How pregnancy impacts adult cyanotic congenital heart disease

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Mrs S., 19 y.o., 22 WG

- Pulmonary atresia with aorto-pulmonary collaterals
- Progressive exertional dyspnea since the first trimester: NYHA III
- Oxygen Sat = 78%.
- Laboratory values: hematocrit=66%

• How should this complicated patient be managed? Should one recommend acute endotracheal intubation, phlebotomy or termination of her pregnancy?
<table>
<thead>
<tr>
<th>Shunt with normal or restricted pulmonary blood flow: normal PVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Pulmonary outflow tract obstruction</td>
</tr>
<tr>
<td>• Tetralogy of Fallot</td>
</tr>
<tr>
<td>• ccTGA and VSD and pulmonary stenosis</td>
</tr>
<tr>
<td>• Pulmonary atresia with VSD and aortopulmonary collateral vessels</td>
</tr>
<tr>
<td>• Univentricular heart with pulmonary outflow tract obstruction</td>
</tr>
<tr>
<td>• Intrapulmonary arteriovenous malformations after bidirectional Glenn anastomosis</td>
</tr>
<tr>
<td>➢ Without pulmonary outflow tract obstruction</td>
</tr>
<tr>
<td>• Fontan with fenestration</td>
</tr>
<tr>
<td>• Ebstein + PFO or ASD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pulmonary vascular disease secondary to a non-restrictive shunt: Increase in PVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ “Simple” CHD</td>
</tr>
<tr>
<td>• Non-restrictive VSD, PDA</td>
</tr>
<tr>
<td>• ASD</td>
</tr>
<tr>
<td>➢ Complex CHD</td>
</tr>
<tr>
<td>• Atrio-ventricular septal defect</td>
</tr>
<tr>
<td>• CCHD without pulmonary outflow tract obstruction: univentricular heart, common arterial trunk, ccTGA+VSD</td>
</tr>
<tr>
<td>• Aorto-pulmonary window</td>
</tr>
<tr>
<td>• Segmental PAH (group 5): Pulm atresia with VSD and MAPCA</td>
</tr>
</tbody>
</table>

Brickner et al, NEJM 2000
Oeshlin et al Heart 2016
Chronic cyanosis: adaptive mechanisms and pathological changes

- Cyanosis with secondary erythrocytosis
  - Infectious disease
  - Hyperviscosity
  - Haemorrhagic and thrombotic complication
  - Cardiorespiratory reserve
  - Renal dysfunction
  - Endothelial dysfunction (myocardial BF, retinal BF)
  - Cerebrovascular complications: stroke & TIA, abscess
  - Gallstones
  - Hemoptysis & PE
  - Hyperuricemia
  - Skeletal complications
  - Infectious disease

CCHD and pregnancy

Hemodynamic changes

Pregnancy

- ↓SVR -10%
- ↑CO 30-50%
  Stroke volume
  Heart rate
- ↑Coagulability
- ↑O₂ consumption
- ↑Blood volume 40-100%
  ↑Red Blood cell mass 25%

- ↑Right to left shunt
- Thromboembolism (PE, Stroke)
- Heart failure
- ↑Physiological anemia

- Hypoxemia
- Hypotension
- ↓CO

- Acidosis
  ↑PVR
  Shock
  Respiratory failure
- ↓Blood volume
  Vasovagal reflex
- ↑Venous return

Delivery
CCHD and pregnancy

Hemodynamic changes

Pregnancy

↓SVR -10%
↑CO 30-50%
↑CO2 consumption
↑Blood volume 40-100%
↑Red Blood cell mass 25%
↑ Right to left shunt
Thromboembolism (PE, Stroke)
Heart failure
↑Physiological anemia
Hypoxemia
Hypotension
↓CO
↓Blood volume
Vasvagal reflex
↑Venous return
Acidosis
↑PVR
Shock
Respiratory failure

Clinical outcomes

Delivery

Cyanosis is an independent predictor of maternal cardiac event (OR= 2 to 6 )

Siu et al, Circulation, 2001
ZAHARA Investigators, JACC 2017 and Eur Heart J, 2010
CCHD without PH,

32% of CV complications

CCHD without PH, change in profile

No maternal characteristics were predictive of CV complications
CARPREG score=1.1 and Zahara score=2.3
Risk estimation of CV complications was 17.5 to 27%

↓CV complications 13% vs. 32%

CCHD associated with PAH

- Maternal mortality decreased in the current era, however this one remains prohibitively high
- HF is the most common complication and is particularly severe
- The highest risk of HF and mortality is during the first 4 weeks after delivery

Ladouceur et al, Heart 2016 Thomas et al, J Am H Ass 2017
## Predictive factors in PAH-CHD (group 1)

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late diagnosis and late hospital admission</td>
<td>Weill et al, JACC, 1998</td>
</tr>
<tr>
<td>Primips</td>
<td>Bedard et al, Eur Heart J, 2009</td>
</tr>
<tr>
<td>Severe PAH (sPAP&gt;50mmHg, or mPAP &gt;35mmHg )</td>
<td></td>
</tr>
<tr>
<td>Low oxygen saturation and erythrocytosis (PAH-CHD)</td>
<td>Ladouceur et al, Heart 2015</td>
</tr>
</tbody>
</table>
CCHD : common management

✓ Management of pregnancy and delivery should always be in a specialized center with multidisciplinary care

✓ Restriction of physical activity, +/- oxygen therapy and hospitalization

✓ Pros and cons of anticoagulation therapy need to be individually weighed (thromboprophylaxis with LMWH should be considered).

✓ Treatment of iron deficiency with caution

✓ Peripartum antibiotic prophylaxis?

ESC guidelines on the management of cardiovascular diseases during pregnancy Eur Heart J, (2011)
Specifically for CCHD with PAH

✓ Targeted PH therapies should be continued or started at least 3 months before delivery

✓ Delivery planning:
  • Early at 32–34/36 weeks
  • Optimal mode of delivery remains controversial
  • Anesthesia: titrated epidural anesthesia, with monitoring of haemodynamics
  • PAH control: i.v. epoprostenol immediately prior and after delivery (some centres)

✓ Multidisciplinary postpartum care
  • To reduce risk of RV failure: advanced PAH therapy, inotropes
  • Aggressive diuretics within the first 72 H

✓ After discharge, frequent clinical and echocardiographic evaluation
CCHD at last Follow-up:

- In CCHD without PAH: 13% developed chronic HF at 3.8 years of median FU

<table>
<thead>
<tr>
<th>NYHA FC</th>
<th>Before pregnancy</th>
<th>At last FU (3.8 Y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>II</td>
<td>22</td>
<td>4 + 1</td>
</tr>
<tr>
<td>III</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td></td>
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</tbody>
</table>

Systemic ventricular function:

<table>
<thead>
<tr>
<th>Function</th>
<th>Before pregnancy</th>
<th>At last FU (3.8 Y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>28</td>
<td>3</td>
</tr>
<tr>
<td>Moderately impaired</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Severely impaired</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

- In CCHD with PAH: 35% decreased in functional class and 2 died at 8.8 years of median FU (natural history of PAH?)

Ladouceur M et al, Circulation. 2017
Ladouceur et al, Heart 2016
Conclusions

• Pregnancy in patients with CCHD is a rare situation and its management should be always in specialized center

• Heart failure is the main maternal complication in this population

• However, the severity of maternal complications remains of concern in CCHD-PH and women should be counselled against pregnancy, or for early termination if pregnant.

• Thromboprophylaxis must be counterbalanced with the hemorrhagic risk

• Preventive measures are critical to avoid a life threatening infection

• Long-term outcome are characterized by a high incidence of chronic HF

• Larger prospective studies on pregnancy-related complications of patients with CCHD are needed to develop more rigorous conclusions and elucidate the impact of pregnancy on this unique patient population
What about fetuses and neonates:

- 71% live births
- Neonatal death =11%, prematurity=85% and SGA=28%
- $\text{SaO}_2 \leq 85\%$ was significantly predictive of miscarriages (OR=3.8, $p=0.04$) and SGA (OR=20.3, $p=0.002$).

<table>
<thead>
<tr>
<th>Factor</th>
<th>Category</th>
<th>Pregnancy, n</th>
<th>Live births, n (%)</th>
<th>p value</th>
<th>SGA n (%complete pregnancy)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>ToF and PA</td>
<td>14</td>
<td>13 (93)</td>
<td>0.22</td>
<td>2 (18)</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>SV</td>
<td>38</td>
<td>24 (65)</td>
<td></td>
<td>9 (36)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ccTGA</td>
<td>12</td>
<td>8 (67)</td>
<td></td>
<td>1 (12.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ebstein</td>
<td>2</td>
<td>2 (100)</td>
<td></td>
<td>1 (50)</td>
<td></td>
</tr>
<tr>
<td>Oxygen saturation, %</td>
<td>≤85</td>
<td>13</td>
<td>9 (75)</td>
<td>0.03</td>
<td>5 (83)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>85-89</td>
<td>22</td>
<td>20 (91)</td>
<td></td>
<td>1 (5.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥90</td>
<td>31</td>
<td>22 (71)</td>
<td></td>
<td>7 (44)</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin level, g/dl</td>
<td>≤16</td>
<td>27</td>
<td>17 (63)</td>
<td>0.07</td>
<td>6 (33)</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>17-19</td>
<td>5</td>
<td>4 (80)</td>
<td></td>
<td>1 (25)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥20</td>
<td>3</td>
<td>0</td>
<td></td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>