are early surgical candidates," (Dean *et al*. 2019; Rajasekaran, 2001). "In adults, a Cochrane analysis of two trials revealed no statistically significant difference in outcomes, including the degree of deformity, neurologic status, bony fusion, resolution of PD, mortality, or functionality (Dean *et al*. 2019; Jutte, 2006). However, both studies excluded patients with paraplegia, disease refractory to medical treatment, or significant extra-spinal disease" (Dean *et al*. 2019; Jutte, 2006). Thus, "the recommendation loses applicability to the population of patients who would not meet those criteria. Furthermore, the cervical or thoracic spine may tolerate a lower degree of compression than the lumbar spine due to cord involvement and venous thrombosis. Our opinion that the cervical or thoracic spine's involvement should significantly lower the threshold for urgent aggressive surgical intervention even in the presence of a stable neurologic exam due to the high risk of venous thrombosis of the spinal cord and subsequent neurologic decline" (Dean *et al*. 2019; Jutte, 2006).

From this case report, therefore, overwhelmingly, early recognition and treatment are necessary to minimize spinal deformity and permanent neurological deficits. "Normative chemotherapy is essential for sterilizing the lesions and preventing recurrence. Also, surgery is an efficient treatment for PD that manifests as kyphotic deformity, neurological deficit, or a vast abscess and postoperative nutritional support is also essential" (Wu *et al*., 2018; Yalniz *et al*., 2000; Wang *et al*., 2017; Shen *et al*., 2015; Shi *et al*., 2012). Wu *et al*. (2018), Polley and Dunn, (2009) stated that those patients with skip lesions are more prone to develop neurological complications than the rest cases, indicating a high surgical intervention incidence. Identification of noncontiguous vertebral TB, symptomatic or not, however, is crucial because it can influence the decision of surgical intervention, the number

Table 4: Anti-tb regimen based on disease category (9, Mohammad *et al*., 2012).

		Treatment regimen	
Disease category	**Tuberculosis patient definition**	**Initial phase (daily or three times weekly)**	**Continuation phase (daily or three times weekly)**
I	New smear-positive New smear-negative with extensive parenchymal involvement New severe extra-pulmonary tuberculosis or severe concomitant HIV infection	2Hours	4 or 6 Hours daily
II	Previously treated sputum Smear positive pulmonary tuberculosis Relapse Treatment after interruption Treatment failure	2 Hours	5 Hours
III	New smear-negative pulmonary tuberculosis Extra-pulmonary tuberculosis	2HRZE	4 or 6 Hours daily
IV	Chronic and MDR tuberculosis	Specially designed standardized or individualized regimens	

of levels instrumented and may dictate the need for bracing of spinal vertebral levels not surgically treated (Wu *et al*., 2018; Yalniz *et al*., 2000; Wang *et al*., 2017; Batirel *et al*., 2015). Surprisingly, "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 additional complications like a paravertebral and epidural abscess, with or without preserved intervertebral discs and quadriparesis/ quadriplegia or paraparesis /paraplegia as the case might be ultimately" (Wu *et al*., 2018; Wang *et al*., 2015; Emel *et al*., 2006; Shen *et al*., 2015).

Challenges of management

Based on our study and previously reported cases, we identified the rarity of this multifocal PD involving all spines, which could be challenging to the clinicians, for the following reasons. "First, nowadays, the presentation of tuberculous spondylitis is variable and atypical, and a large proportion (40%) of the affected noncontiguous sites may also be asymptomatic" (Wu *et al*., 2018; Yalniz *et al*., 2000; Thammaroj *et al*., 2014). Kaila *et al.* in 2007 (Wu *et al*., 2018; Kaila *et al*., 2007) suggested performing whole spine MRI on all patients with suspected spinal infection to aid detection of multiple levels of noncontiguous PD. 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 a single obvious lesion is identified" (Wu *et al*., 2018; Du *et al*., 2008; Khattry *et al*., 2007). "Third, the attending clinician's lack of careful physical examination and experience could predispose to a missed diagnosis, as seen in our index patient," (Wu *et al*., 2018; Emel *et al*., 2006).

Interestingly, some patients may be misdiagnosed as a metastatic tumor or lymphoma, or the imaging findings are not compatible with the physical examination, delaying the diagnosis and treatment (Wu *et al*., 2018; Emel *et al*., 2006).

Consequentially, "these patients may suffer a high risk of death and deformity, which may be reported in the 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 treatment institutions to reduce morbidity" (Wu *et al*., 2018; Kim *et al*., 2014; Khattry *et al*., 2007).

Furthermore, "other intricate challenges might arise not only because of low body immunity associated with HIV disease but also the emergence of the organism's resistance to anti-TB drugs. Low patient compliance in taking the medication appropriately also affects the development of resistant germs.

Surprisingly, one additional challenge is the late presentation for early diagnosis and treatment (anti-TB therapy), as well as a prompt surgical intervention which could ultimately prevent the late complications of quadriplegia or paraplegia, particularly in such individuals with neurological deficits, paravertebral abscess, spinal instability, anti-TB drug resistance, etc.," (Wu *et al*., 2018; Kim *et al*., 2014; Khattry *et al*., 2007).

Moreover, "there have been serious concerns about the public health indices in most tropical African population like ours; an environment where the indices like sanitation, sewage disposal, quality of water supply are such that water-borne gastrointestinal diseases like poliomyelitis, hepatitis viruses, shigellosis, cholera, typhoid enteritis, giardiasis, and amoebiasis are prevalent; endemic poverty, ignorance, high prevalence of HIV infection, and a lack of strict compliance with sanitary standards enforceable by public health authorities play contributory roles" (Alegbeleye *et al*., 2019; Alegbeleye, 2019a- Alegbeleye, 2019b).

Conclusion

While assessing patients with spinal TB, clinicians must recognize skipped multifocal extensive noncontiguous PD as a potential differential diagnosis. Interestingly, physicians have a global resolve that early diagnosis yields excellent results in PD treatment. Increasing back pain requires investigation with a plain radiograph and possibly CT or MRI where the facility exists. Our patient presented with back pain and later quadriplegia. He initially presented to a GP who diagnosed multiple sclerosis and referred him to a tertiary center. A good history and reassessment would have suggested the diagnosis, mostly when multiple sclerosis risk factors were remote. Timely intervention in PD treatment can avoid extensive investigations, treatment delays, and adverse long-term outcomes, including compression fractures with neurological deficits, as seen in our patient. Patients with PD experience severe pain. Therefore measures to alleviate pain should include appropriate spinal bracing and a combination of analgesics, including narcotic analgesics. Finally, clinicians managing such cases should be well informed of the various limitations in such a resources-constrained environment like ours to reduce the risk of attendant morbidities and mortalities.

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