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Q Ateşi'nin Yeterince Farkında Mıyız? Tek Merkez Deneyimi.

Are We Aware of Q Fever Enough? Experience From A Single Centre.

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ÖZ

GİRİŞ: *Q ateşi, Coxiella burnetii'nin neden olduğu bir zoonozdur. Başlıca klinik prezentasyonları pnömoni ve hepatit'tir. Bununla birlikte, birçok farklı klinik prezentasyonlar nedeniyle Q ateşini tanımak güç olabilir. Bu çalışmada, kurumumuzdaki Q ateşi olgularının klinik ve laboratuvar özelliklerini sunarak Q ateşi farkındalığını artırmayı amaçladık.*

GEREÇ ve YÖNTEMLER: *Hastanemiz veri tabanındaki Q ateşi tanılı hastalar retrospektif olarak değerlendirilmiştir. Hastaların karakteristikleri, başvurudaki klinik ve laboratuvar değerleri kaydedilmiştir.*

BULGULAR: *Bu çalışmaya toplam altı hasta dahil edilmiştir. En sık ateş, iştahsızlık ve bitkinlik gibi semptomlar olmak üzere çeşitli klinik prezentasyonlar gözlenmiştir. En sık laboratuvar anormalliği tüm hastalarda saptanan CRP yüksekliğiydi, LDH ve transaminaz yüksekliği bunu takip etmekteydi. Gerek LDH yüksekliği gerekse transaminaz yüksekliği dört hastada mevcuttu.*

SONUÇ: *Q ateşini teşhis etmek için kullanılan serolojik yöntemler rutin olarak uygulanmamaktadır, bu yüzden Q ateşi olguları kolayca gözden kaçabilir. Biz inanıyoruz ki, endemik bölgelerde nonspesifik antibiyotik tedavisine yeterli yanıt vermeyen hastalarda Q ateşi daha çok araştırılmalıdır.*

Anahtar kelimeler: *Coxiella burnetii, Q ateşi, Türkiye*

ABSTRACT

BACKGROUND: *Q fever is a zoonosis caused by Coxiella burnetii. The main clinical presentations are pneumonia and hepatitis. However, it can be difficult to recognise Q fever due to many different clinical presentations. In this study, we aimed to increase the awareness of Q fever by presenting clinical and laboratory features of Q fever cases from our institution.*

MATERIALS and METHODS: *Patients with a diagnosis of Q fever in our hospital database were evaluated retrospectively. Patient characteristics as well as clinical and laboratory values at presentation were recorded.*

RESULTS: *A total of six patients were included in this study. Various clinical presentation was observed such as fever, anorexia and malaise as the most common symptoms. The most common laboratory abnormality was CRP elevation as being detected in all patients followed by LDH and transaminase elevations. both were found in four patients.*

CONCLUSION: *Serological methods used to diagnose Q fever are not routinely performed, so Q fever cases can be missed easily. We believe that Q fever should be investigated further in patients from endemic regions who did not give adequate response to nonspesific antibiotic treatment.*

Keywords: *Coxiella burnetii, Q fever, Turkey*

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INTRODUCTION

Q fever is a zoonosis caused by Coxiella burnetii, an obligate intracellular bacterium. Main reservoirs are cattle, goats and sheep (1,2). The disease is spread to humans through contaminated respiratory aerosols from the secretions of infected animals. Incubation period changes from two weeks to one month (3,4). Several investigatory studies have been conducted in different regions of Turkey, and reported C. burnetii positivity in different percentages (5-10). However, the majority of cases are asymptomatic. In symptomatic cases, clinical spectrum is wide from a self-limiting flu-like illness to serious clinical diseases. Although pneumonia and hepatitis are the most common clinical presentations, various clinical presentations may be encountered such as meningoencephalitis, thyroiditis, endocarditis, mesenteric lymphadenopathy, pancreatitis, hemophagocytosis, hemolytic anemia, transient hypoplastic anemia and epididymoorchitis (11,12). As a result, Q fever can be difficult to diagnose due to many different clinical presentations. We retrospectively reviewed Q fever cases diagnosed and managed in our hospital between November 2014 and April 2016.

MATERIALS and METHODS

Patients with a diagnosis of acute Q fever between November 2014 and April 2016 were evaluated retrospectively in our hospital which is located in the western Black Sea region of Turkey and has a capacity of 350 beds. After obtaining informed consent, patient data were collected from the hospital database. Q fever was considered in patients from rural area who had consistent clinical findings like severe headache, pneumonia and hepatitis and who did not give adequate clinical response to non-specific antibiotic therapy. An immunofluorescence assay is used for the serodiagnosis of Q fever which is the reference method. Thus, acute Q fever diagnosis was made serologically and based on C. burnetii immunofluorescent antibody (IFA) phase 2 IgM positivity (IgM≥ 1/64) and/or concurrent IgM and IgG positivity in a single sample and/or four-fold increase in phase 2 IFA IgG titers in repeat sample obtained at least two weeks later (13). Consistent with this knowledge, we made the diagnosis of Q fever according to above mentioned criteria. A total of six patients were included in this study. Baseline laboratory tests, including white cell count, hemoglobin, alanine aminotransferase, aspartate aminotransferase, LDH and CRP levels, were recorded.

RESULTS

There were six patients included in the current study (5 males and 1 female). The patients' clinical presentations were shown in (Table 1). The mean age of the patients was 48.5 years.

Clinical presentation was various with fever, anorexia and malaise as the most common symptoms. Four patients had respiratory symptoms (dispnea, cough, pleuritic chest pain) whereas three patients had severe headache. All of the cases had been living in rural area. Additionally, two patients with respiratory symptoms had a recent history of travelling abroad (Saudi Arabia).

Underlying diseases were found in four patients. One patient had lung cancer and three patients had cardiac diseases. Two of the latter had valvulopathy as one of them had mild mitral and tricuspid valve insufficiency and the other one had prostetic mitral and aortic valve. In addition, we could not document animal contact in our patients.

Clinical manifestations of our patients were summarized as pneumonia in four patients, hepatitis in two patients (accompanied by pneumonia in one of these) and endocarditis in one patient. The patient, who presented with syncope and impaired consciousness, was admitted with an initial diagnosis of acute cerebrovascular event. It was learned that he underwent prostetic mitral and aortic valve replacement two months ago. Cranial computed tomography demonstrated acute hemorrhagic infarct in the left lobe. Transesophageal echocardiography showed jet flow through a fistula between the left atrium and aorta. Fundoscopic examination revealed right parafoveal roth spot. Later on, the patient was diagnosed with early prostetic valve infection according to Duke criteria for infective endocarditis. There was no growth in blood culture. Q fever was considered due to inadequate clinical response to non-specific antibiotic treatment. Although

Table 1. Clinical presentations, treatments and outcomes of Q fever cases from Turkey

Reference	Presentation	Treatment	Outcome
Patient 1	Pneumonia	Doxycycline	Recovery
Patient 2	Pneumonia	Levofloxacin	Recovery
Patient 3	Pneumonia + maculopapular rash	Doxycycline	Recovery
Patient 4	Hepatitis + pneumonia	Doxycycline	Recovery
Patient 5	Pneumonia	Doxycycline	Recovery
Patient 6	Prostetic valve endocarditis	Doxycycline and co-trimoxazole	Recovery
Yeşilyurt *et al.*[17]	acute hepatitis	doxycycline	Recovery
Köse *et al.*[18]	headache + splenomegaly	ampiciline/sulbactam and ciprofloxacine	Recovery
Yıldırmak *et al.*[19]	deep jaundice	ceftriaxone	Recovery
Korkmaz *et al.*[20]	autoimmune hemolytic anemia + tubulointerstitial nephritis	chlarithromycin, steroids and hemodialysis	Recovery
Karabay *et al.*[21]	Crimean Congo hemorragic fever-like presentation	chlarithromycin	Recovery
Yılmaz *et al.*[22]	peritonitis	doxycycline, ciprofloxacin and rifampicin	Recovery
Yavuz *et al.*[23]	endocarditis and aortitis	doxycycline, hydroxycloroquine, ciprofloxacin, aortic valve and graft replacement	Exitus

histopathological examinations were not performed, Q fever serology was positive in this case.

The most common laboratory abnormality was CRP elevation as being detected in all patients followed by LDH and transaminase elevations, both of which were found in four patients. Although four patients had raised transaminase elevations, two of them had evident hepatitis (AST and/or ALT>2 x ULN). Leukocytosis and anaemia was detected in two and three patients, respectively.

During the hospital stay, acute Q fever patients did not develop any complications. However, Q fever endocarditis case was admitted to intensive care unit at first. The next day, the patient was transferred to the ward due to improvement in his clinical status. Four of the patients were treated as inpatient, their follow-up period was uneventful, all of them showed clinical improvement and discharged from the hospital.

DISCUSSION

Q fever is an endemic zoonosis in Bolu province of Turkey. The disease still saves its importance in this region (14). It has a wide clinical spectrum in symptomatic cases sometimes making the diagnosis difficult (15), so a high index of clinical suspicion is required. In fact, the incidence of Q fever is less than expected (14). We think that this situation might be related to insufficient use of serological tests, which are not included in routine diagnosis. In the present study, we aimed to increase the awareness of this disease by presenting clinical and laboratory features of six Q fever cases from our institution.

Similar to a previous study by Vanderbeke et al. (13), males were more frequently affected by Q fever compared to females in our series (5 vs.1). More occupational exposures of men and protective role of estrogen in women were shown to cause this situation in experimental models (16).

We could identify an evident risk factor in four patients in our series. One of our patients had lung carcinoma, whereas three patients had cardiovascular disease. On the other hand, deterioration of immune system with advanced age is a well-known issue. Consistent with this knowledge, elderliness can be regarded as a relative risk factor. There is only one elderly patient in our series at the age of 70 years.

Q fever can be transmitted via infected domestic cattles, goats and sheeps and the main (17). Close contact with cattle, goats or sheeps suggested aerosol transmission of Q fever. Although compatible epidemiological history is very important in the

diagnosis, unfortunately, the importance of animal contact can be ignored by the patients (18). So, this important diagnostic clue should be investigated in detail by the physicians. Travelling abroad can also be stated as a risk factor for transmission of C. burnetii, since two patients in our study had a recent travel history (14). Main clinical presentations of C. burnettii infections are pneumonia and hepatitis, however various clinical presentations may be encountered (11,12).

Diagnosis of Q fever pneumonia is based on clinical and radiological findings, however, there is not a specific Chest X-ray finding of Q fever pneumonia (19). Out of four patients presented with pneumonia symptoms, three of them had infiltrations on chest X-ray. On the other hand, a small number of patients who present with acute Q fever develop endocarditis, which is likely an autoimmune complication of early infection. Q fever endocarditis usually occurs in patients with underlying cardiac valve disease. So, we think that our case developed endocarditis during acute Q fever. Vegetations may not be seen on echocardiography due to smooth aspect or subendothelial localization (20).

The most common treatment of Q fever is oral doxycycline 100 mg twice per day for 14 days in acute cases (3). One of our patients with pneumonia was treated with levofloxacin for two weeks. However, the case with early prostetic valve infection was treated with doxycycline and then with co-trimoxazole for a total of 18 months. The remaining four patients were treated with doxycycline for a duration of two-to-four weeks.

Patients' outcomes are usually satisfying, only a small portion of patients progress to chronic or life-threatening course. Mortality risk is high in endocarditis cases when the diagnosis is delayed (3,20). Four of our patients were managed as inpatient and two patients were managed as outpatient. However, all of them recovered completely without sequel.

We searched previous Turkish literature for previous Q fever cases and found individual case reports. Clinical presentations, treatments and outcomes of Q fever cases from Turkey were summarized in (Table 2).

To the best of our knowledge, our study is the largest Q fever case series from a single institution in Turkey.

Table 2. Clinical presentations, treatments and outcomes of Q fever cases from Turkey

Yeşilyurt *et al.*[21]	acute hepatitis	doxycycline	Recovery
Köse *et al.*[22]	headache + splenomegaly	ampiciline/sulbactam and ciprofloxacine	Recovery
Yıldırmak *et al.*[23]	deep jaundice	ceftriaxone	Recovery
Korkmaz *et al.*[24]	autoimmune hemolytic anemia + tubulointerstitial nephritis	chlarithromycin, steroids and hemodialysis	Recovery
Karabay *et al.*[25]	Crimean Congo hemorragic fever-like presentation	chlarithromycin	Recovery
Yılmaz *et al.*[26]	peritonitis	doxycycline, ciprofloxacin and rifampicin	Recovery
Yavuz *et al.*[27]	endocarditis and aortitis	doxycycline, hydroxycloroquine, ciprofloxacin, aortic valve and graft replacement	Exitus

CONCLUSION

The diagnosis of Q fever is sometimes difficult because of nonspecific nature of signs and symptoms.

Epidemiological data is the most important way in the diagnosis. We believe that Q fever should be investigated more in the presence of persistent fever despite non-specific antibiotic therapy in endemic regions. Serological tests should be repeated in suspected cases at least two weeks later and further diagnostic methods should be considered.

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