

## Case Report

# Brucellosis: the First Case of King Chulalongkorn Memorial Hospital and Review of the Literature

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*Brucellosis remains a major zoonotic disease worldwide. It has never been reported at King Chulalongkorn Memorial Hospital (KCMH). The authors describe the first case of brucellosis in KCMH, and also review all previous reports in Thailand. The presented case was a 52-year-old Thai man, living in Phetchabun Province, who was diagnosed with idiopathic pulmonary fibrosis two years prior to admission. He presented with prolonged fever, dry cough, weight loss of eight kg over three months, hepatosplenomegaly, and pancytopenia. Blood and bone marrow cultures grew *Brucella melitensis* at 72 hours of incubation. A slide agglutination (Rose Bengal) test was also positive for *Brucella* antibody. He had been exposed to contaminated placenta of his goats that had spontaneous abortion in the past few months before his illness. The patient was successfully treated with gentamicin, doxycycline, and rifampicin. Clinicians should have a high index of suspicion when evaluating patients presenting with prolonged fever and having an exposure risk of brucellosis.*

**Keywords:** *Brucellosis, Brucella melitensis, Zoonosis, Prolonged fever*

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Brucellosis remains a major zoonotic disease worldwide especially in the Mediterranean region, the Middle East, and Latin America<sup>(1-4)</sup>. It can be caused by any of the four species of *Brucella* (B); *B. melitensis* can be acquired from goats, sheep, and camels, *B. abortus* from cattle, *B. suis* from hogs, and *B. canis* from dogs. Brucellae are small, non-motile, non-spore-forming, facultative intracellular Gram-negative coccobacilli. Brucellosis is a systemic disease with protean manifestations. It can be categorized into acute, subacute, or chronic disease depending on the clinical course.

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Transmission to humans occurs through the consumption of infected, non-pasteurized animal milk products, through direct contact with contaminated animal parts, and through the inhalation of infected aerosolized particles. After entering the human body, the bacteria will be taken up by local tissue lymphocytes, transferred to regional lymph nodes into the circulation, and subsequently disseminated throughout the body.

Brucellosis has never been reported at King Chulalongkorn Memorial Hospital (KCMH). The authors describe the first case of brucellosis in KCMH and also review all previous reports in Thailand.

### Case Report

A 52-year-old Thai man, living in Phetchabun Province, was hospitalized at KCMH due to fever, dry

cough, and weight loss of eight kg for three months. He was diagnosed with Idiopathic Pulmonary Fibrosis (IPF) two years Prior To Admission (PTA), and was treated with several courses of antibiotics. After diagnosis of IPF at KCMH, he had received oral prednisolone 30 mg and cyclophosphamide 50 mg daily for one month, and discontinued them because of clinical improvement. Three months PTA, he had fever, dry cough, and myalgia. Six weeks PTA, he had epigastric pain and anorexia. He denied having been abroad, and had not been taking any traditional or herbal medications. He did not drink but smoked occasionally. He had no history of tuberculosis contact. He owned a tamarind orchard and a farm of goats, sheep, and cows.

Physical examination revealed a body temperature of 38.1 °C, a pulse rate of 120/minute, a respiratory rate of 24/minute, and a blood pressure of 120/70 mm Hg. The patient was chronically ill. Lymphadenopathy and skin lesions were absent. There were fine crackles of both lungs. Abdominal examination revealed mild-to-moderate hepatosplenomegaly without ascites. Neurologic examination was unremarkable.

A Complete Blood Count (CBC) showed a hematocrit of 36.2%, white blood cell count of 2,970/mm<sup>3</sup> (54% neutrophils, 37% lymphocytes, and 9% monocytes), and a platelet count of 26,000/mm<sup>3</sup>. Liver function test showed a total bilirubin of 1.83 mg/dL, alkaline phosphatase of 317 U/L (42-121), aspartate transaminase of 92 U/L (4-36), alanine transaminase of 46 U/L (4-36), albumin of 3.3 g/dL, and lactate dehydrogenase of 1,020 U/L (100-190). Anti-HIV antibody was negative. Other blood chemistry tests were normal.

Chest radiography showed diffuse reticular infiltrations of both lungs. Abdominal Computed Tomography (CT) revealed hepatosplenomegaly with a few tiny hypodensity lesions within the spleen. No microorganisms were seen on Acid-Fast-Bacilli (AFB)- and modified AFB-stained smears of the sputum. The bone marrow biopsy was performed, and showed normal cellularity with focal aggregation of histiocytes, a few non-caseous granulomata, and rare hemophagocytosis.

Two blood and bone marrow cultures performed by the automated system (BACTEC) subsequently grew Gram-negative coccobacilli at 72 hours of incubation. The organism was identified later to be *Brucella melitensis* by the standard laboratory procedures<sup>(5)</sup>. A serologic test for *Brucella* antibody was performed at the National Institute of Animal Health, Department of Livestock Development, Ministry of Agriculture and Cooperatives, and was positive by a slide agglutination (Rose Bengal) test. After a thorough review of his

history, he had been exposed to the contaminated placenta of his goats that had spontaneous abortion in the past few months before his present illness. The patient was thus treated with gentamicin 240 mg, doxycycline 200 mg, and rifampicin 600 mg daily. The fever subsided after seven days of treatment, and he was discharged home with doxycycline and rifampicin. He was followed up at the outpatient department and was seen for the last time after one month with marked clinical improvement and normal CBC.

## Discussion

Brucellosis is considered a rare disease in Thailand. To the authors' knowledge, only six cases have been reported since 1970 (Table 1)<sup>(6-8)</sup>. The first case was reported in 1970 by Visudhiphan and Nananakorn at Siriraj Hospital<sup>(6)</sup>. The patient was a 34-year-old Thai male farmer from Rayong Province. He had a 15-month fever, chills, marked hepatosplenomegaly, and pancytopenia. Blood and bone marrow cultures grew *B. melitensis*. He was successfully treated with tetracycline 2 g daily for six weeks. The fever subsided on the fourth day of treatment. The second and third cases were reported in 2004 by Manosuthi et al at Ramathibodi Hospital<sup>(7)</sup>. The second case was a 52-year-old Thai man from Kanchanaburi Province. He had a 2-month fever, chills, weight loss, low-back pain, and mild hepatosplenomegaly. He had a history of consumption of non-pasteurized goat milk one month prior to his illness. Blood cultures grew *B. melitensis*. He was successfully treated with doxycycline 200 mg, gentamicin 240 mg, and ciprofloxacin 1,000 mg daily. The fever subsided on the fifth day of treatment. The third case was a 37-year-old male architect from Bangkok. He had a 2-month fever and painful submandibular and occipital lymphadenopathy. He had consumed goat milk one month prior to his illness. Blood cultures grew *B. melitensis*. He was successfully treated with doxycycline 200 mg and rifampicin 600 mg daily for six weeks. The fever subsided on the fifth day of treatment. The fourth, fifth, and sixth cases were reported in 2004 by Chiewcharnyon et al<sup>(8)</sup>. They worked as workers in a goat farm in Satun Province, and had prolonged fever, chills, and generalized myalgia for two months. One of these three cases had a scrotal swelling. Blood cultures did not grow *Brucella*, but *Brucella* antibody was positive by tube and slide agglutination tests, ELISA, and complement fixation test. All were treated with doxycycline 200 mg and rifampicin 600 mg daily for six weeks.

Brucellosis causes nonspecific symptoms and protean clinical manifestations which make it difficult

**Table 1.** A summary of seven cases of brucellosis melitensis in Thailand

No	Year	Hospital	Age(y), sex	Occupation	Province	Risk	Clinical manifestations	Laboratory confirmation	Treatment	Outcome
1 <sup>(6)</sup>	1970	SH	34, M	Farmer	Rayong	NA	15-month fever, hepatosplenomegaly, pancytopenia	Blood and BM cultures	Tetracycline, 6 weeks	Survived
2 <sup>(7)</sup>	2004	RH	52, M	NA	Kanchana-buri	Drank goat milk	2-month fever, low-back pain, hepatosplenomegaly,	Blood cultures	Doxycycline, gentamicin, ciprofloxacin	Survived
3 <sup>(7)</sup>	2004	RH	37, M	Architect	Bangkok	Drank goat milk	2-month fever, lymphadenopathy	Blood cultures	Doxycycline, rifampicin, 6 weeks	Survived
4 <sup>(8)</sup>	2004	-	NA, M	Farm worker	Satun	Contacted contaminated goat parts	2-month fever	Serology	Doxycycline, rifampicin, 6 weeks	Survived
5 <sup>(8)</sup>	2004	-	NA, M	Farm worker	Satun	Contacted contaminated goat parts	2-month fever	Serology	Doxycycline, rifampicin, 6 weeks	Survived
6 <sup>(8)</sup>	2004	-	NA, M	Farm worker	Satun	Contacted contaminated goat parts	2-month fever, scrotal swelling	Serology	Doxycycline, rifampicin, 6 weeks	Survived
7*	2005	KCMH	52, M	Farmer	Phetchabun	Contacted contaminated goat parts	3-month fever, hepatosplenomegaly, pancytopenia	Blood cultures, serology	Doxycycline, rifampicin, gentamicin, 4 months	Survived

BM: bone marrow, KCMH: King Chulalongkorn Memorial Hospital, RH: Ramathibodi Hospital, SH: Siriraj Hospital, M: male, NA: not available

\*Present study

to make a diagnosis. Hematologic complications are common in brucellosis<sup>(9-11)</sup>. Anemia, leukopenia, thrombocytopenia, and coagulopathy can be present, like in our patient who presented with pancytopenia. One possible explanation, which is probably similar to other chronic granulomatous infectious diseases, is due to an interference of bone marrow function by a granulomatous infiltration that is observed in up to 75 percent of cases. Other explanations may include hemophagocytosis, hypersplenism, immune-mediated cell destruction, or chronic disseminated intravascular coagulation.

Respiratory manifestations are rarely observed in brucellosis<sup>(3,12)</sup>. A recent multinational review of cases indicated that approximately 16 percent of cases had pulmonary involvement including alveolar or interstitial infiltrations and pleural effusions<sup>(12)</sup>. The presented patient was diagnosed IPF two years PTA, and was in complete remission despite one month of treatment with prednisolone and cyclophosphamide. This clinical course is unusual for patients with IPF who usually have a more aggressive course. The authors wonder if his clinical manifestations in accordance with diffuse interstitial lung infiltrations might be caused by brucellosis which probably responded to antibiotics and immunosuppressive agents. A careful evaluation of pulmonary symptoms and signs as well as an imaging study after a completion of treatment of brucellosis may confirm, the authors' postulation.

Splenic and hepatic enlargement can be present in 15 to 20 percent of cases<sup>(1-4)</sup>, and abscess may develop in the liver or the spleen, as observed in the presented patient.

Even though the mortality rate is low (approximately 5 percent of untreated cases), untreated or inadequately treated infection can cause debilitating chronic disease involving almost every organ and system<sup>(1-4,13)</sup>. All seven cases of brucellosis in Thailand were successfully treated with tetracycline or doxycycline for at least six weeks, alone or in combination with rifampicin, gentamicin, or ciprofloxacin. However, no long-term follow-up was reported in any case report or series. The relapse rate of brucellosis is unacceptably high especially in cases with monotherapy because *Brucella*, like *Mycobacterium tuberculosis*, is an intracellular bacteria.

Brucellosis has been increasingly reported in humans in the past few years in Thailand. A field epidemiological survey in goats, conducted in Ratchaburi Province in 2003 by the Ministry of Public Health, reported 247 of 365 (67.7%) goat blood samples were

positive for antibody for *Brucella*<sup>(14)</sup>. Animal brucellosis is responsible for enormous economic losses as well as considerable human morbidity since goat milk is gaining more popularity. A control of brucellosis needs practical solutions. Inexpensive, simple, and rapid tests are required to identify and eliminate infected animals. Preventive measures, including education to farmers or workers of better sanitation especially during contact with contaminated animal parts as well as education to the public on consumption of only sterilized or pasteurized milk, should be implemented as soon as possible. Clinicians should have a high index of suspicion when evaluating patients presenting with prolonged fever and having an exposure risk of brucellosis.

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### โรค布鲁เซลโลซิส ผู้ป่วยรายแรกในโรงพยาบาลจุฬาลงกรณ์

เลลานี ไพฑูรย์พงษ์, มนยา เอกทัตร์, ผ่องพรรณ นันทากิสุทธิ, ธีระพงษ์ ตันทวิเชียร, ชุษณา สวณกระต่าย

โรค布鲁เซลโลซิสเป็นโรคติดเชื้อจากสัตว์ที่สำคัญทั่วโลก ไม่เคยมีรายงานโรคนี้ในโรงพยาบาลจุฬาลงกรณ์ รายงานนี้จึงถือเป็นผู้ป่วยรายแรกของโรงพยาบาลจุฬาลงกรณ์ และยังทบทวนรายงานผู้ป่วยทั้งหมดในประเทศไทย ในรายงานนี้เป็นผู้ป่วยชายไทย อายุ 52 ปี อยู่ที่จังหวัดเพชรบูรณ์ เคยได้รับการวินิจฉัยผิดเป็นพังผืดชนิดไม่ทราบสาเหตุ 2 ปี ก่อนมาโรงพยาบาล ผู้ป่วยมาพบแพทย์ด้วยไข้เรื้อรัง ไอแห้ง ๆ น้ำหนักลด 8 กิโลกรัม มา 3 เดือน ตับและม้ามโต และ pancytopenia ผลเพาะเชื้อจากเลือดและไขกระดูกขึ้นเชื้อ *Brucella melitensis* หลังทิ้งไว้ 72 ชั่วโมง ผลการทดสอบแอนติบอดีต่อ *Brucella* ได้ผลบวกโดยวิธี slide agglutination หรือวิธี Rose Bengal ผู้ป่วยมีประวัติสัมผัสสัตว์ของแพะที่แท่งขณะตั้งครอกในช่วง 2-3 เดือนก่อนการป่วย ผู้ป่วยตอบสนองต่อการรักษาด้วย gentamicin, doxycycline และ rifampicin แพทย์ควรสงสัยเป็นอย่างสูงในผู้ป่วยที่มาพบด้วยไข้เรื้อรังและมีปัจจัยเสี่ยงของการเกิดโรค布鲁เซลโลซิส