An Unusual Case of Fever of Unknown Origin

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Case

- Chief complaint: Fever
- HPI: 84 year old woman with history of mitral valve replacement, admitted for fever evaluation
  - Several fevers per week for 2 years
  - Associated fatigue, night sweats, and 25 lb weight loss

Fever History

- Previous work up:
  - Transthoracic and transesophageal echocardiography
  - Bronchoscopy
  - Bone marrow biopsy
  - Temporal artery biopsy
  - Positron emission tomography
  - Multiple computerized tomography scans of head, chest, abdomen, pelvis

Pertinent History

- Mitral valve replacement for mitral regurgitation
  - Two additional mitral valve replacements for regurgitation
  - Aerobic and anaerobic cultures from valves negative

Pertinent History

- Family history unremarkable
- Social history notable for exposure to rabbits, dogs, cats, and raccoons
- Patient up to date on colon and breast cancer screenings

Physical Exam

- Temp 101.2 F, HR 96, RR 16, BP 131/61, O2 sat 95%
- Exam notable for:
  - I/VI systolic murmur at base
  - Trace lower extremity edema

Labs

Initial lab work notable for:

- Hemoglobin/hematocrit 10.3/32, MCV 76
- Platelets 109
- White blood cell count 4.1 (63% neutrophils, 30% lymphocytes, 7% monocytes)
- Normal complete metabolic panel
- C reactive protein 3.6

- Additional work up included:
  - Blood and urine cultures
  - Serum and urine protein electrophoresis
  - Anti-nuclear antibodies
  - HIV 1/2 antibodies
  - Bartonella henselae and Bartonella quintana antibodies
  - Lyme antibodies
  - Erlichia antibodies
  - Babesia antibodies
  - Transthoracic and transesophageal echocardiography
  - Computerized tomography scans of abdomen and pelvis
  - Bone survey

Ultimately the patient's Q fever serologies returned positive

- Phase I antigen antibody 1:2048
- Phase II antigen antibody 1:2048
- Normal range: undetectable

Q Fever

- Zoonotic infection caused by *Coxiella burnetti*
- Pleomorphic gram negative coccobacillus
- Transmitted by goats, sheep, cattle, dogs, cats, rabbits
- Transmission by inhalation of contaminated aerosols
- Disease incidence 0.4 cases per 1 million persons

Source: https://commons.wikimedia.org/wiki/File:Goat_cartoon_04.svg

Q Fever: Acute Infection

- Flu-like illness, hepatitis, or pneumonia
- Frequently self-limited
- Diagnosis: antibodies to Q fever phase I and phase II antigens
- Treatment: Doxycycline for 2-3 weeks
- Mortality <2%

Q Fever: Chronic Infection

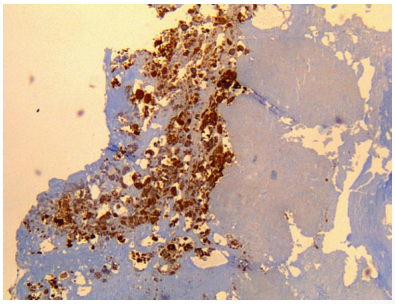
- Endocarditis, hepatitis, osteomyelitis, or chronic vascular infections
- Diagnosis: elevated phase I and phase II antigen antibodies
- Treatment: Doxycycline and hydroxychloroquine for 18 months
- Fatal if untreated, mortality 24% despite treatment

Q Fever Endocarditis

- Most common form of chronic Q fever
- Exclusively in patients with valve pathology
- Can present as fevers, recurrent valvular dysfunction, or congestive heart failure
- Rarely vegetations on echocardiography or thromboembolic phenomenon

Q Fever Endocarditis

- Definitive diagnosis with immunohistochemical stains or PCR from valve tissue
- Revised Duke Criteria include elevated phase I antigen antibody (>1:800) as major criteria



From: Mahamat A, Edouard S, Demar M, Abboud P, Patrice J-Y, La Scola B, et al. Unique clone of *Coxiella burnetii* causing severe Q fever, French Guiana. Emerg Infect Dis [Internet]. 2013 Jul. http://dx.doi.org/10.3201/eid1907.130044

Patient Course

- Started on doxycycline and hydroxychloroquine
- Discharged to home at baseline
- Readmitted 4 months later with progressive heart failure
- Opted for palliative course and died at home

Conclusions: Q Fever

- Caused by Coxiella burnettii
- Endocarditis is the most common chronic form and occurs exclusively in patients with valve disease
- The organism is an obligate intracellular pathogen; It will not grow on blood cultures and vegetations are rare
- Clinicians should have a high index of suspicion in patients with valve disease with unexplained fevers or recurrent valve dysfunction

Thank you!

Thank you to Medical College of Wisconsin Department of General Internal Medicine and Dr. Andrew Petroll for help in preparing this presentation

References

1. AlShukairi, A. N., Morshed, M. G., & Reiner, N. E. (2006). Q Fever Presenting As Recurrent, Culture-negative Endocarditis with Aortic Prosthetic Valve Failure: A Case Report and Review of the Literature. *The Canadian Journal of Infectious Diseases & Medical Microbiology*, *17*(6), 341–344.
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