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*Case Report*

# Clinical Manifestations and Diagnostic Dilemma in Acute Intermittent Porphyria

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## ABSTRACT

Acute intermittent porphyria (AIP) is an autosomal dominant inborn error of heme synthesis typically present in adulthood most often in women in reproductive age group. Porphyria is relatively an uncommon condition and it should be considered in patient presenting with a typical medical, psychiatric and surgical history. Paucity in clinical recognition of porphyria often leads to misdiagnosis, delay in diagnosis and subsequently treatment. Also, signs and symptoms mimic other medical and surgical conditions. The most common porphyria is acute intermittent porphyria. Awareness of porphyria along with the correct diagnostic tests in porphyria could help a long way to overcome the formidable challenges of porphyric patients. Here is a case of 21 years old woman who presented with seizures and abdominal pain treated with antiepileptic drugs initially but later diagnosis as acute intermittent porphyria. This highlights the need for investigation of porphyria in patient with acute abdomen, psychiatric or neurological symptoms.

**Key words:** Acute Intermittent Porphyria, Epileptic Seizures, Acute Abdomen Pain

## INTRODUCTION

Acute intermittent porphyria (AIP) is a rare hereditary disorder of porphyrin metabolism typically present in adulthood most often in women in reproductive age group. [1] It is characterised by episodes of severe abdominal pain, rapidly progressive flaccid paralysis and passage of excess amounts of porphobilinogen (PBG) in urine. [2] There are limited reports on clinical presentation of AIP. Acute abdominal pain is the most common presenting symptom and seizures may precede the diagnosis of AIP. Besides there could be nausea, vomiting, constipation followed by hyponatremia, weakness and neuropathy. Acute intermittent porphyria is due to porphobilinogen deaminase (hydroxymethylbilane synthase) mutation which results in half normal activity. This

discrepancy predisposes heterozygotes patient to the life threatening acute neurovisceral attack that are precipitated by several factors including porphyrinogenic drugs (cyt p450 inducer), alcohol, stress and prolonged fasting. The enzyme deficiency results in excessive accumulation of neurotoxic porphyrin precursor (ALA and PBG). They act in the central and peripheral nervous system to produce acute neurovisceral and psychiatric manifestations.

Ten to twenty percent of all AIP heterozygotes experience AIP attack while the remaining is clinically asymptomatic throughout their life. [3,4] Acute intermittent porphyria is precipitated by drugs like barbiturates, Phenytoin, sulfonamides, acute infections and over-indulgence of alcohol. The clinical picture is dominated by

gastrointestinal and neurological manifestations.

### **CASE REPORT**

Our case was a 21 year old unmarried woman from Thiruvananthapuram, Kerala, India who was brought to the emergency department of our hospital with seizures. The first episode occurred at 2:30am on the day of admission. She had up rolling of eyes, stiffening of limbs, tongue bite and frothing from mouth. Prior to admission in our hospital she went to a nearby private hospital where she was treated with diazepam and phenytoin. She had a second episode of seizure and then brought to our hospital and got admitted in the emergency department. One week prior to admission she had fever, cough, which responded well to medication. She had vomiting for a few days and was nonbilious. Acute abdominal pain started one day prior to admission.

One year back she had a similar episode of seizures which was attributed to hyponatremia when she was treated for Dengue fever. She was given antiepileptic for short duration. Since then she used to get regular attacks of abdominal pain especially during menstruation. There is no family history of seizure or neurological disorder and she is from a non consanguineous marriage. Developmental milestone and scholastic performance was normal. Menarche was at the age of 15 years and she had regular periods with menorrhagia.

On general physical examination she appeared drowsy and non responsive to commands. Her heart rate was 102 beats/minute, BP 140/90 mm to Hg, temperature 98.6F and respiratory rate 18 breaths /minute. There was no neck stiffness or focal neurological deficits.

In routine investigations complete blood count was normal except for mild thrombocytopenia. Hb was 12.3 g%, Total leucocytes count 5,600/cumm and Platelet count 1.31 lakhs/cumm. Result of LFT, RFT, CRP was normal. Serum sodium was low at 108mmol/L. Serum K<sup>+</sup> normal. Thyroid Function Test shows low T<sub>3</sub>, low

TSH with normal T<sub>4</sub> which could represent sick Euthyroid state. USG abdomen, MRI of brain and EEG have been reported as normal.

The patient was admitted under neurology since she presented with seizures. Hypertonic saline was administered to correct hyponatremia along with anti epileptic drugs. Internal medicine department was involved at this point of time for the evaluation of hyponatremia. Due to recurrent hyponatremia seizures and abdominal pain in a woman of reproductive age group AIP was considered as a possibility which could have been missed in the earlier episodes. Since her urine screening for PBG was positive phenytoin was stopped as it is unsafe in AIP patient. 24hr urine PBG was 30.78mg/24hrs as against normal 1.7mg/24hrs. Intravenous hemin was not available so she was treated with carbohydrate load using 10% Dextrose drip & oral glucose. After an initial improvement she developed abdominal pain, hyponatremia and urine incontinence (autonomic neuropathy) which could be probably due to the phenytoin she received earlier.

Our case highlights the importance of suspecting AIP in patients with seizure, hyponatremia, abdomen pain especially in the post pubertal female age group to avoid misdiagnosis, delay in diagnosis and treatment and avoid potentially unsafe drugs to AIP patients.

Treatment of acute attacks involves analgesics for abdominal pain, control of seizures using safe antiepileptic and withdrawal of inciting agent. Intravenous hemin during the attack in most of the times. Dosage is 4mg/Kg once or twice daily. But its availability is a concern. Carbohydrate loading can also be tried in acute attack. A minimum of 300gm carbohydrate per day should be provided orally or intravenously. Electrolyte balance requires close attention.

## **DISCUSSION**

Porphyria is a relatively uncommon condition and it should be suspected in patients presenting with atypical medical, psychiatric, or surgical history.

Paucity of clinical recognition of porphyria often delays diagnosis and consequently treatment. Also, signs and symptoms mimic other common medical and surgical conditions. Hence awareness of porphyria along with proper and accurate diagnostic tests in conjunction could be of great boon to surpass the formidable challenges put forth by porphyric patients. Inappropriateness in diagnosis might result even in death of the patient. <sup>[3,5]</sup>

Acute intermittent porphyria is dominantly inherited and characterized by the half-normal activity of porphobilinogen deaminase. According to clinical features porphyria are broadly classified into neuropsychiatric, dermatological, and mixed forms. The usual clinical presentation of AIP involves abdominal pain, gastrointestinal symptoms and autonomic nervous system disturbances. <sup>[2]</sup> The attacks are precipitated by factors such as drugs, hormones (i.e. estrogens), emotional stress, pregnancy or starvation. These symptoms mimic other medical and surgical illnesses, framing a diagnostic dilemma which leads to misdiagnosis, wrong diagnosis or delay in diagnosis.

Acute intermittent porphyria is caused by a mutation in the gene encoding hydroxymethylbilane synthetase (HMBS) / porphobilinogen deaminase. <sup>[1]</sup> Currently >386 mutations are known in HMBS gene, mostly, missense, nonsense, splicing site mutations, deletions, insertions, or duplications. <sup>[4]</sup> Because AIP is rare and its clinical presentation is heterogeneous, it can be easily misdiagnosed.

Diagnosis of AIP is by biochemical screening by Ehrlich's test and measurement of PBG, ALA and total Porphyrins in urine along with decreased porphobilinogen deaminase activity.

Acute intermittent porphyria can be misdiagnosed as psychosis, Guillain-Barré

syndrome, and chronic hepatitis <sup>[5]</sup> diagnosed AIP as cholecystitis as the presentation was as abdominal pain and gall stone.

## **CONCLUSION**

Acute intermittent porphyria must be included in the differentiated diagnosis of psychiatric, neurological and gastric alteration irrespective of family history is present or not. The screening test Ehrlich test positive shows presence of PBG. If positive it should be followed by estimation of PBG, porphyrins and ALA in urine. This would help a long way in reducing the misdiagnosis or wrong diagnosis of AIP.

Of all types of porphyrias AIP is the most common type. Females usually have more severe symptoms and attacks may be precipitated by menstruation, pregnancy, and use of oral contraceptive. Symptoms may vary considerably in the same patient during different episodes, as well as among patients with AIP. Because the clinical course can vary from acute, self-limiting attacks to attacks that result in chronic or progressive deficits, the attacks may mimic many other psychiatric or medical disorders, making the potential for misdiagnosis. High clinical suspicion and performing simple test (Ehrlich's) and be vital in identifying AIP patients and preventing fatal outcome of the disease due to lack of clinical recognition and delay in diagnosis.

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