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CASE REPORT

A case of Q fever after liver transplantation

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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.[8-13] Overall outcomes are positive, with low morality 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.[8]

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.[14] 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[15], 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:

L.A.P.: Significant care of patient, drafting article, and approval of article. K.P. and H.S.T.: Significant care of patient, critical revision, and approval of article.

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TABLE 1 Q fever serological results

		Initial visit (t)	t + 1 week	t + 5 weeks	t + 7 months	t + 12 months	t + 15 months
Phase I	**IgG**	1:128	1:128	1:128	1:128	1:128	1:64
Phase II	**IgG**	1:128	1: 512	1:128	1:128	1:256	1:32
Phase I	**IgM**	<1:16	<1:16	<1:16	<1:16	<1:16	<1:16
Phase II	**IgM**	<1:16	<1:16	<1:16	<1:16	<1:16	<1:16

t, titer; IgG, immunoglobulin G; IgM, immunoglobulin M.

TABLE 2 Reported cases of Q fever in solid organ transplants

Author (reference)	Age years gender, organ	Country	Time since transplant	Immunosup--pression regimen	Clinical manifestations	Diagnostic confirmation	Treatment, duration	Outcome
Larsen et al.[5]	56, male, kidney	United States	1.5 years	Tacrolimus, sirolimus, prednisone	Acute, complicated by pneumonia, glomerulonephritis	Q fever serologies	Doxycycline, 4.5 weeks	Survived
Godinho et al.[6]	60, male, kidney	Portugal	NA	Sirolimus mycophenolate mofetil, prednisolone	Chronic, prolonged fever, anemia	Q fever serologies	Doxycycline and hydroxychloroquine, NA	Survived
Loudon et al.[7]	5, female, fetal liver + thyroid	United Kingdom	4 years	NA	Acute, then chronic, fevers	Q fever serologies	Tetracycline IV, 4 months	Survived

NA, not available.