Peripartum Cardiomyopathy

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History

- Peripartum cardiomyopathy (PPCM) was first described by Richie in 1849 but was not identified as a distinct clinical state until 1933 when women were noted to have heart failure either late in pregnancy or soon after delivery.

- PPCM has historically been over-diagnosed in the pre-echocardiogram era when dx was based on clinical criteria of heart failure that may not have been true failure (other conditions mimicking).

- Represents about 4% of cases of dilated cardiomyopathy in one series of 1230 patients.
Definition

- Development of cardiac failure in the last month of pregnancy or within 5-6 months of delivery.
- Absence of an identifiable cause of CM.
- Absence of recognizable CM prior to the last month of pregnancy.
- Left ventricular systolic dysfunction on echocardiography (decreased shortening fraction or depressed EF).
Epidemiology - PPCM

- True incidence is unknown but estimates range widely from 1 in 1,300 live births to 1 in 15,000 live births.
- Wide range due to past over-diagnosis due to lack of criteria.
- Accepted incidence appears to be 1 per 3000 to 1 per 4000 live births or about 1000-1300 women/ year in U.S.
Epidemiology - PPCM

- Nigerian women have a 1 per 100 live birth rate of PPCM; thought to be related to the ingestion of lake salt in the immediate post-partum period leading to volume overload.

- There appears to be a predilection for the Southern U.S. compared to other regions in the country.
Risk Factors

- Age > 30
- Multiparity (>3 gestations)
- African descent
- Multiple gestations (twins, triplets, etc.)
- Post-partum HTN, Preeclampsia, Eclampsia
- Selenium deficiency, cocaine use
- > 4 weeks of oral tocolytic therapy
Clinical Presentation

- Rarely seen before 36 weeks gestation or after 5-6 months post-partum.
- Earlier presentations likely represent prior myocardial disease or other cause disease.
- Complaints of dyspnea, DOE, cough, orthopnea, PND, hemoptysis are common.
- Other more non-specific symptoms include CP, fatigue, and abdominal pain (sx of normal pregnancy).
Diagnosis - Studies

- Disqualified are those that have ANY heart failure prior to 36 weeks gestation or > 5 months post-partum, or other cause of heart failure.
- EKG, CXR, and Echocardiography should be done in all that are suspected of having condition.
- Catheterization +/- biopsy more variably done.
- Viral serologies for over-acheivers.
Diagnosis - Findings

- EKG oftentimes sinus tach, Afib rarely, non-specific T wave and ST segment changes, and low voltage. PR and QRS interval changes seen less commonly.

- Echo shows usually reveals left-ventricular enlargement and with global LV dysfunction without LVH. Left atrial enlargement.

- CXR usually shows evidence of cardiac enlargement and pulmonary vascular prominence. May have effusions.
Pathology

- Endomyocardial biopsy has an unclear role. Gross specimens are usually of a flabby myocardium that is dilated with common ventricular thrombi.
- Microscopically myofibril hypertrophy and/or degeneration, fibrosis, and interstitial edema with lymphocytic infiltrate may be seen.
Pathogenesis

- Unclear!
- May represent exaggerated response to pregnancy induced remodeling of myocardium.
- No clear role for hormones of pregnancy.
- Three studies suggest a role for pre-symptomatic myocarditis but results not consistent from study to study.
- When in doubt blame it on the cytokines. It worked for me for 4 years while getting my Ph.D.
Pathogenesis - Immunobiology

- May represent a partial alloimmune response to fetal cells (microchimerism gone awry).
- One study found elevated IL-6, TNF-α, and soluble FasL elevated in 29 PPCM patients when compared to 20 normals.
- Another study found increases in iNOS expression in myocytes of these patients.
Pathogenesis - Immunobiology

- One interesting set of studies found CD4+ PBMC make more IL-2 (lame) when nonspecifically stimulated.
- Interestingly however, there is a paucity of CD4+CD25lo regulatory T cells (T_{reg}) in PPCM sufferers. This may explain why immunosuppression does not appear to work.
- Other more novel therapeutic agent may be useful if they target the effector cells or effector molecules (T cells, blood derived monocytes that induce fibrosis – i.e. PDGF selective Tyrosine kinase inhibitors, endothelin-1 antagonists etc...). **GENE CHIPS AND PROTEOMIC BABY!**
Treatment

- Treatment is that for other forms of congestive heart failure including digoxin, beta-blockade, and after load reduction with ACE-I - keeping in mind safety of these drugs in pregnancy and breast-feeding.

- Evidence for Beta-blockers for delaying progression of myocardial dysfunction with idiopathic DCM and possibly PPCM.
Pregnancy is a hyper-coagulable state.

Stasis of blood in LV a set-up for thromboembolic phenomena in cases of poor LV EF.

Warfarin is class D agent but ok post-partum.

Heparin with low EF in pregnancy.
Treatment - Immunomodulation

- Immunosuppressants such as steroids + azathioprene or cyclosporin not indicated or not clearly indicated.
- IVIG (not surprisingly) has been given with good results especially when given close in time to onset of symptoms.
- In one retrospective study of N=6 PPCM patients vs. 11 controls with IDCMI, IVIG helped restore EF (>10%) in all patients (3 completely back to normal) vs. <40% of controls.
Treatment - Transplantation

- Yikes!
- A last resort when conventional therapy fails. Success rate similar to IDCM patients when transplanted.
- Needless to say, women s/p transplant approach their next pregnancy cautiously.
- Only one report exists of a PPCM gone on to transplant and subsequent pregnancy.
Prognosis

- Based on anecdotal reports or small series but deterioration associated with:
  - Age >30
  - Higher parity (>3)
  - Later onset of symptoms (>7.6 weeks post-partum)
  - Higher LV end-diastolic dimensions (>7.0 cm)
  - Higher mean pulmonary arterial (>38 mm Hg)
  - Higher pulmonary wedge pressure (>24 mm Hg)
  - Conduction defects on presentation
Prognosis - Mortality

- Myocardia that are going to recover usually do so in 6 months from time of diagnosis.
- Otherwise mortality ranges from 25-50% with most death occurring 3 months post-partum.
- Death is usually by over pump failure, thromboembolism, or ventricular arrhythmias.
- One study not so grim, reports on 7% mortality and 7% transplant rate.
Prognosis – Future Pregnancy

- Consensus is that patients with persistent LV dysfunction are at extremely high risk for complications and death with future pregnancies with a mortality of 20%, heart failure in 44%, premature delivery in 37%, and need for abortion on 25%.

- Less risky in those with return to baseline prior to next pregnancy (heart failure is 21% and no mortality).

Up to Date, “Peripartum Cardiomyopathy”

Up to Date, “Causes of dilated cardiomyopathy”


Acknowledgements