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Case Report

Acute Intermittent Porphyria in Childhood Presenting with Hypertensive Emergency and Posterior Reversible Encephalopathy Syndrome

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ABSTRACT

Acute intermittent porphyria is an inherited metabolic disease due to deficiency of the enzyme porphobilinogen deaminase that can affect the autonomic, peripheral and central nervous system. We report an 8 year old female who had presented with hyponatremia, psychiatric manifestations, seizures, hypertension and Posterior Reversible Encephalopathy Syndrome (PRES) with a delayed diagnosis of Acute Intermittent Porphyria. As porphyria is thought to be very rare in pre-pubertal age, in view of the potentially fatal outcome of a severe attack, a high index of suspicion is essential.

Key words: Acute intermittent porphyria, Posterior reversible encephalopathy syndrome, hypertensive crisis.

Introduction

Acute intermittent porphyria (AIP) is one of the porphyrias, a group of diseases involving defect in heme metabolism and that results in excessive secretion of porphyrins and porphyrin precursors. AIP is an autosomal dominant disease that results from defects in the enzyme porphobilinogen-deaminase. This enzyme speeds the conversion of porphobilinogen to hydroxymethylbilane. In AIP, the porphyrin precursors, porphobilinogen and amino-levulinic acid (ALA), accumulate. The predominant problem appears to be neurologic damage that leads to peripheral and autonomic neuropathies and psychiatric manifestations. AIP affects women more than men, with a ratio of 1.5-2:1.[1] Most patients become symptomatic between ages 18-40 years.[1]

Case Report

The patient was an 8 year old female Muslim child, born of non-consanguinous marriage, from lower socio-economic class. At the time of first admission, patient presented with complaints of persistent vomiting, focal convulsion, vague abdominal pain and psychiatric manifestations like confusion, agitation and transient aphasia. Birth, development history and school performance was normal prior to illness. CNS examination, including fundus and routine blood investigations were normal except mild hyponatremia (Serum sodium – 128mEq/L). Repeated blood pressure monitoring revealed BP slightly on the higher side within normal limits with maximum BP recorded once upto 116/70 (90th percentile for age – 117/76). CT scan was also normal. Child was discharged with probable diagnosis of unprovoked convulsion with appropriate follow-up advice.

She was admitted three days later with complaints of focal convulsions. On admission, patient was vitally stable except BP which was 124/72 (95th percentile 122/80). SMR was pre-pubertal and BMI 14.3. Neurological examination including fundus was unrevealing. Serum sodium was 121mEq/L. After admission, the patient had 2 more episodes of seizures. MRI showed asymmetric cortical and subcortical altered signal intensities in bilateral singulate gyrus, right occipital, bilateral parietal and bilateral high fronto-parietal lobes suggestive of PRES (Fig. 1). In spite of appropriate fluid therapy, serum sodium remained persistently between 120-127mEq/L. Serial BP measurements revealed values around 90th

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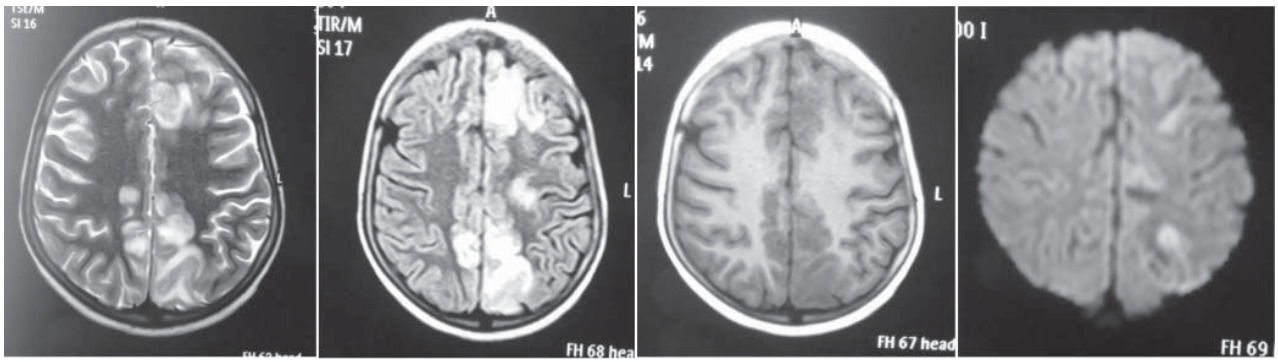

Figure 1: MRI brain contrast images showing asymmetric cortical and subcortical altered signal intensities in bilateral singulate gyrus, right occipital, bilateral parietal and bilateral high fronto-parietal lobes

percentile for age. With the neurologist opinion, EEG was planned. Sodium Valproate was started and the patient was discharged with appropriate follow-up for BP monitoring.

The patient was readmitted within three days with dyspnoea, altered sensorium and clinically hypertensive crisis with BP 148/68 (>99th percentile) (Mean Arterial Pressure 93mmHg). All 4 limbs BP showed no discrepancy. Systemic examination including fundus was normal. Hypertensive crisis was managed with Injectable Labetalol, oral Nifedipine and Injectable Furosemide. During the first 72 hours, vitals were monitored one hourly and anti-hypertensives titrated accordingly. By the third day, the patient was on oral Nifedipine and Labetalol.

CBC, RFT and LFT were normal. Serum sodium was 130mEq/L. She was thoroughly investigated to rule out cardiac, renal or renovascular etiology for hypertension. Urine examination, ASO titre, serum C3 levels and Urinary ferric chloride were normal. 2D ECHO, USG abdomen (including adrenals) and renal Doppler were normal. Parents' BP was normal. 24-hour urinary metanephrine screening test revealed elevated value of 2.3mg/24hours (normal 0-1 mg/24hours).

By 7th day, intermittent tachycardia and laboured breathing was observed. Patient developed muscle weakness in all 4 limbs and palatal palsy. Gradually her urine colour changed from yellow to dark brown to black. She developed icterus and bilirubin was 2.6, which led to suspicion of porphyria. Urine porphyrin levels estimated by Spectrophotometry was 1201.5nmol/L (normal 20-320 nmol/L), indicative of porphyria.

There was no past history of visual disturbances, dark urine, emotional disturbances or cutaneous manifestations in family members. Upon diagnosis of AIP, Valproate was discontinued and she was started on high cabohydrate diet as specific medicine, Hemin is not available. By 15th day, anti-hypertensives were tapered. A nerve conduction velocity (NCV) study was done which showed signs of axonal type of motor polyneuropathy. She was diagnosed as AIP presented with hypertensive crisis, PRES, autonomic disturbance, axonal polyneuropathy and cranial nerve involvement. Enzymatic or gene studies for at-risk relatives could not be done.

Parents were counselled and given written information regarding precipitating factors, list of medications to be avoided, importance of a balanced diet with high carbohydrate content and continuing physiotherapy at home. On follow up, she showed symptomatic improvement and Nifedipine stopped 2 months later.

Discussion

Although occurrence of hypertension during acute attack of AIP is not uncommon, this hypertension is often labile.[2] Malignant hypertension and hypertensive encephalopathy has been reported.[3] However all of these were reported in adults and we could not find any such presentation in children. Hypertension may be associated with autonomic disturbances due to release of catecholamine during an acute episode.[4] It usually occurs secondary to renal ischemia due to arterial spasm as a result of sympathetic overactivity.[2,3] Hyponatremia occurs as a result of SIADH.[4,5] AIP rarely presents with PRES, which is a rapidly evolving neurologic condition characterized by severe headache, visual disturbance, altered consciousness,

and seizures[6]. Classically, MRI reveals edematous lesions located primarily in the posterior parietal and occipital lobes.[7] The pathophysiology of this lesion is most likely due to cerebral vasospasm and loss of autoregulation.[6,8] Other probable mechanisms include neurotoxic effect of excess porphyrin at the hypothalamic level.[9] Peripheral neuropathy, which is predominantly a motor neuropathy of the axonal type, initially affecting mainly the proximal rather than distal muscles, is common.[10] Cranial nerves can also be impaired in cases of AIP, with the facial and vagus nerves being involved more than the others.[9] The accumulation of neurotoxic heme precursors may lead to impaired function of the axonal Na+/K+ pump with consequent alteration in membrane potential to cause neuronal cell death and axonal degeneration.[10]

Conclusion

AIP causes life-threatening attacks of neurovisceral symptoms that mimic many other medical, surgical and psychiatric conditions. Lack of clinical recognition leads to inappropriate diagnostic tests, misdiagnosis and delays effective treatment. In contrast to common presentation of acute abdomen and black urine in the age group of 18-40 yrs, the index patient presented with hyponatremia, neuropsychiatric symptoms and hypertensive crisis. Associated autonomic disturbances such as hypertension, tachycardia and abdominal pain should arouse the suspicion of AIP. Hence, our case was unique in several ways:

1. Early age of onset - Acute intermittent porphyria remains primarily a disease of adult onset.
2. Hypertensive crisis, in contrast to usual presentation of labile hypertension in 36-55% of patients.
3. Marked psychiatric symptoms, observed in 40-60% of patients.
4. Repeated episodes of seizures. Reported incidence is 10-20%.
5. Hyponatremia, seen in around 28% of patients.

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