Case Report

Acute intermittent porphyria: Diagnostic dilemma and treatment options

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Abstract

Acute intermittent porphyria (AIP) presents with diverse group of symptoms making its early diagnosis difficult. Delaying diagnosis and treatment of AIP can be fatal or can cause long term or permanent neurological damage. We present here a case report of AIP where the diagnosis was missed. The diversity of symptoms and details concerning the treatment options for AIP are discussed.

Key words: Acute intermittent porphyria, amino levulinic acid, porphobilinogen

Introduction

The porphyrias are uncommon and complex metabolic conditions caused by deficiencies in the activities of the enzymes of the heme biosynthetic pathway. Acute intermittent porphyria (AIP) is inherited as an autosomal dominant disorder due to deficiency of the enzyme porphobilinogen (PBG) deaminase located in the hydroxymethylbilane synthase (HMBS) gene in chromosome no. 11q23.3.[1]

Case Report

A female patient aged 18 years weighing 35 kg was admitted to the Intensive Care Unit (ICU) in our hospital with complains of diffused dull aching abdominal pain, not related to food habit with occasional nausea and vomiting from 2 months. She was treated with proton pump inhibitors (tablet pentoprazole 40 mg twice daily) and antispasmodic medication (dicyclomin). Gradually she also developed diarrhea, vomiting and progressive weakness of her lower limbs and finally flaccid quadriparesis. At the time of presentation to ICU, she was conscious, oriented, Glasgow coma score (GCS) 15/15, pulse rate 100/min, blood pressure (BP)-130/80 mmHg, normal respiratory and cardiovascular system and flaccid quadriplegia. There was also a history of two episodes of seizure last night. She gave no history of accidental or intentional ingestion of any poisonous substances. Her family history was unremarkable. Initial laboratory investigations showed total leucocyte count 12.0 × 10^9/L with neutrophil 80%, sodium 128 meq/L, chloride 96 meq/L and normal magnetic resonance imaging cervical spine and cerebrospinal fluid analysis. Treatment was started with anticonvulsants (injection phenytoin 100 mg 3 times a day), antibiotics (injection ceftriaxone 1 g twice daily) and correction of the electrolyte imbalance. Over the next 15 days, she developed respiratory muscle paralysis, was intubated and put on mechanical ventilation. Despite all measures she continued to have seizures and labile BP. Gradually she also became delirious with deterioration of GCS to 10. No improvement was observed in her laboratory parameters also. Finally urine PBG was done which was found positive. Electromyography results also demonstrated the presence of severe sensory motor axonal polyneuropathy. Immediately, all porphyrogenic drugs were stopped, phenytoin was replaced by gabapentin and a high-carbohydrate diet (400 to 450 g/day) was started. Treatment with hematin could not be started, due to the difficulty in obtaining the drug. Even after 1-week of therapy there was no improvement in her clinical condition and a decision was made to try hemodialysis. However, eventually she developed sepsis requiring high-ionotropic support which precluded further leading to her demise.

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Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/0970-9185.161683

Discussion

Acute intermittent porphyria also known as "Swedish porphyria" is one of the porphyrias which involves defects in heme metabolism resulting in excessive secretion of porphyrins and porphyrin precursors like amino levulinic acid (ALA) and PBG.[2] AIP is a rare autosomal dominant metabolic disorder characterized by a deficiency of the enzyme PBG deaminase[1] (also known as HMBS or uroporphyrinogen 1 synthetase).

Its prevalence is 2-3 cases per 100000 persons per year.[3] Though it is not much reported in India, it is much prevalent in some parts of the country like Kumar and Maheshwari communities of western Rajasthan.[4]

The patients generally present with neurovisceral symptoms such as pain abdomen (85-95%), vomiting (50%), constipation (50%), peripheral neuropathy (42-68%), seizures (10-16%), delirium, coma and depression.[4] Autonomic disturbances may manifest as urinary retention, paralytic ileus, restlessness, tremor, excessive sweating, tachycardia, and labile BP.[4] Complications like bradycardia and sudden death have also been reported.[5] The attack is often precipitated by environmental factors, reduced calorie intake, medications (barbiturates, calcium channel blockers, antibiotics, antifungals, and hormones), large alcohol intake, nicotine abuse, infection, surgery and psychiatric illness.[3,5] Endo and exogenous steroids have a role in precipitating an acute attack which might be the reason for its frequent finding in females after puberty as in our case.[6]

Diagnosis of AIP is confirmed by detection of porphyrin or porphyrin precursors in freshly voided urine by Watson–Schwartz test using Ehrlich's aldehyde reagent.[7] Classic burgundy red discoloration of long stored urine is also a clue.[7] Quantitative measurements of PBG and ALA in urine or erythrocyte HMBS enzyme test are more reliable confirmatory tests. Heavy metal poisoning (i.e., arsenic and lead and thallium) may simulate AIP making their screening a mandatory requirement.[7]

Porphyric neuropathy typically presents as a motor neuropathy of the axonal type preferentially affecting the proximal musculature with occasional sensory involvement. The predominantly motor neuropathy associated with weakness and areflexia in AIP can mimic Guillain–Barré syndrome.[7] Nerve conduction studies help in differentiating these two conditions as porphyric neuropathy which presents as axonal degeneration lacks the features of demyelinating neuropathy.

Treatment of AIP during acute attack is directed toward decreasing the heme synthesis and production of porphyrin precursors. Removal of precipitating factors, treatment of underlying infection, a carbohydrate diet and intravenous (i.v) heme remains mainstay of treatment of an acute attack. I.V. dextrose in high doses (300-500 g/day) blocks induction of the enzyme and prevents accumulation of precursors. However in severe cases especially if paresis occurs, heme therapy is indicated at 3-5 mg/kg/day for 3-5 days.[8] Heme acts by depressing the ALA synthetase enzyme.[8] The symptoms improve readily on heme therapy generally within 24 h. It is available in the form of hematin (Abott laboratories), heme albumin or heme arginate (Leiras Oy, Turku, Finland).[4] However, as these drugs are not easily available in India we could not use them. Charcoal hemoperfusion and hemodialysis has been used successfully.[9]

Seizure can be controlled by correction of hyponatremia[6] and gabapentine, vigabetin.[6]

Long-term monitoring is required in AIP patients as they are at increased risk for development of chronic renal failure and hepatocellular carcinoma. Screening of the family members even if asymptomatic to detect the genetic defect is important for prevention of an acute attack.[8]

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How to cite this article: Kaur MD, Hazarika N, Saraswat N, Sood R. Acute intermittent porphyria: Diagnostic dilemma and treatment options. J Anaesthesiol Clin Pharmacol 2015;31:407-8.
Source of Support: Nil, **Conflicts of Interest:** None declared.