

## Case report

## Discussion on treatment courses of brucellosis with spondylitis - a report of two cases

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## ABSTRACT

Human Brucellosis is a zoonotic contagious disease caused by *Brucella* infection and is common throughout the world, which can travel through the bloodstream to various organs. Brucellar spondylitis(BS) is the foremost cause of brucellosis's debilitating and disabling complications. We report two sisters with brucellosis complicated by lumbar spondylodiscitis accompanied by cold abscess formation. The diagnosis was based on their symptoms, epidemiological characteristics, laboratory and magnetic resonance imaging(MRI) results. Our therapeutic strategy in these two cases indicate that drug combination and prolongation of the use of antibiotics is a therapeutic strategy worthy of popularizing to reach a greater clearance rate of the infection.

## Introduction

Brucellosis is a zoonotic contagious disease caused by *Brucella* infection and is common throughout the world. More than 500,000 people have brucellosis every year worldwide, and there are approximately 2.4 billion people at risk [4]. In recent years, it has witnessed a gradual increase of patients with brucellosis along with the development of animal husbandry, with an incidence of 2–53% [1]. With the development of tourism and logistics in China, the epidemiology of human brucellosis has become a real threat during the past decades [10].

When *Brucella* infection invades the human body, it travels through the bloodstream to various organs. If it invades the spine, it is clinically called Brucellar spondylitis, or brucellosis spondylitis(BS) [9]. The lumbar vertebrae are involved more frequently (60%) than the thoracic (19%) and cervical vertebrae (12%) [2]. Inflammation caused by brucellosis often involves the spinal cord and nerve roots, leading to neurological symptoms and even paraplegia in severe cases [5]. Spinal involvement is the most crucial cause of the debilitating and disabling complications, which can be either focal or diffuse [3].

Therefore, the choice of antibiotics, the course of treatment, and patient compliance are critical to the treatment and prognosis of the disease. Yet now, drug selection, duration of antibiotic therapy, and the role of surgical intervention remain controversial and prevent the management of spinal brucellosis from being standardized [6].

In our study, two typical case reports about BS are reported. Drug

combination and prolonged use of antibiotics were our therapeutic strategy to reach a great clearance rate of the infection in the two cases.

## Case presentation

## General condition

Two sisters were referred to our hospital successively, one 58-year-old and another 60-year-old, complaining of a 1-week history of intermittent chills and fever, fatigue, severe low back pain(LBP), and other clinical symptoms. They declared no close contact with animals, no recent travel history, or consumption of unpasteurized dairy products, but both had a history of cleaning sheep placenta for cooking soup(In China, some people think the placenta is so nutritious that they eat it in soup.). They had no history of underlying diseases. Laboratory tests including positive blood culture with *Brucella melitensis*, positive Rose Bengal plate test, and > 1:400 in serum agglutination test (SAT) of brucellosis suggested brucellosis. The MRI examination revealed L3-L5 bodies and intervertebral disc spondylodiscitis.

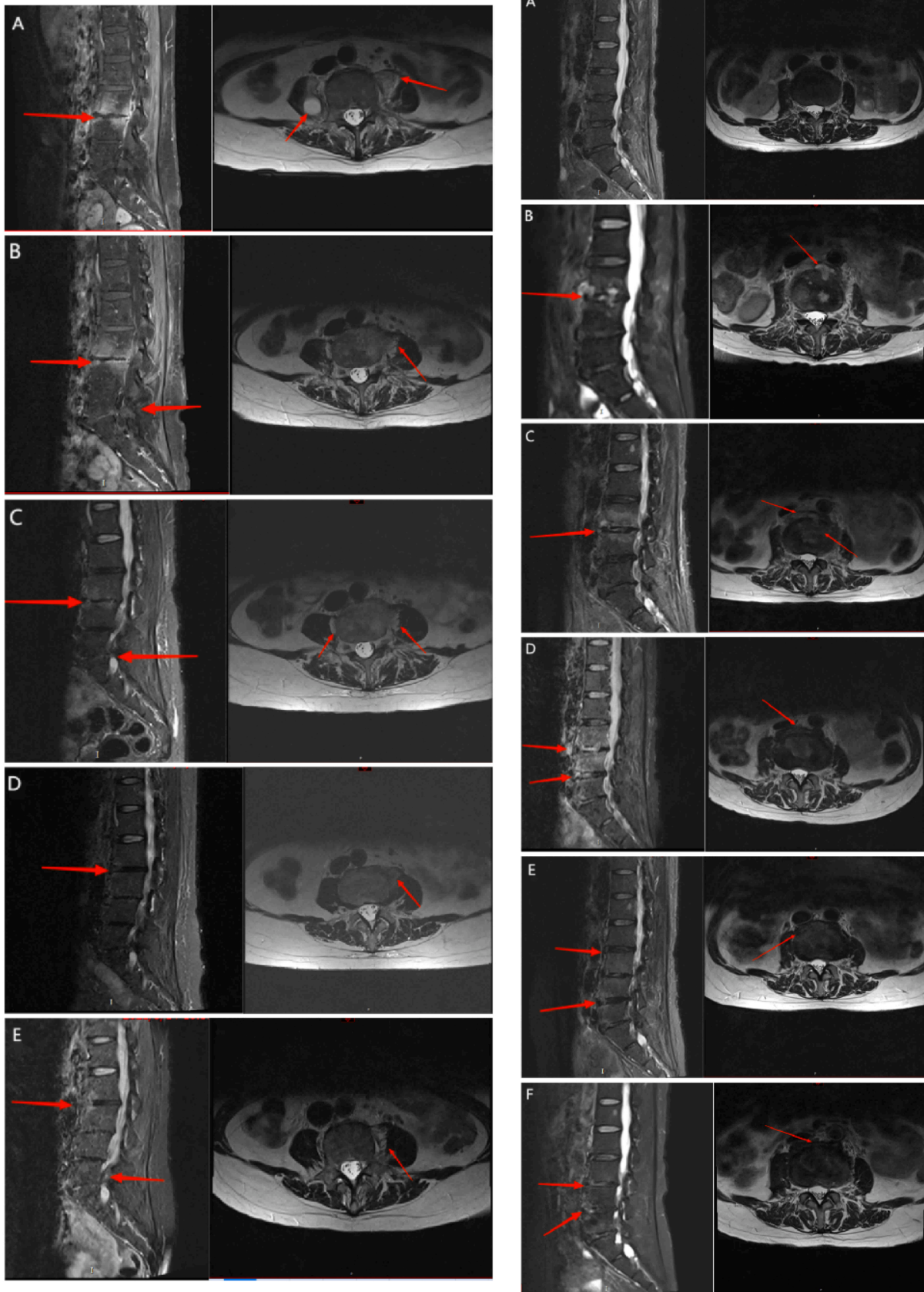
## The therapeutic intervention

## Therapeutic regimen of one patient(sister)

The patient was treated with levofloxacin 500 mg/day for five months (two weeks intravenously followed by sequential oral therapy),

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**Fig. 1.** Contrast enhanced midsagittal and axial T1-weighted magnetic resonance images(MRI) show spondylodiscitis. Figure 1.1 MRI image changes of sister. Figure 1.2 MRI image changes of elder sister.

oral doxycycline 200 mg/day and rifampin 600 mg/day for one year. The patient's temperature returned to normal within three days of treatment. However, the clinical symptom of LBP was not relieved within a short time. The patient's LBP were gradually improved and ultimately improved at one year. She had no neurological deficit and no open surgery.

#### *Therapeutic regimen of another patient(elder sister)*

The patient was treated with oral doxycycline 200 mg/day and rifampin 600 mg/day for ten months, intravenously ceftriaxone 2 g/day for two months, and then oral levofloxacin 500 mg/day for three months. The patient's temperature returned to normal within five days of treatment. The patient's LBP were gradually improved and ultimately improved at nine months. She had no neurological deficit and no open surgery. Fig. 1.

*Imaging changes during treatment (Fig. 1 Contrast enhanced midsagittal and axial T1-weighted magnetic resonance images(MRI) show spondylodiscitis.)*

*Imaging changes during treatment of one patient (Figure 1.1 MRI image changes of sister.):*

( A ) Initial MRI image changes : Contrast enhanced midsagittal and axial T1-weighted magnetic resonance images(MRI) show L3/L4 bodies and intervertebral disc spondylodiscitis, accompanied by multiple cystic abnormal signal foci on both sides(red arrow). ( B ) After one month of treatment: Spondylodiscitis of L3/ L4 vertebrae was the same as before, focus in front of L3 disappeared. However, another abnormal signals appeared at the lower edge of L4 and the upper edges of L5(red arrow). ( C ) After half year of treatment: The focus in front of L3/L4 and beside the psoas major muscles dwindle, but a small amount of exudation of lumbar vertebrae increased(red arrow). ( D ) After one year of treatment: All lesions were absorbed more than before(red arrow). ( E ) After one year of drug withdrawal: All lesions were further absorbed(red arrow).

*Imaging changes during treatment of another patient (Figure 1.2 MRI image changes of elder sister.):*

( A ) Initial MRI image changes: No definite inflammatory changes in the spine were suggested. ( B ) After one month of treatment: Abnormal signals appeared in L3/L4 vertebrae(red arrow). ( C ) After three months of treatment: The lesion range were similar(red arrow). ( D ) After half a year of treatment: The lesion of L3/L4 shrunk than before, but upper margin of L5 vertebrae appeared new focus (red arrow). ( E ) After nine months of treatment:Inflammation of the L3–5 vertebrae was absorbed more than before (red arrow). ( F ) After half a year of drug withdrawal:Inflammation of the L3–5 vertebrae roughly the same as before(red arrow).

## Discussion

According to the World Health Organization(WHO), the treatment regimen for brucellosis consists of a combination of doxycycline (100 mg twice a day) and rifampicin (600 mg/day) (both drugs administered for six months) plus streptomycin(1 g/day IM, 21 days). (WHO., Available at: <https://apps.who.int/iris/handle/10665/43597>.2019). Ulu-Kilic A et al. showed that long-term (usually at three months) antibiotic therapy could effectively prevent relapses in patients[8]. Smailnejad SG et al. showed that different combinations of antimicrobials with an aminoglycoside regimen could treat patients with BS in four months [7]. Zhong Z et al. showed that the therapy duration varied greatly depending on clinical response and ranged between two and six months[11].

2017 edition 《Brucellosis diagnosis and treatment expert consensus》 in China gives advices that the joint treatment can use doxycycline + rifampicin (at least three months) + gentamicin (one week) or

ceftriaxone (one month), or take ciprofloxacin + rifampicin (at least three months). Surgery is recommended for intractable pain and localized abscess formation.

In our case series, two patients received treatment with two or three antibiotics. The spinal lesions of the two patients still progressed after half a year of treatment. The treatment course recommended by WHO and the Chinese 《 Brucellosis Expert Consensus on Diagnosis and Treatment 》 can not control the disease, and the lesions are still progressing after half a year of treatment. According to the improvement of symptoms and absorption of the lesions, the patients were treated for one year and nine months respectively. They had no open surgery. Later MRI images showed that the lesions gradually shrank, and the patients did not have the symptoms of lumbago. Therefore, antimicrobial therapy should be prolonged in complicated spinal brucellosis in particular. But there is no definite conclusion on how long the exact course of medication should be for BS. It's important to combine with improving clinical symptoms, absorption of the local lesion, patient tolerance to drug side effects, patient adherence to treatment, etc. Therefore, it should be handled flexibly according to individual differences. The need for surgical treatment can be determined according to the absorption of the lesion and the improvement of symptoms after the prolonged course of medication. Still, there may be unknown complications, so surgical treatment should be carefully considered.

## Conclusion

Brucellosis infection can cause work-power losses because of misdiagnosis or lack of proper treatment. Insufficient treatment time can lead to uncontrolled or recurrent disease. Although there is no standard therapy protocol for treating BS, early diagnosis and treatment are essential for a successful outcome. Drug combination and prolongation of the use of antibiotics is a therapeutic strategy worthy of popularizing to reach a greater clearance rate of the infection.

## Ethical approval statement

The data in this paper are from clinical cases, no ethics involved. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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## Conflict of interest statement

No potential conflict of interest was reported by the author(s).

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