Indian Journal of Microbiology Research 2024;11(3):222–226

Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Microbiology Research

Journal homepage: https://www.ijmronline.org/

Case Series

A case series of brucellosis: A great mimicker

Sridevi Dinakaran[1], Sandhya Bhat[1]*, Shashikala Nair[1], Prince Solomon[2], Nayyar Iqbal[3], Dilip Shankar Phansalkar[4]

[1]*Dept. of Microbiology, Pondicherry Institute of Medical Sciences, Kalapet, Puducherry, India*
[2]*Dept. of Orthopaedics, Pondicherry Institute of Medical Sciences, Kalapet, Puducherry, India*
[3]*Dept. of General Medicine, Pondicherry Institute of Medical Sciences, Kalapet, Puducherry, India*
[4]*Dept. of Radiology, Pondicherry Institute of Medical Sciences, Kalapet, Puducherry, India*

ARTICLE INFO

Article history:
Received 06-07-2024
Accepted 13-08-2024
Available online 26-09-2024

Keywords:
Fever of unknown origin (FUO)
Spondylodiscitis
Endocarditis
Automated Blood culture
Standard agglutination test (SAT)
Brucellosis

ABSTRACT

Brucellosis is a common zoonotic disease worldwide. Although it is commonly neglected in India, there are pockets where it is prevalent. The disease tends to involve multiple organs, mimicking other illnesses. The symptoms are fever, sweating, and musculoskeletal pain. In 40-70% of patients, musculoskeletal involvement is the most common systemic manifestation. Blood culture, serological tests, and PCR are the available test formats for diagnosing brucellosis. Automated blood culture methods enable earlier diagnosis of brucellosis when presenting as a case of Fever of unknown origin (FUO). Here, we present four cases of brucellosis in a nonendemic area. Of these, two cases presented as *Brucella* spondylodiscitis, mimicking TB spine, one as *Brucella* endocarditis, and the other as acute brucellosis. All four cases were diagnosed with microbiological and radiological diagnostic support and successfully treated as per standard treatment guidelines. The possibility of brucellosis as a differential diagnosis in patients with nonspecific symptoms affecting the bones and unexplained prolonged fever should be considered.

1. Introduction

Brucellosis, a zoonotic infection, is an under-reported disease in India, although there are pockets where the disease is prevalent.[1] Humans acquire brucellosis by consuming unpasteurized milk or exposure to infected animals and their products.[2] It primarily affects the reticuloendothelial system but tends to have a multi-organ involvement. Musculoskeletal involvement is seen in 40-70% of patients.[3] *Brucella* spondylodiscitis can mimic tuberculosis spine by having a similar presentation. Various modalities are available to diagnose brucellosis, such as blood culture, serological tests, and polymerase chain reaction (PCR). The automated blood culture method enables earlier diagnosis, especially in cases of fever of unknown origin. We are reporting a case series of brucellosis presented as a fever of unknown origin.

2. Case Presentation

2.1. Case 1

A 50-year-old man who is a farmer by occupation and worked in a sheep pen in the Middle East presented with a low-grade fever on and off with chills and rigors, night sweats, loss of appetite, arthralgia, loss of weight accompanied by low backache and bilateral lower limb pain for the past two months. He was treated elsewhere with a diagnosis of infective spondylodiscitis suspected of tubercular origin. His MRI revealed a cortical break in the

* *Corresponding author*.
E-mail address: sandhyabhatk@gmail.com (S. Bhat).

https://doi.org/10.18231/j.ijmr.2024.040

L4-L5 region, with a pre-vertebral collection, which was ill-defined, and a mild diffuse bulge with the narrowing of the neural lamina (Figure 1). To relieve the pain, he was managed surgically by disc debridement and interbody fusion of the anterior lumbar was done. Postoperatively, he developed a high-grade fever, for which he was further evaluated. His total leukocyte count was 6,700/μl with neutrophil predominant of 75%. Haemoglobin was 6.6g/dl, so he was transfused two units of packed RBCs. Inflammatory markers like ESR 124mm/hour and CRP 95 mg/dl were also elevated, so a blood culture was sent by automated BacT/Alert bottle. After 75 hours of incubation, it flagged positive. Blood and chocolate agar showed minute moist colonies (Figures 2 and 3). This was identified as *Brucella* species by MALDI-ToF MS (Matrix-assisted laser desorption ionization time-of-flight mass spectrometry), later speciated as *Brucella melitensis* by VITEK 2 (bioMérieux). The patient was started on Tab. Doxycycline 100 mg twice daily with Inj. Amikacin 500mg Q8H.The fever subsided gradually after two days of starting antibiotics, and he improved symptomatically. He was discharged and advised to continue Tab. Doxycycline 100 mg BD and Tab. Rifampicin 900mg OD for another 45 days. He completed the treatment and recovered completely.

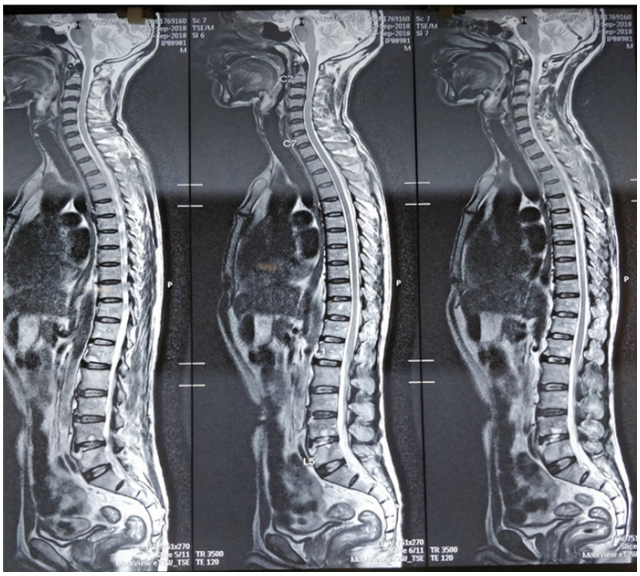

Figure 1: MRI of the spine showed a cortical break in the L4-L5 region with pre-vertebral collection

2.2. *Case 2*

A 42-year-old male complained of fever associated with chills and rigors for four days. He is a shepherd by occupation. Routine investigations were sent, and all were normal. A tropical fever workup was done and found to be negative. He was a known case of hypertension and cerebrovascular accident (CVA). He was also an old

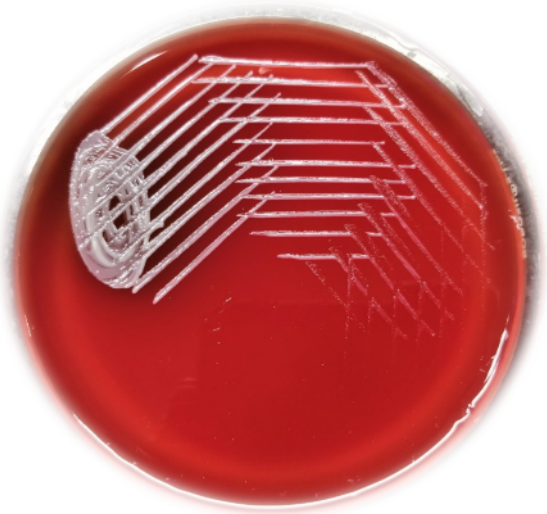

Figure 2: Blood agar showed non-hemolytic minute colonies

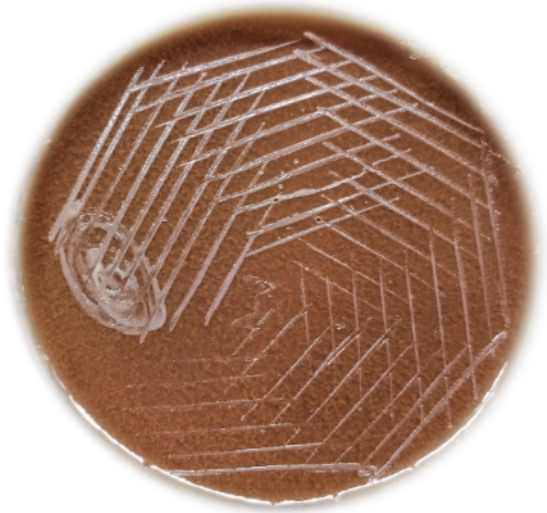

Figure 3: Chocolate agar showed minute moist colonies

case of rheumatic heart disease (RHD) with mitral valve replacement (since 2014) on Warfarin, so the possibility of infective endocarditis was considered and blood samples were sent for culture. A cardiology opinion was obtained, and 2D-ECHO was done, which showed normal valves and chambers, no regional wall motion abnormalities, good ventricular functions, and no vegetation. Three blood cultures were sent, all of which grew *Brucella*, and the standard agglutination test (SAT) was positive for *Brucella abortus* (Table 1). The patient was started on Tab. Doxycycline 100 mg BD with Inj. Gentamicin 300mg OD and Tab.Rifampicin 900mg OD as per *Brucella* endocarditis protocol, and he improved symptomatically; hence, he was discharged. The patient was advised to do Trans-

oesophageal Echocardiography, which he could not do due to financial constraints. He completed the treatment and recovered completely.

2.3. Case 3

A 36-year-old male working in the Middle East in a camel farm complained of multiple joint pain, predominantly involving the large joints, on and off for two months. He had no history of fever, night sweats, loss of weight, or appetite. Blood culture and standard agglutination test were positive for *Brucella abortus* (Table 1). He was started on Tab. Doxycycline 100mg BD for six weeks and recovered completely.

2.4. Case 4

A 21-year-old female complained of lower back pain for three months and got aggravated for one month, for which she was evaluated in a private tertiary hospital. Her MRI showed spondylodiscitis of the D9 and D10 vertebra, suspected of infectious origin (probably TB spine). A CT-guided biopsy was done, and the result was negative for Gene Xpert. She came here for further management. She was evaluated for brucellosis. The standard agglutination test for *Brucella abortus* was positive, and the antibody titers were ≥1:320 (Table 1). The patient was started with Inj. Gentamicin 300mg OD for one week and advised to continue Tab.Rifampicin 900mg and Tab. Doxycycline 100 mg BD for 6 weeks.

Table 1 provides the relevant clinical details of patients (above four cases) with brucellosis.

3. Discussion

Brucellosis is a zoonotic disease that affects individuals exposed to contaminated animal products or who consume unpasteurized milk and milk products.[4] In our study, all of our patients had animal contact or had consumed unpasteurized milk products, which is a significant history of clinically suspected cases of brucellosis.

Among the extrapulmonary tuberculosis cases, Tuberculous spondylitis or Pott's disease comprises around 5%.[4] *Brucella* spondylodiscitis mimics spinal tuberculosis due to its similar clinical presentation and radiological and histopathological features, which is why it is often misdiagnosed.[5] In our case series, two cases were suspected of TB Potts spine, and one was started on an anti-tubercular regime. Unfortunately, in a tuberculosis-endemic country like India, there is a high probability of misdiagnosing brucellosis due to its superimposed presentation.

Brucellosis has varied clinical presentations. To begin with, the constitutional symptoms such as fever accompanied by chills, myalgias, joint pain, headaches, and sweating. Osteoarticular involvement includes spondylitis, spondylodiscitis, sacroiliitis, and arthritis.[1] Spondylitis

Table 1: Relevant clinical details of patients with brucellosis

Case	Age (yrs)	Hb (g/dl)	TLC ($10^3/\mu l$)	CRP (mg/l)	ESR (mm/hr)	SAT	Blood culture Growth	Spine involvement	Animal contact history/consumption of unpasteurized milk products	Suspected TB	Started on ATT	Treatment regimen for brucellosis
Case 1	50	11.5	6.7	28	68	Neg	Yes	Yes	Yes	Yes	Yes	Rifampicin, Amikacin, Doxycycline
Case 2	42	9.7	5.2	26	20	*B.abortus* ≥ 1280	Yes	No	Yes	No	No	Rifampicin, Doxycycline, Gentamicin
Case 3	36	12.7	10.1	-	9	*B.abortus* = 320	Yes	No	Yes	No	No	Doxycycline
Case 4	20	9.8	9.26	3	32	*B.abortus* ≥ 320	Neg	Yes	Yes	Yes	No	Rifampicin, Doxycycline, Gentamicin

Hb: Haemoglobin, TLC: Total leucocyte count, CRP: C-reactive protein, SAT: Standard agglutination test, TB: Tuberculosis, ATT: Anti-Tubercular treatment

and spondylodiscitis are the most frequent presentation of spinal brucellosis, apart from other complications.[6]The spine involvement in brucellosis is seen in 2-54% of cases.[7,8]

It is stated that brucellar spondylodiscitis accounts for 6%- 85%. The lumbar spine was the most common site (60%- 69%), followed by the thoracic or dorsal spine (19%) and cervical spine segments (6%- 12%).[8,9] In our study, two patients were diagnosed with spondylodiscitis. One patient had spondylodiscitis of lumbar vertebrae (L4-L5), and the other had spondylodiscitis of dorsal vertebrae (D9-D10).

At least two of the following findings are required for the diagnosis of spinal brucellosis:

1. Blood and/or bone marrow aspirate culture positive for *Brucella*.
2. *Brucella* standard agglutination test (SAT) titer of 1:160 or higher,
3. Radiography evidence (X-ray /MRI /CT scan) showing skeletal involvement like osteomyelitis or spondylodiscitis and,
4. Tissue biopsy showing non-caseating granulomatous tissue suggestive of brucellosis.[9,10] All four of our patients fulfilled these criteria.

Brucella endocarditis is a rare complication of brucellosis. Generally, it affects both native and prosthetic valves and leads to vegetation in the cardiac valves.[11] The management requires surgical valve replacement and combined antimicrobial therapy.[12] On the contrary, in this case series, we had one patient with a prosthetic valve who did not have vegetation or pulmonary hypertension. He was treated with a combined regimen, and his condition improved.

Laboratory investigations are essential tools in diagnosing brucellosis. It is observed that in brucellosis, the laboratory parameters like total leukocyte count (TLC) are within normal range, and a marginal rise seen in inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are correlating with the current study.[13] All patients had anemia.

The isolation of organisms from bone marrow culture is the gold standard for diagnosing brucellosis. The positivity rate is high in blood and bone marrow cultures. It can range up to 70%.[14] It is a gram-negative coccobacilli, an intracellular, aerobic, non-motile, and slow-growing organism that is often under-reported in resource-limited settings. Automated blood cultures facilitate earlier and more accurate diagnosis. In this study, three out of four patients had growth in blood culture (75%). The yield of blood culture positive is high during the acute phase.The tube agglutination assays are positive for acute and chronic diseases.[15] This notion is seen in this case series as well.

According to WHO guidelines, the treatment regimen includes doxycycline 100 mg BD for 45 days plus streptomycin 1 g daily for 15 days. The other alternative therapy is doxycycline at 100 mg BD for 45 days, plus rifampicin at 15mg/kg/day for 45 days. WHO also suggests that streptomycin may be substituted with gentamicin 5mg/kg/daily for 7–10 days.[16]

There are specific guidelines for osteoarticular brucellosis, but various case reports suggest a triple regimen of Streptomycin (1g daily), Doxycycline (100mg BD), and Rifampin (15 mg/kg daily) will prevent relapses.[17] Similarly, it has been followed in two spondylodiscitis cases.

In this case series, we had one acute brucellosis, two brucellar spondylodiscitis, and one case of *Brucella* endocarditis.

4. Conclusion

Brucellosis is a zoonotic infection transmitted by animals, and human brucellosis can lead to serious health consequences. In *Brucella*-endemic areas, a high index of suspicion and a detailed clinical history of occupation are necessary. Brucellosis is a great masquerader of tuberculosis and is often misdiagnosed, which leads to the unnecessary initiation of a long-term antitubercular regimen. Accurate diagnosis, timely management, and adherence to standard treatment protocols will aid in preventing brucellosis-related complications.

5. Source of Funding

None.

6. Conflict of Interest

None.

References

1. Smits HL, Kadri SM. Brucellosis in India: a deceptive infectious disease. *Indian J Med Res*. 2005;122(5):375–84.
2. Oulkadi L, Amine B, Binoune IE, Rostom S, Bahiri R. Spinal pain revealing brucellar spondylodiscitis: a case report. *Egypt J Intern Med*. 2021;33:1–6.
3. Andrabi SAH, Hamid S, Aijaz S. Brucellosis Masquerading as Spondylodiscitis with Multiple Intervertebral Disc Prolapse. *J Glob Infect Dis*. 2012;4(3):184–5.
4. Papachristodoulou E, Kakoullis L, Louppides S, Panos G. Granulomatous infective spondylitis in a patient presenting with progressive difficulty in walking: the differential between tuberculosis and brucellosis. *BMJ Case Rep*. 2019;12(11):e232540.
5. Lamba AS, Gupta M, Bansal A, Tahlan A, Parmar UPS. Brucellosis Masquerading as Disseminated Tuberculosis: A Clinical Case Report. *Perm J*. 2023;27(3):110–5.
6. Esmaeilnejad-Ganji SM, Esmaeilnejad-Ganji SMR. Osteoarticular manifestations of human brucellosis: A review. *World J Orthop*. 2019;10(2):54–62.
7. Rizkalla JM, Alhreish K, Syed IY. Spinal Brucellosis: A Case Report and Review of the Literature. *J Orthop Case Rep*. 2021;11(3):1–5.
8. Bouaziz MC, Ladeb MF, Chakroun M, Chaabane S. Spinal brucellosis: A review. *Skeletal Radiol*. 2008;37(9):785–90.

9. Tekaya R, Tayeb MH, Amri NE, Sahli H, Saidane O, Mahmoud I. THU0257 Brucella Spondylodiscitis: A Study of Nineteen Cases. *Ann Rheum Dis*. 2015;74:290.
10. Hantzidis P, Papadopoulos A, Kalabakos C, Boursinos L, Dimitriou CG. Brucella cervical spondylitis complicated by spinal cord compression: a case report. *Cases J*. 2009;2:6698.
11. Raju IT, Solanki R, Patnaik AN, Barik RC, Kumari NR, Gulati AS. Brucella endocarditis - a series of five case reports. *Indian Heart J*. 2013;65(1):72–7.
12. Jacobs F, Abramowicz D, Vereerstraeten P, Clerc JLL, Zech F, Thys JP. Brucella endocarditis: the role of combined medical and surgical treatment. *Rev Infect Dis*. 1990;12(5):740–4.
13. Turunc T, Demiroglu YZ, Uncu H, Colakoglu S, Arslan H. A comparative analysis of tuberculous, brucellar and pyogenic spontaneous spondylodiscitis patients. *J Infect*. 2007;55(2):158–63.
14. Godfroid J, Cloeckaert A, Liautard JP, Kohler S, Fretin D, Walravens K, et al. From the discovery of the Malta fever's agent to the discovery of a marine mammal reservoir, brucellosis has continuously been a re-emerging zoonosis. *Vet Res*. 2005;36(3):313–26.
15. Dahouk SA, Nöckler K. Implications of laboratory diagnosis on brucellosis therapy. *Expert Rev Anti Infect Ther*. 2011;9(7):833–45.
16. World Health Organization. Brucellosis; 2020. Available from: https://www.who.int/news-room/fact-sheets/detail/brucellosis#:~:text=The%20incubation%20period%20of%20the,g%20daily%20for%2015%20days.
17. Bayindir Y, Sonmez E, Aladag A, Buyukberber N. Comparison of five antimicrobial regimens for the treatment of brucellar spondylitis:A prospective, randomized study. *J Chemother*. 2003;15(5):466–71.

Author biography

Sridevi Dinakaran, Senior Resident https://orcid.org/0009-0006-8319-0373

Sandhya Bhat, Professor https://orcid.org/0000-0002-4257-9220

Shashikala Nair, Professor and HOD

Prince Solomon, Professor and HOD https://orcid.org/0000-0002-8802-0115

Nayyar Iqbal, Professor https://orcid.org/0000-0002-7063-3677

Dilip Shankar Phansalkar, Professor and HOD

Cite this article: Dinakaran S, Bhat S, Nair S, Solomon P, Iqbal N, Phansalkar DS. A case series of brucellosis: A great mimicker. *Indian J Microbiol Res* 2024;11(3):222-226.