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Analytic Study of Spinal Infections: Clinical Picture, Treatment, and Outcomes in King Fahad Military Medical Complex in Dhahran, Saudi Arabia

Salma Albahrani[1,2*], Amal Shilash[1,3*#], Ayat Albasri[1,4], Sharifah Almuthen[1,4], Sama Tawfiq[1,4], Khalid Alzahrani[1,5], Amjad Darwish[1,5], Muneera Albassam[1,6], Jamil Barhoun[1,2]

[1]King Fahad Military Complex, Dhahran, KSA
[2]Infectious Disease Consultant, King Fahad Military Complex, Dhahran, KSA
[3]Epidemiologist, Infection Control Department, King Fahad Military Complex, Dhahran, KSA
[4]Internal Medicine Department, King Fahad Military Complex, Dhahran, KSA
[5]Neurosurgeon Consultant, King Fahad Military Complex, Dhahran, KSA
[6]Radiology Department, King Fahad Military Complex, Dhahran, KSA
Email: drsalma1@hotmail.com, [#]amalsalshammari@gmail.com, dr.ayat.ali@hotmail.com, dr.sharifah89@hotmail.com, samatawfiq@hotmail.com, khaledalzahrani@hotmail.com, dramjaddarwish@gmail.com, muneera_b@hotmail.com, jamilbarhoun@gmail.com

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Abstract

Objective: To evaluate the prevalence of spinal infection in a hospital located in the eastern region of Saudi Arabia through a retrospective review and to identify the associated etiological agents in terms of clinical picture, treatment, and outcomes. **Design:** Retrospective cross-sectional study. **Setting:** Single hospital in Dhahran, Saudi Arabia. **Patients:** Patients with any type of spinal infection and/or who had undergone neurosurgical intervention for spinal infection between January 2006 and December 2018. **Methods:** We collected data on all patients with an established diagnosis of spinal infection from January 2006 to December 2018 in the King Fahad Military Medical Complex in Dhahran, Saudi Arabia. A validated and structured checklist was used for data collection. Spinal infection diagnosis was based on the clinical manifestation, microbiological evidence, radiological findings, and antimicrobial therapy response. **Results:** Seventeen patients were included in this study, and their mean age was 54.93 years. Twelve of the patients were male and four were female. The approximate time from symptom onset to diagnosis was 2 - 6 months. Most of the patients experienced back pain, with lumbosacral spondylitis being the most commonly cited type (61.11%), followed

*S.A. and A.S. are equally contributed and co first authors.

by thoracolumbar spondylodiscitis (25%) and cervical spondylodiscitis (6.25%). The most frequently isolated organism was *Mycobacterium tuberculosis* (8 patients, 50%), followed by extended-spectrum beta lactamase (ESBL)-producing *Escherichia coli* (4 patients, 25%), *Brucella* spp (3 patients, 18.75%), *Staphylococcus aureus* (1 patient, 6.25%), and *Quambalaria cyanescens* (1 patient, 6.25%). Totally, in 50% of the patients with thoracolumbar and lumbosacra site involvement, tuberculosis spondylodiscitis was observed, while another 50% of the cases showed complications associated with paravertebral abscess that required surgical drainage. **Conclusion:** *M. tuberculosis* was found to be the major cause of infectious spondylodiscitis. Additionally, *Quambalaria cyanescens* was isolated; this is the second reported case of the organism being isolated and the first associated with spinal infection.

Keywords

Spinal Infection, *Mycobacterium tuberculosis*, *Quambalaria cyanescens*, Tuberculosis, Spondylodiscitis

1. Introduction

Spinal infections include spinal abscess, discitis, spondylitis, and paraspinal infection. Spondylodiscitis represents 0.15% to 5% of all osteomyelitis cases, ranging from 1 in 100,000 cases/year to 1 in 250,000 cases/year [1]. Spondylodiscitis is an infection (generally bacterial) of the intervertebral disk and neighboring vertebrae [2]. It includes spontaneous spondylodiscitis (SS), which results from microbial dissemination through the bloodstream from a remote entry portal, and postoperative spondylodiscitis (POS), which is caused by direct inoculation into the intervertebral space [3]. Pyogenic spondylodiscitis can be categorized into different POS types following diagnostic or therapeutic processes in the spinal cord, and into SS types based on whether the infection is community-acquired or nosocomial [4]. Most spondylodiscitis cases show a monomicrobial etiology, with gram-positive bacteria being the most predominantly noted, followed by gram-negative bacteria and yeast. *Staphylococcus aureus* is the most frequently isolated microorganism in such settings [4]. Subacute and chronic spondylodiscitis are caused by a broad range of pathogens, of which *Mycobacterium tuberculosis* is the most prevalent; other bacteria include *Brucella* spp in the endemic regions [5].

Spinal infection established risk factors include an immunocompromised state such as the presence of diabetes, steroid use, liver cirrhosis, end-stage kidney disease, intravenous drug use, and chronic alcoholism [6]. However, postoperative spondylodiscitis tends to occur in younger people and is associated with fewer comorbidities than spontaneous spondylodiscitis. The average age of patients with postoperative spondylodiscitis is 52 years, and many of them have an underlying disease (discal hernia) that requires surgery [7].

The diagnosis of spondylodiscitis is challenging and requires clinical, radiological, and microbiological study. The following requirements must be met for the diagnosis of spinal infection:

1) Condition suggestive of spondylodiscitis (persistent back pain and/or irradiated pain and/or neurological deficiency and/or fever), and abnormal values of laboratory parameters such as white blood cells (WBCs), erythrocyte sedimentation rate (ERS), and C-reactive protein (CRP).

2) Abnormal findings on magnetic resonance imaging (MRI) and computed tomography suggestive of spinal infection.

3) Microbiological or histopathological identification of the causative organism isolated on tissue biopsy.

However, in the early postoperative phase of discitis, MRI is not accurate as the only imaging method to distinguish septic from aseptic discitis and may provide false-negative results.

This study sought to evaluate the prevalence of spondylodiscitis in a single center and describe the associated clinical, laboratory, and diagnostic features. We also aimed to identify the causative organisms and their response to treatment and outcomes.

2. Materials and Methods

This single-center case-series study was conducted at the King Fahad Medical Military Complex (KFMMC) in Dhahran, Saudi Arabia from 2006 to 2018, and included a total of 17 patients. Inclusion criteria were all patients been admitted to KFMMC as a case of infectious spondylodiscitis from Jan 1st, 2006 till Dec 31st, 2018. We excluded any patient who is younger than 12 years old and pregnant women. Data collection was performed via a well-structured checklist. Diagnoses were confirmed by infectious disease consultants and neurosurgeons based on the clinical manifestation, imaging, and microbiological evidence. Data were collected by internal medicine residents using patients' medical records. The diagnosis of infectious spondylodiscitis was established by an infectious disease consultant according to the International Classification of Diseases, 10th edition (ICD-10) [8]. The measurements of exposure, Vital signs: temperature, labs works: ESR, CRP, Blood culture, Radiology: lumbar spine MRI for localization of the pathology all were obtained based on a literature review and included the Charlson comorbidity score [9]. The Charlson comorbidity index (CCI) score: low (0 - 1) or high (≥2). The CCI assigns a score from 0 to 6 for 12 diseases with the sum of the scores serving as a measure of overall comorbidity for each case [10]. Other associated risk factors, as well as the laboratory features at the baseline, 48 hours after treatment initiation and two weeks after treatment. **Table 1** shows all the patients' clinical characteristics. Approval from the institutional review board at KFMMC was obtained before study initiation. The objective of the study was explained to each participant, and informed consent was obtained. Patient data were anonymized and coded to ensure confidentiality.

Table 1. Patients' clinical characteristics.

Patient no.	Diagnosis	Clinical symptoms	Body temperature ˚C	ESR mm/h	CRP Mg/l	WBC count X10/mm	Localization	Culture
1	Discitis	Back pain and weakness of the lower limb	38	62	19	11.3	L3, 4, 5	ESBL-producing *E. coli*
2	Vertebral osteomyelitis	Severe low back pain	38.2	84	299	20.7	C2 - 7 + L5	MSSA *S. aureus*
3	Vertebral osteomyelitis	Back pain, lower limb numbness, fever, weight loss, night sweats	37	53	0.7	14.1	T4 - 7	*M. tuberculosis*
4	Vertebral osteomyelitis	Fatigue and weight loss and decrease of appetite	37.5	52	12	10	T12 - L1	*M. tuberculosis*
5	Vertebral osteomyelitis	Chronic back pain	37	43	24	4.79	L3 - 4	*M. tuberculosis*
6	Discitis	Lower back pain for 3 weeks	38	33	24	10.6	L3 - 4	ESBL-producing *E. coli*
7	Vertebral osteomyelitis	Back pain and pain of the back of the right thigh	36.9	61	71	3.4	L5 - S1	*M. tuberculosis*
8	Discitis	Fever and chills associated with back pain	37	83	6	7.3	L3 - 4	ESBL-producing *E. coli*
9	Vertebral osteomyelitis	Lower limb numbness, weight loss, and low back pain	37	27	negative	4.0	T8 - 9	*M. tuberculosis*
10	Discitis	Severe low back pain, fever associated with knee pain	38.6	62	Negative	4.4	L2 - 3	*Brucella*
11	Vertebral osteomyelitis	Back pain, bilateral lower limb pain, fever, and weight loss for 3 months	37.0	52	24	7.76	L2 - 5	*Brucella*
12	Discitis	Low back pain	38.	62	16	6.17	L2 - 3	*Brucella*
13	Vertebral osteomyelitis	Paraparesis	37	120	48	8.0	T2 - 5	*M. tuberculosis*
14	Vertebral osteomyelitis	Spastic paraparesis and bladder dysfunction	37	9	6	4	L5 - S1	*M. tuberculosis*
15	Vertebral osteomyelitis	Back pain increasing with movement	37	91	48	6	T12 - L1	*M. tuberculosis*
16	Discitis	Back pain and lower limb weakness	38	120	64	12.3	L3 - 4	ESBL-producing *E. Coli*
17	Vertebral Osteomyelitis	Right hip pain with fever for 10 days	37	115	48	17.9	L2 - 3	*Qumbalaria cyanescens*

E. coli, *Escherichia coli*; ESBL, extended-spectrum beta lactamase; MSSA, methicillin-sensitive *Staphylococcus aureus*; *M. tuberculosis*, *Mycobacterium tuberculosis*; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; WBC, white blood cell.

3. Results

Presenting Symptoms and Signs

In the 17 enrolled patients, the disease onset was of a more sub-acute-to-chronic nature. All patients were symptomatic. The most commonly observed symptom was back pain, followed by fever and constitutional symptoms. All patients presented with localized back pain related to the site of infection. Back pain radiating to one or both lower limbs was observed in six patients. One of the patients had lumbosacral back pain radiating to the back of the thigh. One patient had urinary incontinence. Body temperatures ≥ 38˚C were observed in seven patients.

Laboratory Data and Microbiology

Elevated CRP levels were observed in 12 patients. The ESR was increased in all patients (>30 mm/h) except two. Leukocytosis (>10,000 WBCs/mm) was noted in five cases. Standard tube agglutination testing of the initial samples of the two patients with *Brucella*-related spondylitis yielded positive results for antibodies to *Brucella* (titer, ≥1:160). Blood cultures yielded positive results in one patient for whom the titer was <1:160. Pathogens were isolated through biopsy of the tissue from the infected spine in all cases. *Staphylococcus* spp were observed in one case only. *E. coli* was isolated in four patients and all of them showed the ESBL-resistant strain. The majority of the cases (8 patients) had *M. tuberculosis*. Brucellosis was detected in three cases. One case showed a fungal infection related to *Qumbalaria cyanescens*.

In 13 patients, the infection was localized to the lumbar spine. The infection involved more than two contagious vertebrae and the intervertebral disk causing vertebral osteomyelitis. However, in six patients, the infection was limited to the intervertebral disk space without adjacent vertebrae causing discitis.

Treatment

All patients received antimicrobial therapy. The duration of the therapy was based on the clinical response of the patient and/or presence of abscess in the vertebrae and paravertebral space. The choice of therapy was the use of either an antimicrobial agent (imipenem/meropenem for ESBL-producing *E. coli*) or vancomycin for methicillin-resistant *S. aureus* (MRSA). The standard anti-tuberculosis (TB) regimen for all the TB cases (all of which were isoniazid-rifampicin sensitive). For brucellosis, rifampicin and doxycycline for 3 months with an initial seven-day dose of gentamicin were intravenously used. Decompressive laminectomy and abscess drainage together with debridement of the infected bone were performed in most of the patients except for those with brucellosis.

MRI was performed in all patients, and we observed findings characteristic of spinal infection. Ten patients underwent initial MRI. Decrease in the vertebral bodies with intervertebral discs on T1-weighted images, which are considered typical changes, were found. Additionally, we noticed a minimal diffuse disc bulge at two vertebral levels with posterior disc protrusion in one patient at the multilevel disc lesion/paravertebral collections with vertebral end plate enhancement in the lower lumbar region in four patients with TB, two of whom had nerve compression in the lower thoracic region with an intact intervertebral disc space. One TB patient had associated unilateral psoas muscle abscesses.

Outcomes

All patients were followed-up for a median of 4.0 years (minimum 12 months).

The period of admission was a median of 6 days, and none of the patients showed fever from days 1 to 15. In terms of laboratory findings, the CRP and ESR values were normalized. No cases of recurrence or relapse were reported.

Characterization of Risk Factors

As shown in Table 2, diabetes mellitus was observed in five patients, and in three of eight TB patients, a history of previous TB or contact with TB patients was observed as a major risk factor. Five of the patients did not have any predisposing factor for infection. Raw milk ingestion was reported in two of the three brucellosis patients. Previous spinal surgery was cited in three of the patients.

4. Discussion

In this study, *M. tuberculosis* was found to be the major cause of infectious spondylodiscitis, contradictory to previous reports. Additionally, *Quambalaria cyanescens* was isolated; this is only the second reported case of this organism being isolated and the first associated with spinal infection. The pathogenesis of spinal infections has changed dramatically over the past few years. TB used to be the most frequently cited spinal infection type in the 1950s [11]. Nowadays, however, pyogenic infections are more commonly observed. *S. aureus* is the

Table 2. Demographic data of analyzed patients.

Case number	Gender	Age (y)	Pathogen	Predisposing factors	Spinal infection location
1	Female	59	ESBL-producing *E. coli*	Not present (Salmonella in 2016)	L3 - 5
2	Male	64	*S. aureus*	Diabetes mellitus + previous spinal surgery	C2 - 7 + L5
3	Male	19	*M. tuberculosis*	Contact with tuberculosis patients	D4 - 7
4	Male	62	*M. tuberculosis*	Diabetes mellitus + liver cirrhosis	D12 - L1
5	Male	35	*M. tuberculosis*	Family history of tuberculosis	L3 - 4
6	Male	81	ESBL-producing *E. coli*	Infective endocarditis, mitral valve regurgitation	L3 - 4
7	Male	65	*M. tuberculosis*	End-stage renal disease on hemodialysis	L5 - S1
8	Male	85	ESBL-producing *E. coli*	Diabetes mellitus	L3 - 4
9	Male	28	*M. tuberculosis*	Not present	D8 - D9
10	Female	62	Brucellosis	Diabetes mellitus + raw milk ingestion	L2 - 3
11	Male	60	*Brucella*	Raw milk ingestion	L2 - 5
12	Female	62	*Brucella*	Previous spinal surgery	L2 - 3
13	Male	50	*M. tuberculosis*	Not present	D2 - D5
14	Male	60	*M. tuberculosis*	Not present	L5 - S1
15	Male	47	*M. tuberculosis*	Previous spinal surgery + brain TB in 2006	D12 - L1
16	Female	50	ESBL-producing *E. coli*	Not present	L3 - 4
17	Male	80	*Quambalaria cyanescens*	Diabetes mellitus + treated tuberculosis 30 years ago	L2 - 3

ESBL, extended-spectrum beta lactamase; *E. coli*, *Escherichia coli*; *M. tuberculosis*, *Mycobacterium tuberculosis*.

most frequently isolated bacterium in spinal infection patients, accounting for 20% to 84% of all such cases[12] [13], and is observed commonly among intravenous drug abusers [14]. However, we found that *M. tuberculosis* was the most commonly isolated causative organism, associated with the high prevalence of TB in Saudi Arabia. The Ministry of Health in the country reported a TB incidence of 64,345 cases during 1991-2010. Of these, there were 46,827 (73%) pulmonary TB cases and 17,518 (27%) extra-pulmonary TB cases, with Saudis accounting for 52% of the cases (33,468 cases) and non-Saudis for 48% (30,837 cases). The majority (62%) of the patients were male [15]. Additionally, *Enterobacter* spp were observed in 7% to 33% of the cases with pyogenic vertebral infection [12]. The most commonly observed bacteria in this group was *E. coli* [16], which is associated with certain infections such as urinary or gastrointestinal infections, old age, and an immunocompromised state [17]. Brucellosis is still commonly observed in endemic areas, accounting for 12% to 65% of the cases [18]. **Table 3** shows the distribution of the aerobic bacteria isolated from 33 cases of spondylodiscitis in the literature. Saudi Arabia is an endemic region in terms of brucellosis, and the prevalence of the disease in the country is believed to range from 1 to 3 per 1000 cases [19]. Fungal infections are rarely reported in immunocompromised patients [20].

The spinal regions mainly affected were found to be related to the causative organism. Pyogenic infections affect mainly the lumbar regions, followed by the thoracic, cervical, and sacral regions [21], while TB predominantly affects the

Table 3. Aerobic bacteria isolated from 33 cases of spondylodiscitis in the literature

Gram-positive	
Peptococcus spp.	3
Staphylococcus saccharolyticus	1
Peptostreptococcus spp.	3
Clostridium perfringens	1
Clostridium difficile	1
Other *Clostridium* spp.	1
Corynebacterium diphtheriae	2
Propionibacterium acnes	7
Unspecified anaerobes	3
Total	**22**
Gram-negative	
Bacteroides fragilis	2
Bacteroides melaninogenicus	6
Other *Bacteroides* app.	4
Fusobacterium necrophorum	1
Fusobacterium spp.	1
Total	**14**
TOTAL	**36**

thoracolumbar region [22]. Most patients present with more than two affected vertebrae, and 25% of them have skip regions [23].

Patients with spondylodiscitis usually present with vague and non-specific clinical manifestations [24], along with back and neck pain, tenderness, and paravertebral muscle spasm [25]. Pyogenic infections are associated with earlier symptom onset than TB which has more insidious and delayed-onset manifestations.

Radiologically, the three main signs of spinal infection are spinal cord compression, presence of abscesses with regular margins, and presence of bi-lobed epidural abscesses with distinct margins that remain localized under the anterior longitudinal ligament.

Spondylitis is the most frequently occurring and significant complication in brucellosis, with an incidence rate of 2% - 60% [26]. Lumbar vertebrae are the most frequently involved regions, followed by the thoracic and cervical segments [26]. Spinal brucellosis has two forms: focal and diffuse [27]. The abnormal signal intensity in the focal areas in the anterior aspects of an end plate of the vertebra, which is usually localized at the diskovertebral junction, is defined as the focal vertebral osteomyelitis. Diffuse abnormal signal intensity in the adjacent vertebrae and the intervening disk is defined as diffuse vertebral osteomyelitis. Suspicious MRI findings, such as early disc involvement, involvement of the superior endplate underlying the pathological disc, and the presence of epidural abscess call for extra attention by clinicians.

As demonstrated in our patients, back pain was a presenting symptom, the degree of which increased with movement and at night, and was followed by a sensation of stiffness that eventually led to limitations in the patients' activities. Additionally, tenderness was observed on palpation over the involved region, which is a common finding in spondylodiscitis.

The intravenous administration of antibiotics is the treatment of choice for the first two to four weeks, followed by oral antibiotic use [28]. The optimal duration is 6 weeks for parenteral therapy and 6 weeks for oral treatment. Treatment failure is associated with a shorter parenteral therapy duration [28]. However, any treatment discontinuation decision should be based on the clinical improvement of the patient and CRP and ESR normalization. In general, no firm guideline on the duration and choice of antibiotics has been established. The switch to oral antibiotics occurs if there is a decrease of 50% in the CRP and ESR values [29]. Antibiotics should be administered after microbiological samples such as blood culture and/or other bodily fluids with suspicions of infection are obtained. If the results are negative, then an empirical antibiotic therapy for the most commonly noted pathogens is initiated. In cases with suspicions of MRSA, vancomycin is the agent of choice, while in those with gram-negative bacteria, a second/third-generation cephalosporin is used [17]. At admission, the addition of low-molecular weight heparin for 2 - 4 weeks is recommended, as is mobilization, as tolerated, with a brace, corset, or lumbar support belt [17]. For TB-related spondylodiscitis, the usual first-line TB drug (isoniazid + rifampicin + ethambutol + pyrazinamide) must be used first, after which ethambutol and pyrazinamide should be discontinued after 2 months, provided the isolate is isoniazide- and rifampicin-susceptible for a total of 9 - 12 months. For *Brucella*-related spondylodiscitis, doxycycline and rifampicin can be used, both for 3 months, with a once-daily dose of gentamicin intravenously for the first 7 days or ciprofloxacin and rifampicin both for 3 months. Surgical treatment, in the form of spinal cord decompression and the drainage of epidural or paravertebral abscesses, should be considered when antibiotic treatment yields no improvement and disease progression is noted [28].

5. Conclusion

Accurate diagnosis is crucial in cases with spinal infection, especially in the early stages of the disease, as this may reduce the therapy duration and prevent irreversible spinal cord damage. However, as diagnosis is usually delayed in such settings, spondylodiscitis should be considered in the differential diagnosis of patients presenting with fever, root syndrome, and increased CRP and ESR values.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

M. tuberculosis	*Mycobacterium Tuberculosis*
E.coli ESBL	*Escherichia coli* Extended Spectrum Beta-Lactamases
S. aureus	*Staphylococcus aureus*