CASE REPORT

A case of Q fever after liver transplantation

Lindsay A. Petty1, Helen S. Te2, Kenneth Pursell3

1Division of Infectious Diseases, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA
2Division of Gastroenterology, Department of Internal Medicine, University of Chicago Medical Center, Chicago, IL, USA
3Division of Infectious Diseases and Global Health, Department Internal Medicine, University of Chicago Medical Center, Chicago, IL, USA

Correspondence:
Lindsay A. Petty, MD
Department of Internal Medicine
Division of Infectious Diseases
University of Michigan Health System
Ann Arbor, MI USA.

Email: pettyl@med.umich.edu

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/tid.12737

This article is protected by copyright. All rights reserved
Abstract

Coxiella burnetii, the causative agent of Q fever, is a zoonosis that causes both acute and chronic disease in humans. Few cases have been reported in solid organ transplants, and this case highlights the need to include Q fever in the differential diagnosis for fever of unknown origin in solid organ transplant hosts.

Keywords:
Coxiella burnetii, liver transplantation, Q fever

1 INTRODUCTION

Coxiella burnetii is an obligate, intracellular bacterium, and the cause of the zoonosis Q fever. Q fever (from ‘query’) was named in 1935 following an outbreak of febrile illness in an abattoir in Queensland, Australia. Acute disease in humans varies from asymptomatic seroconversion, to a non-specific flu-like illness. Rarely, complications and chronic disease can occur, most often endocarditis.1

Literature review of the medical databases PubMed and Medline using the search terms “Q fever,” “Coxiella,” “transplant,” and “immunocompromised” revealed a paucity of information on Q fever in solid organ transplant hosts, and no reported case in an adult liver transplant. We therefore, to the best of our knowledge, report the first documented case of Q fever in an adult liver transplant patient. We also review the previously published cases of Q fever in solid organ transplant.

2 CASE REPORT

A 51-year-old Egyptian man with hepatitis C-related cirrhosis underwent orthotopic liver transplant in 2007. His maintenance immunosuppressive regimen included mycophenolate mofetil and tacrolimus. He also had a history of latent tuberculosis and had completed 9
months of isoniazid after transplantation. In addition, he had developed insulin-dependent diabetes mellitus.

Seven years after transplantation, he presented with 2 months’ duration of fevers. The patient had routine dental work completed with antibiotic prophylaxis, and noted daily fevers around that time, for which he took acetaminophen twice daily. With the fever, he had associated chills, rigors, palpitations, fatigue, and myalgias. He denied any mouth or jaw pain. He also denied weight loss, night sweats, nausea, vomiting, diarrhea, rash, arthralgias, or cough. He worked as a taxi driver, but had not worked in over a month because of fevers and fatigue. He lived with his wife and four children at home, none of whom had been sick recently. Approximately 1 month prior to feeling ill, he traveled to Egypt to visit family. He stayed in an urban area, although did drive in rural areas with the windows down. He denied drinking unpasteurized milk or eating unpasteurized cheese. He did not have pets at home, and denied any hobbies and injection drug use.

His physical evaluation was unremarkable. He was afebrile and normotensive. He was without facial pain or poor dentition, hepatomegaly, or cardiac murmur or stigmata of endocarditis. His initial laboratory evaluation demonstrated normal kidney function, liver function, and blood counts. Negative infectious work-up included Epstein-Barr virus polymerase chain reaction (PCR), cytomegalovirus PCR, Brucella serologies, blood culture, acid-fast bacilli blood culture. Computed tomography scan of the chest, abdomen, and pelvis was unremarkable. Transthoracic echocardiography was performed, and showed normal valvular function.

His Coxiella burnetii serologies returned with phase I and II immunoglobulin (Ig)G positive results (both 1:128), IgM negative (Table 1). Follow-up testing 1 week later showed an increase in phase II IgG to 1:512, while phase I IgG remained 1:128. He was diagnosed with acute Q fever, and started on doxycycline 100 mg twice daily. After approximately 2 weeks of therapy, his fevers completely resolved, and his energy level had improved. He completed 4 weeks of doxycycline therapy. Serologies checked at 5 weeks and 7 months remained elevated (both 1:128), but the patient was asymptomatic, so the plan was continued monitoring.
One year after the initial diagnosis, the patient presented to clinic with complaints of severe fatigue and chills for 2 months. Serologies were repeated, and showed an increase in phase II IgG to 1:256. He had no other symptoms or lab abnormalities, and repeat echocardiogram was stable and without vegetation. The differential was chronic fatigue post Q fever vs chronic Q fever with an inadequate serologic response in an immunosuppressed patient, so he was started on doxycycline and hydroxychloroquine therapy for potential chronic Q fever. Within 4 weeks, his symptoms had resolved, and at 3 months after this therapy, his serologies had decreased (phase I 1:64, phase II 1:32).

3 DISCUSSION
Q fever, a zoonosis caused by the intracellular bacterium *C. burnetii*, causes disease worldwide with few exceptions, such as New Zealand. Ticks are the main reservoir, but mammals, birds, and arthropods may be reservoirs, most notably farm animals.² It is primarily transmitted by the aerosol route, in particular exposures from parturient cattle. Ingestion of unpasteurized milk or cheese, mother-to-child, and very rarely human-to-human transmission are also possible. However, transmission is also present without known animal contact or ingestion, with likely wind exposure bringing the bacterium long distances.³

In immunocompetent hosts with acute Q fever, up to 50% are asymptomatic. If symptoms present, they are non-specific, including fever, malaise, myalgias, headache, chills, non-productive cough, abdominal pain, nausea, vomiting, and diarrhea. Complications include myocarditis, granulomatous hepatitis, pneumonia, neurologic complications, and miscarriage or pre-term labor. Less than 5% develop chronic Q fever, with pregnancy, valvular heart disease or prosthesis, or older age as risk factors for development of chronic infection.¹,⁴

Only three cases of Q fever have been described in solid organ transplant patients, although it is often listed as consideration in the differential for fever of unknown origin in an immunocompromised host. These cases were two renal transplants in adults ⁵,⁶ and one fetal liver and thyroid transplant for a child with Severe combined immunodeficiency who also developed acute lymphocytic leukemia ⁷ (Table 2). All three patients survived.
More cases are described in non-transplant immunocompromised hosts. Those include patients with rheumatoid arthritis, ankylosing spondylitis, and psoriasis on anti-tumor necrosis factor (TNF)-alpha therapy, and patients with human immunodeficiency virus, Crohn’s disease, Hodgkin’s disease, acute myeloid leukemia, acute lymphocytic leukemia, and bone marrow transplant. Overall outcomes are positive, with low mortality rates.

Treatment for acute Q fever is typically doxycycline for 2 weeks. The ideal duration of therapy for acute Q fever in solid organ transplants is unknown, and in case reports of immunocompromised hosts, typically longer durations have been used. In addition, whether or not a transplant patient on immunosuppression would mount an adequate serological response, particularly in the setting of chronic Q fever, is also unknown, although an adequate serologic response for diagnosis of chronic Q fever was evident in a case of a patient on an anti-TNF-alpha agent.

We treated our patient with 4 weeks of doxycycline, and at the end of therapy his symptoms had resolved and he had a decrease in serological titers, although not complete resolution. In acute Q fever, phase II titers predominate and are greater than phase I. Titers typically peak at 14 days and then persist for 10-12 weeks. Six months after therapy, our patient remained clinically well.

However, at 1 year post therapy, he developed fatigue and chills, and he had a small increase in phase II titers. Typically, phase I IgG >800 is diagnostic of chronic Q fever, one reason it is important to continue to monitor serologies for a decrease in titers over time. While a diagnosis of chronic fatigue after Q fever was considered, therapy was initiated for possible chronic Q fever, given our concern for an inadequate serologic response in the setting of immunosuppression. On therapy, his symptoms resolved and his titers have now decreased.

To the best of our knowledge, this is the first described case of acute Q fever in an adult patient after liver transplantation. This highlights the need to consider Q fever in the differential diagnosis for fever of unknown origin in a liver transplant patient, even without direct animal exposure.

AUTHOR CONTRIBUTIONS:

This article is protected by copyright. All rights reserved

REFERENCES


**TABLE 1** Q fever serological results

<table>
<thead>
<tr>
<th></th>
<th>Initial visit (t)</th>
<th>t + 1 week</th>
<th>t + 5 weeks</th>
<th>t + 7 months</th>
<th>t + 12 months</th>
<th>t + 15 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase II IgG</td>
<td>1:128</td>
<td>1:512</td>
<td>1:128</td>
<td>1:128</td>
<td>1:256</td>
<td>1:32</td>
</tr>
<tr>
<td>Phase I IgM</td>
<td>&lt;1:16</td>
<td>&lt;1:16</td>
<td>&lt;1:16</td>
<td>&lt;1:16</td>
<td>&lt;1:16</td>
<td>&lt;1:16</td>
</tr>
<tr>
<td>Phase II IgM</td>
<td>&lt;1:16</td>
<td>&lt;1:16</td>
<td>&lt;1:16</td>
<td>&lt;1:16</td>
<td>&lt;1:16</td>
<td>&lt;1:16</td>
</tr>
</tbody>
</table>

* t, titer; IgG, immunoglobulin G; IgM, immunoglobulin M.
TABLE 2 Reported cases of Q fever in solid organ transplants

<table>
<thead>
<tr>
<th>Author (reference)</th>
<th>Age years, gender, organ</th>
<th>Country</th>
<th>Time since transplant</th>
<th>Immunosuppression regimen</th>
<th>Clinical manifestations</th>
<th>Diagnostic confirmation</th>
<th>Treatment duration</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larsen et al. 5</td>
<td>5, male, kidney</td>
<td>United States</td>
<td>1.5 years</td>
<td>Tacrolimus, sirolimus, prednisone</td>
<td>Acute, complicated by pneumonia, glomerulonephritis</td>
<td>Q fever serologies</td>
<td>Doxycycline 4.5 weeks</td>
<td>Survived</td>
</tr>
<tr>
<td>Godinho et al. 6</td>
<td>60, male, kidney</td>
<td>Portugal</td>
<td>NA</td>
<td>Sirolimus mycophenolate mofetil, prednisolone</td>
<td>Chronic, prolonged fever, anemia</td>
<td>Q fever serologies</td>
<td>Doxycycline and hydroxychloroquine, NA</td>
<td>Survived</td>
</tr>
<tr>
<td>Loudon et al. 7</td>
<td>5, female, fetal liver + thyroid</td>
<td>United Kingdom</td>
<td>4 years</td>
<td>NA</td>
<td>Acute, then chronic, fevers</td>
<td>Q fever serologies</td>
<td>Tetracycline IV, 4 months</td>
<td>Survived</td>
</tr>
</tbody>
</table>

NA, not available.