LETTER TO THE EDITOR / EDİTÖRE MEKTUP

DOI: 10.4274/mjima.2018.32
Mediterr J Infect Microb Antimicrob 2018;7:32
Erişim: http://dx.doi.org/10.4274/mjima.2018.32

Two Cases of Laboratory-acquired Brucellosis

Laboratuvar Kaynaklı İki Bruselloz Olgusu

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Keywords: *Brucella*, laboratory infection, biosafety cabinet, education, prevention

Anahtar Kelimeler: *Brucella*, laboratuvar enfeksiyonu, biyogüvenlik kabini, eğitim, korunma

Dear Editor,

Brucellosis is a zoonotic disease that is transmitted to humans by infected animals or contaminated animal products. It is caused by *Brucella* species. *Brucella abortus, Brucella melitensis*, and *Brucella suis* are frequently identified as the causative agents in humans[1,2]. *Brucella* spp. can be easily aerosolized and the infective dose is quite low, in the 10-100 range[2,3]. *Brucella* spp. are responsible for 2% of laboratory-acquired infections, and actions/events that pose a risk of transmission to workers include sniffing bacteriological cultures, direct contact with broken skin, mouth pipetting, and sprays/splashes into the eyes/nose/mouth during inoculation[1-4]. Herein, we present two cases of laboratory-acquired brucellosis that occurred as a result of direct contact with or inhalation of blood culture isolates.

A 26-year-old female patient working in a microbiology laboratory was admitted to the Infectious Diseases outpatient clinic with complaints of fever, joint pain, and fatigue for the last three days. On initial examination, her body temperature was 38 °C, blood pressure was 120/80 mmHg, and heart rate was 88/min. No pathological findings were noted in her physical examination. Results of laboratory testing were leukocyte count: 5,230/mm^3 (neutrophil, 60.7%), platelet count: 309,000/uL, aspartate aminotransferase (AST): 34 U/L, alanine aminotransferase (ALT): 45 U/L, urea: 19.3 mg/dL, creatine: 0.85 mg/dL, sedimentation rate: 8 mm/h, and C-reactive protein: 1.75 mg/dL (N<0.8). The patient reported that she had been working in her current position for six months and did not have adequate experience in bacteriology. She also stated that there had been significant *Brucella* spp. growth in blood cultures within the past month and that she conducted bacteriological examination on an open bench outside the biosafety cabinet by sniffing and without using personal protective equipment. Based on this history, she was tested for brucellosis. Other than laboratory exposure, the patient had no history of eating fresh cheese or working with livestock. Rose Bengal test was positive and Brucella Coombs gel test (ODAK *Brucella* Coombs gel test, Toprak Medikal, İstanbul) showed a titer of 1/640. Gram-negative coccobacilli growth in her blood culture was identified as a *Brucella* spp. by conventional techniques. She was diagnosed with laboratory-acquired brucellosis and was administered oral doxycycline 100 mg twice daily and rifampicin 600 mg once daily for six weeks. No recurrence was observed during post-treatment follow-up.

The second patient was a 35-year-old female patient who had worked in the microbiology laboratory for 10 years. She presented to the outpatient clinic after her colleague was diagnosed with laboratory-acquired brucellosis. She reported no complaints in her history other than joint pain and fatigue.

Cite this article as: Sayar Sefa M, Bulut D, Haykır Solay A. Two Cases of Laboratory-acquired Brucellosis. Mediterr J Infect Microb Antimicrob. 2018;7:32.

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Received/Geliş Tarihi: 15.05.2018 **Accepted/Kabul Tarihi:** 19.10.2018

Presented in: Susesi Congress Center, Antalya between 8th and 13th May 2018 as an e-poster (7th EKMUD Congress of Turkey).

Published: 23 October 2018

Her temperature was 36.5 °C, blood pressure was 110/70 mmHg, and heart rate was 78/min. Laboratory testing showed leukocyte count: 6,680/mm^3 (neutrophil, 60%), platelet count: 161,000/uL, AST: 31.7 U/L, ALT: 43 U/L, urea: 26.6 mg/dL, creatinine: 0.73 mg/dL, erythrocyte sedimentation rate: 13 mm/h, and C-reactive protein: 0.54 mg/dL. Rose Bengal test was positive and *Brucella* Coombs gel test (ODAK *Brucella* Coombs gel test, Toprak Medikal, İstanbul) resulted in a titer of 1/160. The patient did not report any history of eating fresh cheese or working with livestock. Blood cultures performed to support a diagnosis of brucellosis yielded Gram-negative coccobacilli. The isolate was identified as a *Brucella* spp. by conventional techniques. She was treated with oral doxycycline 100 mg twice a day and 600 mg rifampicin once daily for six weeks. No recurrence was observed during post-treatment follow-up.

Brucellosis, caused by *Brucella* spp., is transmitted to humans through direct contact with the blood/aborted fetus/uterine secretions/placenta of infected animals and consumption of raw/non-pasteurized infected milk/dairy products[5]. *Brucella infections pose* a low risk for the general community but cause high-risk in terms of transmission to laboratory workers. It is included in risk group 3 in the microorganism risk classification of the World Health Organization[6]. Reported infection attack rates in the laboratory setting are between 30-100%, depending on personnel location and bacterial load[7,8]. Studies investigating the development of laboratory-acquired brucellosis in laboratory personnel have reported widely varying rates such as 5.8%, 11.9%, and 43%[3,7,9]. After two cases of laboratory-acquired brucellosis occurred in our hospital, the other 10 laboratory workers were subjected to *Brucella* screening with serological tests. Other than the two cases reported, no additional cases were detected (overall 16.6%).

Breakage of blood culture bottles or centrifuge tubes is responsible for 20% of laboratory-acquired infections. However, other factors and behaviors that increase the risk of bacterial transmission include lack of experience on the part of the technician identifying *Brucella* isolates, careless examination of unidentified samples sent for analysis, inappropriate laboratory practices such as sniffing cultures and using open benches that do not meet biosafety level 3 requirements while working with *Brucella* isolates, not using personal protective equipment such as gloves, goggles, and masks, and practicing mouth pipetting. We determined that no reported laboratory accident preceded these cases. However, the first patient's history included factors such as significant *Brucella* growth in blood cultures within the past month, inadequate experience in morphologic bacterial identification, and performing microbial identification on an open bench by sniffing, without the use of appropriate personal protective equipment in the laboratory. Despite being more experienced than the first patient, the second patient admitted were also doing the same wrong practices. Although both patients had received the requisite training in laboratory protection measures, their failure to adopt correct behaviors resulted in their infection.

A 2008 report from the Centers for Disease Control and Prevention (CDC) included a risk stratification for laboratory personnel exposed to *Brucella*[3]. According to this classification, high-risk exposure encompasses any person who handles a *Brucella* isolate in a class-2 biosafety cabinet without biosafety level 3 measures, who is within a five-foot radius of an open bench on which these activities are carried out, and all persons present in the laboratory during aerosol-generating events (e.g., centrifuging without sealed carriers, spills or splashes, and tube breakage)[3]. Low-risk was defined as all persons who are further than five feet from someone handling a *Brucella* isolate, without exposure to the high-risk scenarios described above[3,4]. There is minimal risk of transmission to laboratory personnel when *Brucella* isolates are handled with biosafety level 3 measures in a class-2 biosafety cabinet[3]. Traxler et al.[3] reported that of 1724 laboratory personnel, 153 were exposed to *Brucella* spp. (49% of which were high-risk) and that only 0.3% of them developed laboratory-acquired brucellosis. Fiori et al.[8] reported that in personnel follow-ups conducted after laboratory accidents occurring in an experimental microbiology laboratory in Italy, 12 laboratory personnel working in various parts of the laboratory were serologically diagnosed with brucellosis (31% attack rate). The patients presented here handled *Brucella* isolates on an open bench, outside a biosafety cabinet, and were therefore evaluated as having had "high-risk exposure" based on the CDC risk classification.

In conclusion, microbiology laboratories are high-risk environments for the transmission of microbes. The main cause of almost all laboratory exposures that result in infection seems to be the "human factor"[10]. Every laboratory must have clear, concise, and easily accessible written procedures for the use of personal protective equipment, disinfection of equipment and contaminated materials, collection and processing of samples, waste handling, and cleaning spills and splashes[6]. Many laboratory-acquired infections may be prevented with the appropriate use of protective measures[10]. The cases presented here emphasize the importance of personal protective equipment and biosafety cabinet use among laboratory personnel and the need to suspect laboratory-acquired infections when laboratory personnel present to outpatient clinics.

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.S.S., D.B., Concept: M.S.S., D.B., Design: M.S.S., A.H.S., Data Collection or Processing: M.S.S., D.B., Analysis or Interpretation: D.B., A.H.S., Literature Search: A.H.S., M.S.S., D.B., Writing: M.S.S., A.H.S.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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