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Case Report

Unveiling the unusual: a fatal case of brucellosis with multi-organ involvement

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ABSTRACT

Brucellosis in humans is one of the most common zoonoses. The infection is caused by various species of *Brucella* bacteria. Brucella infections frequently affect several organ systems with vague clinical symptoms. Humans typically acquire brucellosis through direct contact with infected animals or consumption of contaminated animal products like unpasteurized dairy. It poses significant clinical challenges due to its varied presentation. The disease manifests with a range of nonspecific symptoms including fever, sweating, fatigue, joint and muscle pain, and loss of appetite. Brucellosis can also affect various organs such as the liver, spleen, heart, and nervous system. Diagnosis often involves blood cultures, serological tests, and polymerase chain reaction (PCR) assays to detect the bacteria or antibodies produced by the immune system. This case report presents the clinical course of patient X, a 58-year-old female who succumbed to death following an unusual presentation of brucellosis. Despite initial diagnostic challenges, the identification of *Brucella melitensis* in her blood marked a critical turning point. The case highlights the importance of considering Brucellosis in patients with persistent fever and multi-organ involvement, emphasizing the need for early recognition and appropriate management.

Keywords: *Brucella melitensis*, *omp31*, Neurobrucellosis, PCR

INTRODUCTION

Brucellosis, a zoonotic infection caused by various *Brucella* species, typically presents with non-specific symptoms, making diagnosis challenging.[1] Though commonly associated with most typical signs of infection like fever, muscle and joint pain, weakness, and enlargement of the liver, spleen, and lymph nodes, the disease can manifest with atypical features, complicating its identification.[2] Human brucellosis is a worldwide disease that is particularly common in developing nations. Every year, over 500,000 new cases of brucellosis in humans are reported globally with approximately 40,000 new cases from India.[3,4] According to Gwida et al, the species *Brucella melitensis*, which infects goats and sheep, and *Brucella abortus*, which infects cattle, result in serious human illness and large financial losses for animal husbandry.[5] Humans contract the disease mostly from eating undercooked meat and dairy products, from direct contact with infected animals, from the placenta, or aborted fetuses.[6] The most common symptoms of infection include fever, malaise, muscle and joint discomfort,

weakness, and enlargement of the liver, spleen, and lymph nodes. However, the disease's clinical manifestations are frequently non-specific.[2,7] All body systems may be impacted, and problems including hepatitis, osteoarthritis, cardiovascular disease, central nervous system malfunction, respiratory symptoms, orchitis and epididymitis are possible. The case highlights the importance of considering brucellosis in patients with atypical symptoms and the need for early recognition to prevent fatal complications.

CASE REPORT

Patient X, 58 years old post-menopausal female, non-diabetic, non-hypertensive presented to the Emergency Department Jawaharlal Nehru Medical College, Aligarh with a history of fever, vomiting, and altered sensorium. The routine biochemical investigations like hemogram, liver function test, renal function test, urine (routine microscopy and culture) and blood culture were normal (Table 1). The workup for the endemic causes of fever like tuberculosis, enteric fever, dengue, and malaria yielded negative results (Table 1).

Table 1: Diagnostic workup of patient-X.

Diagnosis	Result
ELISA for HIV 1, 2	Non-reactive
Urine culture	Sterile
Blood culture	Sterile
Chest X-ray	No abnormality detected
USG abdomen	Normal
Cerebrospinal fluid (CSF)	Sugar-60 mg/dl
	Protein-44 g/l
	TLC-<2/cumm
	India ink stain-negative
	ZN stain-negative
	Gram stain-negative
	Bacterial culture-sterile
	PCR for HSV-non-reactive
pH	7.36
pCO_2	35 mmHg
pO_2	80 mmHg
Na^+	138 mmol/l
K^+	4.0 mmol/l
Ca^{2+}	0.96 mmol/l
Glucose	120 mg/dl
Lactate	1.1 mmol/l
Hematocrit	42%
HCO_3^-	23.4 mmol/l

As per the hospital protocol and clinical presentation of the patient, a lumbar puncture was done and the cerebrospinal fluid (CSF) parameters were normal. The magnetic resonance imaging (MRI) of the brain revealed an infarct in the left caudate nucleus. As she was from a rural background with routine exposure to cattle, serological testing for *Brucella melitensis* was done and it revealed *Brucella melitensis* positivity using the RBPT (Figure 1), IgM, and IgG enzyme-linked immunosorbent assay (ELISA) (Figure 2), and RT-PCR targeting the *omp31* region for *Brucella melitensis* (Figure 3). Because of the critical condition, the patient was initiated on triple drug therapy (doxycycline 100 mg twice daily, rifampicin 600 mg daily, and streptomycin 15 mg/kg body weight/day I.V.). During the hospital course, she developed cardiogenic pulmonary edema (Figure 4) further complicating the clinical picture.

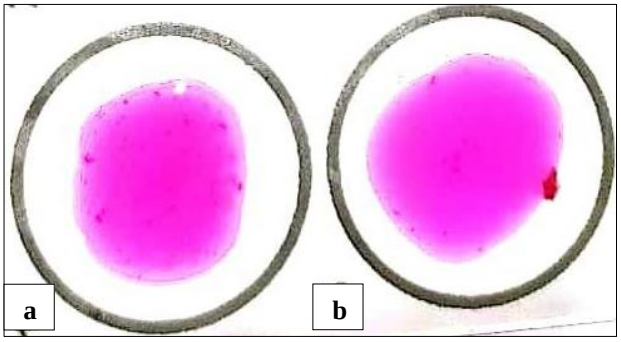

Figure 1: Rose Bengal plate test for human brucellosis (a) control and (b) test.

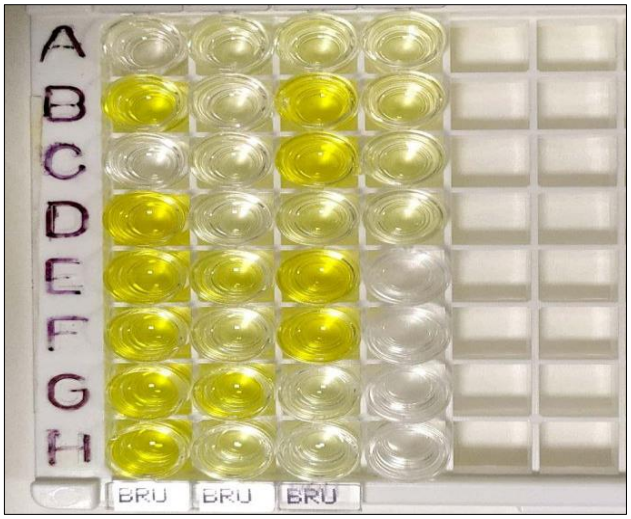

Figure 2: ELISA for IgM anti-Brucella antibodies detection.

Despite intensive management efforts, the patient succumbed to complications associated with cardiac failure. The case highlights the complexity of diagnosing atypical presentations of infectious diseases and the challenges posed by the simultaneous occurrence of multiple organ involvement. Brucellosis, although uncommonly associated with neurological and cardiac complications, should be considered in cases of fever of unknown origin, especially in regions where the disease is endemic. A multidisciplinary approach is crucial for a thorough investigation and timely intervention in such complex cases.

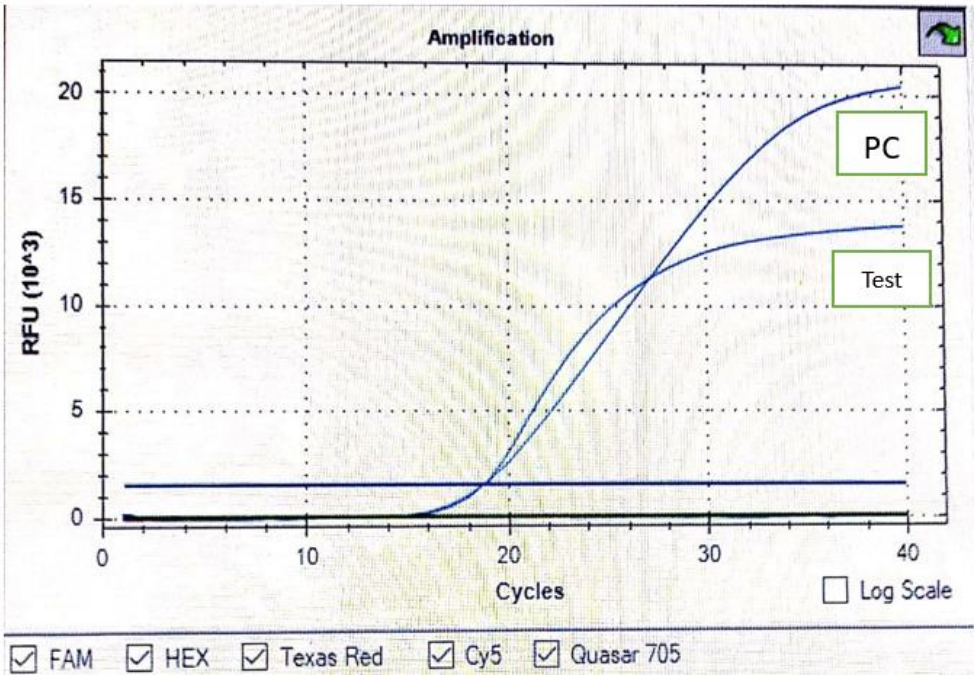

Figure 3: Real-time PCR amplification pattern using the Brucella genus specific probe. Plotting the fluorescence ratio versus the number of PCR cycles allows for real-time amplification monitoring (Ct of positive control: 16, Ct of test sample: 22).

Figure 4: MRI brain of patient X (lacunar infarct is shown by arrows).

DISCUSSION

This case challenges conventional perceptions of brucellosis by showcasing an intricate clinical course involving neurological and cardiac complications. While brucellosis is primarily known for its musculoskeletal and reproductive system involvement, this case underscores the potential for severe multi-organ complications, including the central nervous system and cardiac manifestations. The number of cases of human brucellosis reported globally should only be regarded as a minimum estimate because many patients remain undiagnosed as a result of unusual clinical presentations, incorrect diagnoses, and insufficient surveillance.[8] Major outer-membrane protein (OMP) genes of *Brucella* have recently attracted attention as they exhibit polymorphism to allow differentiation between *Brucella* species and some of their biovars. *B. melitensis* contains two Omps with apparent molecular masses of 25–27 kDa and 31–34 kDa, now designated as omp27 and omp31, respectively.[9] Neurobrucellosis occurs in 5–10% of cases of brucellosis and affects the central (CNS) or peripheral nervous system (PNS).[10,11] The correlation between imaging abnormalities and the clinical manifestations of neurobrucellosis shows subthalamic hemorrhage, mild perivascular enhancement, left caudate lacunae, and diffuse white matter changes.[12,13] The diagnosis of Brucellosis in humans involves the Rose Bengal plate test (RBPT) which is a rapid screening method and the serum agglutination test (SAT). IgM and IgG are also utilized to measure specific antibodies, offering sensitivity and species differentiation. Blood culture, the gold standard, confirms infection through bacterial growth but is slow and difficult. However, with the advancement in technology, real-time polymerase chain reaction (RT-PCR) amplifies Brucella DNA, being highly specific but costlier. Despite extensive investigations, the identification of *Brucella melitensis* emerged as a critical factor in the patient's complex presentation. The chronic lacunar infarct observed on MRI, in conjunction with elevated troponin I, suggests a potential link between brucellosis and cardiovascular manifestations. The elevated vitamin B12 levels,

hepatomegaly, and sterile urine culture adds to the understanding of Brucellosis's systemic impact. The identification of *Brucella melitensis* through various diagnostic modalities like the RBPT, and SAT that detect antibodies, provides a quick insight. ELISA IgM and IgG tests quantify specific antibodies, aiding in stage identification are cheaper and easily available. Although RT-PCR offers a quicker alternative with high specificity, but it comes with a higher cost. The selection of diagnostic tests depends on the specific requirements of each case, often involving a strategic combination for a comprehensive and accurate diagnosis. The MRI brain shows a chronic lacunar infarct in the left caudate is suggestive of neurobrucellosis. The symptoms vary from confusion, seizures, behavior change, and loss of hearing. This case underscores the need for increased awareness among healthcare professionals to consider brucellosis in the differential diagnosis, especially when faced with a complex clinical presentation.

CONCLUSION

This case report emphasizes the critical significance of considering brucellosis as a potential diagnosis in patients with atypical symptoms and multi-organ involvement, particularly in endemic regions. The intricate clinical course of patient X, including neurological and cardiac complications, challenges conventional perceptions of brucellosis and necessitates a multidisciplinary approach to diagnosis and management. The identification of *Brucella melitensis* through various diagnostic modalities, such as serological tests and PCR assays, proved pivotal in uncovering the underlying cause of the patient's complex presentation. This case underscores the importance of heightened awareness among healthcare professionals to facilitate early recognition and appropriate management of brucellosis, thus preventing fatal complications and contributing to the advancement of knowledge in the field of infectious diseases.

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