Chest Pain and a Sore Throat

COURTENEY MACKUEN, MD; JEFFREY FEDEN, MD; BONNIE MARR, MD; WILLIAM BINDER, MD

Case Records of the Brown University Residency in Emergency Medicine

DR. COURTENEY MACKUEN: The patient was a 36-year-old-man who presented to the Emergency Department (ED) with the sudden-onset of substernal chest pain that woke him from sleep just prior to arrival. The pain was sharp and radiated down his left arm. It was associated with shortness of breath and diaphoresis. He had never experienced similar pain previously. The patient was otherwise a healthy, employed, married man with two children at home. He reported subjective fevers and chills three days prior to his visit and had had several loose stools. He also complained of a sore throat and headache for the past several days. He denied cough or runny nose, and he denied abdominal pain. He stated that he had been taking ibuprofen for the past 24 hours because he was simply not feeling "well." The patient denied any illicit drug use and is a former smoker. Ill contacts included his 9-year-old son who was diagnosed with streptococcal pharyngitis approximately two weeks prior to presentation and was treated with amoxicillin for ten days. His family history is only significant for coronary disease in his father at the age of 55. The patient has two dogs and keeps an aquarium.

DR. WILLIAM BINDER: Can you describe his exam?

DR. MACKUEN: This gentleman appeared uncomfortable, and diaphoretic. His blood pressure was 94/64 mmHg, heart rate at 114 beats per minute, temperature of 102.7 degrees Fahrenheit, and oxygen saturation 98% on room air. The patient's exam demonstrated an erythematous posterior pharynx with minimal exudate and mild nasal discharge. He had no cardiac murmurs, rubs, or gallops and his pulses and blood pressures were equal bilaterally. The lung exam was unremarkable and his abdomen was soft, nontender, and nondistended. There was no hepatosplenomegaly. There was no edema in the legs. His neurologic exam was normal.

DR. FRANTZ GIBBS: What were your initial concerns in the evaluation of this patient?

DR. MACKUEN: Of the 130 million emergency department visits in the US, chest pain is one of the most frequently encountered complaints, accounting for over 6 million visits to the nation's EDs annually. The initial focus among emergency physicians is to consider life-threatening conditions, such as acute coronary syndrome (ACS), pulmonary embolism, and aortic dissection. Though sharp pain is atypical for ACS, radiation of pain into the left arm has an odds ratio of 1.7 for ACS. (1) The patient's relatively young age and lack of risk factors reduced the likelihood of ACS, and his fever prompted a broader differential diagnosis.

DR. ALEXIS LAWRENCE: What studies were performed and how did the results affect the differential diagnosis?

DR. JEFFREY FEDEN: National guidelines mandate a 12-lead electrocardiogram (ECG) within ten minutes of ED arrival for all patients presenting with chest pain or possible anginal symptoms. Our patient's ECG (**Figure 1**) shows striking ST segment abnormalities which are generalized to the limb and precordial leads and not associated with the characteristic reciprocal changes suggestive of acute ST-elevation myocardial infarction. ST segment changes like these may be seen in acute pericarditis and benign early repolarization. The ECG changes prompted additional testing including a complete blood count (CBC), basic metabolic panel, and

Figure 1. 12-lead electrocardiogram demonstrating diffuse ST segment changes suggestive of pericarditis rather than myocardial infarction.

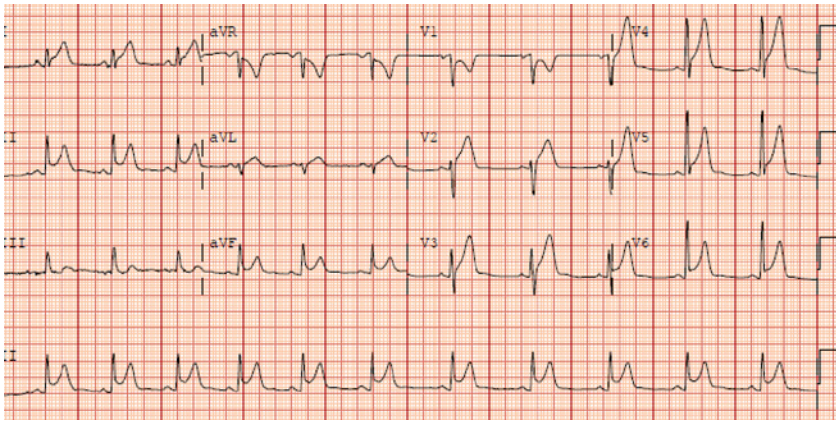

Table 1

WBC	27 x 10 (9)	67% Segs, 13% Bands
Troponin	10.44 ng/mL	
TSH	1.31 uIU/ml	
CRP	227.5 mg/L	
ESR	65 mm/h	
HIV	Non reactive	
Rapid Strep A antigen	Positive	
Heterophile antibody	Negative	

troponin. The CBC revealed leukocytosis with 13% bands, and the troponin was elevated **(Table 1**). A portable chest radiograph was unremarkable. The elevated troponin, taken along with the ECG findings and febrile illness, suggested myopericarditis as a leading diagnosis.

In the United States and other developed countries, viral infections including Coxsackie A and B, Echoviruses, Hepatitis C, Epstein-Barr virus (EBV), Cytomegalovirus (CMV), Respiratory syncytial virus (RSV), Influenza, and many others are the most common causes of myocarditis, pericarditis, and myopericarditis. (2, 3) Approximately 10-20% of cases are associated with connective tissue diseases, cancer, radiation, and post-cardiac injury syndromes. (4, 5) Additional causes include bacterial, protozoal, and parasitic disorders, in addition to medications. (3)

In the developing world, rheumatic fever, dengue and Chagas disease remain important causes of myocarditis. The patient did not report any travel history; therefore, a mono-like illness such as CMV, EBV, or HIV is a more likely cause of his illness. I would also consider checking a throat culture since he further presents with exudative pharyngitis.

DR. MACKUEN: The monospot, HIV, and CMV serologies were negative. A rapid streptococcal antigen test was positive and acute phase reactants were elevated—the erythrocyte sedimentation rate [ESR] was 65 mm/h and the C-reactive protein [CRP] was 227.5 mg/L.

DR. ANDREW NATHANSON: The patient meets some of the criteria for Acute Rheumatic Fever (ARF). How common is ARF and can you review the Jones criteria?

DR. MACKUEN: Rheumatic heart disease still reaches epidemic proportions in low-income and socially-disadvantaged populations worldwide. (6) It is estimated that nearly 20 million people in total are affected globally, and rheumatic heart disease remains a leading cause of heart failure through the 5th decade of life. (7, 8) In the United States (US), the prevalence is much lower at approximately 2 per 100,000. (9, 10) This low prevalence is attributed to better living conditions, antibiotic use against Group A β hemolytic Streptococcus (GABHS) and, more fundamentally, to a shifting (non-rheumatogenic) GABHS serotype. (6, 11)

The original Duckett Jones criteria were published in 1944, modified in 1992, and have traditionally been used to diagnose ARF. Diagnosis requires evidence of GABHS infection (positive throat culture or rapid antigen test, or elevated antistreptolysin O antibody titer) in addition to one major and two minor criteria, or two major and one minor criteria. The major criteria include carditis, arthritis, chorea, subcutaneous nodules, and erythema marginatum. The most common findings are carditis (50-70%) and arthritis (33-66%). The minor criteria consist of fever, arthralgia, elevated ESR/CRP, and PR interval prolongation. (8)

There have been several updates to these criteria, most recently in 2015. (12) The criteria now include echocardiogram as a diagnostic tool for subclinical carditis. Since 1992, there has been increasing debate about the utility of echo in diagnosing subtle heart disease. Previously, carditis was diagnosed using cardiac biomarkers (i.e., troponin) or auscultation for valvular abnormalities. With the 2015 update, echocardiogram may be used to diagnose valvular involvement in the absence of clinical symptoms (Level I evidence).

Although the addition of echocardiography was a major change in 2015, several other small changes are noteworthy. (12) New guidelines separate minor criteria into greater detail depending on the population prevalence of ARF. For example, "arthritis" in low-risk populations was changed to "polyarthralgias." Low-grade fever is included in the minor criteria in high-risk populations and ESR must be greater than 60 in low-risk populations.

DR. BRUCE BECKER: How does one contract acute rheumatic fever? Can it be prevented?

DR. MACKUEN: Acute rheumatic fever is a delayed inflammatory sequela of GABHS and often occurs about two weeks after the initial pharyngitis. Although ARF has been studied for more than 150 years, the exact pathogenesis remains elusive. An autoimmune response causing ARF may be triggered by molecular mimicry between group A streptococcus antigenic determinants and human cardiac tissue. (13) The primary preventive method is treatment of pharyngitis with appropriate antibiotics.

DR. BRIAN CLYNE: Was an echocardiogram performed? Did the patient meet the Jones criteria?

DR. MACKUEN: An echocardiogram showed no evidence of valvular disease and further demonstrated normal left ventricular function. However, the patient's myopericarditis (with an initial troponin elevation) certainly qualifies as one of the major Jones criteria. In combination with elevated inflammatory markers and fever, our patient met two minor criteria for ARF.

DR. FEDEN: There are some limitations to the Jones criteria. As the incidence of ARF has decreased in developed

countries, the Jones criteria are increasingly specific but have reduced sensitivity. An alternative cause can be considered in this case – myopericarditis due to acute streptococcal pharyngitis – but the evidence for this diagnosis is indirect. The absence of valvular disease is occasionally noted in acute rheumatic fever but is an uncommon finding. (9). Additionally, ARF has a median onset of two weeks after an episode of overt or subclinical pharyngitis, unlike this patient who presented acutely.

The pathogenesis of nonrheumatic streptococcal myocarditis has not been elucidated, but it may be due to both cross-reactivity between cardiac M proteins and streptococcal antigens, in addition to a direct insult of pyogenic exotoxins and hemolysins on the myocardium. (14, 15) It is a rarely reported diagnosis. (14, 15, 16)

DR. THOMAS HARONIAN: What happened to your patient?

DR. MACKUEN: The patient was treated with penicillin in the ED, and admitted to the hospital. His troponin peaked at 86.7 ng/mL on hospital day 3, and his symptoms subsided by hospital day 4. He was discharged to home. An echocardiogram one month later still showed no evidence of valvular disease or left ventricular dysfunction. His ECG normalized.

FINAL DIAGNOSIS: Acute rheumatic fever causing myopericarditis without valvular involvement versus nonrheumatic streptococcal myocarditis.

References

1. Goodacre S, Locker T, Morris F, Campbell S. How useful are clinical features in the diagnosis of acute, undifferentiated chest pain? Academic Emergency Medicine. 2002; 9: 203-208.
2. LeWinter MM. Acute Pericarditis. NEJM. 2014; 371: 2410-2416
3. Imazio M, Trinchero R. Myopericarditis: Etiology, management, and prognosis. International Journal of Cardiology. 2008; 127: 17-26.
4. Maisch B, Serovic PM, Ristic AD et al. Guidelines on the diagnosis and management of pericardial diseases executive summary: The Task Force on the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology. European Heart Journal. 2004; 25: 587-610.
5. Seferovic PM, Ristic AD Maksimovic R, et al. Pericardial Syndromes: An update after the ESC guidelines. Heart Failure Review. 2013: 18: 255-266.
6. Seckeler MD, Hoke TR. The Worldwide epidemiology of Acute Rheumatic Fever and Rheumatic Heart Disease. Clinical Epidemiology. 2011; 3: 67-84.
7. Chakravarty SD, Zabriskie JB, Bibofsky A. Acute Rheumatic Fever and Streptococci: The Quintessential Pathogenic Trigger of Autoimmunity. Clinical Rheumatology. 2014; 33: 893-901.
8. Martin WJ, Steer AC, Smeesters PR, Keeble J, Inouye M, Carapetis J, Wicks IP. Post-Infectious Group A Streptococcal Autoimmune Syndromes and the Heart. Autoimmunity Reviews. 2015; 14: 71-725.
9. Burke RJ, Chang C. Diagnositic Criteria of Acute Rheumatic Fever. Autoimmunity Reviews. 2014; 13: 503-507.
10. Cilliers AM. Rheumatic Fever and Its Management. BMJ. 2006; 333: 1153-1156.
11. Essop M, Peters F. Contemporary issues in Rheumatic Fever and Chronic Rheumatic Heart Disease. Circulation. 2014; 130: 2181-2188)
12. Gewirtz MH, Baltimore RS, Tani LY, et al. Revision of the Jones Criteria for the Diagnosis of Acute Rheumatic Fever in the Era of Doppler Echocardiography: A Scientific Statement From the American Heart Association. Circulation; 2015: 131: 1806-1818.
13. Carapetis JR, McDonald M, Wilson NJ. Acute Rheumatic Fever. Lancet. 2005; 366: 155-168.
14. Khavandi A, Whitaker J, Elkington A, Probert J, Walker PR. Acute Streptococcal myopericarditis mimicking myocardial infarction. American Journal of Emergency Medicine 2008;26: 638.e1-638.e2.
15. Said SAM, Severin WPJ. Acute NonRheumatic Myopericarditis Associated with Group A Hemolytic Streptococcal Tonsillitis in a male ICU-nurse. The Netherlands Journal of Medicine. 1998; 53: 266-270.
16. Karjalainen J. Streptococcal tonsillitis and acute nonrheumatic myopericarditis. Chest. 1989: 95: 359-363.

Authors

Courteney MacKuen, PGY4, Alpert Medical School of Brown University.

Jeffrey Feden, MD, Assistant Professor, Dept. of Emergency Medicine, Alpert Medical School of Brown University.

Bonnie Marr, MD, former Emergency Medicine Resident, Alpert Medical School of Brown University.

Willliam Binder, MD, Associate Professor of Emergency Medicine Alpert Medical School, Brown University.

Correspondence

William Binder, MD
Emergency Medicine Foundation
593 Eddy St
Providence, RI 02903
401-444-5411
Fax 401-444-4307
William_Binder@brown.edu