85-Year-Old Man With Chest Pain

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An 85-year-old man presented to the emergency department with 3 hours of left-sided chest pain. He described the pain as an abrupt onset, intense, sharp, and pleuritic discomfort radiating to the left trapezius ridge.

His past medical history included hypertension, dyslipidemia, and coronary artery disease (CAD). Notably, only days before his presentation, he was dismissed from hospital after having sustained an inferior myocardial infarction caused by acute thrombotic occlusion of his right coronary artery (RCA). He underwent successful percutaneous coronary intervention (PCI) with multiple stent implantations to his RCA. He reports adherence to his medications: aspirin, clopidogrel, metoprolol succinate, and atorvastatin. He denies recent use of tobacco, excess alcohol, or illicit drug use.

Physical examination revealed an elderly man in no acute distress. Vital signs demonstrated that he was afebrile (36.7 °C [98.06 °F]), with a pulse rate of 60 beats per minute, blood pressure of 90/46 mm Hg, respiratory rate of 21 breaths per minute, and oxygen saturation of 94% while breathing room air. Cardiac examination revealed normal heart tones without murmur, friction rub, or gallop. Jugular venous pulsations were non-elevated. Lung auscultation revealed adequate air movement without wheezes or pulmonary rales. No peripheral edema was detected. Chest pain was not reproducible to chest-wall palpation; however, the patient's pain visibly worsened upon deep respiration and positional changes, especially lying supine.

A 12-lead electrocardiogram (ECG) revealed an ectopic atrial rhythm at 60 beats per minute, with deep, wide Q waves in the inferior limb leads (III > aVF > II); widespread PR-segment depression and up-sloping "concave" ST-segment elevation in leads I, II, aVL, and V2-V6; and PR-segment elevation and down-sloping ST-segment depression in lead aVR (Supplemental Figure 1, available online at http://www.mayoclinicproceedings.org).

Laboratory work-up demonstrated low hemoglobin of 11.6 g/dL (normal 13.2 to 16.6 g/dL) and elevated white blood cell count at 13.6×10^9/L (normal 3.4 to 9.6×10^9/L) with neutrophil predominance of 11.75×10^9/L (normal 1.56 to 6.45×10^9/L). Serum creatinine was 0.89 mg/dL (0.74 to 1.35 mg/dL). C-reactive protein was elevated to 89.4 mg/L (normal <8.0 mg/L). Index troponin T of 612 ng/L was elevated (normal <15 ng/L), and subsequent values were 488 ng/L and 450 ng/L after 2 and 6 hours, respectively.

1. **Which <u>one</u> of the following diagnoses is <u>most consistent</u> with this patient's clinical picture?**
   a) Coronary artery stent thrombosis
   b) Stress-induced cardiomyopathy
   c) Acute pulmonary embolism
   d) Costochondritis
   e) Acute pericarditis

In any patient with known CAD presenting with chest pain, acute coronary syndrome (ie, unstable angina [UA], non-ST elevation myocardial infarction [NSTEMI], or ST elevation myocardial infarction [STEMI]) should be strongly suspected, especially among patients having undergone recent revascularization procedures. Coronary artery stent thrombosis resulting in myocardial infarction (MI) is a serious but fortunately rare post-PCI complication. More than half of patients present with ST-segment elevation in the ECG leads corresponding to the stented coronary artery, whereas the remainder present with UA or NSTEMI.[1] Stent thrombosis is particularly important to consider early (<1 month) after PCI. Nonadherence with dual antiplatelet therapy (ie, aspirin and

platelet $P2Y_{12}$ inhibitors) is 1 of the most powerful predictors of stent thrombosis, especially if this occurs within the first 30 days following stent implantation.[2] However, the patient's nonischemic chest pain syndrome, diffuse ST-segment elevation pattern, and downward-trending cardiac biomarkers suggest an alternative diagnosis.

Stress-induced cardiomyopathy should be considered among patients presenting with chest pain, elevated troponins, and ECG abnormalities. Classically, stress-induced cardiomyopathy will demonstrate characteristic abnormalities on cardiac imaging such as anteroapical regional wall motion abnormalities and systolic "ballooning" of the left-ventricular apex. In general, this condition is diagnosed after the identifying precipitant physical or emotional stressors and confirming the absence of culprit coronary stenoses and/or occlusions.

Acute pulmonary embolism (PE) is commonly recognized as a possible source of pleuritic chest pain, and recently hospitalized patients have an elevated risk of developing venous thromboembolism. Furthermore, PE, especially the massive and submassive variety, is commonly associated with elevated cardiac enzymes. Although a 12-lead ECG does not provide sufficient sensitivity and specificity to diagnose an acute PE confidently, the most commonly observed ECG findings include sinus tachycardia and nonspecific ST-segment and T-wave changes. More specific abnormalities (eg, $S_1Q_3T_3$ pattern, right-ventricular strain pattern, and new right bundle branch block) are less frequently identified.[3] This patient's characteristic chest pain syndrome and ECG abnormalities more strongly favor an alternative diagnosis.

Costochondritis would not explain the patient's accompanying ECG abnormalities or elevated cardiac enzymes. Furthermore, this diagnosis typically presents with reproducible, well-localized chest pain upon palpation.

To establish a diagnosis of acute pericarditis, a patient must meet at least 2 of the following: characteristic chest pain syndrome, pericardial friction rub, typical ECG changes, or a pericardial effusion of more than a trivial size.[4] This patient's description of chest pain and abnormal ECG sufficiently fulfill the diagnostic criteria for acute pericarditis. Pleuritic chest pain that radiates to the trapezius ridge and worsens while lying supine are hallmark symptoms of acute pericarditis. In addition, this patient's ECG demonstrated classic electrocardiographic features of acute pericarditis: widespread "concave" ST-segment elevation and PR-segment depression as well as ST-segment depression and PR-segment elevation in lead aVR. The patient's lack of ST-segment elevation and PR-segment depression in the inferior leads (II, III, aVF) may be mistakenly interpreted as being incompatible with acute pericarditis[5]; however, the absence of ST-segment elevation may be explained by obscuring repolarization abnormalities resulting from the recent MI.

2. **Aside from classical ECG features, which of the following ECG findings _most strongly suggests_ acute pericarditis?**
   a) Deep, wide Q waves in the inferior limb leads
   b) Localized ST-segment elevation in leads I and aVL
   c) Non-sinus P waves
   d) Atrial fibrillation
   e) ST-segment/T-wave ratio ≥ 0.25 in lead V6

The ECG features of acute pericarditis are sometimes not readily apparent. In other circumstances, it can be difficult to distinguish acute pericarditis from other diagnoses, such as early repolarization or STEMI.

Deep, wide Q waves in the inferior limb leads (II, III, aVF) without evidence of acute or evolving myocardial injury (ie, ST-segment elevation) suggest an age-indeterminate or old inferior MI. Although such ECG findings would align with the patient's recent inferior MI, they do not suggest acute pericarditis. Localized ST-segment elevation in leads I and aVL would be more consistent with lateral STEMI.

Non-sinus P waves suggest an ectopic atrial rhythm originating outside of the sino-atrial node. Although the patient's ECG demonstrated an ectopic atrial rhythm, this

rhythm is not known to be associated with acute pericarditis. Although atrial fibrillation is considered to be the most common sustained arrhythmia associated with acute pericarditis, with an incidence of approximately 5%,[6] it is a relatively common arrhythmia that is nonspecific for acute pericarditis.

Calculation of the ST segment/T wave ratio in lead V6 can be helpful in differentiating an early repolarization pattern and acute pericarditis. The ST segment/T wave ratio is calculated by dividing the vertical height of the ST-segment elevation (ie, from the end of the PR segment to the J point) by the T-wave amplitude (ie, from the PR segment to the T-wave peak) (Supplemental Figure 2, available online at http://www.mayoclinicproceedings.org). A ratio greater than 0.24 in lead V6, as seen in this patient's ECG, is suggestive of acute pericarditis.[7] In contrast, early repolarization is typically localized to the precordial leads (V2 to V4) and exhibits J-point elevation ($\geq$0.1 mV) with a slurred or notched morphology.

Further evaluation included a chest x-ray demonstrating a normal cardiac silhouette, chronic emphysematous changes, and no evidence of a pleural effusion or pulmonary venous congestion.

3. **Which one of the following diagnostic tests is the most appropriate next step in evaluation of this patient?**
   a) Serial ECGs
   b) Coronary angiography
   c) Transthoracic echocardiogram (TTE)
   d) Transesophageal echocardiogram (TEE)
   e) No additional work-up

Acquisition of serial ECGs may be essential to the evaluation of patients with confirmed or suspected acute coronary syndrome (ACS) but has limited clinical value among patients with acute pericarditis. Coronary angiography would be the most appropriate next step for patients presenting with ACS. Although there is no absolute indication for TTE in the setting of a clear presentation of pericarditis lacking hemodynamic instability and physical examination findings suggestive of tamponade (eg, elevated jugular venous pulsations), TTE would be the most

appropriate diagnostic test of choice among patients having recent MIS. TTE acquisition allows for the evaluation of potentially dangerous precipitant causes or sequelae related to the patient's recent MI (eg, left-ventricular pseudoaneurysm). Furthermore, echocardiography allows for the identification of large or rapidly progressive pericardial effusions capable of causing cardiac tamponade. Although TEE may be considered among patients who have difficult or limited transthoracic imaging windows, it is a more invasive imaging modality than TTE. No additional work-up would be inappropriate at this stage of evaluation, as serious post-MI complications may be an explanation for the patient's acute pericarditis.

TTE showed borderline left-ventricular enlargement, left-ventricular ejection fraction of 56%, unchanged inferior regional wall motion abnormalities consistent with his recent MI, mild right-ventricular enlargement with mildly decreased systolic function, no significant valvular heart disease, and no pericardial effusion.

4. **Which one of the following would be the most useful next step in this patient's case?**
   a) Repeat transthoracic echocardiogram in 1 week
   b) Stress echocardiogram
   c) Antinuclear antibody assay
   d) Hemodynamic cardiac catheterization
   e) Cardiac magnetic resonance imaging (MRI)

Repeating a TTE in 1 week can be considered among patients with refractory or recurrent symptoms and in those with known pericardial effusion that may increase in size and/or produce cardiac tamponade. Stress testing would not be indicated in a patient with a well-established history of CAD and lack of ischemic symptoms.

Among patients for whom there is concern for causative connective tissue disorder, an antinuclear antibody assay may be considered; however, there was no reason to suspect an underlying autoimmune etiology in our patient's case.

Hemodynamic cardiac catheterization can be considered among patients suspected to have constrictive pericarditis but inconclusive echocardiogram findings. As our patient did not present with clinical features suggestive of constrictive pericarditis (eg, right-sided heart failure) or demonstrate suggestive echocardiographic findings (eg, interventricular dependence), further evaluation employing an invasive diagnostic procedure is not warranted.

Our patient presented with an acute pericarditis with coexistent troponin elevation. Elevated troponins may be explained by a nonischemic release of cardiac enzymes brought on by attendant inflammatory damage to superficial but underlying myocardium (ie, myopericarditis). In fact, the extent of cardiac enzyme elevation has been shown to correlate with degree of myocardium involved.[8] Cardiac MRI would be useful in determining causation for the patient's elevated troponins: coexisting myopericarditis, new unrecognized ischemic injury, and/or lingering biomarker elevation from washout following his recent MI.

Cardiac MRI revealed diffuse pericardial enhancement and thickening consistent with suspected acute pericarditis but no myocardial edema or delayed enhancement to suggest concomitant myocardial involvement. Regional wall motion abnormalities and delayed subendocardial enhancement consistent with previous RCA territory infarct were also observed. Given the patient's classical presentation of acute pericarditis, recent MI, and aforementioned imaging findings, he was diagnosed with peri-infarction pericarditis.

5. Which one of the following therapy regimens is the most useful for this patient?
   a) Therapeutic pericardiocentesis
   b) Loading dose of 325 mg of aspirin and 600 mg of clopidogrel
   c) 650 mg of ibuprofen 3 times daily until symptom resolution and 0.6 mg of colchicine twice daily for 1 month
   d) 1 mg/kg/day of prednisone followed by a slow taper and 0.6 mg of colchicine twice daily for 6 months
   e) 2 g of aspirin daily until resolution of symptoms and 0.6 mg of colchicine twice daily for 3 months

In general, the treatment goals for acute pericarditis are to relieve pain, resolve inflammation, and prevent recurrence. Therapeutic pericardiocentesis would be the most appropriate next step for patients with large pericardial effusions, with or without cardiac tamponade. A 1-time dose of 325 mg of aspirin and 600 mg of clopidogrel is a preferred loading regimen for patients with ACS expected to undergo PCI.

Nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine are preferred agents to treat most forms of acute pericarditis. Although 650 mg of ibuprofen 3 times daily until resolution of symptoms, plus 0.6 mg of colchicine twice daily for 1 month, may provide satisfactory treatment for viral or idiopathic variants of pericarditis, the inadequate duration of colchicine dosing lends to an increased risk of recurrence of disease. The suggested duration for initial cases of acute pericarditis is at least 3 months of colchicine and 6 months for recurrent cases.

The combination of colchicine and glucocorticoids (eg, prednisone) may be considered in patients having contraindications to NSAIDs (eg, renal failure). A slow steroid taper and colchicine therapy for 3 months may be used for those with their first episodes of acute pericarditis; however, because of an increased risk of recurrent pericarditis, glucocorticoids are a less efficacious treatment option.[9]

In the setting symptomatic pericarditis during the early post-MI period, aspirin is the preferred NSAID choice.[4] The patient was initiated on high-dose aspirin (2 g daily) in combination with 0.6 mg of colchicine twice daily for 3 months. A proton-pump inhibitor was also added for gastric protection. Two weeks after hospital discharge, the patient was without chest pain.

DISCUSSION

Acute pericarditis accounts for approximately 5% of patients who present to emergency

departments with nonischemic chest pain.[10] In developed countries, the large majority of cases is idiopathic or presumed viral in origin, whereas tuberculosis is the most common etiology in developing countries.[4] Other causes of pericarditis include MI, chest trauma, renal failure, malignancy, radiotherapy, medications, autoimmune disease, and other infectious processes.

According to the guidelines put forth by the Task Force on the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology on management of pericardial disease, the diagnosis requires the presence of at least 2 of 4 symptoms or signs: chest pain consistent with pericarditis, pericardial friction rub, characteristic electrocardiographic features, and pericardial effusion.[4] In certain clinical contexts, the diagnosis of acute pericarditis may be less clear. For example, in our post-MI patient, the expected ECG changes of acute pericarditis were likely obscured by his recent inferior MI. Moreover, the lack of pericardial friction rub on physical examination and absence of a pericardial effusion on TTE may make the diagnosis more difficult to establish. Furthermore, a recent hospitalization for MI and elevated biomarkers, as it was in our patient's case, may easily inspire an anchoring bias to other the common causes of chest pain (eg, MI or acute PE). Thus, it is important to consider alternative causes for increased cardiac enzymes such as acute pericarditis with myocardial involvement (ie, myopericarditis).

Peri-infarction pericarditis is a rare post-MI complication characterized by inflammation pericardium occurring within days after MI. Its incidence has drastically declined with the emergence of effective and rapid revascularization strategies such as PCI.[11] Peri-infarction pericarditis often demonstrates similar clinical findings to other forms of acute pericarditis, but it is not uncommon for patients to present without classical symptoms.

Pericardial effusion commonly coexists with peri-infarction pericarditis and is a known predictor of poor prognosis.[12] The routine use of echocardiography among patients suspected of having peri-infarction pericarditis is essential to identify patients with large or rapidly progressive pericardial effusions capable of causing cardiac tamponade. Cardiac MRI may be helpful to identify and/or examine the extent of coexistent myopericarditis.

Peri-infarction pericarditis is normally self-limited, responds well to medical therapy, and has low risk of recurrence. Unlike the treatment of acute viral or idiopathic pericarditis, current guidelines recommend avoiding extended duration anti-inflammatory therapies (ie, NSAIDs and glucocorticoids), noting the lack of evidence that such a strategy alters clinical outcomes.[9] In early post-MI patients, high-dose aspirin until resolution of symptoms, colchicine for 3 months, and proton-pump inhibitor for gastric protection are appropriate.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

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CORRECT ANSWERS: 1. e. 2. e. 3. c. 4. e. 5. e