A 61-year-old man with a past medical history of type 1 diabetes mellitus, hypertension, hyperlipidemia, and alcohol use disorder presented to the emergency department with epigastric abdominal pain, nausea, and vomiting. He normally consumed 4 to 6 cans of beer per day and had done this for numerous years. His last drink was 2 days before presentation, when he had his usual amount of alcohol intake. Home medications included aspirin 81 mg, atorvastatin 10 mg, and an insulin pump. The insulin pump used aspart. It had a basal dose of 17.5 units per day and a maximum total bolus dose of 25 units per day. His hypertension was managed by nonpharmacologic methods. He was evaluated 1 day earlier for similar symptoms and was found to have cellulitis at the pump injection site. He was given 10 units of intravenous (IV) regular insulin and a prescription for cefalexin 500 mg to be taken every 6 hours for 7 days. Later, he had sharp epigastric pain with vomiting, which prompted him to seek further care.

At presentation, the patient was afebrile and had a heart rate of 71 beats/min with a regular rhythm, blood pressure of 149/75 mm Hg, and oxygen saturation of 98% on breathing of room air. Cardiac and pulmonary examination findings were unremarkable. He had epigastric tenderness on abdominal examination but no rebound or guarding. His skin was dry, and there was a small area of erythema on the right lower quadrant. Mucous membranes were moist, and clinically he appeared euolemic. Neurologic examination findings were within normal limits.

Laboratory studies yielded the following (reference ranges provided parenthetically): hemoglobin, 14.1 g/dL (13.5 to 17.5 g/dL); leukocyte count, 10.3 × 10⁹/L (3.4 to 9.6 × 10⁹/L); platelets, 244 × 10⁹/L (135 to 317 × 10⁹/L); sodium, 134 mmol/L (135 to 145 mmol/L); potassium, 5.0 mmol/L (3.6 to 5.2 mmol/L); creatinine, 0.81 mg/dL (0.74 to 1.35 mg/dL); bicarbonate, 14 mmol/L (22 to 29 mmol/L); glucose, 326 mg/dL (70 to 100 mg/dL); blood urea nitrogen, 10 mg/dL (8 to 24 mg/dL); β-hydroxybutyrate, 7.2 mmol/L (<0.4 mmol/L); albumin, 4.3 g/dL (3.5 to 5.0 g/dL); lipase, 11 U/L (13 to 60 U/L); lactate, 4.2 mmol/L (0.5 to 2.2 mmol/L); alanine aminotransferase, 22 U/L (7 to 55 U/L); aspartate aminotransferase, 54 U/L (8 to 48 U/L); alkaline phosphatase, 81 U/L (40 to 129 U/L); hemoglobin A₁c, 8.0% (4.0% to 5.6%); and troponin T, 363 ng/L (≤15 ng/L). On arterial blood gas analysis, pH was 7.399 (7.350 to 7.450); P<sub>CO₂</sub>, 33.7 mm Hg (35 to 45 mm Hg); P<sub>O₂</sub>, 69.9 mm Hg (83 to 108 mm Hg); and HCO₃⁻, 20.4 mmol/L (22 to 26 mmol/L).

Urinalysis was positive for ketones and revealed a glucose concentration above 1000 mg/dL. Electrocardiography was performed, which showed nonspecific T-wave abnormalities in the anterior leads but otherwise was within normal limits. Findings on chest radiography and computed tomography (CT) of the abdomen and pelvis were unremarkable. No evidence of aortic calcifications was noted on CT imaging.

1. Which of the following is the most likely diagnosis?
   a. Acute pancreatitis
   b. Diabetic ketoacidosis (DKA)
   c. Alcohol withdrawal
   d. Hyperglycemic hyperosmolar syndrome
   e. Alcohol ketoacidosis

The diagnosis of acute pancreatitis requires at least 2 of the following 3
characteristics: symptoms consistent with acute pancreatitis; serum lipase level at least 3 times the upper limit of normal; and characteristic imaging findings on CT, magnetic resonance imaging, or ultrasound. Diabetic ketoacidosis (DKA) has 3 major characteristics: hyperglycemia, anion gap metabolic acidosis, and presence of ketones in the blood or urine. He had findings consistent with DKA. The Diagnostic and Statistical Manual of Mental Disorders (fifth edition) criteria for alcohol withdrawal are based on the following 4 characteristics:

1. The abrupt discontinuation (or reduction) of heavy and prolonged alcohol use.
2. Two or more of the following symptoms after the reduction of alcohol:
   a. Autonomic hyperactivity
   b. Increased hand tremors
   c. Nausea/vomiting
   d. Insomnia
   e. Visual, tactile, or auditory hallucinations
   f. Psychomotor agitation
   g. Anxiety
   h. Generalized tonic-clonic seizures
3. The development of the symptoms causes distress or an inability to function in social, or occupational environments.
4. These symptoms cannot be explained by another medical/psychiatric condition.

Although he meets some criteria for alcohol withdrawal, his symptoms are more likely explained by DKA. He is unlikely to have hyperosmolar hyperglycemic state. This condition occurs in patients with type 2 diabetes. In this state, there is an insignificant amount of ketoacid accumulation, and the glucose levels are frequently higher than those seen in DKA (>600 mg/dL). Altered mental status is also a common presenting comorbid condition. Hyperosmolar hyperglycemic state is incorrect because the patient was a type 1 diabetic, without a change in mental status; glucose levels were, in this case, less than 600 mg/dL, and ketones were present in the urine.

He did not have alcoholic ketoacidosis. This diagnosis is made by clinical history and glucose levels. Alcoholic ketoacidosis is present in patients with nutritional deficiencies and alcohol use disorder with recent binge consumption. Symptoms include abdominal pain, nausea, and vomiting before presentation. Patients appear hypovolemic and manifest signs of acute alcohol withdrawal. In alcoholic ketoacidosis, the glucose levels are frequently less than 275 mg/dL, which is somewhat lower than the levels frequently found in patients with DKA.

The patient's insulin pump was discontinued, and an insulin drip was started. A basic metabolic panel was scheduled to be collected every 4 hours to assess for electrolyte abnormalities while the patient was receiving the insulin drip.

2. Which of the following laboratory test values will be falsely elevated in this condition?
   a. Phosphorus
   b. Creatinine
   c. Sodium
   d. Triglycerides
   e. Lipase

Phosphorus levels will be falsely elevated. Total volume depletion causes contraction of the extracellular fluid, contributing to the overall appearance of increased phosphorus levels. The administration of fluids and insulin will normalize these abnormalities without the need for additional interventions. However, if serum phosphate concentration is below 1 mg/dL or 0.32 mmol/L, IV repletion should be strongly considered.

Creatinine concentration can acutely rise in DKA, but this is a reflection of the hypovolemic state rather than a false elevation.

Sodium levels may appear acutely low. This is because of osmotic pressure from the excess glucose. Glucose will cause a shift of water out of cells and dilute the sodium concentration.

Excess glucose and lack of insulin favor the production of triglycerides in DKA. Triglycerides serve as the substrate for ketosis in hepatocytes.
Lipase levels are elevated in DKA. However, the mechanism of why this occurs has yet to be elucidated.

Repeated troponin determinations at 2 and 6 hours were 542 ng/L and 617 ng/L, respectively. The electrocardiogram was unchanged from the previous recording. There was no evidence of ST-segment elevation or depression, and he denied chest pain.

3. What is the most likely trigger for this patient’s DKA?
   a. Acute pancreatitis
   b. Insulin pump malfunction
   c. Sepsis
   d. Myocardial injury
   e. Recent initiation of cefalexin

Acute pancreatitis is a common trigger for DKA, but he did not meet the required criteria.

Insulin pump malfunction can also trigger DKA. However, the infusion set was recently repositioned, and he had adequate supply of aspart.

Sepsis needs to be ruled out in an acutely ill patient. Vital signs were within normal limits, and white blood cell count was mildly elevated. The only source of infection was the cellulitis. The evidence at hand did not support sepsis as the cause of DKA.

Myocardial injury was the most likely cause. In patients with diabetes, the clinical presentation may be more subtle because of neuropathy arising from long-standing damage to peripheral nerves. The epigastric pain probably reflected an atypical presentation of cardiac ischemia, which is supported by the increasing troponin levels.

Cefalexin has not been associated with DKA. Medications that reportedly are associated include fluoroquinolones, thiazide diuretics, second-generation atypical antipsychotics, and beta blockers. The sodium-glucose cotransporter 2 inhibitors have also been reported to trigger DKA and are not recommended for use in patients with type 1 diabetes.

The cardiology team was then consulted. They recommended continued treatment of DKA, initiation of medical therapy for a non-ST-segment elevation myocardial infarction (NSTEMI), and transthoracic echocardiography to investigate for any regional wall motion abnormalities.

4. Which of the following medications should be administered acutely for this patient?
   a. Angiotensin-converting enzyme (ACE) inhibitor
   b. Tenecteplase
   c. Sodium bicarbonate
   d. Unfractionated heparin
   e. Subcutaneous insulin

An angiotensin-converting enzyme (ACE) inhibitor should not be started acutely because of the possibility of hypotension in an acute myocardial infarction (MI). Before hospital discharge, this medication may be prescribed if there is evidence of left ventricular dysfunction or concomitant hypertension. Given his diabetes, an ACE inhibitor or an angiotensin receptor blocker would be considered a valuable addition for renal protection.

Tenecteplase, a thrombolytic, is administered only in ST-segment elevation myocardial infarctions. Patients must meet certain criteria before fibrinolytic therapy is chosen. These criteria include chest pain characteristic of an acute MI for 12 to 24 hours, inability to receive revascularization in a timely fashion, presence of a new ST elevation seen on 2 contiguous leads, and presence of a new left bundle branch block.

A randomized clinical trial determined the benefit of bicarbonate therapy to increase the pH of acidic patients to 7.3 or higher. There was a decrease in 28-day mortality and need for dialysis in patients who were acidic and had severe acute kidney injury. There would be no benefit of sodium bicarbonate for this patient, whose pH was greater than 7.3.

Anticoagulation should begin once a patient is diagnosed with an NSTEMI. Early implementation of antiplatelet therapy and anticoagulation has been demonstrated to yield marked survival benefit in acute MI.
For patients who will undergo invasive coronary angiography within 48 hours, unfractionated heparin is preferred. These patients should receive a loading dose of aspirin (162 to 325 mg) and a P2Y12 inhibitor (clopidogrel or ticagrelor) before intervention. The P2Y12 inhibitor may initially be withheld if there is a high suspicion that the patient will need coronary artery bypass grafting. Our patient received a loading dose of aspirin but not a P2Y12 inhibitor.

In DKA, subcutaneous insulin would not be the initial treatment. Guidelines recommend the initiation of IV insulin.

A heparin drip was started; metoprolol tartrate 25 mg was prescribed, and aspirin 325 mg was administered. Transthoracic echocardiography showed new regional wall motion abnormalities at the apex of the left ventricle along the posterolateral wall; the ejection fraction was greater than 50%. Invasive coronary angiography was scheduled to occur after optimization of the DKA.

5. Which of the following would warrant urgent invasive coronary angiography for this patient?
   a. Acute-onset atrial fibrillation
   b. Sudden resolution of angina
   c. Presence of regional wall motion abnormalities on echocardiography
   d. Prior MI
   e. Presence of ventricular arrhythmias

New-onset atrial fibrillation would not be an indication for invasive angiography as its development is likely to be reflective of multiple stressors. By itself, it is unlikely to compromise cardiac function.

Sudden resolution of angina would not prompt an urgent invasive strategy. Persistent angina despite analgesic therapy would prompt expedited intervention.

Wall motion abnormalities are expected in an MI. However, if there are no signs of acute heart failure or cardiogenic shock, invasive coronary angiography can be delayed, given ongoing critical illness (ie, DKA).

Prior history alone does not equate to needing urgent angiography.

Ventricular arrhythmias are a foreboding feature and would prompt urgent invasive coronary angiography. These rhythms can cause hemodynamic compromise and increase the likelihood of death.

Patients who do not need urgent coronary angiography should undergo appropriate risk stratification. Two stratification scores are the Global Registry of Acute Coronary Events (GRACE) and Thrombolysis in Myocardial Infarction (TIMI).

The TIMI score is calculated on the basis of 7 binary variables: age of 65 years or older, presence of 3 or more risk factors for coronary heart disease, known coronary stenosis of 50% or more, presence of ST-segment elevation or depression on electrocardiography, 2 or more anginal episodes in the last 24 hours, troponin elevation, and use of aspirin in the last 7 days. Higher scores correlate with increased number of major cardiac adverse events at 14 days.

The GRACE score is based primarily on 8 characteristics: age (>30 years), Killip class, systolic blood pressure (<200 mm Hg), presence of ST changes, cardiac arrest, creatinine level, troponin level, and heart rate (>50 beats/min).

A TIMI score below 3 and a GRACE score below 108 are considered lower risk, but the overall clinical context must always be taken into account. Our patient had a TIMI score of 3 and an in-hospital GRACE score of 111, which supported the need for an invasive approach.

After 37 hours, blood glucose levels were between 140 and 180 mg/dL, and he underwent coronary angiography. He was not reloaded with aspirin before the procedure. There was a 99% stenosis in the middle left anterior descending artery and a 90% stenosis in the second diagonal branch. A drug-eluting stent was successfully placed in the mid left anterior descending artery, and there was percutaneous transluminal coronary angioplasty to the second diagonal branch. He did well and was transitioned back to his home insulin pump. He was discharged home on the following medications: metoprolol, high-
intensity atorvastatin, lisinopril, aspirin, and clopidogrel.

DISCUSSION

Diagnosis of DKA and identification of the underlying trigger are paramount to ensuring prompt, appropriate treatment. Pancreatitis and alcohol withdrawal can mimic the symptoms of DKA, which underscores the importance of a comprehensive clinical history. The 2 most frequent causes of DKA are nonadherence to insulin therapy and the presence of an infection (commonly pneumonia or urinary tract infections). In patients with long-standing diabetes, MI may be manifested with atypical symptoms and should always be considered in the differential diagnosis.

The incidence of death is nearly 30% in patients presenting with both DKA and MI. Troponin elevation in DKA is not an uncommon phenomenon, and determination of its clinical significance may be difficult to discern without invasive testing. In DKA, the acidosis disrupts the sarcoplasmic reticulum of the cardiac myocytes, causing an increase in intracellular calcium and, ultimately, myocardial stunning and proteolysis. In addition, there are increased circulating catecholamines, which increase myocardial demand and cause elevated troponins in patients with diminished coronary blood flow reserve. Last, elevated free fatty acids lead to ketone body formation and decreased uptake of glucose by cardiac myocytes. Because glucose is the primary energy substrate for cardiac myocytes, this state is damaging to cells and promotes the release of troponin.

Optimal DKA management should adhere to a defined DKA protocol that includes recommendations for insulin dosage and fluid management. It is important to allow clearance of ketones and free fatty acids before glucose levels normalize and patients are transitioned back to their home insulin regimen. There should be an overlap of at least 2 hours of the home subcutaneous regimen and IV drip before discontinuation.

Patients presenting with any signs of severe complications from the underlying MI should be evaluated for an urgent invasive approach. Our patient received coronary angiography within 37 hours, which was relatively early in the hospital course. The GRACE and TIMI scores can be used to assist with risk stratification in patients who are having an NSTEMI. Patients with lower scores may still undergo early invasive coronary angiography if the clinical context is appropriate.

Before discharge, it is important that all patients who have had percutaneous coronary intervention with stenting be started on a beta blocker, statin, and dual antiplatelet therapy (DAPT). An ACE inhibitor may be added if cardiac function has decreased significantly after the event. Current recommendations promote the use of DAPT in all patients who have had an MI. In those who have undergone revascularization, DAPT also serves to prevent thrombosis within newly placed stents. The duration of DAPT should ideally be 1 year for all MIs but may be truncated in those at higher risk for major bleeding. On discharge, patients who have suffered from an MI should also be referred for cardiac rehabilitation.

Potential Competing Interests: The authors report no competing interests.

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