Young Man With Chest Pain, Headache, and Muscle and Joint Pain

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Which test—antistreptolysin O titers, coronary angiography, enzyme-linked immunosorbent assay (ELISA), Western blot testing for Borrelia burgdorferi, or genetic testing for long QT syndrome—would help you diagnose a young man with worsening chest pain, frontal headache, and diffuse muscle and joint pain?

For several weeks, a 35-year-old man has had worsening chest pain, frontal headache, and diffuse muscle and joint pain. The patient was initially treated conservatively with ibuprofen for a presumed viral syndrome. However, because of his minimal response to the NSAID and a strong family history of early cardiac disease (his father had a “heart attack” at age 40), he is hospitalized.

HISTORY
The patient was previously healthy; he takes no long-term medications. He does not smoke or use illicit substances. He works as a professional arborist in southeastern Pennsylvania and frequently spends time in areas of heavy foliage. However, he has been unable to work regularly since the onset of his symptoms.

PHYSICAL EXAMINATION
Temperature is 37.2°C (99°F); heart rate, 52 beats per minute; blood pressure, 110/60 mm Hg; and oxygen saturation, normal on room air. No rashes, lymphadenopathy, or oral lesions are noted. Aside from bradycardia, results of a cardiac examination are normal. The lungs are clear, and the abdomen is normal. There is diffuse joint tenderness with palpation and deep inspiration, especially along the costosternal joints; no effusion is noted. Results of a neurologic examination are nonfocal.

LABORATORY AND IMAGING RESULTS
Results of a complete blood cell count and serum chemistry panel are all normal. Serum total cholesterol level is 133 mg/dL. Erythrocyte sedimentation rate is 54 mm/h. Cardiac troponin levels are less than 0.05 ng/mL on admission (normal range, 0.05 to 0.5), and at 8 and 16 hours thereafter. Chest radiograph shows no active disease. ECG reveals first-degree atrioventricular (AV) block, with a PR interval of 0.32 millisecond; otherwise it is normal. A transthoracic echocardiogram shows normal left ventricular function with no pericardial effusion. Myocardial perfusion imaging reveals no evidence of ischemia; however, the maximum heart rate with exercise is only 95 beats per minute (target rate, 157 beats per minute). During the exercise portion of the study, frequent episodes of Mobitz type I and type II conduction delays are noted; these continue intermittently on telemetry for several hours afterward. Which of the following studies is most likely to lead to the diagnosis?

A. Antistreptolysin O titers.
B. Coronary angiography.
C. Enzyme-linked immunosorbent assay (ELISA) and Western blot testing for Borrelia burgdorferi.  
D. Genetic testing for long QT syndrome. CORRECT ANSWER: C

Antistreptolysin O titers (choice A) are helpful in the evaluation of acute rheumatic fever. However, none of the major Jones criteria for that illness—arthritis, carditis, chorea, and subcutaneous nodules or erythema marginatum—are present here. This patient has tenderness mainly in the costochondral joints; there is no history of migratory arthritis in the large joints more typical of rheumatic fever. There is no evidence of murmurs or pericardial effusions, and he has a normal ejection fraction. Although the onset of rheumatic fever can be subtle, characterized chiefly by mild carditis, the lack of hard evidence for any of the major diagnostic criteria make this entity very unlikely. PR prolongation does occur in 25% of patients with acute rheumatic fever but is neither specific for nor diagnostic of the disease.

The patient had a normal perfusion imaging scan. While it is true that he did not achieve the target heart rate, the absence of ischemic changes on the ECG and of elevated troponin levels at any point in the course of his illness make ischemia unlikely. Moreover, ischemia is not a common cause of isolated heart block. The clinical scenario here is much more suggestive of a systemic illness than of coronary artery disease; coronary angiography (choice B) is thus inappropriate.
Long QT syndrome can cause cardiac arrhythmias, syncope, and even sudden death. However, the prolonged QT interval will be evident on the ECG. Here, the PR interval is prolonged. In addition, the arrhythmias most likely to be seen are torsade de pointes and ventricular tachycardia—not heart block. Thus, there is no basis for genetic testing for long QT syndrome.

Lyme disease can potentially account for all of this man's symptoms. Moreover, his history of working in heavily wooded areas in a region where Lyme disease is endemic gives further weight to this diagnostic possibility. Lyme disease is caused by *B. burgdorferi*, a spirochete transmitted by the *Ixodes scapularis* tick nympha.

**Symptoms of Lyme disease.** The disease typically begins with erythema migrans, a localized, round rash with central clearing at the site of the tick bite. This rash can appear from 3 to 5 days following the bite; it is not recognized in about 20% of infected patients. The rash stage is usually accompanied by flu-like symptoms. About 10% of patients with Lyme disease have no symptoms. Rheumatologic, neurologic, and cardiac manifestations can occur in subsequent weeks and months. About 60% of patients with untreated Lyme disease experience bouts of arthritis in the months following infection, usually in the knees and other large joints. Neuroborreliosis develops in about 15% of untreated patients within weeks of infection, resulting in a range of symptoms. These can include headache, cranial nerve palsy, neck stiffness, and lymphocytic meningitis. Cardiac abnormalities occur in about 5% of untreated patients within several weeks of infection. Typically, findings include varying degrees of high-grade AV block, myocarditis, and mild heart failure.¹

**Diagnosis of Lyme disease.** Diagnosis is based on the history, symptoms, exposure to infected ticks, physical findings, and serologic testing when appropriate. Patients with erythema migrans do not require serologic testing. For patients, such as this man, in whom erythema migrans is not noted but who have at least 1 symptom or manifestation consistent with Lyme disease, 2-step antibody testing (an ELISA and Western blotting for *B. burgdorferi* antibodies) (choice C) is appropriate. The CDC recommends that all specimens found to be positive or equivocal on ELISA be tested with a standardized Western blot test. Specimens found to be negative on ELISA need not be tested further. However, if Lyme disease is strongly suspected, even though the initial ELISA result is negative, it is recommended that the test be repeated during the convalescent phase of the illness (weeks 2 through 4) if the initial test was done during the acute phase. In the first 2 weeks following infection, 20% to 30% of ELISAs yield negative results. In patients with acute illness of less than 1 month's duration and positive or equivocal results on ELISA, measure IgG and IgM antibodies with a Western blot test. After 1 month of infection, only IgG antibodies can be used to establish the diagnosis.

**Outcome of this case.** A presumptive diagnosis of Lyme disease was made. Intravenous ceftriaxone was started empirically and continued for 21 days; the presenting symptoms and conduction abnormalities gradually resolved. Diagnosis was confirmed by a positive result on a 2-step antibody test. After the patient returned to work, he began wearing protective clothing and using insect repellent—and “tick checks” are now part of his post-work routine.

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