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Case report

Presentation and diagnosis of acute Q fever in Portugal — A case series

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ABSTRACT

Q fever is a worldwide zoonotic infection caused by the obligate intracellular bacterium *Coxiella burnetii* that can course with acute or chronic disease.

This series describes 7 cases of acute Q fever admitted in a Portuguese University Hospital between 2014 and 2015.

All cases presented with hepatitis and had epidemiological history. Diagnosis was done by PCR on majority (5) and by serology and PCR in only 2.

Serological tests can be negative in the initial period of the disease. Molecular biology methods by polymerase chain-reaction are extremely important in acute disease, allowing timely diagnosis and treatment.

Introduction

Q fever is a worldwide zoonotic infection caused by the obligate intracellular bacterium *Coxiella burnetii* [1,2] that can course with acute or chronic disease [3].

The most commonly identified sources of human infection are farm animals such as cattle, goats and sheep, [4] and transmission results mainly from inhalation of contaminated aerosols [5].

The acute clinical manifestations of Q fever range from asymptomatic seroconversion (50%–90% of patients) to severe disease [1,2]. Symptomatic patients usually present with an *influenza*-like illness with varying degrees of pneumonia and hepatitis [3].

Immunofluorescence assay is the reference method for serodiagnosis of Q fever. There is also evidence of high sensitivity and specificity of PCR in specialized laboratories [5].

The recommended treatment for acute disease is doxycycline 100 mg twice daily for 14 days, but starting antibiotic after the third day of disease may not change the outcome [3].

This series describes 7 cases of acute Q fever admitted in a Portuguese University Hospital between 2014 and 2015. Our aim is to describe the clinical presentation of this disease in our setting, highlighting the difficulties of achieving the diagnosis, due to its unspecific clinical behaviour, the absence of a clear history of zoonotic exposure and/or the frequently negative serology early in the course of the disease. We also want to emphasize the importance of molecular methods for timely diagnosis.

Material and methods

This case series includes the patients who fulfilled all the following criteria: age over 18 years, admission to Infectious Diseases Department in an University Hospital in Porto, Portugal, between 2014 and 2015 with the diagnosis of acute Q fever, based on compatible clinical picture and positive serology or PCR during hospital stay or follow up, without an alternative diagnosis.

Patients were identified through our hospital's patient database and clinical information collected from medical records.

For each case, we report relevant data, such as: prior medical history, epidemiological context for exposure to *Coxiella burnetii*, disease clinical presentation, laboratory results (Tables 1 and 2), treatment and follow-up.

Q fever diagnosis was based on serology, using an indirect immunoenzyme assay to test phase II IgG antibodies against *Coxiella burnetii* in human serum *(Delta Biologicals N° DBE-080®)*, and a real time polymerase chain reaction (PCR) assay targeting the insertion element (IS1111), which detect DNA in blood [14].

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Case reports

Patient 1, a 47-year-old man who lived in Lousada (Fig. 1), a rural area nearby a sheep farm, was admitted with acute hepatitis in January 2014. He presented with a history of fever, asthenia, vomiting, diarrhoea and choluria for 8 days. He had been prescribed clarithromycin (500 mg/d), 5 days before, without improvement.

On physical examination, he was febrile (39 °C), had abdominal tenderness on the right lower quadrant, liver was palpable 2 cm below the costal margin; the remaining physical examination was normal. An abdominal ultrasound showed a hepatomegaly (19 cm) and diffuse steatosis.

His lab results are shown on Table 1. Serologies for HIV, Hepatitis B and C were negative. He was immune to Hepatitis A.

Given the persistence of fever and increased inflammatory markers he was started on cefotaxime. Three days later serology and PCR results were positive for *C. burnetii*. A diagnosis of acute Q fever was assumed and doxycycline was started.

Echocardiography was unremarkable. Liver biopsy revealed a chronic granulomatous process; granulomas contained lipidic vacuole surrounded by a fibrinoid ring. Patient completed 21 days of antibiotic therapy with full clinical recovery.

Patient 2, a 47-year-old man from Rio Tinto (Fig. 1), who worked in an abattoir, was admitted with a history of fever in October 2014. He presented with a six day history of fever, headache, photophobia, chills, loose stools (without blood, mucus or pus) and vomiting.

At admission, he was febrile (39 °C) and the reminder of physical examination was unremarkable. Blood tests are described in Table 1; serologies for HIV, Hepatitis B and C were negative. Echocardiography showed normal global ventricular systolic function.

Q fever diagnosis was based on the detection of *C. burnetii DNA* in blood; serology was negative. The patient completed 21 days of doxycycline with full clinical recovery.

During follow- up, repeated serologic test showed positive IgG for *C. burnetii*.

Patient 3, a 31-year-old man who lived in a rural area in Águas Santas (Fig. 1), with farmers in the surroundings and with no prior medical history, presented to the Emergency Department with a 4-day history of prostration, fever (maximum of 39,4 °C), anorexia, nausea and one episode of vomiting. On admission he was febrile and adynamic but the remaining physical examination was unremarkable. Blood results are shown in Table 1. Viral serologies were negative. Abdominal ultrasound revealed hepatomegaly. Chest radiography was normal. He was admitted to the Infectious Diseases Department in January of 2015.

Patient's clinical condition progressively worsened and he was put on Ceftriaxone for suspected leptospirosis and admitted in our Intensive/Intermediate Care Unit.

Despite a negative Q fever serology on admission, diagnosis of Q fever was made after a positive PCR for *C. burnetii* in blood. Other causes of fever and acute hepatitis were excluded.

Oral doxycycline was started on the 3rd day after admission, with clinical improvement. At follow-up he was asymptomatic and repeated serology that was positive (IgG).

Patient 4, a 26-year-old man who lived in a urban area in Águas Santas (Fig. 1), whose father worked in an abattoir, presented to the emergency department in February 2015 with an 8-day history of fever, headache, myalgia and occasional vomiting.

Physical examination was unremarkable except for fever. Blood work is shown on Table 1. Abdominal ultrasound showed hepatosplenomegaly, and chest radiography was normal.

Patient was started on ceftriaxone 2 g for suspected leptospirosis. On the 2nd day after admission, he became asymptomatic. Leptospirosis blood PCR was negative and *Coxiella burnetii* DNA was positive so doxycycline was started. Patient was discharged at day 5 Ecocardiography did not show any valvular lesions. At follow-up serology became positive (IgG).

Patient 5, a 22-year-old woman who lived in an urban area in Ermesinde (Fig. 1) with sporadic contact with rural areas, and with a personal history of scoliosis and chronic rhinosinusitis, was admitted in February 2015 with a 5-day history of fever, upper abdominal pain, constipation and anorexia. On physical examination she was febrile and had palpable and tender hepatomegaly. Blood tests are shown in Table 1; Abdominal ltrasound showed an enlarged liver (18 cm); chest radiography was normal. On the 2nd day of hospital admission she was put on Ceftriaxone, abdominal symptoms began to improve but fever persisted. PCR was positive for *Coxiella burnetii* as serologic test, IgG and IgM. Patient was discharged with doxycycline.

Patient 6, a 72-year-old man who lived in a rural area in Porto (Fig. 1), with goats in the backyard (one of them had an abortion 3 weeks earlier), was admitted in July, 2015 with a 7 day history of fever, anorexia and malaise. Besides fever, physical examination was unremarkable.

Blood work is revealed on Table 1. Serologies for HIV, hepatitis B, hepatitis C, and *C. burnetii* were negative.

After 4 days of hospitalization, the patient had a remarkably improvement and was discharged. At follow-up (7 days later), *C. burnetii* DNA in blood was positive so Q fever was assumed and

Table 1
Relevant epidemiological data and main laboratory results on admission.

Laboratory parameters	Reference levels	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Admission date		02/01/2014	28/10/2014	30/01/2015	13/02/2015	26/02/2015	03/07/2015	04/08/2015
Day of fever		8	6	4	8	5	7	3
Epidemiological data		Yes	Yes	Yes	Yes	Yes	Yes	Yes
WBC ($\times 10^9$ cell/L)	4.0–11.0 $\times 10^9$L	6.3	6.2	6.92	4.25	5.56	9.64	5.64
PMNL (%)	53.8–69.8%	82%	80%	84%	57%	59.6%	66.6%	48%
Platelet count ($\times 10^9$ cells/L)	150–400 $\times 10^9$L	164	155	77	115	125	186	107
AST (IU/L)	10–37 U/L	332	186	152	82	158	91	76
ALT (IU/L)	10–37 U/L	481	289	271	206	197	125	108
SGGT (IU/L)	10–49 U/L	571	148	285	132	221	177	38
APT (IU/L)	30–120 U/L	238	157	194	113	178	145	85
Total bilirrubin	<1.2 mg/dL	1.81	0.76	3.24	1.45	1.19	0.54	0.68
Direct bilirrubin	<0.4 mg/dL	0.91	0.25	2.11	0.54	0.47	0.11	0.16
aPTT	24.5–36.5 s	35.9	31	40	31.8	43.7	35.5	32.6
PT	9.5–14.5 s	13.2	12.2	17	13	13.5	12	12.4
CRP (mg/L)	<3 mg/L	145.9	103.6	240	106	179	148.7	88.7

WBC: white blood cells; PMNL: polymorphonuclear leukocytes; AST: aspartate aminotransferase; ALT: alanine aminotransferase; SGGT: serum gamma-glutamyl transferase; APT: alkaline phosphatase level; aPTT: activated partial thromboplastin time; PT: prothrombin time; CRP: C-reactive protein.