Peripartum cardiomyopathy (PPCM) is a rare but serious cause of heart failure occurring in the last month of pregnancy or the first 5 months postpartum. The current definition of PPCM only includes patients with left ventricular systolic dysfunction. The authors present a case of peripartum heart failure with normal ejection fraction and propose that the definition of PPCM be expanded to include left ventricular diastolic dysfunction. Because the mortality and morbidity of patients with PPCM are higher in women who experience a subsequent pregnancy after a prior episode of pregnancy-related heart failure, a revised definition of PPCM has important potential implications.

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By definition, peripartum cardiomyopathy (PPCM) is a disorder of left ventricular (LV) systolic dysfunction. However, that description was formulated decades ago, before the role of LV diastolic dysfunction in heart failure was recognized. It is now known that diastolic dysfunction is common and frequently precedes left ventricular systolic dysfunction. In early 2008, Wells and Little published the first case of a patient with isolated diastolic dysfunction as a cause of PPCM. Here we describe a second case with hopes that it will promote further reports of this entity and lead to an exploration of the definition of PPCM that incorporates diastolic dysfunction. A more comprehensive definition of PPCM should add to our understanding of the pathophysiology of this rare but serious condition.

Report of Case

A 38-year-old primigravid white woman at 39 5/7 weeks gestation was admitted to the hospital on April 13, 2008, for induction of labor because of advanced maternal age and term pregnancy. She was physically fit and exercised on a regular basis before her pregnancy. Her pregnancy was uncomplicated and routine screening throughout the pregnancy was within normal limits, except for a positive group B streptococcus culture, which was obtained at 35 4/7 weeks. Her blood pressure remained normal, and she gained 35 pounds in weight.

Early the next day, she was taken to cesarean section because she failed to progress with labor. During surgery, the estimated blood loss was 700 mL. She received 2200 mL of intravenous (IV) Ringer’s lactate solution and had a urine output of 150 mL. In recovery, she received 1200 mL of IV Ringer’s lactate solution and voided 400 mL. The IV solution was continued at 125 mL per hour until the next day when it was discontinued due to a hemoglobin level of 8.5 mg/dL. She was discharged home on postoperative day 3 with oral ibuprofen 600 mg three times daily, of which she took 4 pills, and propoxyphene. Physical examination was normal, with a firm fundus and no edema.

The patient was readmitted to the hospital on postpartum day 4 with shortness of breath. She had noticed progressive ankle edema beginning soon after her discharge home. She became dyspneic with room ambulation. On examination, the blood pressure was 114/70 mm Hg. The heart rhythm was regular at 60 beats per minute, and the respiratory rate was 16 breaths per minute. Breath sounds were diminished in the lung bases. She had mild pretibial edema.

The chest radiograph showed normal heart size with bilateral infiltrates consistent with vascular congestion (Figure). A computed tomography scan of the chest excluded pulmonary embolism. Relevant laboratory findings were as follows: hemoglobin, 10.2 gm/dL; hematocrit, 31.9%; BNP (brain-type natriuretic peptide), 507 ng/mL; and prolactin, 147.7 ng/mL (normal [SD] value for day 4 postpartum is 238 [21] ng/mL). The echocardiogram demonstrated normal LV size and wall thickness. Left ventricular ejection fraction was greater than 50%. Tissue Doppler index and mitral flow characteristics were consistent with stage II diastolic dysfunction (Table). She improved rapidly with diuresis, and was discharged home on furosemide, 20 mg daily.

The patient returned for outpatient follow-up 6 weeks.
later on June 3, 2008. At that time, she was asymptomatic, except for the usual fatigue of a new nursing mother. She had resumed a walking program. With the baby stroller, she covered 1 mile in 20 minutes without symptoms. Findings from a cardiopulmonary examination were normal. An echocardiogram showed resolution of diastolic dysfunction (Table).

**Comment**
Peripartum cardiomyopathy is a rare cause of heart failure that affects women late in pregnancy or in the early postpartum period. The incidence of PPCM varies widely, with a reported incidence of from 1:300 to 1:15,000 deliveries in the United States; 1:1000 in South Africa; and 1:300 in Haiti. Risk factors for PPCM include age greater than 30 years; African descent; multiparity; pregnancy with multiple fetuses; history of preeclampsia, eclampsia, or postpartum hypertension; maternal cocaine use; and more than 4 weeks of tocolytic therapy. When remission occurs, it happens early, within the first 6 months.

Currently, three criteria are required to meet the definition of PPCM:

- development of cardiac failure in the last month of pregnancy or within 5 months of delivery
- absence of identifiable cause for heart failure
- absence of recognizable heart disease before the last month of pregnancy

A modified definition for PPCM and prognosis was proposed in 1999. To the standard criteria, the authors added these strict echocardiographic criteria:

- LV ejection fraction less than 45%, fractional shortening less than 30%, or both
- end diastolic LV dimension greater than 2.7 cm/m²

Because of the high maternal mortality associated with PPCM, Hibbard et al also proposed a pharmacologic echocardiographic stress test that might be useful to determine LV contractile function and could reproduce the hemodynamic stress associated with pregnancy.

**Diastolic Dysfunction**
Diastolic dysfunction is now recognized as a common cause of heart failure, perhaps representing up to 50% of all heart failure patients, with a similar dire prognosis. The diagnosis of diastolic dysfunction is a relatively new practice. Because of this, the descriptors have evolved over the past 2 decades, initially using LV inflow Doppler echocardiography measurements and now incorporating left atrial volume and tissue Doppler imaging. As with the diagnosis of many other conditions, the clinical diagnosis of diastolic heart failure (DHF) incorporates patient characteristics with findings from diagnostic tests (ie, echocardiography) and other laboratory parameters.

Despite improvements in identifying patients with DHF, the relationship between this condition and its counterpart—systolic heart failure—is still debated. Recently, the European Society of Cardiology issued a consensus statement on the diagnosis of DHF using the terminology “heart failure with normal left ventricular ejection fraction.” In a subsequent report, Handoko and Paulus, contributors to the consensus statement, recognized that this terminology implies that DHF may not be a “distinct clinical entity differing from systolic heart failure,” but instead, these two conditions could be “suc-
cese phenotypes of the same heart failure syndrome. Similarly, we suggest that diastolic dysfunction could be a successive phenotype of systolic dysfunction in PPCM.

Pathophysiology of Pregnancy-Induced Cardiomyopathy

The assessment of cardiac function during pregnancy, labor, and delivery needs to incorporate features of the fluid and hemodynamic changes associated with pregnancy and the effect of the gravid uterus. During a normal cesarean section, about 800 mL of blood is lost. After delivery of the baby, there is an abrupt increase in venous return, in part because of autotransfusion from the uterus, but also because the baby no longer compresses the inferior vena cava.

During a normal pregnancy, women develop cardiac hypertrophy and delayed LV relaxation. This hypertrophy is felt to be similar to that associated with exercise, and it typically regresses after childbirth, with a return in LV diastolic function.

Various theories have been offered to explain the mechanism of PPCM, including viruses and autoimmune reactions. It remains a diagnosis of exclusion. Physicians’ understanding of PPCM was advanced significantly by studies on a mouse model of dilated cardiomyopathy. Hilfiker-Kleiner et al showed that the 16-kDa cleavage product of prolactin is a major contributor to PPCM. Further, the authors demonstrated that bromocriptine mesylate, a drug that blocks prolactin, reduced mortality in a small cohort of 6 women.

Clinical Implications of Redefining PPCM

The mortality and morbidity associated with PPCM are high. Because of the relative rarity of the condition, the mortality rates are compiled from data gathered from several centers and summarized in review articles. The mortality rates were previously in the range of 18% to 50% and now have improved to 9% to 15%. The LV ejection fraction normalizes in only 50% of patients and are most likely to return to normal in patients with LV ejection fractions greater than 30% at presentation.

We propose that the criteria for PPCM be re-evaluated in terms of patients with diastolic dysfunction. There would be several reasons for such a change. One would be to provide the basis of a more comprehensive study of the natural history of this entity. A second would be to enrich the current understanding of the pathophysiology of PPCM.

The third reason would be to gain more information about the relationship of parity to the risk of development of the syndrome. If patients with relatively mild volume overload postpartum actually had diastolic dysfunction, which was unrecognized at the time, they could be at risk for more severe heart failure with a subsequent pregnancy. A prospective survey of such patients could be of considerable value.

Limitations

The clinical presentation of the patient described in the current report represents the intersection of rare and common medical conditions. Peripartum cardiomyopathy is rare and has several possible causes; there is limited understanding of its pathophysiology apart from the well-defined role of prolactin in some patients. This mirrors the situation with heart failure with normal ejection fraction (diastolic heart failure), which is very common but also is characterized by limited understanding of the condition; it is a heterogeneous syndrome with multiple possible causes.

While the echocardiogram is helpful to understand heart failure, the parameters are not specific to the illness and there are significant limitations to the method. For example, the ejection fraction to meet criteria for PPCM is less than 45%, which is within the range of measurement error of a normal ejection fraction of 50%.

In the present report, we cannot exclude the possibility that the patient’s ejection fraction was much lower in the early peripartum period or that a rapid recovery occurred from the time of hospital readmission to the first echocardiogram. Likewise, we cannot be certain that the heart failure demonstrated in our patient reflects a distinct cardiomyopathy manifest by transient DHF. Although our patient received standard fluids and medications, it is possible that her condition is one of simple volume overload.
Conclusion
Peripartum cardiomyopathy is a rare but serious condition affecting women in the last month of pregnancy or the first 5 months postpartum. The pathophysiology of PPCM is consistent with the known cellular events associated with LV diastolic function. The current definition of PPCM was formulated before the present recognition of the important role of diastolic function in heart failure and only includes patients with systolic dysfunction.

We propose that this patient should be considered as an example of peripartum heart failure that might be peripartum cardiomyopathy. She has met all of the standard clinical criteria for PPCM except that of LV systolic dysfunction. We speculated that the LV failure in PPCM may be similar to that in other conditions in that there is a successive phenotype with systolic dysfunction representing a more severe form.

References

When all parts of the human body are in line, we have perfect health. When they are not, the effect is disease. When the parts are readjusted, disease gives place to health.

Andrew Taylor Still, MD, DO
1828-1917