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A 37-year-old man with chest pain, ECG changes, and elevated cardiac enzymes

A 37-year-old African American man presents to the emergency department with chest pain and dyspnea, which began suddenly 30 minutes ago. The pain is severe, pressure-like, nonradiating, and pleuritic.

His heart rate is 88 beats per minute, blood pressure 135/72 mm Hg, respiratory rate 12 per minute, and oral temperature 38.5°C (101.3°F). His oxygen saturation by pulse oximetry is 99% while breathing room air. He is given sublingual nitroglycerin, but this does not alleviate his pain.

On physical examination, he is a physically fit man in obvious distress. His jugular veins are not distended, and no lymph nodes are palpable in his neck. The heart sounds are muffled without murmurs, but a faint pericardial friction rub is heard that persists even when he holds his breath. His lungs are clear to auscultation, his abdomen is normal, and his lower extremities are warm, with normal pulses and no edema. Of note, neither a Kussmaul sign nor a paradoxical pulse is present. An electrocardiogram is ordered (**FIGURE 1**).

While blood samples are being drawn, we learn more about his history. He has hypertension, for which he takes amlodipine (Norvasc), and gastroesophageal reflux under control with esomeprazole (Nexium). He says he does not have hyperlipidemia, diabetes, or coronary artery disease and his surgical history is unremarkable. He says he does not smoke, rarely drinks, and does not use any drugs. No one in his family has had premature coronary artery disease.

He says he has had similar symptoms in the past few months, which resulted in two emergency room visits. Electrocardiograms at those times were unremarkable, and a stress test was negative for ischemia.

A computed tomographic (CT) scan of the chest was also obtained during one of those visits. The scan was negative for a pulmonary embolus but incidentally showed liver hemangiomas.

He goes on to add that his chest pain has recently increased in frequency, and it has occurred daily for the past 5 days. The pain is not related to exertion, occurs throughout the day, and is associated with significant shortness of breath. It worsens when he is taking a deep breath and improves when he leans forward. Although he is febrile, he says he has had no fevers or chills in the past. He gives no history of weight loss, cough, orthopnea, or paroxysmal nocturnal dyspnea, but has been experiencing malaise, weakness, and myalgia for the past month. His review of systems is otherwise negative.

He has had similar symptoms for the past few months, but now they are worse

The patient's initial laboratory results are shown in **TABLE 1**.

WHAT IS THE CAUSE OF HIS CHEST PAIN?

1 Which is the most likely cause of this patient's chest pain?

- ☐ Acute myocardial infarction
- ☐ Acute pericarditis
- ☐ Myocarditis
- ☐ Pulmonary embolism
- ☐ Aortic dissection
- ☐ Pneumonia

Dr. Krasuski has disclosed that he has received honoraria from Pfizer for teaching and speaking and honoraria and consulting fees from Actelion for teaching, speaking, and consultation.

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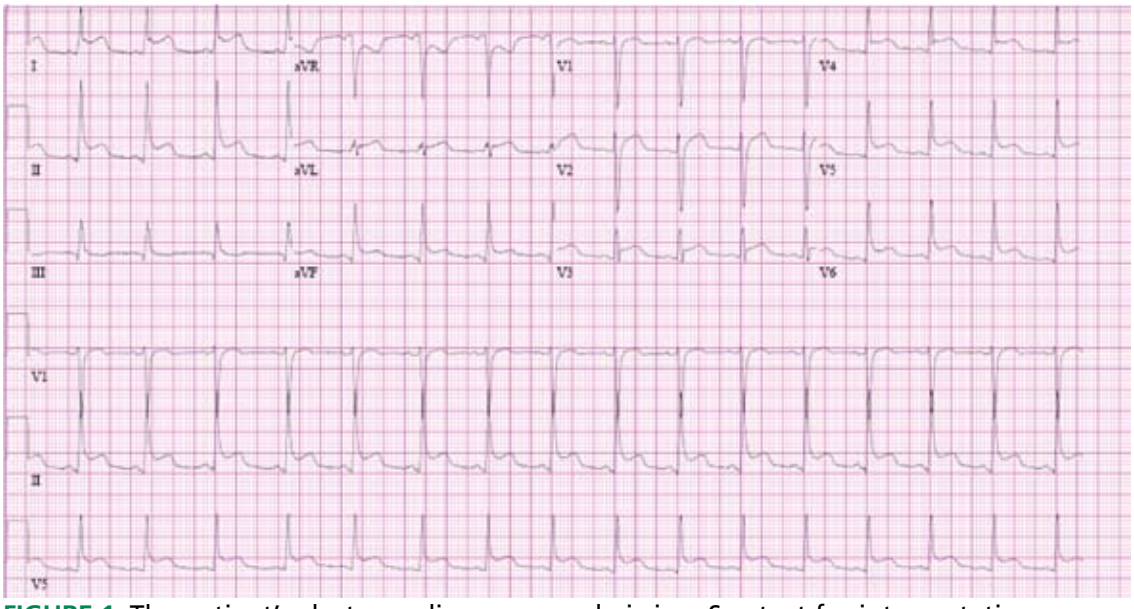

FIGURE 1. The patient's electrocardiogram on admission. See text for interpretation.

Acute myocardial infarction. This is a young man with chest pain, ST-segment elevation, and elevated cardiac enzymes. Acute myocardial infarction should always be included in the differential diagnosis of such a patient, as recognizing it early and making an effort to rapidly restore blood flow to the myocardium can greatly improve the clinical outcome. However, particular features in his electrocardiogram and the duration and nature of his chest pain suggest another diagnosis.

The ECG changes of acute pericarditis may be difficult to distinguish from those of acute MI

Acute pericarditis causes pleuritic chest pain with diffuse ST-segment elevation, and its electrocardiographic changes may be difficult to distinguish from those of ischemia. The features in our patient's electrocardiogram that point to pericarditis are[1]:

- ST-segment elevation that is concave upward, occurring in all leads except aVR
- T waves concordant with ST-segment deviation
- PR-segment depression, sparing V_1 and aVR
- PR-segment elevation and ST depression in aVR.

Pleuritic chest pain is the most common symptom in acute pericarditis. A prodrome of fever, myalgia, and malaise is also common, especially in younger patients.[2] On physical examination, a pericardial friction rub is pathognomonic.

Our patient has most if not all of the classic features of acute pericarditis. Elevated cardiac enzymes, which this patient has, are not a classic feature of pericarditis and are generally considered a marker of cardiac ischemia. However, because the myocardium is adjacent to the pericardium, the acute inflammatory process of acute pericarditis may also result in myocardial injury, resulting in release of creatine kinase-MB.[3]

An increase in cardiac troponin is also frequently observed in acute pericarditis, reflecting biochemical evidence of inflammatory myocardial cell damage.[4] Furthermore, cardiac troponin can be elevated in several other medical conditions,[5] such as ischemic heart disease, congestive heart failure, myocarditis, pulmonary embolism, severe pulmonary hypertension, significant left ventricular hypertrophy, renal failure, sepsis, critical illness, and subarachnoid hemorrhage. Therefore, cardiac enzymes are not good markers to distinguish between acute myocardial infarction and acute pericarditis. However, echocardiography is an effective way to help differentiate pericarditis from myocardial ischemia in the setting of elevated troponins and electrocardiographic changes, by determining if wall-motion abnormalities are present or absent.

Hence, the diagnosis of acute pericarditis should take into account the combination of the clinical picture, electrocardiographic findings, and laboratory values. Overreliance on any of these in isolation can lead to misdiagnosis.

TABLE 1

The patient's laboratory values on admission

TEST	RESULT	NORMAL RANGE
Creatine kinase	502 U/L	30–220
Creatine kinase-MB	13.7 ng/mL	0–8.8
Creatine kinase-MB%	3%	0–4
Troponin T	1.59 ng/mL	0.0–0.1
White blood cell count	12.93×10^9/L	4–11
Neutrophils	80.2%	40–70
Lymphocytes	10.4%	22–44
Red blood cell count	4.21×10^{12}/L	4.5–6.0
Hemoglobin	12.2 g/dL	13.5–17.5
Platelet count	256×10^9/L	150–400
Glucose	150 mg/dL	65–100
Blood urea nitrogen	18 mg/dL	10–25
Creatinine	1.2 mg/dL	0.7–1.4
Sodium	139 mmol/L	135–146
Potassium	4.4 mmol/L	3.5–5.0
Chloride	99 mmol/L	98–110

TABLE 2

Some specific causes of acute pericarditis

Infections

Viral (echovirus, coxsackievirus, adenovirus, cytomegalovirus, hepatitis B, infectious mononucleosis, HIV/AIDS)

Bacterial (*Pneumococcus, Staphylococcus, Streptococcus, Mycoplasma,* Lyme disease, *Haemophilus influenzae, Neisseria meningitidis)*

Mycobacterial *(Mycobacterium tuberculosis, Mycobacterium avium-intracellulare)*

Immune-inflammatory diseases

Connective tissue disease (systemic lupus erythematosus, rheumatoid arthritis, scleroderma, mixed)

Late postmyocardial infarction (Dressler syndrome), late postcardiotomy or postthoracotomy, late posttrauma

Drugs

Procainamide (Procanbid), hydralazine (Apresoline), isoniazid (Nydrazid), cyclosporine

Neoplastic disease

Breast and lung carcinoma, lymphomas, leukemias

Radiation

Trauma

Blunt and penetrating, postcardiopulmonary resuscitation

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Pulmonary embolism is another common cause of acute-onset pleuritic chest pain and dyspnea. Electrocardiographic changes can include ST-segment elevation, and cardiac enzymes can be elevated, although this is uncommon.

Myocarditis is commonly due to infections, collagen vascular diseases, or medications. Hallmarks of this disease are elevated cardiac enzymes and myocardial damage that results in reduction in heart function.

Aortic dissection typically causes a sharp, tearing chest pain that radiates to the back. This diagnosis is unlikely in this patient.

Pneumonia. Although our patient did not have a cough and no crackles were heard on lung examination to suggest pneumonia, his fever, pleuritic chest pain, and leukocytosis with a left shift warrant a workup for it. A parapneumonic effusion could manifest with fevers and pleuritic chest pain. However, the acuity of the symptoms and the characteristic electrocardiographic changes and elevated cardiac enzymes are better explained by the other diagnoses, notably acute pericarditis.

ACUTE PERICARDITIS: WHAT IS THE CAUSE?

2 Which is the most common cause of acute pericarditis?

- ☐ Idiopathic
- ☐ Neoplasm
- ☐ Autoimmune
- ☐ Tuberculosis

Most (approximately 80%) of cases of acute pericarditis are idiopathic.[6,7] In a study in 100 patients with acute pericarditis,[6] a specific cause was identified in only 22. The most common identified cause was neoplasm, which was present in seven patients: four with lung cancer and one each with breast carcinoma,

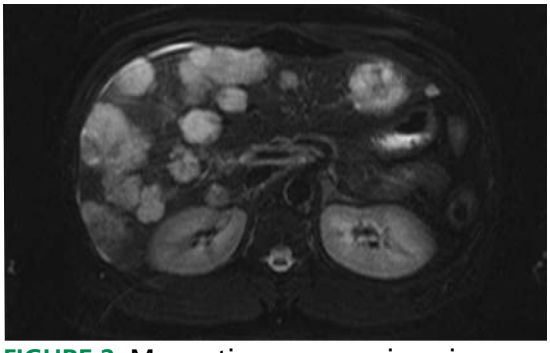

FIGURE 2. Magnetic resonance imaging shows multiple lesions in the liver.

cystic duct adenocarcinoma, and cardiac angiosarcoma.

A more recent study in 453 patients revealed similar results: 377 (83.2%) of the cases were idiopathic, 23 (5.1%) were neoplastic, 17 (3.8%) were due to tuberculosis, 33 (7.3%) were autoimmune, and 3 (0.7%) were purulent. Of note, viral causes are categorized as idiopathic, since the diagnostic workup is usually unsuccessful and treatment is empiric[6]; therefore, most of the so-called idiopathic cases are likely viral. TABLE 2 summarizes the most common specific causes of acute pericarditis.

Pericardial effusion has many possible causes

CASE CONTINUES: PERICARDIAL EFFUSION

The patient is admitted to the hospital for additional workup. His fever, myalgia, and chest pain persist, though the pain is less intense than before.

A chest roentgenogram and transthoracic echocardiogram are ordered and blood cultures are drawn.

The roentgenogram shows marked cardiomegaly, bilateral small pleural effusions, and minimal atelectatic changes in the lungs.

Echocardiography reveals a normal ejection fraction (60%) and a moderate-sized pericardial effusion without evidence of tamponade.

3 Which is the most common cause of pericardial effusion?

- ☐ Idiopathic
- ☐ Infection
- ☐ Malignancy
- ☐ Collagen vascular disease

Pericardial effusion is relatively common after acute pericarditis but also has many other possible causes. In a study of 204 patients with pericardial effusion,[8] 48% of cases were labeled as idiopathic. Of the remaining 52%, the most common specific diagnoses were infection (16%) and cancer (15%). Collagen vascular disease accounted for 8% of the cases and included systemic lupus erythematosus, rheumatoid arthritis, and scleroderma.

Although small pericardial effusions are common in pericarditis, larger pericardial effusions or failure to respond to therapy necessitates additional workup.[2]

In our patient, an extensive workup is initiated to look for bacterial, viral, fungal, and autoimmune causes of pericardial effusion, but the results of the workup are negative.

TREATING ACUTE PERICARDITIS

4 Which is the most appropriate treatment for acute pericarditis?

- ☐ Steroids
- ☐ A nonsteroidal anti-inflammatory drug (NSAID) or aspirin
- ☐ Opioids
- ☐ Colchicine
- ☐ Colchicine plus an NSAID or aspirin

An NSAID or aspirin is the basis of treatment for acute pericarditis and is very effective in relieving symptoms. Aspirin 2–4 g daily, indomethacin (Indocin) 75–225 mg daily, or ibuprofen (Motrin) 1,600–3,200 mg daily are prescribed most often; ibuprofen is preferred because it has a lower incidence of adverse effects than the others.[9]

Colchicine is recommended in addition to aspirin or NSAIDs for the treatment of acute pericarditis. Although in the past colchicine was reserved for recurrent pericarditis, the Colchicine for Acute Pericarditis (COPE) trial[10] found it to be beneficial for first episodes of pericarditis as well.[10] In this study, patients were randomized to receive conventional treatment with aspirin 800 mg every 6 or 8 hours or aspirin at the same dose combined with colchicine 0.5 to 1.0 mg daily. Colchicine showed significant benefit over conventional therapy, resulting in reduced rates of recurrence.

CASE CONTINUES: HEPATIC LESIONS ON MRI

Although aspirin and colchicine were started at the time of admission, our patient's symptoms fail to improve. A suspicion remains that a neoplastic disorder could be the underlying cause of the presentation and could explain his chronic malaise, pericardial disease, and fever. In view of the liver hemangiomas reported previously on CT, we decide to evaluate the liver further with magnetic resonance imaging (MRI).

To our surprise, the MRI reveals innumerable hepatic lesions, some of which show radiographic features consistent with hemangiomas, while the remainder are atypical and appear to warrant a biopsy (FIGURE 2). An oncology consultation is obtained and the need for biopsy is confirmed.

Since our patient's symptoms have improved significantly during the past few days and his fever has resolved, biopsy is scheduled on an outpatient basis. Biopsy with ultrasonographic guidance is performed a week later and yields a pathologic diagnosis of hemangioma. The improvement, however, is short-lived, and his pain and dyspnea recur after 2 months. A follow-up echocardiogram is ordered.

A remarkable echocardiographic finding

To our astonishment, the echocardiogram reveals a mass in the right atrial free wall and right ventricle that appears to be invading the myocardial tissue (FIGURE 3).

The original echocardiogram that was performed a little over 2-1/2 months ago is re-reviewed. It very subtly suggests a complexity to the pericardial effusion in the area of the current mass, apparent only when the two studies are directly compared. Clearly, there has been interval development of a mass easily detectable by echocardiography. Although a small mass may have been obscured by the pericardial effusion in the original echocardiogram, the development of a mass of this size in such a short time suggests a rapidly growing tumor.

Cardiac MRI is performed, which confirms the finding and characterizes the mass as measuring 5.1 by 4.8 cm within the pericardial space adjacent to the right atrium and atrioventricular groove and adherent to the right atrium. There are small excrescences of soft tissue through the midportion of the right atrial wall, suggesting tissue invasion (FIGURE 4).

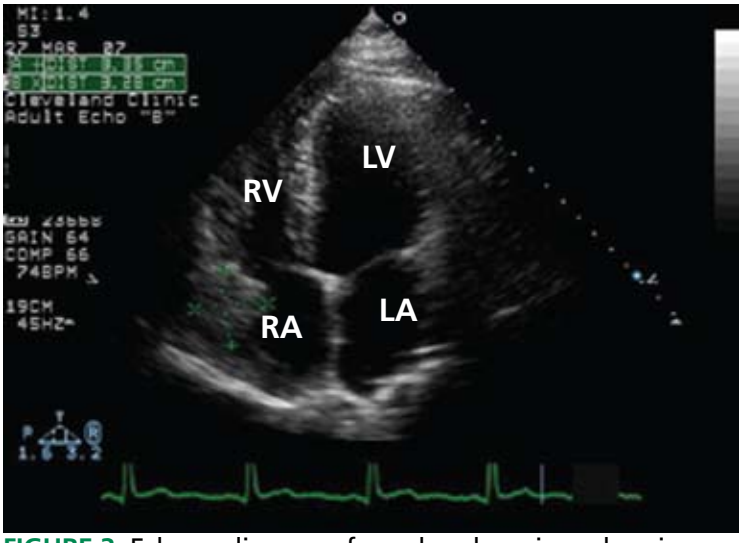

FIGURE 3. Echocardiogram, four-chamber view, showing the tumor (crosshairs) in the right atrium (RA). LA = left atrium, LV = left ventricle, RV = right ventricle.

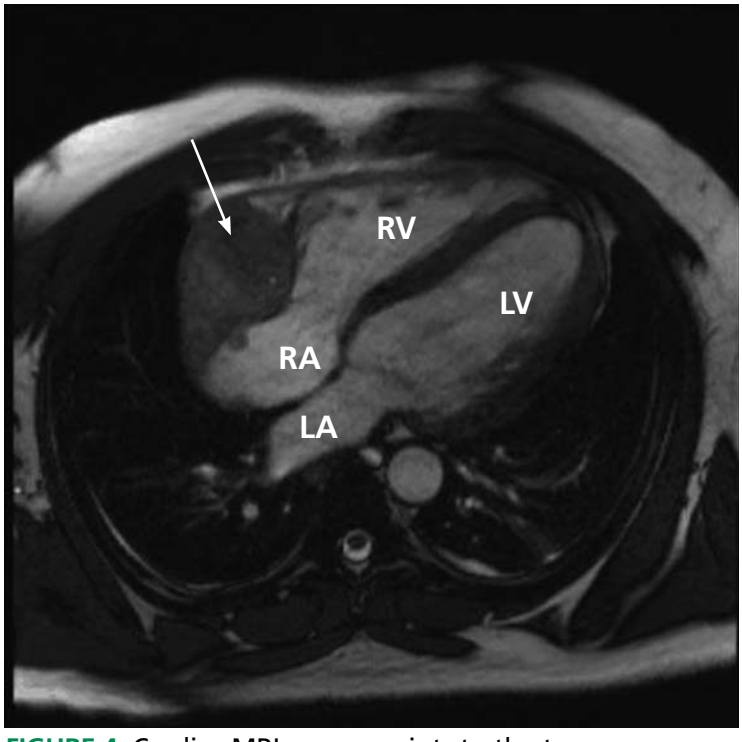

FIGURE 4. Cardiac MRI; arrow points to the tumor. RA = right atrium, RV = right ventricle, LA = left atrium, LV = left ventricle.

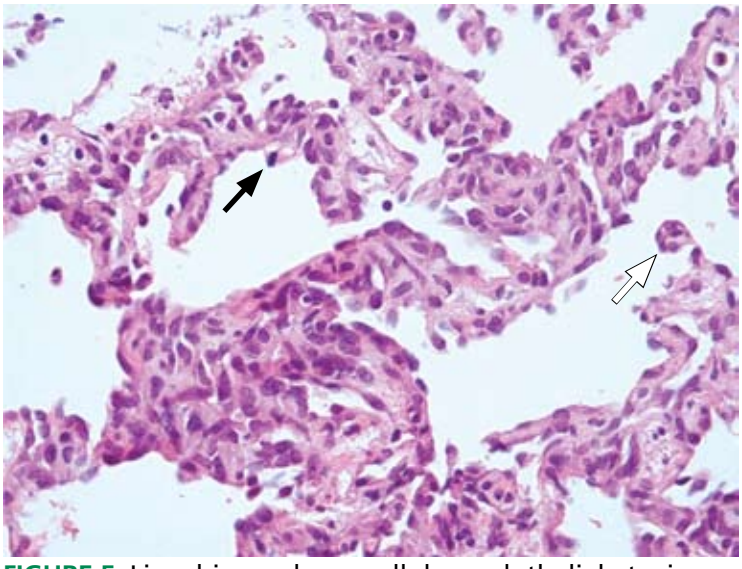

FIGURE 5. Liver biopsy shows cellular endothelial atypia with mitotic activity (black arrow), growth along the hepatic sinusoids, and papillary tufting (white arrow), all features of low-grade angiosarcoma.

CARDIAC TUMORS

5 Which is the most common primary cardiac tumor?

- ☐ Myxoma
- ☐ Papillary fibroelastoma
- ☐ Sarcoma
- ☐ Lymphoma

The mass has grown large in only 2-1/2 months, suggesting it is a rapidly growing tumor

Primary cardiac tumors are rare, with an incidence on autopsy series ranging between 0.0017% and 0.33%,[11,12] making them far less common than metastases to the heart.

Myxomas are benign cardiac tumors and are the most common primary cardiac neoplasm. Approximately 80% of myxomas originate in the left atrium, typically presenting with one or more of the triad of intracardiac obstruction, systemic embolization, and constitutional symptoms.[14]

Cardiac papillary fibroelastomas, the second most common cardiac tumors, are benign and predominantly affect the cardiac valves.[15]

Only one-fourth of all cardiac tumors are malignant. Nearly all of these malignant tumors are sarcomas, with angiosarcoma being the most common morphologic type, accounting for 30% of primary cardiac sarcomas.[13]

Primary cardiac lymphomas are extremely rare and account for only 1.3% of all primary cardiac tumors.[16]

A DIAGNOSIS IS MADE

Fluorodeoxyglucose (FDG) positron-emission tomography is done, and shows a hypermetabolic right-sided pericardial tumor in addition to several suspicious hepatic lesions with heterogeneously increased FDG uptake. Biopsy with ultrasonographic guidance is performed again and reveals tissue consistent with hemangioma in addition to other areas with features strongly suggestive of a low-grade angiosarcoma (FIGURE 5). Pathology findings are unable to differentiate primary cardiac angiosarcoma from a metastatic cardiac tumor; however, given the multiple liver lesions and the presence of a solitary cardiac mass, this is most likely a primary cardiac tumor with metastasis to the liver.

CARDIAC ANGIOSARCOMA

Cardiac angiosarcoma, the most common malignant primary cardiac tumor, has a predilection for the right atrium.[13] These tumors tend to occur between the third and fifth decade of life and are three times more common in men than in women. Cardiac sarcomas proliferate rapidly and commonly extend into the pericardial space, causing pericardial effusion in up to one-fourth of patients.

Surgical resection is the treatment of choice, but due to the location and extent of involvement, complete resection is often difficult. Also, distant metastases are present at the time of diagnosis in 80% of cases, precluding a surgical cure.[17] Adjuvant chemotherapy, radiotherapy, and even heart transplantation do not substantially improve the survival of these patients.[18–20] Because no effective treatment is available, the prognosis is dismal, with a median survival of 6 to 12 months.

Our patient is discharged home to follow up with an oncologist and initiate chemotherapy. ■

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