CASE REPORT

Acute porphyria: An unusual case of quadriparesis, hypertension, recurrent severe cyclic abdominal pain, and seizures

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Abstract

Porphyria refers to a rare group of genetically inherited or acquired disorders that arise due to reduced metabolic activity of any of the enzymes in the haem biosynthetic pathway. Defect in any enzyme causes the presentation of symptoms of porphyria. The epidemiology of Acute Intermittent Porphyria (AIP) is complicated because of its rarity and delay in diagnosis.

We present the case of a seven-year-old girl who presented with multisystem involvement; her symptoms were quadriparesis, hypertension, recurrent severe cyclic abdominal pain, and seizures. These symptoms together were not explained by the differentials taken into account. She presented before puberty with no family history of such conditions, while being born of consanguineous marriage. Her symptoms along with urinary porphobilinogen positivity test helped to reach the diagnosis of AIP in the absence of cutaneous manifestations.

This case highlights the variable presentation of porphyria and emphasises the importance of appropriate and timely diagnosis and management in these patients.

Keywords: Porphyria, Acute intermittent porphyria, Erythropoietic porphyria, Hepatic porphyria, Hepato-erythropoietic porphyria, Porphyria cutanea tarda.

DOI: https://doi.org/10.47391/JPMA.7390

Submission completion date: 19-09-2022
Acceptance date: 27-05-2023

Introduction

Porphyria can be termed an unusual group of hereditary inborn errors of metabolism that result due to a lack of the enzymes responsible for conducting the biosynthetic haem generation pathway, leading to a pathogenic build-up of "haem precursors (such as Porphobilinogen (PBG), δ- or 5-aminolaevulinic acid) and porphyrin".[1]

Porphyria is classified into two groups: (a) location of the primary overproduction of porphyrin precursors, which comprises hepatic and erythropoietic porphyria; or (b) based on clinical manifestation, which includes acute and chronic porphyria.[2,3]

Acute hepatic porphyria (AHP) can be classified as a set of life-threatening disorders caused by inborn metabolic errors that trigger acute periodic neurovisceral attacks. They include acute intermittent porphyria (AIP), hereditary coproporphyrin (HCP), variegate porphyria (VP), and delta- or 5-aminolevulinic acid (ALA) dehydratase deficiency or Doss porphyria (ALADP).[2,4,5]

The most predominant type of AHP is AIP, with a prevalence rate of 5/per 100,000 individuals in the United States of America. The other common forms of AHP are VP (approximately 1/30,000 citizens) and HCP (approximately 2/1,000,000 citizens in Denmark). A higher frequency of VP has been recognised in Afrikaner inhabitants of Dutch descent in South Africa and Finland; this is linked to a founder effect. ALAD porphyria is very uncommon; though several cases have been identified, the prevalence is slightly more than a few hundred.

In the United States of America, the frequency of all the varieties of porphyria collectively is estimated to be about 1 in 25,000, whereas global prevalence is estimated to be between 1 in 500 and 1 in 50,000 individuals, varying from region to region.[6,7]

Acute porphyria is a rare but potentially life-threatening condition and is difficult to diagnose due to its non-specific and wide spectrum of clinical manifestations.[8]

Genomic association might be involved in variations in penetrance, although the underlying genes involved are still unknown.

Given the rarity, variable presentation, and potential life-threatening nature of acute porphyria, it is crucial to enhance awareness among healthcare professionals regarding this condition. By presenting this unusual case of quadriparesis, hypertension, recurrent severe cyclic abdominal pain, and seizures in a seven-year-old girl, we aim to highlight the importance of early recognition and timely management of acute porphyria. Increased understanding of the diverse clinical manifestations of

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porphyria can lead to improved outcomes and enhance the quality of care provided to these patients. Thus, this case report serves as a valuable addition to the existing literature, reinforcing the significance of prompt diagnosis and appropriate interventions in individuals with acute porphyria.

Case Report

A seven-year-old female patient, with no underlying comorbidities, presented to the Paediatric Intensive Care Unit (PICU) of National Institute of Child Health (NICH), a tertiary care hospital in Pakistan, on November 5, 2019. The patient, who was up to date with routine immunizations, was referred to the hospital by her parents, who belonged to the same kinship. She complained of severe abdominal pain, fever, fits, and shortness of breath.

Approximately 21 days prior to admission, the patient began experiencing severe cyclic abdominal pain that was unresponsive to analgesic therapy. The pain was localised to the epigastric area and radiated to the whole abdomen and back. It was accompanied by fever, red-coloured urine, up-rolling of the eyes, and shortness of breath. The patient had no history of acute or episodic gastrointestinal or neuropsychiatric complaints.

The patient had an unremarkable birth history and achieved all developmental milestones according to age. Her intelligence quotient was average. No similar complaints were reported in the patient's parents, other four siblings, or second-degree relatives.

Upon physical examination, the patient was noted to have tachypnoea, tachycardia, and was vitally unstable with blood pressure above the 99th percentile for her age. She was also below the fifth percentile for height and weight. Chest auscultation revealed decreased air entry and crepitation on the left basal side of the lung, while abdominal examinations were normal. Cranial nerve function tests were normal during neurological assessment, but motor strength assessments were decreased. Temperature, vibration, proprioception, light touch, and pinprick stimuli were within the usual range.

Haematological investigations and blood biochemistry, including transaminases and lipid profile, were within normal limits except for constant hyponatremia across multiple levels (average 128mEq/L) and haemoglobin of 9g/dl (microcytic hypochromic anaemia). However, the peripheral smear showed no signs of haemolysis, and Liver Function Tests were within the appropriate range.

To rule out infectious aetiology and screen for Guillain-Barre Syndrome, a lumbar puncture was conducted. Cerebrospinal fluid examination revealed a glucose level of 75 mg/dL (standard range 45-80 mg/dL) and a protein level of 20 mg/dL (normal range 12-0 mg/dL), with no presence of cells and no positive Gram staining.

Antinuclear antibodies (ANA), anti-smooth muscle antibodies (ASMA), and anti-mitochondrial antibodies (AMA) were not observed. Examination for infectious diseases, including HIV, HBV, HCV, HSV1, HSV2, and tuberculosis, revealed no evidence of these diseases.

X-ray chest showed consolidation on the left side of the lung, and ultrasonography of the abdomen revealed left kidney hydronephrosis and abrupt narrowing of the left ureter at the junction of the left iliac vessels, probably due to kinking of the ureter. No apparent calculus was identified in the visualised dilated course of the left ureter, and the right iliac vessels were also not visualised. The radiology team advised an MRI, which revealed microinfarcts in the kidneys. Based on the presence of these microinfarcts, variegate porphyria was suspected.

CT scan of the brain was normal, while CT scans of the abdomen revealed multifocal parenchymal infarct in the spleen and both kidneys; incidental horseshoe-shaped kidneys were also noted. A 24-hour urine test for urinary porphobilinogen showed a significant increase in levels, indicating porphyria.

The patient was managed symptomatically due to unavailability of haematin in Pakistan and steroids were also administered. Despite this regimen, the patient's condition did not improve, and she expired after 18 days. Her siblings were screened for porphyria, but all the markers returned normal. A possible link to oestrogen surge was speculated as a precipitating factor, as the patient was approaching puberty. However, further investigations were required to confirm this hypothesis.

Discussion

Porphyria can be termed an unusual group of hereditary inborn errors of metabolism that result due to a lack of enzymes responsible for conducting the biosynthetic haem generation pathway, owing to a defective gene coding for the enzyme, the disorder may be induced or genetic. The absence of any of the enzymes may result in a variety of clinical symptoms, including neurovisceral, cutaneous, or mixed symptoms.[9,10]

The involvement of kidneys has been seen in 'Variegate Porphyria',[11] which is characterised by defective function of the enzyme protoporphyrinogen oxidase, and is a very rare genetic condition.[11] As genetic testing for this enzyme is not available in Pakistan, it was not possible to reach a definite diagnosis.

The sign and symptoms of AIP can appear at any time regardless of age, starting at puberty, however, it is highly frequent in the 30s. The classic trio of an acute attack is abdominal pain, peripheral neuropathy, and altered mental state, which are observed in half of the patients.[12]

Our patient presented with a variety of multisystem involvement symptoms including quadriparesis, hypertension, recurrent severe cyclic abdominal pain, and seizures. The differentials considered were unable to justify the combination of such manifestations. The significance of neurological manifestations was prioritised over intermittent abdominal pain, resulting in the initial diagnostic conundrum.

Meningoencephalitis, acute disseminated encephalomyelitis (ADEM), Guillian-Barre Syndrome, and recurrent paralysis were also significant differential diagnoses in our situation. Meningoencephalitis was ruled out by the worsening of symptoms even after adequate antibacterial and antiviral treatment. Results of CSF, DR, and MRI of the brain ruled out ADEM and Guillain-Barre Syndrome (GBS). In the absence of cutaneous symptoms, a combination of characteristics such as periodic abdominal pain, neurological findings, and hypertension accompanied by a urinary porphobilinogen positivity test enabled us to diagnose AIP.

The patient is distinctive in the way that she presented before puberty and had no family background. There were no such complaints from either the parents or the siblings.

Starvation, exogenous influences that cause the production of microsomal cytochrome P450 in the liver, such as sulphonamides, barbiturates, endogenous steroid hormones, chloroquine, griseofulvin, and many other medications, acute infections, the luteal phase of the menstrual cycle, fasting, and excessive alcohol consumption may all cause acute attacks.

Because of its prevalence and late detection, the epidemiology of AIP is complex. Prevalence of AIP differs; the frequency of AIP is high in England, Ireland, and Scandinavia.[13] In the general adult population, the prevalence of AIP ranges from 1-to 8 per 100,000.[13]

Hospital and laboratory findings such as transient abdominal pain with neurological symptoms such as seizures, hypertensive crisis, dysautonomia, elevated urinary porphobilinogens, enzyme analysis, or DNA mutation analysis are used to diagnose porphyria.[14]

Management involves the termination of an acute attack, symptomatic relief, and avoiding precipitants.[8]

Intravenous haem is the treatment of choice. Cimetidine is cheaper than Hermin, hence is an effective substitute for treating acute attacks; administering 800mg/day till ALA levels return to normal.[8,14]

Increased carbohydrate intake can resolve mild attacks by inhibiting delta-ALA synthetase.[8,14]

In refractory cases, a liver transplant has been suggested. Supportive treatment for hypertension, electrolyte imbalance, and pain control should be addressed accordingly.[15]

A limitation in our case report is that it does not involve the complete treatment of the patient.

Conclusion

This case demonstrates the complex appearance of porphyria and stresses the significance of considering the disease as a differential even if the patient is young and has existing neurological indications, and presents with vague neurovisceral indications or ambiguous neurological decay. Appropriate and timely diagnosis and management of these patients is essential.

Informed Consent: The patient's parents provided written consent for the publication of this case report.

Disclaimer: None.

Funding Sources: None.

Conflict of Interest: None.

Data Availability: The authors declare that data supporting the findings of this study are available within the article.

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