JOURNAL OF COMMUNITY HOSPITAL INTERNAL MEDICINE PERSPECTIVES, 2017
VOL. 7, NO. 2, 100–102
https://doi.org/10.1080/20009666.2017.1317535

Taylor & Francis
Taylor & Francis Group

CASE REPORT

Acute intermittent porphyria: a test of clinical acumen

Rashmi Dhital[a], Sijan Basnet [b], Dilli Ram Poudel [b] and Khema Raj Bhusal [c]

[a]Department of Internal Medicine, Universal College Of Medical Sciences, Bhairahawa, Nepal; [b]Department of Internal Medicine, Reading Health System, West Reading, PA, USA; [c]Department of Internal Medicine, Manmohan Memorial Medical College, Kathmandu, Nepal

ABSTRACT

Acute intermittent porphyria (AIP) is a rare autosomal dominant hepatic porphyria due to deficiency of hydroxymethylbilane synthase (HMBS), also known as porphobilinogen deaminase leading to accumulation of porphyrin precursors. However, gene defect alone is usually not sufficient to cause an acute attack, and many extrinsic factors play a role. Diagnostic tests are defined, but clinical suspicion is often delayed as symptoms mimic other common conditions. We report a case of a 18-year-old male with severe, persistent, and generalized abdominal pain along with marked hyponatremia, with subsequent development of altered mentation needing intensive care. He improved after infusion of intravenous dextrose. AIP can mimic many common surgical and medical conditions such as appendicitis, cholecystitis, pancreatitis, etc., and may lead to extensive diagnostics or surgical intervention if missed. Diagnosis of AIP requires high clinical suspicion. It should be considered in a patient with recurrent abdominal symptoms, intractable hyponatremia, along with neurological manifestations. Early diagnosis and treatment can prevent recurrent episodes and can potentially be lifesaving.

Abbreviations: AIP: Acute intermittent porphyria; ALA: Aminolevulinic acid; PBG: Porphobilinogen

ARTICLE HISTORY
Received 27 January 2017
Accepted 4 April 2017

KEYWORDS
Acute intermittent porphyria; porphyria; clinical acumen

1. Introduction

Acute intermittent porphyria (AIP) is an inherited metabolic disease with a prevalence of symptomatic disease in 1–2 per 100 000 [1,2]. It is an autosomal dominant hepatic porphyria characterized by a partial deficiency of hydroxymethylbilane synthase (HMBS), also known as porphobilinogen deaminase, an enzyme involved in heme biosynthesis [1,3]. Deficiency of HMBS results in accumulation of upstream products like delta-aminolevulinic acid (ALA) and porphobilinogen (PBG). The accumulation of these products is amplified by certain medications, alcohol, infections, low caloric intake, or hormonal imbalances during menstrual cycle and pregnancy [1]. Although the deficient enzyme and accumulated metabolites are easily detectable, diagnosis is often unsuspected because it is rare and can mimic many other common conditions [4]. Here we present a case of 18-year-old male with recurrent attacks of undiagnosed abdominal pain.

2. Case story

An 18-year-old Nepali male presented to the emergency department (ED) with severe, persistent and generalized abdominal pain for five days. At times, the pain was severe enough to require multiple doses of morphine. He also complained of severe, intermittent cramping pain in all of his limbs. In addition to that, he had a 10-day history of pain at the tip of the penis along with burning micturition.

The patient had similar episodes of acute pain at three instances in the past, at the ages of 10, 13, and 17 years. Each time, he was hospitalized with no clear diagnosis to explain his pain. He, however, could temporally relate those episodes to fasting and inadequate caloric intake. Treatment consisted of repeated high doses of analgesics. He had no known history of other medical conditions. He denied use of alcohol or any recreational drugs. He had no family history of similar symptomatology.

At presentation, he was hypertensive (160/110 mmHg), tachypneic (20 breaths/min) and tachycardic (105/min) but afebrile. He was anxious and was clutching his abdomen. Abdomen was nontender and without guarding or rigidity. No organomegaly was noted. Extremities were not swollen or tender. There was no motor weakness. On examination of skin there was no blistering, scarring, or erythema. Genital exam was noncontributory (no urethral discharge or ulcers).

Diagnostic lab tests were significant for a sodium level of 106 mEq/L. He was admitted to the intensive care unit and hypertonic saline was started for treatment of hyponatremia. Urinalysis revealed 10–12 white blood cells per high power field. Ceftriaxone

CONTACT Rashmi Dhital rashmi046@gmail.com Department of Internal Medicine, Universal College of Medical Sciences, Bhairahawa, Nepal

was initiated empirically pending culture and sensitivities. Renal and liver function tests were normal. An abdominal-pelvic computed tomography (CT) with intravenous contrast did not reveal any potential cause of his pain. He received multiple high doses of analgesics without much relief, up to 5 mg morphine every four hours. He was persistently hypertensive with repeat blood pressure measurements of 166/106 mmHg and 160/100 mmHg the next day. He was started on propranolol for high blood pressure and tachycardia.

On the following day, he developed altered mentation in the form of fluctuating levels of orientation, agitation, irritability, confusion, and visual hallucination (seeing animals) in the ICU. These neuropsychiatric manifestations were not reported in prior attacks. Lumbar puncture done to rule out meningoencephalitis was normal. Head computed tomography (CT) and magnetic resonance imaging (MRI) were both normal for acute or chronic changes. Alprazolam was started for anxiety, and chlorpromazine was initiated for hallucination and psychotic features. Sodium level remained low at 112 mEq/L even with hypertonic saline treatment.

At this point, acute intermittent porphyria (AIP) was suspected and urine was sent for porphobilinogen (PBG) and delta-aminolevulinic acid (ALA). Urine from this sample was noticed to be cola colored in the lab. The results of urine PBG and ALA results came back positive - about 20 times elevated (PBG: 90 mg/24 hours and ALA 68 mg/24 hours; normal levels: PBG: 4 mg/24 hours; ALA: 0–7 mg/24 hours). Diagnosis of acute porphyria (attack) was made. The patient was treated with glucose loading of 10% dextrose followed by maintenance. Intravenous hematin was not used due to unavailability and prohibitive costs.

Three weeks later, the patient was discharged in good condition and counselled to avoid fasting, stress, alcohol, and smoking, and to take an adequate carbohydrate containing diet. He was also given a list of drugs to avoid and was advised to wear a medical alert bracelet notifying that he was a porphyria patient.

3. Discussion

Even though AIP is an autosomal dominant (AD) condition, our patient did not have a positive family history. Almost 90% of patients who inherit this disorder remain asymptomatic for lifetime [5]. This could be explained by the fact that the gene responsible for AIP has an incomplete penetrance so that the disease often exists in a latent form (i.e., without clinical or biochemical manifestations) and family history may not be imminent [6]. The onset of symptoms usually occurs in adolescence, with females being more affected than males [7]. However, our patient was an adolescent male, with an onset of symptoms since childhood. The attack of acute porphyria in our patient was probably precipitated by urinary tract infection. Infection is attributable to precipitation of acute attack in as high as 29% cases [8]. His three prior episodes were supposedly triggered by fasting. Fasting and inadequate carbohydrate intake have been shown to precipitate acute porphyria attack in as many as 12% of cases [8].

Elevated PBG (precursor of porphyrin) in urine is highly sensitive and specific for acute (attack of) porphyrias (AIP, hereditary coproporphyria, and variegate porphyria). In an appropriate clinical scenario (e.g., unexplained abdominal pain and vomiting) qualitative positive PBG urine screen is enough to initiate treatment without confirming the type. However, a much better test is to measure the 24-hour or even spot urine total PBG. The cornerstone of management of acute attack of porphyria includes intravenous hemin along with avoidance of contraindicated drugs and other precipitants, and administration of high dose opiates for pain management [9,10]. However, hemin is not available and the cost of procurement is very high in developing nations like Nepal [11]. Our patient received only IV glucose in addition to symptomatic management. For diagnosing specific type of acute porphyria, plasma and stool samples should preferably be collected before initiating the therapy. Confirmatory tests for AIP are plasma and stool porphyrins which are usually normal and plasma fluorescence emission spectroscopy may demonstrate an emission peak at 620 nm. Unlike other types of acute porphyrias, AIP does not have cutaneous manifestations [9,10].

Even though genetic testing is considered as the 'gold standard' for diagnosis and screening in families, it could not be performed in our patient due to similar financial and logistic reasons as above.

Early clinical recognition is crucial for patients with acute neurovisceral attacks. The diagnosis is often delayed by many years and has been reported to be as long as a mean of 15 years [12]. Our patient was diagnosed at least 10 years after his first clinical attack. The invaluable clues to correct diagnosis are gastrointestinal symptoms (acute abdominal pain in 85–90% of attacks), severe intractable hyponatremia and orange colored urine on exposure to light, in association with neurologic symptoms [13,14], and all of these were present in our patient.

Neurological manifestations are probably due to the neurotoxic effects of porphyrin precursors, ALA being the most significant. Abdominal pain is a sign of autonomic neuropathy, due to splanchnic dysfunction such as intestinal dilatation or spasm [15].

In AIP, pathophysiology of hyponatremia is only partly understood and can be associated with the

syndrome of inappropriate antidiuretic hormone secretion, also contributed to by gastrointestinal or renal sodium loss [13]. In contrast to cutaneous porphyrias, AIP patients are not photosensitive due to absence of porphyrin accumulation [16].

4. Conclusion

AIP is a mimic of many common surgical and medical conditions like appendicitis, cholecystitis, pancreatitis etc., and may result in extensive diagnostics or surgical intervention if missed. Diagnosis of AIP requires high clinical suspicion. It should be considered in a patient with recurrent abdominal symptoms, intractable hyponatremia, along with neurological manifestations. Early diagnosis can prevent recurrent episodes and can be potentially lifesaving.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

Sijan Basnet http://orcid.org/0000-0002-8324-2827
Dilli Ram Poudel http://orcid.org/0000-0003-2350-719X
Khema Raj Bhusal http://orcid.org/0000-0003-0813-2019

References

[1] Pischik E, Kauppinen R. An update of clinical management of acute intermittent porphyria. Appl Clin Genet. 2015 September;201: DOI:10.2147/TACG.S48605
[2] Herrick AL, McColl KEL. Acute intermittent porphyria. Best Pract Res Clin Gastroenterol. 2005;19(2):235–249. DOI:10.1016/j.bpg.2004.10.006
[3] Besur S, Schmeltzer P, Bonkovsky HL. Acute porphyrias. J Emerg Med. 2015;49(3):305–312. DOI:10.1016/j.jemermed.2015.04.034
[4] Ventura P, Cappellini MD, Biolcati G, et al. A challenging diagnosis for potential fatal diseases: recommendations for diagnosing acute porphyrias. Eur J Intern Med. 2014;25(6):497–505. DOI:10.1016/j.ejim.2014.03.011
[5] Sykes RM. Acute intermittent porphyria, seizures, and antiepileptic drugs: a report on a 3-year-old Nigerian boy. Seizure. 2001;10(1):64–66. DOI:10.1053/seiz.2000.0473
[6] Whatley SD, Badminton MN. Acute intermittent porphyria. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews(®). Seattle (WA): University of Washington, Seattle;1993. [cited 2016 Aug 10]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1193/
[7] Stein JA, Tschudy DP. Acute intermittent porphyria. A clinical and biochemical study of 46 patients. Medicine (Baltimore). 1970;49(1):1–16.
[8] Kauppinen RMD, Mustajoki PMD. Prognosis of acute prophyria: occurrence of acute attacks, precipitating factors, and associated diseases. Medicine (Baltimore). 1992;71(1):1–13.
[9] AIP, HCP, VP & ADP. American Porphyria Foundation. 2009. Mar 13. [cited 2017 Mar 26]. Available from: http://www.porphyriafoundation.com/for-healthcare-professionals/types-of-porphyria/AIP
[10] Stein PE, Badminton MN, Rees DC. Update review of the acute porphyrias. Br J Haematol. 2017;176(4):527–538. DOI:10.1111/bjh.14459
[11] Dosi R, Ambaliya A, Patell R, et al. Challenges in the diagnosis and treatment of a case of acute intermittent porphyria in India. J Postgrad Med. 2013;59(3):241. DOI:10.4103/0022-3859.118056
[12] Bonkovsky HL, Maddukuri VC, Yazici C, et al. Acute porphyrias in the USA: features of 108 subjects from porphyrias consortium. Am J Med. 2014;127(12):1233–1241. DOI:10.1016/j.amjmed.2014.06.036
[13] Straume Z, Skuja V, Proskurina A, et al. Think porphyria: case report and review of literature. Exp Clin Gastroenterol. 2015;7:69–77.
[14] Anderson KE, Bloomer JR, Bonkovsky HL, et al. Recommendations for the diagnosis and treatment of the acute porphyrias. Ann Intern Med. 2005;142(6):439–450.
[15] Pischik E, Kauppinen R. Neurological manifestations of acute intermittent porphyria. Cell Mol Biol Noisy–Gd Fr. 2009;55(1):72–83.
[16] Wetterberg L, Thunell S, Zetterlund P. Why is the patient with acute intermittent porphyria not light sensitive? Acta Derm Venereol Suppl (Stockh). 1982;100:73–74.