MAYO CLINIC

86-Year-Old Man With Atrial Fibrillation and Dyspnea on Exertion

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See end of article for correct answers to questions.

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An 86-year-old man with a history of atrial fibrillation (AF) and lower extremity venous stasis ulcers presented to our primary care clinic to establish care. He had dyspnea on exertion that had worsened from baseline limiting his capacity to perform basic activities of daily living including getting dressed. He also had progressive lower extremity swelling for several years and had received ongoing treatment of his venous stasis ulcers from a local vascular surgeon.

The patient was taking metoprolol tartrate, 25 mg twice a day, for symptomatic AF diagnosed at an outside institution. His other medications included fish oil and aspirin, 325 mg daily. He reported no nonsteroidal anti-inflammatory drug use or excessive salt intake. He had not experienced any cough, sputum production, angina, syncope, presyncope, paroxysmal nocturnal dyspnea, orthopnea, or sleep apnea and did not use tobacco or alcohol.

On examination, the patient was able to speak in full sentences but with difficulty. His blood pressure was 135/89 mm Hg, pulse rate was 93 beats/min, respiratory rate was 18 breaths/min, and oxygen saturation was 97% while breathing room air. His body mass index was 26 kg/m^2. Cardiovascular examination revealed an irregularly irregular rhythm, normal S_1 and S_2, and no murmurs, rubs, gallops, or heaves. The point of maximal impulse was enlarged and laterally displaced. There was mild jugular venous distention with a jugular venous pressure of 9 cm and normal waveforms. On pulmonary examination, bibasilar crackles without wheeze were noted. Abdominal examination findings were normal. Examination of the lower extremities revealed 3+ pitting edema involving both knees and healing venous stasis ulcers.

1. **Which *one* of the following is the *most likely* cause of the patient's dyspnea on exertion?**
   a. Heart failure (HF)
   b. Chronic venous thromboembolism (CVTE)
   c. AF
   d. Chronic obstructive pulmonary disease (COPD)
   e. Myocardial ischemia (MI)

The patient presented with clinically important progressive HF with New York Heart Association class III-IV symptoms. Heart failure should be distinguished from other causes of dyspnea including MI, CVTE, and COPD. Chronic venous thromboembolism is a cause of chronic dyspnea and pulmonary hypertension and may present with peripheral edema and jugular venous elevation. However, the absence of parasternal heave, prominent S_2, and risk factors for venous thrombosis in our patient make CVTE unlikely. Atrial fibrillation is a common arrhythmia that typically presents with palpitations and is associated with HF,[1] but it would not explain the clinical presentation in this patient. Pulmonary diseases such as COPD or emphysema are unlikely to present without cough and sputum production in a patient with no smoking or exposure history. Myocardial ischemia can present with exertional dyspnea. However, the clinical examination findings of jugular venous distention, peripheral edema, and pulmonary congestion make HF the most likely diagnosis.

The decision was made to pursue an outpatient evaluation for suspected HF.

2. **To evaluate this patient's HF, which *one* of the following is the *most useful* diagnostic test?**
   a. B-type natriuretic peptide (BNP)
   b. Computed tomography of the chest
   c. Ventilation-perfusion scan
   d. Transthoracic echocardiography
   e. Cardiac angiography

The initial evaluation of patients with HF should include a complete blood cell count, urinalysis, serum electrolyte panel, thyroid function tests, lipid measurements, renal and hepatic function tests, chest radiography, and

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12-lead electrocardiography.[2] B-type natriuretic peptide is not a reliable measure of the severity of chronic HF[2]; however, elevated levels of BNP may lend weight to a suspected diagnosis of HF. Chest computed tomography would be helpful in assessing parenchymal change but is not indicated in this patient because there is low pretest probability of pulmonary disease. A ventilation-perfusion scan would be helpful in the diagnosis of CVTE as a cause of pulmonary hypertension leading to HF but would not be the first test to establish a diagnosis of HF.[3] Comprehensive transthoracic echocardiography with Doppler flow studies is an essential part of the initial evaluation of HF and is the single most useful diagnostic test.[2] Echocardiography can help establish whether abnormalities of the myocardium, heart valves, or pericardium are present and which chambers are involved. This information is important because patients often have more than one cardiac abnormality that contributes to the development of HF.[2] Evaluation for MI with coronary angiography should be part of the initial evaluation for most patients with new-onset or worsening HF. However, the diagnosis of HF should be established before proceeding with cardiac catheterization.

Laboratory studies yielded the following results (reference ranges shown parenthetically): hemoglobin, 16.5 g/dL (13.5-17.5 g/dL); leukocytes, 9.7 $\times$ 10^9/L (3.5-10.5 $\times$ 10^9/L); platelet count, 176 $\times$ 10^9/L (150-450 $\times$ 10^9/L); potassium, 5.1 mmol/L (3.6-5.2 mmol/L); serum urea nitrogen, 25 mg/dL (8-24 mg/dL); creatinine, 1.2 mg/dL (0.8-1.3 mg/dL); N-terminal pro-BNP, 4118 pg/mL (<138 pg/mL); and thyrotropin, 4.7 mIU/L (0.3-5.0 mIU/L). Urinalysis revealed proteinuria (1+).

Chest radiography documented mild cardiomegaly, no overt pleural effusions, and a tortuous aorta but no other abnormalities. Electrocardiography revealed AF with a ventricular rate of 81 beats/min and right axis deviation. Low voltage was also present. On echocardiography, left ventricular (LV) systolic function and chamber size appeared normal. The calculated LV ejection fraction was 59%. The mitral annulus media E/e′ ratio was 33.3, consistent with severely increased LV filling pressure and ventricular septal thickness. No regional wall motion abnormalities were noted. Results of strain imaging examination, performed to assess LV function and global averaged LV longitudinal peak systolic strain, were abnormal at −7% (normal, −18% or less). Mild to moderate left atrial enlargement was noted. The right ventricular (RV) size was normal, but a moderate to severe decrease in RV systolic function was observed. Estimated RV systolic pressure was 32 mm Hg (systolic blood pressure, 130 mm Hg). No serious valvular disease, intracardiac mass or thrombus, or pericardial effusion was detected.

The patient's echocardiographic findings, including increased ventricular wall thickness, diastolic dysfunction, and worsened strain pattern, were suggestive of infiltrative cardiomyopathy. Cardiomyopathies are divided into 3 major functional categories: dilated, hypertrophic, and restrictive. Restrictive cardiomyopathy is the least common form and consists of infiltrative and noninfiltrative subtypes. The 2 most likely conditions for infiltrative cardiomyopathies are amyloidosis and sarcoidosis.[4,5] Sarcoidosis typically presents in young to middle-aged people, rarely first manifesting with cardiac disease.[6] Given our patient's age and the absence of other pulmonary symptoms, a work-up for amyloidosis was pursued.

3. Which *one* of the following is the *best* test to establish a diagnosis of amyloidosis in this patient?

a. Serum protein electrophoresis (SPEP) and urinary protein electrophoresis (UPEP) with immunofixation
b. Free light chain (FLC) analysis
c. Fat aspiration biopsy
d. 24-Hour urinary protein collection
e. Bone marrow biopsy

The initial SPEP and UPEP should always be performed in combination with serum immunofixation. Immunofixation is done in order to determine and confirm monoclonality and to distinguish the immunoglobulin heavy and light chain class if an M protein is identified. The serum FLC assay is a sensitive antibody-based assay that can detect low concentrations of monoclonal FLCs in the serum. Fine-needle aspiration of abdominal fat is a simple, safe procedure with more than 80% positivity and is the currently preferred method for diagnosing amyloidosis. Additionally, abdominal fat tissue