Brucella melitensis Infection Following Military Duty in Iraq

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Impacts

- Undiagnosed brucellosis can lead to delayed treatment and ongoing symptoms.
- Active military personnel may seek medical care in civilian facilities. Healthcare providers should be aware of diseases that are less prevalent in the US, but common in the Middle East and other areas of active duty in those with relevant travel history to prevent delayed treatment.
- Clinical laboratory workers can be exposed to Brucella through improper laboratory procedures. Laboratories should handle specimens and unidentified cultures with appropriate caution and use personal protective equipment to minimize risk.

Introduction

Brucellosis (undulant fever or Malta fever) is a common zoonotic disease worldwide (Pappas et al., 2006a,b). However, the incidence in the United States is <0.5 cases per 100 000 population; 100–200 cases are reported annually to US public health officials (Centers for Disease Control and Prevention, 2009). Brucella spp. are environmentally stable gram-negative cocccobacilli, which are transmitted through numerous routes including direct animal or environmental contact, consumption of raw or poorly cooked animal products, and aerosol (Pappas et al., 2005, 2006a,b). Additionally, Brucella spp. are classified as category B biodefense agents and possible bioterrorism agents (Pappas et al., 2006a,b).

Brucella abortus, Brucella melitensis, Brucella suis and Brucella canis are recognized human pathogens with distinct animal reservoirs of cattle, sheep and goats, swine and dogs respectively (Pappas et al., 2006a,b). Illness in animals, notably livestock, often manifests as abortions or other reproductive problems. Brucellosis is typically a febrile illness with non-specific symptoms, but can cause localized effects in certain organ systems (Dahouk et al., 2007). The incubation period for human brucellosis infections varies from 5 days to 5 months (typically 2–3 weeks). Clinical symptoms vary widely from patient...
to patient but most commonly include recurring (undulant) fever, night sweats, malaise, sleeplessness, arthralgias, headaches and neuropsychiatric symptoms (Glynn and Lynn, 2008).

Brucellosis in the US is primarily due to *B. melitensis* infection acquired via consumption of high-risk foods or travel outside the US to endemic areas (Glynn and Lynn, 2008). Consideration and diagnosis of brucellosis by clinicians, especially in non-endemic regions like the US, can be delayed. *Brucella*’s tendency to evade host defence mechanisms can lead to the characteristic waxing and waning, atypical, or non-specific clinical signs, while the persistence of antibodies sometimes makes interpretation of serology difficult (Queipo-Ortuno et al., 2008). Delays in diagnosis and treatment can lead to substantial clinical complications (Noviello et al., 2004). *Brucella* spp. grow slowly, and culture techniques can present risks to laboratory personnel (Mantecon et al., 2008). Common serological tests utilized for diagnosis include serum agglutination test and enzyme-linked immunoassays (Memish and Balkhy, 2004). Genotypic analysis has been used by public health officials to assist in identifying the likely geographical location where the infection originated or was acquired (Bricker and Halling, 1994; Whatmore et al., 2006; Gerberding et al., 2008; Gopaul et al., 2008).

Brucellosis is a reportable condition in Tennessee. For each case, public health investigation is conducted to assess potential bioterrorism implications, determine likely exposures and implement control measures.

We describe a case of *B. melitensis* infection diagnosed in a US soldier residing in Tennessee following his second deployment to Iraq. Clinical course, diagnosis and public health follow-up, including genetic analysis of the *B. melitensis* isolate, are discussed.

### Methods

Following notification of positive laboratory tests for *Brucella*, an investigation was conducted to assess potential exposures. Information regarding exposure history, clinical course, diagnosis and treatment were ascertained by review of medical records and interviews with the patient and medical providers. Laboratory diagnosis was conducted using standard methods. Genetic characterization and analysis were conducted by the Centers for Disease Control and Prevention (CDC) Bacterial Zoonosis Branch as previously described (Gerberding et al., 2008). Routine state public health laboratory follow-up after failure to diagnose a select agent at the local healthcare facility prompted further investigation. A standardized questionnaire and serological monitoring were used to assess risky laboratory procedures among Military Treatment Facility (MTF) laboratory personnel.

### Results

The case-patient was a 23-year-old married male soldier. He had returned to the US in November 2006 following his second deployment in Iraq, where he was involved in combat and patrol operations. In January 2007, he presented to the MTF with complaint of recurring post-exercise knee pain and swelling for the previous 2 months. Physical examination findings were normal; oral temperature was 36.8°C, and he was treated with ibuprofen. He presented again in February 2007 complaining of acute severe back pain in addition to the knee pain, with no abnormalities noted on physical examination. The patient was treated with diazepam and ibuprofen and referred to physical therapy. However, worsening pain with focal right-sided hip pain, right thigh pain, and continued knee and back pain occurred over the next month. Magnetic resonance imaging (MRI) of the left knee and lumbar spine revealed no abnormalities. At the end of March 2007, the case-patient became febrile (38.5°C), which prompted additional laboratory and radiology work-up. Magnetic resonance imaging at this time showed severe synovial effusions in the left knee and substantial fluid collection in the medial popliteal fossa compatible with a large Baker’s cyst. Magnetic resonance imaging of the spine found nothing unusual. Arthrocentesis of the right knee yielded 20 ml of fluid that showed positive string sign and straw colour, suggesting normal synovial fluid.

In the first week of April 2007, the patient presented to the MTF emergency room complaining of fever, severe back pain and difficulty ambulating. He was admitted to the inpatient ward for 1 week. Urine cultures at the MTF grew *Escherichia coli*, and blood cultures grew organisms identified only as ‘diptheroid’ by MTF laboratory staff. Magnetic resonance imaging showed accumulation of fluid within the left lateral pelvis anterior to the sacroiliac joint. Differential considerations at this time included autoimmune arthralgia, Reiter syndrome, ankylosing spondylitis, Lyme disease and syphilis. The case-patient was treated with Ciprofloxacin for positive urine cultures until transfer to a regional public hospital.

At the regional hospital, the patient exhibited undulating fever. Urine and blood cultures demonstrated no growth. Parvovirus, cytomegalovirus, human immunodeficiency virus, tuberculin, Lyme disease and several rheumatological test results were negative. A computerized tomography (CT)-guided aspirate of the left sacroiliac joint was performed and yielded 1 ml of fluid, which was cultured. *Brucella melitensis* was identified at the Tennessee Department of Health, Division of Laboratory Services. Therapy included rifampin and doxycycline, and the patient was discharged 1 week later. Follow-up examinations as late as June 2007 found mild persistent...
hip and back pain and slight asymmetric accumulation of intra-articular fluid of both hips.

When the case-patient was interviewed, he denied both direct contact with livestock and eating unapproved foods. He stated that his unit had marched through herds of goats and played football on fields where livestock had been grazing.

Twenty-five of 26 laboratory workers were considered to have had risky exposure to \( B. \) melitensis; two of these had serological evidence of exposure based on a positive IgM antibody titre by commercial enzyme immunoassay (EIA). One reported plating the specimen without using a hood or adequate personal protective equipment (PPE). The other worked in close proximity to the bench with inadequate PPE. Seropositive laboratory workers did not exhibit any clinical signs and were treated with rifampin and doxycycline. Serological monitoring of all laboratory workers continued for 6 months with no additional positive results.

Genetic characterization and analysis of the \( B. \) melitensis isolate performed at the CDC Bacterial Zoonosis Branch in Atlanta, GA, indicated that the infecting subtype was consistent with other isolates of the Middle Eastern region. Comparison with isolates from USA, Thailand, Israel and Qatar/Egypt showed that the isolate was most closely related to Qatar/Egypt isolates.

**Discussion**

Brucellosis infection among travellers and military personnel returning from endemic regions is an infrequent, but long recognized problem. The first human case of brucellosis in the US was in an Army officer who contracted the disease in Puerto Rico in 1898 (Nicoletti, 2002). More than a century later medical and public health implications of such cases remain relevant. This report of \( B. \) melitensis infection illustrates important medical and public health considerations for dealing with non-endemic zoonotic diseases. Due to delayed diagnosis, the duration of infection was extended, increasing the risk of complications and exposures.

Symptoms of brucellosis are usually non-specific and include fever, sweating, malaise, weight loss, fatigue, headaches, arthralgia and myalgia. Osteoarticular manifestations are the most frequent focal complication, often affecting the spine and sacroiliac joints (Rajapakse, 1995; Dahouk et al., 2007). However, some clinicians do not associate brucellosis with bone or joint illness. This soldier’s illness was characterized by severe skeletal pain accompanied by mild systemic illness, which possibly led to the initial focus on autoimmune diagnoses and delayed the diagnosis of brucellosis. Morbidity associated with delayed recognition and treatment of brucellosis is well documented (Kattar et al., 2008). Clinicians assessing recent travellers with these types of symptoms should be aware of travel history and consider brucellosis as a possible diagnosis.

Laboratory workers were exposed to Brucella through improper laboratory procedures. Laboratories should handle specimens and unidentified cultures with appropriate caution and use PPE to minimize risk. According to CDC recommendations, clinicians should note when brucellosis is suspected on laboratory submissions (CDC, 2007). As a biosafety level three organism, suspected *Brucella* spp. should be handled with PPE that includes protective laboratory clothing, gloves, face and eye protection and respiratory protection. Laboratory personnel should refer to CDC recommendations for laboratory barrier precautions.

Medical record review and this patient’s history demonstrated that symptoms began after return to the US and not during deployment. Possible exposures were assessed including food and direct animal and environmental contact. Only US approved food and water were reported consumed while deployed, although exposure to sheep and goat pasturing areas was reported. Military personnel in endemic areas are typically instructed in risk reducing measures concerning food consumption and animal contact. Despite these directives, previously published reports link brucellosis among soldiers to eating locally produced goat cheese products (Nguyen, 2007).

Important lessons are provided by this case of *B. melitensis* infection. Delayed diagnosis can lead to repeated laboratory testing, increasing medical complications and laboratory exposures. Even in this military hospital setting, where examination and treatment of recently deployed personnel is part of the daily routine, brucellosis was not considered by clinicians or laboratory personnel. It remains important for healthcare providers and laboratory workers to remain vigilant for rare, non-endemic diseases among recent travellers, including military personnel.

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**References**


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