A 33-year-old previously healthy white woman (gravida 1, para 1) who recently delivered a healthy baby girl via elective cesarean section experienced acute shortness of breath approximately 6 hours after delivery. Her pregnancy was complicated by development of preeclampsia without severe features at 32 weeks. Because of her preeclampsia, she underwent elective cesarean section at 37 weeks’ gestation. She received routine prenatal care and was up-to-date on all vaccinations and screenings. Her medical history, social history, and family history were unremarkable. Her only medication was a prenatal multivitamin.

Six hours after cesarean delivery, acute shortness of breath developed. Vital signs were notable for a body mass index of 28.6 kg/m², temperature of 36.5°C, heart rate of 114 beats/min, blood pressure of 142/81 mm Hg, and oxygen saturation of 88% while she breathed room air. Chest radiography revealed prominent bilateral interstitial pulmonary opacities consistent with pulmonary edema without cardiomegaly. Electrocardiography (ECG) revealed sinus tachycardia, normal QRS complexes, and no ST-segment or T-wave changes. The presence of lower extremity edema prompted bilateral lower extremity ultrasonography, which was negative for deep venous thrombosis. Given the patient's tenuous status, she was transferred to the intensive care unit (ICU) for further management.

On arrival to the ICU, she was tachycardic and tachypneic. Her oxygen saturation was 96% while receiving 3 L of oxygen via nasal cannula. Physical examination findings were notable for an elevated jugular venous pressure approximately 6 cm above the clavicle. Cardiac examination revealed audible S₁ and S₂ with a faint S₃. Pulmonary examination identified bilateral basal crackles. Neurologic, abdominal, musculoskeletal, and skin examination findings were unremarkable.

Laboratory studies revealed the following (reference ranges provided parenthetically): hemoglobin, 13.3 g/dL (11.6 to 15.0 g/dL); white blood cell count, 14.1 × 10⁹/L (3.4 to 9.6 × 10⁹/L); and creatinine, 0.62 mg/dL (0.59 to 1.04 mg/dL). Her initial highsensitivity cardiac troponin T level was 37 ng/L, 2-hour troponin T value was 35 ng/L (≤10 ng/L), and N-terminal pro-B-type natriuretic peptide concentration was 422 pg/mL (<82 pg/mL).

1. Given this patient’s clinical presentation, which one of the following is the most likely diagnosis?
   a. Acute coronary syndrome (ACS)
   b. Pulmonary embolus
   c. Peripartum cardiomyopathy
   d. Spontaneous coronary artery dissection
   e. Amniotic fluid embolus

This patient appears to have heart failure given her physical examination evidence of S₃ and crackles noted on pulmonary auscultation. Her chest x-ray is also concerning for pulmonary edema. Although ACS could certainly cause decompensated heart failure, this patient does not have traditional risk factors for ACS, ECG results are reassuring, and her troponin levels are not changing. A pulmonary embolus is certainly part of the differential diagnosis of this patient’s acute shortness of breath, especially given her postpartum status. However, a pulmonary embolus would not usually cause pulmonary edema. In addition, a pulmonary embolus, and an amniotic fluid embolus for that matter, severe enough to cause a new oxygen requirement might also be expected to result
in hypotension of varying degree, which was absent in this case. Peripartum cardiomyopathy is the most likely diagnosis in this patient. Peripartum cardiomyopathy usually occurs in late pregnancy or the early postpartum period. This type of cardiomyopathy can cause acute left ventricular dysfunction and typical heart failure symptoms including shortness of breath, pulmonary edema, and bilateral lower extremity edema. Spontaneous coronary artery dissection would also be included in the differential diagnosis of this patient’s condition. However, it typically presents with ECG changes, substernal chest pain, and substantially elevated and changing troponin levels, as would also be typical in ACS, none of which were evident in this patient. Amniotic fluid embolus is a life-threatening diagnosis that almost invariably occurs during or immediately after labor. Typical features of amniotic fluid embolus include tachycardia, hypotension, tachypnea, and bleeding due to disseminated intravascular coagulation. This patient’s clinical picture was not suggestive of this etiology.

Intravenous diuresis with furosemide was initiated. With diuresis, she had excellent urine output and her shortness of breath improved. Transthoracic echocardiography revealed severe left ventricular enlargement, severe generalized left ventricular hypokinesis, and a calculated left ventricular ejection fraction (LVEF) of 23%. The right ventricular size and function were normal. Transthoracic echocardiography also identified moderate-severe functional mitral valve regurgitation secondary to left ventricular enlargement.

2. Which one of the following factors most likely contributed to the development of peripartum cardiomyopathy in this patient?
   a. History of multiple gestations
   b. Obesity (body mass index >30 kg/m²)
   c. White race
   d. Substance abuse
   e. Preeclampsia

A history of multiple gestations is a well-described risk factor for the development of peripartum cardiomyopathy, but this patient had no prior gestations. Obesity is a proposed risk factor for the development of peripartum cardiomyopathy; however, this patient would be considered overweight and not necessarily obese, which would not carry the same risk. White race is not a known risk factor for the development of peripartum cardiomyopathy, although being of African descent is a risk factor for unknown reasons. Substance abuse, especially cocaine use, during and after pregnancy is a proposed risk factor for development of peripartum cardiomyopathy. This patient reported no substance abuse, and her social history was unremarkable. Her most important risk factor for the development of peripartum cardiomyopathy is preeclampsia. There is evidence that preeclampsia may be a risk factor for the development of peripartum cardiomyopathy because of shared physiologic mechanisms that predispose the patient to endothelial dysfunction and oxidative stress.

The patient continued to improve with diuretic therapy. Given her clinical improvement, medical therapy was initiated. Because she wished to pursue breastfeeding her infant, medications had to be chosen carefully.

3. In view of this patient’s newly diagnosed peripartum cardiomyopathy, which one of the following medications is not considered compatible with breastfeeding?
   a. Furosemide
   b. Enalapril
   c. Metoprolol succinate
   d. Sacubitril-valsartan
   e. Digoxin

Women who present with peripartum cardiomyopathy should be treated according to guideline-directed medical therapy for heart failure with few exceptions. The initial step in treatment is to treat hypervolemia with diuretics. Furosemide is the most commonly used diuretic and has the most evidence for its use. In patients without overt pulmonary congestion, cautious diuresis is strongly recommended because overdiuresis can decrease blood flow to the placenta in pregnant patients and can decrease the volume of breastmilk production in breastfeeding women.
angiotensin-converting enzyme inhibitors (ACEIs) being contraindicated during pregnancy, their use is recommended and included in guideline-directed medical therapy for heart failure, with enalapril and captopril considered safe during breastfeeding. β-Blockers, such as metoprolol succinate, are also part of guideline-directed medical therapy for heart failure, and breastfeeding is not a contraindication to their use. The PARADIGM-HF (Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure) trial has recently paved the way for sacubitril-valsartan to be recommended in guideline-directed therapy for systolic heart failure, but this trial did not include postpartum or breastfeeding women. The use of sacubitril-valsartan is limited to case reports of postpartum cardiomyopathy in women who are not breastfeeding. Thus, this medication needs more rigorous studies in breastfeeding mothers before it can be recommended. Digoxin does have a limited role in the treatment of peripartum cardiomyopathy and is typically used in cases that are refractory to standard therapy with ACEIs and β-blockers. Digoxin has been found to be safe in breastfeeding mothers.

After intravenous diuresis, we initiated treatment with metoprolol tartrate and enalapril. The patient tolerated medical therapy well. Her vital signs and symptoms improved, and she was able to be transferred to the medical ward 3 days after ICU admission.

4. If this patient initially presented with fulminant cardiogenic shock and hemodynamic instability, which one of the following medications would be recommended and would require cessation of breastfeeding?
   a. Ibuprofen
   b. Bromocriptine
   c. Pentoxifylline
   d. Losartan
   e. Estrogen-progesterin oral contraceptives

There is no evidence for the use of ibuprofen in the management of cardiogenic shock or peripartum cardiomyopathy. In fact, the use of ibuprofen may worsen cardiogenic shock and may cause an acute kidney injury among other complications. The underlying pathophysiology of postpartum cardiomyopathy is thought to involve the cleavage of prolactin hormone. It is thought that genetic alterations in regulatory genes may predispose patients to certain enzymatic reactions involving prolactin, resulting in the generation of vasoinhibin. Vasoinhibin is a proinflammatory molecule that promotes myocyte apoptosis. This hypothesis has been supported by the use of bromocriptine in the treatment of postpartum cardiomyopathy. A proof-of-concept study involving 20 patients found that participants receiving bromocriptine had improved recovery of left ventricular function compared with patients receiving placebo. Current European guidelines endorse bromocriptine use in patients with severe postpartum cardiomyopathy or cardiogenic shock. United States guidelines do not currently endorse specific treatment recommendations for peripartum cardiomyopathy. Further, bromocriptine is a dopamine receptor agonist and would require cessation of breastfeeding due to prolactin inhibition. Thus, bromocriptine as a rescue measure would be the recommended therapeutic option if this patient had presented with cardiogenic shock. Pentoxifylline is another medication that has mechanistic plausibility in the pathogenesis of postpartum cardiomyopathy, but given the limited supporting data on efficacy and safety, it is not currently recommended in any guidelines. Losartan is an angiotensin receptor blocker and is not indicated if the patient has cardiogenic shock because starting this medication may cause unfavorable hemodynamic changes. Estrogen-progesterin oral contraceptive pills are not advised for treatment of peripartum cardiomyopathy or cardiogenic shock. Estrogen-progesterin oral contraceptive pills are contraindicated given the risk of fluid retention and heart failure exacerbations and in the acute setting may be detrimental to cardiovascular hemodynamics. Some forms of birth control may be indicated after stabilizing the patient but are not indicated in the acute setting.
The patient continued to do well, and her heart failure symptoms were well controlled with optimal medical therapy. Throughout her hospitalization, telemetry did not identify any arrhythmias or abnormalities. Five days after admission, the patient and her newborn baby were discharged from the hospital with a regimen of metoprolol succinate, enalapril, and furosemide. Before discharge, her overall prognosis was discussed as well as her increased risk of recurrent symptoms if future pregnancies are attempted.

5. Given this patient’s illness course and current condition, which one of the following is a poor prognostic factor for her overall recovery?
   a. White race
   b. Episodes of cardiac arrhythmias
   c. Electrocardiogram with a QRS duration of more than 120 ms
   d. Family history of nonischemic cardiomyopathy
   e. LVEF of 23% at diagnosis

White race is considered a favorable prognostic factor. African American women have been found to have reduced recovery and a prolonged course for unknown reasons. Any form of cardiac arrhythmia, including ventricular arrhythmias and heart block, would predispose the patient to increased morbidity and sudden cardiac death. Sudden cardiac death has been reported in women with severely decreased LVEF on presentation as well as women who have completely recovered LVEF. This patient did not have any arrhythmias or ECG changes. A personal or family history of an underlying nonischemic cardiomyopathy is certainly a poor prognostic marker of left ventricular systolic function recovery. In fact, a personal or family history of nonischemic cardiomyopathy may represent a familial dilated cardiomyopathy syndrome that would be indistinguishable from peripartum cardiomyopathy, thus complicating diagnosis and prognosis. This patient did not have a personal or family history of cardiomyopathy. Multiple studies have documented the relationship between echocardiographic parameters and patient outcomes. Left ventricular ejection fraction and left ventricular end-diastolic dimension have been reported to provide prognostic information about overall prognosis. This patient’s LVEF was 23% at the time of diagnosis. An LVEF of less than 30% has been found in multiple studies to portend a poor prognosis in terms of cardiac recovery. Most women have improvement in left ventricular systolic function within 6 months, but only a minority of women who have an initial LVEF of less than 30% will completely recover.

Three months after discharge, repeated transthoracic echocardiography revealed an LVEF of 51%, mild left ventricular enlargement, and no valve abnormalities. The patient continues her β-blocker and ACEI therapy and is asymptomatic. Her infant continues to do well.

DISCUSSION
Peripartum cardiomyopathy is defined as a decrease in left ventricular systolic function occurring during the last month of pregnancy or in the first 5 months of the postpartum period. The incidence of peripartum cardiomyopathy is thought to be increasing because of older maternal age and increased recognition of this clinical entity. There are multiple proposed pathophysiologic mechanisms for the development of peripartum cardiomyopathy. However, the most accepted mechanism involves the role of prolactin. In genetically susceptible individuals, there may be activation of enzymes that cleave prolactin to proinflammatory proteins that lead to cardiac myocyte apoptosis. This hypothesis has been supported in the literature by the use of bromocriptine. Bromocriptine has been tested in multiple studies in the past with promising results. However, current US guidelines do not recommend bromocriptine as first-line treatment, and this medication is usually reserved for extremely ill patients or patients with cardiogenic shock. Bromocriptine is not universally recommended in the United States because
it suppresses lactation and has been associated with thrombotic complications. \(^1\,^3\) All patients presenting with heart failure should also receive guideline-directed medical therapy. During the postpartum period, diuretics, enalapril, and \(\beta\)-blockers are safe during breastfeeding and are first-line treatments. Most women experience recovery of their left ventricular function within 6 months after diagnosis if their initial LVEF is greater than 30\%\(^,\,\!^1\,^\,\!^3\) Even with this high proportion recovering left ventricular function, there is a high rate of recurrence of peripartum cardiomyopathy in subsequent pregnancies no matter the initial echocardiographic findings. \(^1\,\!^1\,\!^2\) In women with recovered LVEF, there was a 20% risk of left ventricular dysfunction in subsequent pregnancies. \(^1\,\!^\,\!^1\,\!^4\) Thus, patients and their families should know the risk of future pregnancies and should participate in a shared decision-making process with a multidisciplinary health care team.

**Potential Competing Interests:** The authors report no competing interests.

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**REFERENCES**

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