Acute Intermittent Porphyria: A Diagnostic Challenge for Endocrinologist

Tao Yuan, Yu-Hui Li, Xi Wang, Feng-Ying Gong, Xue-Yan Wu, Yong Fu, Wei-Gang Zhao

Department of Endocrinology, Key Laboratory of Endocrinology, The Ministry of Health, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing 100730, China

Key words: Acute Intermittent Porphyria; Hydroxymethylbilane Synthase Gene; Hyponatremia; Syndrome of Inappropriate Antidiuretic Hormone Secretion

Introduction

Acute intermittent porphyria (AIP) is an autosomal dominant inborn error of metabolism caused by deficiency of porphobilinogen (PBG) deaminase, also known as hydroxymethylbilane synthase (HMBS), the third enzyme in the heme biosynthetic pathway. The clinical features of AIP are attributed to heme depletion and accumulation of heme intermediates PBG and aminolevulinic acid (ALA), proximal to the defect.[1] Multiple organ systems can be affected in patients with AIP. The typical porphyria attacks are characterized by gastrointestinal symptoms, sympathetic overactivity, neurologic manifestations, and psychological symptoms. Most of the patients suffered from the typical symptoms of AIP were adult females. We reported an adult male patient diagnosed as AIP by finding a mutation in the HMBS gene after recurrent abdominal pain for 10 years.

Case Report

A 45-year-old male patient was hospitalized in the Endocrinology Department because of "recurrent abdominal pain for 10 years" in November 2013. He experienced lower abdomen pain, nausea, vomiting, and constipation 10 years ago. He was operated after diagnosed as "intestinal obstruction", but the reason of intestinal obstruction was not known. In the next decade, there were several attacks similar to the first onset of abdominal pain, usually induced by eating a lot of food not easily been digested or drinking alcohol. He was treated as intestinal obstruction with the supportive treatment every time. In February 2012, he experienced recurrent urinary retention after onset of intestinal obstruction, irritability, hallucinations and delirium, lower limbs muscle pain, weakness, and hyponatremia. After supplement of sodium, the symptoms of hallucinations and delirium disappeared. In September 2013, he had abdominal pain, nausea, vomit, and the serum potassium was normal, sodium was 119.7 mmol/L, chloride was 87.3 mmol/L. He subsequently developed dark-colored urine without excretion of stone, lower limbs muscle pain, fatigue, sleepiness, and illusion. He had increased urinary sodium (the excretion of sodium in urine was 257.09 mmol/24 h) at the same of hyponatremia. Chest computed tomography scan was normal. Electromyography showed the nerve conduction velocity of the right nervus peroneus communis was decreased. The patient was treated with restriction of the intake of water and supplement of sodium by oral. Serum sodium was gradually returned to normal. He had smoked and drunk for 20 years. There was no family history. Physical examination revealed normal in vital signs. There was no attack of abdominal pain and neurological symptoms when he was admitted in our hospital. The serum and urine electrolytes analysis, plasma hormone levels of thyroxine and cortical were all in normal range. The dark-colored urine and the patient's symptoms raised the possibility of AIP. We collected the dark-yellow color urine he urinated in our hospital although there was no attack of abdominal pain or hyponatremia. The urine turned to dark-red color after 2 h sunshine. Random urine PBG was positive. Genomic DNA was extracted from peripheral white blood cells, and all the 15 exons of HMBS gene were amplified. Sequencing of the HMBS gene was positive for a missense mutation G>A in exon 9 of HMBS, R173Q (CM900131) confirming the diagnosis of AIP. A targeted mutation testing was recommended to the children of the patients.

Discussion

The overall prevalence of clinically manifest AIP is estimated to be 50–500/million. The disease manifests typically in adult

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.160621

Address for correspondence: Prof. Wei-Gang Zhao, Department of Endocrinology, Key Laboratory of Endocrinology, The Ministry of Health, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences. Beijing 100730, China
E-Mail: xiehezhaoweigang@163.com

women in their second through fourth decades of life. The attacks are often linked to menstrual cycles, highlighting the importance of endogenous steroids, especially progesterone, in pathogenesis.[2] The most common presenting is severe abdominal pain, nausea, vomiting, diarrhea, or constipation. Neurologic symptoms may also develop, including flaccid paralysis, seizures, neuropsychiatric and urinary symptoms such as retention or incontinence and constipation. Many patients report passing red to brown urine that may darken when exposed to air, light and warmth. Such findings should alert clinicians to consider the diagnosis of acute porphyria. Hyponatremia is a common electrolyte abnormality that occurs during acute attacks. Factors that contribute to hyponatremia include syndrome of inappropriate antidiuretic hormone secretion, vomiting and resuscitation with high volumes of dextrose solutions given intravenously.[3] Our patient had the typical gastrointestinal and neurologic symptoms of AIP attacks, but he was diagnosed as intestinal obstruction with unknown reason for 10 years. It means that for those intestinal obstruction patients with unknown reasons, we should consider the possibility of rare diseases such as AIP especially when he has red to brown urine.

Acute intermittent porphyria can be precipitated by conditions that increase hepatic heme synthesis such as medications, stress, starvation, severe illness, infection, surgery, smoking, and alcohol. The trigger factor of abdominal pain may be smoking and alcohol in our patient. The patient can be diagnosed by increased PBG or ALA excretion in urine. DNA analysis is recommended after clinical diagnosis of AIP to aid in genetic counseling so that asymptomatic family members who are carriers can be identified. It allows for early diagnosis and appropriate management in order to avoid or minimize disease complications. Until, more than 385 different mutations in the HMBS gene have been reported. There were no phenotype-genotype relationships reported in literature. Our patient had the R173Q missense mutation of HMBS gene, which has been reported in other literatures.[4,5] For the therapy of AIP, the patients should be treated with a high carbohydrate intake (at least 300 g/d), especially when the patient is fasting. Patients with nausea and/or vomiting will need to receive dextrose with sodium and potassium intravenously, and fluid requirement will vary from patient to patient. Thus, it is vital to frequently monitor electrolytes. Changes in the rate and type of intravenous fluid administered should be made based on electrolyte values.[2] In conclusion, AIP is extremely rare among adult men. We report this case to emphasize the clinical presentations of AIP including concomitant underlying gastrointestinal disorders and electrolytes imbalance (especially hyponatremia) that can confound the diagnosis.

References

1. Anyaegbu E, Goodman M, Ahn SY, Thangarajh M, Wong M, Shinawi M. Acute intermittent porphyria: A diagnostic challenge. J Child Neurol 2012;27:917-21.
2. Besur S, Hou W, Schmeltzer P, Bonkovsky HL. Clinically important features of porphyrin and heme metabolism and the porphyrias. Metabolites 2014;4:977-1006.
3. Bloomer JR, Bonkovsky HL. The porphyrias. Dis Mon 1989;35:1-54.
4. Schneider-Yin X, Hergersberg M, Schuurmans MM, Gregor A, Minder EI. Mutation hotspots in the human porphobilinogen deaminase gene: Recurrent mutations G111R and R173Q occurring at CpG motifs. J Inherit Metab Dis 2004;27:625-31.
5. Puy H, Gouya L, Deybach JC. Porphyrias. Lancet 2010;375:924-37.

Received: 08-01-2015 **Edited by:** Ya-Lin Bao

How to cite this article: Yuan T, Li YH, Wang X, Gong FY, Wu XY, Fu Y, *et al*. Acute Intermittent Porphyria: A Diagnostic Challenge for Endocrinologist. Chin Med J 2015;128:1980-1.

Source of Support: Nil. **Conflict of Interest:** None declared.