71-Year-Old Man Presenting With Postoperative Chest Tightness

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A 71-year-old man with a medical history of acute myeloid leukemia in remission after chemotherapy and stem cell transplant, chronic graft-versus-host disease, type 2 diabetes mellitus on insulin, and high-grade invasive adenocarcinoma of the transverse colon presented for laparoscopic right colectomy. Preoperative evaluation revealed no cardiovascular abnormalities, with an electrocardiogram (ECG) showing only first-degree atrioventricular (AV) block and a transthoracic echocardiogram showing normal systolic function, with an ejection fraction of 67%, 6 months before his presentation. He was placed under general anesthesia and underwent a laparoscopic colectomy without any complications. Shortly after recovering from the procedure, the patient began to experience a sensation of uneasiness and jitteriness followed by bandlike chest tightness. He was hemodynamically stable, with a heart rate of 76 bpm, blood pressure of 126/67 mm Hg, oxygen saturation of 99% on room air, and a temperature of 36.3°C. He did not complain of any associated symptoms, including no shortness of breath, dizziness, or loss of consciousness.

Physical examination was notable for normal rate and rhythm, with a 1/6 systolic murmur heard over the left upper sternal border, clear lung fields bilaterally, postsurgical findings over the abdomen, 1+ edema bilaterally over the ankles, and normal neurologic examination findings.

1. Which *one* of the following would be the *most appropriate* first course of action?
   a. Administer lorazepam 1 mg orally
   b. Reassure the patient
   c. Order an ECG
   d. Order a chest radiograph
   e. Order an abdominal radiograph

Administering lorazepam or reassuring the patient without investigating the cause of a recently postsurgical patient's new symptoms would not be appropriate. The risk of perioperative complications is high in this patient, and his symptoms need to at least be evaluated. In particular, risk of cardiac complications is high after intra-abdominal procedures,[1] and the quickest and most efficient way to evaluate for those complications is an ECG. Although a chest radiograph could help evaluate for lung pathology such as a pneumothorax, the patient exhibited no difficulty breathing and no signs on examination to suggest such an etiology. Furthermore, he maintained oxygen saturations of 99% on room air. If other investigations did not reveal a source, this may be pursued next. An abdominal radiograph would help evaluate for abdominal pathology such as a bowel perforation; however, his abdominal examination is benign, and this test would likely be of low yield.

An ECG was ordered that revealed new T-wave inversions in V_2-V_6 and a prolonged QTc to 528 milliseconds from a baseline of 456 milliseconds, in addition to his baseline first-degree AV block. Given these changes, a troponin T level was ordered, which was elevated to 0.13 ng/mL (to convert to µg/L, multiply by 1) (reference range, <0.01 ng/mL) in addition to a hemoglobin level of 10.3 g/dL (to convert to g/L, multiply by 10) (reference range, 13.5-17.5 g/dL), potassium level of 4.3 mmol/L (reference range, 3.6-5.2 mmol/L), and creatinine level of 1.2 mg/dL (to convert to µmol/L, multiply by 88.4) (reference range, 0.8-1.3 mg/dL). The troponin T level was serially evaluated at 3 hours (0.13 ng/mL) and 6 hours (0.13 ng/mL).

See end of article for correct answers to questions.

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2. Which *one* of this patient's risk factors would *most strongly* increase his risk of a perioperative cardiovascular event?
   a. Previous malignancy
   b. First-degree AV block
   c. Creatinine level of 1.2 mg/dL
   d. Diabetes mellitus treated with insulin
   e. Hemoglobin level of 10.3 g/dL

A commonly used and well-validated perioperative cardiac risk model is the Revised Cardiac Risk Index outlined by Lee et al.[2] In an analysis of 2893 consecutive patients undergoing noncardiac surgery, 6 independent risk factors were identified. Previous malignancy was not among the risk factors identified. Although conduction disease in general would be something to consider in preoperative evaluation, first-degree AV block has not been shown to be correlated with an increase in perioperative cardiac risk. Renal dysfunction was among the 6 factors identified; however, a creatinine level greater than 2 mg/dL was the identified threshold. Diabetes mellitus treated with insulin was also 1 of the 6 identified risk factors and the best option. The relative risk of a cardiac event in patients who were being treated with insulin compared with those who were not was 3.5 in the original cohort and was confirmed as a risk factor in the validation cohort.[2] Anemia was not identified as a risk factor for perioperative cardiac complications but should be considered when deciding the appropriateness of a patient for surgery.

Given that the troponin level did not exhibit a significant change and his recent surgery, the decision was made to proceed with noninvasive management. A transthoracic echocardiogram was ordered that showed global akinesis of the apical and midventricular segments circumferentially. The patient was noted to have a reduced ejection fraction of 23%. He was also found to have an apical left ventricular thrombus. An N-terminal-pro brain-type natriuretic peptide level was elevated at 7190 pg/mL (to convert to ng/L, multiply by 1) (reference range, $\leq$103 pg/mL). Although coronary angiography is the standard option for further investigation, the team and the patient decided to pursue further noninvasive imaging because of his postoperative status. Cardiac magnetic resonance imaging (MRI) with gadolinium enhancement was performed and showed decreased wall motion of the mid and apical left ventricle without any delayed enhancement, a left ventricular ejection fraction of 41%, and the previously noted apical left ventricular thrombus. The lack of delayed enhancement suggests a lack of infarction or myocarditis, which would be consistent with stress-induced cardiomyopathy.[3] The patient continued to deny any chest pain, palpitations, shortness of breath, orthopnea or other signs of ischemic cardiac disease or congestive heart failure.

3. Given the previously noted findings, which *one* of the following would you use to treat the newly found left apical thrombus?
   a. No acute treatment, follow up in 3 months
   b. Surgical thrombectomy
   c. Intravenous heparin bridging to warfarin
   d. Intravenous thrombolysis
   e. Low-dose aspirin and clopidogrel

The main risk associated with an intracardiac thrombus is a cardioembolic event, primarily stroke. The risk of embolic complications has been reported to be as high as 10%, often occurring within the first 3 months.[4] It would be inappropriate to forego any acute treatment in this patient given the major risk of further complications. Surgical thrombectomy is a potential option. However, it is typically reserved for either highly mobile and large thrombi protruding from the ventricle or thrombi resistant to medical therapy. The present patient's thrombus did not seem to show any of the characteristics that would warrant surgical intervention at this time. The best option in this patient would be intravenous heparin bridging to oral warfarin. Heparin is used for at least 5 days when initiating warfarin to mitigate the initial procoagulation and prothrombotic effect that warfarin can have. Lovenox can also be used instead of heparin for a similar effect. Anticoagulation has been shown to

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reduce the risk of embolic events, especially if started early.[5] Intravenous thrombolysis has been trialed in the past and did have success in resolving thrombi. However, many patients experienced either embolic or hemorrhagic complications, and thrombolysis is typically not recommended today.[6] It would, however, be contraindicated in our patient, who recently underwent major abdominal surgery. There is a lack of evidence that antiplatelets such as aspirin and clopidogrel have shown benefit in resolution of thrombi, or in prevention of embolic events in this scenario, and would not be indicated.

The patient was initiated on intravenous heparin and bridged to oral warfarin with a target international normalized ratio range of 2 to 3. He continued to be asymptomatic and was scheduled for further follow-up and evaluation. He was also reinstated on his previous medications, including furosemide.

4. Given the diagnosis of stress-induced cardiomyopathy, in addition to furosemide, which *one* of the following medications would you prescribe for this patient?
   a. β-Blocker
   b. Potassium-sparing diuretic
   c. Cardiac glycoside (digoxin)
   d. Nondihydropyridine calcium channel blocker
   e. Class III antiarrhythmic agent

Although definitive management has not been specifically tested, most experts agree that β-blockade is an essential part of therapy for stress-induced cardiomyopathy. It is thought that catecholamine release plays a major role in the pathogenesis of the cardiac dysfunction, and impeding that effect ideally would lead to improved outcomes.[7] This hypothesis has not been formally tested at this time, however. Although diuretics play an important role in congestive heart failure as well, a potassium-sparing diuretic such as spironolactone is not needed at this time, given that he is already taking furosemide. A cardiac glycoside or digoxin would play no role in the management of this situation. He has exhibited no arrhythmia to warrant addition of this medication, and there would be no indication to initiate digoxin for heart failure. A nondihydropyridine calcium channel blocker such as diltiazem may play a role if the patient had concomitant atrial fibrillation and needed rate control. However, these medications act on calcium channel receptors in the myocardium and would not provide the same catecholamine blockade as would a β-blocker. Although some patients with stress-induced cardiomyopathy can exhibit arrhythmias such as ventricular tachycardia, the present patient has not shown any signs of this. An antiarrhythmic drug such as amiodarone would be unnecessary at this time.

The patient continued with adjuvant chemotherapy for his adenocarcinoma and did well over the next couple of months. He returned for follow-up 3 months later and had experienced no interval chest pain, palpitations, shortness of breath, syncope, or orthopnea. His physical examination was notable for a mildly elevated jugular venous pressure and 2+ pitting edema over the ankles. He went for a repeated echocardiogram.

5. Which *one* of the following is the *expected* prognosis for patients with stress-induced cardiomyopathy?
   a. Complete recovery within 4 to 8 weeks
   b. Progressive congestive heart failure requiring eventual transplant
   c. Stable congestive heart failure requiring long-term medical management
   d. Recovery with rehabilitation over 1 to 2 years, but long-term repeated episodes of stress-induced cardiomyopathy
   e. Sudden cardiac death within 1 year

Multiple series have shown that patients generally have resolution of their left ventricular systolic dysfunction after being diagnosed as having stress-induced cardiomyopathy. Most patients will see almost complete recovery of systolic function within 8 weeks.[7] They typically do not need long-term medical management or require evaluation for transplant. The rate of recurrence is less than 10%.[8] There is also no evidence that they are at a higher risk for sudden cardiac death. Patients tend to have similar expected survival

as age-matched controls. Typically, patients who experience stress-induced cardiomyopathy after a major illness do have a higher mortality, although likely related to their underlying disease.[9]

The patient's echocardiogram showed resolution of his systolic dysfunction, with his ejection fraction improving to 57% and only mild residual apical hypokinesis. The apical thrombus had resolved entirely, and his anticoagulation was discontinued. His lower extremity edema and volume status were thought to be at least partially related to his ongoing cancer treatment.

DISCUSSION

Perioperative cardiac complications are, unfortunately, a common clinical scenario. It is important to keep risk factors in mind when evaluating appropriateness for surgery. The Revised Cardiac Risk Index model identified 6 independent risk factors, including high-risk surgery, history of ischemic heart disease, history of heart failure, history of cerebrovascular disease, diabetes mellitus treated with insulin, and a creatinine concentration greater than 2.0 mg/dL.

Stress-induced cardiomyopathy, also known as Tako-Tsubo cardiomyopathy or apical ballooning syndrome, is a rare but important diagnosis to keep on the differential diagnosis for a patient who presents with symptoms suggesting acute coronary syndrome. It is estimated that the incidence is as high as 1% of patients presenting with an initial diagnosis of acute myocardial infarction.[10] Although the pathophysiology is not entirely known, a couple of theories have been proposed. Principal among them is that catecholamine release triggers the syndrome by causing myocardial stunning. This would be in line with the observation that it often occurs after a stressful event. Furthermore, Wittstein et al[11] reported that plasma catecholamine levels were elevated in patients with stress-induced cardiomyopathy compared with Killip class III myocardial infarctions. As in the present patient, malignancy has been associated with the diagnosis, with 1 series identifying up to 5% of presentations associated with a malignancy.[9]

Patients typically present with symptoms and findings similar to an acute coronary syndrome, including angina, ECG changes to suggest ischemia, and elevated cardiac biomarkers. Initial ECG changes can show a transient ST-segment elevation, often in the precordial leads.[9] Later in the clinical course, repeated ECG may show T-wave inversions and a prolonged QTc, as seen in the present patient. The most suggestive or classic finding is on echocardiography. Stress-induced cardiomyopathy is known for its characteristic pattern of wall motion abnormalities: hypokinesis or akinesis of the apical and middle segments of the left ventricle, with sparing of the basal segments, that extends beyond 1 vascular territory.[7] Diagnosis requires the absence of obstructive coronary artery disease and plaque rupture. Coronary angiography is the gold standard test to rule out obstructive disease or plaque rupture. Coronary angiography was not pursued in our patient given his postoperative state and the desire to pursue noninvasive imaging. The proposed Mayo Clinic criteria also include the absence of pheochromocytoma and myocarditis.[7] Cardiac MRI, as seen in the present patient, can be particularly helpful in the evaluation because it may reveal wall motion abnormalities as described previously, but without any delayed gadolinium enhancement, which would suggest ischemia or myocarditis.[3] In addition, CT angiography of the coronaries could be used to evaluate for coronary plaque in the event that an angiogram is contraindicated.

Optimal management has yet to be robustly investigated, but most experts rely on β-blockade and typical congestive heart failure management until cardiac function recovers. The impetus behind β-blockade is to try to interrupt any further catecholamine action on the heart. The prognosis for stress-induced cardiomyopathy is generally very good, with most patients seeing systolic dysfunction resolve within 8 weeks.[7,8] Long-term survival has been shown to be similar to that of a general age-matched population.

With the advent of thrombolysis and percutaneous coronary interventions, the incidence of left ventricular thrombus has declined.[6] However, it remains an important

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complication after acute myocardial infarction and in scenarios where there is stasis of blood in the cardiac chambers, such as stress-induced cardiomyopathy. In fact, the incidence of left ventricular thrombus has been reported to be as high as 1.3% of patients with stress-induced cardiomyopathy.[12] The primary goal of treatment is prevention of cardioembolic phenomena, in particular, stroke. Most of the evidence for anticoagulation in the setting of left ventricular thrombus has come from patients after an acute myocardial infarction. It has been shown that anticoagulation is associated with an 86% reduction in the rate of embolic events in that setting.[5] Most experts feel that it is reasonable to extrapolate that data to patients who develop a left ventricular thrombus in the setting of stress-induced cardiomyopathy. Current recommendations are to initiate heparin and warfarin therapy and continue with heparin for at least 48 hours and until the patient's international normalized ratio is therapeutic at 2 to 3. Anticoagulation should then continue for at least 3 to 6 months. If in 3 to 6 months the thrombus has resolved and ventricular function has normalized, it may then be reasonable to discontinue anticoagulation. There are currently limited data regarding using direct oral anticoagulants in this scenario, and this may be a future area of research.

Thus, apical ballooning syndrome should be high on one's differential diagnosis, especially in the setting of an acute stressor. Cardiac MRI can be helpful in differentiation from ischemia. Supportive therapy with β-blockade is recommended for patients, and most recover left ventricular function within 8 weeks. Appropriate cardiovascular imaging with at least echocardiography is recommended to document systolic function and wall motion abnormalities and to rule out thrombus formation. Especially with apical ballooning syndrome, reduced apical wall motion and stasis may lead to an apical thrombus necessitating anticoagulation. Furthermore, robust data are necessary in the form of large studies to determine optimal therapy and long-term management of Takotsubo cardiomyopathy, as much of the current recommendations stem from observational studies and expert opinion.

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