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사람 브루셀라증 진단을 위한 배양 검사의 중요성

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Importance of Culture for Diagnosing Human Brucellosis

Human brucellosis is a newly emerging infectious disease in Korea, and the number of the patients with this disease has rapidly increased in recent years. To evaluate the most reliable method in diagnosing human brucellosis, a retrospective study was conducted. Medical records of patients admitted or followed-up at the outpatient department of a tertiary care university hospital during the past 5 years were reviewed. Among a total of 32 human brucellosis patients (24 males and 8 females), 21 (65.6%) were positive for standard tube agglutination test (STA) but negative for blood or bone marrow culture, 7 (21.9%) were positive for both STA and culture, and 4 (12.5%) were STA negative but culture positive. Based on these findings, we recommend that physicians include blood and/or bone marrow culture to obtain definitive diagnosis when clinical symptoms and signs strongly suggest the human brucellosis, even when STA is negative.

Key Words: Brucellosis, Standard tube agglutination, Culture

Brucellosis is a major zoonosis in humans and domestic animals, particularly in the Mediterranean region, Western Asia, and a part of Africa and Latin America [1, 2]. The first case of human brucellosis in Korea was reported in 1939. The patient was a Japanese livestock worker living in Seoul who was infected with *Brucella abortus*. No additional clinical cases of human brucellosis have been reported until 2001, after which its number has rapidly increased to become one of serious public health problems.

Although confirmation of brucellosis requires isolation of the bacterium from the blood or tissue samples [3], several serologic tests have been developed to facilitate the diagnosis of human brucellosis: standard tube agglutination test (STA), anti-human globulin test, indirect fluorescence antibody test, and enzyme-linked immunosorbent assay. The most frequently applied method to diagnose human brucellosis is serologic screening with STA. STA titer above 1:160 in conjunction with a compatible clinical presentation is considered to be diagnostic [3, 4]. The sensitivity of blood culture varies depending on individual laboratory practices and how actively blood culture is pursued. Since the positive blood culture rate of *B. abortus* ranges from 15% to 70% [5], most diagnosis of

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human brucellosis has been done by STA, not by culturing blood or bone marrow, in Korea. However, we have experienced 4 cases of STA negative human brucellosis that were diagnosed by culturing blood or bone marrow in patients with compatible clinical manifestations. This finding prompted us to perform a retrospective study to investigate the most reliable method for diagnosing human brucellosis. Therefore, medical records of patients with human brucellosis who were admitted or followed-up at the outpatient department of a 1,050-bed tertiary care university affiliated hospital in Jeonju, Korea, from February 2003 to September 2007 were reviewed. Patients' serologic antibody titers obtained from STA and the results of blood and/or bone marrow cultures were evaluated.

Human brucellosis is defined as a case that presents with compatible clinical findings, is epidemiologically linked to contact with suspected/confirmed animals or contaminated animal products, and shows positive results on laboratory tests (STA ≥1:160 or culture positivity). STA was performed at Jeollabuk-do Institute of Health and Environmental Research. And the bacteriological identification of *Brucella* species was carried out at the Division of Zoonoses, Center for Immunology and Pathology, National Institute of Health, Seoul, Korea.

There were a total of 32 human brucellosis patients (24 men and 8 women), and their median age was 46 years old. As for the occupation, 29 (90.7%) were livestock workers, 1 (3.1%) a veterinarian, 1 (3.1%) an inseminator, and the remaining 1 (3.1%) a student. The student's father was a livestock worker who also had human brucellosis (Table 1).

Among a total of 32 patients, 11 (34.4%) were *Brucella* positive in blood or bone marrow cultures and 28 (87.5%) were STA positive. Further analysis showed that 21 (65.6%) were positive for STA but negative for blood or bone marrow culture, 7 (21.9%) were positive for both STA and culture, and 4 (12.5%) were STA negative but culture positive (Table 1).

Table 1. Demographic Features of Cases with Brucellosis at Chonbuk National University Hospital from 2003 to 2007

Sex	
Male/Female	24 (75%)/8 (25%)
Age (median, year)	46
Occupation	
Livestock worker	29 (90.7%)
Veterinarian	1 (3.1%)
Inseminator	1 (3.1%)
Student	1 (3.1%)
Diagnostic method	
Culture (+)/STA (+)	7 (21.9%)
Culture (+)/STA (-)	4 (12.5%)
Culture (-)/STA (+)	21 (65.6%)

STA, standard tube agglutination assay.

In 4 patients who were culture positive for *Brucella* but negative for STA, they presented with clinical symptoms such as fever, chills, fatigue, arthralgia, and myalgia; *B. abortus* was cultured from the blood in two patients and from the bone marrow in the remaining two patients (Table 2). Among the aforementioned four cases that only showed culture positivity, the first case was a livestock worker who presented with definite clinical manifestations compatible with human brucellosis but whose STA titer was 1:80. Her blood culture was positive, and *B. abortus* was the causative organism. The second case was a livestock worker as well, who also showed clinical manifestations compatible with human brucellosis but had STA titer of 1:80. In this patient, however, blood culture was negative and the diagnosis of human brucellosis by *B. abortus* could only be made after subsequent bone marrow culture. The third case was a high school teenage girl whose parents were livestock workers; her father was diagnosed with human brucellosis and was treated for 8 weeks. She had clinical manifestations compatible with human brucellosis but her STA titer was negative (1:40). Repeated blood cultures were all negative, and only after bone marrow culture could infection by *B. abortus* be diagnosed. The fourth case was a dog handler. There was no epidemiological linkage with bovine brucellosis in this case but human brucellosis was suspected because he had several clinical manifestations compatible with the disease. Although his STA titer was within normal range (<1:20), blood culture was positive for *B. abortus* and thus, could be diagnosed as human brucellosis.

According to our retrospective review, the false negative result of STA was 12.5%. This result suggests that more than 10% of human brucellosis could be missed when tested only serologically.

In this study, we found that among patients who had <1:80 antibody titer with STA, some were later diagnosed with human brucellosis based on the results from blood or bone marrow culture. Therefore, when a patient presents with compatible clinical symptoms for brucellosis and there is high suspicion of epidemiologic association, it could be recommended that blood/

Table 2. Brucellosis Culture Positive Cases with Negative STA

Case	Age (year)/sex	Occupation	SAT	Site	Symptoms
1	38/F	Livestock worker	1:80	Blood	Fever, chill, fatigue, headache, anorexia, arthralgia
2	46/M	Livestock worker	1:80	BM	Fever, chill, fatigue
3	14/F	Student	1:40	BM	Fever, back pain, abdominal pain, arthralgia, headache, nausea
4	52/M	Dog handler	1:20	Blood	Fever, chill, myalgia

STA, standard tube agglutination test; BM, bone marrow.

bone marrow culture be performed, even in the presence of negative STA, to obtain a reliable diagnosis of human brucellosis.

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