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Qazi, Mustafa; Weimer, Anita C.; Bedard, Brenden; and Kennedy, Byron S., "Q-fever in a Refugee After Exposure to a Central New York State Livestock Farm" (2016). Health Science Faculty Publications. 14.
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Q-fever in a refugee after exposure to a central New York State livestock farm

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ABSTRACT

Q-fever is a zoonotic disease caused by Coxiella burnetii that can create an acute or chronic form of the illness. In March 2014, Q-fever was identified by serology and Real-time Polymerase Chain Reaction (RT-PCR), in a 62 year-old male that was a Nepalese refugee. The male visited a livestock farm with a slaughterhouse in rural Central New York State, twenty-two days prior to onset of symptoms. He had direct handling of goats on this farm prior to slaughter. We describe the case presentation of his illness and the public health epidemiological investigation.

Key words: Public health, Q-fever, real-time polymerase chain reaction (RT-PCR), refugee

Introduction

Q-fever, an ubiquitous zoonotic disease, is the result of a resistant, obligate intracellular gram-negative bacterium Coxiella burnetii that infects humans after coming in contact with an infected animal or contaminated environment or aerosols.[1‑3] Inhalation of airborne C. burnetii bacterium from contaminated animal birth fluids/placental tissues or dust contaminated with animal excreta or fluids is the most frequent means of transmission to humans.[4] Transmission can also occur through direct contact with infected animals, primarily cattle, sheep, and goats, and their products, such as wool, raw milk, or manure/fertilizer.[2,3] There have been reports of Q-fever cases related to human exposure to pigeons, dogs, and rabbits and of the possibility of transmission of infection via ticks due to the fact that about 40 species of ticks have been found to carry C. burnetii.[2,4] According to the Centers for Disease Control and Prevention (CDC), 3% of healthy adults in the United States have antibodies to C. burnetii along with 10‑20% of adults in high-risk occupations such as veterinarians and farmers, this suggests past infection with the bacteria.[1] C. burnetii is highly infectious only requiring a single organism to cause disease, in addition it is resistant to heat and drying, and has the ability to survive months to years in an environment.

Persons infected with Q-fever can develop either an acute or chronic form of the illness. In general, symptoms of acute illness develop 2‑3 weeks after an exposure.[1] There are estimates that between 50% and 60% of cases are asymptomatic.[1,4] The most common symptoms reported with acute Q-fever are fever, malaise, chills and/or sweats, headache, and myalgia. The patients may frequently present clinically with a nonspecific febrile illness that could include pneumonia.
or hepatitis.[2,4] The mortality rate for acute Q-fever is 1-2%.[4] Of acutely infected individuals, <5% will develop chronic Q-fever symptoms. The range of onset from acute infection to chronic illness can be anywhere from 6 weeks to months, years or decades after the initial infection.[2,5] Chronic Q-fever can develop after symptomatic or asymptomatic infections. The patients may present with endocarditis [60-78% of cases], infection of aneurysms or vascular prostheses [second most common form], chronic infection after pregnancy [third most common form], chronic hepatitis, osteomyelitis, septic arthritis, chronic pulmonary infections, and chronic fatigue syndrome.[2,4,5] The mortality rate for chronic Q-fever endocarditis is reported by CDC as 25-60% in untreated patients.[1]

**Clinical Case**

A 62-year-old Nepalese male with past medical history notable for type-2 diabetes mellitus, gastroesophageal reflux disease, hypertension, hyperlipidemia, remote history of alcohol abuse, tobacco smoking history, and latent tuberculosis (TB) infection presented with intermittent fevers and lethargy of about 3 weeks. The patient came to the United States as a refugee from Nepal in 2010 and had not traveled abroad since then. He was treated with 9 months of isoniazid [INH] for a positive TB skin test with negative chest x-ray as a part of the refugee TB program at the Monroe County Department of Public Health [MCDPH], Rochester, NY.

The patient first presented to his primary care physician [PCP] on 24 January 2014 with complaints of fatigue and fever and was told he was likely to have influenza. He then went to the emergency department at Strong Memorial Hospital [SMH] in Monroe County, NY on 26 January 2014 for fevers and an episode of nonbilious emesis. He was treated with intravenous [IV] fluids and discharged home after stabilization. Labs at that time were fairly unremarkable showing only mild elevation in liver function tests [LFTs], aspartate aminotransferase [AST] = 103, and the alanine aminotransferase [ALT] = 81.

He was admitted at SMH on 7 February 2014 for persistent fevers, nausea, emesis, and abnormal LFTs including hyperbilirubinemia with clinical jaundice. There was a significant language barrier initially for the providers, but the infectious disease [ID] doctor was able to glean history from the patient when it was realized that both could communicate in Hindi. History was also obtained from his family members who spoke English. According to his sons, the patient had fever up to 102 degrees Fahrenheit at home. He denied diarrhea, rash, dysuria, headache, back pain, abdominal pain, arthralgia, or myalgia. There was a history of osteoarthritis of both knees with occasional swelling for the past 2 years that was unchanged. The patient also denied cough, congestion, sore throat, or flu-like symptoms. The patient denied recent sexual activity. No drug allergies were noted. He did not have pets at home. His current home medications included Neurontin, Lantus, Tylenol, and Prilosec. He was mildly confused at presentation, for which a computed tomography (CT) head scan was negative for acute findings. He had a temperature of 101.5 degrees Fahrenheit on the day of admission. CT of the abdomen/pelvis showed splenomegaly, thickened gallbladder, fatty liver, and mildly enlarged periperal lymph nodes. His influenza and respiratory syncytial virus [RSV] tests were negative and blood cultures had remained sterile. Stool studies were unrevealing. Inflammatory markers, such as erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP], were elevated at 85 and 135, respectively. He was treated for about 48 h with broad spectrum anti-infective agents including Zosyn (Piperacillin/Tazobactam), which was discontinued with unrevealing culture data. Daily fevers that ranged between 100.4 degrees Fahrenheit and 102.2 degrees Fahrenheit persisted, which are suggestive of a noninfectious etiology or an infection secondary to a pathogen not covered by the antibiotic. His LFTs started to trend to normal but remained elevated at the time of the ID consult. The patient was found to be immune to hepatitis B and testing for Hepatitis C was negative. Cytomegalovirus [CMV] was negative, and Epstein–Barr virus [EBV] was immunoglobulin G [IgG] positive and immunoglobulin M [IgM] negative. Blood Cultures x 6 showed no growth. **Clostridium difficile** was negative, and serum ferritin was 1845. His total iron binding capacity [TIBC] was low at 203 (250-450 µg/dL) as was his iron saturation of 30 [45-170 ug/dL]. Antimitochondrial antibody [AMA] and F-Actin antibody [Ab] were elevated at 34 (0-20 units) and 45 (0-19 units), respectively, smooth muscle Ab, IgG titer was <1:20.

On examination, his vital signs were stable, he was alert, but appeared chronically ill and fatigued. His neck was supple, no cervical lymphadenopathy and no oral lesions were observed, and his dental hygiene was poor. A lung exam revealed bibasilar crackles. His heart had a regular rate and rhythm without murmur or rub. The abdomen was soft and nontender without masses. No spinal or costovertebral angle tenderness was elicited. His extremities had trace edema, no peripheral stigmata endocarditis and no rash was noted.

The ID team requested further infectious work-up, including serum cryptococcal antigen [Ag], Syphilis...
The investigation began with contacting the upstate NY animal farm to buy fresh goat meat. This farm is located in a large part of the Nepalese community (NYS) Electronic Clinical Laboratory Reporting System (ECLRS). In addition, an ECLRS report was received on 3/19/14 showing a positive C. burnetti DNA, qualitative real-time PCR collected on 25 February 2014 on this patient. All New York State (NYS) local health departments are mandated to investigate positive lab results on suspected cases of Q-fever under NYS sanitary code 10 NYCCR 2.10, 2/14. The investigation began with contacting the PCP and a review of the hospital record. The PCP did not have any information on possible exposures to Q-fever, but was concerned after review of the recent hospital admission. A Nepalese interpreter was used by the PCP, who was familiar with this patient and was able to give the MCDPH a phone number for the patient’s son, who spoke English. Convalescent blood testing for Q-fever IgG and IgM was drawn on 16 March 2014 for confirmation. The MCDPH interviewed the patient’s son on 19 March 2014. The NYS Q-fever questionnaire was used in this proxy interview, which included questions regarding the case’s symptoms and onset date, travel history, and contact with livestock/animals or their products. The son reported that his father was disabled and did not work. The patient lived with his wife and two sons. No contacts of the patient were reported as ill with similar symptoms. The onset of symptoms was reported as around 20 January 14 with fever, weakness, and then confusion that brought him to the hospital. The patient reportedly had no travel since coming to the United States several years ago. Exposure to animals was initially denied, until further questioning with regard to types of food eaten and where they shopped/acquired their food revealed that the family goes to a farm to get chickens and goat meat about once every month. This farm is located in a

Epidemiological investigation

On 11 March 2014, the MCDPH received serum positive results for Q-fever IgG antibody [Ab] for phase I (4,096) and phase II (65,536) and positive IgM Ab for phase I (16,384) and phase II (262,144) [collected on 25 February 2014 at SMH] from a reference lab via the New York State (NYS) Electronic Clinical Laboratory Reporting System (ECLRS). In addition, an ECLRS report was received on 3/19/14 showing a positive C. burnetti DNA, qualitative real-time PCR collected on 25 February 2014 on this patient. All New York State (NYS) local health departments are mandated to investigate positive lab results on suspected cases of Q-fever under NYS sanitary code 10 NYCCR 2.10, 2/14. The investigation began with contacting the PCP and a review of the hospital record. The PCP did not have any information on possible exposures to Q-fever, but was concerned after review of the recent hospital admission. A Nepalese interpreter was used by the PCP, who was familiar with this patient and was able to give the MCDPH a phone number for the patient’s son, who spoke English. Convalescent blood testing for Q-fever IgG and IgM was drawn on 16 March 2014 for confirmation. The MCDPH interviewed the patient’s son on 19 March 2014. The NYS Q-fever questionnaire was used in this proxy interview, which included questions regarding the case’s symptoms and onset date, travel history, and contact with livestock/animals or their products. The son reported that his father was disabled and did not work. The patient lived with his wife and two sons. No contacts of the patient were reported as ill with similar symptoms. The onset of symptoms was reported as around 20 January 14 with fever, weakness, and then confusion that brought him to the hospital. The patient reportedly had no travel since coming to the United States several years ago. Exposure to animals was initially denied, until further questioning with regard to types of food eaten and where they shopped/acquired their food revealed that the family goes to a farm to get chickens and goat meat about once every month. This farm is located in a

With respect to imaging, the abdominal CT was unrevealing for any hepatic or splenic lesions but showed some periportal lymph node enlargement; chest CT revealed small effusion with no consolidations, hepatobiliary (HIDA) scan and transthoracic echocardiogram (TTE) were both negative for any abnormalities. A liver biopsy was performed on 24 February 2014, which showed macrovesicular steatosis; mild steatohepatitis; well-formed nonnecrotizing granulomas; and portal, periportal, and pericellular fibrosis. Up to this point, the patient continued with almost daily low-grade fevers of unknown origin (FUO) so testing for uncommon pathogens was then considered, including Q-fever serology testing, as well as getting a bone marrow biopsy to evaluate for granulomatous disease and possible miliary TB. A malaria (Vivax/Ovale) smear was requested and was negative. After 20 days of admission, fevers abated and patient remained afebrile for more than 48 h. In light of increasing patient and family frustration, the patient was discharged home with only the C. burnetti serology pending. The patient was instructed to return to the emergency department if fever resumed or new symptoms developed.

Up to this time, no epidemiological link was recognized and the patient’s presentation led ID doctors to believe that some sort of autoimmune phenomenon could be causing the symptoms. When the Q-fever results came back positive, the patient was called by ID and asked to come in for evaluation and treatment. At this clinic visit on 21 March 2014, the patient’s son confirmed that their family (along with a large part of the Nepalese community) had been going to an upstate NY animal farm to buy fresh goat meat. This established a convincing epidemiological link. The son also reported that the animals were slaughtered by the farm owner and then the family skinned the goat themselves. No animal parturition was witnessed, but young calves were in the vicinity. Other than feeling tired and fatigued, the patient was now asymptomatic and afebrile at home, with the return of his appetite as well. Although the ID doctors did not feel the patient had risk factors associated with progression to a chronic Q-fever infection (valvular heart disease, endovascular grafts, arterial aneurysms, and/or an immunocompromised state) as a precaution, the patient was given treatment with doxycycline 100 mg orally twice daily for 2 weeks. The patient followed up in 4 weeks at the infectious disease clinic at SMH. At the 4-week follow-up appointment, the patient had completed his 2 weeks of treatment with doxycycline, he was jovial and more energetic and denied fevers or any other symptoms.

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Screen; Brucella Ab, hepatitis E and A, and human immunodeficiency virus (HIV) 1 and 2 Ag/Ab were negative. He had normal renal function and his blood chemistry was unremarkable except for mild hyponatremia of 124 that went as low as 121 on day 6 of admission. The complete blood count did not have leukocytosis or any remarkable findings except mild thrombocytopenia. Haptoglobin was mildly elevated at 250 mg/dL, and on flow cytometry his cluster of differentiation 4 (CD4) count was 320. Angiotensin-converting enzyme (ACE) levels were normal and Ceruloplasmin levels were only mildly elevated at 38 (0-30 mg/dL).

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different county about 1.5 h away from Monroe County. They do not consume raw milk or other dairy products from this farm. It was described as a large farm with goats, sheep, pigs, rabbits, chickens, which are being sold for meat, with a slaughterhouse onsite where the consumer can kill their own animal or have the farm staff kill it. The patient and his family (four sons) all went to this farm where they went into the fields and physically caught and carried a goat on 29 December 2013, 22 days prior to the patient’s onset of symptoms. The patient was involved in this process and handled the goat. The goat was then brought to the onsite slaughterhouse where the farm staff killed the goat and packaged it up for the family to take home to consume. On the same visit, the family also purchased a chicken that they killed themselves in the farm slaughterhouse and then brought home to consume.

Results

It was learned later in the investigation that an additional serum specimen was taken from the patient at SMH on 8 February 2014 (at the beginning of his hospital admission), these sample results were not initially reported by the reference lab, but also came back IgG and IgM positive as well as DNA PCR positive. Per the request of the NYS Department of Health [NYSDOH], the Q-fever IgG serum specimen drawn from the patient on 25 February 2014 was forwarded by the reference lab to the NYSDOH Wadsworth Laboratory, Albany, NY, and was confirmed positive for phase I (8,192) and phase II (32,768) antibodies. Of note when the number of phase II antibodies is higher than that of the phase I antibodies, the results suggest acute infection with Q-fever.\(^2\) Convalescent testing done on 16 March 2014 came back from the reference lab showing IgG AB’s for phase I (4,096) and phase II (262,144), these results show greater than a fourfold rise in phase II IgG results between acute and convalescent titers thus confirming Acute Q-fever in this patient.\(^3\)

Public health response

After the MCDPH discovered the likely source of this Q-fever case, the next steps were to ensure follow-up/treatment of the patient, surveillance of other possible cases, and follow-up with the farm. At the initial interview with the patient the MCDPH recommended that the patient follow-up with SMH regarding treatment and follow-up testing, this was the PCP’s recommendation as well. The name of the farm, where the patient was exposed to livestock was unknown at the initial proxy interview, but this information was captured by the ID team at SMH at the follow-up visit and passed it on to the MCDPH. The NYSDOH was contacted early on in this investigation by the MCDPH for guidance and recommendations regarding testing, interpretation of results, and surveillance. The NYSDOH was able to confirm that no other recent Q-fever cases in New York had exposure to the same farm as this case. The NYSDOH also reached out to the county where the farm was located to inform them of this case’s exposure and ask about possible cases in the area, which there were none. The MCDPH requested that the NYSDOH reach out to the NYS Department of Agriculture and Markets [NYS Ag and Mkts] with regard to contacting the farm owner to discuss the connection between his farm and this case and provide education. A doctor from the NYS Ag and Mkts was able to speak with the farm owner on this matter. Discussion points included how common Q-fever is in sheep, goats, and cattle, cautioning the farmer on the handling of birth fluids/ fetal membranes/placentae of livestock, which includes taking steps to minimize exposure to persons on his farm (in fields and slaughterhouses), and not letting the public assist with animal births. In addition, the farmer was educated on regulations regarding the sale of unpasteurized milk and milk products. It was recommended that owners/employees/consumers with concerns about their health after exposure to the farm should be directed to a physician or local health department. The ID doctors at SMH also offered to this patient and his family to see any member of the Nepalese community who was experiencing symptoms and had a similar exposure at the goat farm.

Conclusion

The incidence of Q-fever in NYS per the NYSDOH from 2009-2014 has been 24 confirmed cases. Per the NYSDOH, there have been six confirmed cases in the Western New York Region, where Monroe County is located during that time frame. It has been speculated that C. burnetii could be an unknown cause of cases of community-acquired pneumonia, this is most likely due to the fact that it cannot be distinguished “from other causes of community-acquired pneumonia solely on the basis of radiographic findings.”\(^6\) Physicians should suspect acute Q-fever in patients with pneumonia, a prolonged fever of greater than 10 days, and an increase in liver enzymes.\(^7\)

There have been outbreaks of Q-fever in the Netherlands from 2007 to 2009, which reported around 4,000 cases, with about 50% of acute cases being hospitalized, as well as an outbreak in the United States (Washington and Montana) in 2011 with 21 identified cases.\(^5,7,8\) This illustrates the possibility of large outbreaks of Q-fever.\(^5,7,8\) Bjork et al. [2011 US outbreak] point out that many patients, including an 11-year-old child, suffered long durations of illness.
(months) and even had an appendectomy, because they were not properly diagnosed and did not receive proper treatment.\[^8\] Exposure history from the Monroe County case was not known during hospitalization and test results for Q-fever were not available, so a diagnosis of Q-fever was not made and treatment was not started. If a clinician is suspecting Q-fever treatment should not be delayed and should ideally be started within 3 days of onset to decrease the length and risk for complication of Q-fever.\[^2,8\] Doxycycline is the most effective treatment.\[^2\]

It is important for health-care professionals to obtain a complete history of their patients to include the following information: Occupation, where they live, contact with someone who has been ill, travel history, any farm or domestic animal exposures (or exposure to animal products), blood transfusion history, tick exposure, along with the clinical picture, to evaluate for a possible Q-fever diagnosis and to make appropriate treatment decisions.\[^2\]

**Conflicts of interest**

There are no conflicts of interest.

**References**