CASE REPORT

Acute intermittent porphyria

Dr. Arvind Kumar D[1], Dr. Srinivas V[1,*] and Dr. Sravan Kumar S[1]

[1] Department of Internal Medicine, Krishna Institute of Medical Sciences, Minister Road, Secunderabad-500003, Telangana, India.

Abstract

17-year-old female, came with complaints of abdominal pain, vomitings, hypertension. Three days before admission she developed severe abdominal pain, backache and generalised body pains with extreme weakness. These symptoms worsened over 3 days, accompanied by nausea, vomiting, and emotional instability [1]. Her medical history is notable for 6 similar attacks with abdominal pain and vomiting. She took no medications. On admission she was lethargic but oriented. On day 4 of hospital stay patient developed generalised tonic clonic seizure, hyponatremia, fall in haemoglobin, and during this episode there was pinkish discoloration of urine. With suspicion of porphyria, urine was sent for porphobilins estimation, which was positive. 24 hour urine for porphoblilinogen, was elevated and there were decreased levels of PBG-deaminase activity. Patient was treated with high carbohydrate intake and correction of electrolyte disturbances. Haematin and heme arginate were not used, due to the difficulty to acquire the medication.

Keywords: Acute intermittent porphyria; autosomal dominant metabolic disorder; porphobilinogen deaminase enzyme

***Corresponding author:** Dr. Srinivas V, Department of Internal Medicine, Krishna Institute of Medical Sciences, Minister Road, Secunderabad-500003, Telangana, India.

Received 5 February 2015; *Revised* 18 March 2015; *Accepted* 25 March 2015;.Published.31.March.2015

Citation: Arvind Kumar D, Srinivas V, Sravan Kumar S. Acute intermittent porphyria. J Med Sci Res. 2015; 3(2):75-78. DOI: http://dx.doi.org/10.17727/JMSR.2015/3-014

Introduction

Acute intermittent porphyrias (AIP) a rare autosomal dominant metabolic disorder resulting from a disorder in the hepatic pathway of heme biosynthesis, caused by decrease of the porphobilinogen deaminase enzyme levels (PBG-D). It is characterized by generally intermittent signs and symptoms including abdominal pain, nausea, vomiting, constipation or diarrhoea, abdominal bloating, adynamic ileus, urinary retention or incontinence, tachycardia, tremor, fever, peripheral neuropathy, and psychiatric disorders. Many factors can trigger an AIP crisis, among them are noteworthy hypocaloric and low-carbohydrate diets. Abdominal pain is the most characteristic symptom and generally the earliest, being diffuse and possibly accompanied by nausea and vomit. Rarely, generalised epileptic fits and neuropsychiatric disturbances may occur.

Case report

A 17-year-old woman came to the emergency department with a history of abdominal pain a 5 days duration, emotional instability and autonomic dysfunction along with episodes of tachycardia and hypertension with similar complaints since last 2 years. She had intermittent, localized, severe, sharp epigastric and periumbilical pain associated with vomiting. The pain usually started 2 to 3 days prior to the beginning of her menstrual cycle and generally lasted for the length of the cycle. There was no other obvious exacerbating or relieving factors. She reported no burning or additional pain on micturition and no history of fever, chills, diarrhoea, constipation, melena and hematochezia.

Medical history was significant during the 6 previous hospital admissions, at which time extensive work-ups had been performed to determine the cause of her hyponatremia, irregular menstruation, and abdominal pain; no specific diagnosis had been reached on these occasions. The patient had no history of psychiatric illness, sexual intercourse, sensitivity to the sun, smoking, drinking, or illicit drug use. Menarche occurred at the age 12 years.

Physical examination revealed a thin woman of fair complexia in mild distress. Heart rate was 108 bpm. The abdomen was scaphoid, with mild tenderness on deep palpation (mostly periumbilical); there was no hepatosplenomegaly. Auscultation of the abdomen revealed reduced bowel sounds. Pelvic examination revealed no tenderness is cervical motion or adnexal tenderness; there were no visible ulcers or lesions on speculum examination.

Results of serum electrolyte measurement were notable for a serum sodium level of 132 mEq/L (normal, 135–145 mEq/L). Other serum electrolyte levels and plasma levels of urea nitrogen, creatinine, and glucose were within normal limits. Results of a complete blood count and liver function tests also revealed no abnormal readings. Results of urinalysis showed a few erythrocytes. Ultrasonography of the abdomen showed complex right adnexal cystic leision. MRI of the abdomen showed complex cystic lesion in right ovary. Diagnostic possibilities include haemmorghic cyst with hemosiderin layering and endometriotic cyst.

Subsequent hospital course

The patient was admitted in the hospital and was treated with oral administration of analgesics and antiemetics and intravenous administration of dextrose. On the 4th hospital day, patient developed generalised tonic clonic seizure. Her CBP showing haemoglobin 9.6 gm/dl, WBC 23000, magnesium 1gm/dl, serum sodium level decreased to 109 mEq/L, urine sodium level was 121mEq/L, serum osmolality was 217 mOsm/kg H_2O (normal, 275–295 mOsm/kg H_2O), and urine osmolality was 356 mOsm/kg H_2O (normal 50–1400 mOsm/kg H_2O).These laboratory findings were all consistent with the syndrome of inappropriate secretion of antidiuretic hormone. Intravenous administration of fluids was discontinued, and she was placed on fluid restriction, which increased her serum sodium level.

Based upon clinical and laboratory findings, acute porphyria was suspected. Then urine for porphoblilinogen was carried out, it was positive. Then levels of the delta aminnolevulinic acid and of porphoblilinogen in 24h urine was carried out, with significant increase of both(delta aminnolevulinic acid: 308µmol/gm creatinine, ref- <56µmol/g creatinine; porphobilinogen 473µmol/gm creatinine, ref- <12.3µmol/gm creatinine), low PBG deaminase acivity (8.32nmol/L/s ref; 18.5-23.21nmol/L/s). Once diagnosis was confirmed, treatment was immediately begun with a carbohydrate rich diet, correction of dyselectrolytemias.Hematin and heme arginate were not used, due to the difficulty to acquire the medication. The patient was discharged 5 days later with complete resolution of symptoms. She was placed on a high-carbohydrate diet and was advised to avoid prolonged periods without eating and to use medications, only after consulting with her family physician.

Discussion

Acute intermittent porphyria pertains to a group of at least eight distinct genetic diseases, in addition to acquired forms known as porphyrias. Estimated occurrence is 5 to 10 in every 100,000 persons. AIP is the main porphyria, causing acute symptoms, that may be severe and with risk to life, but of short duration. Typically AIP crises take place after puberty [2] and are more frequent in women than in men. Under normal conditions the enzyme deficiency is not sufficient to trigger crises. Other factors are needed to induce symptoms.

As such, about 80% of bearers of deficiency from enzymatic activity never present any symptoms (called individuals with 'latent" AIP) and some of the others suffer only light occasional symptoms. Environmental factors play an important role in the unleashing and course of this disease. Many drugs (barbiturates, anticonvulsants, calcium channel blockers, some sedatives, antibiotics, antifungal and hormones) as well as consumption of large amounts of alcoholic drinks, tobacco or hypocaloric and low carbohydrate diets may activate the symptoms. Stress as a result of infection, another eventual concomitant disease, surgery or psychological disorder also may sometimes be involved in the genesis of a porphyries crisis. Abdominal pain is one of the most characteristic symptom and usually the earliest. Often, it is very intense, diffusedly located in the abdomen and does not respond to typical analgesics, that when used, may worsen the crisis. Nausea, vomiting, constipation, urine retention, arrhythmias, hyper or hypotension [3] besides hydro electrolytic disorder, notably hyponatremia may appear together with the pain. This may be secondary to a series of factors such as diarrhoea, vomit, low intake and especially excessive renal loss and inadequate secretion of anti-diuretic hormones (ADH) [4], Symptoms of peripheral neuropathy include muscle weakness in the upper and lower limbs, changes in sensitivity and motor neuropathy with cranial nerve involvement may develop (leading to symptoms such as dysphagia, diplonia and facial paralysis). The most severe central nervous system impairment may lead to seizure and even to bulbar paralysis [5] with respiratory failure and death. Psychiatric findings include hysteria, anxiety, apathy or depression, phobias, psychosis, agitation, delirium, sleepiness or coma [6].

The early diagnostic hypothesis of AIP may be possible when there is a family history of the disease or if there is a high level of suspicion. The first step for diagnosis of AIP is, during crises, ALA and PBG in 24 hours urine [7]. In crises, the excreted quantity of both may be many folds. Even without crises, the value of both may be high, which permits diagnosis of latent AIP in a next of kin of the bearer of symptomatic AIP. Measurement of the PBG deaminase enzyme activity or HMB synthase in red blood cells is sufficient to confirm diagnosis of AIP in 95% of cases. Definitive diagnosis, in patients with characteristic symptoms and higher dosage of ALA and PBG or in a first degree relative, is performed by survey for the mutant gene through a molecular genetic test, with a detection capacity of the mutant gene of over 98%.

Acute attacks of AIP should be managed with administration of appropriate narcotic analgesics for pain control and appropriate antiemetics for nausea and emesis. A minimum daily intake of 300 g of carbohydrates also is required during attacks. If oral intake is inadequate, carbohydrates should be administered intravenously [8]. Dextrose has been shown to decrease the urinary excretion of porphyrin precursors in patients with AIP. Intravenous heme therapy [9] is also effective in managing acute attacks. Early heme therapy for acute attacks is advocated and is associated with improved outcomes, as measured by length of hospitalization. Heme is taken up by hepatocytes, in which it causes negative feedback for the activity and synthesis of ALA synthase, the rate-limiting enzyme.

Heme can be administered intravenously as hematin (heme albumin and heme arginate are alternatives) in dosages of 3 to 4 mg/kg body weight per day for 4 days, beginning as soon as possible after the onset of the attack. Patients receiving heme therapy should be monitored for complications of coagulopathy, thrombophlebitis, and hemolysis.

Recently, cimetidine [10] has been used for hematin resistant AIP. Cimetidine may be a more cost-effective and easily administered alternative to hematin therapy. The optimal dosage and duration of treatment with cimetidine have not been established and are likely to be patient specific. Daily oral doses of 800 mg have typically been used. In addition to its potential for treatment, cimetidine may also have a role in prophylaxis of acute episodes by maintaining a baseline suppression of ALA synthase activity.

Conclusion

Acute intermittent porphyria should be included in the differential diagnosis of neurological, psychiatric and gastroenterological alterations when results of all other exams are normal. Attention must be given to patients undergoing procedures involving stress, substantially limit the total caloric intake, potentially triggering crises.

Conflict of interest

The authors declare no conflict of interest.

References

1. Acute Intermittent Porphyria - PubMed - NCBI. Available on January 2015 from: http://www.ncbi.nlm.nih.gov/pubmed/20301372
2. Jones B, Brzezinski WA, Estrada CA, Rodriguez M, Kraemer RR. A 22-year-old woman with abdominal pain. J Gen Intern Med. 2014; 29(7):1074–1078.
3. Nabin A, Thapa LJ, Paudel R, Rana PVS. Acute intermittent porphyria with SIADH and fluctuating dysautonomia. Kathmandu Univ Med J (KUMJ). 2012; 10(38):96–99.
4. Tébar MT, Aguilera L. Acute intermittent porphyria and inappropriate ADH syndrome. Rev Esp Anestesiol Reanim. 2010; 57(5):311–313.
5. Tracy JA, Dyck PJ. Porphyria and its neurologic manifestations. Handb Clin Neurol. 2014; 120:839–849.
6. Bautista O, Vázquez-Caubet JC, Zhivago EA, Dolores Sáiz M. From metabolism to psychiatric symptoms: psychosis as a manifestation of acute intermittent porphyria. J Neuropsychiatry Clin Neurosci. 2014; 26(2):E30.
7. Marsden JT, Rees DC. Urinary excretion of porphyrins, porphobilinogen and δ-aminolaevulinic acid following an attack of acute intermittent porphyria. J Clin Pathol. 2014; 67(1):60–65.
8. Doss M, Sixel-Dietrich F, Verspohl F. "Glucose effect" and rate limiting function of uroporphyrinogen synthase on porphyrin metabolism in hepatocyte culture: relationship with human acute hepatic porphyrias. J Clin Chem Clin Biochem. 1985; 23(9):505–513.
9. Fuchs T, Ippen H. Treatment of acute intermittent porphyria with a new protein-bound lyophilized hematin. Dtsch Med Wochenschr. 1987; 112(34):1302–1305.
10. Siepmann M, Stölzel U, Sieg I, Leo-Rossberg I, Riecken EO, et al. Cimetidine in treatment of acute intermittent porphyria. Z Gastroenterol. 1993; 31(4):246–249.