Peripartum Cardiomyopathy: An Update

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27 YO HF  G₂P₁  IUP @ 8 weeks  
diagnosed with HTN at 20th wks of 1ˢᵗ pregnancy.  
Cardiac evaluation including Echocardiogram - WNL.  
Asymptomatic until 32 wks when she was delivered by  
C-section B/O preeclampsia & fetal distress.  
Baby girl born with bradycardia, required pacemaker &  
died 16 days post partum.
Peripartum Cardiomyopathy

Admitted @2½ mo post partum for CHF.

LVEF was 25% by Echo with normal thallium scan.

Treated with Lasix, Cozaar, Digoxin, Coreg with complete recovery of symptoms and some improvement of LVEF to 30%.

Patient became pregnant again 2 mo Later.
Peripartum Cardiomyopathy

- Definition.
- Incidence.
- Clinical manifestations.
- Outcome.
- Predictors of failure to recover and other complications.
- Treatment.
- Risk of subsequent pregnancy.
<table>
<thead>
<tr>
<th>PERIPARTUM CARDIOMYOPATHY</th>
<th>DEFINITION</th>
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<tbody>
<tr>
<td>An idiopathic cardiomyopathy presented during the 2\textsuperscript{nd} and 3\textsuperscript{rd} trimester of pregnancy or within several months postpartum and associated with depressed LV systolic function.</td>
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</table>
PPCM – Time of Diagnosis

(Elkayam et al. Circulation 2005;111:2050)

N=123

Number of patients

Early

Traditional

Weeks

Months PP
PPCM
Early Presentation

♥ 35 yo female G₂ P₁ IUP @ 25 wks, previously healthy, transferred to USC 8 days after admission to another hospital for SOB, found to be hypertensive and in pulmonary edema which required intubation.

♥ Echocardiogram – mild LV enlargement with diffuse hypokinesis, LVEF 25%, mild MR and mild TR.
PPCM
Early Presentation

♥ Cardiac catheterization – elevated LVEDP, normal coronaries.

♥ Patient was treated with IABP, IV NTG, Hydralazine and Furosemide and improved.

♥ Transferred to USC and delivered 2 days after admission.

♥ Echo 1 wk PP: LVEF - 32%, LVEDD – 5.5 cm.

1 yr PP: LVEF ~ 50%, LVEDD – 4.2 cm.
### Comparison between Traditionally and Early diagnosed PPCM patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Traditional (N=100)</th>
<th>Early (N=23)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31 ± 6</td>
<td>30 ± 6</td>
<td>0.67</td>
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<tr>
<td>Parity</td>
<td>2.1 ± 1.7</td>
<td>1.9 ± 1.5</td>
<td>0.64</td>
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<tr>
<td>Hx of gestational HTN</td>
<td>43%</td>
<td>30%</td>
<td>0.56</td>
</tr>
<tr>
<td>Twin Pregnancy</td>
<td>13%</td>
<td>26%</td>
<td><strong>0.009</strong></td>
</tr>
<tr>
<td>LVEF at Diagnosis</td>
<td>31 ± 12%</td>
<td>30 ± 12%</td>
<td>0.72</td>
</tr>
<tr>
<td>LVEF at Last F/U</td>
<td>46 ± 14%</td>
<td>44 ± 16%</td>
<td>0.54</td>
</tr>
<tr>
<td>Duration of F/U (Months)</td>
<td>6 ± 7</td>
<td>7 ± 9</td>
<td>0.52</td>
</tr>
<tr>
<td>Mortality</td>
<td>9%</td>
<td>13%</td>
<td>0.7</td>
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</table>

(Elkayam et al. Circulation 2005;111:2050)
Peripartum Cardiomyopathy
Clinical Profile in the U.S.

- Although PPCM is diagnosed mostly during the 1\textsuperscript{st} gestational month (week), \textasciitilde 20\% of cases present during the 2\textsuperscript{nd} and 3\textsuperscript{rd} trimester prior to last gestational month.

- Clinical profile as well as LVEF at diagnosis and rate of recovery are almost identical in both groups.
Recent surveys in the US and Canada (Circ 2004;110:III 520) found a ratio of 1~ 2300 live births (~1300 cases/year).

Higher incidence reported in South Africa (1:1000) and in Haiti (1:300).
Possible reasons for increased incidence of PPCM

- Older patients age (≈ 4 yrs increase in age of 1\textsuperscript{st} delivery since 1970. Birth in women 35-39 and 40-44 yrs increased 43% and 62% respectively).
- Increased number of multiple gestations (≈121000 in 2001 vs ≈68000 in 1980).
- Improved diagnostic capabilities.
periartum Cardiomyopathy
Clinical Presentation

- CHF signs and symptoms.
- Arrhythmias (with or without CHF)
- Thromboembolism.
- Asymptomatic LV dysfunction.
<table>
<thead>
<tr>
<th>PPCM Thromboembolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Coronary emboli.</td>
</tr>
<tr>
<td>(Tx heart inst J 2004;31:442).</td>
</tr>
<tr>
<td>▪ Biventricular thrombi.</td>
</tr>
<tr>
<td>▪ Pulmonary embolism.</td>
</tr>
<tr>
<td>▪ Peripheral embolization.</td>
</tr>
<tr>
<td>(Ann Cardiol Angiol 2003;52:382).</td>
</tr>
<tr>
<td>▪ Thrombotic cerebral infarct.</td>
</tr>
</tbody>
</table>
Outcome in 123 Patients With PPCM

Recovery: LVEF ≥50% at last F/U
59%

Persistent LV dysfunction at last F/U
41%

Heart Transplantation
4%

Death
10%* (Including 2 pts who died post transplantation)
LV Ejection Fraction in 52 Patients with Complete Set of Measurements

- Diagnosis: 30 ± 11%
- 6 months postpartum: 45 ± 13%
- 12 months postpartum: 48 ± 11%
- Last F/U: 46 ± 14%

*p<0.0000001 vs LVEF at diagnosis
Predictors of Persistent LV dysfunction

- Severity of LV insult (dilatation and systolic dysfunction) at time of diagnosis.
- Evidence for myocardial cell damage with Troponin T level >0.04 ng/ml at time of diagnosis (Hu CL et al Heart 2007;93:488-90).
- African American race.
Recovery of LV function in 55 pts with PPCM

Amos et al AHJ 2006;15:509-513
PREDICTORS OF RECOVERY OF LV FUNCTION IN PPCM IN THE US
(Bitar, Elkayam et al Circulation 2005)

Total Patients
154 Patients

Echocardiogram Data at 6 months Post Partum unavailable
= 32 patients

Total Patients Included in Study
122 Patients
## Logistic Regression Analysis results

<table>
<thead>
<tr>
<th>Groups Compared</th>
<th>Odds Ratio</th>
<th>Standard of Error</th>
<th>P Value</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2 vs Group 1</td>
<td>4.8</td>
<td>3.2</td>
<td>0.016</td>
<td>1.3-17.4</td>
</tr>
<tr>
<td>Group 3 vs Group 1</td>
<td>6.1</td>
<td>3.8</td>
<td>0.004</td>
<td>1.8-20.7</td>
</tr>
</tbody>
</table>

**Group 1 (Baseline EF 10%-20%)**
**Group 2 (Baseline EF 21-30%)**
**Group 3 (Baseline EF 31-45%)**
Is the normalization of LV function complete post PPCM?
# Contractile Reserve in Pts with PPCM and Recovered LV Function

Lampert et al, AJOG 1997;176:189

<table>
<thead>
<tr>
<th></th>
<th>PPCM at diagnosis</th>
<th>PPCM at study entry</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>94 ± 34</td>
<td>70 ± 12</td>
<td>73 ± 11</td>
</tr>
<tr>
<td>ESD (cm)</td>
<td>5.0 ± 0.5</td>
<td>3.3 ± 0.4</td>
<td>3.1 ± 0.2</td>
</tr>
<tr>
<td>EDD (cm)</td>
<td>6.1 ± 0.4</td>
<td>5.1 ± 0.5</td>
<td>4.6 ± 0.3</td>
</tr>
<tr>
<td>SF (%)</td>
<td>18.8 ± 4.5</td>
<td>35 ± 3.0</td>
<td>32 ± 2.0</td>
</tr>
<tr>
<td>CO (L/min)</td>
<td>4.1 ± 1.2</td>
<td>5.1 ± 1.3</td>
<td>5.0 ± 0.3</td>
</tr>
<tr>
<td>CI (L/min/m²)</td>
<td>2.4 ± 0.7</td>
<td>2.9 ± 0.3</td>
<td>3.0 ± 0.3</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>54 ± 33</td>
<td>71 ± 11</td>
<td>73 ± 17</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>110 ± 20</td>
<td>85 ± 14</td>
<td>77 ± 7</td>
</tr>
<tr>
<td>TVR (dynes/sec/cm⁵)</td>
<td>2413 ± 1195</td>
<td>1389 ± 301</td>
<td>1268 ± 218</td>
</tr>
</tbody>
</table>
Contractile Reserve in Patients With PPCM and Recovered Left Ventricular Function

Lampert et al. AM J Ob Gyn 1997; 176:189
PPCM
Spontaneous Deterioration of LV Function After Normalization

LVEF - 16%.

♥ June 1992 – Patient recovered,
LVEF ~ 55%

♥ September 1995 – Fainting episode while moving furniture in her office,
LVEF - 35-40%, Atrial fibrillation.
PPCM
Spontaneous Deterioration of LV Function After Normalization

♥ Symptoms attributed to atrial arrhythmias.

♥ April 2000 – Syncope, LVEF 28% by Echo, normal coronaries by angio.

♥ September 2000 – Sudden death.
LONG-TERM SURVIVAL IN PTS WITH INITIALLY UNEXPLAINED CARDIOMYOPATHY
(Felker et al NEJM 2000;342:1077)
PPCM – INTERVAL FROM END OF PREGNANCY TO DEATH

Major adverse events in PPCM
(Goland, Elkayam, Circulation Suppl 2006)

182 patients.
≥ MAEs in 46 pts (25%).

- Death – 13 pts, 40% sudden death.
- Heart transplantation – 11 pts.
- Temporary circulatory support – 2 pts.
- Cardiopulmonary arrest – 6 pts.
- Pulmonary edema – 17 pts.
- Thromboembolic complications – 5 pts.
- ICD or pacemaker implantation – 10 pts.
Major adverse events in PPCM
(Goland, Elkayam, Circulation Suppl 2006)

- ≥ 1 week delay in diagnosis after onset of symptoms reported in 59% of all cases.
- MAEs preceded the diagnosis of PPCM in 50% of pts.
- 32% of surviving patients without cardiac transplantation, had residual brain damage.
Major adverse events in PPCM
(Goland, Elkayam, Circulation Suppl 2006)

Significant predictors of MAEs

1. LVEF ≤ 25% (HR = 4.2, CI:2.04-8.64).

2. Non Caucasian ethnic background (HR 2.16, CI:1.17-3.97).
**PERIPARTUM CARDIOMYOPATHY**
Why are we missing it?

Symptoms and signs that can mimic heart failure during normal pregnancy

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Physical Findings</th>
</tr>
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<tbody>
<tr>
<td>Decreased Exercise Capacity</td>
<td>Distended neck veins</td>
</tr>
<tr>
<td>Tiredness</td>
<td>Leg edema</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Palpable RV impulse</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>Pulmonary basilar rales</td>
</tr>
<tr>
<td>Palpitations</td>
<td>Functional murmurs</td>
</tr>
<tr>
<td>Lightheadedness</td>
<td></td>
</tr>
<tr>
<td>Syncope</td>
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</table>
peripartum Cardiomyopathy

Reported associated conditions

- Maternal age > 30 yrs – YES (55%)
- Multiple pregnancies – YES (58%)
- Black – NO (20%)
- Poor nutrition - NO
- Twin pregnancies – YES (15%)
- History of HTN / Preeclampsia – YES (42%)
- Long-term (>4wks) tocolytic Tx - YES (19%)
PERIPARTUM CARDIOMYOPATHY

Treatment
Peripartum Cardiomyopathy
Therapeutic considerations during pregnancy

Safe Drugs:
- Digoxin
- Nitrates
- Hydralazine
- Heparin
- Diuretics
- Beta blockers

Unsafe Drugs:
- ACE-I
- Nitroprusside
- Amiodarone
- Coumadin
Peripartum Cardiomyopathy

Therapeutic considerations post partum

- ACE-I, Beta blockers, aldosterone receptor antagonists and Coumadine until LV function normalizes.
- Temporary mechanical support (IABP, LVAD) may be useful as bridge to recovery of LV function.
Preliminary data suggest benefit of immunosuppressive and immunomodulating therapy (pentoxifylline), as well as treatment with bromocriptine, an inhibitor of prolactin.
PPCM and Pentoxifylline
Combined Endpoint of Poor Outcome

(Death, Class III-IV @ last FU, Failure to increase EF >10%)

Treatment with pentoxifylline – the only independent predictor of outcome on logistic regression analysis

P=0.03
PERIPARTUM CARDIOMYOPATHY

SUBSEQUENT PREGNANCY
PREGNANCY ASSOCIATED CARDIOMYOPATHY
Index Pregnancy
N=123

- 1st: 42%
- 2nd: 17%
- 3rd: 17%
- 4th: 10%
- 5th: ≥ 14%
SUBSEQUENT PREGNANCY

- A 28 YO Caucasian female G1. P1. (Delivered 11/24/04) who was seen on 11/1/06 for consultation.
- The patient developed progressive weight gain and edema which started at 30 weeks gestation and were associated with orthopnea and SOB. The findings were attributed to Preeclampsia which was diagnosed 2 weeks later and she was urgently delivered by a C section.
- After discharge from the hospital she continued to experience DOE and orthopnea and was diagnosed with CHF when admitted with ileus as a complication of her C section.
SUBSEQUENT PREGNANCY

- Diagnosis was supported by a CXR which showed pulmonary congestion and BNP level of 1400 pg/ml.
- An Echocardiogram which was obtained in the ER showed 4 chamber enlargement and LVEF of 20-25%.
Changes in LV Size and Function in PPCM

- LV end diastolic diameter
- LV end systolic diameter
- LV ejection fraction

25%  28%  36%  43%  51%  58%  58%

0.0  10%  20%  30%  40%  50%  60%

2.0  3.0  4.0  5.0  6.0

0 days  9 days  14 days  18 days  2 months  7 months

11/24/04  12/5/04  12/8/04  12/12/04  1/27/05  6/22/05

5.7 cm  5.3 cm  5.0 cm  4.9 cm  4.9 cm
SUBSEQUENT PREGNANCY

- Patient is presently at the NYHA functional class I and exercises regularly.
- Patient and her husband are interested in having more children.
- But was told by her physician that subsequent pregnancy may be associated with 50% incidence of maternal mortality.
Outcome of Subsequent Pregnancies in PPCM
(Elkayam et al NEJM 2001;344:1567)
Maternal Complications Associated With Subsequent Pregnancy*

*including aborted pregnancies

- A: HF Symptoms
  - 21%
  - 21%
- B: >20% Decreased LVEF
  - 44%
  - 25%
  - 14%
- A: >20% Decreased LVEF at F/U
  - 31%
- B: Maternal Mortality
  - 0%
  - 19%
Maternal Complications in women without abortions

- HF Symptoms: 26% A, 50% B
- >20% Decreased LVEF: 17% A, 33% B
- >20% Decreased LVEF at F/U: 9% A, 42% B
- Maternal Mortality: 0% A, 25% B
### Outcome of Subsequent Pregnancies in Women With PPCM (Elkayam U, Eur Heart J 2002)

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Index &amp; Pregnancy</th>
<th>F/U</th>
<th>Subsequent Pregnancy</th>
<th>F/U</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>50</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>50</td>
<td>32</td>
<td>46</td>
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<tr>
<td>3</td>
<td>45</td>
<td>60</td>
<td>19</td>
<td>50</td>
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<td>4</td>
<td>43</td>
<td>65</td>
<td>47</td>
<td>58</td>
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<td>5</td>
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<td>67</td>
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<td>9</td>
<td>30</td>
<td>55</td>
<td>40</td>
<td>40</td>
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<tr>
<td>10</td>
<td>44</td>
<td>59</td>
<td>35</td>
<td>20</td>
</tr>
<tr>
<td>Mean</td>
<td>34±12</td>
<td>58±7*</td>
<td>43±13**</td>
<td>45±10***</td>
</tr>
</tbody>
</table>

* = p<0.0001 vs. A; ** = p<0.01 vs. B; *** = p=0.01 vs. B
OUTCOME OF SUBSEQUENT PREGNANCY IN PTS WITH PERSISTENT LV DYSFUNCTION

  16 pregnancies in 15 pts.
  8 experienced worsening HF and 1 died 10 month PP.

  5 of 6 pts showed deterioration of LV function and 2 died of HF within 8 weeks PP.
Subsequent pregnancy may lead to a significant and persistent depression of LVEF, to CHF and even death.
Clinical and functional deterioration are more likely in patients with persistent LV dysfunction but can also occur in pts who normalize their LV function.