A RARE METABOLIC DISORDER PORPHYRIAS NEUROLOGICAL MANIFESTATIONS

KALPANA R RADHAKRISHNAN
Department of Neurology,
STANLEY MEDICAL COLLEGE AND HOSPITAL

Abstract:
Porphyrias are a group of rare metabolic disorders. Porphyrias have a large spectrum of clinical manifestations. 17 year old, male was admitted with fever, recurrent vomiting, seizure and altered sensorium. In addition, he had hyponatremia and syndrome of inappropriate antidiuretic hormone secretion (SIADH). Subsequently, the patient developed a high blood pressure-labile hypertension, posterior reversible encephalopathy syndrome (PRES) and an acute areflexic quadriplegia with a predominant proximal weakness with preserved ankle jerks. The above features of labile hypertension, SIADH, acute areflexic quadriplegia with preserved ankle jerks in the background of abdominal complaints in the form of recurrent vomiting and encephalopathy made us consider the possibility of porphyria. Urine samples tested positive for porphyrin precursors qualitatively and quantitatively. This case is presented for its rarity and to highlight the varied spectrum of clinical manifestations of porphyria.

Keyword:
porphria, labilehypertension, hyponatremia, SIADH, areflexic-quadriplegia preserved-ankle jerks

Abbreviations:
SIADH — syndrome of inappropriate antidiuretic hormone, PRES — posterior reversible encephalopathy syndrome, GBS — Gullian Barre Syndrome.

Porphyrias are a group of rare metabolic disorders resulting from deficiency of specific enzymes in the heme biosynthesis pathway causing accumulation of porphyrin and their precursors, leading to a variety of neurological, hematological and dermatological manifestations. The term porphyria derived from Greek means ‘purple urine’. A diagnosis of porphyria should be considered in patients with unexplained neuro psychiatric features, recurrent attacks of abdominal pain or cutaneous photo sensitivity. The commonest form of porphyria, acute intermittent porphyria usually presents as acute attacks of abdominal complaints such as abdominal pain / vomiting, encephalopathy and peripheral neuropathy.
Case vignette:
17 yr old male who was apparently healthy 4 days ago, was admitted with complaints of fever (high grade intermittent with rigors) and recurrent vomiting for the past 3 days with 1 episode of generalized seizure followed by altered sensorium since morning O/E patient was semiconscious, GCS 6/15, febrile, no meningeal signs, PERL, CNS – no focal neurological deficit, fundi normal and other systems examination was normal. Patient was suspected to have CNS infection, work up for infectious etiology, CT brain imaging & CSF analysis was done, but the above investigations were not contributory. Patient was empirically treated with parenteral antimalarials and supportive therapy. Patientsensorium improved over the next 3 days, conscious, oriented and obeying commands. However on the 5th day of admission, patient had two episodes generalized seizures following which the patient’s sensorium deteriorated again. The blood pressure was high(BP 140/110 mmHg) and MRI brain revealed bilateral parieto occipital vasogenic edema suggestive of posterior reversible encephalopathy syndrome(PRES). EEG showed severe diffuse non specific electro physiological dysfunction and epileptiform discharge in bilateral regions. Seizures were treated with loading dose of parenteral phenytoin followed by maintenance dose. Antihypertensive, Ca+channel blocker was added for the control of blood pressure. In spite of the antihypertensive the blood pressure kept fluctuating between normal and labile hypertension with PRES and flaccid quadriplegia (with normal S.k+ of 4.3meq/l) with retained ankle jerks, made us think to consider the possibility of porphyria. Review of history revealed that the patient used to have abdominal pain on and off in the past that was relieved with antacids! Urine sample for ALA and PBG was positive. Urine on sunlight exposure turned burgundy wine colour.24 hr urinary porphobilinogen(PBG) was 78.80 mg/day (normal 0 – 3.4 mg/day and aminolevulinic acid(ALA) was 116.60mg/day (normal 1- 7 mg/day), consistent with the diagnosis of porphyria. Other investigations – complete hemogram, renal and liver function tests, blood sugar, urine routine were normal. Ultrasonogram whole abdomen with renal arteries doppler was normal. Echocardiogram was normal. Urine & blood culture sensitivity showed no growth. CXR was normal. S CPK was 150 IU/L. Vasculitic workup ANA, RA factor, APLA, SS-A SS-B were negative. 

On day 7, patient developed acute flaccid areflexic quadriplegia. Proximal power of all limbs was 3/5 whereas the distal power was near normal. The DTR were absent however the ankle jerks were preserved. The serum potassium was 4.3 meq/l . The nerve conduction study of both upper and lower limbs, done on the day of onset of quadriplegia was normal. The above features of abdominal complaints in the form of recurrent vomiting,encephalopathy,labile hypertension with PRES ,SIADH and flaccid quadriplegia (with normal S.k+ of 4.3meq/l) with retained ankle jerks, made us think to consider the possibility of porphyria.
MRI brain T2 flair of this patient, showing Bilateral parieto-occipital hyperintensities MRI brain ADC of this patient showing hyperintensities in the bilateral parietal regions and the corresponding areas on DWI were isointense suggestive of vasogenic edema of PRES

Urine sample of the patient before sunlight exposure

Urine sample of the patient after sunlight exposure

The patient was treated with glucose loading, the precipitating drugs and causes were carefully avoided, and the vitals were closely monitored and maintained. Fluid and electrolyte balance was maintained. However the patient’s condition worsened with progressive limb weakness. Subsequently the patient developed respiratory muscle weakness and aspiration necessitating mechanical ventilation and the patient succumbed to the disease on the 25th day of admission.

Discussion:
The acute encephalopathy of porphyria manifests as altered sensorium or psychiatric features, seizures and SIADH. Porphyric neuropathy is predominantly motor and autonomic. The short axons are preferentially involved in porphyric neuropathy and causing predominant proximal, symmetrical weakness initially and later involves the distal muscles. The deep tendon reflexes may be completely absent except for preserved ankle jerks. The sensory complaint, if present, is a sensory loss over the face trunk and proximal limbs.
The autonomic involvement causes abdominal pain, constipation, labile hypertension, tachycardia, fever, dilated pupils and cardio respiratory collapse. In our patient, initially, when he presented with fever, recurrent vomiting, seizures and altered sensorium, CNS infection was suspected but the CT brain imaging and infectious etiology workup including CSF analysis was normal. As the patient developed hypertension and PRES vasculitic workup and renal arteries doppler were done which were negative. Subsequently, the patient developed SIADH and acute areflexic quadriaparesis, a Gullian barre syndrome like picture. This clinical spectrum of labile hypertension, SIADH, acute areflexic quadriaparesis with preserved ankle jerks in the background of encephalopathy and abdominal complaint in the form of recurrent vomiting, gave the clue to the diagnosis of porphyria. Urine samples tested positive for porphyrin precursors qualitatively and quantitatively and there was a burgundy red wine colour change of urine on exposure to sunlight.

Porphyrias are caused due to inherited disturbance in heme biosynthesis. Prevalence is 1-2 per 100,000. There is a higher incidence of porphyria in psychiatric than in general population(1). Clinical features of acute intermittent porphyria(AIP) are abdominal pain in 80% of the patients with an acute attack, vomiting in 50%, constipation 50%, labile hypertension in 31% and fever in 16% of the patients(2). Hyponatremia is often associated with acute attacks of AIP and may be associated with SIADH(5) The most common presenting symptom of an acute attack is abdominal pain (3). The most common physical sign of AIP is tachycardia seen in 80% the patients with acute attacks (4). Sudden death in porphyria is attributed to cardiac arrhythmias. There are conditions that can precipitate an acute attack in a patient with porphyria. The common precipitating factors for an acute attack are drugs (barbiturates, alcohol, ketamine, anticonvulsants like phynetoin, carbamazepine, sodium valporate, antibiotics like sulphonamides, centrally acting agents viz metoclopramide, alpha methyl dopa, chlorpropamide, chloroquine, NSAIDS etc, starvation, low carbohydrate diet, stress, severe physical exertion, surgery, trauma and hormonal changes. Acute attacks of AIP should be managed with narcotic analgesics for abdominal pain, phenothiazines for nausea and vomiting. A minimum daily intake of 300gms of carbohydrate is required during acute attacks. Early heme therapy for acute attacks is advocated. Heme causes negative feedback inhibition of ALA synthetase, the rate limiting enzyme in heme synthesis pathway. Heme is administered intravenously as hematin in doses of 3 – 4 mg / kg body weight/ day for 4 days. Patients receiving heme therapy should be monitored for complications of coagulopathy, thrombophlebitis and hemolysis.

**Conclusion:** This case is presented for its rarity. In the presence of abdominal complaint as recurrent vomiting, encephalopathy in the form of altered sensorium, seizures and SIADH, the presence of labile hypertension, GBS like acute flaccid areflexic quadriaparesis causing a predominant proximal, symmetrical weakness with preserved ankle jerks, porphyria should be considered.

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