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Peripartum Cardiomyopathy - A Brief Review

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ABSTRACT

Peripartum cardiomyopathy although a rare diagnosis is one of the prominent cause of maternal morbidity and mortality. Heart failure in the puerperial period was recognised in the early 19th century. In 1930 its pathogenesis was attributed to be a consequence of pregnancy. Later in 1971, their case series of 27 patients who developed peripartum cardiomyopathy following delivery were published and the term "peripartum cardiomyopathy" was termed.

Keywords: Pregnancy, Peripartum cardiomyopathy, Maternal mortality, Peripartum heart failure, Bromocriptin

INCIDENCE

The incidence of Peripartum cardiomyopathy (PPCM) has a wide geographic variation [1,2]. Previously healthy pregnant women have a low incidence of 0.1% of pregnancies but the morbidity and mortality is high ranging from 7% to 50% [3]. The incidence of PPCM is more common in the older, multiparous woman and is more frequently associated with twins and toxemia. Despite the rare occurrence of PPCM it is the fifth leading cause of maternal mortality. The survivors of PPCM have a high rate of left ventricular dysfunction and may require heart transplant [4]. This article describes in brief about the diagnosis, ethiopathogenesis and management of PPCM.

DEFINITION

PPCM has been defined by various medical associations. Few important ones are as follows:

- European Society of Cardiology on the classification of cardiomyopathies defines PPCM as a non-familial, non-genetic form of dilated cardiomyopathy associated with pregnancy [5].
- Workshop held by the National Heart Lung and Blood Institute and the Office of Rare Diseases defined PPCM as the development of heart failure in the last month of pregnancy or within 5 months post-partum in the absence of an identifiable cause of heart failure or the absence of recognizable heart disease prior to the last month of pregnancy or LV systolic dysfunction demonstrated by classical echocardiographic criteria. The latter may be characterized as an LV ejection fraction <45%, fractional shortening <30% or both, with or without an LV end-diastolic dimension >2.7 cm/m^2 body surface area [4].
- Heart Failure Association of the European Society of Cardiology Working Group on PPCM 2010 defined it as PPCM is an idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular systolic dysfunction towards the end of pregnancy or in the months following delivery, where no other cause of heart failure is found. It is a diagnosis of exclusion. The left ventricle may not be dilated but the ejection fraction is nearly always reduced below 45%.
- American heart association defines PPCM as heart failure develop in the last month of pregnancy or within 5 months of delivery with Heart pumping function is reduced, with an ejection fraction (EF) less than 45% (typically measured by an echocardiogram). EF is how much blood the left ventricle pumps out with each contraction. A normal EF can be between 55% and 70% and no other cause for heart failure with reduced EF can be found.

The most widely used in clinical practice is that given by Workshop held by the National Heart Lung and Blood Institute and the Office of Rare Diseases.

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Etiopathogenesis

The exact etiology is yet to be identified, however many factors have been proposed that might play a role in the development of PPCM. The prominent among them being hormonal imbalances, inflammation, viral agents, autoimmune response and genetic predisposition [6].

Hypertension, gestational diabetes, malnourishment, excess salt and smoking also have found to predispose to the development of PPCM [6].

Pregnancy enhances cardiac angiogenesis and also induces an increase in oxidative stress on the cardiac myocytes. The regulation of this angiogenesis is heart is critically dependent on Signal transducer and activator of transcription 3 (STAT3). STAT3 is a master transcriptional factor involved in a broad spectrum of adaptive and innate immune functions such as Th17 differentiation and epithelial regeneration. The absence of cardiomyocyte STAT3 in the postpartum heart causes increased oxidative stress due to blunted induction of the antioxidant enzyme mitochondrial antioxidant manganese superoxide dismutase (MnSOD). As a consequence, expression of cardiac cathepsin D is increased, which in turn, induces a detrimental conversion of Prolactin hormone into its anti-angiogenic 16 kDa derivative. The generation of 16 kDa prolactin greatly accelerates the negative effects of oxidative stress and activated cardiac cathepsin D [7].

Inflammation

Patients prone to develop PPCM have an increased level of pro inflammatory agents such as TNF-alpha, interferon gamma, C-reactive protein, Fas-Apo-1, NT-proBNP and IL-6 [8]. Fas/Apo-1 an apoptotic marker is significantly increased in patients with PPCM and correlates with severity of LV dysfunction. Proteins involved in cardia remodelling such as matrix-metallo-proteinace-2 is also increased in patients with PPCM when compared to healthy postpartum patients [8]. All these findings point towards the role of inflammatory mechanism in the development of PPCM.

Viral pathogens

Parvovirus B19, human herpes virus 6, Epstein-Barr virus and human cytomegalovirus genomes were identified from endomyocardial biopsy specimens from patients with PPCM. These findings stress upon the virus-associated inflammatory changes in peripartum cardiomyopathy [9].

Genetics

Patients with a familial history of dilated cardiomyopathy are more prone to develop PPCM. Abnormal immune response to circulating fetal antigens in maternal blood has also shown to cause and worsen PPCM. However AHA classifies PPCM as acquired and non-familial.

Risk factors

Several obstetric and non-obstetric factors increase the overall relative risk for the development of PPCM. The important ones being listed below [10].

- African-American ethnicity
- Age
- Preeclampsia
- Multiparity
- Multiple gestations
- Obesity
- Smoking
- Chronic hypertension
- Prolonged use of tocolytics
- Twin gestation
- Toxemia

CLINICAL PRESENTATION

The diagnosis of PPCM needs a high degree of suspicion. Most cases with PPCM present in the first four months postpartum and around 10% of cases are diagnosed in the ante natal period in the last trimester [11]. The patient usually presents with dyspnoea, cough, haemoptysis and orthopnea.

A lateral shift of apical impulse, tachycardia, presence of s3 gallop, new onset of tricuspid or mitral regurgitation, dilated neck veins, tender hepatomegaly, pitting pedal odema, pulmonary edema are few of the signs which can be picked up in patients with PPCM.

Chest x-ray

Chest x-ray shows non-specific features of cardiomegaly, pleural effusion and pulmonary congestion.

Electrocardiogram

ECG in patients with PPCM shows ST-T wave abnormality, QT interval prolongation, QRS widening, LV hypertrophy, and atrial fibrillation. Although these are non-specific finding it often helps the treating doctor to further investigate for PPCM.

Endomyocardial biopsy is required in some cases to exclude the inflammatory etiology of acute heart failure.

DIAGNOSTIC CRITERIA

According to workshop held by the National Heart Lung and Blood Institute and the Office of Rare Diseases, PPCM is to be considered if the following criteria are met [4].

- The development of heart failure in the last month of pregnancy or within 5 months post-partum in the

absence of an identifiable cause of heart failure or the absence of recognizable heart disease prior to the last month of pregnancy.

- LV systolic dysfunction demonstrated by classical echocardiographic criteria.
- LV ejection fraction <45%, fractional shortening <30% or both.
- With or without an LV end-diastolic dimension >2.7 cm/m^2 body surface area.

MANAGEMENT

The treatment protocol for the management of PPCM should be individualised according to the patients presenting complaint and its severity. The treating team should include a cardiologist. The main management follows the protocols that involved in treating cardiac failure. PPCM is treated according to the European Society of Cardiology guidelines for heart failure in pregnancy [12]. Addition of Bromocriptin in the management of patients with PPCM greatly improved Left ventricular function and decreased morbidity in such patients [13]. Bromocriptin blocks prolactin and prevents the onset of disease. However Bromocriptin is associated with an increased risk of thromboembolism. One week addition of Bromocriptin to standard heart failure treatment has found to significantly reduce morbidity in patients with PPCM.

After delivery, standard therapy for heart failure is recommended in PPCM including beta-blockers, ACE-inhibitors/AT1-blockers, mineralocorticoid receptor antagonists (MRA) and diuretics. However diuretics are avoided in the antenatal period as it impairs placental circulation and potentially harms the fetus *in utero*. Inotropins may be used in patients with hypotension or in patients with cardiogenic shock [12]. Hemodynamic instability in pregnant PPCM patients should prompt decision for early delivery. If possible vaginal delivery is preferred [14]. Anti-coagulant therapy can be used to prevent thromboembolic phenomenon due to hypercoagulable state and immobilisation.

Another drug which has shown a great deal in decreasing the morbidity in patients with PPCM is Pentoxifyllin due to its anti-TNF-α activity [15].

Intravenous immunoglobin therapy in patients with PPCM improves the ejection fraction and significantly reduced inflammatory cytokines.

PPCM can lead to chronic heart failure in 50% of cases despite optimal medical treatment. Such patients are benefitted with cardiac resynchronization therapy [16].

PPCM imposes a life threatening risk of ventricular tachyarrhythmia and sudden cardiac death. Patients with severely reduced LV Ejection Fraction have an elevated risk for ventricular tachyarrhythmias. Therefore, use of the Wearable Cardiac Defibrillator should be considered in all women with early-stage PPCM and severely reduced LVEF during the first 6 months after initiation of heart failure therapy [17].

In patients with refractory acute heart failure, an extra corporal life support system may be used for stabilization. As some PPCM patients showed continues improvement in cardiac function up to 5 years after diagnosis [18], heart failure treatment and follow up may be continued in patients with persistently reduced LV ejection fraction for several years or even lifelong. However on an average most patients require standard heart failure medication for upto 12 months.

PROGNOSIS

In patients with PPCM cardiac dysfunction re-emerges frequently in the peri- and post-partum phase. A study showed 20% recurrence of PPCM in subsequent pregnancy [19]. PPCM patients should be advised not to get pregnant again. The use of an intrauterine device is recommended for PPCM patients since hormonal contraceptives may interact with heart failure medication. Permanent sterilisation is ideal in these patients and vasectomy to be encouraged in partners.

CONCLUSION

Peripartum cardiomyopathy although a rare diagnosis is one of the prominent cause of maternal morbidity and mortality. Previously healthy pregnant women have a low incidence of 0.1% of pregnancies but the morbidity and mortality is high ranging from 7% to 50%. Despite the rare occurrence of PPCM it is the fifth leading cause of maternal mortality. PPCM cardiac dysfunction re-emerges frequently in the peri- and post-partum phase. And has a 20% recurrence of PPCM in subsequent pregnancy. PPCM patients should be advised not to get pregnant again and permanent sterilisation methods should be practiced if possible.

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