Acute intermittent porphyria presenting with neurological emergency: Review of six cases

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Acute intermittent porphyria presenting with short duration of gastrointestinal symptoms followed by rapidly progressive fulminant neurological syndrome during first attack is relatively uncommon. It is a neurological emergency and mimics many other psychiatric and medical disorders and can be fatal if it remains undiagnosed and untreated. Further, specific treatment in the form of Heme arginate is not universally available and very costly, so high clinical suspicion and early diagnosis and management of acute attack and prevention of further attacks are very important. We report a series of six cases who presented with convulsion and/or polyneuropathy early in the course of disease to highlight this fact.

Key words: Acute intermittent porphyria, convulsion, neurological emergency

Acute intermittent porphyria (AIP) is an autosomal dominant disorder, resulting from partial deficiency of porphobilinogen deaminase (PBGD) enzyme in the haem biosynthetic pathway.[1] The presentation of AIP as an acute abdomen is well known, but a short duration of gastrointestinal symptoms followed by a rapidly progressive course of neuropsychiatric manifestations including peripheral neuropathy, respiratory paralysis, seizures and loss of consciousness during the first attack may also occur. The relationship of seizures with porphyria is complex and the most common description is the presence of acute symptomatic generalized seizure occurring in the context of AIP in relapse.[2] Convulsive seizure may be the presenting symptom of an acute relapse.[3] The knowledge of convulsion in AIP is very essential because the use of enzyme-inducing antiepileptic drugs can cause worsening of the convulsion leading to death. Thus, a strong clinical suspicion, early diagnosis and adequate management of convulsion and prevention of further attacks are of paramount importance in reducing the morbidity and mortality.

We present a report of six cases who had convulsion and/or other severe neurological dysfunction along with fulminant course of illness.

Case Report

We present a report of six cases of AIP who had convulsions and/or other neurological manifestation along with fulminant course of illness [Table 1]. Soon after suspicion of AIP, urine and blood samples were collected for Watson-Swartz test, urine PBG level, routine cytology, blood biochemistry and electrolyte estimation and patients were put on high carbohydrate diet by oral root or Ryle's tube along with intravenous glucose so as to provide at least 400g of glucose to the patient each day. All the patients were kept under close observation so that they can be put on ventilatory support if required. One patient needed ventilatory support for five days. Apart from the observations as written in Table 1, one pregnant woman had rapid deterioration in her condition and therefore was advised to go for MTP (Medical Termination of the Pregnancy) after which she improved. Those patients who developed convulsion were treated by gabapentin and IV lorazepam. All the patients recovered fully in the course of one week to four months.

Discussion

Early in the last century, Waldenstrom[4] called AIP as the little imitator distinct from the more common manifestation of neurosyphilis. The severe constipation and episode of abdominal pain, hypertension and tachycardia seen during an acute attack of porphyria may be because of an autonomic neuropathy. A predominantly axonal neuropathy, which can be acute

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Table 1: Clinical profile of the patients with acute intermittent porphyria presenting with neurological emergency

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age (years)	36	15	15	28	21	17
Sex	Male	Male	Female	Female	Female	Male
Past history AIP	Yes	No	Yes	Yes	Yes	No
Family history	No	Yes	Yes	Yes	No	Yes
Precipitating factors	Alcohol	Fever	Unknown	Pregnancy	Pregnancy	Drugs (ATT)
Gastrointestinal symptoms						
Pain abdomen	Yes	Yes	Yes	Yes	Yes	Yes
Constipation	Yes	Yes	No	Yes	Yes	Yes
Nausea and vomiting	No	No	Yes	Yes	Yes	Yes
Diarrhea	No	No	Yes	No	No	No
Psychiatric manifestations	Yes	Yes	Yes	Yes	Yes	Yes
Neurological manifestations						
Peripheral neuropathy	Yes	Yes	Yes	No	Yes	No
Respiratory paralysis	Yes	Yes	No	No	Yes	No
Cranial nerve involvement	No	No	No	No	Yes	No
Sphincter involvement	Yes	Yes	No	No	Yes	No
Seizures	Yes	Yes	Yes	Yes	No	No
Loss of consciousness	Yes	Yes	No	Yes	Yes	Yes
Time interval between onset of symptoms and neurological complications (days)	1-2	4 -5	2	2	1	3
Other relevant parameters						
Blood pressure (mmHg)	170/110	130/174	124/82	150/96	130/88	154/94
Pulse rate / min	120	84	78	104	80	96
Watson-Swartz test	Yes	Yes	Yes	Yes	Yes	Yes
Urine PBG (0-4) mg/day	21.42	24.93	31.62	Not done	Not done	12.40
Urine ALA (1-7) mg/day	13.17	47.28	47.23	Not done	Not done	22.40
USG abdomen	Normal	Normal	Normal	Normal	Normal	Normal
Serum Na^+ / K^+	Normal	Normal	Normal	Normal	126 meq/L (Na^+)	Normal
CT Head	Normal	Normal	Normal	Not done	Not done	Normal
NCV	Not done	Axonal	Normal	Not done	Not done	Not done
EEG	Normal	Normal	Not done	Not done	Not done	Not done
Treatment given						
Gabapentin	Yes	Yes	No	No	No	No
Propanolol	Yes	No	No	Yes	Yes	Yes
IV Dextrose	Yes	Yes	Yes	Yes	Yes	Yes
Chlorpromazine	Yes	Yes	No	Yes	Yes	Yes
Ventilator Support	No	Yes	No	No	No	No
I.V. Lorazepam	No	Yes	Yes	No	No	No
Other	No	No	No	No	MTP	No
Recovery	2 weeks	4 month	1 week	1 week	3 month	2 week

ATT: Anti tubercular treatment, MTP: Medical termination of pregnancy

and involve the bulbar cranial nerves and respiratory muscle is well described.[5]

Involvement of the central nervous system is comparatively less common. Several mechanisms have been proposed to explain the neurological symptoms of AIP, which includes overproduction of ALA and PBG and their accumulation in nervous tissue exhibiting neurotoxic properties.[6,7] Convulsion can occur at any time during acute illness but acute symptomatic seizures are a well recognized feature of porphyria in relapse[8,9] and subsequent use of enzyme-inducing antiepileptic drugs can cause a worsening of condition and new symptoms, such as acute neuropathy and respiratory paralysis. Further, it is less well documented that these manifestations can occur as a rapid progressive course during the first attack of AIP. All the cases presented in this series attended the emergency room with almost similar attacks of AIP with short duration of gastrointestinal symptoms followed by very rapidly progressive course of neuropsychiatric manifestations in the form of peripheral neuropathy, respiratory paralysis and seizures with loss of consciousness. In four patients there was no past history of similar episodes and they were not known cases of AIP. Family history of AIP was present in four cases. Four of our cases (no. 1-4) presented with gastrointestinal symptoms and seizure, case no. 5 with pain abdomen and polyneuropathy and case no. 6 presented with pain abdomen and altered sensorium. No definitive cause was revealed for CNS dysfunction except in case no. 5 in which hyponatremia was documented. Diagnosis of all cases was done by past history of similar episode, family history of AIP, clinical feature and Watson-Swartz test and further confirmed by quantitative PBG / ALA estimation, but further evaluation by PBG deaminase enzyme assay or mutation analysis was not done because these tests are

not available.

Heme arginate (IV) is the treatment of choice and very effective if given early in the course (within one-two days) of illness and leads to biochemical reemission followed by clinical improvement in one to two weeks but it is less effective if treatment is delayed.[10,11] Limitations for using heme arginate are that it is not universally available, very costly (four-day course costs approximately $8000) and can cause severe coagulopathy and anaphylactic reactions sometimes.

Since definite diagnostic facilities are not available widely, high clinical suspicion and early diagnosis by Watson-Swartz test and effective management of acute attacks is very important in reducing mortality and morbidity.[11] Acute intermittent porphyria should always be considered as differential diagnosis in case of abdominal pain with neuropsychiatric manifestation, whether family history of AIP is present or not. Finally, once the diagnosis has been confirmed, the family members must be screened for the PBGD enzyme level and/or mutation analysis to diagnose asymptomatic carriers.

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