MAYO CLINIC

84-Year-Old Woman With Chest Pain

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See end of article for correct answers to questions.

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An 84-year-old woman presented to the emergency department with an 8-hour history of persistent substernal chest pain. The pain intensity was rated a 6 on a scale of 1 to 10, radiated to the shoulder blades, and was worse with deep breathing and lying flat. She denied dyspnea, orthopnea, palpitations, or lower-extremity edema. She had no history of cardiac disease. Her medical history was notable for well-controlled rheumatoid arthritis and hypertension. Her medications included triamterene and hydrochlorothiazide (37.5 and 25 mg/d) for hypertension and methotrexate for rheumatoid arthritis (15 mg/wk), which she had stopped taking 8 weeks earlier after recent hip surgery.

Her heart rate was 74 beats/min, blood pressure was 127/72 mm Hg, and respiratory rate was 25/min. Her temperature was 36.8°C, and oxygen saturation was 97% on ambient air. Initial examination by emergency department staff revealed an alert, well-appearing, white woman in no acute distress. No cardiac murmurs were noted, pulses were equal throughout all extremities, and there was no appreciable jugular venous distention. Pulmonary, abdominal, neurologic, and extremity examination was unrevealing. No lymphadenopathy or rash was noted. A chest radiograph revealed a normal cardiac silhouette and normal-appearing lung fields. An electrocardiogram (ECG) was obtained (Supplemental Figure, available online at http://www.mayoclinicproceedings.org), revealing ST-segment elevation in anterior, inferior, and lateral leads. Given the ST-segment elevation in the context of new-onset chest pain, the institutional ST-segment elevation myocardial infarction (STEMI) protocol was activated; she was given heparin, aspirin, and clopidogrel and taken immediately for coronary angiography.

1. **On the basis of the available clinical information, what is the *most likely* cause of the patient's chest pain?**
   a. Acute myocardial infarction (AMI)
   b. Acute pericarditis
   c. Cardiac tamponade
   d. Pulmonary embolism
   e. Aortic dissection

New-onset chest pain with ECG ST-segment elevation is concerning for AMI, which may be investigated by checking serum cardiac biomarker levels. However, the pleuritic and positional nature of the pain and the presence of diffuse ST-segment elevation in both limb and precordial leads should lead one to suspect acute pericarditis. Closer inspection of the ECG revealed that in addition to diffuse ST-segment elevation, PR depression was also evident in leads I and II, with PR elevation in aVR. These characteristics and the absence of reciprocal ST depression are more consistent with acute pericarditis than AMI.[1] The history of recently untreated rheumatoid arthritis further supported this notion.[2]

In the triage of patients with chest pain, life-threatening emergencies should first be considered. In cardiac tamponade, one would expect marked hypotension due to impaired cardiac output, jugular venous distention, and muffled heart sounds, none of which were present. Similarly, she did not have hypoxemia, respiratory distress, lower-extremity erythema or edema, or history of thromboembolic events, making pulmonary embolism unlikely. The absence of a widened mediastinum on chest radiography and her hemodynamic stability did not support a diagnosis of aortic dissection.

In this patient's case, her initial triage directed her to coronary angiography for presumed STEMI. Angiography revealed moderate diffuse atherosclerotic coronary artery disease with a 90% stenosis of the first obtuse marginal coronary artery, and balloon angioplasty and stenting were performed. She was then transferred to the coronary care unit. Her initial serum troponin T level was less than 0.01 ng/mL and remained negative at 3- and 6-hour intervals, ruling out AMI. On review of the ECGs, the diffuse nature of the ST-segment elevation and PR depression was evident. In addition, cardiac auscultation revealed a pericardial friction rub, and the patient described ongoing pleuritic chest pain. Thus, despite her angiographic findings of moderate coronary atherosclerosis, acute pericarditis was diagnosed as the cause of her symptoms.

2. **After ECG and chest radiography, which of the following is the *most appropriate* imaging modality to aid in diagnosis?**
   a. Echocardiography
   b. Coronary angiography
   c. Computed tomographic angiography of the chest
   d. Cardiac magnetic resonance imaging
   e. Right-sided ECG

In patients with clinical signs of pericardial inflammation, echocardiography should be performed to evaluate for pericardial effusion or tamponade. The

American College of Cardiology and the European Society of Cardiology recommend that clinical evaluation include physical examination, ECG, chest radiography, serum cardiac biomarkers, and echocardiography.[3,4]

Immediate angiography with percutaneous coronary intervention is indicated for STEMI and may also be helpful in diagnosis of coronary vasospasm. However, when acute pericarditis is the most likely diagnosis, echocardiography is more appropriate. Computed tomographic angiography of the chest is appropriate for diagnosis of pulmonary embolism. However, strong evidence was lacking to support this diagnosis, and with a Wells score of 0, this patient would be considered low risk.[5] Cardiac magnetic resonance imaging is helpful in the evaluation of several cardiac conditions and might be used later to demonstrate signs of pericardial or myocardial changes in myopericarditis or to assess myocardial necrosis after AMI but is unnecessary in the urgent evaluation of chest pain with ST-segment elevation. Right-sided ECG may be performed to evaluate for a right ventricular myocardial infarction but is not helpful in the evaluation of acute pericarditis.

Our patient underwent echocardiography immediately after admission to the coronary care unit, and this demonstrated a normal left ventricular ejection fraction without regional wall motion abnormalities and no evidence of pericardial effusion, tamponade, or myocardial dysfunction.

3. **Which *one* of the following causes of her suspected diagnosis is *most likely* to result in normal ECG findings?**
   a. Uremia
   b. Viral infection
   c. Autoimmune disease
   d. Radiation
   e. Idiopathic

The pericardium is composed of the fibrous outer parietal layer and the inner visceral layer, which contacts the epicardium. Acute pericarditis is typically marked by inflammation of the visceral pericardium, with inflammatory infiltration of the epicardium and subepicardium. This inflammation causes characteristic ECG changes, such as diffuse upsloping ST-segment elevation and PR depression, the latter representing pericarditis over the atria. However, in uremic pericarditis, much of the inflammation is confined to the fibrous parietal layer, without direct myocardial involvement, resulting in minimal or no ECG changes.[6] In contrast, the other causes of acute pericarditis typically result in ECG changes. In this patient, typical ECG changes were seen, and the most likely underlying cause was her rheumatoid arthritis, although an idiopathic cause could not be excluded.

4. **Which of the following is the *most appropriate* initial treatment for this patient's condition?**
   a. Pericardiocentesis
   b. Prednisone
   c. Additional course of methotrexate
   d. High-dose aspirin therapy
   e. Oral colchicine only

Pericardiocentesis is effective for draining large pericardial effusions, particularly in the setting of cardiac tamponade. However, there was no evidence of either a pericardial effusion or tamponade in this patient. Prednisone is sometimes used as an adjunctive therapy in refractory cases, although it is not recommended as monotherapy because it has been demonstrated to increase the risk of recurrence.[7] Readministering an anti-inflammatory medication, such as methotrexate, for a patient with rheumatoid arthritis and uncontrolled inflammation is appropriate. However, this would not result in immediate, substantial relief and would thus be inadequate monotherapy. For treatment of acute pericarditis, high-dose aspirin and/or nonsteroidal anti-inflammatory drugs (NSAIDs) are first-line therapy. Colchicine is an adjunctive treatment that may be added to standard therapy to reduce risk of recurrence but is not recommended as monotherapy.[7]

Because this patient was found to have coronary artery disease and underwent stent placement, her anti-inflammatory regimen consisted of aspirin, 650 mg 4 times daily. In addition, the rheumatology department was consulted, and per their recommendations, a 2-week prednisone taper was added (given her untreated rheumatoid arthritis) and her weekly methotrexate was resumed. This regimen resulted in immediate and substantial symptomatic improvement.

5. **Which of the following features would be associated with a *more favorable* prognosis in her newly diagnosed condition?**
   a. Association with trauma
   b. Immunosuppression
   c. Absence of a fever
   d. Subacute onset
   e. Connective tissue disease

Clinical features associated with poorer prognosis in acute pericarditis include a temperature greater than 38°C, immunosuppression, subacute onset, oral anticoagulant therapy, association of the pericarditis with trauma, and presence of severe pericardial effusion or tamponade.[8] Thus, absence of fever is a favorable prognostic sign. These features

help in appropriate triage of patients because the presence of any of these symptoms may indicate the need for hospitalization for initiation of therapy and monitoring. Presence of connective tissue disease has not been demonstrated as a risk factor for worse outcomes in acute pericarditis.

Our patient did not present with any of these poor prognostic indicators and was predicted to recover fully with appropriate treatment. She was discharged home after a 48-hour hospitalization with a prednisone taper, high-dose aspirin, ongoing methotrexate therapy, and arrangements for early follow-up.

DISCUSSION

A number of conditions, both cardiac and noncardiac, can produce chest pain. Electrocardiography is an integral and early part of any evaluation of chest pain and helps guide clinical decisions. The presence of ST-segment elevation should raise suspicion for AMI, requiring immediate reperfusion therapy. However, other conditions can produce ST-segment elevation in the absence of an acute coronary syndrome. These conditions include early repolarization, hyperkalemia, acute pericarditis, left ventricular hypertrophy, left bundle branch block, pulmonary embolism, coronary vasospasm (Prinzmetal angina), Brugada syndrome, and immediate postcardioversion changes.[1]

Appropriate triage should always begin with a thorough history and physical examination. In a stable patient, more time may be available for a complete examination. A careful cardiopulmonary examination is paramount. Presence of a friction rub on cardiac auscultation is pathognomonic for acute pericarditis. However, this condition must be distinguished from a pleural friction rub, which varies with the respiratory cycle. Classically, a pericardial rub produces a scratching or squeaking sound and has 3 components: (1) atrial systole, (2) ventricular systole, and (3) ventricular diastole. The presence of a pericardial friction rub along with supporting history and ECG changes should obviate the need for coronary angiography.

In addition to the history and physical examination, evaluation for acute pericarditis involves ECG, chest radiography, serum cardiac biomarkers, serum markers of inflammation (which may be elevated), and transthoracic echocardiography. The chest radiograph helps to rule out other causes of chest pain and may show an enlarged cardiac silhouette in the setting of a large pericardial effusion. Cardiac biomarkers may suggest myocardial infarction, although mild elevations may be seen in acute pericarditis up to 50% of the time when underlying myocardium is involved (myopericarditis). Transthoracic echocardiography is useful in evaluation of pericardial disease, with particular attention to the presence of effusion or tamponade physiology.

The ECG is extremely useful because there are well-documented ECG stages in the progression of acute pericarditis. In the initial hours to days (stage 1), diffuse ST-segment elevation is seen (concave upward) in the precordial and limb leads. PR depression may also be seen in the limb and lateral precordial leads (V_5 and V_6) and PR elevation in aVR, reflective of an atrial injury current. Stage 2 shows resolution of these changes. Stage 3 is characterized by diffuse T-wave inversion, and stage 4 (late) is marked by normalization of the T waves.[9] Two conditions commonly mistaken for acute pericarditis by ECG include AMI and early repolarization. Features that help distinguish acute pericarditis from AMI include widespread upwardly concave ST-segment elevation without reciprocal ST depression, in contrast to the vascular territory–specific, upwardly convex ST-segment elevation with associated reciprocal changes in AMI. Additional distinctions include absence of Q waves and resolution of ST-segment elevation before the appearance of T-wave inversion. Early repolarization, a normal variant typically seen in young males, produces diffuse upsloping ST-segment elevation without Q waves or reciprocal changes. However, it does not cause chest pain and does not typically produce the PR depression seen in acute pericarditis. Further, the ST/T ratio (ST-segment height from baseline divided by T-wave height) is characteristically greater than 0.25 in acute pericarditis and less than 0.25 in early repolarization.[10]

Despite these well-described ECG characteristics, misdiagnosis of STEMI is common. A recent review[11] of all incident cases of acute pericarditis at the Mayo Clinic, Rochester, Minnesota, from 2000 to 2006 found that 16.8% of these patients underwent coronary angiography because of suspicion of myocardial infarction and that the frequency was 5-fold higher among those with ST-segment elevation. Furthermore, up to one-third of these patients had some degree of angiographic coronary artery disease. This finding highlights the diagnostic dilemma facing clinicians treating patients with chest pain and further underscores the necessity of thoughtful clinical decision making.

When the diagnosis of acute pericarditis is made, the question of an underlying cause arises. Approximately 65% of the time the cause is idiopathic or infectious (most commonly viral but also bacterial, fungal, or parasitic). Other causes include inflammatory (rheumatoid arthritis, lupus, scleroderma, and others), metabolic (uremia, gout, and myxedema), neoplastic (primary pericardial or secondary to metastasis), traumatic conditions (blunt chest trauma, cardiac surgery, and after pericardiot-

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omy), and post–myocardial infarction Dressler syndrome (which is rare in the modern era).[2] Given the wide range of potential causes, extensive testing for all possible causes is not routinely performed, and any specific testing should be guided by clinical features. For our patient, her recently untreated rheumatoid arthritis was the most likely predisposing factor.

Regardless of the inciting cause, treatment generally consists of oral high-dose NSAID (or aspirin) therapy for suppression of pericardial inflammation. This therapy may consist of ibuprofen, 400 to 800 mg 3 times daily, aspirin, 650 to 1000 mg every 6 hours, or indomethacin, 50 mg 3 times daily. Intravenous ketorolac has also been used. Treatment duration is typically 1 to 4 weeks and is guided by symptoms, with gradual dose tapering. Approximately 70% to 80% of patients will have adequate relief with this therapy alone.[12] In those who do not, colchicine may be added as an adjunct. Concomitant use of NSAIDs and colchicine has been shown to reduce the risk of treatment failure and recurrence.[7] In addition, glucocorticoids may be considered in cases associated with connective tissue diseases or in those refractory to NSAID therapy. However, their use has been called into question because some studies have shown an increased risk of recurrence with high-dose cortico steroids, although lower-dose cortico steroids may mitigate these risks.[7] Prolonged or repeated cortico steroid courses may also increase osteoporosis risk, and preventive bisphosphonate therapy and/or calcium and vitamin D supplementation should be considered in such cases. Furthermore, high-dose NSAID therapy increases the risk of gastrointestinal complications; thus, consideration should be given to acid suppression therapy for gastroduodenal protection.

Long-term prognosis in acute pericarditis is very good. However, recurrences are fairly common (15%-30%), depending on the underlying cause.[12] In recurrent cases, first-line treatment remains NSAIDs, whereas colchicine may be added to reduce the risk of recurrence.[7]

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SUPPLEMENTAL ONLINE MATERIAL

Supplemental online material is available for this article at http://www.mayoclinicproceedings.org.

Abbreviations and Acronyms: **AMI** = acute myocardial infarction; **ECG** = electrocardiogram; **NSAID** = nonsteroidal anti-inflammatory drug; **STEMI** = ST-segment elevation myocardial infarction

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CORRECT ANSWERS: 1. b. 2. a. 3. a. 4. d. 5. c