INTRODUCTION

Heart failure during pregnancy was first noted in 1849. But the first description as a distinctive form came only in 1930s. In 1971 Demakis described 27 patients with the disease and named this as a syndrome peripartum cardiomyopathy (PPCM).

The European Society of Cardiology recently defined PPCM as a form of dilated cardiomyopathy that presents with signs of heart failure in the last month of pregnancy or within 5 months of delivery, where no other causes heart failure is found. It is a diagnosis of exclusion. The LV may not be dilated but the ejection fraction is nearly always reduced below 45%.

It occurs 1 in every 2289 live births in the United States. The rate varies in other populations with highest in Haiti, where 1 case occurs in every 300 live births. Environmental and genetic factors, differences in cultural practices, and standards of perinatal care may account for this regional disparity.

Etiology

The aetiology and path physiology are poorly understood, but inflammation plays an important role and markers of inflammation (CRP, TNF) are elevated in many patients. Myocarditis, cardiotropic viral infection, chimerism, and apoptosis play a role.

Myocarditis

The prevalence of Myocarditis in patients with PPCM ranged from 9-78% in different studies. However the presence or absent of Myocarditis alone does not predict the outcome of PPCM.

Cardiotropic Viral Infection

After a viral infection, a pathologic immune response occur which inappropriately target native cardiac tissue, leading to cardiac dysfunction. Bultmann found several viral (parvovirus B19, HHV6, EBV, CMV) DNAs in endomyocardial biopsy specimen of patients of PPCM.

Chimerism

Cells from the fetus provoke an immune response in mother. Serum from patients with PPCM has been found to contain autoantibodies in high titres, which are not present in serum from patients with idiopathic cardiomyopathy.

Apoptosis and Inflammation

Experiments on mice suggest that apoptosis of cardiac myocyte has a role in PPCM. Fas and Fas ligand are cell surface proteins that play a key role in apoptosis. Study from South Africa, 100 patients with PPCM followed for 6 months. 15 patients died, and those who died had significantly higher plasma level of Fas/Fas ligand.

Recent studies suggest that PPCM is a vascular disease, with cardio angiogenic imbalance and an excess of antiangiogenic signalling that is accentuated by preeclampsia. The placenta in late pregnancy secretes vascular endothelial growth factor (VEGF) inhibitors like soluble Flt1, and plasma level of sFlt1 is abnormally high in women with PPCM.

Other report suggest role of cleaved prolactin in PPCM, which is powerful antiangiogenic, proapoptotic, and proinflammatory agent.

Who is at Risk?

Multiparity

Advanced maternal age (>30 years)

Multifetal pregnancy

Preeclampsia and Gestational hypertension

African- American race

Symptoms and Signs

Common symptoms include breathlessness, cough, orthopnea, and paroxysmal nocturnal dyspnea. Most affected patients have New York Heart Association (NYHA) class III or IV function. Other symptoms include nonspecific fatigue, malaise, palpitations, chest and abdominal discomfort, and postural hypotension.
Anticoagulation should be continued until left ventricular function is normalized.

Warfarin is probably safe during the first 6 weeks of gestation, but there is a risk of embryopathy if the warfarin is taken between 6 and 12 weeks of gestation. It is relatively safe during the 2nd and 3rd trimesters but must be stopped and switched to a heparin several weeks before delivery. Warfarin can cause spontaneous fetal cerebral hemorrhage in the 2nd and 3rd trimesters. Unfractionated heparin/low molecular weight heparin can be used safely during pregnancy.

Investigation

CXR/XPA View: Cardiomegaly with or without pulmonary venous congestion/pulmonary edema (Figure 1).

ECG: Left ventricular hypertrophy, Non-specific ST-T changes, atria or ventricular arrhythmia and conduction defect (Figure 2).

Echocardiography: LV dilatation with global hypokinesia, Left Ventricular Ejection Fraction < 45%, mitral regurgitation, pulmonary hypertension with dilated RA, RV, and TR and Pericardial effusion.

Management of PPCM

The treatment of PPCM is same as for other form of congestive heart failure, except that Angiotensin converting enzyme inhibitors (ACEI) and Angiotensin receptor blockers (ARB) are contraindicated in pregnancy. Aldosterone antagonist should be avoided, because of antiandrogenic effect on fetus.

NON PHARMACOLOGICAL: salt restriction (4 gm/day), water restriction (< 2l/day)

Pharmacological

Preload reduction: diuretics and nitrates (nitroprussides are not recommended due to potential cyanide toxicity)

Afterload reduction: hydralazine, nitrates, amlodipine

 Ionotropes: digoxin, dopamine, dobutamine are used in severely low cardiac output cases.

Beta-blockers and Anticoagulant

Antiarrhythmic: quinidine, procanamide, and digoxin

Early fetal delivery may be required in women with heart failure. Cesarean section is preferred mode of delivery in hemodynamically compromised patients.

Guidelines of Anticoagulant Therapy

Patients with evidence of systemic embolism, with severe left ventricular dysfunction, or documented cardiac thrombosis should receive anticoagulation.

Anticoagulation should be continued until left ventricular function is normalized.

Cardiac arrhythmias and sudden cardiac arrest have also been reported. Physicians should consider PPCM in any peripartum patients with unexplained breathlessness with raised BNP.

Common signs of PPCM include pedal edema, hepatomegaly, raised jugular venous pressure, presence of tachycardia with gallop rhythm, evidence of mitral or tricuspid regurgitation, pulmonary crepitations, left ventricular hypertrophy. The differential diagnosis includes accelerated hypertension, diastolic dysfunction, pulmonary embolus, and obstetric complications such as preeclampsia, eclampsia, and amniotic fluid embolism.

Cadiac Transplantation

It is indicated in patients with severe heart failure not responding to maximal drug therapy, however only 3000 hearts are available worldwide for transplantation. Therefore ventricular assist devices are indicated as a bridge to transplantation. Patients with symptomatic ventricular arrhythmia should be considered for defibrillator implantation.

Newer Therapies

Pentoxyfylline – improves left ventricular function and outcome.

Intravenous immunoglobulin – improves the ejection fraction and significantly reduces the level of inflammatory cytokines.

Immunosuppressive therapy – may have a role in patients with proven myocarditis.

Bromocriptine – it is a novel drug for targeted therapy of PPCM. Recent data discovered that blockade of prolactin by bromocriptine prevented the onset of disease in an experimental model of PPCM and appeared successful in small pilot trials. Bromocriptine is associated with increase risk of thromboembolism so Concomitant heparin anticoagulation should be given.

Duration of Treatment

Treatment for heart failure should continue for 6-12 month in patient whom ventricular function return to baseline within 6 month, others will require treatment till normalization of LV function or life long.

Prognostic Factors

The measure determinant of prognosis is recovery of left ventricular function. 30% of patients return to baseline ventricular function within 6 months. The usual cause of death in patients with PPCM is progressive heart failure, arrhythmia, or thromboembolism. Usually PPCM had good prognosis with 5 year survival rate of 94%. There is an initial high risk period with mortality of 25-50% in the first 3 month postpartum. Patients with persistent cardiomegaly at 6 months have a reported mortality of 85% at 5 years. QRS duration >120ms or more and positive troponin T measured 2 weeks after PPCM carry bad prognosis. Increased Risk of persistent left ventricular dysfunction is associated with LVEF < 30%, LVEDD > 5.6cm, left ventricular thrombus, and African American race.
**Risk of Relapse and Recommendation for Future Pregnancies**

Future pregnancies carry a risk of relapse of PPCM even after full recovery of LV function. If LV function came to baseline, next pregnancies have no contraindication, although carries high risk of relapse. If LV function has not recovered, subsequent pregnancies are contraindicated. If LV function has partially recovered, and then dobutamine stress echocardiography should be done and if there is normal response then pregnancy is allowed.

**CONCLUSION**

High level of suspicion is required when a pregnant woman presents with signs of heart failure. The prognosis is best when peripartum cardiomyopathy is diagnosed and treated.

Early. Pregnant women should receive standard heart failure therapy. It is better to avoid ACEI/ARBs, or warfarin in first trimester because of potential teratogenic effects. Targeted therapies (for example, intravenous immunoglobulin, pentoxifylline, and bromocriptine) show promise but need further clinical evaluation before they can be widely adopted. An initial left ventricular end-diastolic dimension less than 5.5 cm, a LVEF > 30%, may predict a better outcome. Subsequent pregnancies may carry a high risk of relapse, even in women who have fully recovered left ventricular function.

**References**

1. Heart failure association of the ESC working group in PPCM. (silva et al 2010)