

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 haemoglobin 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–Whitney *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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