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A CASE OF ACUTE INTERMITTENT PORPHYRIA

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Abstract :
Acute Intermittent Porphyria (AIP) is a rare hereditary disorder of heme metabolism, characterised by episodes of gastrointestinal, psychiatric, or neurologic symptoms.We report a case of young female presenting with recurrent attacks of abdominal pain with seizures and peripheral motor neuropathy.The diagnosis of acute intermittent porphyria was confirmed by the presence of urine porphobilinogen and patient recovered with supportive therapy.
Keyword : Acute Intermittent Porphyria,Porphobilinogen,Hematin

CASE REPORT:

23 yr old female resident of Nellore was admitted with 1 week history of episodic diffuse colicky abdominal pain,associated with nausea and vomiting associated with passing dark red coloured urine.About 3 days later she developed acute onset progressive weakness of all the four limbs and became bedridden within next 2 days prior to hospitalization.In the past 1 year she had 4 similar episodes of abdominal pain not associated with weakness.She had episodes of generalized tonic clonic seizures in the last 2 months without limb weakness.Her relatives gave history of altered behavior with episodes of aggression in the last 1 month. No h/0 fever, skin rashes,photosensitivity,arthralgia,bleeding tendencies,abdominal distension,jaundice,headache,blurring of vision,dysphagia,nasal regurgitation,sensory disturbances,bowel and bladder disturbances.No h/o other comorbid illness like diabetes,hypertension,asthma,tuberculosis.She is unmarried with regular menstrual cycles.She was born of non-consanguinous marriage with 2 siblings and death of an elder sibling at the age of 16 yrs with similar illness. On examination she is thin built,irritable,with hirsutism, afebrile,anemic,not icteric with adequate hydration with normal pulse and blood pressure.Neurological examination revealed flaccid quadriparesis with areflexia with intact sensory

system and cranial nerves.Examination of abdomen,cardiovascular and respiratory system did not reveal any abnormality.

PHOTO SHOWING WASTING AND HIRSUTISM

Laboratory investigations showed a Hemoglobin- 7.6 g/dl,Total leukocyte count – 5800/cu mm,Differential count – P50%, L44%, E1%,M5%,Plateletcount–2 lakhs and ESR-45 mm/hr.Peripheral smear revealed microcytic hypochromic anemia.Serum electrolytes,serum amylase,liver and renal function tests were normal.Urine for Hemo and Myoglobin negative.Serology for HIV,Hepatitis B and Hepatitis C were negative.Cerebrospinal fluid analysis revealed Sugar 66mg/dl,protein 49 mg/dl with occasional lymphocytes.MRI Brain was normal.Urine Porphobilinogen was strongly positive.Nerve conduction studies revealed reduced amplitudes of compound-muscle action potentials on the motor nerves.The sensory nerve studies were normal.Screening of other family members for porphobilinogen was negative.

A provisional diagnosis of Acute Intermittent Porphyria was made on the basis of positive family history, typical clinical features and presence of Porphobilinogen (PBG) in urine of the patient. Patient was treated with high dose of carbohydrates along with other symptomatic measures and physiotherapy.Patient showed gradual improvement in muscle power and at the time of discharge adviced about the drugs precipitating the attacks. **DISCUSSION:** The word “porphyria” derives from the Greek word *porphuros*[1]*, which means red or purple.The porphyrias are a group of rare metabolic disorders arising from reduced activity of any of the enzymes in the heme biosynthetic pathway. The disorders may be either acquired or inherited through a genetic defect in a gene encoding these enzymes.*

Porphyrias can be classified as either ***hepatic or erythropoietic***[3]*, depending on whether the heme biosynthetic intermediates that accumulate arise initially from the liver or developing erythrocytes, or as* ***acute or chronic****, based on their clinical manifestations.*

Acute Porphyrias[2,6]*:Present during adult life with acute attacks of neurologic manifestations and elevated levels of one or both of the porphyrin precursors, ALA and PBG. Neuroporphyrias:Acute intermittent porphyria (AIP),ALA-dehydratase porphyria (ADP). Neurocutaneousporphyrias:Hereditary coproporphyria (HCP), variegate porphyria (VP).*

Chronic Porphyrias*:Present before or after puberty with cutaneous manifestations. Porphyria cutanea tarda (PCT), congenital erythropoietic porphyria (CEP) and erythropoietic protoporphyria (EPP).* ***ACUTE INTERMITTENT PORPHYRIA (AIP)***[4] *Acute intermittent porphyria is an autosomal dominant disorder resulting from partial deficiency of porphobilinogen deaminase enzyme in heme biosynthetic pathway.*

Estimated occurrence is 1 to 2 in every 100,000 persons, with the most common incidence in the Northern European countries such as England, Ireland and Sweden. In India[24], AIP has been reported from various parts of the country and some specific communities in Rajasthan have been found to be especially susceptible.Manifestations of AIP occur commonly after puberty and the female preponderance suggest the role of estrogens in activating the disease.Common precipitating factors include endogenous and exogenous steroids, porphyrinogenic drugs[5] (phenobarbitone,phenytoin,carbamazepine,rifampicin,spironolactone,etc.), alcohol ingestion and low-calorie diet.

CLINICAL MANIFESTATIONS: Abdominal pain, peripheral neuropathy, and changes in mental status are the classic triad of an acute attack.

GASTROINTESTINAL[6]**:**Abdominal pain is the initial manifestation in 85% of acute attacks usually steady and poorly localized.Other manifestations include nausea,vomiting, abdominal distension and constipation.

NEUROLOGICAL[7,8,9,10,11]**:** Peripheral neuropathy occurs due to axonal degeneration[12,13] primarily affects motor neurons.Cranial nerve involvement,bulbar and respiratory paralysis and seizures can occur.

AUTONOMIC:

Tachycardia, hypertension, restlessness, tremors, and excessive sweating occurs due to sympathetic overactivity.

PSYCHIATRIC:[15]Anxiety, insomnia, depression, disorientation, hallucinations, and paranoia can occur in acute attacks.

ELECTROLYTE DISTURBANCES: Hyponatremia,hypokalemia, andhypocalcemia.Hyponatremia occurs due excess vomiting,diarrhea and SIADH[14].

LONGTERM COMPLICATIONS: Hypertension[16],chronic renal disease and hepatocellular carcinoma[17].

DIAGNOSIS:[18,19,20] A definitive diagnosis requires demonstration of PBG Deaminase 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.Watson Schwartz test is based on a colour reaction with Ehrlich's aldehyde reagent, an acidic solution of paradimethylaminobenzaldehyde.The porphobilinogen and chromogen it forms always remain in the aqueous phase. It has a sensitivity of only 40% –69%.Measuring the 24-hour urinary excretion of porphobilinogen and aminolevulinic acid during a symptomatic period is the most helpful method of determining whether a particular set of symptoms and signs are due to acute porphyria.During an acute attack, acute intermittent porphyria is distinguished from variegate porphyria or hereditary coproporphyria by normal or near-normal levels of fecal porphyrin. Reduced activity of erythrocyte porphobilinogen deaminase further supports the diagnosis of acute intermittent porphyria.HMB synthase activity in erythrocytes or genetic mutation analysis detects asymptomatic carriers.

TREATMENT:[21]

Management strategies in acute episodes of porphyria are limited and therapy is mainly supportive.Treatment mainstays include identifying and limiting possible precipitants, maintaining adequate intake of carbohydrates atleast 300g/day and fluids,narcotic analgesics for abdominal pain,benzodiazepines like clonazepam for seizures and administering haem arginate. Hematin[22,23] most typically in the form of haem arginate acts by negative feedback, suppresses aminolevulinic acid synthase, the rate-limiting enzyme in the heme biosynthetic pathway, with a resultant dramatic decline in porphyrin production. Within hours of heme administration,the overproduction and overexcretion of aminolevulinic acid and porphobilinogen are normalized.Within 2 to 4 days, most patients with acute porphyria show clinical improvement

DIFFERENTIAL DIAGNOSIS:

Lead poisoning and Hereditary tyrosinemia

CONCLUSION: Acute intermittent porphyria should always be considered in a case of abdominal pain with neuropsychiatric manifestations.Since definitive diagnostic facilities are not routinely available high index of clinical suspicion along with Watson Swartz test will help in the management of acute attacks and reducing the morbidity and mortality.Once diagnosis is made screening of family members for asymptomatic carriers should be done.

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