Clinical Case Reports International

Research Article
Published: 01 Apr, 2023

Clinical and Epidemiological Characteristics of Q Fever in Hospitalized in UCC Republic Srpska Banja Luka in 2016

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Abstract

We retrospectively analyzed clinical and epidemiological characteristics of Q fever in 28 patients hospitalized at the University Clinical Center Republic Srpska in Banja Luka from February 1st to April 30th, 2016. The source of the bacteria *Coxiella burnetii* was an infected herd of sheep. The epidemy lasted from February to April 2016. During this period 28 people got ill. Besides having high temperature and fever the people suffered from exhaustion, fatigue, nausea, vomiting and diarrhea as well as confused condition. Chest X-ray revealed interstitial pulmonary infiltrates in the majority of patients, localized in a single pulmonary lobe (25 or 89.3%). Pleural effusion was recorded in 3 (10.7%) patients. In their treatment tetracyclines (doxycycline) were used and azithromycin and ciprofloxacin for treating the smaller number of ill people. Doxycycline showed the best clinical efficacy. All patients were cured. In this epidemia, the Q-fever in people was caused by the infected sheep and contaminated area in which the infected sheep stayed.

Keywords: Q-febris; Clinical characteristics; Epidemiology

Introduction

Q-fever is a zoonosis caused by the intracellular gram-negative bacterium *Coxiella* (C.) *burnetii*, which is distributed worldwide, except in New Zealand [1]. Q-fever in animals usually causes a clinically inapparent infection. Q-fever in humans can be an acute or chronic disease, and they differ in duration, clinical presentation and serological test findings. Acute Q-fever can be asymptomatic or manifest as a short-term febrile illness, atypical pneumonia, and granulomatous hepatitis [2]. Chronic Q-fever is most often presented as endocarditis, and less often as endovascular infection, chronic infection during pregnancy, chronic hepatitis, chronic lung infection and infections of the locomotor system [2]. Endocarditis is responsible for 60% to 70% of cases of chronic *C. burnetii* infection [3]. It is a disease of some wild and almost all domestic animals, among which it is maintained and transmitted by vectors (ticks). Among domestic animals, the most common hosts are ruminants, but it has also been proven in horses, pigs, camels, bison, rabbits, squirrels, mice, wild game, domestic poultry and wild birds. The most common source of infection for humans is sheep, goats and cattle. The causative agent, *C. burneti*, is excreted in the milk of infected animals, and there are extremely many causative agents in amniotic fluid, sheaths, lochia secretions and on wool [4]. Humans are usually infected by inhaling dust contaminated with *C. burnetii* bacteria and by contact with infectious materials, during childbirth, abortion or slaughter. In humans, the infection is manifested by a severe headache, high fever, pain in the back and joints, and atypical pneumonia usually occurs. In the chronic form, a person can suffer from endocarditis and hepatosplenomegaly, and the outcome can be fatal.

In our country, Q-fever regularly appears at the end of winter or in spring, during the lambing of sheep, so it is extremely seasonal. In previous years, Q-fever in our country was more frequent and associated with nomadic sheep grazing. The last Q-fever epidemic in the Banja Luka region occurred in 2004. In 2015, 42 cases of this zoonosis were registered in the Banja Luka region. Epizootics and epidemics have been described in various countries. Nebreda et al. In 2001, it was described in Spain by Serbezov et al. 1999 in Bulgaria and Slovakia, Literak and Rehacek, 1996) in the Czech Republic and Slovak Republic, Tringali and Mansueto 1987 in Italy [5].

The goal of the paper was to show the importance of this disease, a zoonosis that occurs in our area, especially in the differential diagnosis of unclear febrile conditions, by presenting the Q fever epidemic.

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Received Date: *15 Mar 2023*
Accepted Date: *28 Mar 2023*
Published Date: *01 Apr 2023*

Citation:
Verhaz A, Roganović T, Ritan S, Petrović M, Pavlica B, Narić S. Clinical and Epidemiological Characteristics of Q Fever in Hospitalized in UCC Republic Srpska Banja Luka in 2016. Clin Case Rep Int. 2023; 7: 1520.

Material and Methods

In the period from February 1st to April 30th, 2016, 28 people, 23 men and 5 women, fell ill with Q-fever. Most of the patients were from Banja Luka, the Lauš settlement (80%), and 20% from the surrounding towns, Čelinac, Kotor Varoš, Gradiška, Han Kola. The youngest patient was 31 and the oldest 66. The affected population consisted of 82.1% men and 17.9% women. The extracted blood was sent to the Department of Microbiology, UKC RS Banja Luka for serological testing for Q-fever.

The diagnosis of Q-fever was made by detecting specific antibodies by enzyme immunoassay (ELISA, Virion-Serion, Wützburg, Germany). Specific IgM and IgG antibodies to the *C. burnetii* phase 2 antigens, which appears in the acute phase of the disease, and specific IgG antibodies to the *C. burnetii* phase 1 antigens, which are indicative of the chronic form in addition to elevated antibodies to the *C. burnetii* phase 2 antigens, were determined. diseases. IgM antibodies to *C. burnetii* phase 2 antigens as well as IgG antibodies to *C. burnetii* phase 1 antigens were expressed quantitatively and were considered positive if the measured extinctions were greater than the extinctions for the standard control sample that determined the assay cutoff. IgG antibodies to *C. burnetii* phase 2 antigens were expressed quantitatively and a titer result greater than 30 U/mL units per mL was considered a positive finding. Values of 20 U/mL to 30 U/mL were considered a borderline finding. IgM antibodies for phase 2 antigens and IgG antibodies for phase 1 *C. burnetii* can be expressed as index values, i.e., the ratio of the measured extinction for the serum and the extinction of the cutoff value of the test. An index value greater than 1.1 is considered positive, while the threshold score is an index value of 0.9 to 1.1.

Results

Incubation in humans ranged from two to three weeks. In sick people, the most common symptoms were elevated body temperature (some higher than 40C), nausea, vomiting, diarrhea, fatigue and malaise. An elevated temperature is the dominant sign in all patients, and in most patients, it was over 39°C. Headache of high intensity, especially in the frontal part and retrobulbar, was pronounced in most of the patients. Cough as a significant sign was dry and irritating with admixtures of blood in the sputum in only one patient. Atypical pneumonia developed in 100% of patients. Liver damage manifested by elevated values of Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), and Gamma Glutamyl Transferase (γGT) was recorded in 19 (67.8%), 17 (60.7%), and 10 (35.7%) of the patient. The value of aminotransferases in one patient was increased more than five times expressed in international units per ml (i.j/ml); AST 349 IU/ml and ALT 1422 IU/ml. Serological tests included testing of serum from a group of patients, taken about 10 days after the onset of the disease, in the group of patients a significant titer of antibodies to *C. burnetii* was demonstrated. In the treatment, doxycycline was most often used, and in some cases, azithromycin and ciprofloxacin. All applied antibiotics and chemotherapeutics were effective in the treatment.

Discussion

Q-fever is known in humans as primary atypical pneumonia, seven-day fever, desert fever, Balkan flu, Italian fever, Crimean fever and Cretan pneumonia [6]. People who work with animals, veterinarians, cattle breeders and workers in slaughterhouses are most often exposed to the infection. During February, March and April 2016, a total of 28 patients were treated in the UKC RS Banja Luka, 21 in the Clinic for Infectious Diseases, six in the Clinic for Pulmonary Diseases and one patient for Internal Diseases.

The sick mostly came from the Banja Luka settlement of Lauš, who came into contact with sheep infected with *C. burnetii*. Airborne route of infection, inhalation of contaminated dust. In this epidemic, there was contact of most people with a herd of infected sheep, and a part with a contaminated area. It is known that *C. burnetii*, in the form of spores, can survive for a long time in the external environment and cause disease in people who have been in contact with infected aerosol [2]. In addition, it has been confirmed that *Coxiella* can be blown by the wind to greater distances [2,6]. The resistance of the bacterium *C. burnetii* to adverse environmental conditions, especially to desiccation, played a crucial role. The authors state that *C. burnetii* remains infectious in an aerosol for up to two weeks, and in the soil for up to five months. In dried material, the causative agent can survive from 30 to 500 days [6]. Just one *C. burnetii* bacterium is enough to cause disease in a susceptible person. This agent can be developed for use as a biological weapon and is considered a potential terrorist threat. Human-to-human transmission is rare. Kruszewska et al. described the possibility of sexual transmission of Q-fever in humans. The research was conducted on nine pairs of shepherds from Poland who worked seasonally in Spain. After returning to Poland, shepherds and their wives fell ill with Q-fever. *C. burnetii* was isolated from urine and semen samples of men. Cases of Q-fever in pregnant women have been described. Hellmeyer et al. describe placentitis and premature birth in 30%, slow fetal growth in 46%, spontaneous abortion in 22% and fetal death in the womb in 7% of cases [7].

Q-fever belongs to acute febrile diseases. The clinical symptoms were as follows: elevated body temperature, in some patients higher than 40°C, accompanied by fever. Other symptoms included cough, chest pain, headache, myalgias, nausea, vomiting and diarrhea, fatigue, malaise, confusional state (delirium). An X-ray of the lungs was performed in all patients upon admission to the hospital, and in 100% of patients an interstitial infiltrate was detected, located in one lung lobe (25 or 89.3%). Pleural effusion was registered in three (10.7%) patients.

28 or 100% of patients had an elevated CRP value. 9 or 32.1% had a CRP value of 10 mg/L to 100 mg/L, 101 mg/L to 200 mg/L 16 or 57.2%, and 201 mg/L to 300 mg/L 3 or 10.7% of patients. Liver damage manifested by elevated values of aspartate aminotransferase, alanine aminotransferase, and gamma glutamyl transferase was present in most of our patients. One third of patients, 9 of them (32.1%) had normal aminotransferases. Also, blood cultures were taken from all hospitalized patients, and sputum from some patients for bacteriological processing.

The disease was serologically confirmed in 28 patients. They were treated with tetracycline (doxycycline) for fourteen days, and a few patients with azithromycin and ciprofloxacin. In the initial therapy, some of the beta-lactam antibiotics were used in the majority of patients 20 (71.4%). Most of the patients were hospitalized, and some were treated on an outpatient basis. Various antibiotics (mainly beta-lactams, quinolones, azithromycin) were administered to patients on an outpatient basis, before hospitalization, in 85.7% (24 patients), which indicates a sometimes premature and quick decision to include antibiotics.

C. burnetii is innately resistant to beta-lactam antibiotics and aminoglycosides, and sensitive to tetracyclines, co-trimoxazole, rifampicin and fluoroquinolones. Mortality of untreated chronic Q-fever can be more than 65% [2,8]. Adequate antimicrobial therapy significantly reduces mortality, but the causative agent is difficult to eradicate, which is why prolonged antimicrobial therapy is needed. Monotherapy with any of these antibiotics reduces the symptoms of chronic Q-fever. According to *in vitro* research, inside the phagosome where *C. burnetii* is located is an acidic medium that may be responsible for the loss of the bactericidal properties of some antibiotics. When antimicrobial therapy is stopped, disease relapses often occur, which is why combined antimicrobial therapy is preferred [9]. Pebody et al. found respiratory disorders in 57% of patients with Q-fever, heart disease in 7% and hepatitis in 5%. Marrie lists headache, myalgia and pneumonia as the main symptoms of Q-fever. Connolly et al. found pneumonia in 62.8%, influenza-like illness in 24.6%, heart problems in 9% (endocarditis), and hepatitis in 1.6% of Q-fever patients [9-11]. We did not have endocarditis in our patients. No deaths were registered.

Conclusion

In the differential diagnosis of unclear febrile conditions, the clinician should consider Q-fever, both acute and chronic form of the disease, especially if the patient has an indicative epidemiological history.

In vitro, tetracyclines, quinolones, rifampicin, co-trimoxazole and macrolides are active against *C. burnetii* [2,12], but the drug of choice in the treatment of Q-fever is doxycycline in a daily dose of 200 mg [12]. Macrolides and co-trimoxazole are recommended for children and pregnant women [12].

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