Psychiatric Manifestations in three cases of Acute Intermittent Porphyria

Lt Col Neatu Narang*, Surg Cdr A Banerjee*, Lt Col J Kotwal*, Maj Jasmeet Kaur**, Brig YV Sharma**, Lt Col CS Sharma#

MJAFT 2003; 59 : 171-172

Key Words : Acute Intermittent Porphyria; Delta-Aminolevulinic Acid; Organic Psychotic Disorder; Porphobilinogen

Introduction

The porphyrias are a heterogeneous group of inborn errors of metabolism caused by inherited enzyme defects in the heme biosynthesis pathway. The commonest form is the Swedish or 'acute intermittent' type inherited through an autosomal dominant gene on chromosome 11, resulting in a 50% reduction of porphobilinogen deaminase activity [1]. As a result of these enzymatic deficiencies, metabolic intermediates, mainly δ -aminolevulinic acid and porphobilinogen are produced in excess, accumulate in tissues, and result in neurovisceral symptoms [2].

Acute attacks are most common in third decade and rare before puberty; five times more common in females than males. Only 10-15% of gene carriers develop the clinical syndrome. A third of patients have no family history, the condition having remained latent or unidentified for several generations [3]. The majority of attacks are precipitated by identifiable factors though some appear to arise spontaneously [4]. The symptoms of acute intermittent porphyria are episodic in nature. Psychiatric manifestations occur with a high prevalence and the clinical picture is usually coloured with clouded consciousness, paranoid features and schizophrenia-like reactions.

Three cases of Acute Intermittent Porphyria manifesting with predominantly psychiatric symptomatology are presented. The detection of autonomic hyperactivity, confusion and disorientation at the height of psychotic manifestations, raised the possibility of an underlying organic pathology. An intracranial space-occupying lesion was excluded by MRI. These patients tested positive for porphobilinogen in urine by Watson Schwartz test on repeated occasions. They showed satisfactory response to symptomatic management for psychosis, high carbohydrate diet and vitamin supplementation. The diverse clinical profile

of the patients is discussed.

Case Report 1

A 26 year old male cook presented with sudden development of gross behavioural abnormalities of one week duration. The individual was noticed to be confused and disoriented. He spoke irrelevantly and exhibited emotional lability. He indulged in acts which were uncharacteristic of his previous attitude. He was found hiding in bushes for which he could not offer any plausible explanation. On being brought to the unit Medical Inspection Room, he broke a bottle and injured his hand, also showed violent tendencies towards others and required physical restraint.

Patient was febrile, confused and had altered sensorium. Autonomic instability in the form of profuse diaphoresis, tachycardia, tachypnea, labile blood pressure (systolic varying between 130-160 mm Hg and diastolic between 90-106 mm Hg) and tremors, was present. Mental status evaluation (MSE) revealed neglect of self-care and hygiene, uncooperative and negativistic attitude, vacant stare with variable, unpredictable psychomotor activity. He was perplexed, spoke irrelevantly and incoherently and showed hallucinatory behaviour. Delusions of persecution and nihilism were present and he was easily distractable. He lacked insight into his illness, judgement and biorhythms were grossly impaired. Upon attempting an IV line, he committed another deliberate self-harm with scissors onto his abdomen.

Case Report 2

A 34 year old non-alcoholic male manifested with behavioural abnormalities of three months duration. While performing duties of advance winter stocking at a high altitude recovery post, he developed belief that his colleagues were conspiring against him. At his behest, his duty location was changed, but his "persecutors" followed him.

Examination showed, an emaciated and anorectic individual having autonomic hyperactivity. MSE revealed a well kempt, but perplexed and hypervigilant individual with poor reality testing. He had auditory hallucinations and well systematized delusion of reference and persecution with

*Classified Specialist (Psychiatry), Military Hospital, Kirkee, Pune, *Classified Specialist (Medicine & Neurology), INHS Asvini, Colaba, Mumbai, *Classified Specialist (Pathology), Armed Forces Transfusion Centre, Delhi, **Graded Specialist, (Pathology), Command Hospital, Eastern Command, Calcutta, **Comandant, Military Hospital, Ambala Cantt #Addl Advisor, (Psychiatry), Command Hospital, Northern Command, C/o 56 APO.

formation of paranoid pseudocommunity.

Case Report 3

27 year old Sapper performing duties in strenuous environment became withdrawn and mute, not comprehending simple instructions. History revealed gradual progression of symptoms over two months. He visualized ghosts, snakes and animals in walking state, which frightened him. While on leave, he sought assistance of a faith healer who performed religious ceremonies but did not afford any relief.

MSE showed disheveled appearance, an uncooperative and noncommunicative demeanor. There was severe degree of psychomotor retardation, blank stare into space, no spontaneous utterances and poverty of speech. Emotional responses were blunted and attention span was brief. Visual and auditory hallucinations with predominantly nihilistic contents, were elicited.

There was no past history of psychiatric disability in these three cases. Family history did not reveal evidence of genetic loading. Premorbid personality was stable in all cases. There was evidence of alcohol abuse in case one. Laboratory investigations revealed normal hepatic, renal and cardiac functions. Cerebro spinal fluid (CSF), biochemical and serological profiles were normal. Blood counts, EEG, and MRI brain were within reference limits. Nerve conduction study was abnormal in case one, revealing segmental conduction block. Porphobilinogen (PBG) was detected in urine by Watson Schwartz test for seven consecutive days in all the cases. They were diagnosed as Acute Intermittent Porphyria.

Using the International Classification of Diseases, tenth revision (ICD-10) nomenclature, the following psychiatric comorbid diagnoses were made :

- Case 1 - Organic schizophrenia - like disorder
- Intentional self-harm
- Case 2 - Organic delusional disorder
- Case 3 - Organic catatonic disorder

The patients were managed with antipsychotic drugs, high carbohydrate diet, tab pyridoxine 100 mg daily, supportive measures and psychotherapeutic interventional modalities. Case one required augmentation with seven ECTs administered under Inj diazepam 10 mg IV in view of his repetitive deliberate self-harm attempts. All the individuals showed gradual but adequate response to treatment. Upon remission of psychotic symptomatology, they were discharged back to respective units on maintenance antipsychotic medications. They have been advised to avoid the precipitating porphyrogenic agents, a list of which was given to each.

Discussion

The clinical profile of Acute Intermittent Porphyria may not always be the classical triad of abdominal symptoms, neurological features and psychiatric manifestations. Mental disorders accompany the acute

attacks in 25-75% of cases, and psychiatric symptoms may dominate the picture as illustrated by our case series. The spectrum of psychiatric symptoms may vary from emotional disturbance to acute depression, anxiety, and sometimes restlessness and violence. Acute confusional state can progress to delirium, with hallucinations, delusions and disorganised behaviour [2,5].

Psychotic developments may obscure other aspects of the disorder and lead to a primary diagnosis of depressive illness or acute schizophrenia. High degree of suspicion is warranted as to detect this metabolic abnormality. The revelation of dysautonomia and confusional state at the height of the psychotic presentation in these patients led us to launch an exhaustive search for an underlying organic pathology. The intracranial space occupying lesion was excluded by MRI of brain. The detection of PBG in urine by Watson Schwartz test on repeated occasions clinched the diagnosis.

Autonomic instability is an invariable accompaniment as elucidated in our cases. Tachycardia, labile blood pressure, tremulousness and diaphoresis were detected in all the cases. However, the sympathetic overactivity did not require any specific treatment and these autonomic features resolved gradually. Neuropathy complicates less than 20% of attacks. It is predominantly a motor peripheral neuropathy, which manifests as muscle weakness, diminution of tendon reflexes, paraesthesiae or pain in the limbs. The porphyric neuropathy is attributed to axonal degeneration [2]. Amongst these three cases, only one had segmental conduction block that responded to pyridoxine.

The severity of psychiatric manifestations was related to the duration of excretion of PBG in urine. An acute episode is typically associated with significantly elevated urine PBG, often more than 10 times the upper limit of the reference interval. During asymptomatic intervals, this abnormality may resolve, however persistently elevated PBG in remission correlates with an increased risk of an acute attack [6].

Important precipitating factors that are known to induce acute porphyria attacks in susceptible persons include reduced caloric intake, stress, infections, alcohol ingestion and drugs like barbiturates, anticonvulsants, sulphonamides and oral contraceptives [4]. These conditions or medications directly or indirectly stimulate δ -aminolevulinic acid (ALA) synthetase activity via induction of cytochrome P450 or heme oxygenase, which results in an increased biosynthesis of heme and the various intermediate porphyrins.

Excessive alcohol intake in case one and overwhelming physical stress of working in uncongenial areas in case 2 and 3, were the apparent precipitators in our case series. Recognition and avoidance of such precipitating events is a key part of the treatment program for porphyria.

Although the exact mechanism underlying these psychotic manifestations is unclear, various hypotheses have been put forth, including :

Direct neurotoxicity caused by PBG and δ -ALA [7].

Decreased GABA concentration by inhibition of its release by ALA [1].

Decreased activity of hepatic tryptophan pyrrolase, a heme-dependent enzyme leading to increased levels of brain tryptophan and increased turnover of 5-HT.

Decreased plasma melatonin levels, which enhance ALA-mediated lipid peroxidation [8].

We conclude that Acute Intermittent Porphyrria in psychiatric population is not uncommon. Routine screening for porphyria in the first episode of psychosis and major depression can detect this preventable metabolic disorder, otherwise likely to be missed.

References

1. Kappas A, Sassa S, Galbraith RA, Nordmann Y. The porphyrias. In : Scriver CR, Beaudet AL, Sly WS, Valle D, editors. *The metabolic basis of inherited disease*. 6th ed. New York : McGraw-Hill, 1989;1305-66.
2. Thadani H, Wassif W, Deacon A, Peters T. Neuropsychiatric manifestations of acute intermittent porphyria. *J Psychiatric Case Reports* 1997;2:29-35.
3. Meyer UA, Schuurmans MM, Lindberg RL. A review of the pathogenesis of the neurological manifestations of the acute porphyrias. *Seminars in Liver Disease* 1998;18:43-52.
4. Kauppinen R, Mustajoki P. Prognosis of acute porphyrias : occurrence of acute attacks, precipitating factors, and associated diseases. *Medicine* 1992;71:1-13.
5. McColl KEL, Dover S, Fitzsimons E, Moore MR. Porphyrin metabolism and the porphyrias. In : Weatherall DJ, Ledingham JGG, Warrell DA, editors. *Oxford textbook of medicine*. 3rd ed. Oxford : Oxford University Press, 1996;1388-99.
6. Elder GH, Smith SG, Jane Smyth S. Laboratory investigation of the porphyrias. *Ann Clin Biochem* 1990;27:395-412.
7. Bonkovsky HL. Advances in understanding and treating "the little imitator", acute porphyria. *Gastroenterology* 1993;105:590-4.
8. Monterio H, Bechara EJH, Abdalla DSP. Free radicals involvement in neurological porphyrias and lead poisoning. *Mol Cell Biochem* 1991;103:73-84.

* * * * *

One professor at school (an econ prof) had a strict policy that the hourly examinations were done at the bell and anyone who kept writing on their exam after the bell would take a zero on the exam. Well, one guy kept writing on his exam for a while after the bell and then confidently strode up to turn it in.

The prof looked at him and said "don't bother to hand that paper in...you get a zero for continuing after the bell."

The guy looked at him and said, "Professor, do you know who I am!!"

The professor replied, "No, and I don't care if your dad is president of the United States...you get a zero on this exam"

The guy, with a enraged look on his face, shouted, "You mean you have no idea who I am???"

The professor responded, "No, I've no idea who you think you are."

With that, the guy said "good," plunged his exam into the middle of the stack of other students exams, and did a hasty retreat from the examination room!!!

* * * * *