

Case Report

Beyond the Usual Suspects: Human Brucellosis Presenting with Pyrexia of Unknown Origin: A Case RevisitedRuwanthi Bandara^{1*}, Chamara Sarathchandra²¹Department of Medicine, Faculty of Medicine, University of Peradeniya.²Department of Medicine, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka.**Abstract**

Brucellosis is a bacterial zoonosis, transmitted to humans via close contact with infected animals and consuming contaminated food products. Although bovine brucellosis remains endemic in Sri Lanka, there is a serious lack of data on human brucellosis. However, a study done in Sri Lanka reports an overall seroprevalence of 8.4%.

We report an 18-year-old schoolgirl who presented with a prolonged febrile illness. She gave an occasional exposure to domesticated cattle. The Enzyme-linked Immunosorbent Assay (ELISA) for *Brucella* became positive with a significant titre. She was successfully treated with doxycycline and rifampicin to achieve a complete recovery.

Keywords: Human brucellosis, Pyrexia of unknown origin

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Introduction

Brucellosis is a bacterial zoonosis transmitted to humans via close contact with infected animal secretions, ingestion of contaminated food products, and consumption of unpasteurised milk. It is caused by a gram-negative, non-spore-forming, non-encapsulated intracellular coccobacillus. [1] Annual incidence varies across regions of the world, ranging from fewer than 2 to 500 cases per 1,000,000 persons per year [2]. There are eight species of *Brucella*, and four are known to infect humans. They are *B. melitensis* (sheep), *B. abortus* (cattle), *B. suis* (pigs) and *B. canis* (dogs) [3].

Sri Lanka is an endemic country for bovine brucellosis, with a significantly high prevalence in the North Central, North Western, and Eastern provinces [4]. The overall prevalence of brucellosis in cattle was 4.5-5.5%,

whereas it was 3.5- 4% in buffaloes [4]. Among the domesticated cattle, *B. abortus* is the most frequently reported strain [5]. The epidemiology of human brucellosis in Sri Lanka remains poorly studied. The first suspected case was reported over four decades ago [6]. Since then, only two authenticated cases have been reported from Sri Lanka. A case of epidural abscess caused by *B. melitensis* was reported in 2018 at Teaching Hospital Karapitiya; however, it was likely an imported case, as the patient had worked as a shepherd in Kuwait and consumed raw camel milk [7]. The second case, a 16-year-old girl with indigenously acquired *B. abortus sacroiliitis*, was published in 2023 [8]. However, a 2019 study reports an overall seroprevalence of 8.4% for human brucellosis; the seroprevalence among individuals with no animal contact is 4.0% [9]. These findings suggest that many cases of human *Brucella*

infection remain unreported and possibly underdiagnosed.

We report a case of a schoolgirl with pyrexia of unknown origin with an exposure to domesticated cattle. She was infected with *B. abortus* and seroconverted following treatment. To our knowledge, this is the third confirmed clinical case of human brucellosis in Sri Lanka.

Case report

An 18-year-old schoolgirl from Kurunegala in North-Western province presented with intermittent high-grade fever and chills for one month. She was febrile with high spiking fever, with a temperature of 38.8 °C (102 °F), pulse rate 104/minute, and blood pressure 110/80 mmHg. She was pale, but had no jaundice, lymphadenopathy, organomegaly or skin rashes. Her cardiovascular and respiratory examinations were normal.

Investigations revealed a low haemoglobin (9 g/dl), a low total leukocyte count (4420/mm³), and a platelet count of 198,000/mm³. Blood picture showed a mild hypochromic microcytic anaemia compatible with iron deficiency, and a left shift of neutrophils, suggestive of ongoing infection. Although her serum ferritin level was within the normal range, serum transferrin saturation was low (8.9%), indicating iron deficiency. The normal ferritin level may be explained by its role as an acute-phase reactant; it was low but had risen to a normal level due to inflammation. Blood biochemistry showed a blood urea of 8.4 mg/dl, serum creatinine 0.8 mg/dl, aspartate aminotransferase (AST) 6IU, alanine aminotransferase (ALT) 23IU, albumin/globulin ratio of 1.4, sodium 137 meq/L, potassium 4.2 meq/L. Erythrocyte sedimentation rate (ESR) was 76mm in the 1st hour, and C-reactive protein (CRP) was 58 mg/L. Blood and urine cultures were repeatedly sterile. Blood smear for malaria and Mantoux test were negative. Vasculitis screening was negative. Basic ultrasonic imaging of the abdomen was normal.

There was no clinical, microbiological or echocardiographic evidence of infective endocarditis. Viral panel, including cytomegalovirus (CMV), Epstein-Barr virus (EBV), and retroviral studies, was negative.

Revisiting the history revealed occasional exposure to domestic cattle, although she denied using unpasteurised milk. Brucellosis was considered in the differential diagnosis, and the serological assay for *Brucella abortus* became positive. [Brucella IgM by ELISA 17.72 DU (>11 DU positive) and Brucella IgG

3.88 DU (<9 DU negative)]. This was confirmatory of acute brucellosis. She was started on doxycycline 100 mg twice daily and rifampicin 300mg once daily for six weeks after a consultation with the microbiologist. Patient responded well to treatment, and she remained well and free of complications with a normal CRP level on the sixth-month follow-up.

Discussion

This case represents one of the very few documented cases of human brucellosis in Sri Lanka in recent decades. Despite the known endemicity of bovine brucellosis in several regions of the country, the paucity of reported human cases has contributed to a false sense of security and diagnostic oversight among clinicians. By highlighting this patient's clinical course and diagnostic process, this case serves to raise awareness and emphasise the need for heightened clinical suspicion and improved surveillance of brucellosis in Sri Lanka.

Sri Lanka is an endemic country for bovine brucellosis; however, human brucellosis is rarely reported [4]. Brucellosis is acquired by direct inoculation through cuts, skin abrasions, or conjunctiva, from handling animal tissues or secretions, inhalation of infected aerosols or by ingestion of unpasteurised milk or contaminated meat [10]. Farmers, veterinarians, abattoir workers, and lab personnel are more prone to the infection [11]. A history of travelling to endemic areas, consuming raw milk or meat, or having close contact with a susceptible animal should raise clinical suspicion.

Most of the patients (78%) will present with fever [12]. Untreated brucellosis shows an undulating fever pattern (Fever persists for weeks before an afebrile period, followed by a relapse), which is distinct from most other tropical infections. Fifty per cent of patients will have associated musculoskeletal symptoms, mainly osteomyelitis, septic arthritis and metastatic abscess formation [12]. It can also cause hepatosplenomegaly, pneumonia complicated with empyema and lung abscesses. Ten to twenty per cent develop significant lymphadenopathy. Genito-urinary system involvement manifests as epididymo-orchitis, prostatitis, salpingitis and pyelonephritis. Neurological involvement causes depression, lethargy, lymphocytic meningoencephalitis that mimics neuro-tuberculosis and cerebral abscesses. Endocarditis occurs in 1% of cases [12]. There is an increased incidence of fetal loss and preterm delivery among pregnant mothers with brucellosis, but compared to animals, the tendency is much less pronounced [13].

The diagnosis is guided by clinical suspicion, a history of potential exposure, a presentation consistent with the disease, and supporting laboratory findings (Brucella antibodies [IgM and IgG] or Brucella culture). The combined sensitivity and specificity for both IgM and IgG brucella antibodies by the ELISA method vary considerably, reported to be 92% - 100% and 55% - 84%, respectively [14].

Our patient had above clinical and laboratory parameters for the diagnosis of brucellosis, but she did not have significant organ involvement, possibly due to being diagnosed relatively early.

Treatment goals are to control symptoms and minimise complications. Multi-drug regimens are utilised to reduce the relapse rate, which is common with monotherapy. For non-complicated patients, doxycycline 100mg twice daily with rifampicin 600 – 900 mg per day for six weeks is recommended, with a relapse/failure rate of about 10%. Substituting rifampicin with streptomycin (0.75-1 g daily for 14 to 21 days), together with doxycycline has been shown to reduce the relapse rate to 5-10 % [15]. Triple drug regimen of doxycycline, rifampicin and an aminoglycoside was deemed superior to dual therapy and should be considered in all complicated patients [15-17]. Neurobrucellosis needs prolonged treatment for approximately three to six months, including ceftriaxone supplementation [18]. Before commencement of treatment with rifampicin, tuberculosis must always be excluded. Treatment protocols for brucellosis during pregnancy are controversial, and the data available are inadequate. Prophylaxis is recommended with rifampicin and doxycycline for three weeks after low-risk exposure, and for six weeks after major exposure. Following completion of therapy, the patient should ideally be followed for two years to detect a relapse.

Prevention is achieved through live attenuated vaccines; however, these vaccines are not yet available for humans. The mainstay of prevention is active immunisation of animals, slaughter of infected animals, and pasteurisation of milk before consumption.

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In the current era of superbugs, brucellosis is a neglected zoonotic disease. However, with the looming threat of bioterrorism, brucellosis is regaining importance. Due to its moderately infectious nature via the aerosol route, ease of culture from infected material, ease of transfer, storage, and dissemination, it is an attractive pathogen for use as a potential agent in biological warfare [19]. Therefore, the modern physician should be familiar with the clinical presentation in anticipation of re-emergence.

It is also recommended to survey the status of human brucellosis in the country by analysing notified and suspected cases, and to arrange follow-up to detect relapses early.

Conclusion

This case highlights the importance of considering brucellosis in the differential diagnosis of prolonged fever, even in individuals with only occasional exposure to domesticated animals. Our patient, an 18-year-old schoolgirl with pyrexia of unknown origin, was ultimately diagnosed with *Brucella abortus* infection and achieved complete recovery with the timely initiation of doxycycline and rifampicin therapy. The absence of complications and sustained remission at six months underscores the value of early recognition and treatment. This case also illustrates that human brucellosis may be underdiagnosed in Sri Lanka despite the continued endemicity of bovine infection. Increasing clinical awareness, improving diagnostic access, and strengthening collaboration between human and veterinary health sectors are essential steps toward early detection and prevention of similar cases in the future.

CREDIT statement

Ruwanthi Bandara: investigation, patient management, conceptualisation, writing original draft; Chamara Sarathchandra: patient management, validation, writing: reviewing and editing.

Consent

The patient and her mother gave informed written consent for publication.

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