Lesson 253: PreAnesthetic Assessment of the Patient With Peripartum Cardiomyopathy

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NEEDS STATEMENT
Patients may present at term with peripartum cardiomyopathy (PPCM)—which is often unrecognized during pregnancy. The anesthesiologist may be called on an emergency basis and should have an understanding of the pathophysiologic processes that underlie this condition. An appropriate plan for perioperative care can then be devised. Obstetric emergencies have been identified by committee as important knowledge for the practitioner.

TARGET AUDIENCE
Anesthesiologists

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If you would like to write a CME lesson in Anesthesiology News, please send an e-mail to Elizabeth A.M. Frost, MD, at ElizFrost@aol.com.

LEARNING OBJECTIVES
At the end of this activity, the participant should be able to:
1. Define PPCM.
2. Manage a parturient who presents with signs and symptoms of congestive heart failure.
3. List the specialty consultations that are appropriate for the patient with PPCM.
4. Identify the risk factors for precipitating PPCM.
5. Discuss the importance of echocardiography in the diagnosis and definition of PPCM.
6. Understand the indications for invasive monitoring.
7. Identify the drugs that should not be administered to the parturient until after delivery.
8. Present an anesthetic plan for a patient with PPCM.
9. Summarize the viral, autoimmune, or genetic mechanisms of action that may be involved in the etiology of PPCM.
10. Describe the normal physiologic changes of pregnancy and their role in provoking PPCM.

CASE HISTORY
A 35-year-old Caucasian woman, with a height of 5 ft 6 in, a weight of 250 lb, and a history of chronic hypertension (which had been treated with labetalol 200 mg bid) and gestational diabetes, underwent an emergency Caesarean section at 36 weeks for possible placental abruption. She was dyspneic postoperatively—attributed in part to her obesity. The results of a ventilation-perfusion scan and echocardiography were normal. Two days after discharge from the hospital, she returned to the emergency room with dyspnea, orthopnea, and general malaise. Bilateral pleural effusions and a pericardial effusion were detected. Thoracentesis was attempted, but the fluid was believed to be loculated. The patient was unable to tolerate an attempt to place chest tubes under local anesthesia because of excessive discomfort and oxygen desaturation. She was scheduled to undergo emergency treatment for the alleviation of increased intrathoracic pressure and insertion of a pericardial window under general anesthesia.

PREANESTHETIC ASSESSMENT

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S
ome of the earliest descriptions of heart failure in the puerperium—the period from the end of the third stage of labor until complete involution of the uterus (approximately 3-6 weeks)—were offered by Gouley et al in 1937. They reported 7 cases as a distinct clinical syndrome. In each case, heart failure developed insidiously during the later months of pregnancy and became life-threatening during the puerperium.1 At around the same time, Hull and Haldeman2 described their observations of puerperal heart failure. They noted that not all women in whom heart failure developed after childbirth had a normal heart before pregnancy; rather, most had preexisting organic heart disease, often caused by hypertension or rheumatic fever. However, all the patients identified in their study in whom cardiac failure developed were thought to have had a normal heart before pregnancy.

Peripartum cardiomyopathy (PPCM), a rare syndrome, is a type of heart failure associated with pregnancy. Toxic postpartum cardiomyopathy was the early name physicians gave this disease because it was observed mostly after delivery.2 The designation was later changed to PPCM to account for cases diagnosed before delivery. PPCM is believed to be a distinct clinical syndrome because of the occurrence of most cases in the puerperium period. It may, however, reflect an unmasking of previously undiagnosed heart disease by the hemodynamic stresses and complications of pregnancy, and it may be conditioned by such factors as poor nutrition, familial or hereditary abnormalities, autoimmune mechanisms, and unsuspected myocarditis, or by some as-yet-unknown cause. The diagnosis of PPCM may best be considered as one of exclusion.3

Physiologic Changes of Pregnancy
Pregnancy causes significant physiologic changes to the cardiovascular system, in addition to other systems; such changes put stress on the maternal heart and circulation. Resulting effects include increased cardiac output secondary to increased blood volume and decreased afterload or systemic vascular resistance, and a physiologic anemia secondary to increased plasma volume relative to the volume of red blood cells. Beginning early in gestation and peaking around 28 weeks, blood volume and cardiac output increase by 50%. Systemic vascular resistance falls by more than 50% to a mean of 850 dyne-s-cm⁻², and the heart rate rises approximately 10% to 20% above the rate before pregnancy. A flow murmur may be detected. Supine hypotensive syndrome and aortocaval compres-
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The symptoms, signs, and pathologic (usually associated

Given that there are approximately 4 million

in addition to ascites.

Peripheral edema occurs in approximately one third

of healthy gravid women.

Incidence and Epidemiology

Worldwide, the incidence of PPCM is approximately 1 in

3,000 to 1 in 15,000 pregnancies—with a higher incidence

in Africa historically. Most cases in the United States have

been reported among African-American women from the

South. Incidence rates of PPCM are reported to be 1 case

per 6,000 live births in Japan, 1 case per 1,000 in South

Africa, and 1 case per 350 to 400 in Haiti. A high prevale-

ence of the disease in Nigeria may be related to the Haussa

tradition of ingesting kanwa (dried lake salt) while lying on

heated mud beds twice a day for 40 days postpartum. The

high salt intake leads to volume overload. 6

Epidemiologic studies have found that the disease occurs

most commonly in obese, black, multiparous women who are

more than 30 years old and is associated with Caesarean

delivery, multiple gestations, preeclampsia, and chronic

hypertension. 7 Given that there are approximately 4 million

annual deliveries in the United States, about 1,000 US

women each year will acquire PPCM; for many, it will be

fatal. 8 The incidence rate in the United States is currently

believed to be about 1 per 3,000 to 1 per 4,000 pregnancies.

Although PPCM is an uncommon condition and accounts for

fewer than 1% of the cardiovascular problems associated

with pregnancy, the mortality rate ranges from 18% to 56%.

Many survivors have severe morbidity; heart transplantation

may even be necessary. 9 The majority of cases (82%) occur

in the first 3 months postpartum. Only 7% of cases develop in

the last month of pregnancy. 10 A recent analysis of maternal

mortality in North Carolina found cardiomyopathy to be the

leading cause of maternal death in that state. 11

Diagnosis

When PPCM develops during the last month of pregnancy, it

is difficult to diagnose by signs and symptoms alone, because

some of the same symptoms—fatigue, orthopnea, and

pedal edema—are common during late pregnancy. PPCM is a
dilated cardiomyopathy of uncertain etiology, as previously

defined by Demakis et al 12 and amended by the National Heart,

Lung, and Blood Institute and Office of Rare Diseases work-

shop. 13 The 4 accepted criteria for an accurate diagnosis are the

following:

• cardiomyopathy presenting between the last month of

  pregnancy and the first 5 months postpartum
• the absence of a preexisting cause for heart failure
• the absence of a history of cardiac failure
• the presence of specific echocardiographic criteria, includ-

  ing left ventricular systolic dysfunction with a depressed

  left ventricular ejection fraction of <40% and fractional

  shortening of <30% on an M-mode echocardiogram. 14

These findings distinguish PPCM from diastolic dysfunc-

tion caused by preeclampsia. 7

Expected echocardiographic findings include left ventricu-

lar enlargement and global systolic dysfunction with or with-

out left ventricular hypertrophy, and they may include left atrial en-

largement, mitral and tricuspid regurgitation, pericardial effu-

sion, atrial and ventricular thrombi, and a holosystolic murmur of mitral regurgitation, an S 3, and left ventricular dilation can be seen in normal pregnancy. 15

The end-diastolic pressures in both ventricles are often elevat- ed (the left more than the right), and consequently the mean
atrial pressures are also elevated to abnormally high levels.

Stress echocardiography can be used to assess and evalua-
t heart disease during pregnancy and indicates the need for

cardiac catheterization. Results of coronary arteriography are

generally found to be normal. For patients who do not

respond to initial treatment for congestive cardiac failure, car-
diact catherization, viral serologic testing, and endomyocar-
dial biopsies should be considered on a case-by-case basis.

Serologic testing excludes unusual causes of cardiomyopathy,
including viral (eg, HIV) and rickettsial infections, toxoplasmo-
sis, syphilis, and Chagas’ disease (trypanosomiasis), and alpha-

hemop木地板. Systemic disorders such as collagen vascular disease,
sarcoidosis, thyrotoxicosis, and pheochromocytoma should also be excluded. The differential diagnosis further includes congenital and connective tissue disorders, which may also be associated with

PPCM is temporarily related to pregnancy in that 93% of cases occur in the postpartum period. In patients with preex-

isting heart disease, one might expect a deterioration in car-
diac status during the period of maximum cardiovascular load

(ex, during pregnancy). If cardiac failure recurs during subse-
quent pregnancies, it tends to manifest clinically in the peripar-
tum period. By definition, PPCM develops between 36 weeks

of gestation and 5 months postpartum. Patients who have

underlying heart disease (eg, valvular, ischemic, or myopathic) typically become symptomatic in the second trimester.

Before the use of echocardiography, a diagnosis of PPCM may have erroneously been given to patients with undeter-

mined, otherwise unexplained left heart failure or with

the clinical syndrome of pulmonary heart failure. 16 As a diagnostic tool, echocardiography can reveal occult ventricular dysfunction that may occur serendipitously in the presence of the increased hemo-
dynamic burdens of pregnancy. Echocardiography assesses

ventricular size and valvular structure and contractility, and it enables a diagnosis of systolic or diastolic dysfunction, allowing better management and long-term care of the patient. Reduced systolic function causes incomplete left ventricu-

lar emptying, an elevation in left ventricular end-diastolic pres-
sure, and ultimately an increase in pulmonary capillary hydrostatic pressure. 17 The symptoms, signs, and pathologic

findings in PPCM are not different from those seen in other

forms of congestive cardiomyopathy. It has been argued that

PPCM may be a form of occult primary congestive cardiomypathy made overt by the pregnant state.

Before a diagnosis of PPCM is considered, other condi-
tions associated with perinatal heart failure (eg, infectious myocarditis, toxic or metabolic disorders, and ischemic or

valvular heart disease) should be excluded. Also to be ruled

out are complications of late pregnancy, including toxemia

and anemic or pulmonary embolism, which may cause heart

failure. The peripartum patient with dyspnea carries a broad
differential diagnosis that encompasses infectious causes

(e.g., pneumonia, bronchitis, and upper respiratory illnesses),

obstructive lung diseases (including asthma and emphyse-

ma), anemia, acute respiratory distress syndrome, congestive

heart failure, myocardial infarction, and pericardial effusion.

Presentation

PPCM is a dilated cardiomyopathy that can deteriorate into congestive heart failure; the evident signs and symp-
toms are those of left ventricular failure with pulmonary edema. In most cases, the onset is gradual or insidious. In a few patients, acute symptoms of dyspnea and pulmonary edema develop. After confinement and resumption of nor-
mal activity, the patient may notice swelling of the ankles and noc-turnal cough progressing to orthopnea. 14 Depend-

ing on the severity of the disease, the patient may experi-
ence symptoms of fatigue, shortness of breath, dyspnea on

exertion, paroxysmal nocturnal dyspnea, chest pain or dis-

comfort, orthopnea, and palpitations. Signs may include the

following: generalized edema and anasarca, ankle swelling,

cough, hemoptysis, jugular venous distention, hepatic con-

gestion, hepatorenal reflex, pulmonary rales, cyanosis, an

apical holosystolic murmur, and an early diastolic gallop heart best heard at the apex (associated with an alternation in ventricular filling) and radiating to the aorta, and an accentuated, audible S 3 (usually associated with hypertensive cardiac disease characterized by altered ventricular compliance). There may be a loud pulmonic valve component of the S 3 in addition to asceres.

On examination, the patient with PPCM has congestive heart failure with tachycardia, a narrow pulse pressure, and

cold extremities, and she is diaphoretic. The heart may be

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enlarged on palpation. Cardiomegaly is defined as a heart size greater than one half of the internal thoracic diameter. A left ventricular thrust at the apex and/or a right ventricular heave may be felt. A chest X-ray may show cardiomegaly, pulmonary vascular congestion, and pericardial and pleural effusions. Patchy infiltrates, and interstitial congestion in the lower lung fields with vascular redistribution, indicate congestive heart failure. A single chest X-ray, nuclear study, or angiography performed during the antepartum period exposes the fetus to less radiation than the theoretical acceptable allowance. Organogenesis is complete after the first trimester, and radiographic studies after this period are believed to present a low risk to the fetus. Appropriate shielding should be performed, however.

The electrocardiogram may appear normal or show ST-T wave abnormalities and left ventricular hypertrophy—appreciated by a large S wave in lead V1 and a large R wave in lead V5, totaling more than 35 mm. Voltage may be low, normal, or high. The more common electrocardiographic abnormalities are left atrial enlargement, recognized by a large and wide terminal portion of a diphasic P wave in lead V1; premature ventricular contraction (PVC); tachycardia; and atrial fibrillation. First-degree heart block and bundle-branch block can also be present in dilated cardiomyopathy. The blood pressure may be elevated, normal, or lowered.

Systemic embolization is not uncommon in these patients, reflecting the formation of mural thrombi in dilated and hypokinetic heart chambers. Walsh at al found embolic phenomena, particularly to the kidneys, in 53% of patients; pylonephritis is a complication in about 40% of cases. Patients with PPCM may also present initially with neurologic symptoms, as from cerebral embolism. For example, in one study, transient ischemic attacks developed in a patient at 3 months postpartum. Another patient had undergone mantle field radiotherapy with doxorubicin chemotherapy as part of a multidrug regimen for Hodgkin’s disease 5 years earlier. Given the long time frame, chronic cardiomyopathic effects might not have been expected. However, doxorubicin causes a delayed, cumulative, dose-dependent cardiomyopathy that can occur during, or even long after, completion of treatment. Doxorubicin must be discontinued when congestive heart failure, secondary to diffuse cardiomyopathy, develops. The total cumulative dose should not exceed 550 mg/m² because the risk for congestive heart failure increases markedly with larger doses.

In a review by Veille, postpartum cardiac and renal failure as a mode of presentation of PPCM has been described in possible association with congestive heart failure and pre-natal renal failure. In a recent case report, dyspnea developed in a postpartum patient; the chest X-ray findings were consistent with congestive heart failure, and an echocardiogram demonstrated a left ventricular ejection fraction of 30% with moderate mitral regurgitation. Titors for coxsackievirus were negative, and titors for cytomegalovirus—consistent with a previous infection—were slightly elevated for IgG, but negative for IgM. The patient had an elevated D-dimer level (>500 ng/mL). Spiral chest computed tomography with contrast showed questionable changes in the upper lung fields, equivocal for small pulmonary emboli. Results of a hypercoagulable screen that included levels of factor V Leiden, G20210A, and anticardiolipin antibody were negative. In the hospital, the patient responded to treatment with furosemide, digoxin, an angiotensin-converting enzyme inhibitor, and warfarin. A repeat echocardiogram indicated that her ejection fraction had increased to 40%. By hospital day 6, the patient’s condition had significantly improved, and she was discharged. The diagnosis was congestive heart failure with possible pulmonary embolism.

Etiology

The etiology of PPCM is controversial; its exact cause is unknown. Predisposing conditions associated with an increased risk for PPCM include increased maternal age, multiparity, twin or multiple gestation, preeclampsia, chronic hypertension, black race, and obesity. Elevated blood pressures (systolic >140 mm Hg and/or diastolic >90 mm Hg) and hyperreflexia with clonus suggest preeclampsia. From case reports and anecdotal experience, ejection fractions as low as 10% to 15% have been documented in patients with severe preeclampsia, with subsequent normalization of echocardiograms within 3 to 6 months. Preeclampsia has been listed as a risk factor, but it may have been the diagnosis in some reported cases. Accelerated hypertension may be an important factor in the etiology of PPCM; it has been reported to occur in up to 30% of cases. A study by Demakis and colleagues concluded that the incidence of PPCM is significantly higher in women older than 30 years of age, in their third or subsequent pregnancy, and with twins or toxemia. Twin pregnancies have been reported in 7% to 10% of PPCM cases. Increased demands on existing maternal physiologic changes may be contributory. Other proposed risk factors include volume overload, poor nutrition, low selenium levels, viral infection, autoimmune disorders with autoantibodies, hormonal disorders, genetic disorders, alcoholism, and the physiologic stress of pregnancy. Examples of nutritional deficiencies include inadequate iron (causing anemia) and protein (which may predispose to edema). The concentration of cases among blacks living in poor social conditions in specific urban environments, along with a declining prevalence of the disease for the past 20 years at Charity Hospital, New Orleans, La, would suggest environmental causes (eg, the delayed effects of malnutrition).

The striking clinical similarity between PPCM and the cardiac form of beriberi (caused by a deficiency of thiamine, or vitamin B₁) is evidence of the possible role of malnutrition in the pathogenesis of PPCM. Beriberi is endemic in Southeast Asia, where white rice is the main food. In the United States, beriberi is primarily seen in those with chronic alcoholism and malnutrition. Thiamine is important in carbohydrate metabolism. In special situations—such as patients with an overactive metabolism or prolonged fever, or who are pregnant or breast-feeding—the thiamine requirements can be increased; this can lead to an uncommon form of cardiovascular disease called wet beriberi. This condition, involving a rapid onset of symptoms and acute heart failure, is often fatal. Wet beriberi is known to cause sudden death in young migrant laborors in Asia whose diets consist of white rice.

One theory about a possible link between viral myocarditis and PPCM is that a virus triggers an autoimmune reaction in the myocardium, and because the immune system is suppressed during pregnancy, the virus can replicate in unchecked fashion. Studies in mice have shown an increased susceptibility during pregnancy to myocarditis caused by coxsackievirus and echoviruses. In pregnant women, enhanced suppressor cell activity has been demonstrated. Immunologic function returns to normal soon after childbirth, which allows the patient’s condition to stabilize, with relief of symptoms and regression of hemodynamic abnormalities.

Another possible cause of PPCM is a maternal immunologic response to fetal antigen. This idea is based on the hypothesis that fetal cells that escape into the maternal blood circulation are not rejected because of a suppressed immune system in pregnancy and the weak immunogenicity of fetal antigen. It is hypothesized that if such fetal cells lodge in the cardiac tissue during pregnancy, they are recognized as non-self after delivery, when immune competency is regained, and hence an autoimmune response may be triggered. PPCM may be caused by autoimmunity to myocardial proteins released during viral myocarditis, or cross-reactivity with myometrial proteins released during parturition.

Knobel et al have postulated that the fast involution of the uterus after delivery results in the fragmentation of tropocollagen by collagenolytic enzymes—causing the release of actin, myosin, and their metabolites. Antibodies against actin cross-react with myocardial tissue, and the patient acquires a cardiomyopathy. Rand and colleagues described a case of stillbirth in a parturient with cardiomyopathy and myocardial antibodies (IgG) that could have crossed the placenta. The case may be analogous to neonatal myasthenia gravis, thyrotoxicosis, or thrombocytopenic purpura, in which autoantibodies transmitted across the placenta cause disease in the baby. If not fatal early on, the effect may be a transient one that clears in the weeks following birth.

Other factors that contribute to the development of PPCM include unusual maternal anemia, delivery by Caesarean section, and maternal infection and fever, all of which...
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increase cardiac output. Besides an increased frequency and intensity of postpartum anemia and infection associated with Caesarean delivery, surgery stimulates the production of antidiuretic hormone and fluid retention that persists for several days. Anemia—both the chronic form from iron deficiency and the acute form from hemorrhage at delivery—is common in women with peripartum heart failure. Significant and glycogen granules. Autopsy commonly follows blood loss resulting from Caesarean delivery. As noted by Seftel and Susser in 1961, of 2 patients in South America who succumbed to what was thought to have been PPCM, one actually had Chagas’ disease and the other patient had milary tuberculosis at autopsy.16

Although historically PPCM has been described more often in black populations, it has also been reported in other population groups, including Asians (Koreans, Japanese, Chinese, and Indians) and Caucasians.17, 18 African-Americans, who may be predisposed to elevated blood pressure and many of whom have inadequate access to medical care, are also at elevated risk for sickle cell anemia. This condition is associated with ventricular hypertrophy and possible congestive heart failure (presumably from long-standing anemia and chronically increased cardiac output); in addition, the development of myocardial hemochromatosis is possible. Secondarily increased red blood cell breakdown with the deposition of hemosiderin into the myocardial fibers.20

The onset of lactation is associated with a rise in blood pressure; thus, suppression of breast-feeding has been suggested as part of the management of PPCM.19 Prolactin is inhibited by bromocriptine, a dopamine agonist. The nutritional requirements of a lactating woman are increased, and those with underlying heart disease may decompensate without essential vitamins. Lactation and decreased thiamine levels have been associated with heart failure. Seftel and Susser found that the two thirds of patients in whom heart failure developed during the first 10 weeks postpartum were lactating. A high rate of breast-feeding was usual among the African women they studied. At 5 months, 92% of infants were still being suckled; at 12 months, the figure was 77%.

Obesity, particularly in persons with a body mass index >30, is associated with left ventricular hypertrophy—a powerful independent predictor of cardiovascular morbidity and mortality.21

Prolonged tocolytic therapy with β-adrenergic receptor agonists (eg, terbutaline and ritodrine) has been reported to cause pulmonary edema. Chest pain may occur with β2-sympathomimetic therapy. The β2 agonists terbutaline and ritodrine suppress premature labor by inhibiting uterine contractions; they also have some β1-adrenergic receptor activity, which accounts for side effects including tachycardia, arrhythmia, myocardial ischemia, mild hypotension, hyperglycemia, and hypokalemia. β1-Adrenergic agonists produce glycogenolysis, gluconeogenesis, and subsequent insulin secretion. Mechanisms of pulmonary edema include such noncardiogenic causes as β-sympathomimetically induced sodium retention leading to volume overload, increased pulmonary capillary permeability, and decreased plasma oncotic pressure. Stimulation of the jugulomembranous cells by β1-adrenergic agonists causes the release of renin, which results in fluid retention and increased blood pressure.22 As previously discussed, patients may have a preexisting subclinical cardiomyopathy that is simply unmasked by tocolytic therapy.23 Prolonged β1-stimulation also results in receptor downregulation. An early diagnosis and the institution of medical treatment for this form of cardiomyopathy are critical because they may affect the patient’s long-term prognosis.

The increased number of premature and low-birth-weight babies in patients with PPCM hints that a disease process may be present earlier in gestation than is suggested by the patient’s actual clinical presentation.5

Pathology

The pathologic findings of PPCM on gross examination include dilation of the heart, with an increase in heart weight (sometimes to double the normal weight of 300-350 g) and pericardial fluid. Hypertrophy and mural thrombi occur primarily in the left side of the heart but can be found on both sides.13, 19 The myocardium appears soft, flabby, and pale. The valves and coronary arteries appear normal. The microscopic findings include a loss of myocardial fibers with interstitial edema. A cellular infiltrate, composed mostly of lymphocytes, suggests a viral cause. Polymorphonuclear leukocytes are seen if a bacterial or parasitic infection is involved. Invasion by fibroblasts and fibrosis are seen in chronic disease. There may also be an increase in the size and number of mitochondria and glycogen granules. Autopsy results from patients with PPCM reveal gross evidence of severe myocardial disease of recent origin.

Management at Time of Delivery

The delivery of a healthy fetus generally depends on the mother’s health during pregnancy. An improvement in maternal cardiac output helps ensure adequate uteroplacental perfusion. Acute maternal hypoxia may cause fetal distress. Vaginal deliveries are preferred because third-spacing of fluid, endometritis, and pulmonary emboli occur much less frequently than with Caesarean deliveries.27 Cae-
sarean sections are reserved for cases in which obstetric complications are present.

If a parturient’s cardiac status can be stabilized with medical therapy, the induction of labor is usually recommended. In parturients with acute cardiac decompensation, a Caesarean section may be considered because of their inability to tolerate the prolonged stress of labor.

Anesthetic Management

Parturients with PPCM require special anesthetic care during labor and delivery. Invasive monitoring, including the placement of an arterial line and pulmonary artery catheter, can be used to assess the hemodynamic status and guide management. If cardiac decompensation occurs, a vasoactive agent such as nitroglycerin or nitroprusside for preload and afterload reduction is indicated. Dopamine, dobutamine, or milrinone may be needed for isotropic support.28 Data from the pulmonary artery catheter are used to guide pharmacologic therapy to achieve optimal hemodynamic status. Plotting the cardiac output against the preload is useful to evaluate pathologic states and optimize drug therapy. Starling’s law of the heart relates cardiac output and left ventricular end-diastolic volume.29 Excessive filling pressures, however, may decrease cardiac output, and overdistention of the ventricle may cause incompetence of the atrioventricular valves. Important indices of ventricular performance—including blood pressure, heart rate, stroke volume, cardiac output, and cardiac index—are plotted against measures of ventricular preload; these include left ventricular end-diastolic pressure, left atrial pressure, pulmonary capillary wedge pressure, and, in some cases, central venous pressure. Pulmonary and peripheral edema may develop when hydrostatic pressures increase or oncotic pressure is low, causing a net transfer of fluid and electrolytes out of the capillary blood into the interstitial spaces.30 A lower serum oncotic pressure that can predispose the patient to noncardiogenic pulmonary edema in the presence of other stresses has been associated with preeclampsia, multiple gestations, and multiparity.7

If hepatic disease has been used, it must be discontinued before delivery because of the occurrence of epidural hematomas, the American Society of Anesthesiologists recommends that women receiving full-dose low-molecular-weight heparin should not be administered spinal or epidural anesthesia for 24 hours after the last injection.27 Regional anesthesia reduces afterload, relieves pain, and decreases tachycardia. A key component of anesthetic management is the early administration of labor analgesia to minimize the cardiac stress associated with pain. Epidural or intrathecal anesthetic techniques offer advantages in the hemodynamic management of the parturient, and also provide excellent analgesia. With the use of data from invasive monitoring to guide fluid management and the titration of vasoactive drugs, the slow induction of epidural anesthesia is a safe and effective technique in parturients with PPCM. In fact, the sympathomimetic-induced reduction in afterload that occurs with epidural anesthesia can improve myocardial performance.32
When the patient is suspected of having a low cardiac output, regional analgesia can be initiated by administering only opioids. Hemodynamic stability may be more easily maintained, and the need for a sympathetic block with local anesthetic is avoided. Supplemental intravenous or intrathelial local anesthetic is sometimes required to provide adequate analgesia for the second stage of labor and delivery. With Cesarean deliveries, a continuous epidural technique is usually the best option. The hematologic status is carefully followed; fluid management is guided by appropriate monitoring while the depth of anesthesia is slowly increased.

When a Cesarean section is required, general anesthesia is sometimes necessary because of fetal distress or acute maternal decompensation. Maternal oxygen consumption increases 20% at term, which contributes to a decrease in the oxygen reserve—emphasizing the need for preoxygenation. Anesthetic drugs with myocardial depressant effects should not be administered to patients who have a dilated cardiomyopathy. The use of a high-dose opioid technique for the induction and maintenance of anesthesia is often preferred. A slow maternal circulation time may make the patient vulnerable to a drug overdose if additional agent is administered because of a presumption of insufficient dosage. Trained neonatal specialists must be available to manage neonatal depression when a high-dose opioid anesthetic is selected. The events and interventions surrounding labor and delivery— including uterine contractions, surgical procedures, blood loss, and the I.V. administration of fluid and anesthetic agents—place increased demands on the patient’s heart. Systemic hypotension, pulmonary edema, hypoxemia, myocardial ischemia, and dysrhythmia may develop. The cardiac output may increase by up to 65% in the puerperium because of the release of venacaval obstruction and the autotransfusion of uteroplacental blood back into the maternal circulation. Noninvasive echocardiography and pulse oximetry may be used throughout the antepartum period. Objective hemodynamic monitoring may reveal a more compromised patient than symptoms would indicate.

**Treatment**

Historically, extreme congestive heart failure was treated with phlebotomy, the rotation of lourniquets, and supplemental oxygen. In addition, pleural effusions required thoracocentesis, and patients with ascites may have required abdominal paracentesis. Pericardial tamponade due to fluid required placement of a window.

Currently, patients with PPCM who experience a first episode of heart failure generally respond to conventional therapy. This includes the administration of supplemental oxygen, diuretics, and digitalis; a low-sodium diet (2 g/d sodium chloride); and the administration of anticoagulants if indicated. Symptoms usually abate quickly. Bed rest is no longer recommended for patients with PPCM because of the potential for thromboembolism.

The inferior vena cava ascends on the right side, and so mothers should be managed with left uterine displacement to prevent supine hypotension syndrome or aortocaval compression and subsequent uterine–placental insufficiency.

Because organogenesis is completed by the end of the first trimester, pharmacologic therapy for PPCM should have little effect on the fetus. Hydralazine is secreted in breast milk. The infant is exposed to a very small percentage of the dose, and no adverse effects have been reported in newborns. The transplacental passage of digoxin has been widely documented. Because of this pharmacokinetic property, digoxin has been used to treat fetal tachyarrhythmias in utero. Digoxin is also secreted in breast milk. The infant is exposed to a very small percentage of the dose, and no adverse effects have been reported in newborns. Digitalis increases the force and velocity of myocardial contractions and controls atrial fibrillation—which occurs in 20% of patients. Cardiac dysrhythmia may be treated with a variety of antiarrhythmics. Electric cardioversion, used in the treatment of paroxysmal atrial tachycardia, is said to have no adverse fetal effects.

The maternal complications of diuretic therapy may include pancreatitis, volume contraction, alkalosis, hyperglycemia, hypokalemia, hyponatremia, and hyperuricemia. A bleeding diathesis has been reported in the neonates of patients who have taken diuretic agents during pregnancy. Pregnant patients are at increased risk for thromboembolic complications because of the well-known hypercoagulable state of late pregnancy, which is associated with increased concentrations of coagulation factors II, VII, VIII, and X and plasma fibrinogen, and the augmentation of platelet adhesiveness. Such changes may persist for as long as 4 to 6 weeks postpartum. Antiocoagulants are indicated in patients with a markedly enlarged heart, a history of embolization, atrial fibrillation, or a significantly reduced cardiac output. Oral anticoagulants such as warfarin have been classified by the US Food and Drug Administration as class D agents (contraindicated in pregnancy); these agents cross the placenta and are associated with fetal teratogenic effects. During the period before delivery, heparin is the anticoagulant of choice. Given its short half-life (1-2 hours, depending on the dose), heparin can be discontinued before delivery to prevent maternal hemorrhage. Although heparin has several adverse side-effects—including depletion of antithrombin III, thrombocytopenia, and premature maternal osteoporosis—these are seen infrequently in patients with PPCM, who usually require short-term therapy. Heparin or warfarin may be secreted in breast milk; however, neither drug is said to cause any significant anticoagulant effect in the breast-fed infant. An advantage of unfractionated heparin over low-molecular-weight heparin is that the level of anticoagulation can be assessed by obtaining an activated partial thromboplastin time.

Patients whose condition does not improve within 2 weeks of standard therapy for congestive heart failure should be considered for endomyocardial biopsy; those with evidence of myocarditis may benefit from immunosuppressive therapy. A retrospective study by Blockurt et al41 found benefits for immunosuppressive therapy in PPCM patients who had findings of myocarditis on endomyocardial biopsy. During early follow-up, the patients given immunosuppressive therapy showed a greater increase in their ejection fraction than did the patients treated conventionally.

It is important to appreciate that results from biopsy material obtained early in the onset of PPCM may differ from results from biopsy material obtained later in the course of the disease. Myocardial biopsy results in the first week following the onset of symptoms were positive in 4 (67%) of 6 patients in a study by O’Connell and colleagues. Results of biopsies performed after the first week were...
negative—possibly because the window of sensitivity had been missed. Melvin et al. obtained a positive therapeutic response after the administration of immunosuppressive agents to patients with viral myocarditis, as confirmed by biopsy. Although the study lacked a control group, treatment with prednisone and azathioprine resulted in clinical improvement in the 3 patients studied; the effects coincided with a loss of inflammatory infiltrate on follow-up biopsy.

Immunosuppression with azathioprine therapy seems to result from interference with nucleic acid metabolism at steps required for lymphoid cell proliferation, which follows anti-genic stimulation. Immunosuppressive therapy (eg, with corticosteroids or azathioprine) may be useful in patients with dilated cardiomyopathy associated with collagen vascular disease or sarcoidosis, or in those with evidence of active inflammation on endomyocardial biopsy.36 For patients whose condition does not improve with conventional medical therapy, or who have persistent cardiomegaly or moderate to severe mitral regurgitation, invasive interventions (eg, placement of a pacemaker, intra-aortic balloon pump, or left ventricular assist device) and referral to a cardiac transplant center should be considered. Studies indicate that patients with PPCM have survival rates after transplantation comparable to those of age-matched women receiving heart transplants for other causes. However, patients with PPCM show a marginally higher rate of biopsy-proven early rejection, and thus they require more aggressive cytolytic therapy. Cardiac transplantation has been performed successfully in patients with PPCM.43,44 Nevertheless, complications may include rejection and malignant neoplasia. Outcome data on pregnancies among heart transplant recipients demonstrate that despite frequent complications— including preclampsia, preterm labor, chronic hypertension, graft rejection, and, in infants, premature birth or small size for gestational age—such pregnancies can be successfully managed in high-risk centers.39,40

Prognosis

The hemodynamic stresses of pregnancy, along with one or more of the previously discussed risk factors for PPCM, may precipitate a cardiomyopathy or unmack a previously undiagnosed cardiomyopathy in otherwise medically stable individuals. The prognosis for these patients is guarded. In the United States, the overall mortality rate ranges from 25% to 50%—with 25% to 50% of these patients dying within the first 3 months postpartum. Death may occur suddenly or result from chronic, progressive congestive heart failure, arrhythmia, and embolization.41 The mortality rate from embolic phenomena has been reported to be as high as 30%.42 The most common causes of death are congestive heart failure, which is frequently exacerbated by pulmonary emboli, and supraventricular arrhythmias, such as atrial fibrillation and atrial flutter.43 When patients are first seen, it is difficult to differentiate between those who will continue to have cardiomegaly and those whose heart will return to normal size. The long-term prognosis appears to be related to how quickly the heart normalizes. In approximately 50% of patients, the heart size returns to normal within 6 to 12 months after the onset of disease. The prognosis is poor for patients who have cardiomegaly for 6 months or longer.44 As with other forms of heart failure, it has been suggested that the prognosis is related to left ventricular size or the severity of left ventricular dysfunction at the time of initial presentation. Patients whose heart size returns to normal can lead active lives if they are asymptomatic, but they should avoid competitive exercise. Patients whose heart size does not return to normal should lead restricted lives commensurate with their cardiac disability.45,46 Humans found that the infants of women presenting with PPCM after delivery had a good outcome, whereas the infants of mothers who presented with PPCM before delivery had a less favorable outcome.47

Future Pregnancy

PPCM tends to recur during subsequent pregnancies. Controversy remains as to whether patients with previous PPCM whose left ventricular function is presumed recovered can safely undergo another pregnancy. If a patient conceives again, serial echocardiographic monitoring of her cardiac function is recommended. Such patients decompensate earlier and have more severe symptoms. A diobutamine challenge test to determine left ventricular shortening has been recommended to use to predict cardiac performance in case of future pregnancies. During routine echocardiography, cardiac reserve was found to be lowered in patients thought to have recovered from PPCM. These women may have subclinical, resid- ual systolic dysfunction that does not become evident until the myocardium is subjected to significant hemodynamic stress (eg, during another pregnancy).47 Some cardiac failure can be anticipated in 50% to 88% of patients during a subsequent pregnancy.48 Demakis and colleagues reported a 50% mortality rate in patients who became pregnant again and whose heart had not returned to normal size.49 Appropriate birth control measures are strongly recommended for patients with an enlarged heart. However, oral contraceptives may best be avoided because of an increased risk for thromboembolism. Birth control pills inhibit antithrombin III, resulting in a hypercoagulable state. In summary, if the heart of the patient with PPCM returns to normal size, subsequent pregnancies may be tolerated. If, however, the heart remains enlarged, future pregnancies exacerbate myocardial damage, often leading to intractable congestive heart failure and death.

Management of the Case Described

The patient had had 2 previous pregnancies. The first infant, suspected of having PPCM, was premature and died. The second pregnancy was complicated by preeclampsia and a large placental abruption, but the baby was delivered vaginally. The current pregnancy had apparently not been complicated by preeclampsia, and there was no abortion recognized during an emergency Caesarean section—performed because of abdominal pain and the possibility of a repeat abortion. The patient was readmitted to the hospital, and her laboratory test results showed the following values: hemoglobin, 106 g/dL; potassium, 4 mEq/L; creatinine, 0.9 mg/dL; blood glucose, 99 mg/dL; albumin, 1.8 g/dL. The patient was a nonsmoker and did not drink alcohol. Her blood pressure was 140/94 mm Hg, and her heart rate was 98 beats/min. After she was preoxygenated with 100% oxygen and air, a pH of 7.4, PaO₂ of 35 mm Hg, and PaCO₂ of 50 mm Hg. She was administered oxygen at 4 L/min via a nasal cannula. After preoxygenation of the patient, an endotracheal tube was placed and general anesthesia induced with propofol, 80 mg and a sufentanil infusion; fentanyl 30 mg and vecuronium were also administered. Anterior and posterior chest tubes and a pericardial window were placed. After muscle paralysis had been reversed, the patient was returned to the recovery room and maintained with assisted ventilation. Mild positive end-expiratory pressure was established with a Jack- son-Reesee Mapleson breathing circuit to permit more time for recovery from anesthesia, and to better assess the patient’s respiratory abilities. Only 50 to 75 mL of fluid was removed from presumed loculated areas. The lung mechanics were not improved, and she was returned to the operating room for a thoracotomy. General anesthesia was again induced with the same technique and maintained with 100% oxygen, isoflurane, and sufentanil. The attempted placement of an arterial line was unsuccessful. The surgery lasted 1 hour. The patient received an infusion of 1,500 mL of lactated Ringer’s solution; 500 mL of pleural effusion fluid was evacuated. The patient was again transferred to the recovery room, where she received assisted ventilation. Nebulizer therapy and furosemide were administered. After tracheal extubation, she was taken to the intensive care unit. Later that evening, she was taken to the cardiac catheterization laboratory. The cardiologist interpreted the bedside echocardiogram as an indication of severe, global, diffuse left ventricular hypokinesis. The ejection fraction was estimated at about 22%. Mild mitral valve regurgitation was present, and the left ventricular wall thickness appeared normal. Dipyridamole and phenoxyphrine infusions were initiated. A pulmonary catheter was placed, which recorded a cardiac index of 2.5 L/min·m⁻², systemic vascular resistance of 771 dyn·s·cm⁻⁵, pulmonary artery pressures of 54 mm Hg systolic and 40 mm Hg diastolic, and
a pulmonary capillary wedge pressure of 15 mm Hg. The central venous pressure was 16 mm Hg. Subsequently, the patient was transferred to a tertiary care hospital where she remained intubated for approximately 2 weeks. Her ejection fraction improved considerably.

**Conclusion**

Patients with PPCM are best managed with early diagnosis, prompt treatment, and careful follow-up to minimize myocardial damage. Based on the observations and published findings of many clinicians, it is difficult to reconcile pregnancy as the sole cause of PPCM. In the rare event that PPCM develops during pregnancy, the patient’s prognosis is worse than that of a patient with peripartum cardiac failure resulting from multiple, compounding cardiovascular events associated with the stresses of parturition. The care of patients with PPCM consists of a multidisciplinary effort that requires the collaboration of a high-risk obstetrician or maternal-fetal medicine/perinatologist, a cardiologist, an obstetric anesthesiologist, and a neonatologist. Therapy must be individualized to address maternal cardiovascular function, gestational age, and fetal status.

As the field of diagnostic medicine has grown and become more sophisticated, the number of diagnoses of PPCM has decreased. With the increasing use of echocardiography and angiography, many cases that would previously have been diagnosed as PPCM may now be found to be more likely caused by ischemic, valvular, or other cardiomyopathic disease. It is possible that separate disease entities—with different causes but a similar clinical presentation—have been lumped together under the label of PPCM. In patients with mild heart disease, unrecognized in the nonpregnant state, overt heart failure may develop when they are exposed to the hemodynamic stress of pregnancy, which can then be compounded by other factors, such as operative delivery, toxemia, anemia, infection, and administered drugs. The diagnosis of PPCM is best considered as a diagnosis of exclusion.

**References**