MJSBH July-December 2012|Vol 11|Issue 2

Acute intermittent porphyria presenting as recurrent limb weakness.

Binod Karki[1], Prakash Raj Pande[1], Arun Sharma[1], Rajeeb Kumar Deo[1].
[1]Department of Internal Medicine, Shree Birendra Hospital.

ABATRACT
Acute intermittent porphyria is a rare autosomal dominant condition of porphyrin metabolism resulting from the half-normal Hydroxy methyl bilane synthase activity. The disorder can present with protean manifestation ranging from acute abdomen, psychosis to gross peripheral neuropathy thus making the diagnosis challenging and misled most of the times. A case of Acute intermittent porphyria with extreme neurological involvement in form of acute onset quadriparesis is presented in this paper.
Keywords: porphyria, limb weakness, quadriparesis.

INTRODUCTION
Acute intermittent porphyria (AIP) is a rare autosomal dominant type of hepatic porphyria resulting from the half-normal HMB (Hydroxy methyl bilane) synthase activity[1]. It is characterized by episodes of severe abdominal pain, rapidly progressive flaccid paralysis and passage of excess amounts of porphobilinogen (PBG) in urine[2]. Acute intermittent porphyria is the second most common form of porphyria; porphyria cutanea tarda being the most common[3]. High index of suspicion is required to diagnose the case as most patients can be wrongly diagnosed as some other medical conditions. We present a case of young male with extreme neurological involvement in the form of acute onset quadriparesis requiring ventilatory support who was previously wrongly diagnosed as a malingerer.

CASE REPORT
A 35 year old gentle man presented to Emergency of our hospital with complaints of inability to move all four limbs for two days duration and difficulty in breathing for four hours. He had pain abdomen, vomiting and diarrhoea preceding the weakness which was managed as a case of acute gastroenteritis by a local medical shopkeeper. Examination revealed acute flaccid quadriparesis with absent reflexes in all four limbs with respiratory rate of 40/min and SPO_2 of 80 % on high flow oxygen at 5 L/min via mask. Arterial blood gas analysis showed PaO_2 of 55 mm Hg only with pH of 7.22. In view of impending respiratory fatigue and arrest, he was intubated, shifted to ICU and put under mechanical ventilation.

His previous medical documents were reviewed, which revealed that he had repeatedly visited hospital with number of different complaints for the last four years. The complaints ranged from acute abdomen, many times managed as Acid Peptic disease, hypertension in Medical OPD, admitted and discharged as Guillian Barre syndrome and he was even consulted Neurpsychiatrist. He was also counseled for possible malingering as he was repeatedly coming to the hospital with bizzare symptoms.

His basic investigations including complete blood count, renal function test and liver function test were unremarkable. His CXR and ECG were normal. With one of the differentials as acute intermittent porphyria, we asked the ICU nurse to keep his urine in a glass container out in the sun, and surprisingly it turned dark brown within an hour (as shown in figure1). Urine sent for porhobilinogen was also positive and he was diagnosed as a case of acute intermittent porphyria.

He was immediately put on carbohydrate loading with intravenous Dextrose infusion 300 g/day. Subsequently he developed Right lung pneumonia but managed successfully with appropriate antibiotics and he was extubated on fifth day. His weakness of all four limbs slowly improved and with persistent physiotherapy now he is able to move around with the support of a stick. He is under rehabilitation therapy at our hospital.

Correspondence:
Maj. Dr. Binod Karki
Department of Internal Medicine,
Shree Birendra Hospital, Kathmandu, Nepal.
Email: binodkarki@yahoo.com
Phone: +977-9841253747

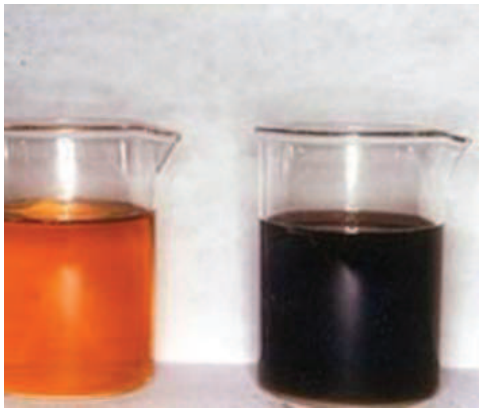

Figure 1. Urine may appear dark during attack after standing in the sunlight. (source : http://www.porphyriafoundation.com/about-porphyria/types-of-porphyria/AIP)

DISCUSSION AND REVIEW OF LITERATURE

AIP is the most common acute porphyria and is caused by a deficiency of hepatic PBG deaminase activity. The prevalence of AIP varies, with a higher incidence reported in England, Ireland, and Scandinavia[4]. There is no literature available regarding the actual incidence of porpyria cases in Nepal. Clinical features of AIP consist of heterogeneous manifestations of acute neurovisceral attacks; there is no cutaneous involvement. The most common signs and symptoms of AIP are abdominal pain (80%), constipation (50%), nausea and vomiting (50%), tachycardia (40%), hypertension (31%), urine discoloration (25%), and fever (16%)[5].

The most common manifestation being abdominal pain; it forms differential diagnosis in acute abdomen. The neurological manifestation is in the form of motor neuropathy and peripheral neuropathy in the form of symmetrical motor weakness involving the arms. The neuropathy is believed to result from axonal degeneration. Cranial nerves can also be impaired in cases of AIP, with the facial (VII) and vagus (X) nerves being involved more than the others. Several mechanisms have been proposed to explain the neurological symptoms of AIP, which includes overproduction of Aminolevulinic acid (ALA) and PBG and their accumulation in nervous tissue exhibiting neurotoxic properties.[6] In the present case, there was short gastrointestinal symptom followed by rapidly progressive course of neurological manifestations in the form of peripheral neuropathy and respiratory paralysis and in the following days he developed pneumonia as a complication.

Hospitalization is usually required for treatment of severe symptoms of acute intermittent porphyria (AIP), monitoring of respiration, electrolytes, and nutritional status, and the intravenous administration of medication (eg, carbohydrates, hemin). Monitoring in an intensive care unit is warranted if the patient's vital capacity is impaired.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.Glucose is important alternative when hemin is not available, which reduce porphyrin precursor excretion. Intravenous treatment with 300 to 500 grams of glucose, usually administered as 10 percent solution is recommended.[7]

In order to prevent future attack, multiple inciting factors must be addressed and avoided. List of medicines known to produce attacks of intermittent porphyria are given in table 1. Dietician may play role in advising diet high in carbohydrate (60 to 70 percent of total calories).

Table 1. Drugs unsafe in porphyria

Carbamazepine
Co-trimoxazole
Dapsone
Etamsylate
Ketoconazole(systemic)
Barbiturates
Chloramphenicol
Clonidine
Danazole
Erythromycin
Ethosuximide
Griseofulvin
Methyldopa
Nalidixic acid
Pyrazinamide

source: http://www.porphyria-europe.com/03-drugs/selecting-drug-unsafe.asp

REFERENCES

1. Longo DL, Kasper DL, Jameson LJ, Fauci AS, Hauser LS, Loscalzo J. Harrison's Principles of Internal Medicine. 18th ed. New York:McGrawHill; 2011:
2. Becker DM and Kramer S. The neurological manifestations of porphyria A review. Medicine, 56: 411-423, 1977.
3. James, William D.; Berger, Ass; et al. (2006). Andrews' Diseases of the Skin: clinical Dermatology. Saunders Elsevier
4. Kappas A, Sassa S, Galbraith RA, Nordmann Y. The porphyrias. In: Scriver CR, Beaudet AL, Sly WS, Walle D,editors. The metabolic and molecular bases of inheriteddisease [book on CD-ROM]. 7th ed. New York: McGrawHill; 1997:2103–59.
5. Suarez JI, Cohen ML, Larkin J, et al. Acute intermittent porphyria: clinicopathologic correlation. Report of a case and review of the literature. Neurology. 1997;48:1678–84.
6. Pierach CA, Edwards PS. Neurotoxicity of delta-aminolevulinic acid and porphobilinogen. Exp Neurol. 1978;62:810-4.
7. Anderson KE, Bloomer JR, Bonkovsky HL, et al. Recommendations for the diagnosis and treatment of the acute porphyrias. Ann Intern Med. 2005;142:439.