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Jacobs Journal of Medical Diagnosis and Medical Imaging

Research Article

# Monitoring Diagnosis and Treatment of Infectious Spondylodiscitis

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*Received:* 04-29-2015

*Accepted:* 06-06-2015

*Published:* 06-25-2015



## Abstract

The objective of this study was to describe the more consistent findings of pyogenic, brucellar, and tuberculous spondylodiscitis and to improve the early diagnosis and treatment strategies of infectious spondylodiscitis. The etiological distinction of 72 patients was made on the basis of clinical and routine laboratory evaluation, microbiological, histopathological and radiological grounds. The diagnosis of infectious spondylodiscitis was performed by imaging techniques. The patients were diagnosed as tuberculous (28%), brucellar (54%), and pyogenic (18%) spondylodiscitis. The mean age of the patients were 54.7±13.9 years, being 53% as female, and 47% as male. Fever (56.9%), back pain (95.8%), and clinical instability (27.7%) were the predominant symptoms. Erthrocyte sedimentation rate, C-reactive protein, and leukocyte counts were 61.6±31.5 mm/h, 7.2±7.5 mg/dL, and 9000±3906.7 / $mm^3$, respectively. The most common location of spondylodiscitis was the lumbar spine (50.0%), followed by lumbosacral (26.4%), and thoracic spine (15.3%). All the patients were treated for at least 12 weeks or longer up to 15 months. Surgery was performed for nine (12.5%) cases. After one-year follow-up of completion therapy, all cases were found to recover without functional sequelae. As presence of characteristic imaging features in the early diagnosis and management of infectious spondylodiscitis, isolation or demonstration of the etiological agent was also essential for monitoring infectious spondylodiscitis.

**Keywords:** Pyogenic; Tuberculous; Brucellar; Spondylodiscitis; Diagnosis; Treatment

## Introduction

There has been a considerable increase in patients of infectious spondylodiscitis, which accounts 2-4% of all osteomyelitis cases in the last decades [1,2]. Despite the advanced medical technology, the diagnosis of this disease and differentiating it from degenerative diseases, non-infective inflammatory lesions, and spinal neoplasms are difficult. The clinical features can be subtle and misleading and delays in diagnosis can lead to increased mortality (18-31%), morbidity, and neurological deficit [3].

Patients with vertebral osteomyelitis are usually referred to spinal surgery specialists. Although there is an increasing

move away from surgical intervention towards conservative therapy, percutaneous drainage of abscess may be indicated [3]. Due to the fact that the distinctive disease findings referring to the causative agent of infectious spondylodiscitis are not well defined, early diagnosis and treatment of spinal infections are difficult for surgeons and infectious disease specialists. The objective of this study was to highlight areas of uncertainty for the medical diagnosis and treatment strategies of pyogenic, brucellar, and tuberculous spondylitis and to describe the more consistent findings of the disease in an endemic setting.

## Materials and Methods

**Patients:** The study included 72 retrospectively followed adult vertebral osteomyelitis patients diagnosed by magnetic resonance imaging in the infectious disease clinic of a teaching and research hospital for five consecutive years. The patient data were collected with a patient observation form used to record the information about clinical, laboratory and radiological results, surgical interventions, therapy, and the clinical outcome. Patients with nosocomial vertebral infections were not included to the study protocol. Consultations from neurosurgery or orthopaedics departments were asked when necessary.

**Evaluation of clinical and laboratory aspects:** Past history, clinical findings, and routine laboratory records on microbiological, histopathological, and radiological grounds were evaluated. Laboratory tests observed for all cases were leukocyte count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Wright's test, plain vertebral roentgenograms, and magnetic resonance imaging (MRI) of the involved spinal vertebra region. Bacterial cultures from blood, body fluid, and/or tissue samples were obtained; and histopathology of the skeletal biopsy samples were examined when available. The patients suspected of tuberculous spondylodiscitis have examined by chest computerized-tomography (CT).

**Diagnosis:** The diagnoses of spontaneous spondylodiscitis were made on medical imaging (MRI). The etiology of spondylodiscitis was based on clinical history, radiological features, histopathological and microbiological grounds. At the time of a patient's admissions, CT-guided percutaneous needle biopsy or open biopsy on the preference of the spine surgeon was conducted for 26 cases in which the clinical and radiological diagnoses were uncertain. The patients with brucellar spondylodiscitis (BS) were diagnosed on positive clinical and laboratory findings (≥1/160 titers of brucella agglutination tests and/or positive blood cultures). The diagnoses of pyogenic and tuberculous (TB) spondylodiscitis were based on positive Gram or Ziehl-Neelson stained slides and/or bacterial growth of the organisms. Presence of caseation granulomatosis on histopathological examination confirmed TB spondylodiscitis (TS).

**Therapy and clinical outcome:**Treatment was directed towards the etiology documented by microbiological, histopathological, and radiological findings. Duration of medical treatment was determined according to the etiologic agent and the kind of medication chosen. The patients with pyogenic spondylodiscitis (PS) were treated with an appropriate antibiotic approximately 4-6 weeks through intravenous route, followed by the oral intake of the same antibiotic or antibiotics for 6-8 weeks or more. For the treatment of TS, isoniazid, rifampin, pyrazinamide, and streptomycin combination were preferred as long as there was no contraindication or side effects for these medications. The patients with TS were treated with standard doses of isoniazid, rifampin, pyrazinamide, and streptomycin (or ethambutol) for two months and then by isoniazid, rifampin, and pyrazinamide by an additional one month, followed by isoniazid and rifampin. The treatment duration was between 12 to 18 months. Brucellar spondylodiscitis was treated with streptomycin (1 g/daily) for 21 days, and doxycycline (100 mg twice daily) and rifampicin (600 mg once daily) for three to six months. In severe cases streptomycin was switched to ciprofloxacin at the 21th day of treatment.

Patients underwent surgery when there was significant and progressive neurological deficit with large soft tissue compression on the spinal cord and a destructive lesion disrupting the stability of the spinal bone by the evaluation of the spine surgeon. The kind of surgery implemented for the cases was not documented in the study.

All the patients were followed-up by clinical status, inflammatory biomarker responses, and signs of plain radiography or MRI improvements. Persistence of increased ESR and CRP levels or deteriorating clinical and radiological signs within the second month considered as treatment failure or lack of response.

**Statistical analysis:** For statistical analysis chi-square test has been used. $p>0.05$ was evaluated as significant.

## Results

The patients were diagnosed as tuberculous (28%), brucellar (54%), and pyogenic (18%) spondylodiscitis (PS). The mean age of the patients were 54.7±13.9 years, being 53% as female, and 47% as male (Table 1). Twenty-six patients were referred to neurosurgical or orthopaedics clinics while 46 were admitted to medical (3 internal medicine, 1 neurology, 1 physical therapy and rehabilitation, and 41 infectious diseases) clinics. Patients with TB spine infections had sequelae pulmonary lesions on chest radiograms or CT's (9 cases), one suffered from active pulmonary tuberculous disease, and three patients had family TB history. Among spondylitis cases cardio-vascular system disease complications (24 patients) were the predominant underlying diseases, followed by diabetes mellitus (12

cases), immunosuppression (3 cases), chronic renal failure (3 patients), and chronic obstructive pulmonary disease (2 cases).

**Table 1.** Demographic features of the patients with spondylodiscitis (%).

| | **Pyogenic** n=13 (18) | **Tuberculous** n=20 (28) | **Brucellar** n=39 (54) |
|---|---|---|---|
| **Age** | 55.30 ±12.53 | 54.40 ±17.31 | 54.74 ± 12.73 |
| **Gender** (female) | 8 (62) | 10 (50) | 20 (51) |
| **Admission** | | | |
| Surgical wards | 6 | 10 | 10 |
| Medical wards | 7 | 10 | 29 |
| **Time from onset of symptoms** | | | |
| 1 weak-1 month | 4 (30.8) | 2 (10.0) | 5 (12.8) |
| 1-4 months | 5 (38.4) | 6 (30.0) | 16 (41.0) |
| >4 months | 4 (30.8) | 12 (60.0) | 18 (46.2) |
| **Past history** | | | |
| Tuberculous* | 1 (7.7) | 13 (65.0) | 0 |
| **Underlying disease** | 10 | 16 | 18 |

*Sequelae TB lesion on chest radiogram or CT, family histoy related to TB, or active pulmonary

Fever (56.9%), back pain (95.8%), and clinical instability (27.7%) were the predominant symptoms (Table 2). The most frequent neurological findings were paraparesis (8 patients), followed by paraplegia (3 patients), and tetraparesis (2 patients) at presentation. The most common location for spondylodiscitis was the lumbar spine (50.0%), followed by lumbosacral (26.4%), and thoracic spine (15.3%).

Erythrocyte sedimentation rate (ESR), C-reactive protein (CPP), and leukocyte counts were 61.6±31.5 mm/h, 7.2±7.5 mg/dL, and 9000±3906.7 / $mm^3$, respectively at presentation. In 59 (81.9%) patients the diagnosis were confirmed on microbiological and/or histopathological basis. One patient with a negative Wright test gave positive signal for brucella growth on blood culture system (Table 3).

All the patients showed normal ESR and CRP levels within 2 to 3 months of therapy. All the patients were treated for at least 12 weeks (up to 15 months). Surgery was performed in nine cases (12.5%). One-year after the completion of therapy, all cases were found to recover without functional sequelae.

**Table 2.** Predominant clinical features and surgical implementations of the patients with spine infections (%).

| | **Pyogenic** n=13 (18) | **Tuberculous** n=20 (28) | **Brucellar** n=39 (54) |
|---|---|---|---|
| **Symptoms** | | | |
| Malasia and weakness | 7 (53.9) | 9 (45) | 17 (43.6) |
| Back pain | 13 (100) | 18 (90) | 38 (97.4) |
| Clinical instability | 7 (53.9) | 10 (50) | 3 (7.7) |
| **Physical findings** | | | |
| Fever | 5 (38.4) | 12 (60) | 20 (51.3) |
| Neurologic finding | 2 (15.4) | 9 (45) | 2 (5.1) |
| **Vertebral level involved** | | | |
| Thoraco-lumbar | 1 (7.7) | 5 (25) | 3 (7.7) |
| Thoracic | 2 (15.4) | 8 (40) | 1 (2.6) |
| Lumbar | 8 (61.5) | 4 (20) | 24 (61.5) |
| Lumbo-sacral | 2 (15.4) | 1 (5) | 10 (25.6) |
| Cervical | 0 | 1 (5) | 0 |
| Cervico-thoracic | 0 | 1 (5) | 1 (2.6) |
| Thoraco-lumbo-sacral | 0 | 1 (5) | 0 |
| **Surgical interventions** | | | |
| Needle/Open Biopsy | 9/2 | 5/7 | 2/1 |
| Surgery | 1 | 5 | 3 |

The observation of the chest computerized-tomography (CT) of eight patients with TS showed sequelae lesions related to TB infection. Two patients were diagnosed as miliary tuberculosis and one as TB pleurosy. One patient was diagnosed as TB meningitis and spondylodiscitis clinically and by laboratory documentation of the cerebrospinal fluid (CSF). Two patients with spine infection which were not microbiolocically or histologically proven, were diagnosed as miliary tuberculosis, as well.

The statistical analysis was most significant in tuberculous infection of the vertebra, the thoracic region was most frequently involved (p>0.05)

**Table 3.** Laboratory findings of the patients with spondylodiscitis (%).

| Parameters | Pyogenic n=13 (18) | Tuberculous n=20 (28) | Brucellar n=39 (54) |
|---|---|---|---|
| ESR mm/h | 66.76 ± 36.86 | 75.95 ± 29.08 | 52.43 ± 28.24 |
| CRP mg/dL | 6.46 ± 8.22 | 6.62 ± 5.30 | 7.78 ± 8.30 |
| Leucocyte/mm$^3$ | 9446.15±6444.84 | 10795±4071.14 | 7930.76±2043.36 |
| Wright test | Negative | Negative | 38 Positive (97.4) 1/354.73±1/362.24 |
| Blood culture positivity | 0 | 0 | 10 (25.6) |
| Non-spesific biopsy culture positivity | 9 (69.2) (6/9 *S. aureus)* | 0 (0 of 7) | 0 |
| TB-spesific biopsy culture positivity | 0 | 7 (35)* | 0 |
| TB-specific surgical material culture positivity | 0 | 4 (20) | 0 |
| Brucella-specific surgical material culture positivity | 0 | 0 | 2 (5.1) |
| Histopathologic examination | 3/3 non-specific infection | 5/7 TB-specific infection | 2/2 non-specific infection |
| Spondylodiscitis | 13 | 20 | 39 |
| Soft tissue involvement | 10 (76.9) | 16 (65) | 32 (82) |
| Abscess | | | |
| Paravertebral | 2 (15.4) | 6 (30) | 9 (23.1) |
| Epidural | 1 (7.7) | 1 (5) | 6 (15.4) |
| Both | 2 (15.4) | 0 | 0 |
| Psoas abscess | 2 (15.4) | 5 (25) | 2 (5.1) |

*One TB specific culture positivity was from CSF sample

## Discussion

Magnetic resonance imaging was the unique technique in the diagnosis of all cases in the study. This imaging tool was regarded as the most sensitive (91-96%) and specific (92.5-97%) modality for early detection of vertebral osteomyelitis [4,5]. In more than 50% of cases the typical features of spondylodiscitis were apparent on MRI in the first two weeks [5]. In our study all cases were diagnosed as infectious spondylodiscitis by MRI within 1-week and >4 months depending upon admission to the wards (Table 1). Computerized tomography yielded positive findings in the early stages and could also be used to guide disc biopsy or drainage of a paravertebral collection[5].

In the present study most of the patients (87.5%) responded to non-operative treatment, with resolution of pain and spontaneous fusion within one year whereas half to three-quarters of all patients responded to non-operative treatment [5]. A significantly higher rate of TS patients underwent surgery in both the present and previous study [2]. In present study patients with TS suffered from additional extrapulmonary TB such as four cases of miliary tuberculosis and among them one with concurrent TB pleurosy, and one patient with TB meningitidis. Therefore, the follow-up of the disease course of these patients required careful evaluation and multidisciplinary approach.

Brucellar (54%) and tuberculous (28%) spondylodiscitis were more common than pyogenic (18%) spondylodiscitis in Turkey where the diseases were endemic. In Portugal, like other Mediterranean countries brusellosis and tuberculosis were frequently diagnosed in one study with 140 patients over a 24-year period [6]. Pyogenic bacteria accounted for most of the cases where brusellosis and tuberculosis were not endemic [7,8]. Tuberculous of spine accounted for 1-2% of all TB infections and 25-60 of all bone and joint infections caused by TB [3,4]. Spondylitis was among the most frequent and serious complications of brucellosis [9,10]. Spinal involvement in brucellosis ranged from 2 to 30% in reported studies [3].

Gender distribution was not statistically meaningful in the present study. In previous presentations males were affected more frequently than women with the ratios of 1.5-3.1 [3,5]. This finding might be attributed to the fact that pyogenic bacteria were not the etiologic cause of many cases. In general, pyogenic spondylitis was preceded by infection elsewhere, most commonly the genitourinary tract [1,3,5]. Tuberculous infection generally affected adults in fourth and fifth decades while the peak incidence of pyogenic spondylitis was seen in the sixth and the seventh decades [3]. The mean age distribution was somewhat similar in some of previous studies as well as in the present study [11].

Regardless of the causative agent, the most frequent clinical finding [2] was spinal pain (97.3%), followed by such consti-

tutional symptoms as lack of appetite, weakness, nocturnal sweating (74.6%), and fever (72%). In the present study, fever was the dominant symptom in patients with TS and BS (Table 2). In a previous study 33/75 patients were presented with neurological symptoms. Neurological involvement, which was one of the most important symptoms of spinal tuberculosis, was reported in previous [2] and present studies as 23-76% and 45%, respectively. It was stated that it resulted from a compression on spinal cord, nerve roots, and cauda equina. In addition, spinal deformities due to caseous granulomas in TS patients might lead to neurological symptoms and neurological deficits [2,12].

Erythrocyte sedimentation rate was significantly higher in patients with TS in present and also in a previous study [2] from Turkey. Leukocyte count and ESR were relatively lower in brucellar spondylitis than in tuberculous or pyogenic spondylitis. Leukocytosis was, however, suggestive of pyogenic spondylitis rather than tuberculous or brucellar spondylitis [13]. No significant difference relating to white blood cell count among bacterial agents of spondylodiscitis was reported in present study.

There were involvements in the lumbar, thoracic, cervical, and sacral vertebras. In tuberculous infection of the vertebra, the thoracic region was most frequently involved while infection of the lumbar region was more commonly affected in brucellar and pyogenic spondylodiscitis [3,8,10,13-16]. This finding was significant in the present study. Detecting by imaging technologies, psoas, paravertebral and epidural abscess were serious complications. Psoas abscess was observed more commonly in cases with TS [2], and in concurrence with the present study (25%). Soft tissue involvement was seen more frequently in patients with BS (82%) and epidural abscess was also more common among BS patients. Paravertebral abscess formation was observed in cases with PS and TS (Table 3). In one previous article it has been underlined that paraspinal abscess may occur up to approximately 50% of TB of the spine whereas the frequency of paraspinal abscess complicating brucellosis has been reported in approximately 12% [3].

Conservative management generally started intravenously followed by oral antibiotics. If the organism remained undetermined then broad-spectrum antibiotics with anti-staphylococcal coverage were recommended [5]. Grados et al. [17] reported that in uncontrolled studies, treatment for 4 to 8 weeks was associated with markedly increased recurrence rates compared to those treated for 12 week or longer. If the ESR and CRP showed a 50% reduction and there was no pain from instability or neurologic deficits, then a switch from intravenous to oral therapy was appropriate. An earlier switch to oral treatment had been advocated only if the CRP was normal even after two weeks [17]. Patients should be followed up throughout treatment and for 1 year after its completion in order to detect relapses. During therapy, patients should be monitored by CRP and ESR levels, and should be examined by using plain radiographs at 1 and 3 months into antimicrobial therapy, then 3 months after cessation of therapy. Reduction in back pain and recovery of constitutional symptoms suggested successful treatment. Magnetic resonance imaging was of limited value in assessing recovery. Imaging findings might actually worsen while patient was improving clinically. Magnetic resonance imaging was useful for initial assessment of spontaneous infectious spondylodiscitis. Persistent or increased gadolinium enhancement seen in the context of clinical improvement did not necessarily represent deterioration or treatment failure. Some degree of contrast enhancement might be present for many months [10,12,18]. In one study in patients with spine infections, it was documented that soft tissue findings, not skeletal findings, should be the focus of clinicians interpreting follow-up MR imaging results [19].

Surgery might be indicated for the following reasons: resolution of significant spinal cord or radicular compression, prevention or correction of biochemical instability and deformity, management of severe persistent pain, drainage of abscess [10,20,21]. Surgical therapy also reserved for patients who failed to respond clinically to antibiotic therapy alone [21,22]. Some authors also recommended an open biopsy to identify pathogen if percutaneous biopsy was negative. Epidural abscesses were generally managed by surgical or percutaneous drainage, particularly in the cervical and thoracic spine where the canal was narrow and neurological dysfunction may progress rapidly [5]. Hadjipavlou et al [1] found that patients treated conservatively reported residual back pain more often than those treated surgically (64% versus 26.3%). However in contrast to the previous study, in the present study surgery was performed in nine cases and only one patient suffered from back pain who was medically treated. In our series after one-year of follow-up completion therapy, all cases were found to recover without functional sequelae. Delay in diagnosis or management was detrimental to outcome [5].

Streptomycin for 14 days and doxycycline plus rifampin for four months was a better regimen for therapy of brucellar spondylitis. They had no relapse with this regimen [23,24]. Some recommended the use of a combination of doxycycline and ciprofloxacin for a period of 3 months [25].

Isoniazid, rifampin, pyrazinamide, and streptomycin combination was the preferred medications for the treatment of TB spondylodiscitis. The four-drug regimen (with ethambutol instead of streptomycin) was given as a first-line treatment for four months followed by isoniazid, rifampicin and ethambutol for an additional at least eight months in one of previous studies with lumbar or lumbosacral tuberculous spondylodiscitis [21].

## Conclusion

Radiological imaging evaluations have gained importance in the diagnosis and treatment monitoring of all the spinal infections. As presence of characteristic imaging features, isolation or demonstration of the etiological agent is also essential for monitoring infectious spondylodiscitis. Infectious pathology must be considered in a patient presenting with back pain and fever. Prognosis of spondylodiscitis is strongly associated with early diagnosis and specific medical treatment which has been directed towards the etiology and the follow-up of the disease course requires a multidisciplinary approach.

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