CASE REPORT

Worsening abdominal pain leading to false laparotomy: A case of acute intermittent porphyria

Tehreem Farah[1], Hania Batool[2], Nasir Ashraf[3], Fatima Qayyum Abbasi[4], Aisha Nasir[5]

Abstract

Acute intermittent porphyria (AIP), one of the most severe types of acute hepatic porphyria, is an autosomal dominant inherited disorder of heme biosynthesis. We present a case of a 16-year-old girl who presented with severe abdominal pain, subjected to a laparotomy and later developed seizures and other neurological manifestations. Initial investigations showed hyponatraemia. Magnetic Resonance Imaging of brain showed cerebritis. She underwent several investigations including an ultrasound of abdomen, a computed tomography scan of abdomen and pelvis, cerebrospinal fluid routine examination and culture, and autoimmune investigation which were found to be normal. Later urine porphobilinogen levels were found to be raised. The diagnosis was made based on investigation and clinical symptoms. AIP should be suspected when a patient presents with chronic abdominal pain and neurological symptoms.

Keywords: Acute Intermittent Porphyria, false laparotomy, appendicitis, acute abdomen, hyponatremia, tonic-clonic seizures.

DOI: https://doi.org/10.47391/JPMA.10209

Introduction

Acute intermittent porphyria (AIP) is among the severe types of acute hepatic porphyria (AHP). It is rare and inherited in an autosomal dominant pattern caused by a mutation in the gene coding for Hydroxymethylbilane Synthase; the third enzyme in the heme synthesis chain. This reduces enzymatic activity up to 50% of the reference range.[1,2] Although very common among acute porphyria, AIP has a very low prevalence of approximately 5 cases per 100,000 people.[3] The patient with AIP may develop typical symptoms of an acute attack and can be considered a manifest AIP or present with no clinical manifestations called latent AIP.[4] AIP is clinically a triad of severe colicky abdominal pain, neurological dysfunction, and psychiatric changes.[5] Some patients may also present with partial seizures. Usually, urine darkens to red or brown on exposure to air, light, and heat. Patients are asymptomatic between attacks.[4]

Genetic analysis for mutation is the gold standard for diagnosing specific AHP, but it is not recommended as a first-line investigation because of its low penetrance. So, the cause of acute symptoms during the attack is the elevation of urinary amino levulinic acid (ALA) and porphobilinogen that helps in diagnosis.[6]

Due to its rare presentation, it is among the most commonly misdiagnosed illnesses[7] and consequently, can result in fatality.[8] Multiple case studies in the past report misdiagnosing AIP as appendicitis,[7] cholecystitis[1] and Guillain–Barré Syndrome[9] leading to unnecessary medical and surgical interventions that could have been prevented.

Case Study

This study reports the case of a 16-year-old girl seen in January 2023, with her guardian's consent, who presented with sudden, severe, and generalized abdominal pain for the past seven days. The pain was colicky and with no associated symptoms. Initially, she was treated for gastroenteritis for 4 days with ciprofloxacin and metronidazole in a nearby hospital. The patient showed no improvement and was advised to undergo an ultrasound abdomen, which revealed a 4.2mm renal stone in the upper pole of the right kidney. The patient was prescribed antipyretics and nonsteroidal anti-inflammatory drugs for three days, slightly reducing discomfort. The computed tomography scan yielded unremarkable results. Although, there was no evidence of appendicitis, an appendectomy was done on the seventeenth day since the onset of her illness resulting in no improvement in pain. She had an episode of generalized tonic-clonic seizure 4 days post-operatively, for which she presented to our emergency department (ED) at Pakistan Institute of Medical Sciences (PIMS). Seizures were generalized and were accompanied with up rolling of eyes, frothing from the mouth, and urinary incontinence. Her seizures were managed via levetiracetam with an initial loading dose of 1.5g followed

[1,2]Department of Obstetrics and Gynaecology, Pakistan Institute of Medical Sciences, Islamabad, Pakistan; [3]Department of General Medicine, Pakistan Institute of Medical Sciences, Islamabad, Pakistan; [4]Final Year MBBS Student, Federal Medical College, Islamabad, Pakistan; [5]Final Year MBBS Student, Dera Ghazi Khan Medical College, Dera Ghazi Khan, Pakistan.

Correspondence: Tehreem Farah. e-mail: tehreemfarah10@gmail.com
ORCID ID: 0009-0006-4797-1105

Submission complete: 06-07-2023 **Review began:** 30-09-2023
Acceptance: 24-07-2024 **Review end:** 25-05-2024

by a maintenance dose of 500mg twice daily, and investigations were done. All results were unremarkable except for serum electrolytes, which showed hyponatraemia (117mmol/L; normal levels: 135-145mmol/L). This was managed timely by 3% hypertonic saline administered intravenously (IV) and 24-hrs sodium monitoring yielded a noticeable improvement in pain.

During her 6-hour stay in the ED, she had another seizure that lasted 1 minute, occurring 2 hours after the previous one. These seizures were again controlled by Levetiracetam 500 mg twice daily. When her symptoms briefly improved, she was shifted to an in-patient department where she underwent three similar episodes of seizures lasting 1 to 2 minutes, occurring three hours apart. She was then started on IV diazepam and dextrose. The patient experienced dizziness and confusion between seizures with no paraesthesia, amnesia, or other neurological signs. Ceftriaxone, acyclovir, and vancomycin were administered and discontinued when the cerebrospinal fluid routine examination and culture did not show any abnormality. Magnetic resonance imaging of brain showed focal mild gyral swelling in the superior parietal regions bilaterally and right frontal lobe anteriorly, which was suggestive of focal cerebritis. Dexamethasone 8mg three times a day for three days was prescribed. Subsequently, a workup for hyponatraemia was repeated, and the results are illustrated in Table in the appendix.

Table: Characteristics of the participants (n=470).

Investigations	Results	Reference
Urine sodium	86mmol/L	40-220 mmol/L
Urine potassium	14.3mmol/L	60-80 mmol/L
Urine chloride	84mmol/L	98-106 mmol/L
Urine osmolality	327mOsm/kg	250-900 mOsm/kg

Systemic lupus erythematosus, tuberculosis and autoimmune encephalopathy workup were also conducted, with anti-nuclear antibodies, anti-double stranded DNA antibody, lupus anticoagulant and xpert mycobacterium tuberculosis. All were found to be normal. In addition to the tests above, an increased urine porphobilinogen level of 70 mg/dl suggested the presence of AIP. Furthermore, the erythrocyte sedimentation rate was raised to 46mm/hour while procalcitonin levels were found to be normal.

She was treated with dextrose, saline and diazepam for seizures as haematin was unavailable. Later she was discharged on levetiracetam 500mg twice daily. There were two follow-up visits, one with abdominal pain and the other with abdominal pain and seizures.

Discussion

To the best of our knowledge, this is the first reported case of AIP with worsening abdominal pain leading to false laparotomy in Northern Pakistan. This case highlights the importance of recognizing AIP as a cause of abdominal pain to avoid unnecessary surgery. This case report also serves as a reminder that autosomal dominant diseases without a family history can appear due to de novo mutations. Although case reports from Pakistan have been published previously, they have focussed on different presentations. For example, one report described a young female diagnosed with Acute disseminated encephalomyelitis whose subsequent diagnosis of AIP was found to be the primary trigger for the initial CNS inflammation.[10] Another study from Pakistan highlights a case of deteriorating motor neuropathy and recurrent abdominal pain, eventually diagnosed as acute porphyria, with significant improvement observed after plasmapheresis, underscoring the importance of considering acute porphyria in patients with acute abdominal symptoms.[11] A local study suggested the case of a seven-year-old girl who presented with multiple system involvement; her symptoms were quadriparesis, hypertension, repeated cyclic abdominal pain and seizures. These symptoms were not sufficient for the differentials to reach a final diagnosis. 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.[12] In our patient, the case remained misdiagnosed for an extended period. Patient's family history was insignificant, although an autosomal dominant disease presents with a known case in the family. Approximately 90% of the patients are without symptoms for a long time.[5] It is more symptomatic and prevalent in females, especially of reproductive age.[7] Before coming to our hospital, our patient was treated for gastroenteritis and renal stones and had a laparotomy for appendicitis, but her abdominal pain did not settle. The patient underwent a negative laparotomy for the acute abdomen on suspicion of appendicitis. She presented with generalized tonic-clonic seizures and hyponatraemia on the fourth postoperative day and later with altered sensorium. Neurological dysfunction in AIP results from neurotoxic implications of porphyrin precursors, in which ALA is the most imminent.[2] Abdominal pain is considered a manifestation of autonomic neuropathy resulting from splanchnic dysfunction. One of the most frequent electrolyte abnormalities in AIP is hyponatraemia, as shown in our case[7] and its pathology can be linked with the syndrome of inappropriate anti-diuretic hormone secretion

caused by sodium loss via the gastrointestinal tract.[5]

Initially, gastroenteritis and appendicitis were suspected, which later, with the development of neurological symptoms, changed to meningoencephalitis, cerebritis, autoimmune encephalitis, systemic lupus erythematosus, and tuberculosis. The diagnosis was made on raised urine porphobilinogens (PBG) levels, which are sensitive and specific for an acute attack of various types of porphyria, including AIP. In a scenario where abdominal pain and vomiting remain unexplained, qualitative urine analysis for PBG indicates initiation of treatment for the disorder without knowing the type.[2] Empiric treatment was given according to the differential diagnosis and was stopped when test results were unremarkable. After diagnosis, she was provided supportive treatment.

She underwent unnecessary medical and surgical intervention. Therefore, acute unexplained presenting signs and symptoms should always raise suspicion and PBG levels should be advised, which can build its way to a definitive diagnosis.[7] A delayed diagnosis not only risks unnecessary investigations but also endangers the patient's life. A high index of suspicion and vigilance is crucial for prompt identification. IV haematin (3–4 mg/kg) is effective, with heme arginate considered a safer option. Additional measures include IV dextrose and a high-carbohydrate diet to reduce the severity of the attack. It can suggest screening and genetic counselling of first degree relative at risk.[13] Therefore, when dealing with unexplained abdominal pain and hyponatraemia along with neurological symptoms, physicians should keep AIP as a differential diagnosis.

Conclusion

The case emphasizes the importance of considering AIP as a diagnosis when a patient presents with abdominal pain and neurological symptoms. AIP is often misdiagnosed because of its nonspecific symptoms and complex presentation that may lead to unnecessary investigation and treatment. Although rare, it should be considered a differential to enable early diagnosis and avoid unnecessary investigations.

Disclaimer: None.

Conflict of Interest: None.

Funding Sources: None.

References

1. Phillips JD. Heme biosynthesis and the porphyrias. Mol Genet Metab 2019;128:164-77. doi: 10.1016/j.ymgme.2019.04.008.
2. Spiritos Z, Salvador S, Mosquera D, Wilder J. Acute Intermittent Porphyria: Current Perspectives And Case Presentation. Ther Clin Risk Manag 2019;15:1443-51. doi: 10.2147/TCRM.S180161
3. Sardh E, Barbaro M. Acute Intermittent Porphyria. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, et al, eds. GeneReviews®. Seattle, WA: University of Washington, Seattle; 1993-2024.
4. Sharma AG, Pandit K, Gupta S, Kumar V. Acute Intermittent Porphyria in Prepubertal Child-diagnostic and Therapeutic Challenges in India: A Case Report and Literature Review. Indian J Crit Care Med 2022;26:390-4. doi: 10.5005/jp-journals-10071-24133
5. Wang B. The acute hepatic porphyrias. Transl Gastroenterol Hepatol 2021;6:24. doi: 10.21037/tgh-2020-01
6. Gonzalez-Mosquera LF, Sonthalia S. Acute Intermittent Porphyria. Treasure Island, FL: StatPearls Publishing; 2024.
7. Indika NLR, Kesavan T, Dilanthi HW, Jayasena KLSPKM, Chandrasiri NDPD, Jayasinghe IN, et al. Many pitfalls in diagnosis of acute intermittent porphyria: a case report. BMC Res Notes 2018;11:552. doi: 10.1186/s13104-018-3615-z
8. Hudgins K. Porphyria: A Rare, Complicated, and Misdiagnosed Disease. Crit Care Nurs Q 2019;42:192-7. doi: 10.1097/CNQ.0000000000000253
9. Son WC, Kim J, Kim DY. Importance of Screening Acute Intermittent Porphyria in Severe Sensorimotor Polyneuropathy Misdiagnosed as Guillain–Barré Syndrome: A Case Report. J Electrodiagn Neuromuscul Dis 2020;22:86-9. doi: 10.18214/jend.2020.00017
10. Sheikh AAE, Sheikh AB, Sagheer S, Tariq U, Bukhari MM, Fatima Z, et al. Acute Intermittent Porphyria: A Rare Cause of Acute Disseminated Encephalomyelitis. Cureus 2018;10:e2989. doi: 10.7759/cureus.2989
11. Maqbool U, Khan MA, Maqbool A, Aslam W, Naseem MA. The Management of Motor Neuropathy With Plasmapheresis in a Patient With Acute Porphyria: A Case Report. Cureus 2023;15:e43196. doi: 10.7759/cureus.43196
12. Gowa MA, Abidi SMA, Khan M, Jamal G, Nawaz H. Acute Porphyria: An Unusual Case Of Quadriparesis, Hypertension, Recurrent Severe Cyclic Abdominal Pain, And Seizures. J Pak Med Assoc 2023;73:2089-92. doi: 10.47391/JPMA.7390
13. Ahmed I, Ahmed E, Zaidi BH, Ansari JK, Nisar S. A young girl with fits. J Ayub Med Coll Abbottabad 2015;27:232-3.

Author Contribution:

TF: Case selection, data acquisition, literature search, drafting and final approval.
HB: Case selection, data acquisition, literature search, editing and final approval.
NA: Patient care and guardian's consent, data acquisition, conceptual modification of case, supervision, reviewing, editing and final approval.
FQA: Study design, literature search, writing, editing and final approval.
AN: Study design, literature search, writing, revision and final approval.