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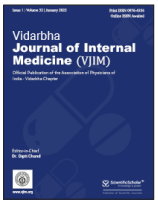

Case Report

Neuropsychiatric Manifestation of Acute Intermittent Porphyria: A Case Report

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ABSTRACT

Acute intermittent porphyria is a rare hereditary metabolic disorder with heme biosynthesis. Because of the wide and non-specific symptomatology of porphyria, diagnosis of porphyria is often missed or usually misdiagnosed as polyneuropathy or encephalopathy, or psychiatric disease. This case report is a reminder to physicians regarding porphyric neuropathy and psychiatric involvement associated with porphyria.

Keywords: Acute intermittent porphyria (AIP), Hydroxymethylbilane synthase (HMBS), Delta-aminolevulinic acid (ALA), Porphobilinogen (PBG), Acute porphyric neuropathy

INTRODUCTION

Acute intermittent porphyria (AIP) is an autosomal dominant, inherited metabolic disorder of porphyrin metabolism. It is caused by a partial deficiency of hydroxymethylbilane synthase, the third enzyme in the heme biosynthesis pathway.[1,2] This results in the accumulation of upstream metabolic products, such as delta-aminolevulinic acid (ALA) and porphobilinogen (PBG). ALA and possibly PBG are believed to be neurotoxic and affect the autonomic, peripheral, and central nervous systems, thereby causing related symptoms, including severe abdominal pain, hypertension, respiratory failure, and quadriplegia. It is also characterised by psychiatric manifestations such as hysteria, anxiety, depression, phobias, psychosis, organic disorders, agitation, hallucination, delirium, and altered consciousness ranging from somnolence to coma.[3,4] Because of this wide spectrum and non-specificity of symptoms, diagnosis of porphyria is often missed.

Neurological complications usually result from severe episodes of acute attacks.[5] About 10–40% of patients may have symptoms of peripheral nerve damage during an AIP attack, but they are usually only mildly affected. However, in the present case, the patient had neuropathy that presented intensely, with a relatively unusual severe clinical picture.

CASE REPORT

A 17-year-old female patient presented to the emergency department and consulted the surgeon with the complaints of severe colicky abdominal pain for the past 2 days. The patient was having diffuse abdominal pain. Her ultrasonography of abdomen and abdominal X-ray, serum lipase, and amylase level were normal. Her blood pressure was about 150/100 mmHg and she had a pulse rate of 130/min. The patient was tachypneic and was disoriented. The patient also had a third-person auditory hallucination. The patient was referred to the medicine department for hypertension and tachycardia. History was obtained from the patient's mother. She recollected that the patient used to get similar episodes of abdominal pain for the past 2 years almost every month, 7–8 days following her menstrual period. They had consulted multiple doctors but a definite diagnosis was not made. Her mother also gives a history of seizure 6 years ago for which she was evaluated and she never had a recurrence in this past year, and therefore, she was not on any treatment. No family history of similar complaints was present. On examination, she was emaciated and was having diaphoresis and tremors of hands. No cutaneous lesion was present. Because of abdominal pain, neuropsychiatric disease, and associated autonomic dysfunction urine, PBG was done and was found to be positive; hence, diagnosis of AIP was made. Classic discolouration of urine colour on exposure to sunlight was also demonstrated. Psychiatry consultation was done in view of hallucination and they gave the impression of organic schizophrenia like disorder. In the emergency department itself, the patient developed one episode of seizure for which she was hospitalised. She was treated with levetiracetam.

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However, the patient developed levetiracetam-induced psychosis and was started on brivaracetam 50 mg BD after obtaining neuro physician and psychiatrist opinion. CT head was normal. RBS, serum electrolytes, and oxygen saturation were normal. Renal function tests, liver function tests, and complete blood count were within normal limits. The patient was drowsy following the seizure episode. Thereafter, she developed acute onset of weakness of both lower limbs with a power of 4/5 in proximal muscles and 3/5 in distal muscles. It was associated with urinary incontinence and constipation. Cranial nerve examination was normal. Deep tendon reflexes were absent in lower limbs and plantar was absent. After 3 days, the weakness progressed to involve upper limbs and the patient went into respiratory failure over the next 2 days and had to be intubated and ventilated mechanically. Magnetic resonance imaging brain and spinal cord were within normal limits. EMG-NCV study revealed acute-onset motor neuropathy with reduced CMAP with normal conduction velocity.

The patient was treated with a high carbohydrate diet and dextrose-containing intravenous fluids, brivaracetam, antipsychotic drugs, and mechanically ventilation. Tachycardia was controlled with beta-blockers. The patient is currently admitted in intensive care units and ventilated and is improving. She has regained consciousness and the power of lower limbs has not improved yet.

DISCUSSION

AIP is a rare metabolic disease due to the PBG deaminase gene on chromosome 11. A 50% reduction in the enzyme is responsible for the disease activity, but only 10% with this defect suffer from AIP. The remaining 90% remain asymptomatic and may not even demonstrate an elevated level of ALA and PBG in urine.[4]

Even though AIP is the most common hepatic porphyria, the overall prevalence of clinically manifest AIP is estimated to be 50–500/million and incidence is about 5/100,000 people.[6,7] The diagnostic clue toward AIP, in this case, was based on the classical triad of abdominal symptoms, neurological features, and psychiatric manifestations.[8]

Between 10% and 40% of patients with porphyria may exhibit symptoms of peripheral nerve damage during an AIP attack and patients are usually mildly affected. It is rare for the development of severe peripheral nerve damage, such as that which caused the quadriplegia described in our case report. Cranial nerve involvement usually occurs in 75% of cases, but in our case, cranial nerve involvement was not there. Neuropathic symptoms in most patients reach their peak at about 2 weeks after onset.[9]

The neuropathy in porphyria is typically an acute axonal motor neuropathy but there are some characteristic features. Proximal muscles are predominantly affected in 80% of patients; this was true in our patients also. Sensory involvement is present only in 60% of cases. In our patient, sensory involvement was absent. Acute porphyric neuropathy shares many things in common to GBS, ascending type of paralysis predominantly motor neuropathy with many features of respiratory paralysis and autonomic involvement.

Pischik *et al*. concluded that 11% of patients diagnosed with AIP have previously undiagnosed acute porphyria; this is because physicians commonly misdiagnose this cause of acute polyneuropathy or encephalopathy.[10]

Autonomic neuropathy occurs in 90% of patients, which usually involves both sympathetic and parasympathetic systems, especially during an acute period which usually resolves with an acute period. Autonomic manifestations usually include tachycardia (most common), sweating, diarrhoea, constipation, or sphincter disturbances. Hypertension and tachycardia are usually elevated due to catecholamines.[9]

The spectrum of psychiatric symptoms may vary from emotional disturbance to acute depression, anxiety, and sometimes restlessness and violence. An acute confusional state can progress to delirium, with hallucinations, delusions, and disorganised behaviour. Our patient had hallucinations and an acute confusional state. 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.

CONCLUSION

Porphyria is a disease that can present as the acute abdomen or as autonomic dysfunction or as neuropathy or as a psychiatric illness. This may cause misdiagnosis and unnecessary interventions. Hence, a high index of suspicion should be kept in individuals presenting with the classic triad of porphyria, and urinary PBG level should be assessed.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conlicts of interest

There are no conflicts of interest.

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