A 78-year-old man presented with a constant, substernal, sharp, nonradiating chest pain of 6 hours’ duration; he rated the pain’s severity as 5 on a 10-point scale. He denied previous chest discomfort. His chest pain was preceded by 1 day of epigastric abdominal pain and episodes of nausea and nonbloody emesis. He described the epigastric pain as constant, sharp, and band-like, noting that it was exacerbated by food. Findings were otherwise unremarkable on a complete review of systems. Before this illness, he had exercised daily by jogging on a treadmill.

His medical history was notable for diet-controlled diabetes mellitus, hypertension, hyperlipidemia, giant cell arteritis, and remote tobacco abuse. He denied a family history of premature coronary artery disease (CAD). His medications included amlodipine, atenolol, hydrochlorothiazide, lisinopril, pravastatin, and aspirin.

His vital signs were as follows: blood pressure, 158/77 mm Hg; pulse, 78 beats/min; temperature, 36.1°C; respiratory rate, 16 breaths/min; and saturation while receiving 2 L of oxygen, 95%. He was in no acute distress, and cardiac, vascular, pulmonary, abdominal, musculoskeletal, neurologic, and integument findings were unremarkable. Review of findings on electrocardiography (ECG) revealed new abnormalities not previously seen on ECG (Figure). Atelectasis of the left base was noted on chest radiography.

1. Given these findings, which one of the following is the most likely etiology of this patient’s presentation?
   a. Pulmonary embolism
   b. Pneumonia
   c. Esophageal rupture
   d. Aortic dissection
   e. Acute coronary syndrome (ACS)

   Pulmonary embolism may cause chest discomfort but is unlikely in this hemodynamically stable patient without dyspnea who has a low probability of pulmonary embolism (Wells Score, 0). Although pneumonia can produce abdominal discomfort, the absence of fever, cough, or infiltrate on chest radiography makes this diagnosis unlikely. Esophageal rupture typically occurs after esophageal instrumentation or vigorous vomiting and usually results in chest pain; pneumomediastinum may be present on chest radiography. Our patient had no such history and his chest radiograph was unremarkable. Aortic dissection can produce tearing chest and abdominal pain. Aortic dissection also can result in unstable vital signs, unequal pulses, and possibly a new murmur of aortic regurgitation. This patient had no risk factors, such as connective tissue disorders, history of aortic aneurysm, or a bicuspid aortic valve. A recent study of patients presenting with chest pain found increased odds ratios of myocardial infarction (MI) with a presentation including nausea or vomiting. Given the history and ECG changes, this patient’s presentation is consistent with ACS.

   The patient was given 324 mg of chewable aspirin and sublingual nitroglycerin. His initial troponin value was 0.018 ng/mL (reference ranges provided parenthetically) (<0.01 ng/mL). The patient was administered intravenous unfractionated heparin, intravenous nitroglycerin, and oral metoprolol and was then transferred to our institution for further management.

   At the time of our evaluation, the patient’s ongoing chest pain was less severe. His examination revealed minimal diffuse abdominal tenderness without rebound or guarding and normal bowel sounds. A follow-up ECG showed no relevant changes. Follow-up laboratory testing revealed the following: troponin, 0.02 ng/mL (<0.01 ng/mL); an elevated leukocyte count, 18.0 × 10⁹/L (3.5-10.5 × 10⁹/L); an elevated neutrophil count, 16.8 × 10⁹/L (1.7-7.0 × 10⁹/L); and random glucose level, 190 mg/dL (70-140 mg/dL).

2. Given these findings, which one of the following is most appropriate in the management of this patient?
   a. Switch unfractionated heparin to low-molecular-weight heparin (LMWH)
   b. Administer intravenous morphine
   c. Administer a loading dose of oral clopidogrel
   d. Give an additional dose of enteric-coated oral aspirin
   e. Administer intravenous tenecteplase

   Although LMWH was shown to be more effective than unfractionated heparin at 30 days for prevention of recurrent angina, MI, or death, transitioning between different heparins is not recommended; in fact, studies have shown increased rates of death and MI in those who crossed over...
as compared with those who did not. Further, LMWH increases risks of hemorrhagic surgical complications because of its long half-life. Although adverse events have been suggested with morphine use, continued chest pain usually indicates ongoing ischemia, and administration of intravenous morphine is reasonable. Morphine is thought to provide relief through 3 mechanisms: (1) analgesia through μ-receptor activation; (2) decrease in anxiety and sympathetic drive; and (3) decreased preload and myocardial oxygen demand. The administration of clopidogrel or glycoprotein IIb/IIIa inhibitors is a class IA recommendation in the setting of ACS. However, the possible need for coronary artery bypass grafting makes immediate clopidogrel administration a less attractive option; in such cases, glycoprotein IIb/IIIa inhibitors should be considered instead. In this setting, the maximum recommended dose of aspirin is 324 mg. Chewable aspirin is recommended because of enhanced buccal absorption and decreased time to effective platelet inhibition. Tenecteplase, a thrombolytic agent, is indicated for ST-segment elevation MI but not for non-ST-segment elevation MI.

An important consideration in evaluating this patient with ACS is his Thrombolysis in Myocardial Infarction risk score of 6, which predicts a 41% risk of all-cause mortality, new or recurrent MI, or severe ischemia requiring urgent revascularization. An early invasive management strategy was planned, but before catheterization the patient noted increasing abdominal pain. Follow-up examination revealed stable vital signs but also the development of abdominal guarding with rebound tenderness that was prominent in the right lower quadrant. Findings on urgent bedside transthoracic echocardiography (TTE) were not consistent with acute MI. Lipase, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and bilirubin levels were normal. However, the patient’s lactate level was elevated at 3.0 mmol/L (0.6-2.3 mmol/L).

3. Which one of the following is the most appropriate next step?
   a. Initiation of intravenous antibiotics
   b. Abdominal ultrasonography
   c. A follow-up point-of-care lactate level
   d. Computed tomography (CT) of the abdomen and pelvis
   e. Transesophageal echocardiography

   The patient’s history and physical examination findings could point to an abdominal infection; however, without further evaluation of the pain, initiation of antibiotics would not be the most appropriate next step. The differential diagnosis of his abdominal pain includes appendicitis, inflammatory bowel diseases, diverticulitis, small bowel obstruction, ruptured viscus, and ischemic bowel. Although ultrasonography can visualize the appendix, the other conditions cannot be diagnosed and require further imaging. Obtaining a second lactate level will not help because normal lactate values do not rule out pathology, nor do elevated levels establish a diagnosis secondary to its lack of specificity. With leukocytosis, peritoneal signs, and lactic acidosis, it is necessary to search for the aforementioned causes; CT of the abdomen and pelvis would provide the most relevant information. In this case, TTE is generally sufficient to identify regional wall motion abnormalities (RWMAs) and transesophageal echocardiography would not provide any additional information to justify the risks of procedural complications.

   Findings on CT (a dilated thick-walled appendix, an obstructing appendicolith, and a few small gas bubbles next to the appendiceal tip) were consistent with acute appendicitis.
4. In addition to surgical consultation, which one of the following is indicated in the management of this patient?

a. Perform preanesthesia medical examination
b. Initiate intravenous vancomycin
c. Perform coronary catheterization
d. Administer intravenous protamine sulfate
e. Discontinue intravenous heparin

The patient’s signs and symptoms were attributed to a pseudomyocardial infarction (PMI) secondary to ruptured appendicitis. Briefly, PMI is a condition of chest pain, ECG changes, and cardiac troponin elevation that mimics MI without CAD. When the need for surgical intervention is emergent, a preanesthesia medical examination is unnecessary because it delays life-saving surgery and may yield results that cannot be addressed immediately. Vancomycin is a gram-positive antimicrobial agent and, in this case, empirical antibiotic therapy should be aimed against intraabdominal gram-negative aerobes and anaerobes to prevent wound infection and abscess formation. Coronary catheterization is not indicated because ACS was not the underlying cause of the patient’s symptoms, and further cardiac testing could be considered after treatment of his acute appendicitis. Because of potential risks associated with its administration, protamine sulfate is typically used in the setting of uncontrollable or anticipated major bleeding and heparin overdose. Laparoscopic appendectomy is a minimally invasive procedure with a low bleeding risk and unfractonated heparin has a short half-life; therefore, immediate discontinuation of heparin would be the best approach.

On the day after laparoscopic appendectomy, the patient’s troponin levels and ECG findings normalized, and he was discharged with primary care and cardiology follow-up.

5. Which one of the following would be the most appropriate test to evaluate this patient’s risk of CAD?

a. Dobutamine stress echocardiography
b. CT coronary angiography
c. Exercise ECG
d. Coronary angiography
e. Adenosine sestamibi perfusion study

Dobutamine stress echocardiography provides information on the presence and extent of inducible myocardial ischemia, while assessing left ventricular function, chamber size, and valvular function. It is indicated when patients cannot exercise or when baseline ECG abnormalities interfere with interpretation of stress ECG; this was not the case in our patient. Although CT coronary angiography is a noninvasive test for determining coronary anatomy and major epicardial coronary disease, it would not be the best screening tool because of the associated radiation exposure, risk of contrast reaction, and cost. In this patient, who is capable of exercising and whose resting ECG has returned to normal, the most appropriate test would be exercise ECG. Coronary angiography should only be considered in patients with a high pretest probability of left main or triple-vessel CAD or for those whose occupation (ie, airplane pilot) requires a definitive diagnosis. An adenosine sestamibi perfusion study localizes areas of perfusion limitation and can also determine ejection fraction and myocardial viability. However, this test should not be a first-line test for a patient with good exercise capacity.

Stress testing 2 months later was negative for ischemia. With risk factor management, the patient continues to do well.

DISCUSSION

Awareness of PMI continues to grow. This syndrome requires a high index of suspicion in the face of universally accepted criteria for MI. However, the 2007 definition of MI acknowledges that a number of conditions can mimic and confound the diagnosis. Thus, understanding PMI is imperative to preventing improper patient care.

Ischemic ECG changes, including ST-segment elevation, ST-segment depression, and T-wave inversion, can be produced by a wide variety of both cardiac and noncardiac conditions. Conditions such as apical ballooning syndrome, coronary vasospasm, myopericarditis, left ventricular hypertrophy, bundle branch blocks, Brugada syndrome, and arrhythmogenic right ventricular cardiomyopathy can all produce ischemic ECG changes, but interpretation within their clinical context and presentation can help physicians to make the correct diagnosis. Noncardiac conditions such as pulmonary embolism, cerebrovascular accidents, seizures, and medications (ie, digoxin) can also produce similar ECG changes; however, because of their unique presentations, clinicians are usually able to differentiate such entities from MI.

Although cardiac troponin has been considered specific for myocardial necrosis, it is too without false positives. The etiologies that have already been discussed, along with the systemic inflammatory response syndrome and renal failure, can all elevate troponin levels and, combined with ECG abnormalities, can lead to an inappropriate diagnosis of MI. Further, the immunoassay for cardiac troponin is subject to interference by a number of factors, including heterophilic antibodies (which occur in autoimmune diseases or after exposure to foreign antigens), rheumatoid factor, excess fibrin, microparticles, and analyzer malfunction.

In several reports, PMI presented with intraabdominal pathologies, such as acute pancreatitis, duodenal perforation, cholecystitis, and perforated appendicitis. Severe metabolic stress from shock or abnormal renal function has
also been implicated.\textsuperscript{14,25} The underlying mechanism remains under investigation and is thought to be secondary to vagal responses leading to hypotension, decreased coronary perfusion, myocardial depression, increased myocardial oxygen consumption, and subsequent myocardial ischemia with corresponding electrical changes and biomarker elevations.\textsuperscript{20,26}

Further, during these conditions, derangements in sodium, potassium, and calcium levels can modify the cardiac action potential, producing ECG abnormalities.\textsuperscript{20,25}

When PMI is suspected, we suggest invoking another defining criterion for MI by cardiac imaging. Early bedside TTE is a relatively fast and effective modality to detect ischemic RWMA.\textsuperscript{11} In acute chest pain syndromes (without elevation in cardiac biomarker values), the absence of substantial RWMA has a negative predictive value of 95%.\textsuperscript{27} Even with elevated troponins, the absence of RWMA should increase suspicion for PMI.

Furthermore, if the anatomic distribution of RWMA is discordant to the ECG changes, a non-ACS diagnosis should be suspected (eg, apical ballooning syndrome or myocarditis). If findings on TTE raise doubt about the ACS diagnosis, then the presenting history, findings on examination, and diagnostic studies should be reviewed. Once an alternative explanation is found, management of this condition is expected to produce resolution of the PMI.

Although PMI is not secondary to substantial CAD, studies have suggested that it is not a benign condition. Post hoc analysis of TACTICS-TIMI-18 showed that patients without angiographically evident stenosis who satisfied the definition of ACS with troponin elevations on presentation had a 6.3% rate of death, infarction, or rehospitalization for ACS at 6 months.\textsuperscript{28} Several other studies have shown similar outcomes\textsuperscript{29,30}, thus, these patients should be labeled as having an intermediate-risk profile for recurrent cardiovascular events and require follow-up stress testing and risk factor management.

REFERENCES


Correct answers: 1. e, 2, b, 3, d, 4, e, 5, c