Original Article

Deformity Progression in Non-Tuberculous Spinal Infection

Pengsuwan G, MD[1], Chotivichit A, MD[1], Korwutthikulrangsri E, MD[1]

[1]Siriraj Spinal Unit, Department of Orthopaedic Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Spinal infection accounts for 2 to 7% of all musculoskeletal infections. Surgical treatment is normally indicated in concurrent neurological deficit that requires decompression, and in failure of medical treatment. Spinal deformity and instability are also potential indications for surgical treatment. Few studies have investigated the factors associated with deformity progression.

Objective: To investigate the incidence of and factors associated with the development of spinal deformity in non-tuberculous spinal infection.

Materials and Methods: A retrospective review of patients diagnosed with spinal infection by clinical and imaging study at Siriraj Hospital (Bangkok, Thailand) from January 2009 to December 2015 was conducted. The exclusion criteria were suspected or confirmed diagnosis of tuberculous infection, age under 18 years, no radiographic study available, and/or loss to follow-up before 6 months. Radiographic parameters at initial presentation and at follow-up were recorded. Cobb angles that changed more than 10 degrees, or vertebral height loss of more than 15% compared to the initial measurement were defined as deformity.

Results: There were 62 non-tuberculous spinal infections included in the present study composed of 30 females and 32 males with a mean age of 61.3 years (range 28 to 89). The most common site of infection was the lumbar spine (65.1%), followed by the thoracic spine (26.7%)then cervical spine (7.9%). Location of infection was a significant factor associated with deformity (p = 0.006) Causative pathogen was identified in 35 patients (56.5%). The most frequently observed organism was *S. aureus* (16.1%), followed by *E. coli* and *S. agalactiae* (both 9.7%). Spinal deformities were detected in 39 patients (62.9%). Surgical treatment was performed in 35 patients (56.5%).

Conclusion: In the present study, 62.9% of patients developed deformity, and most commonly in the lumbar spine. Location of the infection and number of the infected vertebrae are the significant factors associated with deformity progression.

Keywords: Spinal deformity, Spinal infection, Spondylodiscitis, Osteomyelitis, Bacteria, Non-tuberculous

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The spine is a susceptible site of infection in the body. The spine accounts for 2 to 7% of all musculoskeletal infections[1], and these infections are more common in older age. Infection can affect the intervertebral disc (discitis), vertebral body (spondylitis, vertebral osteomyelitis), both disc and bone (spondylodiscitis), and/or the epidural space (spinal epidural abscess). The common causative organisms are bacteria, mycobacterium, and parasite. Hematogenous spread, direct inoculation, and spread from adjacent infected vertebra are the typical sources of infection.

Non-surgical treatment with antimicrobial is the effective treatment in 89 to 94% of cases[2-4]. Surgical treatment is typically indicated in concurrent neurological deficit that requires decompression, and in failure of medical treatment[5,6]. Spinal deformity and instability are also potential indications for surgical treatment. Few studies have investigated the factors associated with deformity progression. Accordingly, the aim of the present study was to investigate the incidence of and factors associated with the development of spinal deformity in non-tuberculous spinal infection.

Correspondence to:

Korwutthikulrangsri E.

Clinical Lecturer of Orthopedic Surgery, Siriraj Spinal Unit, Department of Orthopaedic Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand.

Phone: +66-2-4197969, **Fax:** +66-2-4197967

E-mail: ekkapoj.kow@mahidol.ac.th

Materials and Methods

The authors performed a retrospective study of non-tuberculous spinal infection at Siriraj Hospital, Bangkok, Thailand. Medical records and radiographic studies of 62 patients that were diagnosed and treated during the January 2009 to December 2015 study period were reviewed. The inclusion criterion was diagnosis of spinal infection by clinical and imaging study. Patients were excluded if there was suspicion of or confirmed diagnosis of tuberculous infection, age under 18 years, no radiographic study available, and/or loss to follow-up before 6 months.

Outcome assessments

Demographic, clinical, and radiographic data were collected, recorded, and analyzed. Radiographic parameters at initial presentation and at follow-up were recorded using same position standard anteroposterior and lateral radiographs. Angulation of the spine was measured by Cobb method. The angle between the upper end plate of the vertebra

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cephalad to the infected vertebra, and the lower end plate of the vertebra caudal to the infected vertebra was measured. The difference in height between the infected vertebra and it's upper and lower normal vertebra were recorded. In radiographic evaluation, Cobb angle that changed more than 10 degrees or vertebral height loss of more than 15% compared to the initial measurement were defined as deformity[7-9].

Statistical analysis

All statistical analyses were performed using the Statistical Package for Social Sciences version 18.0 (SPSS, Inc., Chicago, IL, USA). The statistical significance level was defined as $p<0.05$. Descriptive statistics were used to summarize demographic data and clinical characteristics. Mean and standard deviation or median and range were used to describe continuous data, frequency and percentage was used to describe categorical data. Independent t-test was used to compare age between the deformity and non-deformity groups, and Chi-square test or Fisher's exact test was used to evaluate potential risk factors for spinal deformity.

Results

There were 62 non-tuberculous spinal infections included in the present study. There were 30 females and 32 males with a mean age of 61.3 years (range: 28 to 89). The diagnosis was spondylodiscitis in 44 patients (70.9%), followed by osteomyelitis in 11 patients (17.7%). Most patients have normal to overweight BMI (40.3% and 38.7%, respectively). Forty patients had underlying disease, including diabetes mellitus, hypertension, dyslipidemia, renal impairment, and hepatitis infection. There was no statistically significant difference for gender, age, BMI, or underlying disease between the deformity and non-deformity groups. The duration before admission was 6.7 weeks (range: 1 day to 24 weeks) (Table 1).

Location of infection is the factor that was significantly associated with deformity progression (p = 0.002). Most infections occurred at the lumbar spine (65.1%), followed by the thoracic spine (26.7%) and cervical spine (7.9%).

The number of infected vertebrae is another factor that associated with deformity progression (p = 0.006). One vertebra was infected in 12.9% of cases, two vertebrae were infected in 77.4% of cases. All patients with 1-level infected vertebra had deformity progression, while 62.5% of patients with 2-level involvement showed progression.

Causative organism was identified in 35 patients (56.5%). There were 19 patients with Gram-positive bacteria, 17 patients with Gram-negative bacteria, and 1 patient had mixed Gram-positive and Gram-negative bacteria isolation. The causative organism could not be identified in 23 patients and there was no specimen for culture in 2 patients. *Staphylococcus aureus* was the most commonly isolated organism (10 patients, 16.1%) (Figure 1), followed by *Escherichia coli* and *Streptococcus agalactiae* (group B) were the second most common organisms found in 6 patients (9.7%) each. There was no difference between the types of causative organisms in the deformity group (10 Gram-positive vs. 12 Gram-negative; p = 0.2).

Surgical treatment was performed in 35 patients (56.5%). In this group, spinal deformity was found in 21 patients (60%), and non-deformity was found in 14 patients (40%) (Figure 2). There was no statistically significant difference between patients who did and who did not undergo surgery, and there was no significant difference in deformity progression between the surgery and non-surgery groups (Table 2).

Discussion

Spinal infection is potentially devastating pathology. It can lead to severe back pain, deformities, neurological deficit, and even death. The incidence of spinal infection ranges from 0.2 to 2.4 per 100,000 per year, and its estimated mortality rate ranges from 2 to 4%[10-13]. Bacterial

Table 1. Demographic and clinical characteristics

Variable	Total	Deformities (n = 39)	Non-deformities (n = 23)	*p*-value
Gender, n (%)				
Female	30	17 (43.6)	13 (56.5)	0.325
Male	32	22 (56.4)	10 (43.5)	
Age (years)				
Median (range)		62 (28 to 89)	59 (32 to 75)	0.144
Mean ± standard deviation		63.08±12.81	58.35±10.95	
BMI categories, n (%)				
Underweight (<18.5 kg/m^2)	7	6 (16.7)	1 (5.0)	
Normal (18.5 to 22.9 kg/m^2)	25	17 (47.2)	8 (40.0)	0.270
Overweight (>23 kg/m^2)	24	13 (36.1)	11 (55.0)	
Underlying disease, n (%)				
Yes	40	28 (71.8)	12 (52.2)	0.170
No	22	11 (28.2)	11 (47.8)	
Diagnosis, n (%)				
Spondylodiscitis	44	26 (74.3)	18 (90.0)	0.357
Osteomyelitis	11	9 (25.7)	2 (10.0)	

infections are becoming more and more common. Hematogenous spread from the remote area of infection is the major route. Sepsis, intravenous infection, and pulmonary or urinary tract infection are the most common sources of bacteremia.

The majority of patients with bacterial spinal infection present with insidious onset of back or neck pain, and approximately 30% present with neurological deficit[14]. Other findings include constitutional symptoms, such as fever, weight loss, nausea/vomiting, anorexia, and lethargy. Bacterial lodge at the metaphysis area due to slow blood flow causes occlusion of blood supply to vertebra. This subsequently leads to avascular necrosis and bone infarct. Together with bacterial proteolytic enzymes that destroy the vertebral end plate and intervertebral disc, infection can spread to the intervertebral disc and/or adjacent vertebral body. This leads to spinal instability, deformity, and/or neurological compromise.

The present study found that 62.9% of patients

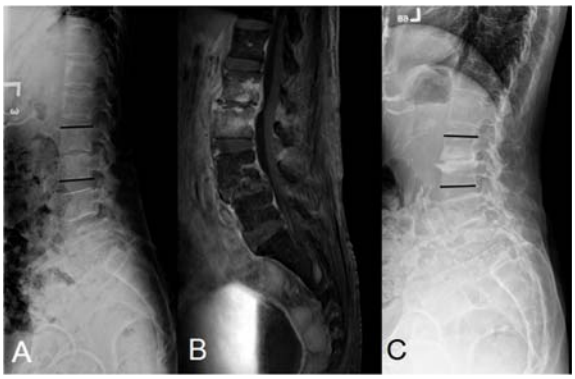

Figure 1. A 71-year-old women presented with severe back pain without neurological deficit for 2 weeks. Her initial film (A) shows segmental lordosis of 10 degrees at L2 to 3. MRI (B) shows osteomyelitis at L3 body with right psoas abscess. Her culture was positive for MSSA, and she was treated with IV antibiotics. At the 2-year follow-up, no spinal deformity was observed at this segment. Film (C) shows marginal osteophyte at L2 to 3 with autofusion, and L2-3 lordosis of 6 degrees.

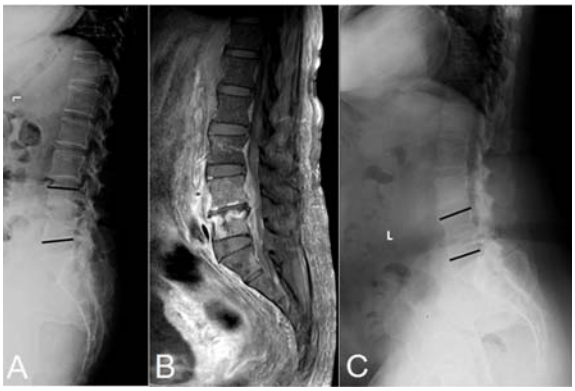

Figure 2. A 59-years-old female with underlying ESRD and cirrhosis presented with severe back pain with bilateral leg weakness for 2 weeks. Preoperative images (A and B) show spondylodiscitis at L4 to 5. Lordotic angle at L4 to 5 was 7 degrees. She underwent operative debridement without instrumentation. Tissue and blood culture were positive for *E. coli*. Her 6-year follow-up film (C) shows progressive deformity at lumbar spine, and progression of the L4-5 angle to 5 degree of kyphosis.

Table 2. Infection and surgical data compared between patients with and without deformities

Variables	Total	Deformities (n = 39)	Non-deformities (n = 23)	*p*-value
Location of the infection, n (%)				
Cervical	5	3 (7.5)	2 (8.7)	
Thoracic	17	5 (12.5)	12 (52.2)	0.002
Lumbar	41	32 (80.0)	9 (39.1)	
Number of infected vertebrae, n (%)				
1	8	8 (20.5)	0 (0.0)	
2	48	30 (76.9)	18 (78.3)	0.006
≥3	6	1 (2.6)	5 (21.7)	
Organism, n (%)				
Gram-positive	19	10 (25.0)	9 (47.4)	
Gram-negative	17	12 (30.0)	5 (26.3)	0.200
No growth	23	18 (45.0)	5 (26.3)	
Surgery, n (%)				
Yes	35	21 (53.8)	14 (60.9)	
No	27	18 (46.2)	9 (39.1)	0.609

with spinal infection developed spinal deformity. The site of infection is the factor that was significantly associated with progressive deformity. Our data showed that 32 out of 41 (77.5%) patients with spinal infection located in the lumbar spine had at least one deformity progression. A previously published study by Srinivasan, et al reported that 44% of patients developed at least 1 deformity, and the only variable significantly associated with deformity was the anatomical location of infection (bone, disc, epidural space). They also found the presence of epidural abscess to be associated with lower odds of deformity[13]. In present study, lumbar spine was the mainly affected region (66.1%), followed by thoracic spine (27.4%) and cervical spine (8.1%). This is consistent with the findings of Noh, et al[15] who reported 51.6% in the lumbar region, and 25.6% in the thoracic spine.

The most common organism identified in the present study was *S. aureus*, which is consistent with many previous reports. The incidence of *S. aureus* infection in the spine was reported to range from 20% to 84% among patients with non-tuberculous spinal infection[10]. Reported risk factors include age older than 50 years[16] and intravascular devices. Other organisms that we identified in the present study are *Escherichia coli* and *Streptococcus agalactiae*. Enterobacteriaceae accounts for 7-33% of infections, and most cases are *E. coli*[10]. Belzunegui, et al reported that *E. coli* was isolated in 20% of patients aged over 63 years, and in 0% of younger patients with vertebral osteomyelitis[17]. In the present study, *Streptococcus agalactiae* was isolated in 6 patients (9.7%), which is surprisingly high for this uncommon pathogen. This group B Streptococcus is the common cause of bacteremia and meningitis in neonates. There are few case reports of vertebral osteomyelitis in adults[18-21]. Garcia-Lechuz, et al reviewed 12 cases of vertebral osteomyelitis due to group B Streptococcus, and most patients had chronic underlying disease[22]. All of the cases in the present study had slow progressive vertebral osteomyelitis. There were 23 patients (37%) in whom the causative pathogen could not be identified. This is comparable to the previous reports in literature. Blood culture successfully identified the causative organism in 40 to 60% of cases, and culture from biopsy tissue was positive in 43 to 78% of cases[10,23]. Bhagat, et al reported that 26 out of 69 patients (37.7%) had negative culture on blood culture, CT-guided biopsy, or open biopsy[24]. Kasalak, et al conducted a systematic review of percutaneous biopsy in suspected spondylodiscitis and found positive culture in 10 to 52% from initial biopsy, and 60% in secondary culture[25]. The cause of culture negative can be explained by several reasons. Antibiotics given before the specimen was obtained[26], such as empiric antibiotics in patients with sepsis, may cause culture negative. In contrast, Marschall, et al reported pathogens were identified in 66% of cultures with no observed association with prebiopsy antibiotics[27]. Other causes of culture negative include variability in culture difficulty among organisms, confinement of organisms in a certain section of tissue that was not included in the biopsy specimen, and biopsy of inflamed tissue.

The present study has some mentionable limitations. First, the retrospective design of the present study rendered it vulnerable to incomplete or missing data. Second, the included cases were treated by different surgeons, which means that there could have been variability in technique. Third, all included data were derived from the database of a single center. Fourth, the relatively small size of our study population may have given the present study insufficient statistical power to identify all significant differences and associations. Fifth, there were no data available that the authors could use to evaluate quality of life after treatment. Sixth and last, measurements were performed by one physician, so there was no inter-intra observer reliability analysis performed.

Conclusion

Spinal infection can lead to various adverse consequences. Early recognition and treatment are important for improving outcome and preventing morbidities. Spinal deformity is a major cause of morbidity. In the present study, 62.9% of patients developed deformity, and more common in the lumbar spine. Location of the infection and number of the infected vertebrae are the significant factors associate with deformity progression. Further study in a much larger study population may reveal other significant factors. These findings will help to reduce the incidence of deformity and the onset of other morbidities, and both of these improvements will enhance outcomes and patient quality of life.

What is already known on this topic?

Spinal infection can lead to spinal deformity.

What this study adds?

The incidence of spinal deformity was as high as 62.9%, and location of infection and number of infected vertebrae were found to be significantly associated with deformity progression.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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