INTERMITTENT ACUTE PORPHYRIA

(A Report of Three Cases)

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Introduction

Intermittent acute porphyria (IAP) is the commonest form of porphyrias, which are a group of metabolic disorders characterized by overproduction, accumulation, and excretion of intermediates of haem biosynthesis. IAP is transmitted as an autosomal dominant trait with variable expressivity [1]. Of about 180 cases reported from India, 116 cases were clustered in Bikaner district of Rajasthan [2]. We report 3 more cases encountered in a hospital in a district neighbouring Bikaner over a period of 2 years. All 3 of our cases belonged to regions other than Bikaner.

CASE REPORTS

Case No. 1

Mrs GD, aged 25 years, resident of Jodhpur district of Rajasthan, presented with recurrent episodes of abdominal pain, vomiting, constipation, and oligo-dysuria of 3 years duration. She had taken treatment for these episodes from various sources without any lasting relief and at times even aggravation. On examination the abdomen was soft with diffuse tenderness and no organomegaly. Other general physical, systemic, and gynaecological examination was unremarkable. Blood counts, urinalysis, metabolic parameters and chest radiogram were normal. Plain radiogram abdomen showed some distended loops of intestine. Two days after hospitalization she developed acute urinary retention and had to be catheterized. Tachycardia and hypertension (BP 140/100 mm of Hg) were the other new findings at this stage. Renal metabolic parameters, serum electrolytes, and ECG were normal. Urine examination for porphobilinogen (PBG) by Watson-Schwartz test [3] was negative. Over the next 8 days she had 3 more episodes of acute urinary retention requiring catheterization. Blood pressure recordings varied from 140/90 to 160/120 mm of Hg. Urine examination for PBG was repeatedly negative. Treatment was started with

Nephrol and propranolol for hypertension and antispasmodics for abdominal colicky pain. Barium meal and follow through, ultrasonography of abdomen, serum amylase, gastroduodenoscopy and intra-venous urography (IVU) were normal.

On the 16th day after hospitalization she became drowsy and lapsed into coma. There were no features of raised intracranial tension. Neurological examination was normal apart from hypotonia and hyporeflexia. Urine repeated for PBG was now positive and remained so for next 3 days. She was treated with heavy doses of parenteral glucose (2.5 litres of 20% dextrose over 24 hours) and all other drugs were withdrawn. She regained full consciousness within 18 hours but had quadriplegia with motor power grade 4/5 and hyporeflexia. She was maintained on high carbohydrate diet. Subsequent recovery was uneventful and she regained full motor power in 10 days time. During 6 months follow-up period, she had remained asymptomatic and normotensive without any anti-hypertensive medication. She denied any history of similar illness in close family members but despite repeated requests none of her family members appeared for examination of urine.

Case No. 2

MB, a 36-year-old soldier, resident of Nepal, presented with complaints of dull constant abdominal discomfort with intermittent episodes of colicky pain, vomiting, and constipation of 7 days duration. There was no history of diarrhoea or dysuria. There was no relevant past or family history. Examination showed no pallor, icterus, or lymphadenopathy. Pulse was 94/minute and blood pressure 190/100 mm of Hg. Abdomen was soft with mild diffuse tenderness and no organomegaly. There was no neurological deficit and optic fundi were normal. Blood counts, urinalysis, renal metabolic parameters, electrolytes, chest radiogram, ECG, ultrasonography of abdomen and IVU were normal. In view of presentation with pain abdomen, tachycardia, and hypertension, possibility of IAP was thought of as confirmed by positive urine test for PBG. He subsequently became asymptomatic though blood pressure remained high requiring antihypertensive therapy with propranolol. He continued to have porphobilinogenuria.

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Case No. 3

SK, a 23-year-old serving soldier, resident of Patiala district of Punjab, presented with acute colicky upper abdominal pain and vomiting of 2 days duration. There was no fever, diarrhoea, or dysuria. General physical examination was normal apart from tachycardia and blood pressure recording of 140/90 mm of Hg. Abdomen was soft with no localized tenderness. Investigations showed polymorphonuclear leucocytosis (TLC 16300/cmm with 86% polymorphs). All other relevant investigations were normal. He was managed conservatively for a possible acute abdominal condition in the surgical ward with parenteral fluids. Urine when collected for examination turned dark on standing raising the suspicion of IAP. This was confirmed by a positive Watson-Schwartz test. On high carbohydrate diet, he became asymptomatic and subsequently ceased to have detectable porphobilinogenuria. He denied history of similar illness in his family members.

Discussion

IAP is an uncommon entity in clinical practice. Various epidemiologic studies have shown a high prevalence of IAP in Bikaner district of Rajasthan [2,4,5]. All other series are of sporadic cases from different parts of the country. Case number 2 belonged to Nepal. This is probably the first case being reported from that country.

Abdominal features predominate in all clinically manifest acute attacks of IAP. Gunther described the diagnostic triad of abdominal pain, vomiting, and constipation [6]. We saw this triad in 2 patients and abdominal pain with vomiting in the third. Cardiovascular features include tachycardia and hypertension, which were present in all 3 patients. The importance of the triad of abdominal pain, tachycardia, and hypertension in suspecting porphyria has been described in two earlier studies [7,8]. Hypertension, seen commonly during the acute crisis of IAP, can persist even after the acute attack. This was seen in our second patient. Church et al reported deaths due to complications of chronic hypertension in 5 out of 19 porphyric subjects in their study [9].

Detection of PBG in urine by qualitative method of Watson and Schwartz is a simple and valuable screening test for the diagnosis of an acute attack of IAP, but false-positive and false-negative results are possible. The test is positive only when the concentration of PBG in urine is three to five times the upper limit of normal but during episodes of neuropsychiatric dysfunction the test is almost always positive [1]. In our first patient, despite a strong clinical suspicion the di-

agnosis could not be confirmed since the test was repeatedly negative during in the early course of illness. It was only when the patient developed neurological features that the test became positive. In the Watson-Schwartz test, extraction using chloroform and butanol removes frequently occurring substances that interfere with the test [3]. In between attacks, the levels of porphobilinogen may be increased but may also be normal [10]. Quantitative tests for PBG and amino laevulinic acid (ALA) in urine by chromatographic methods should be employed to confirm both positive and negative results of Watson-Schwartz test but these are not available routinely. However, the definitive test for diagnosis, whether the patient is symptomatic or not, is to measure PBG deaminase in red blood cells [11].

In the treatment of an acute attack of IAP, intravenous administration of glucose at a rate of 20 g/hour is recommended. Increased carbohydrate load reduces ALA synthetase activity and can be enough to treat some patients. If the patient does not improve within 48 hours of continued glucose infusion or if neuropsychiatric symptoms progress, intravenous infusion of haematin should be tried. The other proposed therapeutic measures include use of a gonadotropin releasing hormone analogue as prophylactic therapy in women in whom the attacks are related to the menstrual cycle [12], oral cimetidine [13], and tin-porphyrins [14].

The most important measure in the management, however, is prevention of acute attacks by avoiding provocative factors such as drugs, steroids, alcohol excess, and deliberate fasting.

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