



The Quandary of the Quotidian Fever

A case of acute Q-fever with bone marrow granulomas

Jonathon Judkins, MD^{1,2}; Jonathan Taylor, MD^{1,2}; Tae-Soo Kim, MD^{1,2};

Olga Danilova, MD, PhD³; Claire Zeigler, MD^{1,2}; Rianna Wurzburger, MD^{1,2}

¹Department of Medicine, Oregon Health & Science University; ²Department of Medicine, ³Department of Pathology, VA Portland Healthcare System



Introduction

Q fever is a rare zoonotic infection caused by the bacterium *Coxiella burnetii*, typically transmitted through infected livestock, meat or dairy. The culprit exposure may not always be obvious, and the symptoms are often subtle and nonspecific.

Case Description

HPI:

A 62-year-old long-haul truck driver with a history of diabetes and coronary artery disease presented with a 1-month history of nocturnal fevers, drenching night sweats, weight loss, and general malaise. He denied recent travel or obvious animal/environmental exposures.

INITIAL EXAM:

T 98.4°F, BP 94/58, HR 99, RR 16, SpO2 98%

No rash, murmur, lymphadenopathy

INITIAL LABS:

AST 58, ALT 86, AlkP 182, Tbil1 0.9
ESR 34, CRP 69.9, LDH 537, ferritin 1768
Pit 89 (baseline ~200)

SUBSEQUENT LABS:

Negative infectious labs:

- Bartonella, Brucella, Mycobacteria
- Malaria/blood parasite smear
- HIV, HAV/HBV/HCV, RVP, CMV, West Nile, HSV1/2, VZV, HHV-8
- Dimorphic molds
- Blood cultures
- Echocardiogram (endocarditis)

Negative rheumatologic labs:

- Actin, C3/C4, α-DNA Ab

Positive labs:

- ANA 1:80, speckled pattern
- RF 69.9
- α-SSA Ab
- EBV IgG (IgM and PCR neg)
- Q-fever phase II IgM and IgG

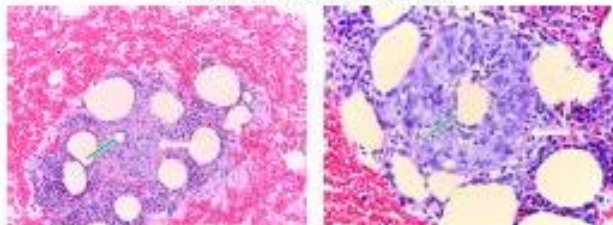
IMAGING:

CT C/A/P: hepatosplenomegaly, enlarged mediastinal lymph node, lung nodule

PET-CT: Increased uptake in R mandible (known poor dentition), sacrum, and L adrenal with no evidence of lymphoma or other malignancy

Bone Marrow Analysis of Our Patient

MARROW HISTOPATHOLOGY



Bone marrow biopsy and clot section (H&E, 200X, 400X) showed non-caseating "doughnut ring" granulomas, as seen above. The granulomas are composed of a central vacuole (green arrow) surrounded by epithelioid histiocytes and neutrophils with an outer fibrin ring (red arrow). This type of granuloma can be suggestive of Q-fever infection, but is not pathognomonic. See other common etiologies below.

MARROW PCR AND STAINING

- EBV, TB, and fungal stain negative
- Bacterial, fungal, and TB PCR negative
- No immunophenotypic evidence for leukemia, lymphoma, or plasma cell neoplasm

MARROW FLOW CYTOMETRY

- No evidence for leukemia, lymphoma, or plasma cell neoplasm
- No increase in CD34+ blasts
- Polyclonal B cells and plasma cells
- Normal CD4:CD8 ratio

Common Bone Marrow Granuloma Etiologies⁶

Infectious	Malignant	Other
Mycobacteria	Lymphoma	Sarcoidosis
Histoplasmosis	ALL/AML/CML	Other autoimmune
CMV/EBV	Multiple myeloma	Procainamide
Q fever	Colon/lung/ovarian cancer	Sulfonamide
Brucellosis	Sarcoma	Foreign bodies
Typhoid fever		Chronic renal failure

Common Q-Fever Symptoms and Labs¹

Symptom	%	Lab Abnormality	%
Asymptomatic	60	↑ AST/ALT	62
Fever	91*	↑ ESR	55
Headache	51*	Thrombocytopenia	35
Pneumonia	27*	Anti-smooth muscle antibody	20
Rash	11*		

*Percentage of asymptomatic patients

Hospital Course

During his hospitalization, he suffered from persistent, daily nocturnal fevers (Tmax 38.8 °C) and profuse night sweats but was otherwise asymptomatic. An infected molar was removed without resolution of fevers.

On further questioning after *Coxiella burnetii* serologies returned positive, he reported occasionally transporting raw beef. He was diagnosed with acute Q-fever, treated with 14 days of doxycycline, and was asymptomatic at follow-up one month later.

Discussion

- Acute Q-fever presents with a non-specific constellation of symptoms and lab findings, which can present a diagnostic quandary for clinicians
- Typically asymptomatic, but isolated fever is the most common symptom¹⁻²
- Elevated AST/ALT, elevated ESR, and thrombocytopenia are the most common lab abnormalities^{1,2}
- Can cause generalized immunological arousal and false-positive autoimmune assays. This may have been the cause of the positive ANA, RF and SSA antibodies in our patient.
- Bone marrow granulomas can be seen in infections, connective tissue disease, sarcoidosis, malignancies, and secondary to certain medications⁴⁻⁶
- With no unique pattern of lab findings or pathognomonic symptoms, the diagnosis of acute Q-fever must be made serologically or via bacterial nucleic acid testing, with testing largely based on risk factors and exposures uncovered during thorough history taking

Teaching Points

- Q-fever is usually asymptomatic; the most common symptom is isolated fever
- The most common lab abnormalities are elevated AST/ALT, elevated ESR, and thrombocytopenia
- Bone marrow granulomas can narrow a differential, but are not diagnostic in acute Q-fever or other etiologies
- HISTORY-TAKING IS IMPORTANT!

References

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