

‘Seize this pain’

Case Presentation



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Case

34 year old woman presenting with 2 weeks of severe, intensifying,
diffuse abdominal pain

Histories

Past medical history

- **Migraines**
- Rosacea

Past surgical history

- **C-section** (5 years prior to presentation)
- Wisdom teeth removal

Family history

- **Recurrent abdominal pain – father**
- Colon cancer – maternal aunt, age 31
- CAD – paternal grandmother
- Lung cancer – paternal grandmother

Social history

- Married, has a 5 yr old daughter
- Homemaker, side-business of photography
- No alcohol, smoking or illicit

Home meds

- Cyclobenzaprine (Flexeril) 10 mg TID
- Acetaminophen-hydrocodone (Vicodin) PRN

Presentation

- 2 weeks of abdominal pain - progressive, now 10/10
 - Epigastric, flanks, radiating to lower abdomen
 - Sudden and sharp shooting, but also diffuse pain at baseline
 - no particular relationship to food intake
- Low back pain, radiating to feet
- Sporadic abdominal and back pain over the past year, lasting few minutes to days
- 3 weeks prior to presentation – diagnosed with a urinary tract infection and started on trimethoprim-sulfamethoxazole
- Other symptoms on ROS – nausea, occasional emesis, decreased appetite, constipation, 5 pound weight loss since symptom onset, ?hematuria

Presentation

- Physical exam

- Temp 36.8 C, **BP 179/118 mm Hg, HR 144 bpm**, RR 18 pm, satting 100% on RA, BMI 24.7
- Young woman, dry mucous membranes, tachycardic
Abdomen: soft, non-distended, **tender to palpation all over abdomen but especially on R side**, reduced bowel sounds
- Normal neurological exam, no jaundice, no stigmata of chronic liver disease, no CVA tenderness

- Initial labs

- WBC 8.2k, Hb 12.6, Plt 286k, INR 1.1
- Na 136, K 3.7, Cl 98, CO2 24, BUN 17, Cr 0.7, glucose 98
- Alb 3.5, T.protein 7.2, T.bili 0.8, AST 28, ALT 47, Alk phos 67
- Lactate 1.4
- Amylase 54, lipase 181

NORMAL

Presentation

- Other labs

- Urinalysis: **Hazy orange color**, 1-5 WBC, 1-5 RBC, >20 SE, 1+ Bacteria.

“Substances that cause abnormal urine color may affect the readability of the reagent test strips. *Due to intense urine color, the results of the occult blood, leukocyte esterase, nitrites, glucose, urobilinogen, protein and ketones were not reported.*”

- Imaging

- CT A/P with contrast: No acute changes, underdistended colon, normal-appearing abdominal organs
- Abd US: no ovarian torsion

- Treated with IV hydromorphone (Dilaudid) and IV ondansetron (Zofran)
- Admitted to medicine floor for management of uncontrolled pain and ?UTI

Course

- Floor management: IV Dilaudid -> IV Toradol (ketorolac). IVFs for tachycardia. Repeat UA.
- 36 hours post-admission (hospital day 2 at 1:46am):
 - Husband woke up to choking sounds coming from patient, **patient unresponsive**
 - Condition A called → downgraded to C
 - Afebrile, BP 160/100 mm Hg, HR 140 bpm, RR 20 pm, satting 96% on RA
 - **Non-verbal, bilateral nystagmus, moving all limbs simultaneously -> seizure**
 - Per husband, patient was **hallucinating** earlier in day (horses on wall, shapes on ceiling)
 - Labs: notable for **Na of 117 (138 at presentation)**, other labs unchanged
- Transferred to MICU for management of hyponatremia and generalized tonic-clonic seizure
- In the MICU, remained hypertensive and tachycardic
- Labs in 4 hours: Na 110. Urine reddish orange but 0 RBCs seen.
- CT head negative, CT chest negative, EEG showed mild diffuse encephalopathy without epileptiform activities or seizures

Course

- Renal, neuro and GI teams consulted

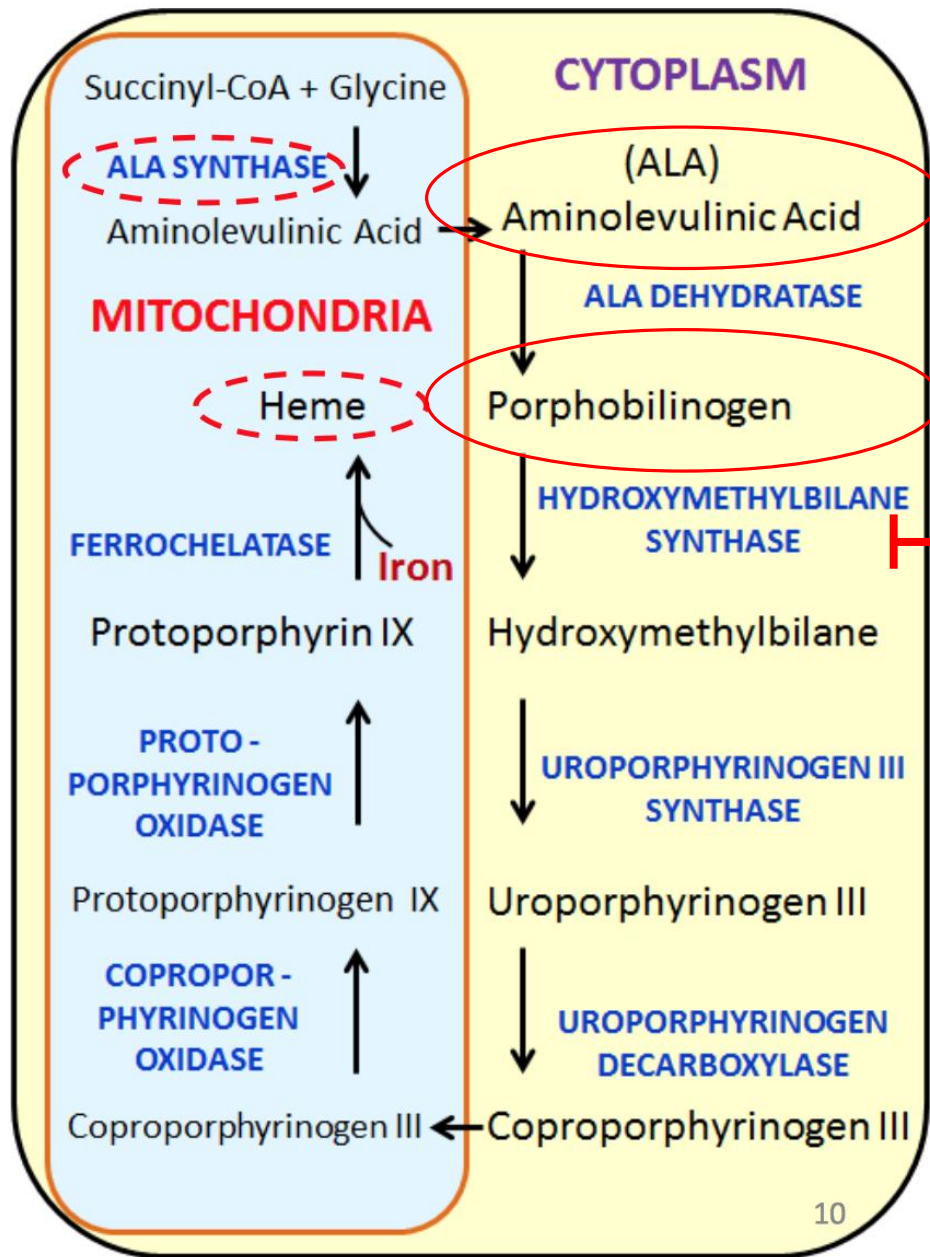
Differential Diagnosis for her abdominal pain?

Differential Diagnosis

- Cyclobenzaprine toxicity?
- Vasculitis?
- Acute Intermittent Porphyria (AIP)?

What test do you order to diagnose AIP ?

- Spot urine porphobilinogen (PBG)
- Returned at **160 mg/g creatinine (normal <2.3)**
--> **diagnostic of acute intermittent porphyria**



Acute Intermittent Porphyria (AIP)

- Acute hepatic porphyrias: metabolic disorders caused by alterations of enzyme activity in the heme biosynthesis pathway -> **AIP is the most common**
- Prevalence: 5 cases/100,000 people
- AIP
 - Caused by HMBS deficiency
 - Autosomal dominant, female predominant
 - Low penetrance: 80% of mutation carriers are asymptomatic

AIP: Clinical features

- Think **neurovisceral symptoms**
 - ✓ abdominal pain, vomiting, constipation
 - ✓ autonomic neuropathy: tachycardia, hypertension
 - ✓ peripheral neuropathy: sensory loss, weakness
- Most common electrolyte abnormality: **hyponatremia**
- **Urine appears red-brown** due to presence of porphyrins
- Over time, can lead to chronic pain

Acute intermittent porphyria incidence of signs and symptoms

Abdominal pain	85 to 95%
Vomiting	43 to 88%
Constipation	48 to 84%
Muscle weakness	42 to 60%
Psychiatric symptoms	40 to 58%
Limb, head, neck, or chest pain	50 to 52%
Hypertension	36 to 54%
Tachycardia	28 to 80%
Convulsion	10 to 20%
Sensory loss	9 to 38%
Fever	9 to 37%
Respiratory paralysis	9 to 14%
Diarrhea	5 to 12%

AIP: acute intermittent porphyria.

From Annals of Internal Medicine, Anderson KE, Bloomer JR, Bonkovsky HL, et al, Recommendations for the diagnosis and treatment of the acute porphyrias, Vol 142, Pg 439. Copyright © 2005 American College of Physicians. All Rights Reserved. Reprinted with the permission of American College of Physicians, Inc.

AIP: Triggers

- ✓ **Medications** (induce hepatic ALAS1 and hepatic cytochrome P450):
 - Barbiturates, Phenytoin, Anti-epileptics
 - Metoclopramide
 - **Sulfonamides**
- ✓ **Ethanol use**
- ✓ **Smoking**
- ✓ **Sex hormones**
 - Progesterone
 - Testosterone
- ✓ **Starvation**
- ✓ **Stress**

AIP: Management

- ✓ For mild cases (pain without paresis or hyponatremia) or until IV hematin is available, use IV dextrose (D10W, 300-400mg/day)
- ✓ IV Hematin: 3-4 mg/kg/day mixed with albumin, administered via central line (suppresses ALAS1)
- ✓ New FDA-approved therapy (Nov 20, 2019): **givosiran**
- ✓ Narcotics for pain, chlorpromazine for nausea/vomiting
- ✓ Genetic testing for family

AIP: Management

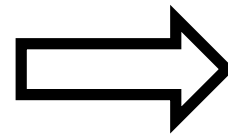
- ✓ Refer to **hematologist**: usually takes charge of hematin infusions
- ✓ Refer to **hepatologist**:
 - Persistent elevations in AST, ALT
 - HCC surveillance: **risk of HCC** (upto 27%), even without cirrhosis¹
 - Liver Transplantation: may be an option, especially for severely affected patients without advanced motor neuropathy

1. Review of hepatocellular cancer, hypertension and renal impairment as late complications of acute porphyria and recommendations for patient follow-up. Stewart MF, J Clin Pathol. 2012 Nov;65(11):976-80. Epub 2012 Jul 31.

AIP: Our patient

- ✓ Started on **IV hematin infusions**, gradual resolution of pain and autonomic symptoms
- ✓ Initially, for tachycardia, started on a **beta-blocker**
- ✓ For hyponatremia, **3% hypertonic saline** and **DDAVP**, then transitioned to urea with fluid restriction
- ✓ At home, instructed to **increase carbohydrate intake** if she developed mild symptoms, and present to the ER for IV hematin if symptoms persisted
- ✓ Genetic testing performed, has an HMBS mutation
- ✓ Following with hematology – plan is for annual ultrasound, AFP, LFTs for monitoring for liver damage/HCC screening

Take-home message



**Spot urine PBG
(porphobilinogen)**

- Send out to Quest/Mayo Clinic
- Protect sample from light and heat

Quiz question

- How did 'porphyria' get its name?
- From the Greek word '*porphyrus*', which means '*purple*'



Thank you

Urine in acute intermittent porphyria



Photograph of urine from a normal subject (left) and a subject with acute intermittent porphyria (middle). The colors are compared with a dilute aqueous solution of red wine (right).

AIP: acute intermittant porphyria

Provided by Shigeru Sassa, MD, PhD.

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