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Update on treatment options for spinal brucellosis

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Abstract

We evaluated the efficacy and tolerability of antibiotic regimens and optimal duration of therapy in complicated and uncomplicated forms of spinal brucellosis. This is a multicentre, retrospective and comparative study involving a total of 293 patients with spinal brucellosis from 19 health institutions. Comparison of complicated and uncomplicated spinal brucellosis was statistically analysed. Complicated spinal brucellosis was diagnosed in 78 (26.6%) of our patients. Clinical presentation was found to be significantly more acute, with fever and weight loss, in patients in the complicated group. They had significantly higher leukocyte and platelet counts, erythrocyte sedimentation rates and C-reactive protein levels, and lower haemoglobulin levels. The involvement of the thoracic spine was significantly more frequent in complicated cases. Spondylodiscitis was complicated, with paravertebral abscess in 38 (13.0%), prevertebral abscess in 13 (4.4%), epidural abscess in 30 (10.2%), psoas abscess in 10 (3.4%) and radiculitis in 8 (2.7%) patients. The five major combination regimens were: doxycycline 200 mg/day, rifampicin 600 mg/day and streptomycin 1 g/day; doxycycline 200 mg/day, rifampicin 600 mg/day and gentamicin 5 mg/kg; doxycycline 200 mg/day and rifampicin 600 mg/day; doxycycline 200 mg/day and streptomycin 1 g/day; and doxycycline 200 mg/day, rifampicin 600 mg/day and ciprofloxacin 1 g/day. There were no significant therapeutic differences between these antibiotic groups; the results were similar regarding the complicated and uncomplicated groups. Patients were mostly treated with doxycycline and rifampicin with or without an aminoglycoside. In the former subgroup, complicated cases received antibiotics for a longer duration than uncomplicated cases. Early recognition of complicated cases is critical in preventing devastating complications. Antimicrobial treatment should be prolonged in complicated spinal brucellosis in particular.

Keywords: Brucellosis, spondylitis, spondylodiscitis, treatment
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Introduction

Brucellosis, the most common bacterial zoonosis in the world, is still endemic in many developing countries. Spinal involvement in brucellosis is seen in 6–12% of cases and is the foremost cause of the debilitating and disabling complications [1–4]. The treatment regimens recommended by the World Health Organization (WHO) for brucellosis consist of the combination of doxycycline and rifampicin (both drugs administered for 6 weeks) or alternatively doxycycline plus streptomycin. Complicated spinal brucellosis requires a prolonged therapy (≥8 weeks), but the ideal treatment regimen and the optimal duration of the antibiotics in these cases are not known [5]. High relapse rates were reported in a previous series, in spite of the prolonged antibiotic treatment, and the role of surgery still remains controversial [6].

Complicated spinal brucellosis is a rare complication of vertebral osteomyelitis, extending to neighbouring vertebrae and the paravertebral and epidural spaces. Several case reports and series presenting spondylodiscitis with abscesses have been published in the literature [1,6]. However, treatment options and the duration of therapy have not been evaluated separately. The aim of this multicentre study was to assess the efficacy and tolerability of commonly used antibiotic regimens, and optimal duration of therapy in complicated and uncomplicated forms of spinal brucellosis.

Patients and Methods

We performed a multicentre, retrospective and comparative study involving a total of 293 patients with spinal brucellosis from 19 health institutions. Demographic and epidemiological characteristics, clinical and laboratory findings of the patients, methods used in laboratory diagnosis of disease, antibiotic regimens and the course of treatment were recorded. The comparison of two groups of patients with complicated and uncomplicated spinal brucellosis was statistically analysed.

The diagnosis of brucellosis with spinal involvement was established according to the presence of all of the following three criteria.

1. A clinical picture compatible with spondylodiscitis or spondylitis.
2. Absence of any aetiology other than brucellosis that can explain spinal involvement.
3. Microbiological evidence of brucellosis
   a. Isolation of *Brucella* from blood or other body fluids or tissue samples.
   b. Serological evidence of the disease.

Serological diagnosis of the disease included the following.

1. A Wright's seroagglutination test titre of 1/160 or higher.
2. Non-agglutinating antibodies measured using Coombs' test at a titre of 1/320 or higher.
3. Four-fold or greater rise in serum antibody titres measured at least 2–3 weeks apart.

Definitions

1. Brucellosis: clinical findings in accordance with the disease, along with the aforementioned microbiological evidence [7].
2. Classification: according to the duration of symptoms, brucellosis was classified as acute (<8 weeks), subacute(8–52 weeks) and chronic(>52 weeks) brucellosis [8].
3. Spinal brucellosis was defined as clinical and radiological or scintigraphical evidence of inflammation of one or more vertebrae and/or discitis in a patient with brucellosis. Any extension of infection through paravertebral and epidural spaces, the psoas muscle or radicles with/without neurological involvement is defined as complicated spinal brucellosis.
4. Therapeutic failure was assessed by clinical and laboratory evaluation of patients in relation to the parameters of continuation and/or deterioration of symptoms, absence of a decline in ESR and CRP levels and worsened imaging findings during treatment.
5. Relapse was defined as a recurrence or exacerbation of pain, unexplained fever, night sweats, weight loss, re-elevation of ESR and CRP levels, new vertebral lesions and recurrent bacteraemia.
6. Sequelae were defined as persistent pain, abnormal physical findings or functional limitation for longer than 6 months after treatment.

Statistical analysis

Data analysis was performed using SPSS 15.0 software. The data were defined using numbers, percentages, average, median, standard deviation and 1st–3rd quartiles. Normal distribution of the continuous values was assessed by the Kolmogorov–Smirnov test. The *t*- test was used for variables if normally distributed and Mann–Whithney *U*-test if not. The chi-squared and Fisher's exact tests were used for comparison of discrete variables; a p value of <0.05 was considered statistically significant. Any variable having a p value of < 0.25 was selected as a candidate variable, and these variables

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(considered to be clinically significant) were analysed to determine the factors affecting the success of the treatment. Backward LR analysis was used to obtain the best model. Variables with $p < 0.10$ were included in this model.

Results

A total of 293 patients with spinal brucellosis were enrolled in this study. The ages of the patients ranged between 14 and 85 years (51.4 ± 16.2) and 156 (53.2%) of them were male. Out of 293 patients, 128 (43.7%) were employed within animal husbandry, 231 (78.8%) were consuming unpasteurized raw milk and dairy products, 24 (8.2%) were dealing with veterinary care, and two (0.7%) were laboratory workers.

Patients were classified into the acute (n = 132, 45.1%), subacute (n = 123, 42.0%) and chronic (n = 28, 9.6%) stages of the disease. The mean duration of symptoms for all patients was 21 weeks. The most common clinical symptoms among all patients were backache (90.8%), debility (69.6%), arthralgia (61.4%) and fever (58.4%). Hepatomegaly and splenomegaly were determined in 13.0% (38 patients) and 10.9% (32 patients) of all patients, respectively. The standard tube agglutination test (STA) was used in 291 patients; it was positive at a titre of ≥1:160 in 283 (97.2%) patients. Enzyme-linked immunosorbent assay (ELISA) was used for the diagnosis of 16 (5.4%) patients. Blood culture was obtained from 185 patients and *Brucella* spp. were isolated in 62 (33.5%) of them. Among subtyped isolates, 32 isolates (51.6%) were identified as *B. melitensis* and 15 isolates (24.2%) were *B. abortus*. The rate of isolation of *Brucella* spp. from blood cultures was 32.0% in complicated cases, compared with uncomplicated cases ($p < 0.05$). Cultures from the abscess were obtained in 20 patients and yielded the pathogen in 10 samples (50.0%), with five of them identified as *B. melitensis*.

Complicated spinal brucellosis was diagnosed in 78 (26.6%) patients. The clinical presentation was found to be significantly more acute (with fever and weight loss) in the complicated group. Laboratory profiles of the complicated cases differed from the uncomplicated cases. They had significantly higher leukocyte and platelet counts, erythrocyte sedimentation rates and C reactive protein levels compared with the uncomplicated cases. However, they had lower haemoglobin levels. Demographic, clinical and laboratory characteristics of the two groups are listed in Table 1.

The diagnostic imaging methods used in patients with spinal brucellosis were MRI alone in 226 patients (77.1%), bone scintigraphy alone in two patients (0.7%) and CT alone in two patients (0.7%) out of 293 patients. More than one imaging technique was performed in 63 (21.5%) patients (MRI and scintigraphy in 34 patients, MRI and CT in 24 patients, and MRI, CT and scintigraphy in five patients). Single regional involvement of the spine was seen in 234 (79.9%) patients and 59 patients (21.1%) had diffuse involvement (>2 vertebral bodies). Considering the involvement of a single vertebral body, the lumbar region was the most frequent vertebral level (470/656, 71.6%), followed by the thoracic region (90, 13.7%), sacral region (61, 9.2%) and cervical (35, 5.3%) region (Fig. 1). The involvement of the thoracic spine was significantly more frequent in complicated cases. Spondylodiscitis was complicated with paravertebral abscess in 38 patients (13.0%), prevertebral abscess in 13 patients (4.4%), epidural abscess in 30 patients (10.2%), psoas abscess in 10 patients (3.4%) and radiculitis in 8 (2.7%) patients.

Various antibiotics (rifampicin, doxycycline, ciprofloxacin, trimetroprim and sulphamethoxazole, and aminoglycoside) and their combinations are used in the treatment of spinal brucellosis. The five major combination regimens were as follows.

1. Doxycycline 200 mg/day, rifampicin 600 mg/day and streptomycin 1 g/day (DRS).
2. Doxycycline 200 mg/day, rifampicin 600 mg/day and gentamicin (DRG).
3. Doxycycline 200 mg/day and rifampicin 600 mg/day (DR).
4. Doxycycline 200 mg/day and streptomycin 1 g/day (DS).
5. Doxycycline 200 mg/day, rifampicin 600 mg/day and ciprofloxacin 1 g/day (DRC).

There was no significant therapeutic difference between these antibiotic groups; the results were similar regarding the complicated and uncomplicated groups separately (Table 2). Patients were mostly treated with doxycycline and rifampicin with or without an aminoglycoside. These two combinations were compared according to the duration of the antibiotic therapy in patients with therapeutic success. Complicated cases received antibiotics for a longer duration than uncomplicated cases (Table 3). The clinical and therapeutic characteristics of the two groups are compared in Table 4. Patients treated with DR were more likely to be chronic ($p < 0.05$) and weight loss was present significantly more frequently in patients treated with DR and an aminoglycoside.

Side-effects attributed to each antibiotic were evaluated by the prescriber clinicians. Nausea and vomiting (n = 18; 6.1%) were the most frequently reported side-effects (Table 5). Doxycycline was the most switched (n = 8) antibiotic due to gastrointestinal intolerance (nausea, vomiting, oesophagitis, gastritis and abdominal pain). The side-effects attributed to rifampicin that resulted in switching were also due to gastrointestinal intolerance, and skin eruptions reported in two patients. The new regimens

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TABLE 1. Comparison of demographics and clinical and laboratory data for complicated (Group I) and uncomplicated (Group II) spinal brucellosis cases (*n* = 293)

Variable	Group I (*n* = 78)	Group II (*n* = 215)	p-value
Mean age ± SD, years	55.7 ± 14.8	49.8 ± 16.4	0.014
Male sex, *n* (%)	46 (59.0)	110 (51.5)	0.236
Risk factors, *n* (%)			
Animal husbandry	32 (41.0)	96 (44.7)	0.573
Consumption of unpasteurized milk	58 (74.4)	173 (80.5)	0.239
Veterinary/laboratory worker	2 (2.6)	22 (10.2)	0.034
Symptoms and signs, *n* (%)			
Fever	53 (67.9)	118 (54.9)	0.045
Debility	59 (75.6)	145 (67.4)	0.177
Lack of appetite	45 (57.7)	102 (47.4)	0.121
Sweating	46 (59.0)	119 (55.3)	0.580
Arthralgia	47 (60.3)	133 (61.9	0.803
Backache	67 (85.9)	199 (92.6)	0.081
Weight loss	29 (37.2)	50 (23.3)	0.018
Hepatomegaly	14 (17.9)	24 (11.2)	0.126
Splenomegaly	10 (12.8)	22 (10.2)	0.530
Disease classification, *n* (%)			
Acute	46 (59.0)	86 (40.0)	0.004
Subacute	30 (38.5)	93 (43.3)	0.462
Chronic	2 (2.6)	26 (12.1)	0.014
Relapse	2 (2.6)	15 (7.0)	0.153
Other organ/system involvement, *n* (%)			
Joint	5 (6.4)	32 (14.9)	0.054
Sacroiliac joint	6 (7.0)	45 (20.9)	0.008
Testicles	2 (2.6)	3 (1.4)	0.612
Others	5 (6.4)	2 (0.9)	NS
Involvement of vertebral region, *n* (%)			
Cervical	7 (8.9)	9 (4.2)	0.111
Thoracic	18 (23.1)	29 (13.5)	0.048
Lumbar	65 (83.3)	187 (86.9)	0.427
Sacral	15 (19.2)	41 (19.1)	0.975
Co-morbidities, *n* (%)			
Diabetes mellitus	13 (16.7)	26 (12.1)	0.308
Chronic renal failure	0 (0.0)	4 (1.9)	0.577
Malignancy	2 (2.6)	2 (0.9)	0.289
Immunosupression	0 (0.0)	3 (1.4)	0.568
Hypertension	5 (6.4)	5 (2.3)	0.137
Other	9 (11.5)	14 (1.4)	0.612
Laboratory data (mean + SD)			
Leukocyte (cells/mm^3)	7460 ± 2152	6785 ± 2519	0.006
Haemoglobin (g/dL)	12.1 ± 1.80	12.6 ± 1.70	0.047
Platelet (cells/mm^3)	293154 ± 102317	251237 ± 87403	0.001
Erythrocyte sedimentation rate (mm/hr)	51.55 ± 27.8	42.97 ± 26.6	0.018
C-reactive protein (mg/L)	45.7 ± 43.3	29.7 ± 33.0	0.003
Aspartate aminotranspherase (IU/mL)	29 ± 16	35 ± 30	0.296
Alanine aminotranspherase (IU/mL)	33 ± 27	36 ± 33	0.948
Lactate dehydrogenase (IU/mL)	245 ± 102	253 ± 150	0.402
Creatine phosphokinase (IU/mL)	91 ± 118	63 ± 46	0.582
Isolation of *Brucella* spp. from blood cultures[a], *n* (%)	25 (32.1)	37 (17.2)	0.006
Brucella melitensis	13 (52.0)	19 (51.4)	0.960
Brucella abortus	9 (36.0)	6 (16.2)	0.074

[a]Sixty-two patients were culture positive for *Brucella* spp., with 32 positive for *B. melitensis* and 15 positive for *B. abortus*.

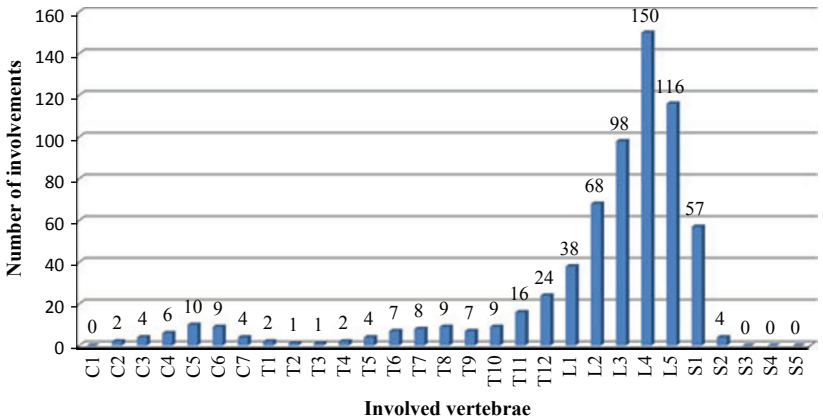

FIG. 1. The distribution of involvement of each vertebra according to the radiological imaging techniques in spinal brucellosis cases (*n* = 293).

(*n* = 10) included ciprofloxacin (*n* = 9) and/or trimethoprim/sulphamethoxasole (*n* = 6) instead of the discontinued antibiotic due to side-effects.

The average time for the resolution of clinical findings can be described as follows: resolution of the fever after 6.5 days (range, 1–45 days), erythrocyte sedimentation rate declined

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TABLE 2. Comparison of success of antibiotic regimens in complicated and uncomplicated spinal brucellosis

Patient groups	Regimens	Successful, *n* (%)	Failure, *n* (%)	p-value
Uncomplicated (*n* = 215)	DS	5 (100)	0 (0.0)	0.470
	DRS	94 (92.2)	8 (8.8)	
	DRG	14 (100)	0 (0.0)	
	DRC	6 (85.7)	1 (14.3)	
	DR	70 (90.9)	7 (9.1)	
	Others	9 (90)	1 (10)	
Complicated (*n* = 78)	DS	2 (66.6)	1 (33.3)	0.816
	DRS	36 (92.3)	3 (7.7)	
	DRG	8 (100)	0 (0.0)	
	DRC	4 (100)	0 (0.0)	
	DR	17(94.4)	1 (5.6)	
	Others[a]	5 (83.3)	1 (6.7)	

D, doxycycline; S, streptomycin; R, rifampicin; G, gentamicin; C, ciprofloxacin.
aOther: DR plus trimethoprim/sulphamethoxasole or ceftriaxone.

TABLE 3. Comparison of durations of successful antibiotic regimens between groups (*n* = 239)

Patient groups	DR, median week (1st–3rd quartiles)	DR plus aminoglycoside, median week (1st–3rd quartiles)	p-value
Complicated (*n* = 61)	16 (12–23)	20 (12–35)	0.130
Uncomplicated (*n* = 178)	12 (12–13.25)	12 (12–16)	0.876
p-value	0.241	0.001	

D, doxycycline; R, rifampicin; aminoglycoside, gentamicin or streptomycin.

TABLE 4. Comparison of demographics and clinical, microbiological and treatment data of spinal brucellosis cases according to the two main antibiotic regimens (*n* = 258)

Variable	DR (*n* = 95)	DR plus aminoglycoside (*n* = 163)	p-value
Female gender, *n* (%)	45 (47.4)	92 (56.4)	0.159
Mean age ± SD, years	49.6 ± 17.9	51.5 ± 15.2	0.537
Duration of symptoms, median weeks (1st–3rd quartile)	12 (6.75–24.0)	12 (4.0–20.0)	0.267
Disease classification, *n* (%)			
Acute	39 (41.1)	73 (44.8)	0.560
Subacute	34 (35.8)	76 (46.6)	0.090
Chronic	17 (17.9)	10 (6.1)	0.003
Relapse	7 (7.4)	8 (4.9)	0.415
Isolation of *Brucella* spp. from blood or abscess	24 (25.3)	31 (19.0)	0.237
Symptoms and signs, *n* (%)			
Fever	56 (58.9)	95 (58.3)	0.917
Fatigue	64 (67.4)	118 (72.4)	0.393
Lack of appetite	47 (49.5)	82 (50.3)	0.897
Sweating	56 (58.9)	89 (54.6)	0.497
Back pain	89 (93.7)	148 (90.8)	0.413
Weight loss	13 (13.7)	52 (31.9)	0.001
Hepatomegaly	12 (12.6)	20 (12.3)	0.932
Splenomegaly	12 (12.6)	16 (9.8)	0.483
Paravertebral abscess, *n* (%)	17 (18.1)	39 (24.5)	0.233
Spinal surgery needed, *n* (%)	8 (8.4)	20 (12.3)	0.338
Treatment failure, *n* (%)	8 (8.4)	11 (6.7)	0.620
Sequelae, *n* (%)	3 (3.2)	3 (1.8)	0.672

Aminoglycoside, gentamicin or streptomycin.

after 37.4 days (range, 1–330 days), and CRP normalized after 31.9 days of treatment. Radiological improvement was observed after 165.5 days (range, 24–730 days) of treatment. Therapeutic failure was reported in 23 patients (7.85%), relapse was reported in 17 (5.8%) patients and sequelae were reported in eight (2.7%) patients. The sequelae in patients with brucellosis were as follows: five patients developed chronic pain, one patient developed neurogenic bladder, one patient developed paraplegia, and difficulty in walking was observed in one patient. Death was reported in one patient.

Surgery was performed in 32 patients (41.0%) and percutaneous abscess drainage was performed in three (3.8%) of the complicated cases. The surgical procedure consisted of open abscess drainage in 18 (23.0%) of the complicated cases. Laminectomy was performed in five cases (6.4%) and discectomy in two (2.7%) out of 78 complicated cases. Other surgical procedures performed were as follows: laminectomy plus discectomy in two patients (2.7%), laminectomy plus open abscess drainage in two patients (2.7%), discectomy plus open abscess drainage in one patient (1.3%), and open abscess drainage plus cordectomy in one patient (1.3%).

Discussion

Brucellosis is an endemic zoonotic disease prevalent in rural areas of Turkey [9]. Although many organs and systems may be involved, osteoarticular disease is the most common complication in brucellosis [1–4]. This is a multicentre study of 293 patients with spinal brucellosis from different regions of the country.

Clinical presentations of the patients were mostly acute or subacute, as the mean duration of symptoms was 21 weeks. Currently, due to widespread use of imaging techniques, most patients are diagnosed in the early stages of the disease, in contrast to previous studies reporting subacute or chronic presentation [10]. As the corpus vascularization is insufficient, [11] older patients are more prone to spinal involvement and also contagious complications. The average age of our patients was 51 years. Moreover, patients in the complicated group were significantly older than those in the uncomplicated group.

The disease can affect the entire vertebral column and, similarly to previous studies, the lumbar region was the most frequently involved vertebral region, followed by the thoracic, sacral and cervical regions. Multiple and contagious involvement of vertebral bodies, which has been known to suggest particularly tuberculous spondylodiscitis [12], was detected in one-fifth of our cases as well. Brucellar involvement of multiple vertebral bodies was reported to be around 9–30% in previous studies [13,14]. Infection extending from the vertebrae to the neighbouring tissues, including epidural and para-prevertebral tissues, psoas muscles and radicles, was detected in a quarter

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TABLE 5. Side-effects attributed to antibiotics used in the treatment of spinal brucellosis

Side-effects	Rifampicin	Doxycycline	Streptomycin	Ciprofloxacin	Trimethoprim/ sulphamethoxasol	Total
Nausea and vomiting	2	14	1		1	18
Hepatotoxicity	3					3
Oesophagitis		2				2
Gastritis	1					1
Skin eruptions	3	4		2	2	11
Thrombo cytopenia		1				1
Autotoxicity			3			3
Abdominal pain		1				1
Facial numbness			1			1
Dizziness			3			3
Total (*n*)	9	22	8	2	3	44

of the patients with spinal involvement. Similar manifestations of spinal involvement are observed both in tuberculosis and brucellosis; furthermore, these diseases are endemic and important public health problems in Turkey.

Serology is the leading diagnostic tool in brucellosis and thus almost all patients in this study had a positive tube agglutination test. These basic tests should be considered and performed as an initial step in the differential diagnosis of spondylodiscitis [8]. On the other hand, the isolation of the organism from either blood or tissue culture is the definite diagnosis of the disease as seronegative cases have been reported [15]. Seronegative sponylodiscitis seems to be a rare entity and was only detected in eight (2.7%) patients in this study. As the bacteraemia is intermittent and the previously reported prevalence in the literature is 41–56% depending on the timing of the culture[13], the blood cultures yielded positive results in one-third of our patients. Although *B. melitensis*, which is the most virulent of all species of *Brucella*, was the prominent strain identified, *B. abortus* was also considerably common, being associated with a quarter of cases.

Antibiotics are the mainstay of brucellosis treatment, with combinations recommended to prevent the high relapse rates reported with monotherapy. Several dual or triple antibiotic combinations for spinal brucellosis have been compared in different studies [1–3,16–19]. The most frequently proposed and used combinations include streptomycin. Despite the known side-effects of streptomycin, favourable results were reported in brucellosis with bone and joint involvement. Ototoxicity and dizziness were the most prominent side-effects of the drugs among our patients. However, they were not switched due to the short-term utilization and reversibility of the side-effects after the discontinuation of the drug. Clinicians may particularly hesitate to treat the disease with streptomycin in the elderly because they are more prone to side-effects. The restricted use of a parenterally administrated drug in clinical practice is another disadvantage of the treatment. On the other hand, streptomycin in combination with doxycycline was reported to have a superior efficacy and lower relapse rates [3,20]. Doxycycline is the backbone of the antimicrobial treatment and it was included in all regimens in our study. However, rather than streptomycin, doxycycline was the most intolerable and switched drug. A triple combination of DRS was used most commonly in our study. After discontinuing streptomycin treatment, patients were treated with DR instead of doxycycline monotherapy. However, the utilization of rifampicin and streptomycin, which are also effective against *M. tuberculosis*, poses the risk of increased mycobacterial resistance in an endemic area. On the other hand, DR was a commonly preferred oral option that was as effective as streptomycin combinations. However, interactions limiting the effectiveness of this combination were previously reported [20]. Combinations including ciprofloxacin were also found to be effective and were proposed as an alternative to these standard regimens, which had higher costs [21]. Ten of our patients were treated successfully with the combinations including ciprofloxacin and it was used as an alternative to problematic drugs just after switching. Our study represents the clinical experience of infectious disease specialists in the treatment of spinal brucellosis in an endemic area and five major combinations were compared in this paper. However, none of these combinations demonstrated superiority in terms of therapeutic success in both complicated and uncomplicated cases.

Patients with spinal brucellosis do not constitute a homogenous group. Complicated spinal brucellosis extending to neighbouring tissue and paravertebral and epidural spaces has been believed to be a relatively rare complication of vertebral osteomyelitis [16,22]. Several case reports and series presenting spondylodiscitis with abscesses have been published [1–3,16,18,22]. However, characteristics, treatment options and the duration of the therapy have not been separately evaluated before. One of the objectives of this study was to compare clinical characteristics and the treatment of complicated spinal brucellosis with uncomplicated cases.

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Complicated cases were detected in a quarter of our patients, and this was a much higher percentage than the rates reported by previous authors. The complicated group of patients was significantly older and was diagnosed more frequently at the acute stage. In contrast, uncomplicated cases were more commonly diagnosed at the chronic stage Accordingly, positive blood cultures were significantly more common among the complicated cases. Thus, these cases seem to manifest with severe symptoms in the acute and bacteraemic period of the disease. Likewise, laboratory findings were more remarkable, more anaemic and with higher levels of acute phase reactants. Although the lumbar vertebrae were the most frequent site of involvement, the thoracic region was affected more significantly in complicated cases.

In case series including patients with paraspinal abscess it was reported that patients were treated for a longer duration depending on the clinical and radiological response [1]. In this study, the duration of treatment was not significantly different between patients treated with DR and those treated with aminoglycoside-including combinations. However, we found that in the DR plus an aminoglycoside arm, the complicated cases needed a longer treatment. Criteria for the response to treatment were resolution of fever within the first week and normalization of CRP level within the first month. Improvement in radiological findings was the final criterion, achieved after an average period of 23 weeks. A recent study showed that the effective treatment should be a triple antibiotic regimen given for a prolonged period of time (minimum 24 weeks). In this small series of patients with spondylitis, all patients achieved complete remission without relapse or sequelae [19]. Given the fact that brief courses of treatment were reported to result in frequent relapses, duration of treatment appears to be a more important issue than antibiotic selection, according to our data.

The role of surgery is another controversial issue in these patients and in most cases medical treatment is adequate for cure. Surgery was performed in two-fifths of our complicated cases. Aspiration of abscess may provide pain relief and sampling for differential diagnosis and this sampling was performed in most of our patients who underwent surgery. Surgical interventions are proposed as the last resort in the case of continuing systemic signs despite adequate antimicrobial therapy, vertebral collapse or septal abscess[14].

In conclusion, antimicrobial treatment should be prolonged in complicated spinal forms of brucellosis. Early recognition of complicated cases is critical in preventing devastating complications. Selection of an appropriate antibiotic combination should be made on the basis of the patient and the population: age, side-effects and ease of application. As MRI provides satisfactory information in the early stages of the disease, it should be repeated at the end of the fourth month of treatment.

Transparency Declaration

The authors declare no conflicts of interest.

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