



Acute Intermittent Porphyria: A Case Report

KEYWORDS

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ABSTRACT Acute intermittent porphyria(AIP) is an autosomal dominant condition resulting from the half normal level of hydroxymethylbilane (HMB) synthase activity required for conversion of porphobilinogen (PBG) to HMB in heme biosynthetic pathway. We report a case of 14 year old boy presented with generalised tonic clonic convulsions, refractory to phenytoin and weakness in both upper and lower limbs with recurrent dull aching abdominal pain. Patient's urine found to be dark coloured on exposure to sunlight and increased urinary PBG levels and nerve conduction study(NCV) showing mononeuritis multiplex. Non-contrast CT brain was within normal limits. Patient responded to tablet clonazepam and intravenous and oral glucose supplements.

INTRODUCTION:

Acute intermittent porphyria is a hepatic porphyria with autosomal dominant transmission resulting from half normal level of HMB synthase. Most heterozygote remains clinically asymptomatic unless exposed to factors that increase the production of porphyrins. Steroids, alcohol, porphyrinogenic drugs, low calorie diets usually precipitate porphyria. Neurovisceral symptoms, axonal degeneration peripheral neuropathy and mental symptoms are common. Cranial nerve involvement in the form of dysphagia, facial paralysis and diplopia may occur. Seizures may be the presenting feature in 15% of patients of AIP.

In our patient of AIP there are predominant neurovisceral symptoms with axonal type mononeuritis multiplex with involvement in IXth cranial nerve with seizures.

CASE HISTORY:

A 14 Year old boy presented with complaints of

- Recurrent abdominal pain since 3 months not associated with diurnal and postural variation.
- Low grade fever since 3 days
- Generalised tonic clonic convulsions since 2 days. Three episodes occurred at home for which patient was taken to the private hospital and was given injection dilantin and referred. Two episodes of GTC occurred in our hospital followed by altered sensorium and patient had urinary retention for which he was catheterised. Patient was treated with quinine, dilantin and mannitol.
- Despite this patient had persistent abdominal pain which was dull aching not localised.
- Next day patient's urine was found to be dark coloured after sun exposure.
- Weakness in both upper and lower limbs progressed over 15 days associated with nasal twang and nasal regurgitation.

O/E: Patient was drowsy disoriented
Febrile
Pulse-90/min
Blood pressure-110/80 mmhg
No neck stiffness

S/E: RS- AEEBS, clear.
CVS-S1S2+ no murmur
P/A-Tender, 3cm hepatomegaly

CNS- IXth cranial nerve involved
Deep tendon reflexes absent
Plantars flexor.

On investigation:

Normal haematological and biochemical profile. Urine PBG level 44-50 mg/l(normal:

0-2 mg/l) by column chromatography method.
Non contrast CT brain was within normal limits.
Fundus was normal.
Ultrasonography of abdomen revealed mild hepatomegaly.

NCV study showed prolonged distal latencies in both peroneals and tibials, reduced compound muscle action potential (CMAPS), normal conduction velocities, both medians show reduced motor amplitude, sensory action potential was normal. All these features were suggestive of mononeuritis multiplex, axonal type.

Patient's above report with clinical findings of seizures, transient urinary retention with dull aching abdominal pain suggested diagnosis of AIP. So patient was treated with oral and intravenous glucose upto 300 mg/day and tablet clonazepam 0.25 mg twice a day. Patient's abdominal pain slowly disappeared over one week while weakness in both upper and lower limbs which was more distally improved over a month.

DISCUSSION:

Acute intermittent porphyria (AIP) is a disorder due to an inherited defect of the haeme biosynthesis pathway and characterised by neurovisceral and neuropsychiatric manifestations, often precipitated by drugs and other exogenous factors¹. The severe constipation and episode of abdominal pain, hypertension and tachycardia seen during an acute attack of porphyria may be because of an autonomic

neuropathy.

A predominantly axonal neuropathy, which can be acute and involve the bulbar cranial nerves and respiratory muscle is well described.²

Involvement of the central nervous system is comparatively less common. Several mechanisms have been proposed to explain the neurological symptoms of AIP, which includes overproduction of ALA and PBG and their accumulation in nervous tissue exhibiting neurotoxic properties.^{3,4} Convulsion can occur at any time during acute illness but acute symptomatic seizures are a well recognized feature of porphyria in relapse^{5,6} and subsequent use of enzyme-inducing antiepileptic drugs can cause a worsening of condition and new symptoms, such as acute neuropathy and respiratory paralysis.

In India, AIP has been reported from various parts of the country and some specific communities have been found to be especially susceptible.

The clinical manifestations of AIP are Gastrointestinal: Nausea, Abdominal pain, Vomiting, Constipation, Diarrhoea.

Neurological: Seizures, Neuropathy, Autonomic, Tachycardia, Hypertension, Sweating, Urinary retention, Psychiatric Agitation AIP must be suspected if a patient presents with a combination of symptoms.

In our study patient presented with recurrent abdominal pain with generalised tonic clonic convulsions with urinary retention.

A definitive diagnosis requires demonstration of specific enzyme deficiency or gene defect. This is possible in only a few advanced centres. To establish the diagnosis, the tests usually done are assay for the determination of porphyrin precursors and porphobilinogen in urine. This is based on a traditional colour reaction with Ehrlich's aldehyde reagent, an acidic solution of paradimethylaminobenzaldehyde⁷. It is also known as the Watson Schwartz test⁸ and the

porphobilinogen and chromogen it forms always remain in the aqueous phase. The extraction with chloroform and butanol remove frequently occurring substances that interfere with the test.

The most commonly interfering substance is urobilinogen which is chloroform soluble and produces a red color with Ehrlich's reagent.

In our study Urine PBG level was 44-50 mg/l(normal: 0-2 mg/l) by column chromatography method.

Acute attacks require a prompt diagnosis, withdrawal of the inciting agent, and treatment with analgesics, intravenous glucose, and haematin. Electrolyte imbalances requires careful monitoring and correction. Treatment with a high carbohydrate diet diminishes the number of attacks in some patients and is a reasonable empirical gesture considering its benignity. A minimum of 300 g/day of carbohydrate should be provided orally or intravenously. Haeme products like haeme arginate in a dose of 3 mg/kg/day for four days, is the recommended specific therapy for AIP⁹ and should be started as early as possible. The administration of this end-product of the haeme biosynthesis pathway improves the underlying biochemical disturbance by reducing porphyrin precursor excretion. Adverse effects commonly seen are phlebitis and coagulopathy. This drug is not routinely available in our country.

Our patient was treated with oral and intravenous glucose upto 300 mg/day and tablet clonazepam 0.25 mg twice a day. Patient's abdominal pain slowly disappeared over one week while weakness in both upper and lower limbs which was more distally improved over a month.

CONCLUSION:

AIP is a rare but often reported disorder. Despite the abundance of articles in literature regarding this disease, there are many problems faced by treating physicians. The diagnosis of this disease can be made with the help of good laboratory support, but most of the recommended tests are not done by many hospital laboratories in India. Porphyrins in urine by colour chromatography costing and lead poisoning/porphyria profile in urine costing are being done by some private laboratories. Intravenous haeme is more effective than glucose in reducing porphyrin precursor excretion.

Thus, we report a rare case report of a 14 year old boy presented with generalised tonic clonic convulsions, refractory to phenytoin and weakness in both upper and lower limbs with recurrent dull aching abdominal pain. Patient's urine found to be dark coloured on exposure to sunlight and increased urinary PBG levels and nerve conduction study(NCV) showing mononeuritis multiplex. Patient responded to tablet clonazepam and intravenous and oral glucose supplements.

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