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Hotel Novotel, Amsterdam City
3-4 May 2018

Porphyria

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Rarities in Acute Care

• **Is acute care needed for porphyria? Yes!**
  - Acute porphyric attacks: abdominal pain and neuropathic symptoms.

  Life threatening, but treatable! So important to recognise

• **Is porphyria a rarity? Yes!**

  This makes it difficult to recognise...
Erasmus MC: only Dutch Porphyria reference center

www.porphryia.eu
The porphyrias:

• Inborn errors in haem biosynthesis: attacks or skin complaints due to light exposure

• Porphyrins are precursors of haem

• Haem, essential part of:
  - Haemoglobin
  - Myoglobin
  - Oxidative phosphorylation (→ ATP)
  - Catalase
  - Peroxidase
  - Cytochrome P450
↑

aminolevulinic acid (ALA) and porphobilinogen (PBG)

In liver

Symptoms!
Case: Female, 21 years of age

• Presents at emergency department with severe abdominal pain and vomiting.
  - Since 3 days, progressive
  - Tired, not well the week before
  - No stools for 3 days

• Past medical history: healthy
• Intoxications: alcohol at parties (student)
• Family history: no abnormalities
• Allergies: None
• Medication: Oral contraception since 2 months

• Physical examination:
  Blood pressure: 155/95 mmHg, Heart rate: 96/min
  BMI: 18.2 kg/m²
  Otherwise completely normal
Blood tests

- CRP 5 mg/l
- Hb, leucocytes, thrombocytes: normal.
- Na 133 mmol/l, K 3.7 mmol/l, Cl 94 mmol/l, Ca 2.33 mmol/l, albumin 41 g/l
- Urea 8.4 mmol/l, Creatinine 98 umol/l
- ASAT, ALAT, LD, AF, yGT, amylase, bilirubin, glucose: normal.
- Blood gas analysis: normal. Lactate 1.0
• Abdominal ultrasound: No abnormalities

=> “diagnosis”: Abdominal pain because of constipation and “unhealthy” eating habits.

• Admitted for four days for rehydration, pain management and laxation.

• Gastroscopy and colonoscopy: normal.
• Blood tests remained normal.
• Discharged with life style advice. But still had pain.

• Same day readmission with a seizure (stiffness of the hand and involuntary twitching of her arm).
• EEG: epileptic activity confirmed.
• MRI cerebrum: no evident abnormalities.
• Discharged 3 days later with levetiracetam (Keppra).

• She felt well for 3 months. Thereafter:
• New episode with severe abdominal pain.

• Day of admission: Unconscious and tetraplegic.

**IS THIS PORPHYRIA?**

*Yes!* PBG and ALA in Urine 30 times elevated!

• Treatment was initiated ASAP.
• It took her over 6 months to recover.
Symptoms of Acute Porphyric Attacks

Look for the “plus sings”
# Symptoms of an Acute Porphyric Attack

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>85-95%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>43-88%</td>
</tr>
<tr>
<td>Constipation</td>
<td>48-84%</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>42-60%</td>
</tr>
<tr>
<td>Psychiatric signs</td>
<td>40-58%</td>
</tr>
<tr>
<td>Pain in the extremities, head or neck</td>
<td>50-52%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>36-54%</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>28-80%</td>
</tr>
<tr>
<td>Convulsions</td>
<td>10-20%</td>
</tr>
<tr>
<td>Sensory loss</td>
<td>9-38%</td>
</tr>
<tr>
<td>Fever</td>
<td>9-37%</td>
</tr>
<tr>
<td>Paralysis</td>
<td>9-14%</td>
</tr>
<tr>
<td>Hyponatraemia</td>
<td></td>
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</tbody>
</table>

*Anderson KE et al, Annals of Internal Medicine, 2005*
Triggers of a porphyric attack

- Drugs that use CYP450: [http://www.drugs-porphyria.org](http://www.drugs-porphyria.org)
- Fasting
- Infections
- Alcohol
- Hormonal changes
- Heavy physical exercise
- Heavy smoking
- Stress?

*Everything that uses haem*
Pathogenesis of acute attacks in AIP

Latent

ALAS-N

ALAS-N

ALA

PBG

PBGD deficiency

Heme-mediated repression

Active

ALAS-N

Drugs, chemicals, steroids

Cytochrome P450

PBGD deficiency

Loss of heme repression

HO-1

Fasting

Heme

Heme

Heme
Diagnosis of an Acute Porphyric Attack

- Urine analysis (portion): **PBG and/or ALA**
- Cheap, quick and easy to perform

- If normal during an attack -> a porphyric attack is excluded

- If elevated (> 4 times): A porphyric attack is very probable
  - Treat attack first!
  - Confirm diagnosis and determine type of porphyria in specialist center
Treatment of an acute porphyric attack:

- Give carbohydrates (e.g. dextrose 10%, 2L/24 h)
- Give analgesic agents (morphine)
- Give β –blockers (propranolol)
- Treat or stop triggering factor

- If severe attack: Haeme arginate (Normosang) 250 mg iv
Counseling:

• Inheritance: autosomal dominant mutation in HMBS gene

• Attacks occur in < 10% of mutation carriers

• Age of onset of attacks: after puberty-45 years

• 80-90% female predominance

Bissell et al, NEJM; 2017
Long-term complications:

• Hypertension
• Kidney insufficiency
• Hepatocellular carcinoma (incidence similar to hepatitis C)

• Recurrent attacks
• Haem dependency with weakly transfusions
• Chronic pain and depression
• Addiction to morfin
• Severely impaired QoL

Neeleman et al, JIMD, 2018
http://porphyria.eu/

http://www.drugs-porphyria.org
QUESTIONS?