

Brucellosis as an Emerging Disease in Thailand: A Report of Three Cases with Review of Literatures

Samruam Danprachankul*

Bongkot Chiewchanyont**

Hatsadee Appassakij***

Khachornsakdi Silpajakul****

*Satun Province Public Health Office, Satun, **Zone 12 Center for Disease Control, Songkla.

Department of Pathology and *Department of Medicine; Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkla

Abstract Human brucellosis, an important zoonosis, had been virtually absent from Thailand for decades before reemerging in 2003 with only 3 published reports. In this study, three additional cases of Thai brucellosis were reported with additional review and summary of all the 38 cases, 35 of whom occurred during the last 5 years and coincided with the implementation of the government policy to promote goat rearing. This reaffirms that brucellosis is an emerging disease in Thailand. Almost all of the patients were adults while only two were children. Most patients presented with prolonged fever with musculoskeletal symptoms and were diagnosed by serologic means. The blood culture was positive for *Brucella* spp. in 12 (31.6%) of 38 cases, half of which were identified as *Brucella melitensis*. The disease usually occurred in small clusters and was occupationally related to goat rearing. Only one patient contracted the disease from sheep. Acquisition of the disease usually followed caprine abortion outbreaks and manual evacuation of infected goat fetuses and/or placenta with unprotected hands was the most important risk factor. Only 3 (7.9%) of patients admitted of ever drinking raw goat milk. Most responded to treatment with antibiotics which consisted mainly of doxycycline and/or rifampicin and/or ciprofloxacin. Physicians should be aware of the possibility of brucellosis in patients who presents with prolonged fever and musculoskeletal symptoms and should inquire about history of occupational risk factors. In addition farmers should be warned about the dangers of contacting with infected animals and trained on hygienic practices in rearing goats.

Key words: brucellosis, Thailand, goats, transmission, placenta

Introduction

Brucellosis, a zoonosis of worldwide importance has been known to exist for at least 2000 years⁽¹⁾ In

animals, the disease affects mainly the genitourinary system leading to abortion causing enormous economic losses.⁽²⁾ Human brucellosis, however, is char-

acterized mainly by fever with more protean manifestations in many organ systems⁽³⁾. The disease, although endemic in the Mediterranean, Middle East and African countries, has been a reemerging disease, reappearing even in industrialized countries^(4, 5). Human brucellosis, a notifiable disease in Thailand, has been considered a rare disease in the country where the first case was reported in 1970⁽⁶⁾. No additional cases were found until 33 years later when two milk-borne brucellosis patients were identified in 2003. Hereby were reported other 3 cases with a comprehensive review of all 35 cases appearing since 2003 reaffirming that brucellosis is a reemerging disease in Thailand.

Cases of brucellosis in Songklanagarind Hospital were identified from log book of the Division of Serology which began to perform the *Brucella* agglutination and the *Brucella* ELISA assays since 2003. Criteria for diagnosis of brucellosis are either the presence of *Brucella* agglutinins \geq 1:160 (sensitivity and specificity = 1.00) and/or *Brucella* IgG or IgM antibody titers \geq 1:1600 and \geq 1:400, respectively (sensitivity and specificity=0.98).^(8,9) Medical charts of patients who had such diagnostic *Brucella* antibody titers were reviewed. Pertinent history, physical signs, symptoms and related- outbreak investigation results were extracted and described in the cases reports section.

In literature review, the databases of the MEDLINE, the Thai Index Medicus (<http://library.md.chula.ac.th>) and the Thailand Weekly Epidemiological Surveillance Report of the National Bureau of Epidemiology, Ministry of Public Health (<http://203.157.15.4>) for cases of Thai brucellosis were covered, using the search terms: brucellosis, Thailand, goat, sheep and outbreak.. Cases identified through these search were reviewed regarding diagnostic methods, demographic data, the year and the province of occurrence, the clinical manifestations, and the reported risk factors of acquisition of the disease.

These cases were tabulated and summarized as separated table.

Cases Report

Case 1 : In March 2004, a 31 year old Thai male farmer from Satun, a province in southern Thailand (figure 1), had intermittent low grade fever for 2 weeks before he developed some macular rash on his chest, right knee arthralgia and right scrotal swelling (orchitis). He went to a community hospital where he received a 3-day course treatment with oral ciprofloxacin. His skin rash and orchitis subsided. However low grade fever persisted with night sweats and palpitation. In May 2004, night fever recurred together with scrotal swelling, this time in the left side. He took 600 mg rifampicin and 200 mg doxycycline daily as suggested by his relatives before being referred to Songklanagarind Hospital 4 days later. Physical examination revealed high (39.7°C) fever and orchitis of the left scrotum. Complete blood count (CBC) was unremarkable. The results of urinalysis and liver function tests were within normal limits. Blood and urine cultures were negative. His serum was 4+ reactive on screening by Rose Bengal test. Further *Brucella* tube agglutination and the IgM, IgG *Brucella* ELISA antibody assays were positive at titers of 1:200, 1:400, and 1:800, respectively (Table 1). These serologic tests revealed diagnostic results of brucellosis^(8,9). He was treated with 1,000 mg. oral ciprofloxacin, doxycycline (200 mg) and rifampicin (600 mg) daily for 6 weeks. The fever and orchitis gradually subsided after several days of treatment. He fully recovered upon follow up 3 months later.

The patient owned a goat farm. In September 2003, an unusually high numbers of abortion and / or mastitis occurred among goats in his farm. This caprine outbreak continued until January 2004 when 50 of the 200 female goats were affected. The patient frequently engaged in assisting the goats during par-

turition. He frequently used ungloved hands removing the goat fetuses and the retained placentas. He also reported having hand injury from a rope during one incident of manipulating these animals.

Case 2 : During mid March 2004, this 33 years old male, co-owner of the same goat farm, developed fever, with chills, myalgia, diffused arthralgia and backache. He took some unknown medicines purchased from a local drug store for 10 days before all of his symptoms subsided. This patient also assisted his partner during manual evacuation of the goat fetuses and the retained placentas. He reported rare use of hand gloves which frequently were torn in these maneuvers. Physical examinations at Songklanagarind Hospital, 2 weeks after defervescence, were unremarkable. However, Brucella agglutination and ELISA antibody assays were indicative of recent Brucella infection (Table 1). He received the same 6 week medications as in case 1. He remained asymptomatic upon follow up 3 months later.

Case 3 : This 18 years old male had been working in this goat farm for a year. His main job was to attend the pregnant goats and assisted the animals during delivery which he always did by bare hands. He also nursed the baby calves and cleaned their frequently ulcerated mouths.

Beginning in April 2004, he developed chronic fever with chills, severe myalgia with pain in the hip, and the knees. He also had some productive cough and reported having some diarrhea. During the subsequent 6 weeks, he went to a local hospital 7 - 8 times and received some medications for a presumed diagnosis of influenza. However, the symptoms persisted and his boss gave him rifampicin and doxycycline which he took for 4 days before being referred to Songklanagarind Hospital. He felt much better and physical examinations at the hospital revealed only a thin and chronically ill adult without fever and abnormal signs. Routine laboratory tests were normal in-

cluding the chest roentgenogram. However, both the Brucella tube agglutinins and ELISA antibody tests were diagnostic of brucellosis (Table 1). He received an additional 6-week course of oral ciprofloxacin, doxycycline and rifampicin and did not have any relapse of the disease upon follow up 3 months later.

Further investigations of the caprine abortion outbreak in this farm by veterinarians from Satun Province Livestocks Office revealed 180 of 560 goats test-positive by Rose Bengal slide agglutination assays. All these Brucella infected animals were neither serological screened nor vaccinated before admittance into the farm. Due to difficulty in controlling the caprine outbreak and the serious consequences for human health imposed by the infected animals, the veterinarians decided to eliminate all the animals in the farm. In addition, all 7 other persons working and or living within the farm underwent a full clinical and serological investigation. Only one worker had history of fever during the preceding 6 months. However, all these 7 persons were tested negative by the Brucella ELISA assays of their sera drawn twice, 2 weeks apart. Only one of these brucellosis - negative workers had history of ever performing manual evacuation of the goat placenta. However, he had quitted doing so during the preceding 3 months. The association between brucellosis and history of handling infected goat fetuses and placentas was statistically significant ($p = 0.033$, Fisher's exact test). All of the workers in the farm, including the three patients denied consumption of goat milk.

Review of human brucellosis in Thailand

Through the databases of the MEDLINE, the Thai Index Medicus (<http://library.md.chula.ac.th>) and the Thailand Weekly Epidemiological Surveillance Report of the National Bureau of Epidemiology, Ministry of Public Health (<http://203.157.15.4>), a total of 38 Thai patients with brucellosis (including the 3 cases

reported above) were compiled. These were summarized in Table 2.

Almost all of the patients were adults. Only two were children^(15,18) and men outnumbered female by 29 to 9. One pregnant patient⁽¹³⁾ had spontaneous abortion during her illness. All except one patient were farmers and/or goatherds. Only one patient contracted the disease from sheep⁽¹⁶⁾ and the risk for *Brucella* infection was not mentioned in another patient⁽⁶⁾. All of the rest acquired the disease from goats, and usually, following caprine abortion outbreaks^(7,10-15,17,18). Presence of *Brucella* infection in the goats were documented in most of these outbreaks.^(7,11-12,15,18) Manual evacuation of goat fetuses and/or placenta with unprotected hands were mentioned as a major risk factor for acquiring brucellosis in 19 (50%) patients. History of milking goats were reported by 7 (18.4%) patients. Only 3 (7.9%) patients admitted of ever drinking raw goat milk^(2,14) while 6 (15.8%) professed of goat placenta consumption⁽¹⁵⁾. Although most of the patients had history of prolonged fever with musculoskeletal symptoms, most responded to treatment with antibiotics which consisted mainly of doxycycline and/or rifampicin and/or ciprofloxacin. Except for five patients of whom the outcomes were not mentioned in the reports, all the others survived.

Discussion

The reviewed patients presented with prolonged fever and musculoskeletal symptoms - characteristic of brucellosis⁽¹⁻³⁾. The durations of fever were over a month in the patients and in many of the cases compiled in Table 2. It was even as long as 15 months in the first case report of brucellosis in Thailand⁽⁶⁾. One of the patients also had orchitis. Although this physical finding may be a clue leading towards a diagnosis of brucellosis⁽¹⁹⁾, it was present in only 3 (7.9%) of the patients (Table 2). The first patient also had rash, an infrequent manifestation of brucellosis⁽²⁰⁾, illustrating

the occasional protean presentation of this disease.

The three patients, like the majority of cases of brucellosis in Thailand (Table 2), were diagnosed by serologic means. Their blood cultures were negative for *Brucella* organisms. This is not surprising in the presence of history of receiving antibiotics prior to culture⁽²⁾. The yield of blood cultures to diagnose brucellosis has been reported to range from 15 - 80 percent^(1,2), of which the lower figure usually occurs in the setting of chronic form of brucellosis⁽⁹⁾. In Thailand, the blood culture was positive for *Brucella* spp. in 12 (31.6%) of 38 cases reported (Table 2). The organism were further identified as *Brucella melitensis* in half of these isolates (Table 2). Although, it is controversial as to whether this species is the most virulent among *Brucella* organisms, *B. melitensis* is the most prevalent etiologic agent of brucellosis worldwide and is associated with either goats, sheep or camels^(1,2,5). Only one patient in Table 2 contracted the disease from sheep and, except for another patient of whom the risk was not mentioned, all the other case reports of human brucellosis in Thailand were associated with goats (Table 2). This disease in Thailand is an occupational infection. The patients were either rural farmers and/or goatherds in close contacts with infected animals. Only one incidence of infection was not occupational - related and occurred in a Bangkokian architect who drank unpasteurized goat milk bought from Ratchaburi Province⁽⁷⁾. Table 2 also showed that Thai human brucellosis usually occurred in small clusters following caprine abortion outbreaks^(7,10-15,17,18) and unprotected manual evacuation of goat fetuses and placenta was the most reported mode of acquisition of the disease in Thailand. Human outbreaks attributed to handling such infected tissues and/or secretions have been rarely reported.^(21,22) This is in sharp contrast with the indirect transmission through the consumption of unpasteurized goat dairy products, which is the most common reported

cause of brucellosis outbreaks worldwide^(1,2,5). Only 3 (7.9%) of patients in Table 2 admitted of ever drank raw goat milk. This low rate of goat milk consumption and the fact that human brucellosis in Thailand is an occupationally - acquired, might explain the uncommon occurrence of brucellosis in Thai children in Table 2. However, eventhough milk-borne brucellosis might play a minor role in brucellosis transmission in Thailand, consumption of goat placenta was mentioned as a risk factor with an odds ratio of 10.8 (95% CI, 1.8-72.9) in a small outbreak of brucellosis in Uttraradit Province⁽¹⁵⁾. Further study on this unusual route of transmission is needed.

From Table 2, it can be seen that human brucellosis had been virtually absent from Thailand for decades before reappearing in 2003 with a striking increase in number of patients during the recent 5 years. Goats also emerged as important reservoirs. This coincided with the implementation of the government policy to promote goat rearing as a profitable livestock to supplement household income for the marginal farmers (One farm - One village Policy)^(11,12). Because goats can be reared in dry lands unsuitable for other types of livestock and need very low maintenance cost in rearing the registered number of goats in Thailand increased from 177,944 in 2002 to 444,744 in 2007, a 2.5 fold increase⁽²³⁾. It was estimated that, in 2007, at least 38,653 Thai households were involved in goat rearing, either as domestic animals or as a small farming⁽²⁴⁾. Goat rearing in Thailand is no longer confined to the Muslim communities in the southern provinces and, in 2007, only one of 76 provinces in the whole Kingdom reported that there is no goat in their province.⁽²⁴⁾ It is also evident that the three provinces (Kanchanaburi, Nakhon Sawan and Prachuap Khiri Khan)⁽¹⁵⁻¹⁸⁾ that had the most recent (2007-2008) outbreaks of human and/or caprine brucellosis are non-southern and also are among the top five provinces that have the largest numbers of goats in the coun-

try⁽²⁴⁾. Brucellosis has become a serious public health threat for Thailand. Eventhough the present low rate of consumption of goat milk and milk products of the people in Thailand may account for the low incidence of the disease, goat milk, promoted as health food, is gaining more popularity among certain groups of people. In addition, goat placenta products were also advertised for use as cosmetics. People should be educated about the dangers of consumption of raw goat milk and milk products. In addition, since there is no human vaccine for brucellosis and the occurrence of brucellosis is directly linked to the status of animal brucellosis, active co-operation between health and veterinary services is crucial that farmers should be warned about the dangers of contact with infected animals and training of hygienic practices in rearing goats is urgently needed.

Conclusion

Brucellosis is reemerging in Thailand. Physicians should be aware of the possibility of brucellosis in patients who presents with prolonged fever and musculoskeletal symptoms and should inquire about history of occupational risk factors. In addition farmers should be warned about the dangers of contacting with infected animals and trained on hygienic practices in rearing goats.

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บทคัดย่อ โรค布鲁เซลโลซิสในประเทศไทย

สำรวม ด่านประชันกุล*, บงกช เขียวชาญยนต์**, หัสดี อภากาศกิจ***, ขจรศักดิ์ ศิลปโภชากุล****

*สำนักงานสาธารณสุขจังหวัดสตูล, **สำนักควบคุมโรคที่ 12 สงขลา, ***ภาควิชาพยาธิวิทยา,

****ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์, หาดใหญ่ สงขลา

วารสารวิชาการสาธารณสุข 2552; 18:643-9.

โรค布鲁เซลโลซิสในคน นับว่าเป็นโรคติดต่อจากสัตว์สู่คนที่สำคัญโรคหนึ่ง โรคนี้ไม่พบในประเทศไทยมานาน ก่อนที่จะพบโรคนี้เมื่อ พ.ศ. 2546 มีรายงานโรคนี้ในวารสารภาษาอังกฤษเพียง 3 รายงานเท่านั้น รายงานฉบับนี้นำเสนอการพบโรค布鲁เซลโลซิสในคนรายใหม่ 3 ราย และทบทวนรายงานโรค布鲁เซลโลซิสในคนไทยทั้งหมด 38 ราย โดยเป็นผู้ป่วยจำนวน 35 ราย ในระยะเวลา 5 ปีที่ผ่านมา ซึ่งเป็นช่วงระยะเวลาที่รัฐบาลมีนโยบายส่งเสริมการเลี้ยงแพะสำหรับเกษตรกร เป็นการยืนยันว่าโรค布鲁เซลโลซิสในคนเป็นโรคอุบัติซ้ำเกิดขึ้นในประเทศไทย ผู้ป่วยส่วนใหญ่เป็นผู้ใหญ่ พบในเด็กเพียง 2 ราย ส่วนใหญ่มาด้วยอาการไข้ระยะเวลานานหลายวันร่วมกับอาการปวดเมื่อยตามกล้ามเนื้อและข้อ การวินิจฉัยโรคทำโดยการตรวจทางซีโรโลยี การเพาะเชื้อจากเลือดพบ *Brucella* spp. 12(31.6%) รายจาก 38 ราย โดยครึ่งหนึ่งพบว่าเป็นเชื้อ *Brucella melitensis* ลักษณะการเกิดโรคมักเกิดเป็นกลุ่มเล็ก ๆ ในเกษตรกรที่มีอาชีพเลี้ยงแพะ มีเพียงรายเดียวที่ติดโรคจากแกะ ลักษณะของโรค布鲁เซลโลซิสมักเกิดภายหลังจากมีโรคแท้งระบาดในแพะ และผู้ดูแลสัตว์เลี้ยงจับซากลูกสัตว์และรกสัตว์ด้วยมือเปล่า ซึ่งเป็นปัจจัยเสี่ยงที่สำคัญที่สุดของโรคนี้ มีผู้ป่วยเพียง 3 ราย (7.9%) ที่มีประวัติคัมมนแพะดิบ การรักษาส่วนใหญ่ได้ผลตอบสนองดีกับยาปฏิชีวนะ doxycycline และ/หรือ rifampicin และ/หรือ ciprofloxacin แพทย์ผู้ดูแลผู้ป่วยพึงตระหนักถึงโรค布鲁เซลโลซิสในผู้ป่วยที่มีอาการไข้นาน และมีอาการปวดกล้ามเนื้อและข้อร่วมด้วย โดยควรซักประวัติเกี่ยวกับอาชีพเสี่ยง และเตือนเกษตรกรผู้เลี้ยงสัตว์ถึงอันตรายจากการสัมผัสกับสัตว์ที่แท้งลูกหรือติดโรค และควรมีการอบรมการเลี้ยงแพะอย่างถูกสุขลักษณะโดยเร่งด่วน

คำสำคัญ: โรค布鲁เซลโลซิส, ประเทศไทย, แพะ, การติดต่อ, รก