Case Report

Acute Intermittent Porphyria: A Rare Inborn Error of Haem Metabolism

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Abstract

A 22 year young boy presented with recurrent abdominal pain, generalized weakness & wasting with hypertension in Medicine ward CMCH. Subsequently he was diagnosed as a case of Acute Intermittent Porphyria (AIP). Though not common, any patient with unexplained abdominal crisis specially young with any peripheral or central nervous system dysfunction should raise the clinician's suspicion of being porphyric patient as prompt management can relieve the patient from progressive neurological damage and disability.

Introduction

Porphyrias are disorder of haem biosynthetic pathway. The one with most serious consequences is acute intermittent porphyria (AIP), inherited as an autosomal dominant disease, remains clinically silent in the majority of the population who carry the trait. Presentation is in early adult life usually around the age of 30yrs and women are more affected than male. The disease is wide spread but specially common in Scandinavia & Great Britain. The disorder is caused by partial deficiency of porphobilinogen deaminse enzyme, leading to increasd excretion of Amino Laevulanic Acid (ALA) and Porphobilinogen (PBG) in the urine[1,6].

The presentation is with acute relapsing and remitting neurological syndrome, invariably with acute abdominal pain and features of autonomic dysfunction such as tachycardia, hypertension, and constipation. Other frequent association includes neuropsychiatric manifestations like depression, anxiety, psychosis, convulsion. Often there is profound hyponatraemia due to inappropriate ADH release. Neuropathy is predominantly motor (70%) & can lead to quadriplegia with respiratory muscle paralysis.Cranial & sensory nerves may be affected. Skin is never affected like other photosensitive porphyria.

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There is no proven explanation for the episodic pattern of these attacks. However they are often provoked by drugs, diet,alcohol and even fasting. In a significant number of cases no precipitant can be identified[2,4].

The diagnosis can be confirmed by demonstrating an increased amount of PBG in the urine during an attact. Freshly voided urine is of normal colour but it may turn dark upon standing in light and air . All family members should be screened to detect latent cases[3,1]. Treatment with a high carbohydrate diet diminishes the number of attack in some patients. Acute attacks may be life threatening and equire prompt diagnosis and withdrawal of the inciting agent and treatment with narcotic analgesic and intravenous high conc. glucose and haem arginate which inhibit ALA synthase activity and thus reduce ALA and PBG level. The intravenous dose of haem is up to 4mg/kg twice daily for four days keeping in mind about adverse consequences specially phlebitis & coagulopathy. Recovery from severe motor neuropathy may require long time even years. Liver transplantation is an option for patients with disease poorly controlled by medical therapy[1,2].

Case Report: A 22 year old canteen boy, hailing from Chittagong City, admitted in Medicine ward CMCH, on 16-09-2007 with the complaints of episodic attack of severe abdominal pain for the last 3 years, associated with generalized weakness, wasting and walking difficulties for the same duration. Patient elaborated that pain was diffuse, not associated with fever or vomiting but aggravated by fasting and unrelieved by antacids. He had no preceding NSAID intake history, or any history of previous jaundice, diabetes or hypertension. He admitted for several times during relapse of pain but the diagnosis was inconclusive though he improved after symptomatic treatment. There was no history of trauma, sexual exposure, contact with chemicals or alcohol abuse. He had no bladder or bowel difficulty except constipation during attack. His appetite was good and he was not suffering from any respiratory or cardiac disease. No family member was suffering from such illness. On examination, patient was found conscious ill looking, malnourished, mourning with pain, dehydrated, non anaemic & non icteric. No cyanosis,clubbing or pigmentation was found. His temperature was 99F, RR 16/minute, no enlarged lymph node found. Thyroid gland was normal, Pulse 140/m, regular & BP 170/100 mmHg in supine position and 140/90 mmHg in standing position. Bed side urine colour was normal on fresh sample but later on it became red-tea colour (Figure 1).

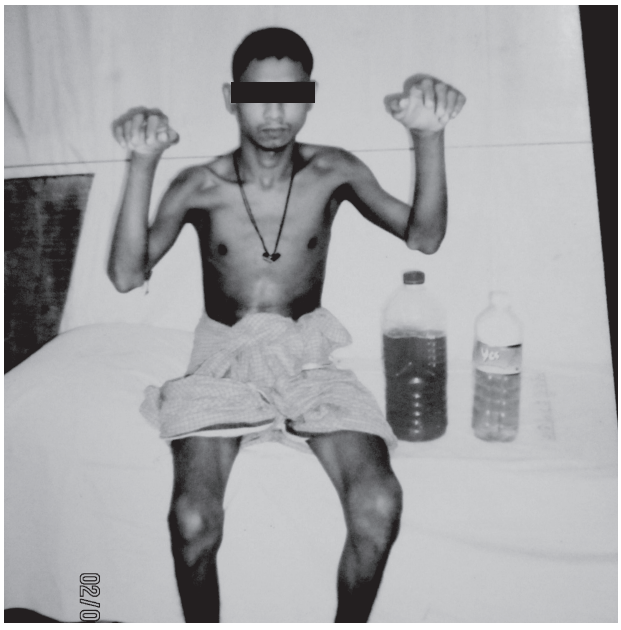

Figure 1: The patient of acute intermittent porphyria with peripheral neuropathy evidenced by wrist and foot drop. There is sample of freshly voided urine of normal colour (left side) and dark reddish urine (right side) after exposure to sun light.

Abdominal examination showed diffuse tenderness on deep palpation but no hepatosplenomegaly, ascitis or visible veins was found. Hernial orifices were intact. Genitourinary system examination revealed no abnormality. On neurological examination higher cerebral function was found normal, no cranial nerve palsy was seen. Wasting of muscles of both upper and lower limbs was present with hypotonia .Muscle power diminished in both limbs (3/5) in all groups. Superficial reflexes were present but deep reflexes were diminished in both upper and lower limbs, more marked distally, Planter reflexes were flexor, gait was high stepping, no tremor or involuntary movement was present. No sensory abnormality was detected; vibration and joint position sense were normal, Romberg's sign was negative. No peripheral nerve thickening or no sign of meningeal irritation found. From history and clinical examination we suspected the patient suffering from porphyric neuropathy and investigated to establish the case as well as excluding other possibilities.

The laboratory profile was as follows:

Hb% II gm|dI ESR 15 mm in 1st hr. TC 8.5×10^/L. Platelet 220×10^9/L
Urine R/E: Suger-Nil. Albumin-Nil, Pus cell - o-2|HPF RBC Nil
RBS: 85 mg/dl, PBF: Eosinophilia.

Serum Na+ 128 mmo1/L, creatinine 0.7mg/dl

Bilirubin0.3mgI/L, HBsAg-Ve.SGPT 89 UL, Serum amylase 79 U/L.

TSH:2.51 mU/L, VDRL: Non reactive

X ray chest P/A Clear, ECG Sinus Tachycardia. Plain X-ray Abdomen. A/P normal

USG Whole Abdomen ,Endoscopy of upper GIT and Echocardiography- normal

Slit skin smear from ear & forehead: negative for mycobacterium lapre.

NCV: Motor poly neuropathy

Urine for porphobilinogen: PBG Positive

Thus the diagnosis was established as a case of an acute intermittent porphyria.

The Patient had a stormy course in hospital with recurrent severe colicky abdominal pain which was controlled by intravenous opoid analgesics. Dehydration and hyponatriemia were corrected by 5% Dextrose Saline infusion. There was labile hypertension and tachycardia which was controlled by propranolol. 25% glucose infusion & plenty oral glucose rich fluid intake helped in subsiding episodes of severe pain. The patient was discharged after a period of 20 days hospital stay.He was given chart of harmful drugs that may precipitate the condition. During discharge his condition was stable, neurological deficit was significantly improved and hypertension was controlled. His family members were advised to screen for urine porphobilinogen in the specialized centre.

Discussion

An acute attack of AIP varies considerably in its clinical presentation and patients may be referred to an internist, surgeon, neurologist, psychiatrist or gynaecologist. A high level of clinical suspicion is necessary in order not to miss the diagnosis which is based on relatively simple laboratory examination for porphobilinogen . An increased urinary excretion of porphobilinogen in the absence of lead poisoning points towards a diagnosis of acute intermittent porphyria. Our patients did not have any history of contact with lead substances . Moreover no clinical feature of lead poisoning like bluish discoloration of gums due to lead sulfide deposition (burton's line) or Basophilic stippling in red blood cells was absent[4,5].

A brief review of the haeme biosynthetic pathway is outlined in order to explain the fundamental defect in AIP (Figure 2).

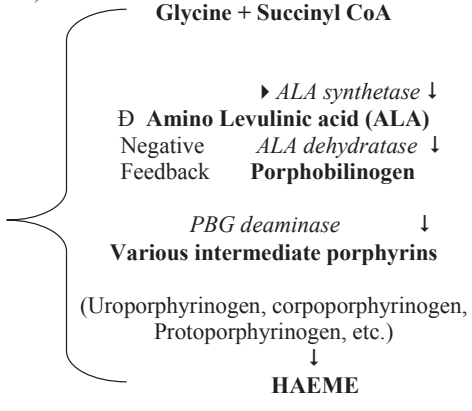

Figure 2 : Biosynthetic Pathway of heam

ALA synthetase is the first and also the rate limiting enzyme in the pathway. In AIP there is reduction in the enzyme PBG deaminase , resulting in diminished haem synthesis causes induction of the rate limiting enzyme ALA synthetase via a bio feedback machanism and thus results in high level porphobilinogen(PBG) in the blood and urine. PBG is generally so strikingly increased during an attack of AIP , quantitative event on spot sample rather than a 24 hour collection of urine is highly informative. During collection of urine a dark plastic jug should be used to protect the sample from light as porphyrin are fluorescent substances which on exposure to light and air oxidize and turn intensely reddish. During shipping it is stored in a refrigerator or in an ice chest[1,4].

The diagnosis of AIP is always an important item of medical information even when there is no symptom. It may influence the choice of drugs to treat other medical conditions, surgery and anesthesia. Some drugs are potentially dangerous like sulphonamide , Tranquilizers and sedative, Griseofulvin, Carbamazepine, Phenytion, Valproate, OCP,Alcohol, Rifampicin,Tetracycline, Diclofenac. Some drugs are probably safe like Narcotic analgesic, Aspirin, Acetaminophen, Chlorpromazin, Peniciline, streptomycin, Glucocorticoid, Insulin, Atrophin, SSRI etc. If a question of drug safety arises a physician or medical centre specialized in prophyria should be conducted[6,8].

Acute attacks require a prompt diagnosis, withdrawal of the inciting agent, and treatment with narcotic analgesics, intravenous glucose and haematin. Electroyte imbalances requires careful monitoring and correction. Treatment with a high carbohydrate diet diminishes the number of attack in some patients. A minimum of 300gm/day of carbohydrate should be provided orally or intravenously. Haeme products like haeme arginate, is the recommended specific therapy for AIP 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 costly drug is not routinely available in our country.So management stratigies for this rare disease should be planned to relieve symptoms, prevent inciting factor, avoiding harmful drugs and taking plenty glucose rich fluids regularly in our perspective[1,2,7].

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