HeFSSA Practitioners Program 2015
Theme - Women and Heart Failure

08:00 - 08:20     Registration & Breakfast
08:20 - 08:25     Welcome and Thank You to Sponsors
08:25 - 08:30     HeFSSA smartphone patient app (video)
08:30 - 09:15     Implantable devices, women and heart failure
09:15 - 10:00     *Peri-partum cardiomyopathy*
10:00 - 10:30     Tea Break
10:30 - 11:15     Hypertension in pregnancy
11:15 - 11:45     Elderly women with Heart Failure
11:45 - 12:00     Questionnaire
12:00             Departure
CASE STUDY:
Peri-partum cardiomyopathy
A young woman presenting with shortness of breath post partum

NOVEL FINDINGS IN PERIPARTUM CARDIOMYOPATHY
CASE STUDY:
Peri-partum cardiomyopathy

- 25 year old woman
- Sudden onset of shortness of breath
- Medical History: What would you ask?
Medical Hx:

- Symptoms started 6 weeks after delivery,
- SOB gradually increasing over 3 days

Has 2 children, 3 & 4 years old

No cardiovascular risk factors such as: No HT, no diabetes, non-smoker

No FHx

Examination: - what would you expect?
Examination:

- HR 120 bpm
- Pulse: small volume
- BP 95/65
- JVP raised
- Apex: displaced, hypokinetic
- Auscultation: 2/6 pan systolic murmur, gallop sounds
- 2 + pedal oedema, minimal ascites
- Crackles up to mid-zone both lungs

Differential diagnosis?
CASE

- Differential diagnosis:
  1. Cardiomyopathy?
     1. Peripartum?
     2. HIV-associated?
     3. Familial?
     4. Idiopathic?
  2. Rheumatic heart disease?
  3. Pulmonary embolus?
  4. Pericardial disease?
Investigations
Investigations
Case
Echocardiography
Blood tests:
HIV negative, d-dimers negative, normal renal function, CRP in normal range
Diagnosis:
Peripartum Cardiomyopathy (PPCM) with features of poor prognosis:

1. Mitral regurgitation
2. Pulmonary hypertension
Cardiomyopathies

HCM = hypertrophic cardiomyopathy; DCM = dilated cardiomyopathy; ARVC = arrhythmogenic right ventricular cardiomyopathy; RCM = right ventricular cardiomyopathy
<table>
<thead>
<tr>
<th>Reference</th>
<th>Definition/classification of PPCM</th>
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<tr>
<td>European Society of Cardiology on the classification of cardiomyopathies</td>
<td>A non-familial, non-genetic form of dilated cardiomyopathy associated with pregnancy.</td>
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<td>(Dickstein 2008, Eur J Heart Failure)</td>
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<td>AHA Scientific Statement on contemporary definitions and classifications</td>
<td>A rare and dilated acquired primary cardiomyopathy, associated with LV dysfunction and heart failure.</td>
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<td>of the cardiomyopathies</td>
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<td>(Maron 2006, Circulation)</td>
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<td>Workshop held by the National Heart Lung and Blood Institute and the</td>
<td>1) The development of heart failure in the last month of pregnancy, or within 5 months post partum.</td>
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<td>Office of Rare Diseases</td>
<td>2) The absence of an identifiable cause of heart failure.</td>
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<td>(Pearson 2000, JAMA)</td>
<td>3) The absence of recognizable heart disease prior to the last month of pregnancy; LV systolic dysfunction demonstrated by</td>
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<td>classical echocardiographic criteria. The latter may be characterized by an LV ejection fraction &lt;45%, fractional</td>
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<td>shortening &lt;30%, or both, with or without an LV end-diastolic dimension &gt;2.7 cm/m² body surface area.</td>
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<td>Heart Failure Association of the European Society of Cardiology Working Group on PPCM 2010</td>
<td>PPCM is an idiopathic form of 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 causes of heart failure are found. It is a diagnosis of exclusion. The left ventricle is not necessarily dilated, but the ejection fraction is usually below 45%.</td>
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<tr>
<td>Sliwa et al. European Journal Heart Failure 2010</td>
<td></td>
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</tbody>
</table>
1: 3500 - 1:15000 USA*

1:1000 in South Africa#

*Lampert M, Lang RM. Am Heart J 1995

# Sliwa et al. The Lancet 2006

No prospective data from Australia or Europe

Mode of Presentation: PPCM – Symptoms and Signs

**Most common**
- Dyspnoea (NYHA class III-IV)
- Cough
- Fatigue

**Common**
- Lower extremity edema
- Orthopnoea
- Paroxysmal nocturnal dyspnoea
- Palpitations
- Dizziness

**Less common**
- Nocturia
- Right upper quadrant pain (hepatic congestion)
- Chest pain
- Postural hypotension
- Syncope

Symptoms can be subtle to dramatic
Highly variable presentation
Often ignored by patients, nurses and doctors
Mode of Presentation:
Acute, dramatic presentation needing circulatory support

- Prognosis in e.g. PPCM is different from DCM, with a significant proportion of patients normalizing their LV function within the first six months postpartum.
- Left ventricular assisted device (LVAD) may be considered before listing the patient for cardiac transplantation.
- Optimum strategy is not known and discussion between experts on a case-by-case basis may be helpful.
- Thrombotic complications possibly more often because PPCM is a pro-thrombotic condition.
- Size of device also remains a limiting factor as not all fully implantable devices will fit into a small woman.
Breathless woman towards the end of pregnancy/early post partum

ECG or Natriuretic peptides AND echocardiography

Any abnormalities

Cardiology review (consider differential cardiovascular diagnoses of PPCM – table)

All normal

Consider non-cardiovascular causes of breathlessness
Differential diagnoses of PPCM: 2 conditions can co-exists!

- Pre-existing idiopathic dilated cardiomyopathy (IDC) unmasked by pregnancy
- Pre-existing familial dilated cardiomyopathy (FDC) unmasked by pregnancy
- HIV/AIDS cardiomyopathy
- Pre-existing valvular heart disease unmasked by pregnancy
- Pulmonary embolus
- Pre-existing unrecognised congenital heart disease
- Pregnancy associated myocardial infarction
- Hypertensive heart disease
Conclusions: Almost all women suffering from PPCM had an ‘abnormal’ 12-lead ECG. Pending more definitive studies, the ECG appears to be a useful adjunctive tool in both screening and monitoring.

Patients with e.g. shortness of breath due to asthma would not have e.g. LBBB, broad QRS, T-wave inversion.
Echocardiography:
Left Ventricular Dysfunction often with Mitral Regurgitation and Pulmonary Hypertension
Reduced TAPSE, signifying RV systolic dysfunction, is defined as a value of ≤ 14 mm.
Comparison of 35 patients with DCM versus 55 patients with PPCM recruited over the 8 months period.

TAPSE ≤14 mm was found in 54.6% of PPCM patients and in 37.1% of DCM patients.

Mean TAPSE was significantly less in PPCM (12.58+4.27 mm) compared to DCM patients (14.46+3.21 mm), (P <0.028)
Conclusion: Potentially causal mutations in cardiomyopathy-related genes are common in families with both PPCM and DCM. This supports the earlier finding that PPCM can be part of familial DCM. This cohort was particularly characterized by a high proportion of TTN mutations and a low recovery rate in PPCM cases.
Summary of pathogenesis:
Recent studies over the past decade have shown the important role of increased oxidative stress and an abnormal prolactin (16kd) which can be inhibited by the drug bromocriptine.

**Management depending on time of presentation**

**Germany**
- Antepartum: 43%
- 1-3 months postpartum: 17%
- 3-6 months postpartum: 40%

**South Africa**
- Antepartum: 0%
- 3-6 months postpartum: 43%
- 1-3 months postpartum: 57%


Treatment of Heart Failure in women with PPCM (new onset or with previously diagnosed PPCM)

According to standard heart failure guidelines

Non Pregnant

Early Pregnancy

Effect on fetus

Diuretics

Hydralazine

Beta Blocker

Late Pregnancy

Diuretics

Hydralazine

Beta Blocker

Postpartum

Diuretics

Ace-inhibitor

Beta blocker
All patients received diuretic, ACE-inhibitors and Carvedilol.
• Blinded clinical, prospective single-centre, randomized, open-label proof-of-concept trial of women with newly diagnosed PPCM, receiving standard care (PPCM-Std, n=10,) versus standard care plus bromocriptine for 8 weeks (PPCM-Br, n=10).

• Bromocriptine: 2.5 mg twice daily for 2 weeks, followed by 2.5 mg daily for 6 weeks.

• Blinded clinical, hemodynamic and echocardiographic assessment were performed at baseline and 6 months post diagnosis, cardiac MRI was performed 4-6 weeks post diagnosis in PPCM-Br.

• 6-month outcome of their children (n=21) was studied, as mothers receiving bromocriptine could not breast feed.
Bromocriptine promotes recovery of cardiac function and survival in patients with PPCM - first randomized proof-of-concept pilot study


Change in left ventricular ejection fraction from baseline to either death, or survival, at 6 months.

PPCM Br: 28 to 56% versus PPCM Std: 28-36%, p=0.006

PPCM Bromo: 10 % Mortality

PPCM Standard Care: 40% Mortality
85% Improver (IMP)  15% Non-Improver (NIMP)

47% Full recovery

7% transpl.
1% LVAD
1.7% died

47% Full recovery
• Thromboembolic phenomena have been reported frequently in PPCM.
• Hypercoagulable state of late pregnancy may persist up to 8 weeks post partum.
• Low ejection fraction (<35%) - LV thrombus common.
• Warfarin is preferred postpartum and low-molecular way heparin agent of choice in the last weeks of pregnancy in particular if EF < 35% or LV clot has been documented.
• In more than 100 patients treated with Bromocriptine in Germany & South Africa thrombotic events were not observed – unpublished observation.
Breast Feeding

• Based on the postulated negative effects of prolactin sub-fragments (*Hilfiker-Kleiner Cell 2007*), breast feeding is not advised in patients with suspected PPCM, even if this practice is not fully evidence-based.

• Several ACE-inhibitors (captopril, enalapril and quinapril) have been adequately tested in breast feeding women.
Follow up
Patient was seen 1 month, 3 month and 6 month post diagnosis. Her symptoms improved on medication and she was asymptomatic at the 6 months visit.

Medication:
Beta-blockers (carvedilol) was up-titrated to maximal dose
Ace-inhibitor (perindopril) was only tolerated at 4 mg daily as BP remained at 100 mmHg systolic
No digoxin was added as no evidence to use in this condition
Furosemide was stopped and replaced with low dose Hydrochlorothiazide.
Bromocriptine was given at 6.25 daily for 2 weeks followed by 6.25 daily for another 4 weeks
Warfarin was not given as patient had no access to regular INR testing
Follow up II

Echocardiography was repeated after 6 month:
The contractility had improved (LVEF 45%) but not normalized
The patient was advised to continue on medical therapy for another 6 months and to repeat the investigation

Advise on a subsequent pregnancy:
The patient was advised to continue on her contraception and to not plan another pregnancy until the heart had fully recovered (minimum to wait- 2 years)
Conclusion and way forward

- PPCM remains a difficult condition to both diagnose and treat.
- PPCM symptoms mimic typical symptoms of pregnancy/early post-partum period. High index of suspicion warranted.
- Treatment with standard medication and bromocriptine needs to be investigated in larger trials and registries.
- Need to identify biomarkers for facilitating early diagnosis and predicting outcome.
- Long-term prognosis is not well established.
- More awareness for the disease is important!
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