รายงานผู้ป่วย

โรคบรูเซลโลสิส รายงานผู้ป่วย 4 ราย ในโรงพยาบาลพระปกเกล้า

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บทคัดย่อ

บรูเซลโลสิสเป็นโรคในสัตว์โรคหนึ่งที่สามารถติดต่อสู่คน การกินผลิตภัณฑ์จากนมของสัตว์ที่ติดเชื้อ การสัมผัสโดยตรงกับตัวสัตว์ที่ติดเชื้อโดยเฉพาะส่วนรก และการหายใจจากอากาศที่ปนเปื้อน เป็นสาเหตุหลักของการติดต่อ บรูเซลโลสิสเป็นโรคติดเชื้อทั่วร่างกายที่มีอาการแสดงหลากหลาย ผู้เขียนนำเสนอผู้ป่วยติดเชื้อบรูเซลโลสิส 4 รายในโรงพยาบาลพระปกเกล้า โดยผู้ป่วยสามรายมีอาการที่ไม่ค่อยพบในประเทศไทย คือ ผู้ป่วยมีไข้เรื้อรังและสงสัยติดเชื้อที่ลิ้นหัวใจเทียม 1 ราย ผู้ป่วยเส้นเลือดสมองตีบจากการอุดตันของหลอดเลือดสมองและการติดเชื้อที่ลิ้นหัวใจ 1 ราย และผู้ป่วยที่มีไข้เรื้อรังและสงสัยติดเชื้อจากการทำงานในห้องปฏิบัติการจุลชีววิทยา 1 ราย ผู้ป่วยทั้งหมด 4 ราย ตอบสนองต่อการรักษาอย่างดีต่อยาดอกซีไซคลินและยาไรแฟมพิซิน

คำสำคัญ: บรูเซลโลสิส; ติดเชื้อที่ลิ้นหัวใจ; ติดเชื้อจากการทำงานในห้องปฏิบัติการ

Literature Interview

Brucellosis, Four Case Series in Prapokklao Hospital

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Abstract

Brucellosis is one of the zoonotic disease that can transmit to humans. Consumption of infected animal milk products, direct contact with infected animal parts especially placenta and inhalation of infected aerosol particles are the main cause of transmission. It is a systemic infection with protean manifestations. We present the four cases of brucellosis in Prapokklao Hospital (PPKH). The three cases with uncommon presentation in Thailand; one case with prolonged fever and suspected prosthetic valve infective endocarditis, one case with embolic stroke and native valve infective endocarditis and one case with prolonged fever and suspected laboratory acquired infection are included. All of them had good response with doxycycline and rifampicin.

Keywords: brucellosis; infective endocarditis; laboratory acquired infection

Brucellosis, four case series in Prapokklao Hospital

Brucellosis is one of the zoonotic disease that can transmission to humans. In the past, brucellosis was known as “Undulant fever”, “Mediterranean fever” or “Malta fever” and was reported during 17th-19th century.[1] Until late 19th century, it was discovered that human was infected from ingested goat milk.[2] Brucella is small, facultative intracellular gram-negative coccobacilli. It usually cause orchitis, epididymitis, mastitis and abortion in domesticated livestock. Recently, at least eight species of brucella are identified in different animal hosts: Brucella abortus (cattle), Brucella canis (dogs), Brucella melitensis (goats, sheep), Brucella neotomae (desert wood rats), Brucella ovis (sheep), Brucella suis (pigs, reindeer and hares) and two brucella strains from marine mammals.[3] Consumption of infected animal milk products, direct contact with infected animal part especially placenta and inhalation of infected aerosol particles are reported worldwide for human brucellosis.[3]

Brucellosis is a systemic infection with protean manifestations. It usually present with fever, chills, loss of appetite, weight loss, myalgia, joint and back pain.[1] We present the four cases of brucellosis in Prapokklao Hospital (PPKH). The three cases with uncommon presentation in Thailand, one case with prolong fever and suspected prosthesis valve infective endocarditis, one case with embolic stroke and native valve infective endocarditis and one case with prolong fever and suspected laboratory acquired infection are included.

Case I

A 65-year old Thai female patient presented with fever for 6 days. She had type II diabetes mellitus and rheumatic heart disease (RHD) status post mitral valve replacement (S/P MVR). Serial four bottles of blood culture grew unidentified gram negative diplococci which were finally identified Paracoccus yeeii. Ultrasound abdomen showed hepatomegaly. Echocardiogram found no evidence of infective endocarditis. She was treated with ceftriaxone for 25 days and doxycycline for 7 days. Next 6 months, she was admitted due to prolong fever for 4 months. Physical examination showed pale conjunctiva, no icteric sclera, normal valve click and hepatosplenomegaly. Blood culture grew Pseudomonas aeruginosa. She was received ceftazidime for 4 weeks. Four months later, she had recurrent fever and was admitted at PPKH. Serial four bottles of blood culture grew unidentified gram negative rod and was sent for further identification at Department of Clinical Microbiology, King Chulalongkorn Memorial Hospital. Echocardiogram showed suspected a small mitral valve vegetation. Finally, Brucella melitensis was identified and was confirmed with culture and polymerase

chain reaction (PCR) from the National Institute of Animal Health, Department of Livestock Development, Ministry of Agriculture and Cooperatives. Past history was reviewed and found that she was goatherd. All of her twenty one goat died during her illness. She was treated with doxycycline and rifampicin for 7 months with clinical improvement. However she was readmitted later with clinically suspected valve dehiscence and was transferred to medical school hospital.

Case II

A 50-year old man presented with headache for 1 day. Two hour prior to admission, his family found he looked stupor and had left side weakness. He had history of smoking and drinking for 20 years. Physical examination showed systolic ejection murmur grade III, left facial palsy (upper motor neuron) and weakness of left side. CT brain found the large cerebral infarction at the right side. Echocardiogram found the oscillating mass 9 millimeter at anterior mitral valve leaflet with severe mitral stenosis and moderate mitral regurgitation. Craniectomy was done after admission for two days. Serial of six bottles of blood culture grew gram negative rod. He was treated with ceftriaxone 2 grams intravenous once daily. After three weeks of ceftriaxone treatment, he was readmitted for cranioplasty and hemoculture was finally identified Brucella abortus. His treatment was adjusted to rifampicin and doxycycline for 7 months. After that echocardiogram was followed up and found no oscillating mass. He had an elective mitral valve replacement with 3M ball valve 2 month later without complication. He had regular followed up until 3 years later without any problem. Past history was reviewed and found that it had goat raising near his workplace. He denied for ate milk goat or direct contacted with goat.

Case III

A 50 year old woman presented with fever and stupor for 12 days. General physical examination shown unremarkable. She had underlying alcoholic cirrhosis. Her first blood culture grew Pseudomonas spp. She was treated with ceftriaxone, however her fever did not declined. Chest X ray, abdominal fluid tapping and lumbar puncture were done. All of the tests were normal study. Other serial hemoculture grew unidentified gram negative rod, which were finally identified Brucella melitensis. She denied contact goat or consume milk goat or product of milk goat. Her illness was cured after treatment with rifampicin and doxycycline for 6 weeks.

Case IV

A 51 year old woman, laboratory technician in microbiology unit of PPKH, presented with prolonged fever, weight lose 2 kilograms and no other organ specific symptom.

Her blood culture grew Brucella melitensis. Before her illness she contacted with her illed dog and denied consume milk goat or product of milk goat. She had exposure of brucella during identified hemoculture of the third patient about 2-3 months before her illness. The catalase test was done in the open laboratory bench. She was treated with rifampicin and doxycycline for 6 weeks without relapsed of fever. Both serum of the laboratory technician and the third patient were further investigated at the National Institute of Animal Health, Department of Livestock Development, Ministry of Agriculture and Cooperatives. Monospecific serum A&M identified Brucella melitensis biovar 3 for both serum.

Human brucellosis has been reported worldwide. In Thailand, the first case was reported in 1970 by Visudhiphan and Na-Nakorn at Siriraj Hospital.[4] The patient was a 34 year old Thai male farmer from Rayong Province with prolong fever, chills, marked hepatosplenomegaly and pancytopenia. His blood and bone marrow culture grew Brucella melitensis. He was successfully treated with tetracycline 2 grams daily for six weeks. The second and third cases were reported in 2004 by Manosuthi et al at Ramathibodi Hospital.[5] Both patients had history of drinking contaminated milk goat. Since 2003, Goat farming has substantially increased in Thailand as a result of government's agricultural policies for increase income in farmer.[6] Animal brucellosis were found throughout Thailand and the majority cases from 2003 to 2009 were reported from Nakhon Si Thammarat and Kanchanaburi Provinces.[7] From 2003 to 2009, 121 human cases of brucellosis were reported to the Bureau of Epidemiology (BOE), Ministry of Public Health, Thailand, including three deaths from 16 provinces.[7] The first phase of outbreak occurred from consumption of contaminated milk goat and direct contact with infected animal part especially placenta.[5, 8-10] The later phase, until in 2016, Weekly Epidemiological Surveillance report still reported human brucellosis, mainly from direct contact with infected animal part in unregistered goat farm.[11-15] A few data also reported laboratory acquired brucellosis from aerosol contamination in the laboratory room.[16-19] A catalase test, which may generate aerosols, usually do in the open laboratory bench. In our laboratory room, it was done in the open laboratory bench too. Exposure the aerosols during routine identification activities is our hypothesis for brucella infection in our laboratory staff. Serum of the third patient and our staff were further identified. Monospecific serum A&M identified Brucella melitensis biovar 3 for both serum (Table 1). The safety measurement in laboratory acquired infection should be convinced. Any procedures is known to produce aerosols should be minimized or conducted in biosafety cabinets.

Table 1. Summary data of four case series

Patient NO	Year	Age(y), sex	Province	Risk	Underlying disease	Clinical manifestations	Laboratory confirmation *
1	2006	65, F	Chanthaburi	Direct contact illed goat	RHD S/P MVR DM II	Intermittent prolong fever bl-*Paracoccus yeeii* bl-*Pseudomonas aeruginosa*	Blood culture, PCR *B. Melitensis*
2	2007	44, M	Sa Kaeo	Indirect contact goat	Severe MS c mod. MR	Acute headache with alteration of consciousness CT brain : large cerebral infarction	Blood culture *B.abortus*
3	2008	51, F	Rayong	No	Alcoholic cirrhosis	Prolong fever bl-*Pseudomonas spp.*	Blood culture, *B.Melitensis* Monospecific serum A & M *B. Melitensis* biovar 3
4	2008	44, F	Chanthaburi	Laboratory worker	No	Prolong fever	Blood culture, *B.Melitensis* Monospecific serum A & M *B. Melitensis* biovar 3

In animals, brucellosis mainly cause orchitis, infertile, abortion and mastitis which lead to contamination in milk goat.[1-2] For humans, it mainly cause nonspecific symptoms such as prolong fever, chill, fatigue, myalgia, arthralgia and weight loss. Common complication that has been reported is the osteoarticular infection, while the reproductive infection is less found. The previous report is found only orchitis.[13] Brucella endocarditis is another uncommon complication. However, it has been reported worldwide except in Thailand.[20-27] We reported the two cases of brucella endocarditis. The first case was delayed diagnosis due to misidentified the organism. She had strong history of contact with illed goat. It was reviewed after known the causative organism. The second case presented with embolic stroke from infective endocarditis. He denied for direct contact with goat or ate goat milk. However, it had goat raising near his workplace. We presumed that goat raising may caused aerosols and led to the environmental contamination.

Recommendation for treatment of brucellosis is a combination of antibiotic that can penetrate macrophages and can act in the acidic intracellular environment.[28] The two most popular regimen are doxycycline plus rifampicin for 6 weeks and doxycycline 6 weeks plus streptomycin 2-3 weeks.[1, 28, 29] The streptomycin containing regimen is slightly more efficacious in preventing relapse. However, parenteral administration and renal toxicity from streptomycin are the limitation for treatment. All of our four patients were treated with doxycycline plus rifampicin. The third and fourth cases without complication were treated for 6 weeks. The first and second cases with brucella endocarditis were treated for 7 months. In the second case, after complete medical treatment and complete resolution of

oscillating mass from echocardiogram, elective mitral valve replacement was operated two months later without relapse. Early report of the brucella endocarditis found that medical and surgical treatment were needed.[22-23, 26] Delayed identification of the true pathogen and prolonged clinical course which caused complication such as refractory heart failure led to the emergency operation. Common regimens for brucella endocarditis therapy are the combination of parenteral aminoglycoside and doxycycline/tetracycline and rifampicin or cotrimoxazole.[1, 29] Prolonged therapy is recommended at least eight weeks.[1] Indication for valve replacement is not well defined. Recent data for brucella endocarditis therapy had reported successful treatment with both medical therapy 6 weeks through 6 months plus elective surgery and medical therapy alone 6 weeks through 1 year.[20-21, 25, 27, 30-31] In 2012, the literature review found that different in antibiotic regimens were not significantly associated with mortality.[24]

Goat farming is found in all regions of Thailand. Proactive measurement for prevent brucellosis infection in animal such as education program, vaccination and registration of all goat farm are needed for reduced human brucellosis. Differential diagnosis of fever of unknown origin in Thailand should include the brucellosis. Increase accuracy and rapidity for brucella Identification in the laboratory room should be implemented in microbiology training program.

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