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Case Report

Acute intermittent porphyria (AIP) in 27 year old female patient- Case report

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ABSTRACT

Acute Intermittent Porphyria (AIP) is the most common acute and probably the most common inherited porphyria. AIP is caused due to deficiency of hydroxymethylbilane synthase (HMBS). AIP is characterized by a classical triad of abdominal pain, central nervous system abnormalities and peripheral neuropathy. We report a case of 27 year old female patient with recurrent episodes of acute abdominal pain. Patient underwent all laboratory & imaging investigations at our centre.

1. Introduction

Acute Intermittent Porphyria (AIP) is the most common acute and probably the most common inherited porphyria. AIP is caused due to deficiency of hydroxymethylbilane synthase (HMBS). It is inherited in an autosomal dominant fashion with incomplete penetrance, making family studies more challenging, and over 375 mutations have been identified. AIP is characterized by a classical triad of abdominal pain, central nervous system abnormalities and peripheral neuropathy.

We report a case of 27 year old female patient with recurrent episodes of acute abdominal pain. Patient underwent all laboratory & imaging investigations at our centre.

2. Case Report

In Nov 2022, a 27 year old female came to a private clinic. She had the first episode of severe abdominal pain around the umbilicus, stabbing in character which radiated towards the back, associated with nausea and vomiting and persisting for about 2-3 days. She remained asymptomatic for around 2 months after this episode. In February 2023, she had her second episode of similar abdominal pain which persisted for around 2 weeks following which she had backache and rapid progressive weakness. She also had episodes of panic attacks and anxiety during the episodes of abdominal pain. She denied any history of paraesthesia, sphinteric disturbance, epileptic fits during any of the episodes. She was non alcoholic and did not have history of any drug intake prior to both the episodes. She got symptomatic treatment and was relieved.

In March 2023 she had her third episode with severe abdominal pain, now associated with passing dark red color urine and developed rapid progressive weakness in all the four limbs. She was hospitalized and underwent multiple blood, urine and radiological examinations.

Laboratory investigations showed CBC within normal limits. The peripheral smear showed Normocytic normochromic RBC's. ESR was 19 mm in 1^{st} hr. Her Hemoglobin electrophoresis was also normal. Coomb's test (Direct) was Negative. Flow cytometry for PNH was negative. Serum iron level and serum ferritin was low: 30 ug/dl. (normal 37-170 ug/dl and 23.0 ng/ml (normal 10-160ng/ml)respectively. Autoimmune disease was ruled

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out by negative ANA and RA test.

Serological tests for viral markers HIV, HBsAg and HCV antibody were negative.

Urine routine examination showed microscopic hematuria. Urine Porphobilinogen (Quantitative) was positive with value of 0.38 mg/dl (N:0-0.2mg/dl), which was diagnostic for porphyrias.

Blood biochemistry test results were Random blood sugar 112 mg/dl (normal 60-140 mg/ dl), Serum creatinine 0.7 mg/dl (0.7-1.2 mg/dl). Uric acid 6.1 mg/dl (normal 2.5-6.5 mg/dl). Total Bilirubin 0.5 mg/dl (normal 0-1.3 mg/dl). SGPT 45 U/L and SGOT 48 U/L. Serum Alkaline phosphatase 86 U/L and LDH 183 U/L. Serum Calcium was 9.1 mg/dl.

Ca-125 ovarian cancer marker was 42.97 U/ml(N:0-35). Serum Prolactin was 27.52 ng/dl (normal 4.79-23.3 ng/dl). TSH was 2.55 uIU/ml (normal 0.27-4.2). Serum procalcitonin was 90.05 ng/ ml. Mantoux test was negative.

Abdominal sonography revealed bilateral tubo ovarian complex with endometrioma. Xray chest was normal. CT Scan findings were suggestive of Bilateral ovarian endometriomas extending into cul de sac abutting each other (kissing ovaries sign) and abutting the rectum and posterior wall of uterus. (adherence). Gastro-duodenoscopy showed Hiatus hernia.

Special tests were performed for Prophobilinogen screening i.e. Watson Schwartz test, UV Fluorescence test and Hoeschs test. All were positive.

Patient was referred to haemato-oncologist. She was diagnosed as acute intermittent Porphyria (AIP). Urine samples of her parents were negative for this pigment. However, the patient's 17 year old younger brother died two years back with the same symptoms but was undiagnosed.

She was advised to avoid dehydration and hypoglycemia- to drink and eat adequately at all the time. Medication for nausea and vomiting was prescribed and was advised to take glucose/ sugar water as much as possible. I.V. fluid for hydration- 5% dextrose or DNS was to be used as and when required. In acute emergency (for acute attack) I.V. Heme slow infusion was advised. Liberal use of certain pain medications analgesics, anti-anxiety drugs, anti-hypertensive drugs and drugs to treat nausea and vomiting, tachycardia, or restlessness was advised.

She was given a drug list of 13 class of drugs to avoid an attack of AIP. Drugs were Barbiturate, Carisoprodol, Danazol, Primidone, Pyrazolones, Trimethadione, Ethchloevynol, carbamazepine, Nifedipine, sulphamethazole, rifampicin, Ketoconazole and Reproductive steroids such as Progesterone, medroxyprogesterone and testosterone.

3. Discussion

Porphyrin molecules are known as the "pigment of life" for their contributions to heme, the responsible molecule for the color of Red blood corpuscles (RBC's). The Porphyrias are metabolic disorders due to defect in the heme biosynthetic pathway. The Porphyrias are a group of metabolic disorders representing a wide range of clinical symptoms according to the specific enzymatic defect in the heme biosynthetic pathway. The genetic mutation causes consequent overproduction of porphyrins which are the essential intermediates of this pathway.

The acute porphyrias can be either autosomal dominant or autosomal recessive. Autosomal dominant include acute intermittent porphyria (AIP), variegate porphyria and hereditary coproporphyria or autosomal recessive, such as delta aminolaevulinic acid (ALA) dehydratase deficiency. In Europe the prevalence is estimated to 110 be approximately 5.9 per million people in the general population. The worldwide prevalence has been estimated to be between one in 50000 in general population.[1] AIP is more frequent in women between second and fourth decades of life.[2,3] The typical acute porphyria attacks manifest with diverse clinical presentations with neuropathy being frequent in acute intermittent porphyria (AIP). Because of the low penetrance of the gene, the attacks are infrequent; and because of non-specific symptoms, AIP is hard to diagnose.[4,5] Associated symptoms are acute abdominal pain, nausea, vomiting, bodyache, neurological symptoms such as seizures, flaccid paralysis, confusion, hallucination, anxiety, insomnia, palpitation, muscle weakness, and panic attacks. It can be also associated with urinary symptoms such as retention or incontinence. Patients often give history of passing red to brown urine that darkens when exposed to light.

According to Jeans et al.,[6] mortality due to AIP was 3-fold compared to that in the general population during the past 50 years. The major cause of the increased mortality was the porphyric attack itself. Acute attack of AIP can land with triggering factors such as history of certain drug ingestion, excessive alcohol consumption, fasting/ dieting, stress, certain infections or hormonal changes (e.g., menstrual cycle) or hormonal drug therapy.[7,8]

The long-term sequelae of AIP can be hepatocellular carcinoma, hypertension, and chronic kidney disease. Tubulointerstitial lesions are the main mechanism of renal disease, and rising creatinine levels are observed after an AIP attack; therefore, the recommendations are monitoring renal function, avoiding recurrent attacks and nephrotoxic medications.[9]The prognosis of acute attacks is good, with most patients with AIP fully recovering; however, 5% to 20% of patients might have morbidity and mortality, especially in undiagnosed, delayed, or inappropriate treatment.[9]

4. Conclusion

AIP should be diagnosed in any suspected patient presenting with severe abdominal pain, neurological symptoms such

as rapid progressive flaccid paralysis and history of passing dark reddish urine. Examination of the urine during acute attacks for PBG and ALA will help in the diagnosis. There is no specific treatment for porphyria and it is therefore important to prevent the triggers which give rise to acute attack. During acute attacks, the usual first approach is to load the patient with a high carbohydrate diet or intravenously administered dextrose. The hemin infusion is a best treatment for AIP, with efficacy in more than 85% of cases,[10] Definitive treatment is an orthotopic liver transplant.

5. Conflict of Interest

None.

6. Source of Funding

None.

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