

The Clinical Characteristics, Perioperative Management, and Treatment Outcomes of Spinal Tuberculosis Associated With Diabetes Mellitus

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Research article

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Abstract

Background. To report a preliminary experience of surgical treatment for patients with spinal tuberculosis (STB) associated with diabetes mellitus (DM) and discuss the strategic factors that should be considered.

Methods. A retrospective study of DMSTB patients who underwent surgical treatment between January 2012 and April 2018 in our center was carried out. For each patient: demographic information, perioperative management, laboratory examination, radiographic assessments, and clinical outcomes were reviewed.

Results. A total of 17 patients were included (11 males and 6 females), with a mean age of 57.53 ± 9.25 years and a follow-up of 28 ± 3.00 mos. Hypertension, Osteoporosis, and Hypoproteinemia were the most common complication. All patients passed the perioperative period smoothly, the 3 months follow-up showed the CRP and ESR have a significant decline, and the final follow-up shows both CRP and ESR back to normal, and there were a significant improvement of serum albumin levels. The Bone fusion time is 9.88 ± 2.65 mos.

Conclusions. Perioperative management of DMSTB patients is a complicated issue with numerous factors to be considered. Spinal surgery can achieve satisfactory outcomes in these patients if the glycemic level remains well controlled, nutritional supplementation is adequate, and antituberculosis treatment is sufficient.

Introduction

According to the 2020 World Health Organization Global Tuberculosis Report, despite multiple efforts made to reduce the impact of tuberculosis, an estimated 10.0 million people are still newly diagnosed with tuberculosis (TB) each year globally. Diabetes mellitus (DM) is a strong risk factor for the development of TB, as up to 0.35 million cases are attributed to diabetes [1]. People with DM have a 2–3-fold greater chance of developing TB compared with nondiabetic controls because DM leads to impaired immunity, which causes latent TB infection to become active [2, 3]. Besides, DM has negative effects on TB patients' treatment response, which may result in TB treatment failure, relapse after recovery, or even death [4, 5]. What's worse, treatment failure increases the odds of drug-resistant TB, which places a heavy burden on the global TB control program [1]. Considering this, a more aggressive TB treatment strategy for patients with DM is needed.

Spinal tuberculosis (STB), as the most common type of extrapulmonary tuberculosis and a major cause of spinal kyphosis and neurological dysfunction, accounts for nearly half of osteoarticular tuberculosis cases [6]. Epidemiological surveys of spinal tuberculosis associated with diabetes (DMSTB) are lacking. To date, only a few studies have reported the incidence rate of spinal tuberculosis complicated with diabetes. A survey conducted in the United States from 2002–2011 shows that 11.6% of spinal tuberculosis patients have a comorbidity of diabetes [7]. Shi, T. et al. [8] reviewed 967 spinal tuberculosis

patients in southwestern China for 1999–2013 and found 77 (8%) of the patients to have diabetes, and a review of 1378 spinal tuberculosis patients who received surgery from 2007 to 2016 in southcentral China found 63 of the patients (4.6%) to have a comorbidity of diabetes [9].

Previous studies have indicated that DM is a major risk factor for perioperative complications of spine surgery, such as wound infection, prolonged operative time, a longer hospitalization period, and a higher nonunion rate [10, 11]. However, to the best of our knowledge, no study has reported the perioperative treatment of DMSTB, considering the poor general health condition of the DMSTB patients, perioperative treatment is a challenge for spine surgeons for such patients. Hence, the purpose of the study is to report a preliminary experience of our surgical treatment for patients with DMSTB and discuss the strategic factors that should be considered[10].

Materials And Methods

This study was approved by the ethics committee of our hospital, and written informed consent was obtained from all patients. We performed a retrospective study of DMSTB patients who underwent surgical treatment between January 2014 and April 2018. All patients underwent one-stage anterior/posterior approach surgical treatment. For each patient, demographic data, including age (years), gender, residence, chief complaint, length of stay (days), and hospitalization expense (USD) information, were reviewed. Intraoperative blood loss (ml) and surgical complications were also reviewed from digital medical records.

Laboratory examination results

The laboratory examination measured the following: ESR), CRP, albumin, creatinine, uric acid, glycemic, glycosylated hemoglobin (4.0–6.1%). CRP and ESR levels at 3-month follow-up and final follow-up were also recorded. Levels of albumin, creatinine, and uric acid at final follow-up were also reviewed.

Radiographic Measurement and Clinical Evaluation

The range of bone destruction was defined using the vertebral body as a reference from computed X-ray tomography (CT) scans, described as half/1/2,... vertebral bodies. Each fusion of a disc is considered to form one fixation segment. Bone graft fusion was assessed using the radiologic criteria reported by Bridwell et al. [11].

Statistical Analysis

Data for the two groups were compared using independent *t*-tests, Fisher's exact test, and chi-square test depending on the parametric quality of the data analyzed. Statistical analyses were performed using SPSS version 25.0 (IBM). The significance level was set at $p < 0.05$.

Results

General information

A total of 17 patients were reviewed (7 males/4 females) with a mean age of 56.63 ± 9.66 years. All patients were diagnosed with spinal tuberculosis for the first time of the 6 patients were newly diagnosed with DM (Table 1). The lumbosacral region was the most affected, as it had been invaded in 9 of the patients: 3 in L5-S1, 3 in L4–5, 1 in L4-S1, and 2 in L1-L2. Six patients were affected in the thoracic region: 3 in T10–11, 2 in T8–9, and 1 in T8-T11. One patient was infected in the cervical region: C6–7. As for residence, only 3 patients lived in an urban area while 14 patients lived in urban areas (Table 2). Of the 17 patients, 14 cases (82.4 %) were with more than three kinds of concurrent disease, including hypertension, obsolete pulmonary tuberculosis, osteoporosis, and diabetic glomerulopathy (Table 3). The diagnosis of STB was based on clinical presentation, laboratory examination, and radiographic measurements. (Fig. 1A-E). Clinical presentation manifested as back pain, numbness, weakness, and limited activity. As outlined in Table 2, The average erythrocyte sedimentation rate (ESR) preoperation was 74.82 ± 32.16 mm/h, The mean preoperative C-reactive protein (CRP) was 26.13 ± 21.65 ug/ml. The mean preoperative albumin was 35.77 ± 3.53 g/L, indicating that the DMSTB patients are innutrition. And the mean preoperative glycosylated hemoglobin was $6.72 \pm 1.42\%$.

Perioperative Care and Surgical Outcomes

Antituberculosis chemotherapy was applied for at least 2 weeks before surgery with doses of rifampicin (10 mg/kg), isoniazid (5 mg/kg), pyrazinamide (25 mg/kg), and ethambutol (15 mg/kg) respectively. Concurrent disease like hypertension was routinely controlled, the targets were blood pressure below 130/90 mmHg. For DM, subcutaneous insulin injection was used during the perioperative period for both newly and previously diagnosed diabetes. As a common practice, we prefer short-acting insulin before meals and long-acting insulin at 10 pm. Meanwhile, fasting and postprandial glycemic levels should be monitored, and the use of insulin should be adjusted accordingly. As the American Diabetes Association recommends, glycated hemoglobin (HbA1c) levels of <7% are an ideal target for patients with DM [12], and HbA1c levels of between 7% and 8% and random blood glucose levels of <11.1 mmol/l are acceptable targets according to the American College of Physicians [13]. The surgical plans were made based on the radiographic measurement and the significant decline of inflammatory biomarkers like CRP and ESR. The mean operation time was 292.72 ± 56.74 min, the intraoperative blood loss was 627.27 ± 486.34 ml, hospitalization expenses were USD 19713.13 ± 5816.89 , and LOS period was 27.63 ± 10.79 days (Table 1). The CRP and ESR have a significant decrease at the 3 months follow-up ($p < 0.01$) and at the final follow-up, both the inflammatory biomarker and serum albumin have back to normal, combined with a mean bone fusion time of 9.88 ± 2.65 month, indicating that STB has been cured(Table 2).

Postoperative complications

After the operation, four patients had the pulmonary infection, one patient had pulmonary infection complicated with lower extremity venous thrombosis, one patient had lower extremity venous thrombosis,

and three patients had different degrees of delayed wound healing. After active symptomatic support treatment, all patients recovered and were discharged from the hospital.

Discussion

The clinical characteristics of DMSTB

DM is a chronic, complex metabolic disorder that affects different organs and systems, leading to various subsequent complications, such as cardiovascular and microvascular accidents, nephropathy, retinopathy, etc. [14, 15] In our study, DMSTB patient's preoperative complications mainly include pulmonary, cardiovascular, hepatobiliary, and urinary complications, making treatment more difficult. Among these complications, hypertension was the most common one (14/17). Two of the patients had coronary heart disease. Two DMSTB patients had symptoms of renal involvement. For other complications, osteoporosis was seen in 6 of the 17 DMSTB patients (Table 3). It is believed that osteoporosis may occur due to bone microstructure damage caused by diabetes [16]. The level of serum albumin in DMSTB patients was lower than the standard ($35.77 \pm 3.53 \text{ g/L}$), indicating that patients with DMSTB are often malnourished. Moreover, more patients lived in rural areas (14/17) in the DMSTB group, and 6 (35%) of them were newly diagnosed with DM, which may imply that patients living in rural areas have fewer financial resources or less access to health care. In short, DMSTB patients are associated with a greater risk of experiencing preoperative complications and malnutrition and with having fewer financial resources.

Perioperative management of DMSTB

For DM patients who undergo spine surgery, glycemic control is essential. Previous studies have shown that patients with unsatisfactory glycemic control are associated with increased perioperative complication rates and poorer surgical outcomes than those with better glycemic control [17, 18]. It has also been reported that poorly controlled DM has the strongest effects on TB susceptibility and unfavorable TB outcomes [18]. Hence, to achieve better glycemic control for STB patients receiving surgical treatment, subcutaneous insulin injection should be used during the perioperative period for both those with newly and previously diagnosed diabetes. As a common practice, we prefer short-acting insulin before meals and long-acting insulin at 10 pm. Meanwhile, fasting and postprandial glycemic levels should be monitored, and the use of insulin should be adjusted accordingly. As the American Diabetes Association recommends, glycated hemoglobin (HbA1c) levels of <7% are an ideal target for patients with DM [12], and HbA1c levels of between 7% and 8% and random blood glucose levels of <11.1 mmol/l are acceptable targets according to the American College of Physicians [13].

Currently, the recommended anti-TB treatment for combined TB and DM is similar to that for patients with TB only, and the treatment principles of tuberculosis drugs include early, sufficient, whole course, and combined adoption [1]. However, caution should be exercised, as DM is known to be associated with several unfavorable antituberculosis outcomes (drug resistance, drug toxicity, treatment failure, and recurrence) [19]. Hence, antituberculosis treatment for DMSTB should be monitored more closely than

that for non-DMSTB, and adjustments of drug doses and/or regimens should be made following the treatment response, with drug-drug interactions, and with drug side effects. At our center, HREZ4 treatment is adopted to treat DMSTB. For patients with liver and kidney dysfunction or drug-resistant tuberculosis, the use of tuberculosis drugs is adjusted according to the given situation. Recently, with the adaption of gene sequencing in clinics, patients have been recommended for gene sequencing of tuberculosis samples for more individualized treatment [20]. In addition, since DMSTB patients usually have low albumin levels, it is necessary to provide adequate nutritional support during the perioperative period.

The key points in the perioperative treatment of DMSTB

From our experience, the treatment of DMSTB should focus on the following points. Firstly, the delayed diagnosis should be avoided. It should be realized that DM may cause diabetic peripheral neuropathy and vascular disease, which not only accelerated the progress of the disease but also covered up the discovery of spinal tuberculosis. Hence, for DM patients with persistent back pain, MRI or even enhanced MRI is recommended as it has high sensitivity and specificity compared to plain radiographic and CT. Secondly, DMSTB patients often have multiple organs involved, considering this, a thorough examination and preoperatively treating the disease effectively is of great importance before surgery. Thirdly, perioperative nutrition support needs to be emphasized. DMSTB patients are tending toward malnutrition, hypoalbuminemia, or even anemia due to longtime poor appetite and insufficient sleep caused by chronic back pain. Fourthly, as osteoporosis is a common condition in DMSTB patients, Anti-osteoporosis therapy perioperative and enhanced pedicle screw fixation technique is essential for spinal stability reconstruction. Fifthly, postoperative early-stage rehabilitation exercises are recommended to avoid long-term bed rest-related complications.

Study limitations

This study has two main limitations. First, as rates of DMSTB with surgery are low (4.6%) in our study area [9], the retrospective nature of our small sample study may be associated with bias. Second, our study did not consider intra- and interobserver differences associated with bias.

Conclusion

Perioperative management of DMSTB patients is a complicated issue with numerous factors being considered. Spinal surgery can achieve satisfactory outcomes in these patients if the glycemic level remains well controlled, nutritional supplementation is adequate, and antituberculosis treatment is sufficient.

Abbreviations

DM: Diabetes mellitus; STB: Spinal tuberculosis; DMSTB: Spinal tuberculosis associated with diabetes mellitus; LOS: Length of stay; FFU: final follow-up; ESR: erythrocyte sedimentation rate; CRP:C-reactive

protein

Declarations

Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that they have no competing interests.

Authors' contributions

HZ designed the study. LX, MT, and YS performed the data collection, statistical analysis, and data interpretation. GY contributed to manuscript writing. GY and LX contributed to patient enrollment and follow-up. All authors read and approved the final manuscript.

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Tables

Table 1. Demographic of study populations

General information	
Age(yrs.)	57.53±9.25
Gender(male/female)	11/6
Residence(cases)	
Rural	14
Urban	3
Chief complaint(cases)	
Pain	15
Numbness	5
Weakness	4
Limited activity	2
Diabetes history(cases)	
Previous diagnosis	11
New diagnosis	6
Operation time(min)	295.29±52.59
Intraoperative blood loss(ml)	650±459.53
Hospitalization expenses (USD)	18555.52±5891.46
LOS (day)	28±8.92

Abbreviation: USD U.S. dollar, LOS length of stay.

Table 2 Surgical Results of the Patients

Laboratory examination	p Value
CRP	26.13 ± 21.65
ESR	74.82 ± 32.16
Albumin	35.77 ± 3.53
Creatinine	108.37 ± 142.45
Glycosylated hemoglobin	6.72 ± 1.42
3M-CRP	8.51 ± 5.05
3M-ESR	45.17 ± 20.45
FFU-CRP	5.32 ± 7.98
FFU-ESR	24.41 ± 24.49
FFU-Albumin	42.89 ± 2.87
Radiological assessments	
Cervical spine tuberculosis	2
Thoracic spine tuberculosis	5
Lumbar and lumbosacral spine tuberculosis	10
Bone fusion time(mouth)	9.88 ± 2.65
Follow up time(mouth)	28 ± 3.00

Abbreviation: CRP C-reactive protein, ESR erythrocyte sedimentation rate, 3M 3-month, FFU final follow-up, * 3 month follow up compared to preoperation, # Final follow up compared to 3 months follow up, & Final follow up compared to preoperation.

Table 3 Pre- and post-operative complications of the DMSTB patients

Preoperative complications(cases)

Pulmonary complications	
Asthma	1
Bronchiectasia	1
Obsolete Pulmonary Tuberculosis	5
Cardiovascular complications	
Atrial fibrillation	1
Arteriosclerosis	1
Coronary heart disease	2
Hypertension	14
Uremic cardiomyopathy	1
Hepatobiliary complications	
Chronic hepatitis B	1
Cholecystolithiasis	1
Fatty liver	3
Urinary complications	
Prostatic nodule	1
Adrenal nodule	1
Chronic Renal Failure	2
Diabetic glomerulopathy	3
Renal calculus	3
Others	
Anemia	2
Incomplete paralysis	5
Osteoporosis	6
Hyperthyroidism	1
Thyroid nodule	1
Endophthalmitis	2
Brain tumors	1
Colon cancer	1
Total	58
Postoperative complications(cases)	
Pulmonary infection	5
LEDVT	2
Delayed wound healing	3
Total	7

Abbreviations: LEDVT Lower extremity deep venous thrombosis;

Figures

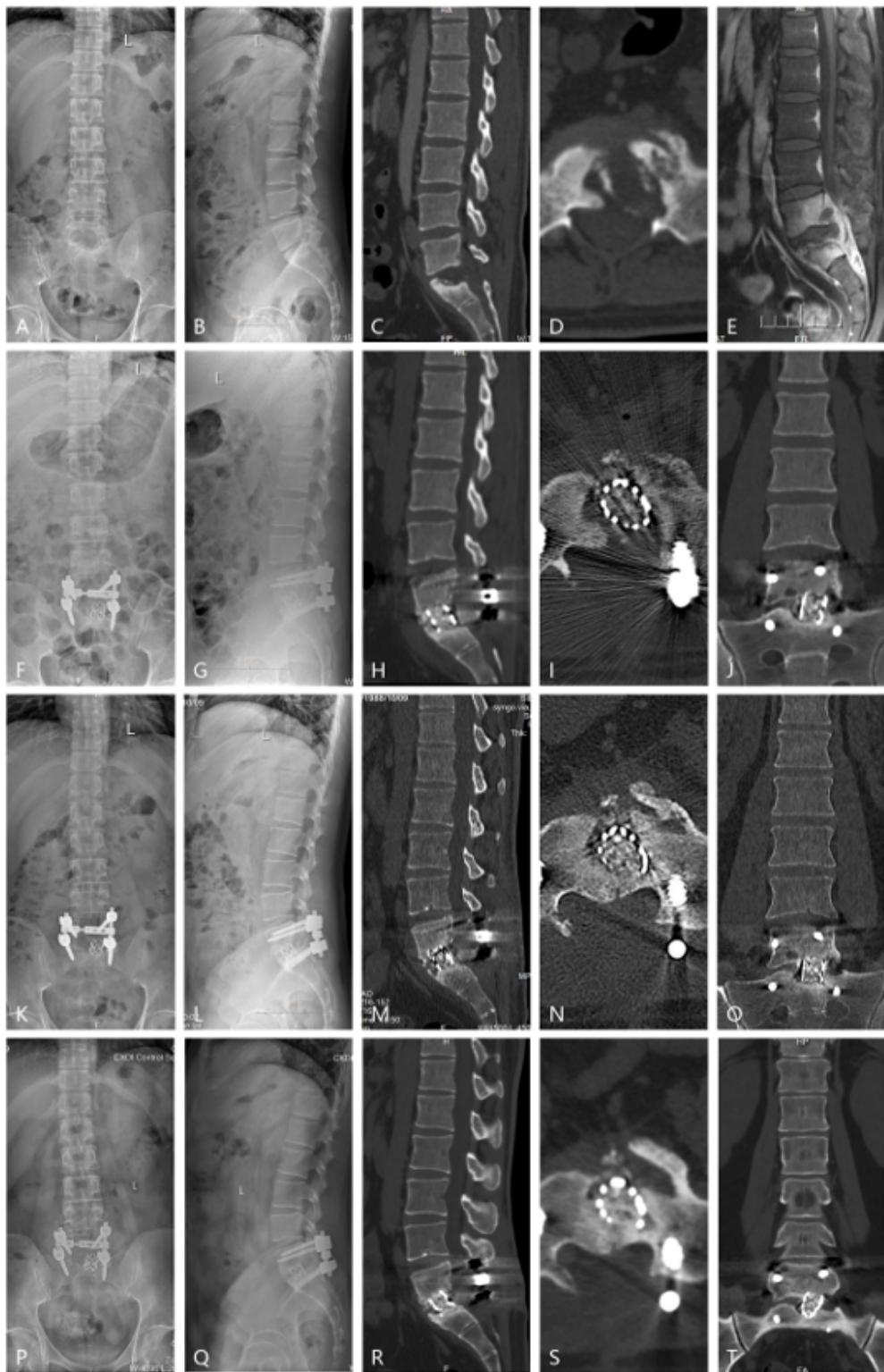


Figure 1

A 42-year-old male was diagnosed as having DMSTB after an eight months history of severe back pain. A-E Pre-operative X-ray, MRI and CT showed that the lesion around the vertebral body of L5/S1 developed an abscess with marked bony destruction. The abscess involved in the spinal canal with cord compromise resulted in neurologic deficit. F-J Post-operative X- ray and CT showed complete resolution of epidural abscess and decompression of neural component. Interbody graft using titanium mesh cages

were placed satisfactorily. K-O 3-mouth follow-up radiographs showed there is no titanium mesh cages displacement. P-T Final follow-up radiographs showed there is good bone fusion.