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*Case Report*

# Brucellosis: An overlooked cause of pyrexia of unknown origin in a child

Jyothi Naik[1], Thirunavukkarasu Arun Babu[1]

[1]Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), Mangalagiri, Andhra Pradesh, India.

***Corresponding author:**
Thirunavukkarasu Arun Babu, Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), Mangalagiri, Andhra Pradesh, India.

babuarun@yahoo.com

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## ABSTRACT

Paediatric brucellosis can be asymptomatic or present as an acute, persistent febrile illness. Limited literature on this disease in the paediatric population often leads to delayed diagnoses or undiagnosed cases. A previously healthy 10-year-old boy presented with a 2-month history of fever and a weight loss of 2 kg. On examination, hepatosplenomegaly was noted. His haemogram showed anaemia and leucopenia. Blood culture identified *Brucella melitensis*, which was sensitive to doxycycline and rifampicin. The Brucella agglutination test further confirmed the diagnosis. He was successfully treated with oral doxycycline and rifampicin. This case highlights the importance of considering brucellosis in the differential diagnosis of children with pyrexia of unknown origin.

**Keywords:** *Brucella melitensis*, Brucellosis, Children, Pyrexia of unknown origin

## INTRODUCTION

Paediatric brucellosis was initially believed to be primarily transmitted through direct contact with animals. However, it is now increasingly recognised that animal products, such as milk and meat, also play a significant role in disease transmission. Children with brucellosis commonly present with fever, anorexia, abdominal pain, night sweats, chills and joint pain. The fever often follows a pattern of frequent remissions, earning it the description of 'undulant fever'. Amongst symptoms, fever and arthralgia are the most prevalent. Physical examination may reveal hepatomegaly, splenomegaly and lymphadenopathy. In paediatric cases, brucellosis is frequently associated with osteoarticular complications, neurobrucellosis and cardiac involvement.

While culture remains the gold standard for diagnosis, *Brucella* species are fastidious and slow-growing, with cultures from primary specimens requiring up to 21 days of incubation. Bone marrow culture offers greater sensitivity than blood culture, but its invasive nature must be considered. Serological testing, particularly the agglutination test, serves as a confirmatory diagnostic method.[1] The standard tube agglutination test is regarded as the reference method. *Brucella*-specific agglutination tests detect bacterial antigens through direct agglutination by specific antibodies, identifying immunoglobulin (Ig)M, IgG and IgA classes. IgM antibodies predominate during acute infection but decline within weeks. In cases of relapse, IgG and IgA levels may transiently rise, whereas IgM levels typically do not.[2]

We report a rare case of brucellosis which was confirmed in a child with pyrexia of unknown origin (PUO).

## CASE REPORT

A 10-year 4-month-old boy presented with a 2-month history of intermittent, high-grade fever occurring 2–3 times/day, accompanied by chills, rigors, headache and a burning sensation in the eyes during febrile episodes. He had also experienced a weight loss of 2 kg over the same period. Over the past 10 days, he exhibited decreased oral intake and appetite. There was no history of rash, joint pain, ear pain, sore throat, cough, or burning micturition. In addition, there was no history of contact with tuberculosis patients or exposure to pets. The child was born through an uncomplicated delivery, and his developmental milestones were normal. Before the presentation, he had sought treatment at multiple hospitals and had been administered various antibiotic and antimalarial medications without any relief from his fever.

On examination, he was stable, with normal vital signs. There were no signs of pallor, icterus, cyanosis, clubbing, or lymphadenopathy. Abdominal examination revealed hepatosplenomegaly, with a liver span of 12 cm and the spleen palpable 3 cm below the costal margin. Both organs were firm in consistency, with regular surfaces and smooth borders. The remainder of the systemic examination was unremarkable.

A working diagnosis of PUO was made, and relevant investigations were conducted. The haemogram revealed a haemoglobin level of 10.2 g/dL, a total leucocyte count of 8 × $10^9$/L (neutrophils 55%, lymphocytes 38%) and a platelet count of 243 × $10^9$/L. The peripheral smear showed mild anisopoikilocytosis with microcytic hypochromic red blood cells and occasional pencil forms. The reticulocyte count was 2%. Liver and kidney function tests were within normal limits. Tropical infections, including dengue, malaria, rickettsial infections, enteric fever and retroviral infections, were ruled out. A tuberculosis workup, including chest radiography, the Mantoux test and gastric aspirate testing for cartridge-based nucleic acid amplification test, was negative. Urine cultures showed no significant growth. The erythrocyte sedimentation rate was 30 mm/h, and the C-reactive protein level was 32 mg/L. Abdominal ultrasound revealed hepatosplenomegaly. Blood culture grew *Brucella melitensis*, which was sensitive to doxycycline and rifampicin. Although brucellosis is uncommon in Andhra Pradesh, a *Brucella* agglutination test was performed and yielded a positive result, confirming the diagnosis. The child was started on oral doxycycline and became afebrile within 6 days. He was discharged home on a combination of doxycycline and rifampicin for 6 weeks.

## DISCUSSION

Brucellosis is a significant re-emerging zoonotic disease with a global distribution. It remains a persistent and serious public health concern, particularly in many developing countries, including India. Also known as Mediterranean fever, Malta fever or undulant fever, brucellosis is caused by bacteria of the *Brucella* genus. Amongst these, *B. melitensis* is responsible for the majority of paediatric cases worldwide, with cattle serving as a key reservoir.[1] High-risk groups include farmers, animal handlers and laboratory personnel. Despite its prevalence, brucellosis continues to be a frequently overlooked disease.

Brucellosis evades the host immune system to establish chronic infections, resulting in a broad spectrum of symptoms ranging from fever, fatigue and joint pain to severe complications such as endocarditis and neurological disorders.[3] The incubation period varies from 5 days to 6 months, and in chronic cases, symptoms may persist for months or even years. A thorough dietary and exposure history is crucial for accurate diagnosis, particularly in non-endemic areas where infection may occur through the consumption of contaminated food.[4] Diagnosing paediatric brucellosis can be particularly challenging due to its non-specific clinical presentation.

Brucellosis can be diagnosed using blood culture, serological tests and molecular methods, each with its strengths and limitations. The choice of diagnostic approach depends on the patient's clinical presentation and the resources available.

In cases of acute brucellosis, the pathogen is often detectable within the standard 7-day incubation period, eliminating the need for subcultures. Matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry provides rapid and accurate identification, but its high cost restricts widespread use. Unlike culture and molecular techniques, serological tests detect antibodies against *Brucella* antigens indirectly, identifying IgM and IgG in the patient's serum.[5]

Genomic techniques provide a rapid and precise method for detecting brucellosis in humans; however, they do not always indicate an active infection, as they may identify genetic material from inactive or dead bacteria. The 16S *rRNA* gene serves as a promising diagnostic target, while species-specific real-time polymerase chain reaction assays are employed for classifying *Brucella* species.

Doxycycline and rifampicin remain the primary treatment options for all forms of brucellosis. A 6-week oral regimen of these antibiotics has demonstrated good efficacy in managing uncomplicated cases. However, *Brucella* species have been known to develop resistance to several commonly used antimicrobial agents. At present, no vaccine is available for human brucellosis.[6] Given its multisystem involvement, brucellosis can mimic various other diseases, and misdiagnosis may contribute to increased morbidity.[7]

## CONCLUSION

This case report highlights the importance of recognising brucellosis as a potential cause of PUO in children. Blood

culture and serological testing for *Brucella* should be conducted without delay in all paediatric patients presenting with PUO. Maintaining a high index of suspicion and performing early serological testing are crucial for timely diagnosis and the initiation of appropriate treatment.

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