Secondary Hypertension in Pregnancy

CSIM Charlottetown 2015

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Objectives
In the context of pregnancy:

- Identify clinical cues that suggest secondary causes of hypertension
- Investigate secondary causes of hypertension
- Interpret laboratory test results such as renin, aldosterone, cortisol and catecholamine levels
Gestational hypertension and preeclampsia = 5-8 % of pregnancies

HTN = 1-5 % of pregnancies

2nd HTN = 0.25% of pregnancies

30%
Causes of secondary hypertension

**Renal:**
- Kidney disease
- Drugs

**Vascular:**
- Aortic coartation
- Renal artery stenosis

**Endocrine:**
- Primary aldosteronism
- Pheochromocytoma
- Cushing syndrome

**Obstructive Sleep Apnea**
Secondary HTN in pregnancy

Rare

1/400 of pregnancies?
Secondary HTN in pregnancy

**Why bother?**
- Associated with maternal and fetal morbidity and mortality
- Often reversible

Ideal to diagnose and treat before pregnancy
Outline

- General clinical clues

- Specific diseases:
  - Vascular disease
  - Endocrine causes
  - OSA
General clues

1- Refractory HTN: 3 + antihypertensive drugs

2- Acute elevation of BP in chronic HTN

3- Less than 30 years old and:
   - Not black
   - No family history of HTN
   - No risk factors (obesity)

4- Hypertensive crisis

5- HTN diagnosed before puberty
Vascular causes

- Coarctation of the aorta

Coarctation of the aorta with severe obstruction of blood flow to the descending thoracic aorta. The descending aorta is supplied by collaterals from the internal thoracic intercostal, subclavian, and scapular arteries.

Vascular causes

- Aortic coarctation

- ACC/AHA recommendations for screening in HTN patients:
  - BP in both arms
  - Feel both radial and femoral pulses simultaneously
  - Take popliteal BP

- Investigation: heart ultrasound
Vascular causes

Renovascular HTN

#1 cause in young adults: fibromuscular dysplasia (FMD)

Clues:

- Refractory HTN
- Abdominal or renal angle murmur

Investigation in pregnancy: renal artery duplex
Vascular causes

- Evolution of renovascular HTN in pregnancy
- Very scarce data
  - Case reports
    - Severe pre eclampsia with fetal death at 20 weeks*
    - Fetal death at 32 weeks **
- Do we miss cases?

**Sellars L. Nephron 1985; 39(3): 280-1
Endocrine causes

- Diagnosis is complex in pregnancy:
- Symptoms of endocrinopathy can resemble those of pregnancy and pregnancy related complications
- The fetoplacental unit alters endocrine functions and hormonal feedback mechanisms
Pheochromocytoma

- Affects less than 2/100,000 pregnancies
- Adrenal secreting tumor most likely to be diagnosed in pregnancy
Pheochromocytoma

Signs and symptoms:

- Classic triad: paroxystic headaches, palpitations and sweating
- Orthostatic hypotension
- Neurologic symptoms
- Weight loss
- Hyperglycemia
Pheochromocytoma

Special finding in pregnancy

Compression of tumor by uterus creating paradoxical supine HTN
# Pheochromocytoma

*Pheochromocytoma rather than preeclampsia*

<table>
<thead>
<tr>
<th>Absent</th>
<th>Present</th>
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<tbody>
<tr>
<td>Edema</td>
<td>Flushing</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>Orthostatic hypotension</td>
</tr>
<tr>
<td>hepatitis</td>
<td>Supine paroxysms</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Palpitations/tachycardia</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>Genetic syndrome: 30%</td>
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*Biggar MA. British Journal of Surgery 2013; jan(2): 182-190*
Pheochromocytoma

🎯 High mortality et morbidity.
🎯 2013 case series: de 77 pregnancies*:
  ✍️ Maternal mortality: 8% = 6= all presenting with HTN crisis
    ✍️ 2 pregnant
    ✍️ 2 during c-section
    ✍️ 2 post partum

🎯 Fetal mortality: 17%
  ✍️ 1 abortion 1st trimester
  ✍️ 8 IUFD and 2 neonatal deaths
  ✍️ 2 deaths with mothers
  ✍️ 3 babies outlived mothers

*Biggar MA. British Journal of Surgery 2013; jan(2): 182-190
Pheochromocytoma

Diagnosis:

- Urinary or plasmatic catecholamines
- Adrenal ultrasound or MRI
Primary aldosteronism

- Number 1 cause of potentially curable HTN

- Less than 50% are hypokalemic

- 3-5% of HTN in adults: under diagnosed
  - Up to 0.25% of pregnancies: where are all the cases?

- Most cases in pregnancy caused by adrenal adenoma
Primary aldosteronism

FIGURE 3. Sequential increases in plasma renin activity (mean ± SE) during normal pregnancy and at 4 to 6 weeks postpartum in a sample of 19 women. The data were normalized to postpartum.
Primary aldosteronism

- Progesterone has anti mineralo corticoid effect:
  - Potential improvement of HTN and hypokalemia

- Diagnosis is difficult:
  - Aldosterone/renin ratio might be suggestive
  - Adrenal ultrasound or MRI

- Case reports of severe HTN and severe preeclampsia
  - Cases seem very heterogeneous
Primary aldosteronism:

- Induced by pregnancy (2 cases) and menopause (1 case)
- Adrenal adenomas with new mutations: express receptors to HCG, LH and/or GNRH
Cushing’s syndrome

Cushing’s Syndrome

Adapted from Marijke Allain-Wooterloud
Cushing’s syndrome

Causes in pregnancy

Excluding iatrogenic and ectopic ACTH

<table>
<thead>
<tr>
<th>Non pregnant</th>
<th>Pregnant</th>
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<tbody>
<tr>
<td>85% ACTH dependent</td>
<td>40% ACTH dependent</td>
</tr>
<tr>
<td>15% ACTH independent</td>
<td>60% ACTH independent</td>
</tr>
<tr>
<td>Rare cases of pregnancy induced</td>
<td></td>
</tr>
</tbody>
</table>

* Malha L. Curr Hypertens Rep 2015; 17: 53
Cushing's syndrome

Central obesity
Amenorrhea
Plethora
Moon face
Acne
Personality changes: depression and mood swings
Stretch marks (purple)
Hyperglycemia (25%)
HTN (68% HTN, 14% preeclampsia)
Muscle wasting
Easy bruising
Cushing’s syndrome

Other complications in pregnancy:
- Osteoporotic fractures
- Opportunistic infections

Fetus:
- Relative protection by placental 11-beta-hydroxysteroid dehydrogenase: converts cortisol to biologically inactive cortisone
- Preterm labor > 50%, IUFD

*Kamoun M. Am J Med Sc 2014; 347(1): 64*
Cushing’s syndrome

Initial diagnosis in pregnancy

- 24 hour urine free cortisol:
  - Should be 3 to 4 times above normal superior value

- Salivary late night cortisol: more than 2-3 times above normal upper limit

- No dexamethasone suppression test: false positives
Cushing’s syndrome

Further testing in pregnancy

Adrenal imaging

High dose dexamethasone (8mg) suppression:
Not well validated

ACTH hard to interpret:
Helps if low
Obstructive Sleep Apnea (OSA)

Screening questionnaires non valid: sensitivity 35% specificity 63%*

- Who should be tested and how?

- Higher prevalence in pregnancy:
  - 8% 1st trimester et 20% third trimester**
  - Risk factors: age and obesity
  - Probable worsening of OSA in pregnancy
  - Improvement post partum

- Experts suggest treating moderate-severe cases

*Olivarez SA. Am J Obstet Gynecol 2010; 202: 552
**Pien GW. Thorax 2014; 69(4): 371
OSA in pregnancy

Association with*:  
- Gestational HTN  
- Pre eclampsia  
- Gestational diabetes  
- Fetal complications

CPAP and pregnancy**,***:  
- Improvement of maternal cardiac output  
- Improvement of fetal movement

Role in chronic HTN in pregnancy?

*Pamidi S. AJOG 2014; 210(52): 52  
** Blyton DM. Sleep 2004; 27: 79  
*** Blyton DM. Sleep 2013; 36(1):15
Conclusions

- Secondary HTN in pregnancy: rare
- Ideally: diagnosis before pregnancy
- Diagnosis of endocrine causes complex during pregnancy
Summary of secondary HTN clues in pregnancy

**General:**
- Refractory HTN
- Worsening of HTN
- Hypertensive crisis
- Before puberty
- Less than 30 yrs and:
  - No family history
  - No risk factors
  - Not black

**Specific:**
- Pheochromocytoma symptoms
- Cushing’s symptoms
- OSA symptoms
- Femoral pulse delay
- Hypokalemia
3: Causes endocriniennes

Phéochromocytome en grossesse:
- Tendance à opérer T2 ou en même temps que césarienne ou accouchement.

Conséquences sur placenta?
- Majorité des cas évoluent bien post surrénalectomie grossesse
- Cas hôpital St-Luc: opérée à 18 semaines, pré éclampsie à 28 semaines et décès du nouveau-né.

*Biggar MA. British Journal of Surgery 2013; jan(2): 182-190
3: Causes endocriniennes

- Hyperaldostéronisme: traitement en grossesse
  - Moins urgent que phéochromocytome à moins que HTA incontrôlée
  - Idéal de diagnostiquer et traiter pré grossesse

- Tx médical:
  - Méthyldopa, amiloride, labetalol, bloqueurs calciques
  - Spironolactone/eplerenone
3: Causes endocriniennes

- Cushing: Traitement en grossesse
- Selon l’étiologie et sévérité
- Traitement médical vs chirurgical
- Médicaments
  - Kétoconazole: effet anti androgène
  - Metyrapone = traitement de choix
Maladies spécifiques

1: Maladies rénales

2: Causes obstructives/anatomiques
   - coarctation aorte
   - Hypertension rénovasculaire

3: Causes endocriniennes:
   - Phéochromocytome
   - Hyperaldostéronisme
   - Cushing

4: Syndrome d’apnée hypopnées du sommeil (SAHS)