**Pheochromocytoma and pregnancy in VHL patients**

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**Pheochromocytoma** is very rare

\[ \pm 0.1-0.6\% \] in patients with hypertension in general outpatient clinics

- Pheochromocytoma is still missed: 0.05 % in autopsy studies!
- Diagnostic delay for pheochromocytoma is \( \pm 3 \) years!
- Timely and proper treatment: possible complete cure

\[ \pm 10-20\% \] in VHL patients / median age of presentation is \( \pm 25-30 \) yrs

Therefore

Early consideration of PHEO is key and this applies in particular to patients with a known genetic syndrome who may harbour a PHEO such as patients with VHL!!

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**Pheochromocytoma and pregnancy**

- Estimated prevalence: 1 in 50,000 full-term pregnancies
- Undiagnosed / untreated: \( \pm 40-50\% \) maternal and fetal mortality

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**Catecholamine physiology in pregnancy**

- Catecholamines do not cross the placental barrier and even in patients with pheochromocytoma umbilical cord blood contains < 10% of maternal catecholamine concentrations
- Fetus: high basal rate of catecholamine secretion but low circulating concentrations due to high intrauterine clearance
- Plasma and urinary catecholamine levels in healthy pregnant women are not or only slightly increased
Fetal risk of surges of released catecholamines

- transient vasoconstriction
- placental abruption
- intrauterine hypoxia

Specific factors to precipitate a pheochromocytoma crisis in pregnancy

- mechanical effects of uterus
- labor
- vaginal delivery
- tumor hemorrhage
- anesthesia
- drugs: analgesics, anti-emetics!

Pre-eclampsia | Pheochromocytoma
---|---
time of presentation of HT\(> 20\) weeks \(\text{any time}\)
paroxysmal headache\(\text{no}\) \(\text{yes}\)
orthostatic hypotension\(\text{no}\) \(10-15\%\)
dema\(\text{possible}\) \(\text{no}\)
proteinuria\(\text{yes}\) \(\text{no}\)
HELLP\(\text{possible}\) \(\text{no}\)

Adapted from Oliva et al. Hypertension 2010; 55: 620.
**Differential diagnosis** pheochromocytoma vs pre-eclampsia

- Paroxysmal hypertension
- Presentation < 20 weeks
- Paroxysmal headache
- Orthostatic hypotension
- Syndromic features
- Nausea
- Possibly present in both
- Proteinuria
- Edema
- HELLP

<table>
<thead>
<tr>
<th>pheochromocytoma</th>
<th>more likely than</th>
<th>pre-eclampsia</th>
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<td>Pre-eclampsia</td>
<td>more likely</td>
<td>Pheochromocytoma</td>
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</table>

**Biochemical testing:**

As in non-pregnant patients with metanephrines as first choice

**Sensitivity**

<table>
<thead>
<tr>
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<th>Hereditary</th>
<th>Sporadics</th>
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<tbody>
<tr>
<td>Plasma Mets</td>
<td>97 (74/76)</td>
<td>99 (137/138)</td>
</tr>
<tr>
<td>Ur. fract. Mets</td>
<td>96 (26/27)</td>
<td>97 (76/78)</td>
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**Specificity**

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<td>Ur. fract. Mets</td>
<td>82 (237/288)</td>
<td>45 (73/164)</td>
</tr>
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**Sampling conditions for metanephines**

**BLOOD**

- After 30 minutes of supine rest!!
- After fasting state (only for methoxytyramine)
- Collect in heparinized tubes on ice

**URINE (24-hours)**

- In container without additives or evt sodiumbisulphite
- Acidify urine in lab to pH 4 before storing
- Also measure creatinine excretion

**Localization of pheochromocytoma**

**Ultrasound:** rapid, readily available but insufficient sensitivity

**MRI** - first choice in pregnancy: no radiation

**CT scan:** unacceptable radiation exposure

**123I-MIBG:** unacceptable: crosses placenta
Presurgical medical treatment

10-14 days

- phenoxybenzamine: crosses the placenta; monitor for first few days (hypotension and respiratory depression)
  - < 1% into maternal milk
- or doxazosin
- ± magnesiumsulphate or calcium entry blockers
- β-adrenoceptor blockade after 1 week α-blockade
- high salt/fluid intake

Surgery

- timing: < 24 weeks or during caesarean section or post partum
- laparoscopic adrenalectomy is safe in pregnancy

Pheochromocytoma and pregnancy

- In patients with an incorrect initial diagnosis (± 30%)† 22-24%
- If diagnosed antenatally: maternal † <5%, fetal/perinatal † <15%
- biochemical diagnosis
- presurgical medical preparation
- MRI but not CT scan or 123I-MIBG scan
- optimal time for tumor resection: < 24 weeks or after delivery

Every patient with VHL disease or mutation
Every untested patient from a positive VHL family ➔ Preconceptional biochemical testing by metanephrines!!

Awareness that a patient might have a pheochromocytoma, particularly in case of known mutations, syndromic features or positive family history, is crucial

Patient ➔ think of it ➔ Midwife; physician

find it ➔ Obstetrician
Endocrinologist
Anesthesiologist
Cardiologist
Pediatrician
Radiologist

remove it

Centers with expertise