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Rare Cases of Multidrug-resistant Tuberculous Spondylitis in Saiful Anwar General Hospital: A Case Series

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Abstract

BACKGROUND: Ten percent of all tuberculosis patients may develop skeletal involvement, and the spine is the most common anatomical location. Tuberculous spondylitis is further complicated by the fast-acid bacilli resistance to the usual chemotherapy regimen (multidrug-resistant/MDR) and its complications. In this case series, we would like to present three MDR tuberculous spondylitis cases effectively treated with tailored chemotherapy regimens and surgical interventions.

CASE REPORT: A series of three patients with MDR tuberculous spondylitis is presented. All three patients presented with back pain, lump, and weakness of both lower extremities. These cases were resolved with a combination of surgical intervention and tailored chemotherapy regiment after MDR resistant detected. Two cases were resolved completely, and only one patient had residual paresthesia on his legs.

CONCLUSION: A combination of MDR antituberculous chemotherapy and surgical intervention leads to an excellent outcome, in which the patient can perform regular daily tasks without pain, even in complicated MDR tuberculous spondylitis cases.

Introduction

Approximately 10% of all tuberculosis patients develop skeletal tuberculosis, and half of those cases affect the spine [1]. From all tuberculous spondylitis cases, an estimated 30% had antituberculous drug resistance, and 1/3 of them had multidrug-resistant (MDR) [2], [3]. The alarming increase of MDR tuberculosis further complicates the management of spinal tuberculosis [4]. This resistance is primarily mediated by genetic mutation induced by suboptimal therapy regimens and the patients' poor adherence [5]. The previous study concludes that Rifampicin and Isoniazid resistance is the most common and usually found simultaneously [6].

A retrospective study showed that the prevalence of MDR tuberculosis in a single tertiary hospital was about 10% [7]. However, the exact prevalence of both skeletal tuberculosis and tuberculous spondylitis in Indonesia is unknown. In our hospital, we observed 14 cases of tuberculous spondylitis in the first half of 2020.

At present, there is no study evaluating the present condition of MDR tuberculous spondylitis in Indonesia. Thus, we would like to highlight three MDR tuberculous spondylitis cases in our hospital, which were successfully managed by a combination of chemotherapy and surgical intervention.

Case Report

Case 1

A 50-year-old woman came with low back pain, muscle sores, and fatigue after walking for 5 years. She did not have any relatives that had tuberculosis disease. After a year, she felt pain and weakness on both legs worsened. The patient was previously diagnosed with low back pain due to muscle spasms and osteoporosis. She underwent physiotherapy for a month, but there was no improvement. A few months later, she realized a large paravertebral abscess, and surgical debridement and abscess evacuation were done. Because the patient's condition persisted after 4 months, she came to our orthopedic clinic. We found large abscesses affecting thoracal XII to

lumbar IV with straight lumbar curvature and slight levoscoliosis deformity apexed at lumbar III secondary to pathological fracture due to infection from X-ray and MRI findings (Figure 1). We diagnosed this case with multi-level thoracolumbar vertebra osteomyelitis and performed redebridement and abscess evacuation. The histopathology examination and culture depicted tuberculosis infection. We started category of one antituberculous chemotherapy and fixated the vertebra with Thoracic Lumbar Sacral Orthoses. Unfortunately, the pain persisted, both legs' weakness progressed, and abscess reappeared 4 months later. The patient received redebridement, decompression posterior stabilization but refused the instrumentation. GenXpert MTB/RIF examination was positive, and we started antituberculous chemotherapy for the next 2 years, the regiment is shown in Table 1. On follow-up, the patient can perform daily tasks without any problem and pain.

Case 2

A 36-year-old male patient complained of low back pain for the previous 6 months. He was on category two antituberculous drug medications for 4 months to treat his MDR pulmonary tuberculosis. The low back pain worsened, and then the patient noticed a lump on his back and weakness on both lower extremities. Radiograph examination revealed large abscess formation, kyphotic deformity at lumbar II–III, and severe destruction of lumbar III vertebral body (Figure 2). We performed surgical debridement and posterior stabilization using pedicle screws and rods from lumbar I–V. The positive results of histopathology, culture, and GenXpert MTB/RIF examination confirmed the spread of MDR tuberculosis to the spine. Antituberculous chemotherapy was started for the next 2 years; the regiment is shown in Table 1. The patient showed good outcomes and can perform daily tasks but with mild paraesthesia on his legs.

Case 3

A 33-year-old woman was presented with intermittent back pain for 8 months accompanied by a lump in the past 3 months and weakness on both lower extremities. The patient had a history of chronic cough, night sweats, weight loss, and denied any contact with tuberculosis patient. Large abscess formation and destruction of lumbar II vertebral body with kyphotic deformity were found in radiograph examination (Figure 3). We conducted abscess evacuation and decompression with posterior stabilization using pedicle screws and rods from thoracal XII to lumbar IV. MDR tuberculosis infection was confirmed by histopathology, culture, and GenXpert MTB/RIF. She started antituberculous chemotherapy, the regiment is shown in Table 1; however, her upper back's pain deteriorated, and the pus came out from the surgical wound 2 weeks later. The abscess spreads from thoracal VII to XI with the destruction of thoracal VIII–X vertebral bodies (Figure 3). The second surgery was carried out for debridement, abscess evacuation, decompression, and additional levels of posterior stabilization from thoracal VI–VII to lumbar III–IV. We continue her antituberculous treatment for the next 1.5 years. On the follow-up, she does not feel any pain on her back and recover without any sequelae.

Discussion

A retrospective cohort in South Africa reveals skeletal involvement in about 1–3% of tuberculosis cases. Most of them involve the spine, and only 4% had MDR tuberculosis [8]. In our hospital for the past 5 years, we observed three MDR tuberculous spondylitis cases, with the most common clinical findings were low back pain, lower extremity weakness, deformity, and lump. Rajasekaran *et al*. concur that back pain is the most

Table 1: Summary of the cases

	Case 1	Case 2	Case 3
Chief complaint	Back pain radiates down to both legs	Back pain is accompanied by cramps and tingling sensation	Back pain is accompanied by tingling sensations and a lump on the back
Physical examination	Abscess in the posterior thoracic region	Abscess in the posterior thoracic region and kyphosis (+)	Abscess in the posterior thoracic region and kyphosis (+)
History of TB treatment	OAT category I: 4 months, drop out OAT category II: 2 months, drop out	OAT category I: s 2 months, drop out	OAT category I: 2 months, drop out
Xpert MTB/Rif Sputum	MTB detected medium RR Detected	MTB detected very low RR Detected	MTB detected very low RR Detected
Chest X-ray	Normal	Lung TB advanced lesion	Normal
MRI lumbosacral	• Pyogenic spondylodiscitis at Th 12-L4 with intraosseous abscess	• Compression fractures at L3 • Spondylolisthesis L2, L3, L4 • TB spondylodiscitis at L2-L3 vertebrae, abscesses and extends to M. Psoas	• Suspected spondylodiscitis due to vertebral TB L1-L2 with bilateral dominant PSOAS abscess at T1-T3
Surgery	Transpendicular Debridement	Decompression laminectomy stabilization and instrumented posterolateral fusion	• Transpendicular Debridement L 3 • Laminectomy in L 2-3 • Posterolateral fusion on Th 12-L1,4,5
Pus culture	No growth of germ colonies (aerobes)	No growth of germ colonies (aerobes)	Negative Coagulase Staphylococcus
Xpert MTB/Rif (Pus)	MTB detected medium RR Detected	MTB detected low RR Detected	MTB detected low RR Detected
TB treatment regiment	8 Cm - Lfx-Cs-Eto-Z/12 Lfx-Cs-Eto-Z (20 months)	8 Cm - Lfx-Cs-Eto-Z-E/12 Lfx-Cs-Eto-Z-E (21 months)	8 Km -Cfz-Cs-Lfx-E/12 Cfz-Cs-Lfx-E (20 months)
Adverse effect	Nausea, vomiting, hyperuricemia, increased creatinine serum, and mild right ear conduction hearing loss	Hypokalemia, tinnitus	Drug induced liver injury, tentament suicide, and sleep disorder

Z: Pyrazinamide; E: Ethambutol; Km: Kanamycin; Lfx: Lefofloxacin; Eto: Ethionamide; Cfz: Clofazimine; Cs: Cycloserine; Cm: Capreomycin.

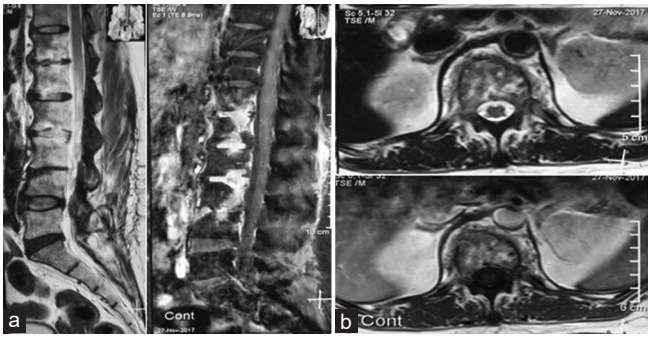

Figure 1: Loss of lumbar lordosis with narrowing of disc space of lumbar II–III; (a) sagittal plane and (b) axial plane of T2-weighted MRI showed marrow enhancement in thoracal XII–lumbar IV vertebral body and destruction of lumbar III–IV with paravertebral abscess formation

common symptom caused by inflammation and rarely radicular [9]. Classic symptoms such as chronic cough, night sweats, and weight loss are present in only one patient.

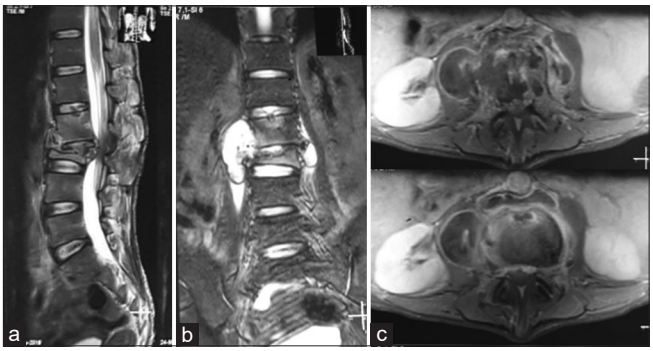

Figure 2: Kyphosis deformity due to destruction of lumbar III; (a) T2-weighted sagittal plane showed lytic lesion of lumbar III vertebral body and intervertebral body destruction with abscess formation extend to spinal canal causing severe thecal sac compression; (b) T2-weighted axial plane with contrast showed abscess in psoas muscle and rim enhancement

Tuberculous spondylitis often involves thoracic vertebra followed by lumbar vertebra. The incidence is decreasing along with the distance from the thoracic vertebra [10]. In all our cases, tuberculous spondylitis

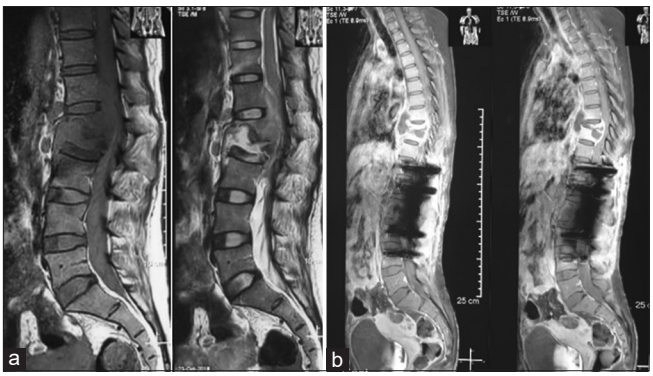

Figure 3: (a) T2-weighted image sagittal plane showed destruction of lumbar II, inferior end plate of lumbar I, and disappearance of psoas line with abscess extend to spinal canal from thoracal XII to lumbar III; (b) abscess formation involving thoracal VII–XII with destruction of Thoracal VIII–X vertebral bodies 2 weeks after the surgery

affects the lumbar vertebrae, and two of them have thoracal involvement. We believe that MDR tuberculosis bacilli are causing more severe vertebra's involvement than the non-MDR bacilli. Rathod *et al*. report a case of MDR tuberculous spondylitis involving the lumbosacral junction [11]. Therefore, further studies are needed to confirm which anatomical predilection would be affected by MDR tuberculosis bacilli.

In Indonesia, all rifampicin-resistant cases are treated with: Kanamycin, levofloxacin, ethambutol, cycloserine, pyrazinamide, and isoniazid. The alternative therapy regimens are levofloxacin, ethosuximide, cycloserine, pyrazinamide, ethambutol, and isoniazid. This therapy is given for 20–26 months; however, this duration can be shortened to 9–11 months [12]. There is still a debate regarding the therapy's effective duration, but the WHO and most experts agree that the effective duration ranges from 9 to 12 months [13]. On the contrary, Kizilbash and Seaworth recommend chemotherapy duration for 18–24 months [14].

Kizilbash and Seaworth state that surgical therapy should be conducted for those with neurologic deficits, intractable pain, considerable kyphotic deformity, spinal instability, and chemotherapy failure [14]. As our patients have neurologic deficits, we performed debridement and posterior instrumentation to prevent further complications. This management in parallel with Li *et al*. study, which mentions similar surgical approaches. Li *et al*. treated the patient with a combination of individualized chemotherapy and surgery that showed satisfactory results similar to the outcomes of our patients [2].

Tuli *et al*. propose the clinical criteria to suspect drug resistance of tuberculous spondylitis. The patients who have taken antituberculous medication for more than 5 months can be suspected as drug-resistant tuberculous spondylitis if they are present with one of the following criteria: Poor clinical and radiological response, fresh lesion osteoarticular tuberculosis, deterioration of spinal deformity, discharging sinus, or wound dehiscence of the previously operated scar [15]. These criteria for suspicion of MDR tuberculous spondylitis are seen in our patients. The first and second patients have poor clinical outcomes even after antituberculosis medication for several months. Wound dehiscence and presentation of pus from the surgical wound are observed in the third patient. Multiple surgeries are conducted in two patients, and all of the patients are given second-line antituberculous medication for more than 1 year. In Indonesia, the diagnosis of MDR tuberculous spondylitis cases is usually late. This is because the time and type of examination required for this diagnosis is quite long so that patient adherence to treatment is poor.

There is not another case series discussing MDR tuberculous spondylitis in Indonesia. For the past 5 years, we found three cases of MDR tuberculous

spondylitis in our hospital. Therefore, future retrospective or prospective studies should be done to better depict this disease entity's condition in Indonesia.

Conclusion

A combination of MDR antituberculous chemotherapy and surgical intervention (debridement, decompression, and stabilization) leads to an excellent outcome, in which the patient can perform regular daily tasks without pain, even in complicated MDR tuberculous spondylitis cases.

Ethical Approval

This study has been reviewed by the authors' Institutional Review Board and all the patients had given written consent.

Author Contribution

- Study Design: Syaifullah Asmiragani, Tjuk Risantoso, Andhika Yudistira, Ery Satriawan, Albert Lesmana, Alva Pribadi, Lasa Dhakka Siahaan.
- Data Collection: Syaifullah Asmiragani, Ery Satriawan, Albert Lesmana.
- Statistical Analysis: None.
- Data Interpretation: Syaifullah Asmiragani, Ery Satriawan, Albert Lesmana.
- Manuscript Preparation: Syaifullah Asmiragani, Tjuk Risantoso, Andhika Yudistira, Ery Satriawan, Albert Lesmana, Alva Pribadi, Lasa Dhakka Siahaan.
- Literature Search: Syaifullah Asmiragani, Ery Satriawan, Albert Lesmana, Alva Pribadi, Lasa Dhakka Siahaan.
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