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A LADY WITH ABDOMINAL PAIN, QUADRIPLEGIA AND HYPONATREMIA

Medicine

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ABSTRACT

Acute Intermittent Porphyria (AIP) the commonest type of porphyria is due to deficiency of porhobilinogen deaminase leading on to accumulation of porphyrin precursors. Clinical diagnosis is often delayed as many of its symptoms mimic other common illnesses. We report a case of 19 year old lady presented to us with quadriplegia, predominantly motor. She also had hyponatremia. In the past she had many symptoms which can occur in AIP, but were overlooked and diagnosis was delayed. This time many past, ongoing and current symptoms like abdominal pain, other autonomic, and neuropsychiatric symptoms were considered together and a clinical diagnosis of porphyria was considered and investigations substantiated it. Diagnosis of AIP require high clinical suspicion and early diagnosis and treatment can prevent recurrence, avoid unnecessary investigations and treatment for many mimickers and will be lifesaving.

KEYWORDS

Acute Intermittent Porphyria, Abdominal Pain, Quadriplegia, High Index Of Suspicion

INTRODUCTION:

AIP is an autosomal dominant metabolic disorder of heme synthesis. Prevalence of symptomatic disease is 1-8 per lakh population (1). It is characterized by a partial deficiency of hydroxymethylbilane synthase (HMBS), also known as porphobilinogen deaminase, an enzyme involved in heme biosynthesis (2, 3). Deficiency of HMBS results in accumulation of precursors like delta-aminolevulinic acid (ALA) and porphobilinogen (PBG). The accumulation of these products is amplified by certain medications, alcohol, infections, low caloric intake, or hormonal imbalances during menstrual cycle and pregnancy (1).The urinary excretion of these precursors is always very high during attacks and lower but not normal between attacks (3,4). When clinical disease is manifest, features include recurrent autonomic dysfunction, expressed as abdominal pain, nausea or vomiting, constipation, tachycardia, and hypertension. Unusual presentations include the syndrome of inappropriate production of antidiuretic hormone (SIADH), fever, leukocytosis and weakness of limbs. Although the accumulated metabolites are easily detectable, diagnosis is often not considered because it is uncommon and can mimic many other common conditions [4]. Here we present a case of 19-year-old lady with history of recurrent attacks of abdominal pain and recently with quadriplegia.

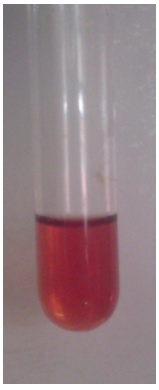
CASE REPORT:

A 19 year old unmarried lady was admitted with complaints of weakness of all four limbs of three months duration. It was gradual onset slowly progressive over this period and the limbs appear flaccid to her. It was symmetrical and progressed from proximal to distal. She had numbness and tingling sensation over the limbs. No diurnal variation. No history of higher mental function abnormalities or cranial nerve symptoms. She is bed bound for the last two months. No history of bowel and bladder involvement, pain over spine, fever or trauma, or any antecedent diarrhea or dysuria and no cardiorespiratory symptoms. She also complains of diffuse dull abdominal pain, intermittent with no radiation. In the past history she had recurrent abdominal pain, anorexia, vomiting, constipation, excessive sweating, unexplained fear and anxiety and one episode of generalized tonic clonic seizure for which she attended several hospitals. No history of joint pains, rashes. She attained menarche at 15 years and for the last three months she is amenorrhoeic. No family history of similar illness.

On examination she was emaciated and pale. No skin lesions. BP was 110/70 mmHg .On another occasion it was 154/94 mmHg associated with hyperhidrosis and was afebrile. Higher mental function examination revealed a depressed mood and cranial nerves were normal including fundus. Bilateral foot drop and wrist drop were present and wasting of upper and lower limb muscles including small muscles was prominent. Hypotonia and Grade 1-2 power of upper and lower limb muscles were noted. Plantar reflex and deep tendon reflexes were absent. Though she had sensory symptoms no signs were present. Skull and spine normal. No signs of meningeal irritation. Abdomen was soft with no obvious swelling. Other systems were normal.

INVESTIGATIONS:

CBC: Hb 10.5 TC 8800 DC N63 L28 M9 HCT 36 MCV 72 PLT 3.46L ESR 70 RDW 16 BU - 13 SCr - 0.7 Na - 129 Potassium - 3.4 Calcium - 6.3 Phosphate - 2.4 FBS - 60 PPBS - 112; Total protein /Albumin - 5.2/2.6 SGOT/SGPT - 67/54 ALP - 78 CXR - Normal; ECG - NSR, HR 90/';USG Abd - NAD, Adrenals normal in size; HIV Negative, HBsAg – Negative, ANA - Negative ,TSH - 3.69; Urine R/E normal ; Stool R/E – NAD; Stool Occult Blood - Negative; CSF study: <5cells , All lymphocytes protein - 30 sugar - 60, no albumino cytological dissociation; Peripheral blood smear - microcytic hypochromic blood picture, no basophilic stippling; Urine Porphobilinogen - positive , Nerve Conduction Study: Motor sensory Axonal neuropathy, No conduction block , No Evidence of demyelination. Even though genetic testing is considered as the 'gold standard' for diagnosis and screening in families, it was not performed in our patient due to financial reasons.



Watson & Schwartz test of urine. Red color suggestive of porphobilinogen or urobilinogen

Chloroform extraction test of urine. clear bottom suggestive of porphobilinogen

A diagnosis of acute intermittent porphyria was made based on the characteristic symptoms of recurrent abdominal pain with nausea vomiting, constipation, other autonomic symptoms like increased sweating and hypertension, seizure episode, axonal neuropathy, hyponatremia and positive urine porphobilinogen.

She was treated with glucose loading of 10% dextrose followed by

maintenance dextrose saline. Intravenous haem arginate was not used due to unavailability and cost .The patient was discharged in ambulant condition with support and advised to avoid fasting, and to consume an adequate carbohydrate containing diet. She was also given a list of drugs to be avoided.

DISCUSSION: Our patient did not have a positive family history even though AIP has autosomal dominant inheritance. Up to 90% of individuals who inherit this condition remain asymptomatic (5).It is due to the fact that the gene responsible for AIP has an incomplete penetrance so that the disease often exists in a latent form and family history may not be evident (6). The symptoms start usually in adolescence, with females more affected than males (7). AIP is characterized by intermittent attacks triggered by many drugs, infection or increased metabolic demand. Elevated PBG (precursor of porphyrin) in urine is highly sensitive and specific for diagnosis of acute attack of porphyrias. In an appropriate clinical scenario qualitative positive PBG urine screen is enough for diagnosis. However, a much better test is to measure the 24- hour or even spot urine total PBG. The cornerstone of management of acute attack of porphyria includes intravenous haem arginate along with avoidance of some drugs and other precipitants, and use of high dose opiates for pain management. However, haem arginate is not available and the cost is very high (8). Confirmatory tests for AIP are plasma and stool porphyrins which are usually normal. Genetic studies are also useful. AIP does not have cutaneous manifestations (9, 10). The diagnosis is often delayed by many years and has been reported to be as long as a mean of 15 years (11).

Porphyric neuropathy (PN) is a well recognized complication and it affects between 10 to 40 percent of acute episodes of AIP. PN preferentially affects proximal motor neurons and weakness is typically more severe in the upper extremities (12). Attacks can range in severity from mild weakness to quadriplegia and can involve the respiratory muscles leading to respiratory failure. The rarity and non-specific symptoms of AIP and PN require a high index of suspicion for an early diagnosis. The presentation can mimic acute Guillain-Barre syndrome; however diagnosis of PN is supported by elevated urinary PBG, Nerve conduction study with primarily proximal axonal polyneuropathy with no evidence of demyelination, and normal CSF analysis without albumino cytologic dissociation. Clues to the diagnosis are gastrointestinal symptoms (acute abdominal pain in 85–90% of attacks), hyponatremia and discoloration of urine on exposure to light, in association with neurologic symptoms and signs. Neurological manifestations are postulated to be due to the neurotoxic effects of porphyrin precursors, ALA being the most significant. Abdominal pain is a sign of autonomic neuropathy, due to splanchnic dysfunction such as intestinal dilatation or spasm. In AIP, pathophysiology of hyponatremia is only partly understood and can be associated with the syndrome of inappropriate antidiuretic hormone secretion, also contributed to by gastrointestinal or renal sodium loss. In contrast to cutaneous porphyrias, AIP patients are not photosensitive due to absence of porphyrin accumulation.

CONCLUSION: Though relatively rare, AIP should be considered as a possibility in all unexplained abdominal pain, constipation, hypertension, neuropsychiatric complaints, autonomic symptoms, seizures, and weakness especially when they occur in combination. Dark or purple discoloration of urine on light exposure and urine porphobilinogen test will add to diagnosis.

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