

Acute Intermittent Porphyrria- Perplexed by the Purple

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ABSTRACT

Porphyrias are rare, genetically inherited group of disorders. The most common disorder among acute porphyrias are the acute intermittent porphyria, which occurs due a defect of the enzyme porphobilinogen deaminase, presenting commonly with a triad of symptoms: visceral abdominal pain, neurological dysfunction and psychiatric disturbances. Non specific myriad of symptoms causes a diagnostic confusion and delay, leading to multiple investigations, unnecessary treatment interventions, high cost of management, with frequent visits to emergency room and a prolonged ward stay. A more perplexing picture appears due to the absence of hard physical findings, and the patients get dismissed for years as "Functional", Malingerers, Mentally ill. In underdeveloped countries, owing to limited investigative procedures, costly laboratory investigations, poor socio-economic status, much reliance on clinical judgment is required.

Keywords: *diagnostic perplexion; Porphyria.*

INTRODUCTION

The porphyrias are a heterogeneous group of overproduction diseases, resulting from genetically determined, partial deficiencies in haem biosynthetic enzymes.¹ Neurological or psychiatric symptoms occur in most acute attacks, and may mimic many other disorders. The diagnosis may be missed because it is not even considered or because of technical problems, such as sample collection and storage, and interpretation of results.¹ The diagnosis of acute porphyrias, however, can be very challenging due to overlapping features amongst the various types.

Here we report a case which caused a similar diagnostic confusion during our assessment and treatment in Nepal Police Hospital. Thorough considerations of multiple differential diagnosis and with evidence from

laboratory results and supportive radiological picture, a diagnosis of acute intermittent porphyria was made.

CASE REPORT

Ms X - Sixteen years old unmarried female, studied upto 10th grade, from a low socio-economic background, a non-smoker and a non-alcoholic presented to the emergency room of Nepal Police Hospital, Kathmandu on 11/7/2017, with chief complaints of pain abdomen since three days and vomiting of same duration.

Abdominal pain was acute on onset, in the epigastric region, colicky in nature, non-radiating, persistent, with waxing and waning intensity. Pain was associated with vomiting which was frequent, non-projectile, non-bilious. Associated with pain and vomiting was constipation of two days duration.

Patient had presented with similar symptoms four months ago, of two weeks duration, along with one episode of unresponsiveness. During that presentation patient was evaluated by the surgical team and provisionally diagnosed as a case of Sub acute intestinal

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obstruction with hyponatremia, was treated symptomatically over three days of in-patient stay and discharged after symptomatic relief. Unresponsive episode was not paid due attention.

During the current admission due to recurrence of similar symptoms, a thorough investigation was carried out by the surgical team, again with a clinical suspicion of sub-acute intestinal obstruction, though per abdominal findings revealed no abnormality. Upper Gastro Intestinal (UGI) Endoscopy revealed, mild antral gastritis which did not explain the severity of symptoms. Ultrasonography (USG) abdomen revealed normal findings except for sluggish bowel movement. USG repeated after five days of admission revealed dilated bowel loops, otherwise normal. Computed Tomography (CT) scan of abdomen was unremarkable for any abdominal pathology.

During ward stay in the current admission, patient developed an episode of unresponsiveness on 15/7/2074 (fifth day of admission), witnessed by the father and the ward nurse. A detail description of the episode was obtained which characteristically showed sudden unresponsiveness, associated with neck deviation towards the right side with stiffening of the whole body and jerky movements of both upper and lower limbs with a tongue bite on the left lateral part of tongue, lasting for about two to three minutes followed by regaining of consciousness, during which the patient would appear confused for next five to six minutes. The patient didn't recall the event. This episode was followed by yet another episode of unresponsiveness after 20 minutes with a fully conscious period in between and was similar in pattern as the previous one. Considering both episodes as Complex partial seizure leading to secondary generalization, patient was shifted to intensive care unit for further observation and care. Electro Encephalography (EEG) done in alert and awake state using the international 10-20 system of electrode placement showed alfa as the posterior dominant rhythm with spiky discharges from left temporal and occipital lobe.

During ICU stay persistent hypertension and persistent tachycardia was observed. The patient didn't have any history of hypertension

or any cardiac abnormality. Echocardiography didn't reveal any abnormality. The laboratory investigations were remarkable for persistent hyponatremia. By this time of evaluation the case was still a diagnostic quagmire-the treating team were not able to come to any conclusive state.

Psychiatry consultation was sought on 22/7/074 to find out, if any psychiatric comorbidity could explain the clinical state. Psychiatric evaluation revealed- presence of a stressor in the form of failure in recent exams with features suggestive of panic attacks. But the Psychiatric symptomatology were not sufficient to explain all the symptoms. The clues which hinted towards an "organic" factor lying underneath all this picture were hyponatremia, persistent tachycardia, persistent hypertension, persistent pain abdomen, persistent vomiting and constipation. This diagnostic confusion led to search for literatures and reverting back to textbooks from which a clue to porphyria was found. Further investigations were requested to find out if these manifestations were compatible with a case of porphyria. Clinically Irritable bowel syndrome was ruled out.

Further investigations revealed:

Laboratory investigations:

- ⊙ Haemoglobin- 11.9 gm/dl Total Leukocyte Count- 4800, Differential count- N-75, L-22, M2, E1, B00
- ⊙ Platelet-150000/ μ L Urea-19 mg/dl, Creatinine- 0.6 mg/dl, potassium- 4mEq/L, Sodium- 126-129mEq/L
- ⊙ Vitamin B12- 548.2 pg/ml (200-1100)
- ⊙ Magnesium- 1.2mg/dl(1.6-2.5)
- ⊙ Calcium- 7.2 mg/dl (8.5-10.5)
- ⊙ Random blood glucose- 96mg/dl
- ⊙ Thyroid function test- FT3 1.7pg/ml(1.2-4.1), FT4 14.7 pg/ml (8.9-17.2), TSH 1.3 μ IU/ml (0.3-4.5)
- ⊙ LFT: SGPT-42, Albumin- 4.5 g/L
- ⊙ C-reactive protein - Negative
- ⊙ Serum Amylase- 46U/L (0-80)

- ⊙ CPK-MB: 14IU/L(<25)
- ⊙ Troponin- I- Negative
- ⊙ Urine R/ME- yellow, alkaline, WBC 1-3, RBC-nil, transparency - clear, epithelial cells-4-6, albumin and sugar-nil.
- ⊙ Infectious screen- TB, HIV, HBSAg, HCVAb, HIV- nonreactive
- ⊙ Peripheral blood smear- Mild anisocytosis with mild hypochromic. Few microcytes, tear drop cells seen. WBCs normal. Platelet adequate.
- ⊙ Iron-114 microgram/dl(60-130)
- ⊙ TIBC- 350microgm/dl(200-400)
- ⊙ Ferritin- 457ng/ml(6.24-264)
- ⊙ Transferrin saturation was calculated from above lab results.
- ⊙ Transferrin saturation- Serum Iron/ TIBC multiplied by 100 (32.57%).
- ⊙ ECG- Normal.
- ⊙ CT abdomen- No abnormality detected. Oral contrast is seen to pass to the distal colic level with no evidence of focal bowel dilatation.
- ⊙ CT / CECT Head- Normal findings.
- ⊙ MRI Head – Posterior reversible encephalopathy syndrome (PRES)
- ⊙ Renal Doppler- Normal.
- ⊙ Urine – positive for porphobilinogen

Finally a diagnosis of acute intermittent porphyria was made and the patient was managed with following medications:

- ⊙ Glucose infusion
- ⊙ Stemetil
- ⊙ Laxatives
- ⊙ Injection Tramadol
- ⊙ Atenolol 50mg OD
- ⊙ Propranolol 20mg BD

- ⊙ Mirtazapine 15mg HS

- ⊙ Patient got symptomatically better after third day of glucose infusion.

- ⊙ Due to unavailability of hematin, it could not be used .

Patient was discharged with complete symptomatic improvement after 19 days of admission.

DISCUSSION

Porphyria is named from the ancient Greek word porphyria, meaning purple. Heme is manufactured in a multistep process. Porphyrias are inherited. With the exception of congenital erythropoietic porphyria (CEP), which is autosomal recessive, all other porphyrias are inherited as autosomal dominant disorders. They invariably result in accumulation and increased excretion of porphyrias and their precursors. There are acute and chronic varieties, each with various clinical subtypes.

The most common acute porphyria is acute intermittent porphyria (AIP), an autosomal dominant disorder of an enzyme called porphobilinogen (PBG) deaminase.² It is an Autosomal Dominant disease. The disease is characterized by a partial deficiency of this enzyme (half normal activity), and thus the symptoms of AIP may not appear until the second or third decade of life. Ms X presented with the clinical signs and symptoms at 16 years of age which is at par with usual age of onset of this disorder. Exposure to a precipitating agent can lead to an earlier presentation.³

Women are more commonly affected than men.⁴ The prevalence of acute porphyria among psychiatric patients is 0.21%-0.48% which was considered to be higher than the typical population as mentioned in the article by Tay et al.⁵ Acute intermittent porphyria has a prevalence of about 1 in 20,000.⁶ Women are affected more than men in the ratio 1.5-2:1 and usually present with symptoms after menarche. Ms X had attained her menarche at 14 years of age. The majority of attacks are precipitated by identifiable factors though some appear to arise spontaneously.⁷

The symptoms are episodic in nature. There is no proven explanation for the episodic pattern of these attacks. However, they are often provoked by drugs such as anticonvulsants, sulphonamides, oestrogen and progesterone, especially the oral contraceptive pill, or by alcohol and even fasting. In a significant number of cases, no precipitant can be identified.⁸ Ms X had undergone an episode of fasting for religious endowments, 24 hrs prior to both episodes of presentation, thus making fasting as a proven precipitating factor for an acute attack in her case.

Diagnosis of an acute porphyria attack is usually suggested by a triad of symptoms: visceral abdominal pain, neurological dysfunction and psychiatric disturbances, such as mental status changes. Of these, abdominal pain is the most troublesome for patients and is the most frequent cause of hospital admission.⁹ Ms X presented with persistent abdominal pain and vomiting which is seen commonly in cases of acute intermittent porphyria.

Frequent spontaneous acute attacks have a highly variable course, lasting from several months to many years, and they are often associated with a markedly impaired quality of life.¹⁰

As has been highlighted already that many of them present with Central Nervous System (CNS) manifestations during the acute attack, at least 20% of them with seizures,¹¹ Ms X also exhibited three episodes of seizures during her two episodes of acute porphyria presentation. Apart from seizures, her clinical examination revealed weakness in all upper and lower limbs, bilaterally.

Various literatures have described about the psychiatric comorbidities in cases of acute intermittent porphyria and vice versa. Psychiatric manifestations occur with a high prevalence and the clinical picture is usually colored with clouded consciousness, paranoid features and schizophrenia-like reactions.¹²

Although psychiatric symptoms in AIP are common, cases with psychiatric symptoms as the only manifestation are rare.¹³ However in a study done by Kuhnelt et al (2000), of hereditary coproporphyria attacks, 28% of patients presented with psychiatric symptoms.¹⁴

Compared with individuals without manifest AIP, individuals with AIP had fourfold increased risks of being diagnosed with schizophrenia or bipolar disorder. First-degree relatives of individuals with AIP had double the risk of schizophrenia and bipolar disorder.¹⁵

Suarez et al. reviewed medical histories of 1039 patients diagnosed with AIP reported in the medical literature and found that the most common psychiatric manifestations were delirium (22%), depression (8%) and psychosis (7%).¹⁶ As reported by Millward, assessment of 90 patients with porphyria revealed anxiety as a relatively stable personality trait with 46% of the group reporting some problem with anxiety and depression.¹⁷ Ms X exhibited symptoms of panic disorder.

Keen observation with high index of clinical suspicion, always surrounded by questions like “why is it happening?” “What could be the cause?” etc (which are the ornaments of a good and astute clinician), drove the team towards dedicated clinical discussions in this case (which should ideally be maintained in each and every patient) and was the key to diagnosis. This case also warns us not to make a psychiatric diagnosis in a haste or jump to psychiatric or functional diagnosis without a thorough and detailed assessment or without ruling out an organic cause.

We are still uncertain about what course this illness will take in future. Due to unavailability of genetic screening techniques, we have not been able to screen the family members. Owing to the high costs of investigations and considering the patient's low socio-economic background the management options remain limited. Owing to their social and poor educational backgrounds, it becomes difficult to explain the disease process and offer any sort of reassurances, causing emotional setback among family members.

CONFLICT OF INTEREST: None.

CONSENT: NMJ case report consent form was signed by the patient.

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