

Granulomatous Hepatitis and Persistent Fever of Unknown Origin: A Case Report

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ABSTRACT

A 41-year-old man presented with persistent fevers and elevated liver enzymes. Percutaneous liver biopsy revealed fibrin ring granulomas and serologic testing confirmed acute Q fever. Interestingly, his fevers did not resolve with doxycycline alone, and he only clinically improved after hydroxychloroquine was initiated. We discuss the differential diagnosis of fibrin- ring granulomas on liver biopsy as well as the clinical features and treatment of Q fever.

Keywords

Fibrin- ring granulomas, Hepatitis, Q fever, Zoonotic.

Abbreviations

INR: International Normalized Ratio, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, FUO: Fever of Unknown Origin.

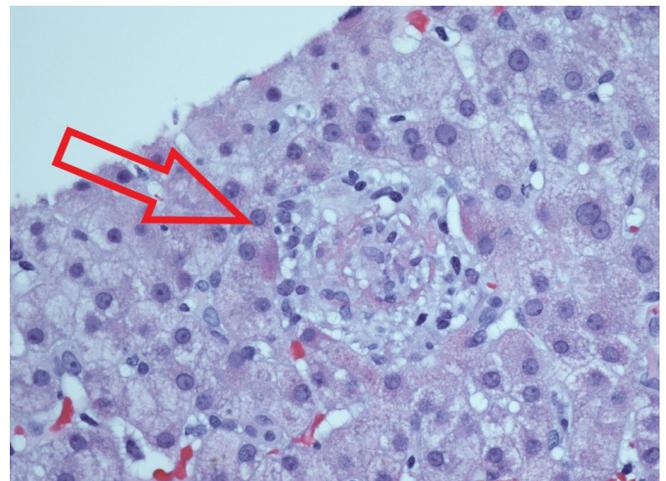
Introduction

Q fever is a rare zoonotic infection caused by the bacteria *Coxiella burnetii*. It has a variety of clinical presentations including granulomatous hepatitis. This histologic finding is characterized by fibrin- ring granulomas on liver biopsy.

Case Report

A 41-year-old man with no significant past medical history was transferred to a tertiary care center for persistent cyclical fevers and elevated liver aminotransferases. Two weeks prior, he developed malaise, profound fatigue, and febrile episodes reaching 39.4 degrees Celsius. He worked as a store manager. He traveled to Missouri two weeks prior to the onset of symptoms. He denied any known contact with animals. Physical exam was unremarkable except for mild hepatomegaly. Laboratory data

was significant for an international normalized ratio (INR) of 2.0, aspartate aminotransferase (AST) 233, alanine aminotransferase (ALT) 139, alkaline phosphatase 223, and total bilirubin 0.7. A comprehensive work up including blood cultures, urine culture, sputum culture, cytomegalovirus, Epstein-Barr virus, fungal titers, and autoimmune serologies were obtained, all of which were normal. He subsequently underwent a percutaneous liver biopsy which demonstrated fibrin- ring granulomas (Figure 1).



Based on the clinical presentation and characteristic fibrin-ring granulomas on liver biopsy, he was started on empiric treatment for Q fever with doxycycline. *Coxiella burnetii* serologies resulted several days later and were notable for an elevated Phase II IgG titer 1:2048 and IgM titer greater than 1:2048 which are diagnostic of acute Q fever. He continued to have daily fevers and abnormal aminotransferases despite being on appropriate antibiotics for eight days, so he was subsequently started on hydroxychloroquine. When he returned to the infectious disease clinic after one month of therapy, his fevers resolved and his aminotransferases improved. The plan was to continue treatment for a minimum of 12 months until his phase II titers became less than 1:200.

Discussion

Q fever is a rare zoonotic infection caused by *Coxiella burnetii* and leads to a wide range of clinical syndromes. Symptoms of Q fever include a non-specific febrile illness, pneumonia, hepatitis, and endocarditis in patients with prosthetic valves. Acute infection virtually always causes fever and is most often a self-limited illness with flu-like symptoms. For more persistent cases of acute Q fever, the most common presenting symptom is fever of unknown origin (FUO) followed by elevated aminotransferases [1]. Human infection most commonly occurs through inhalation of aerosolized excrement from animals infected with the bacteria [2].

Liver biopsy specimens obtained from patients with acute Q fever often demonstrate fibrin-ring granulomas which are suggestive of, but not pathognomonic for the disease. In a case series of 23 patients

with fibrin-ring granulomas, Q fever accounted for the largest proportion, while the remaining cases included leishmaniasis, boutonneuse fever, toxoplasmosis, Hodgkin's disease, allopurinol sensitivity, and idiopathic [3].

The first line treatment for acute Q fever is doxycycline. With appropriate antibiotics, the majority of patients defervesce 72 hours after treatment initiation [2]. Hydroxychloroquine may be added to treat chronic Q fever, also known as persistent localized disease. This particular case is quite rare, in that the patient continued to have fevers despite appropriate first line therapy, and he did not symptomatically or biochemically improve until hydroxychloroquine was initiated.

References

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