Peripartum Cardiomyopathy: a Life Threatening Obstetric Emergency

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Abstract:

Peripartum cardiomyopathy (PPCM) is a rare, life-threatening heart disease of unclear origin and is characterized by heart failure of sudden onset between the final weeks of pregnancy and 5 months after delivery. Incidence varies over geography and ethnicity. Risk factors include advanced maternal age, multiparity, preeclampsia, multiple pregnancy, anaemia, and so many other causes. PPCM is often not diagnosed until late in its course, because of its clinical manifestations are highly variable and a heart disease may not be suspected at first. Frequent presenting symptoms of PPCM, such as lassitude, shortness of breath on mild exertion and coughing are often initially misinterpreted as evidence of pneumonia or as physiological accompaniments of pregnancy and delivery. The clinical picture of PPCM corresponds to a dilated cardiomyopathy (DCM) with signs of severe heart failure. Medical management is similar to other causes of systolic heart failure, except for the ACE inhibitors and angiotensin receptor blockers are avoided in pregnancy. As there are lots of physiological changes during pregnancy and immediately after delivery, it is usually difficult to measure PPCM effectively. Complications include cardiac arrhythmia, thromboembolism, and refractory heart failure. Maternal deaths are not uncommon. Recently the role of abnormal prolactin metabolism and resulting myocardial toxicity have been explored and bromocriptine has shown promise as a potential treatment option.

Key words: Peripartum Cardiomyopathy (PPCM), Heart Failure, Pregnancy, Bromocriptine.

Introduction:

Peripartum cardiomyopathy (PPCM) is a rare and potentially life-threatening form of systolic heart failure affecting women in late pregnancy and first few months after delivery¹. The national heart, lung, blood institute and Office of Rare Diseases have defined PPCM as follows: The development of heart failure in the last month of pregnancy or within 5 months of delivery, the absence of determinable etiology of heart failure, the absence of demonstrable heart disease before the last month of pregnancy, and echocardiographic evidence of left ventricular (LV) systolic dysfunction²-⁴. PPCM is difficult to diagnose and its onset and prognosis are variable. The pathophysiology remains poorly understood; hence treatment options are limited and some possibly are harmful to the foetus¹. An apparently healthy woman can develop severe form of cardiac failure. Around 80% of the symptomatic patients recover, although fewer than 30% achieve complete recovery with normal left ventricular function anatomically and physiologically⁵. The incidence of PPCM varies widely between ethnicities and over geography. The highest reported incidence is in the Hausa and Fulani tribes of Nigeria where the incidence is as high as 1 in 100 deliveries⁶. This high incidence seems related to the unique puerperal practices of these tribes which include postpartum excessive consumption of dried lake salt, warm water baths and laying on heated mud beds leading to a propensity towards volume overload⁷.

Pathophysiology:

Risk factors to develop PPCM include increased maternal age, multiparity, preeclampsia, multiple pregnancy, African descends, use of tocolytics, poverty, tobacco use, malnutrition, and anaemia⁸-¹⁰. The etiology of PPCM is still unknown and many causes have been proposed but not conclusively proven. These include viral myocarditis, abnormal immune response to pregnancy, abnormal response to increased hemodynamic burden of pregnancy, hormonal abnormalities, malnutrition etc¹¹,¹². Here, some ecological factors are described in short.
**Role of prolactin:**

Experimental evidence has implemented abnormal prolactin metabolism as fundamental in the pathogenesis of PPCM. The proposed mechanism is unbalanced oxidative stress leading to the cleavage of the full length 23 kDa prolactin to an antagonistic and proapoptotic 16 kDa form. The full length of 23 kDa prolactin has no adverse effect on the heart. In contrast, high expression of 16 kDa fragment destroys the cardiac microvasculature, reduces in vivo cardiac function and promotes ventricular dilatation\(^\text{13}\). Blockage of prolactin with bromocriptine has been shown to prevent PPCM in experimental models\(^\text{13}\).

**Antagonistic imbalance:**

Data from studies in mice and human suggests that PPCM may be caused by systemic antagonistic imbalance\(^\text{14}\). This may explain why preeclampsia and multiple gestations are risk factors for PPCM.

**Viral myocarditis:**

Several investigations have suggested viral infections as a cause of myocarditis in PPCM. The study of endomyocardial biopsies in PPCM patients found a high prevalence of viral genomes (parvovirus-B19, cytomegalovirus, herpesvirus-6 and Epstein-Barr virus) as well as inflammatory changes consistent with myocarditis\(^\text{15}\).

**Inflammatory cytokines:**

Inflammatory cytokines may play a role in the pathogenesis of and prognosis of PPCM and heart failure, which includes tumor necrosis factor (TNF)-alpha and interleukin-6\(^\text{16}\).

**Abnormal autoimmune response:**

Circulating autoantibodies to selected cardiac tissue proteins were reported by several studies in more than 50% of PPCM patients. Autoantibodies are associated with an increased level of cytokines and are correlated with dilatation of LV and systolic dysfunction\(^\text{4}\).

**Clinical presentation:**

The diagnosis of PPCM is often difficult as its presentation may mimic other causes of systolic heart failure even, exaggerated signs and symptoms of late pregnancy and early puerperium. Common clinical features are as follows:

- Lassitude and exertion
- Dyspnoea
- Paroxysmal nocturnal dyspnoea
- Wet crepitation over the lung fields
- Shadow on the chest X-ray
- Leg edema
- Nocturia
- Palpitation or missed beats
- Newly arrived repolarization abnormalities in the ECG
- Arrhythmia on the ECG
- Systolic murmur
- Impaired left ventricular function
- New-onset secondary mitral regurgitation
- Arterial embolization
- Cerebral emboli\(^\text{17}\)

**Diagnosis of PPCM:**

Variable clinical presentation in a previously healthy young woman causes delay in the diagnosis of PPCM. The first symptoms are often dyspnoea and cough, which are often interpreted as signs of pneumonia or as a physiological consequence of pregnancy and birth. Diagnosis is from clinical features aided by ECG changes and X-ray findings. Misinterpretation of the clinical picture, delayed diagnosis and treatment of heart failure can have detrimental consequences. Observational data suggest that potential specific treatments are only effective if started early\(^\text{18}\).

**Management:**

The management is similar to that of systolic heart failure of other etiologies. In acute heart failure, airway, breathing and circulation should be maintained. Intravenous loop diuretics, mostly furosemide and vasodilators such as nitrates and hydralazine are used for preload and afterload reduction. ACE inhibitors and angiotensin receptor inhibitors can be used in the postpartum period. Inotropic support is provided in cardiogenic shock and pulmonary edema that are refractory to initial management with diuretics and vasodilators. Digoxin may be used as a second line therapy in NYHA class III and IV symptoms in selected patients. Pregnancy and puerperium are hypercoagulable states. Anticoagulation is advised when LVEF falls below 35% or in case of atrial fibrillation or mural thrombi. Beta blockers may be used to treat supraventricular tachyarrhythmia\(^\text{1}\).
New approaches to the treatment of PPCM:

**Bromocriptine:**

A prospective, single-centre, open-label, proof-of-concept pilot study of women with newly diagnosed PPCM randomized patients into those receiving standard care (n = 10) and those receiving standard care plus bromocriptine (n = 10) for 8 weeks. PPCM-Br patients displayed greater recovery LVEF compared with PPCM-Std patients at 6 months. This drug appears to be promising but needs larger trials.

**Mode of delivery:**

In women with PPCM with advanced heart failure, prompt delivery is suggested. Epidural anaesthesia is preferred.

**Breast feeding:**

Breast feeding in not advised in patients with suspected PPCM, ever if this practice in not fully evidence-based. Several ACE-inhibitors (captopril, enalapril and quinapril) have been adequately tested and can be used in breastfeeding women.

**Prognosis:**

Three most important effect of PPCM is left ventricular failure, supraventricular arrhythmia, and sudden death. Studies have reported recovery of LV function at 6 months in 45% to 78% of patients. Mortality rates have varied between 0% and 19% while the rate of cardiac transplantation has ranged from 6% to 11%. Women with a history of PPCM should receive counseling regarding the risk of recurrence in the subsequent pregnancy.

**Conclusion:**

PPCM is a potentially life-threatening illness which usually arises at the last month of pregnancy or shortly after delivery. Early diagnosis is important in these young women. Possibility of PPCM should be kept in mind when a woman after delivery complaining dyspnoea and cough who has no previous history of cardiac compensation. Early diagnosis and systemic approach for treatment can save the life of the women and long-term prognosis is better with improvement of cardiac function and normalization of ventricular size. Maternal mortality ranges from 0% to 19% which actually varies due to the delay in the diagnosis.

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