Acute Intermittent Porphyria

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Introduction

Abdominal pain is one of the most common reasons for a visit to the emergency department. Most of the time, clinicians are able to diagnose a cause of the pain from the patient's history & physical as well as routine lab work & imaging. However, a variety of systemic & extra-abdominal diseases can cause symptoms within the abdomen. When there is no obvious answer, patients are many times labeled as "functional pain."[1] This case report highlights a rare cause of abdominal pain of metabolic origin.

Case Presentation

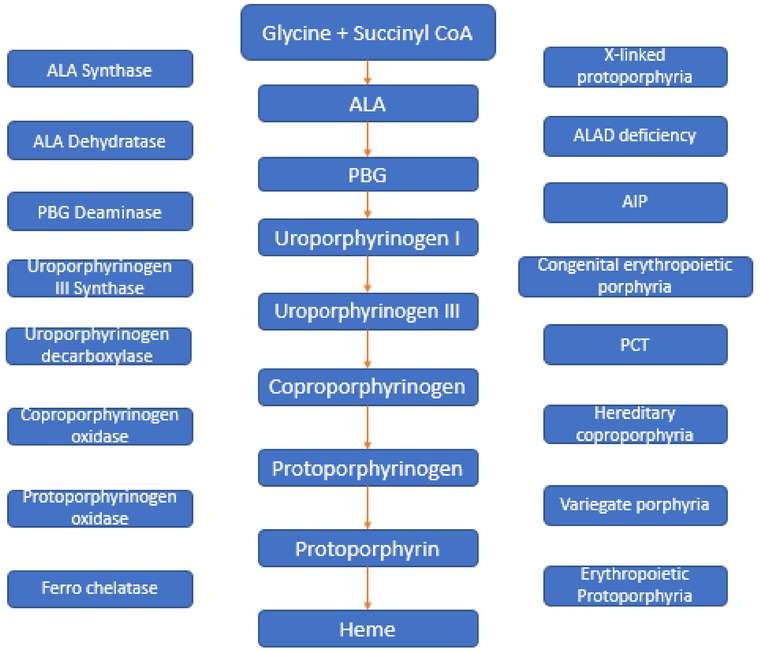
An 18-year old female with no past medical history presented to the hospital with an episode of severe abdominal pain, associated with nausea and vomiting. She had intermittent episodes of similar complaints in the past two years, and attacks usually occurred one week prior to her menses. The patient thought the pain was secondary to her menstrual cycle, and treated these episodes with Acetaminophen & NSAIDs.

She was seen one year ago by her primary care physician, who suspected that she had possible celiac disease and placed her on a gluten-free diet. However, her symptoms did not improve with gluten avoidance. She had also undergone an ultrasound, which did not reveal any cholelithiasis. A few months ago, she was admitted the hospital for similar complaints, and underwent both an upper endoscopy and colonoscopy, both of which were unremarkable, with biopsies negative for Helicobacter pylori & Celiac disease. She was discharged from the hospital at that time with a presumptive diagnosis of functional abdominal pain by the gastroenterology team. She was given Dicyclomine as needed for pain.

On this admission, she was afebrile & hypertensive to 170/90. Additional review of systems included intermittent tingling at her fingertips, which she noticed more frequently. Her father also mentioned that she was extremely anxious and appeared depressed lately. She had no prior diagnosis of anxiety or depression. Labs were notable for a sodium of 126 mmol/L. Imaging, including a CT of her abdomen/pelvis as well as an MR Enterography, were unremarkable. The young patient continued to have pain despite opiate analgesics, which prompted the search for more rare etiologies of abdominal pain.

Given her constellation of vague abdominal pain, neuropsychiatric symptoms & hyponatremia, initial labs to rule out Porphyrias were ordered. Her plasma total porphyrins were 20.1mcg/L (normal 1.0 – 5.6 mcg/L), urine porphobilinogen random was 76 mg/g creat (normal <0.22 mg/g creat) and random quantitative urine porphyrins were extremely elevated.

Her Porphobilinogen Deaminase (PBGD) level was diminished to 5.7 nmol/L/sec (normal ≥7) and was found to have a PBGD mutation. She was diagnosed with Acute Intermittent Porphyria. She was treated with hemin infusions with mild improvement in her symptoms, and oral glucose loading at onset of symptoms. However, her symptoms eventually came back, and she was initiated on monthly Givosiran.



Discussion

The porphyrias are a group of diseases that result from deficiencies of enzymes involved in the heme synthesis pathway. They are divided into two main groups, the cutaneous porphyrias and the acute porphyrias. The cutaneous porphyrias result from the over-production of photosensitizing porphyrins and typically result in skin lesions. The acute porphyrias are secondary to hepatic over-production of porphyrin precursors and may result in potentially life-threatening neurological symptoms.[2]

The four acute porphyrias (acute intermittent porphyria, ALA dehydratase deficiency, hereditary coproporphyria, variegate porphyria) vary in signs & symptoms. Abdominal pain is present in approximately 90%, and dark urine in about 80%. Other features include constipation, paresthesia, nausea, vomiting, hypertension & even ascending paralysis and quadriplegia. Psychiatric features can include depression, confusion, psychosis & even seizures. Hyponatremia is a more common electrolyte abnormality, and is secondary to SIADH. [2]

Acute intermittent porphyria (AIP) is characterized by an accumulation of the neurotoxic heme intermediates, aminolevulinic acid (ALA) & porphobilinogen (PBG).[2] AIP results from a mutation of the porphobilinogen deaminase enzyme and is passed down in an autosomal dominant fashion. Although it is passed down in an autosomal dominant pattern, only approximately 10% of carriers will experience an acute porphyric episode. For this reason, it is difficult to accurately determine the prevalence of the disorder.

During acute porphyric episodes, levels of porphyrins are often greatly elevated. The measurement of urine or serum PBG and ALA over 24 hours may confirm the diagnosis. High levels of PBG may discolor the urine, leading to an amber colored urine that fluoresces under UV light.

The treatment of AIP is mainly supportive. Maintaining a high carbohydrate diet and abstaining from alcohol & smoking are lifestyle changes that can help prevent subsequent acute episodes. There is also a drug database that clinicians can consult, in order to prevent the use of "porphyrinogenic" drugs.

Givosiran is a small interfering RNA (siRNA) directed towards ALAS1, an important enzyme in heme production, and can help reduce the frequency of porphyric attacks.
Patients over age 50 with acute porphyria should be screened for HCC every 6 months.

Conclusion

Abdominal pain is one of the most common reasons for a gastroenterology consult. Acute Intermittent Porphyria is a rare but important disease with an often-delayed diagnosis or missed altogether given its rarity. It is important for physicians to have a high level of suspicion to rule out AIP in patients with suggestive historical findings.

References

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2) Puy H, Gouya L, Deybach JC: Porphyrias. Lancet 2010; 375(9718):924-937