ACUTE INTERMITTENT PORPHYRIA PRESENTING AS ACUTE ABDOMEN

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INTRODUCTION

The porphyrias are a group of diseases characterized by the overproduction of porphyrin compounds and their precursors. In animals, porphyrin synthesis is required for the production of heme. Just as the iron-containing porphyrin heme catalyzes oxidative phosphorylation in animals, the magnesium containing porphyrin chlorophyll catalyzes photosynthesis. As more poetically described by the Nobel prize winner Hans Fischer, porphyrins are the substances that make blood red and grass green.

Though there are several different types of porphyrias, the one with the most serious consequences and the one that usually presents in adulthood is acute intermittent porphyria, which is inherited as an autosomal dominant. Although specific genetic and enzymatic defects are present throughout life, most heterozygous persons never experience symptoms of disease. The disease is common in female of 15-30 years age. The disorder is caused by deficiency of porphobilinogen deaminase activity due to which increased excretion of porphobilinogen and aminolevulinic acid in urine occurs. Among the advances in molecular biology in the past decade are the mapping of the chromosomal locations and sequencing of the genes that code for the enzymes involved in porphyrin biosynthesis, as well as identification of many specific mutations. These may involve point mutations, insertions, or deletions that change the amino acid sequence of an enzyme and thus interfere either with its ability to bind or release intermediates or with its stability. More than 100 distinct mutations affecting the stability or catalytic activity of human PBG deaminase as well as 10 neutral genetic polymorphisms have been identified. The diagnosis may be elusive, if not specifically considered. In contrast to other porphyrias cutaneous photosensitivity is absent in acute intermittent porphyria.

CASE REPORT

A 20 year old unmarried lady was referred to hospital on 26.12.2002 from Agency Headquarter Hospital, Miranshah, with a 3 days history of sore throat, followed by acute abdominal pain and vomiting for which she was operated by a local surgeon with a diagnosis of acute appendicitis, under ketamine anaesthesia. Her recovery was not satisfactory but she was sent home on 3rd postoperative day, while on the way to home, she became drowsy, confused and restless, and also having abdominal pain with vomiting. She was brought back to AHQ Hospital Miranshah from where she was shifted to KTH Peshawar. She was first admitted in Medical ‘D’ Unit and then shifted to Medical ICU. On examination she
was apyrexial but confused and drowsy, having tachycardia and blood pressure of 170/105 mmHg. Her sensory and motor systems were intact, other systemic examinations were unremarkable except dehydration, generalized tenderness of the abdomen and appendectomy scar. Her base line investigations were done, which showed leucocytosis, albuminuria, and raised blood urea. CSF examination was normal. Serum potassium and sodium were low. Abdominal U/S and C.T. Brain were normal LFTs were slightly impaired while HBSAg and HCV antibodies were negative. Urinary uroporphyrin and coproporphyrin were positive. Analgesia, parinatal fluids specially D/water were given, while hematin, the most specific therapy, was not available in the market. The patient recovered completely and was discharged after 10 days of hospitalization.

**DISCUSSION**

The case documents acute intermittent porphyria, one of the rare but important cause of acute abdomen. The primary trigger for the illness in this case was most probably a sore throat and second trigger was an anaesthetic agent ketamine and surgery. The autosomal dominant pattern of inheritance of acute intermittent porphyria results in approximately 50% of normal activity of the enzyme PBG deaminase. With the exception of congenital erythropoietic porphyria and plumoporphria, the porphyrias are usually inherited as an autosomal dominant pattern. Furthermore who are heterozygous for the same enzymatic deficiency, can produce offspring with a much more severe form of the disease; whereas parents who are heterozygous for different enzymatic deficiencies may have offspring with a mixed or so called dual porphyria. The major sites of heme production are bone marrow (erythrocytes) and liver, so the porphyrias are conveniently grouped as erythropoietic, hepatic or both, depending on the site affected. Because of their striking clinical manifestations, their visible urinary chemical markers, and their familial mode of inheritance, the porphyrias were among the earliest diseases to be defined as inborn errors of metabolism.

The acute porphyrias in order of prevalence in North America are acute intermittent porphyria, variegated porphyria, hereditary coproporphyria and ALAD deficiency. As a group, the acute porphyrias are characterized by the occurrence of neurovisceral attacks (neurologic manifestations and abdominal pain).

Each is characterized by several of five "P"s:

1) Onset after puberty. 2) Psychiatric abnormalities. 3) Pain 4) Polyneuropathy and 5) Photosensitivity (found only in HCP and VP). During latency symptoms are absent. However, acute episodes can be precipitated by four "M"s": 1) medicine (including estrogen and alcohol) 2) Menstrual and premenstrual periods 3) Malnutrition (low carbohydrate or fasting) and 4) Medical illness (and surgery). The basic defect in these porphyrias is a partial deficiency of a non rate limiting enzyme. Conversely, isolated erythrocyte PBGD deficiency may occur in persons with normal hepatic enzyme functions, yielding false positive results.

Acute intermittent porphyria should be included in the differential diagnosis of unexplained abdominal pain, acute psychiatric disturbances and acute polyneuropathies. Of assistance in the diagnosis are a positive family history, the presence of pain in the back and extremities as well as in the abdomen, and the acute development of hypertension during the course of the attack. Suspicion should be greater if symptoms occur during menstruation or pregnancy, after exposure to certain drugs, during weight reduction or after surgery.

A urine sample can be rapidly screened for PBG by the Watson – Schwartz or the Hoesch test, both of which utilize Ehrlich's
reagent as a chromagen. Twenty four hours urinary samples should be collected, placed in opaque containers, refrigerated, and delivered to a qualified laboratory for quantitative analysis of ALA, PBG and porphyrins. It is important to avoid drugs known to precipitate attacks. A high carbohydrate diet is also desirable, as is genetic counseling.

Supportive therapy consists of pain relief with meperidine and phenothiazines and intravenous infusion of glucose (400 – 500 gm/day). ‘B’ blockers for the treatment of tachycardia and hypertension. Gabapentin has been used safely for the control of seizures. If rapid improvement does not occur within 24 hours or if motor neuropathy is present, heme therapy should be started immediately which is the most important therapy in severe cases. Improvement is seen usually in 2-7 days. Hematin is also useful when given prophylactically at weekly intervals to women with menstrual exacerbation of AIP. In one study, porphyrin precursor excretion was reduced to near normal levels and symptoms ceased. The prognosis for patients with AIP is probably better than the older medical literature suggests. When full support and continuous respiratory assistance are required, hematin therapy is less effective and the prognosis is poor.

In summary this case demonstrates that

A: In undiagnosed patients regular examination of the patient and looking for the development of new signs, guided us towards the diagnosis. As in our patient the development of abnormal behaviour, hypertension, persistent abdominal pain even after appendectomy lead to us to perform urinary porphyrin level, clinching the diagnosis.

B: Early identification of the etiology of porphyrin symptoms will prevent unnecessary tests and permit prompt treatment.

C: Screening of the family members should be recommended.

REFERENCES


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