Case Report: Outbreak of Human Brucellosis from Consumption of Raw Goats' Milk in Penang, Malaysia

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Abstract. We report the largest outbreak of brucellosis in Penang, Malaysia. Brucellosis is not endemic in this region. The index case was a 45-year-old goat farm owner presented with 3 weeks of fever, headache, severe lethargy, poor appetite, and excessive sweating. He claimed to have consumed unpasteurized goat's milk that he had also sold to the public. Tests were negative for tropical diseases (i.e., dengue fever, malaria, leptospirosis and scrub typhus) and blood culture showed no growth. Based on epidemiological clues, *Brucella* serology was ordered and returned positive. Over a period of 1 year, 79 patients who had consumed milk bought from the same farm were diagnosed with brucellosis. Two of these patients were workers on the farm. Four laboratory staff had also contracted the disease presumably through handling of the blood samples. The mean duration from onset of symptoms to diagnosis was 53 days with a maximum duration of 210 days. A combination treatment of rifampin and doxycycline for 6 weeks was the first line of treatment in 90.5% of patients. One-third of the patients had sequelae after recovering and 21% had a relapse. We highlight the importance of Brucellosis as a differential diagnosis when a patient has unexplained chronic fever.

INTRODUCTION

About half a million cases of human brucellosis occur around the world each year.¹ The principal causing organism worldwide is *Brucella melitensis*, a species of *Brucella* found in sheep and goats. It is the most pathogenic and invasive species followed by *B. suis*, *B. abortus*, and *B. canis*. *Brucella* is a nonmotile, non-encapsulated, facultative intracellular, Gram-negative coccobacillus.²

Human brucellosis is commonly found in countries with rural communities that live in close association with animals, and its prevalence in a region depends on factors such as methods of processing milk and milk products, food habits, socioeconomic status, hygiene, and climate. Endemic in countries in the Mediterranean basin, the Arabian Gulf, the Indian subcontinent and parts of Mexico and Central and South America, this zoonotic disease is predominantly transmitted to humans through ingestion of unpasteurized milk of infected animals and dairy products prepared from such milk. It can also be transmitted through direct contact with fluids and carcasses of infected animals, consumption of its undercooked meat, and through inhalation of airborne infectious particles. These organisms can survive for long periods in dust, dung, water, slurry, soil, aborted fetuses, meat, and dairy products.³

The clinical features of brucellosis are nonspecific and depends on the stage of the disease and the organs and systems involved.⁴ The most commonly reported symptoms are undulating fever, fatigue, malaise, chills, sweats, which may be characterized by a peculiar odor at night, insomnia, headaches, myalgia, arthralgia, anorexia, weight loss, and hepatosplenomegaly.^{1,4} Without the critical epidemiological clue of exposure to animals, consumption of unpasteurized dairy products, or travel to endemic countries, this disease can pose a great diagnostic challenge to the clinician.

Although human brucellosis is rarely fatal, it can be severely debilitating and incapacitating. It can also manifest again after

a long period of quiescence. A man in the United States had a recurrence of brucellosis, which presented as septic shock 50 years after his first infection,⁵ whereas in a separate case, a former abattoir worker was diagnosed with brucellosis 18 years after his known exposure to the risk factors.⁶

Brucellosis can also manifest as a localized disease, affecting the central and peripheral nervous system, and the gastrointestinal, hepatobiliary, genitourinary, musculoskeletal, cardiovascular, and integumentary systems.⁴ Osteoarticular manifestations, specifically peripheral arthritis, sacroiliitis, and spondylitis, are the most frequent complications, occurring in up to 40% of cases in some series.² Although *Brucella* endocarditis is rare, it is the most serious complication, accounting for most of the 5% total mortality rate seen in human brucellosis.⁴

CASE REPORT

An outbreak of brucellosis occurred in Penang, an island on the west coast of Peninsular Malaysia from March 2011 to March 2012. The index case was a 45-year-old goat farm owner who presented to Penang General Hospital with a 3-week history of fever, headache, severe lethargy, poor appetite, and excessive sweating. He owned more than 300 goats and sold its raw, unpasteurized milk to the public. He had also been consuming the raw milk on a daily basis for several months.

Initially, he was investigated for tropical diseases, that is, dengue fever, malaria, leptospirosis, and scrub typhus, but the tests returned negative. Blood culture isolated no pathogen. Based on the history of raw milk consumption, a *Brucella* serology test was ordered. The particle agglutination test for *Brucella* was strongly positive. He was started on oral doxycycline and rifampicin. His fever eventually subsided and he was discharged well.

Following this, another 83 patients presenting with prolonged fever and nonspecific constitutional symptoms were diagnosed with brucellosis. We were able to retrieve 63 patient notes. Two of the patients were workers on the farm. We were not able to confirm if they had contracted the disease through animal contact or consumption of the raw milk. All but four of the other patients had consumed milk bought from the

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same farm. The four patients were hospital laboratory staff who had presumably contracted the disease during handling of the blood samples.

Diagnoses were confirmed using serology (87.3%), blood culture (69.8%), polymerase chain reaction (17.5%), or tissue culture tests (1.6%). *Brucella* enzyme-linked immunosorbent assay (ELISA) immunoglobulin M (IgM) and IgG kits from Viracell (Granada, Spain) were used for detection of antibodies against *Brucella*.

The patients had a mean age of 44 years and more than half (57.0%) of them were males. The mean duration from onset of symptoms to diagnosis was 53 days with a maximum duration of 210 days. The most commonly presenting symptom was fever, followed by fatigue, arthralgia, myalgia, low-back pain, and night sweats. Almost half (47.6%) of the patients had anemia and 12.7% had raised alanine transaminase.

Three patients had spondylitis, whereas another two males developed orchitis. A man was admitted to the Cardiology Department for infective endocarditis and his blood culture subsequently isolated *Brucella*. Unfortunately, he was lost to follow up after receiving treatment. Majority (88.6%) of the patients had systemic illness.

Almost all (90.5%) patients received a combination of oral rifampicin (600 mg daily) and doxycycline (100 mg twice daily) and were on treatment of 6 weeks.⁷ If they had localized disease, they were prescribed the oral regimen as above plus intramuscular streptomycin (1 gm daily).⁸ Some patients were put on trimethoprim-sulfamethoxazole (160/800 mg BD) plus doxycycline.⁷

Of the patients, 41% recovered fully, whereas 21% had a relapse that necessitated another course of oral treatment plus intramuscular streptomycin. Another one-third of the patients recovered but had sequelae, which included difficulty in walking and pain because of osteomyelitis or discitis from spinal infections.

DISCUSSION

This is the largest reported cohort of human brucellosis in Malaysia thus far, demonstrating potential sporadic outbreaks in non-endemic countries. A recent study on the prevalence of *Brucella melitensis* in goats from years 2000 to 2009 showed that the infection has not been fully eradicated in the country yet.⁹ Malaysia has routine serosurveillance performed by the Department of Veterinary Services (DVS) as part of its strategy to eradicate the disease in ruminants and to achieve a disease free status by year 2015.¹⁰

Despite efforts by DVS, several isolated cases of human brucellosis have been reported in the literature involving farmers, veterinarians,¹¹ and laboratory staff.^{12,13} The occurrence of the disease is still low, however, as a study from 2004 to 2009 only found 10 (5.4%) of 184 suspected brucellosis cases to be seropositive.¹¹ Still, the true incidence of the disease could be higher as its nonspecific symptoms usually causes it to be underreported.

There was a long interval between onset of symptoms and diagnosis in our cohort. Patients with consistent symptoms and who claimed to have consumed milk from the farm were tested for brucellosis. Without this important epidemiological clue, diagnosis could have been delayed even longer.

Many claimed they were seen by different doctors, subjected to numerous blood tests, and prescribed antibiotics, antipy-

retics, and analgesics before presenting to the hospital. This demonstrates that a lot of health-care practitioners do not consider the possibility of brucellosis especially in patients with prolonged fever. Delay or misdiagnosis can result in treatment failure, relapses, chronic courses, focal complications, and a high case fatality rate.¹⁴ A study in a small series of patients in northern Australia found the odds of developing complications in a patient with delayed diagnosis to increase by a factor of 26.6.¹⁵ This could explain the fact that less than half of our patients recovered fully. The other patients either had a relapse or a sequelae, which could cause significant distress and financial strain especially when their work is affected. Patients with spondylitis developed long-term sequelae, which required them to attend extensive periods of physiotherapy and rehabilitation. Patients who had localized disease experienced a more complicated course of disease, had to endure more invasive diagnostic tests, and some required modifications to their treatment regimens, increasing their exposure to adverse events from these medications.

Failure to consider brucellosis early can also lead to unintended exposure of laboratory staff to the pathogen. Transmission is usually through inhalation of aerosol particles generated while manipulating the organism in the laboratory. With as little as 10 bacteria required to infect a mice through the respiratory route, it is considered highly infectious when inhaled,¹⁴ making it the most common laboratory-acquired infection.¹⁶ After the first few positive samples, we labeled subsequent samples as suspected brucellosis cases. However, four laboratory staff contracted the disease, presumably during the handling of the specimens. They were given the standard treatment of rifampicin plus doxycycline but two of them developed gastrointestinal symptoms to the medications. The staffs had to go on medical leave for a considerable period and this impacted the work force in the laboratory. The healthy staffs were not given prophylaxis treatment.

Majority of the patients were treated on an outpatient basis with oral medication. Those who had localized disease were given parenteral treatment on top of the oral medications. Many of these patients also opted for daily injections in an outpatient clinic. Most of the patients were compliant but 8% were lost to follow up. The goats owned by the man were culled in accordance to the Brucellosis Eradication Program under DVS.

CONCLUSION

Diagnosis of brucellosis is generally not considered in a non-endemic country. Health-care practitioners should be aware of the possibilities of this zoonotic infection and include brucellosis as a differential diagnosis in patients with nonspecific symptoms and unexplained prolonged fever.

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