Case report • DOI: 10.2478/pneum-2024-0009 • 72 • 2023 • 59-63

Pneumologia

Extensively drug-resistant tuberculosis of the spine: A rare case report

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Abstract

English:

Spinal tuberculosis is the most common form of skeletal extrapulmonary tuberculosis (EPTB). Extensively drug-resistant TB (XDR-TB) is a rare type of multidrug-resistant tuberculosis (MDR-TB) that is resistant to isoniazid and rifampicin, plus any fluoroquinolone and at least one of three second-line injectable drugs (SLI) (i.e., amikacin, kanamycin, or capreomycin) as per the old guidelines.

We present the case of a 13-year-old girl, with lower back pain for 6 months, without other symptoms. She was radiologically diagnosed with tuberculous osteomyelitis without confirmation of acid-fast bacilli. Due to our endemic area, the initial tuberculosis treatment was empiric. The patient received treatment from a private hospital but after 6 months developed lower limb weakness. She was referred to our center where XDR-TB was confirmed by bacteriological examination. She was managed with extended second-line antituberculous chemotherapy according to the new WHO recommendation with a good evolution in the first months of therapy. Appropriate sensitivity-antituberculosis agents and good patient compliance are the keys to ensuring effective treatment of the XDR-TB condition.

Keywords

spinal tuberculosis • XDR-TB • antituberculosis drug

Tuberculoza coloanei vertebrale cu rezistenta extinsa la medicamente - un raport de caz rar

Rezumat

Romanian:

Tuberculoza coloanei vertebrale este cea mai frecventă formă de tuberculoză pulmonară extrapulmonară (TPEP). Tuberculoza pulmonară cu rezistență extinsă (TB-XDR) este o formă rară de tuberculoză pulmonară multi-drog rezistentă (MDR-TB) cu rezistență la izoniazidă, rifampicină, orice fluorochinolonă și cel puțin una din cele trei tuberculostatice injectabile de linia a doua (de ex: amikacină, kanamicină sau capreomicină) așa cum ne precizează ghidurile mai vechi.

Prezentăm cazul unei fetițe în vârstă de 13 ani cu durere lombară dreaptă de aproximativ 6 luni, fără alte simptome. Radiologic s-a diagnosticat cu osteomielită tuberculoasă, fără confirmarea prezenție bacililor acid-alcolo-rezistenți. În contextul zonei noastre endemice, tratamentul tuberculostatic inițial a fost empiric. Pacienta a primit tratament într-un spital privat dar după 6 luni a dezvoltat slăbiciune în mușchii membrelor inferioare. A fost îndrumată în centrul nostru unde s-a confirmat TB-XDR la examinarea bacteriologică. A primit medicamente antituberculoase de linia a doua conform noilor recomandări OMS cu evoluție bună în prima lună de terapie.

Medicamentele antituberculoase cu sensibilitate corespunzătoare și complianța bună a pacientului sunt "cheile" care asigură un tratament eficient în cazul TB-XDR.

Cuvinte-cheie

tuberculoza coloanei vertebrale • TB-XDR • tuberculostatice

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Introduction

Spinal tuberculosis (TB) is the commonest manifestation of skeletal TB.[3] Drug-resistant spinal tuberculosis is an emerging health problem in both developed and developing countries. Globally 20% of people who have multidrug-resistant tuberculosis (MDR-TB) have reported resistance to another potent drug for the treatment of drug-resistant TB, commonly fluoroquinolone. Extensively drug-resistant TB (XDR-TB) is a rare type of MDR TB that is resistant to isoniazid and rifampicin, plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin) as per the old guidelines. XDR-TB, a challenging disease, can be treated if assessed correctly and managed timely [1, 2]. Pott's spine accounts for 2% of all cases of TB, 15% of extrapulmonary, and 50% of skeletal tuberculosis [3]. It spreads through the hematogenous route [3]. Lower thoracic and lumbar vertebrae are the most common sites affected. Clinically, it presents with general symptoms like fever, chills, tiredness and significant weight loss, back pain, tenderness, paraplegia or paraparesis, and kyphotic or scoliotic deformities. Spinal TB is usually secondary to lung or abdominal involvement and rarely may also be the only manifestation of TB [3]. Drug-resistant spinal tuberculosis poses a unique set of challenges, due to difficulty in the procurement of tissues or pus for diagnosis. Spinal TB is a paucibacillary disease. In spinal TB, sputum diagnostics have little utility unless there is concurrent pulmonary involvement [4]. The literature regarding drug resistance in spinal TB and its management is lacking. Drug resistance from a bacteriological perspective is caused by a genetic mutation that makes a drug ineffective against the mutant bacilli. There are described two ways to get XDR-TB: from an inadequate or poorly administered treatment regimen in a clinical setting that allows drug-resistant mutants to become the dominant strain and directly acquired infection from a patient who is already ill. We further present a case of spinal TB with extensively drug-resistant tuberculosis (XDR-TB) treated with second-line antituberculosis drugs.

Case Summary

A 13-year-old girl child, BCG vaccinated, from an endemic area, without immunosuppression (HIV infection or diabetes) or other comorbidities was referred from the Orthopedics department for assessment. She had a history of illness for 6 months when she started having lower back aches. Apart from that, the patient had no complaints of fever, cough, or significant weight loss. There was no evidence of generalized lymphadenopathy, or other systemic involvement. She was evaluated in a private hospital with a positive Tuberculin skin test (TST). The Magnetic Resonance Imaging (MRI) of the dorsal spine was suggestive of D6 vertebral osteomyelitis with a nearly complete (75%) decrease in vertebral height, with pre and paravertebral collection. Chest x-ray was normal and sputum GeneXpert was MTB not detected. Computed Tomography (CT) guided the biopsy of paravertebral soft tissue. The sample tested with the Cartridge Base Nucleic Acid Amplification Test (CBNAAT) for tuberculosis did not detect Mycobacterium Tuberculosis (MTB). An Acid-fast bacilli (AFB) culture report was not done by that center. Given the high prevalence rate of TB in India, she was initiated on empirical anti-tuberculosis therapy (ATT) for drug-sensitive TB according to the National Tuberculosis Elimination Program (NTEP). The treatment was started on a 4-fixed drug combination with each tablet consisting of 4 drugs: isoniazid, rifampicin, pyrazinamide, and ethambutol with doses of 75mg, 150mg, 400mg, and 275 mg each respectively. According to a weight of 30 kg, the patient received 2 tablets orally after breakfast. The patient was compliant with therapy and it was fully supervised for 6 months. However, the patient slowly deteriorated as she started developing bilateral lower limb weakness. Hence she followed up at our hospital for further treatment. On examination, the patient was underweight and with a neurological deficiency (the power in the bilateral lower limb was 3 out of 5). On routine investigations blood parameters were normal. Respiratory system examination was normal. A repeated chest x-ray was normal and sputum GeneXpert MTB was not detected. Again an MRI of the whole spine was suggestive of D5-D7 vertebrae infective spondylodiscitis with the destruction of the D6 vertebral body (Figure 1) along with pre/paravertebral collection and epidural collection. Minimal cord compression was seen at the D6 level (Figure 2). In these circumstances, she was operated on. She underwent posterior decompression with instrumentation. Intra-operative Samples were sent for a GeneXpert, AFB smear, and culture. The patient has no history of MDR contact. Tissue gene Xpert showing MTB detected low rifampicin resistance. In Tissue Mycobacterium Growth Indicator Tube (MGIT) culture grew MTB complex. First-line probe assay (LPA) detected rifampicin and isoniazid resistance. Second-line LPA showed resistance to fluoroquinolones and 2nd line to injectables. The MGIT drug susceptibility testing (DST) showed resistance to Isoniazid, Rifampicin, Pyrazinamide, Ethambutol, Streptomycin, Levofloxacin, Moxifloxacin, Kanamycin, Amikacin, Capreomycin. An extended DST showed resistance to Ethionamide and susceptibility to Clofazimine and Para aminosalicylic acid (PAS). The patient was referred to our department for assessment and was referred to NTEP for initiation of all oral longer Bedaquiline (BDQ) based regimen consisting of weight-adjusted BDQ, Linezolid, Clofazimine, Cycloserine, PAS. Bedaquiline of 400mg was administered

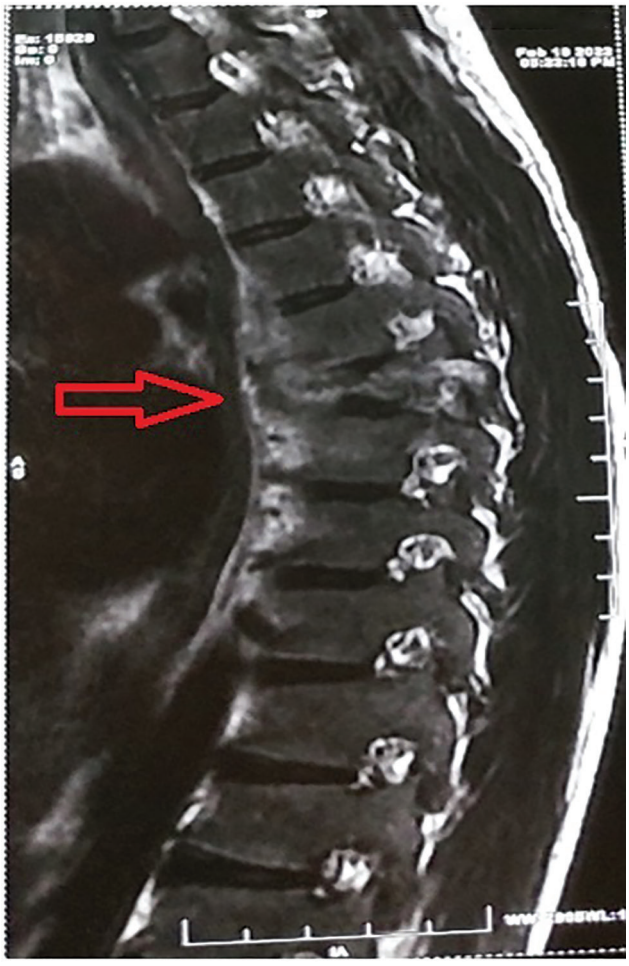

Figure 1. Red arrow suggestive of a complete collapse of the D6 vertebral body with spondylodiscitis of D5-D7 vertebrae.

once daily for the initial 2 weeks followed by 200mg three times a week. Linezolid 600mg, Clofazimine 100mg, Cycloserine 500mg, and PAS 6g were given once daily. The patient improved symptomatically and finally was discharged. The patient is currently followed up after 4 months of therapy and is better without adverse side effects.

Discussion

Skeletal TB occurs due to hematogenous spread and affects most bones. The disease process can start either in the bone or synovial membrane and may spread to other structures in a short time. In skeletal involvement, spine TB is the commonest in the lower thoracic and lumbar vertebrae. The infection spreads and destroys the intervertebral disc, the epiphyseal cortex, and the adjacent vertebrae. The infection spreads beneath the anterior longitudinal ligament to reach neighboring vertebrae. The vertebral body becomes soft causing a wedge

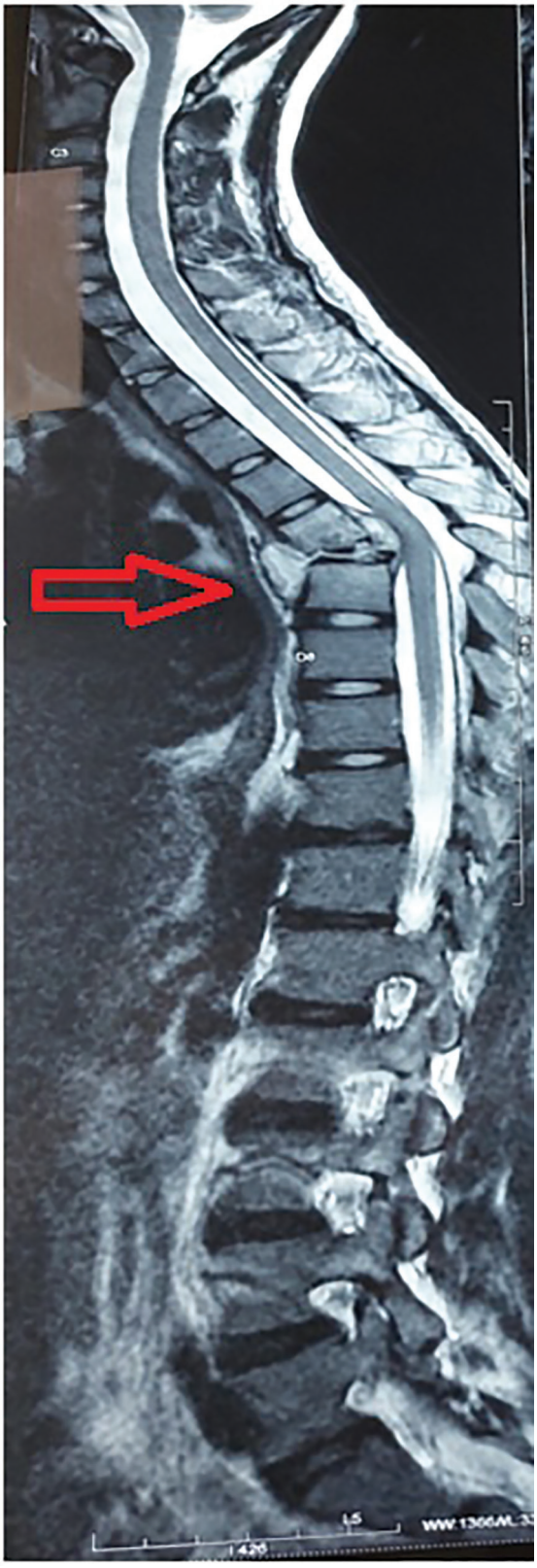

Figure 2. Red arrow suggestive of minimal cord compression at the D6 level.

or total collapse. Anterior wedging is commonly seen in the thoracic spine because a normal kyphotic curve accentuates the pressure on the anterior part of vertebrae. Vertebral TB develops as an exudative lesion due to a hypersensitivity reaction to Mycobacterium tuberculosis. The exudate consists of serum, leucocytes, caseous material, tubercle bacilli, and bone fragments. In the thoracic spine, the exudate may remain confined locally for a long time and may appear in the radiographs as a fusiform or bulbous paravertebral abscess. Tension may force the exudate to enter the spinal canal and compress the spinal cord. Paraplegia is the most serious complication of spinal TB and its occurrence is reported to be as high as 30 percent in patients with spinal TB. Neurological involvement is common when the dorsal spine is involved because the diameter and space of the spinal canal are smallest in the dorsal region. Paraplegia due to spinal TB is also known as Pott's paraplegia. It can be of early or late onset. Early paraplegia develops during the active phase of infection. Paraplegia of late-onset can appear many years after the disease has become quiescent even without any evidence of reactivation. Most commonly paraplegia develops due to mechanical pressure on the cord, but in some, it may occur due to non-mechanical causes.

In the last two decades, multi-MDR, extensively (XDR drug-resistant Mycobacterium tuberculosis (MTB) strains have emerged as a threat to public health worldwide. Drug-resistant spinal tuberculosis poses a unique set of challenges, due to the difficulty of the procurement of tissue for diagnosis. Secondly, spine TB is a paucibacillary disease. Drug-resistant spinal tuberculosis is suspected when the patient is not responding to ATT. In a high disease-burden country like ours with limited resources, patients are often initiated on treatment based on clinic radiological evidence. Primary resistance occurs when a person is infected with mycobacterium that is already resistant to a particular drug. Secondary resistance occurs when drug-resistant organisms emerge as the dominant population during treatment [5]. The major causes of secondary drug resistance are poor adherence to the medication by the patient or inadequate treatment regimens prescribed by a physician [6]. Extensively drug-resistant TB (XDR TB) is a rare type of MDR-TB that is resistant to isoniazid and rifampicin, plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin) as per the old guidelines. As per the new WHO and PMDT guidelines XDR -TB is TB caused by Mycobacterium tuberculosis strains that fulfill the definition of MDR/RR-TB and which are also resistant to any fluoroquinolone and at least one additional Group A drug (bedaquiline - BDQ or Linezolid). A limitation here was, that we initially considered only the resistance to anti-tuberculous drugs mentioned in the older guidelines to manage the patient. Then we fully complied with the new therapy recommendations.

Our patient had a history of therapy for spine TB without any microbiological evidence initially. After 6 months of therapy, the completion of microbiological evidence was pursued. In our case, we assume that Pott's spine due to XDR-TB resulted from acquired resistance, though there was no clear history of exposure to FQ and SLI. XDR Spine TB is very rare with few reported cases. Appropriate sensitivity-antituberculosis agents and good patient compliance are the keys to ensuring effective treatment of the XDR-TB condition.

Funding

None. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

The authors take responsibility for the consent of the patient and that informed consent was obtained.

Data Availability Statement

Data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare no conflict of interest.

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