Journal of Hematology & Thromboembolic Diseases

Mathavan et al., J Hematol Thrombo Dis 2018, 6:2
DOI: 10.4172/2329-8790.1000290

Case Report Open Access

An Interesting Case of Acute Intermittent Porphyria Precipitated During Premenstrual Phase

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Received date: May 05, 2018; **Accepted date:** May 18, 2018; **Published date:** May 24, 2018

Abstract

Acute intermittent porphyria is one of the rare, autosomal dominant, hereditary hepatic porphyria due to deficiency of enzyme Hydroxyl Methyl Bilane synthase (HMB synthase) in the haem synthesis pathway. The condition is characterized by acute abdominal pain and neuropsychiatric manifestations. One of the precipitating causes of AIP is menstruation due to high levels of progesterone. We report an interesting case of AIP precipitated during each cycle of menstruation.

Keywords: Progesterone; Menstruation; Abdominal pain; Porphyria

Introduction

A 22 year old unmarried female, presented with history of recurrent episodes of abdominal pain, especially during her menstrual cycles which was treated as dysmenorrhea. The pain was severe associated with non-bilious non projectile vomiting. Other than the pain, there was no other symptoms suggestive of acute abdomen. Six months prior to presentation patient had an episode of varicella zoster infection which was appropriately treated. During the same period, four months prior to our hospital admission, she was extensively investigated elsewhere for recurrent abdominal pain and definite etiology could not be established. Patient was treated conservatively with proton pump inhibitors and antispasmodic drugs with which she had partial relief. One month prior to our admission, she had an episode of Generalised Tonic Clonic Seizures and altered sensorium without any neurological deficit. She was found to have significant hyponatremia due to SIADH and was managed appropriately. Due to persistent abdomen pain and fluctuating sensorium she reported to our institution. At the time of admission, she was conscious with starring look and decreased responsiveness to call. General examination revealed pallor, but otherwise unremarkable. Other than tachycardia, her vitals were stable. Examination of cranial nerves were normal. She had mild weakness in both lower limb with hypotonia, sluggish deep tendon reflexes with bilateral flexor plantar response. Her sensory system was intact. She had urinary retention with constipation. There were no signs of meningeal irritation and fundus examination normal. A possibility of meningoencephalitis (ADEM), post viral sequelae and metabolic encephalopathy were considered as diagnosis.

Preliminary investigations including complete blood count, ESR, Peripheral smear study, were normal except for mild neutrophilic leukocytosis. LFT showed Albumin Globulin reversal and mild elevation of transaminases. Urine examination showed microscopic hematuria and hemoglobinuria (attributable to contamination by menstruation). Biochemical investigation showed moderate hyponatremia (Na 123 mEq/L) with normal potassium and RFT. Cerebrospinal fluid analysis was done for ADEM which showed normal findings Investigations are shown in the Table 1.

	Day 1	Day 6
Tc	13800 c/mm^3	-
N	76.7	-
E	0.9	-
B	0	-
L	12.3	-
M	10.1	-
Esr	08 mm	-
Rbs	134 mg/dl	-
Bun	18	9
Creatinine	0.6	0.5
Total bili	0.3	-
D.bili	0.09	-
Ast	72	-
Alt	70	-
Alp	69	-
Ggt	92	-
Albumin	2.9	-
Globulin	3.3	-
Sodium	123	136
Potassium	4.7	4.1
Urine		-
Albumin	Nil	-
Sugar	2+	-

Pus cells	06-aug	-
Epithelial cells	03-apr	-
Rbcs	10-dec	-
Ketones	Negative	-
Ph	6	-
Ck total	178	-
Ft3	2.64	-
Ft4	1.02	-
Tsh	4.69	-
S.cortisol	22.19	-
Csf analysis		
Glucose		75
Protein		21.3
Chloride		119
Ada		0.66
Gram stain	-	No pus cells

Table 1: ADEM which showed normal findings investigations.

MRI brain didn't show any abnormality. Inspite of correction of dyselectrolytemia, patient's neuropsychiatric manifestations did not improve. In view of episodic abdomen pain with neurovisceral symptoms with family history of psychiatric disorder in her father, a diagnosis of Acute Intermittent Porphyria was considered. Urine for aminolevulinic acid (ALA) and porphobilinogen (PBG) was done which showed increased urine ALA(50.9 mg/24 hrs) and PBG (54.9 mg/24 hrs). She was managed conservatively with 300 mg dextrose daily. Three months later she presented with severe abdomen pain associated with her menstrual cycle. She was treated with intravenous dextrose and showed dramatic improvement. Since her conditions were mild and not life threatening, hematinic therapy was not considered. Patient was discharged with appropriate advice regarding precipitating factors of porphyria. Patient is on our regular follow up.

Discussion

Acute intermittent porphyria (AIP) is an autosomal dominant disorder, resulting from partial deficiency of enzyme hydroxylmethylbilane synthase (HMB synthase) in the haem biosynthetic pathway. Incidence in Europe is 1:20,0002 and its association with menstruation is noted. We report such case of AIP associated with premenstrual phase and neurological manifestations. Activation of rate limiting enzyme of heme synthesis in liver (ALA synthase) in patients with half normal HMB synthase activity is thought to cause acute attacks in AIP. Most heterozygotes for HMBS mutations remain latent until there is some precipitating conditions where heme synthesis is increased in liver, thus limiting the less available HMB synthase activity and so ALA, PBG, and other intermediates may get accumulated and excreted in urine. AIP manifests at any age from puberty onwards but mostly in the third decade of life [1]. Common precipitating conditions are poor calorie diet or fasting, porphyrinogenic drugs, alcohol, and steroids. Women most commonly have premenstrual attacks due to endogenous progesterone [2]. Studies indicate that progesterone, either endogenous or exogenous, induce attacks of acute porphyria [3]. Progesterone has also been implicated in increased haem catabolism [4]. Levels of progesterone and of its metabolites-are markedly increased during the luteal phase of the menstrual cycle and are considered more important than oestrogens in precipitating AIP attacks [5]. Though acute attacks are seen with exogenous steroids and preparations with progestin, pregnancy is usually well tolerated. Axonal degeneration might cause peripheral neuropathy. Deep tendon reflexes may be normal or brisk but later decreased or absent in advanced neuropathy. Mental symptoms seen in acute attacks include anxiety, insomnia, depression, disorientation, hallucination, and paranoia [1,2]. Seizures can occur due to neurologic effects or to hyponatremia. Treating seizures is difficult as most of the antiepileptics can cause acute attacks of AIP. Hyponatremia is due to hypothalamic involvement and inappropriate vasopressin secretion or from electrolyte depletion. Diagnosis is by increased levels of ALA and PBG in plasma and urine, especially during acute attacks.

Conclusion

AIP should be an important, although uncommon, differential diagnosis in the evaluation of recurrent abdomen pain associated with premenstrual phase in women especially if associated with psychiatric manifestation.

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