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Research Article

Clinical and radiological features of pyogenic and brucellar spondylodiscitis

Spondilodiskit Etkenlerinin Klinik ve Radyolojik Özellikleri

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Abstract

Aim: Since spondylodiscitis continues to be seen with increasing incidence; thus, starting antibiotherapy targeted towards the etiological agent is crucial for reducing complications and mortality. This study aimed to determine the clinical and radiological characteristics of spondylodiscitis' causative microorganisms.

Material and Methods: Patients hospitalized in the Department of Infectious Diseases and Clinical Microbiology with a diagnosis of spondylodiscitis between 2015 and 2023 were retrospectively evaluated.

Results: Low back pain was present in 97.5% of the total 40 patients as the most common symptom. Tissue biopsy culture results were obtained for 21 (52.5%) patients, with culture positivity observed in five (12.5%) patients. Consumption of raw milk/dairy products in the anamnesis and fever were found to be statistically significantly higher in patients with brucellosis ($p < 0.001$, $p = 0.015$), whereas neurological deficits were significantly higher in the pyogenic group ($p = 0.007$). No significant differences were observed between the pyogenic and brucella spondylodiscitis groups in terms of laboratory parameters (sedimentation rate, C-reactive protein, white blood cell count) and magnetic resonance imaging findings.

Conclusion: Since no distinctive clinical and radiological parameters were identified for distinguishing between brucellar and pyogenic spondylodiscitis, serological tests for brucellosis should be investigated when considering the diagnosis, particularly in endemic regions. In cases of pyogenic spondylodiscitis, empirical antibiotic use prior to pathogen isolation may lead to delays in diagnosis and appropriate treatment, potentially resulting in complications such as neurological deficits. Therefore, interventional methods for tissue biopsy culture should be planned before antibiotherapy, especially in patients who do not immediately require antibiotherapy.

Keywords: spondylodiscitis, pyogenic, brucellosis

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Öz

Amaç: Spondilodiskitlerin görülme sıklığı giderek artmaya devam ettiğinden etkene yönelik antibiyo terapiye başlanması komplikasyonları ve mortaliteyi azaltmak açısından önemlidir. Bu çalışmada spondilodiskit etkeni mikroorganizmaların klinik ve radyolojik özelliklerinin belirlenmesi amaçlandı.

Gereç ve Yöntemler: Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği'nde 2015-2023 yılları arasında spondilodiskit tanısıyla yatırılan hastalar retrospektif olarak değerlendirildi.

Bulgular: Toplam 40 hastanın %97,5'inde en sık semptom olarak bel ağrısı vardı. Hastaların 21'inde (%52,5) doku biyopsi kültür sonucu elde edildi, beşinde (%12,5) kültür pozitifliği görüldü. Anamnezde çiğ süt/süt ürünleri tüketimi ve ateş, brusellozlu hastalarda istatistiksel olarak anlamlı derecede yüksek bulundu ($p<0,001$, $p=0,015$), nörolojik defisitler ise piyojenik grupta anlamlı olarak daha yüksekti ($p=0,007$). Brusella ve piyojenik spondilodiskit için ayırt edici klinik ve radyolojik parametre saptanmadı.

Sonuç: Spondilodiskit tanılı hastalarda özellikle endemik bölgelerde bruselloz için serolojik testler istenmelidir. Patojen izolasyonundan önce ampirik antibiyotik kullanımı, tanıda ve uygun tedavide gecikmelere neden olabilir ve nörolojik defisitler gibi komplikasyonlara yol açabilir.

Anahtar Kelimeler: spondilodiskit, bruselloz, pyojenik

Introduction

Spondylodiscitis is an infectious disease that affects the vertebral body, intervertebral disk and paraspinal tissues, and its symptoms are often nonspecific, leading to delayed diagnosis [1]. Spondylodiscitis may arise due to pyogenic (bacterial), parasitic, tuberculosis, brucellosis or fungal infection [2]. The most common finding is pain localized to the infected vertebra and disc area, which increases with physical activity or percussion. The pain typically has an insidious onset and progresses over several weeks to months [3].

The management of spondylodiscitis is achievable through antimicrobial therapy and if necessary, surgical debridement or percutaneous abscess drainage. Tracking patients' treatment response can be challenging and complex. Follow-up should involve monitoring laboratory parameters such as sedimentation rate, C-reactive protein(CRP) and other acute-phase reactants, along with clinical findings and symptoms; radiological follow-up is recommended in patients with therapy failure [4]. However, clinical and laboratory responses may not always be very rapid [5]. In this study, the characteristics of spondylodiscitis cases with different etiologies followed in our clinic were examined, aiming to demonstrate clinical, laboratory and radiological changes in diagnosis and follow-up.

In the study, demographics, clinical and laboratory findings, localization of infection and treatment responses of the patients who were followed up with the diagnosis of spondylodiscitis in the Infectious Diseases and Clinical Microbiology Clinic between 2015 and 2023 were evaluated retrospectively. The diagnosis of spondylodiscitis was made based on clinical presentation, laboratory parameters (acute phase reactants) and magnetic resonance (MR) imaging. Patients with a serum brucella tube agglutination titer of ≥1:160 or positive Brucella spp. growth in blood or tissue biopsy cultures were included in the brucella spondylodiscitis group. Tuberculous spondylodiscitis was diagnosed by Ziehl–Neelsen (EZN) staining, Mycobacterium tuberculosis culture or polymerase chain reaction(PCR) positivity in the tissue biopsy sample, histopathological detection of granulomatous caseation necrosis and response to empirical tuberculosis treatment in cases who had no clinical and laboratory improvement despite receiving at least two weeks of non-specific antibiotherapy. White blood cell count (WBC), sedimentation, CRP and MR imaging of the patients were evaluated at the 1st month, 3rd and 6th months. Patients whose radiological imaging report was compatible with spondylodiscitis were included in the study group. Patients with increased contrast enhancement in the vertebrae, discs, paravertebral and intervertebral areas on MRI images and reported to be compatible with spondylodiscitis were included. Because of the limited number of tuberculous spondylodiscitis cases, the patients were divided into two groups: Brucella and pyogenic (bacterial).

The compatibility of numerical variables to normal distribution was examined using analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Descriptive analyses were summarized using frequency tables for categorical and

ordinal variables, and mean±standard deviation for the age variable. Pearson Chi-Square or Fisher's Exact test was used to compare categorical variables and Mann Whitney U test was used to compare numerical variables. Statistical evaluation was made using the SPSS (20.0.Armonk, NY) software. $P < 0.05$ was considered statistically significant.

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from Ankara Training and Education Hospital Clinical Research Ethics Committee (Permission Date 12.07.2023, Permission number E-23-1307).

Results

Of the 40 patients included in the study, 27 (67.5%) were female, and the mean age of the participants was 61.8 ± 14.4 years (minimum: 22, maximum: 91). Hypertension was the most common comorbidity among the patients, present in 40% of cases. Only two patients had immunosuppression. Almost all cases (n:39) had lower back pain at admission. Only one patient had an individual or family history of tuberculosis. Data regarding the patients' comorbid diseases, medical history and presenting symptoms are described in Table 1.

Table 1. Demographics and baseline clinical characteristics of patients

	n (%)
Diabetes Mellitus	13 (32,5)
Chronic Renal Failure	7 (17,5)
Hypertension	16 (40,0)
Coronary Artery Disease/Congestive Heart Failure	6 (15,0)
Immunosuppression	2 (5,0)
Individual or family history of tuberculosis	1 (2,5)
Consumption of raw milk/dairy products	9 (22,5)
Fever	10 (25,0)
Back pain	39 (97,5)

Eleven patients had brucellar spondylodiscitis, five patients received antituberculous treatment and 24 patients were given non-specific antibiotherapy with a presumptive diagnosis of pyogenic spondylodiscitis. Surgical procedures such as laminectomy, discectomy, corpectomy and abscess drainage were performed on 13 patients (32.5%). A total of 23 patients underwent tissue sampling. Five patients underwent percutaneous abscess sampling, while biopsy sampling guided by Computed tomography (CT) was performed on the remaining five patients. Among the five patients diagnosed with tuberculosis, all showed caseous granulomatous inflammation on histopathological examination, with only one patient testing positive for Tuberculin skin test (TST) and three patients testing positive for interferon-gamma-release-assay (IGRA). None of the patients tissue biopsy EZN staining were positive and Mycobacterium tuberculosis PCR positivity were detected in three of five patients. Serum tube agglutination was above 1/160 in all patients followed with a diagnosis of Brucella spondylodiscitis. Culture results of two patients from whom samples were taken could not be obtained. Characteristics of sampling locations and pathogens, along with administered treatments, are provided in Table 2.

Table 2. Sampling locations and characteristics of pathogens

	n (%)
Procedure for sampling	23 (57,5)
Percutan abscess drainage	5 (12,5)
CT guided biopsy	5 (12,5)
İntraoperative tissue sampling	13 (32,5)
Isolates	
Isolates	19 (47,5)
Without invasive sampling/culture results	16 (40,0)
No bacterial growth	5 (12,5)
Enterobacter cloacae	1 (2,5)
Brucella spp.	1 (2,5)
Klebsiella pneumoniae	1 (2,5)
M.tuberculosis compleks	2 (5,0)
Histopathological examination	
With a result	14 (35,0)
Chronic inflammation, osteomyelitis	9 (22,5)
Caseous granulomatous inflammation	5 12,5)
Treatment	
Non-specific antibiotherapy	24 (60,0)
Antituberculous treatment	5 (12,5)
Treatment of brucellosis	11 (27,5)
TST 17(42,5)	
Negative	13 (32,5)
7mm	1 (2,5)
10mm	1 (2,5)
12mm	1 (2,5)
20mm	1 (2,5)
IGRA	11 (27,5)
Negative	8 (20,0)
Pozitive	3 (7,5)
Brusella tube agglutination	
Negative	29 (72,5)
Pozitive	11 (27,5)

CT: Computed tomography IGRA: İnterferon-gamma-release-assay
TST: Tuberculin skin test

It was found that neurological deficits were statistically significantly higher in the pyogenic group ($p = 0.007$) by comparing causative agents. The existence of fever as

a presenting symptom and a history of consuming raw dairy products were significantly higher in the Brucella spondylodiscitis cases ($p < 0.001$). Lumbar vertebra involvement was the most common (n: 30), but there was no significant difference between the groups regarding the location of infected areas. Although there was a higher incidence of recent surgical and vertebral operations in the pyogenic group, this difference was not statistically significant ($p = 0.157$, $p = 0.217$). The comparison of patients' clinical findings and vertebral involvement locations is presented in Table 3.

Table 3. Comparison of vertebral involvement, clinical features and treatment durations in Brucella and pyogenic groups[1]

	Spondylodiscitis etiology		
	Brucella (n=11)	Pyogenic (n=24)	
Age Mean±SS Median (Min.-Maks.)	 55±17 56 (34-90)	 64±13 66 (22-91)	0,025[2]
Gender, Female	5 (45,5)	17 (70,8)	0,258
Diyebetes Mellitus	3 (27,3)	9 (37,5)	0,709
Chronic Renal Failure	-	7 (29,2)	0,072
Hypertension	2 (18,2)	12 (50,0)	0,137
CAD/CHF	1 (9,1)	5 (20,8)	0,640
Immunosuppression	-	2 (8,3)	1,000
Surgical procedure within the last year	-	5 (20,8)	0,157
History of vertebral operation	1 (9,1)	8 (33,3)	0,217
Neurological deficit	-	11 (45,8)	0,007
Consumption of raw dairy products	8 (72,7)	-	<0,001
Thoracal involvement	2 (18,2)	1 (4,2)	0,227
Lumbar involvement	9 (81,8)	20 (83,3)	1,000
Thoracolomber involvement	1 (9,1)	3 (12,5)	1,000
Sacral involvement	-	6 (25,0)	0,146
Paravertebral abscess	6 (54,5)	11 (45,8)	0,632
Psoas abscess	1 (9,1)	8 (33,3)	0,217
Anterior vertebra	10 (90,9)	21 (87,5)	1,000
Posterior vertebra	4 (36,4)	18(75,0)	0,057
Discitis	9 (81,8)	24 (100,0)	0,092
Vertebra corpus involvement	9 (81,8)	22 (91,7)	0,575
Fever	6 (54,5)	3 (12,5)	0,015
Back pain	11 (100,0)	24 (100,0)	-
Duration of antibiotherapy Mean±SS Median(Min.-Maks.)	 95±61 80 (39-180)	 68±56 42 (4-235)	0,260[2]

[1]Column percentage used.
[2]Mann Whitney U test was used
CAD/CHF:Coronary Artery Disease/Congestive Heart Failure

Laboratory and radiological findings of the patients were evaluated at the beginning of treatment, at the 1st, 3rd and 6th months, and no significant difference was detected in terms of CRP, sedimentation and radiological imaging responses between the brucellar and pyogen groups.

Discussion

Clinical, radiological, and microbiological data need to be evaluated together for diagnosis of spondylodiscitis. In order to prevent complications such as neurological deficits and mortality, early diagnosis is crucial, and antimicrobial therapy targeted to the causative agent should be planned as soon as possible [4]. During follow-up, laboratory parameters and radiological imaging may take longer to normalize, which may not provide sufficient data to detect treatment failure [6,7]. In this study, the characteristics of spondylodiscitis patients with different etiologies and the clinical, laboratory and radiological parameters used in follow-up were evaluated.

Despite the advances in diagnostic tests and radiological imaging, the diagnosis of spondylodiscitis can be delayed due to non-specific symptoms. Back pain, the most common complaint in patients, is a prevalent symptom that can be associated with a variety of clinical conditions [8]. Fever accompanies back pain in approximately 60-70% of cases, as reported in numerous studies [9,10]. In our study, the most common symptom was back pain (97.5%), with fever detected in 25% of patients.

CT-guided vertebra/disc biopsy or intraoperative tissue sample culture is recommended before empirical treatment to determine the etiology of vertebral osteomyelitis. Particularly in patients without signs of sepsis or acute neurological deficits, obtaining tissue culture before starting antibiotherapy is important for targeted therapy [4]. In our study, sampling was performed on 23 patients (57.5%) and tissue culture results could not be obtained for two patients. Only five patients had positive microbial growth. Culture positivity rates have been reported to vary between 20% and 93% in the literature [10,11]. The low isolation rate in our study may be related to the patients' use of empirical antibiotics before sampling especially in the pyogenic group.

Histopathological examination of the tissue sample strongly supports the diagnosis of tuberculous spondylodiscitis. Romdhane et al. reported that 69.1% of tuberculous spondylodiscitis patients with a negative EZN staining and culture were diagnosed by histopathology [12]. In our study, only one of the five tuberculosis patients was found to have

TST >15 mm and three of them had a positive IGRA test. M.tuberculosis complex was isolated from tissue culture of only two patients, PCR found to be positive in three of them and histopathology showed caseating granulomatous inflammation in all patients. In one study all patients had positive PCR results from biopsy specimens(13). Use of molecular diagnostics has a significant role to reach a confirmatory diagnosis for tuberculosis.

Although pyogenic pathogens such as Staphylococcus aureus and streptococci are most commonly reported microorganisms, brucella and tuberculosis as the etiology of spondylodiscitis still hold significance, especially in endemic regions. Numerous studies demonstrate that brucellosis, tuberculosis, and pyogenic pathogens have distinct clinical, laboratory and radiological features [11,14,15]. Consumption of raw milk/dairy products is a significant route of transmission for brucella infection. Consistent with the report of Gök et al., we found a significantly higher consumption of fresh cheese/milk in the brucella group, as expected. Therefore, querying this risk factor in the history of patients with a preliminary diagnosis is important. Unlike the results of Gök et al., fever was significantly higher in brucellar spondylodiscitis in our study. There are also studies reporting that fever is higher in cases of brucella spondylodiscitis [15,16]. This may be related to the antibiotic use prior to admission among the patients in the pyogenic group.

Due to the low number of tuberculosis cases in our study, the pyogenic and brucella groups were compared. Kaya et al. reported significantly higher neurological deficit rate in the pyogenic group, while the presence of paraspinal abscess and thoracolumbar involvement was significantly higher in patients with tuberculosis spondylodiscitis [14]. Similar to Kaya et al., the neurological deficit rate was found to be high in the pyogenic group, but no significant difference was observed between the two groups in terms of involvement regions and the presence of paravertebral abscess.

The lower rate of neurological deficit in the brucella group may be due to the endemic nature of brucellosis in our country, leading to the rapid investigation of serological tests for brucellosis and early initiation of treatment in patients presenting with back pain. Another reason for the poor prognosis in pyogenic infections may be the low rate of pathogen isolation, inappropriate empirical treatment and delayed initiation of targeted treatment. In contrast to Kaya and Gök et al., the lumbar region was more frequently affected in patients without any difference between both groups.

The history of previous vertebral surgery was more common in the pyogenic group, although it was not statistically significant. The higher rates of previous vertebra surgery in pyogenic cases would have been expected to be statistically significant according to the literature [15]. However, this situation was thought to be related to the small number of cases.

The mean WBC, sedimentation and CRP values have been reported to be significantly higher especially in cases of pyogenic spondylodiscitis than in other groups in the literature [10,13,15,17]. Differently, Turunç et al. reported higher levels of acute phase reactants in tuberculous spondylodiscitis [16]. Among laboratory parameters, there were no significant differences in terms of white blood cell count, CRP and sedimentation on admission, at the first, third and sixth months between the two groups. Consistent with our study, it has also been reported that laboratory parameters are not sufficient to distinguish between brucellosis and pyogenic spondylodiscitis, and that there are differences in the detailed radiological evaluation of MR imaging [18]. However, the lower WBC, CRP and sedimentation levels in the pyogenic group may be due to the previous use of anbiotics.

While monitoring the treatment response, the presence of therapy failure or clinical progression symptoms (ongoing fever and back pain, appearance of paraspinal abscess or neurological deficit) and weekly sedimentation and CRP values should be evaluated [4]. With successful treatment, an irregular and slow decrease in the sedimentation rate is expected [19]. CRP decline can typically occur more rapidly. Although a lack of more than 50% decrease in sedimentation within the first month has been associated with treatment failure, it has also been shown that sedimentation response may be slow, especially in the first two weeks. None of our patients had treatment failure and the decrease of sedimentation was observed within months in the pyogenic group (Table 4).

Control radiological imaging is recommended in the presence of clinical and laboratory progression or therapy failure [4]. Especially in the early post-treatment period, MR findings can be stable or progressive [20,21]. In our study, despite achieving clinical and laboratory response in all patients, progression in MR findings was observed in six patients at the 1st month of treatment and in one patient at the 3rd month of treatment among those with pyogenic spondylodiscitis. There was no progression in radiological imaging of any patient at 6 months and no significant change was observed in both groups.

Table 4. Comparison of Laboratory and Radiological Findings in Patients with Brucella and Pyogenic Groups

	Spondylodiscitis etiology		p[1]
	Brucella (n=11)	Pyogenic (n=24)	
WBC Mean±SS Median(Min.-Maks.)	 8.013±2.541 7.980 (4.600-12.530)	 9.187±4.608 8.135 (3.260-24.870)	 0,594
PMNL Mean±SS Median(Min.-Maks.)	 4.793±1.912 4.560 (1.430-8.720)	 6.749±4.665 5.490 (1.530-22.720)	 0,189
CRP Mean ±SS Median (Min.-Maks.)	 54±54 35 (2-173)	 73±85 34 (1-262)	 0,845
ESH Mean ±SS Median (Min.-Maks.)	 66±35 62 (18-140)	 49±31 53 (4-118)	 0,302
First month CRP Mean ±SS Median (Min.-Maks.)	 18±32 5 (1-103)	 30±39 14 (1-164)	 0,072
First month ESR Mean ±SS Median (Min.-Maks.)	 37±31 22 (9-85)	 35±28 23 (1-87)	 0,884
First month MR Similar Regression Progression	 1 (20,0) 3 (60,0) 1 (20,0)	 6 (35,3) 6 (35,3) 5 (29,4)	 -[2]
Third month CRP Mean ±SS Median (Min.-Maks.)	 8±9 3 (1-22)	 33±41 17 (2-120)	 0,223
Third month ESR Mean ±SS Median (Min.-Maks.)	 23±15 16 (9-50)	 51±28 49 (10-86)	 0,071
Third month Similar Regression Progression	 1 (16,7) 5 (83,3) -	 1 (14,3) 5 (71,4) 1 (14,3)	 -[2]
Sixth month CRP Mean ±SS Median (Min.-Maks.)	 10±9 8 (1-25)	 28±39 12 (3-85)	0,830
Sixth month ESR Mean ±SS Median (Min.-Maks.)	 20±11 23 (5-30)	 40±30 35 (9-81)	0,176
Sixth month MR Similar Regression Progression	 2 (33,3) 4 (66,7) -	 1 (25,0) 3 (75,0) -	1,000

1Mann-Whitney U test was used.
2Pearson's chi-square test could not be applied due to cells with frequencies less than five exceeding 20%of the data
WBC: White Blood Cell PMNL: polymorphonuclear leukocytes CRP:C-reactive protein
MR: Magnetic Resonance ESR: Sedimentation

The main limitations of our study include the low rate of tissue sampling, the small number of patients with tuberculosis spondylodiscitis, which prevented us from conducting statistical comparisons with pyogenic and brucella cases, and the lack of data on the clinical course of patients, such as the follow-up of symptoms like back pain and fever, due to the retrospective nature of the study.

No specific clinical and radiological features were identified to differentiate Brucellar and pyogenic spondylodiscitis. Therefore, especially in endemic areas, patients presenting with low back pain require evaluation for brucellar spondylodiscitis. Radiological progression, especially at the 1st and 3rd months, may not be decisive, and follow-up of patients with spondylodiscitis should be based on clinical response and laboratory parameters such as sedimentation and CRP.

Conflict of interest

The authors have no conflict of interest.

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Ethical approval

was obtained from Ankara Training and Education Hospital Clinical Research Ethics Committee (Permission Date 12.07.2023, Permission number E-23-1307).

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