CASE REPORT

Porphyria-induced Postpartum Reversible Posterior Encephalopathy Syndrome

Shri R Sharma[1], Nalini Sharma[2], Baiakmenlang Synmon[3], Yasmeen Hynniewtaya[4]

Abstract

Acute intermittent porphyria (AIP) is a rare condition that needs to be kept in mind where its early recognition, conservative management, and removal of the precipitating factor are the key factors in its management. This "little imitator" presented with varied symptoms is often misdiagnosed. The diagnosis requires a strong index of suspicion as choosing an antiepileptic medication in the management of seizure requires a judicial choice to avoid precipitation of the underlying illness.

Keywords: Acute intermittent porphyria, Encephalopathy, Postpartum period, Seizures.

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An inherited defect in the heme biosynthesis pathway leads to accumulation of pathway intermediates is responsible for AIP. This condition is rare affecting 1 in 75,000 people. Its diagnosis is usually missed or delayed because of its varied presentation.[1] The disease presents with typical symptoms such as recurrent abdominal pain with focal neurological deficit or seizure. Attacks are induced by some particular medications, alcohol intake, endocrine disturbances, fasting, stress, and infections. Antiepileptic drugs and surgical interventions are the most common triggers.[2] Posterior reversible leukoencephalopathy syndrome (PRES) is usually presented with headache, seizure, psychiatric disturbance, and visual obscuration having a classical neuroimaging finding.[3] However, acute attacks during pregnancy are very rare. Posterior reversible leukoencephalopathy syndrome is a rare clinical presentation of acute porphyria. Here, we present a case of a female who suffered the first attack of AIP in the puerperium state presenting with generalized seizures, progressive paralysis, and features of PRES. Appropriate management dramatically changes the outcome in this known debilitating and potentially life-threatening condition.

Case Description

A 20-year-old lady was admitted to us with the history of burning dysesthesia and tingling of her legs for the last 3–5 days. She vaginally delivered a healthy baby 40 days back. She was previously evaluated elsewhere for intermittent abdominal pain for 2 years. Nine months back, she underwent an abdominal ultrasound (USG) and computed tomography with contrast (CECT) of the abdomen, which revealed cholithiasis which was thought to contribute toward the abdominal pain. She was operated upon for this, but the pain persisted post surgery. However, she suffered two episodes of generalized grand mal seizures (GTCS) in repetitive consecutive sequences and was shifted to the critical care unit (CCU) for further management. The patient here suffered one more attack of GTCS when she was given injection lorazepam and a loading dose of levetiracetam.

The patient remained confused and an lower motor neuron (LMN) type of paraparesis was noted with absent stretch reflex. She also had intermittent episodes of aggressiveness and restlessness that were managed with benzodiazepines. Later, she developed bilateral progressive lower limb paresthesia more than the upper limbs, paraparesis, psychomotor agitation, visual hallucinations, and dysautonomia. Neuroleptics and antidepressants were prescribed initially and she developed dysarthria, dysphagia, dyspnea, and quadriparesis. SpO_2 was 82%. As respiratory failure was impending, she was promptly administered oxygen and put on mechanical ventilation under rapid sequence induction. Her SpO_2 rapidly recovered to 100% after intubation. However, she was not able to breathe without supportive mechanical ventilator even after the effect of muscle relaxant had worn off. Weaning from the ventilator was unsuccessful over the next 2 weeks; henceforth, a tracheotomy was performed.

Her brain magnetic resonance imaging (MRI) was performed indicating PRES (Fig. 1). Viral markers, cerebrospinal fluid analysis, heavy metal screen like lead, arsenic and mercury, autoimmune panel like antinuclear antibodies and anti-cardiolipin were negative. Brain MRI performed in our hospital 2 weeks later revealed partial resolution of the white matter lesion. Acute intermittent porphyria (AIP) was confirmed by three times repeated Watson–Schwartz tests in urine. Subsequently, 24-hour urine quantitation of porphobilinogen (PBG) 114 mg/24 hours (normal ≤2.7 mg/24 hours), delta-aminolevulinic acid (ALA) 77.80 mg/24 hours (normal ≤6.4 mg/24 hours), uroporphyrin 746.2 µg/24 hours (normal 3.3–29.5 µg/24 hours) were significantly

[1,2]Shillong, Meghalaya, India

[3,4]Department of Neurology, NEIGRIHMS, Shillong, Meghalaya, India

Corresponding Author: Shri R Sharma, Shillong, Meghalaya, India, Phone: +91 0364 2538083, e-mail: srmsims_sharma@rediffmail.com

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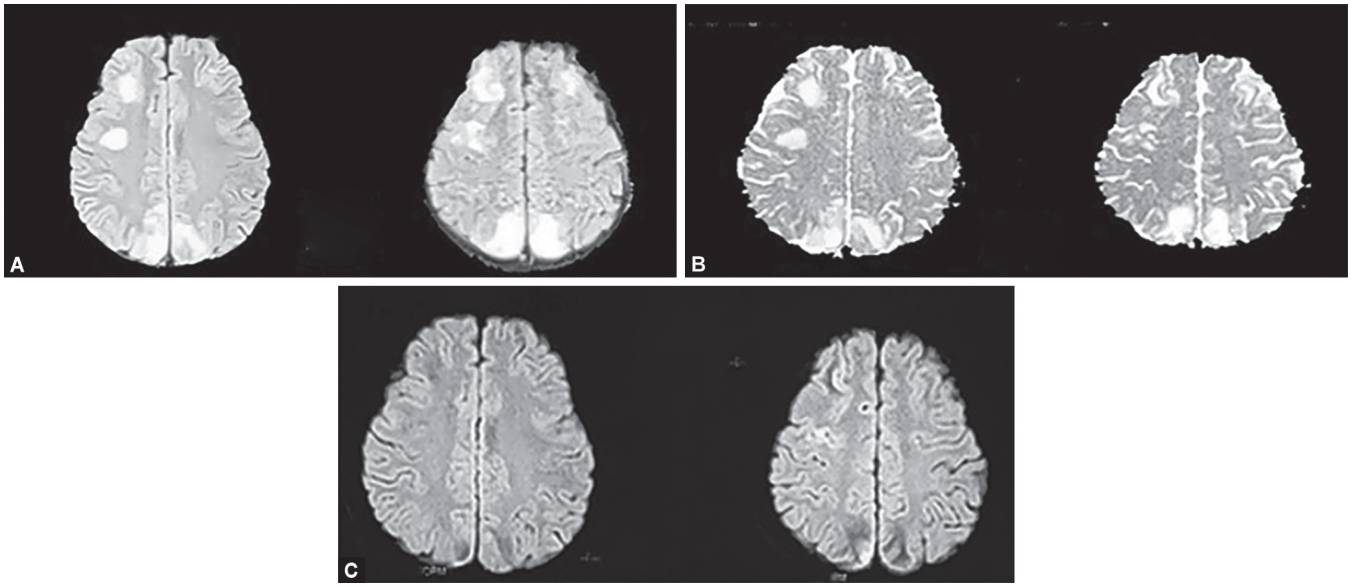

Figs 1A to C: (A) MRI brain axial and FLAIR image showing bilateral symmetrical high-intense signal changes involving parieto-occipital cortex and asymmetrical white matter in bilateral parietal lobes. Corresponding ADC and DWI in (B and C) shows no restriction diffusion RESTR

elevated. Genetic testing identified mutation in the gene coding for hydroxymethylbilane synthase (HMBS), which manifest to development of AIP.

Neuroimaging revealed white matter scattered lesions in the bilateral parieto-occipital and frontal lobes. The patient was administered a high glucose diet and intravenous dextrose. Hematin was unavailable in hospital. However, the patient was finally successfully weaned from the ventilator with no further seizure or abdominal pain, and 1 month later, she was discharged.

Discussion

Acute intermittent porphyria (AIP) is one out of the seven inherited metabolic disorders of heme synthesis. Recurrent abdominal pain is its most common presenting symptom.[1] However, these patients with recurrent abdominal pain are commonly misdiagnosed. Our patient was offered a possible diagnosis of cholelithiasis because of her recurrent abdominal pain. The presence of incidental cholelithiasis makes diagnosis more challenging. Peripheral neuropathy and seizure are the most common neurological presentation of porphyria whereas seizure is a common finding in PRESS.[2] Our case was presented with seizure, so we can conclude that seizures are usually common in AIP patients with PRES.

Posterior reversible leukoencephalopathy syndrome has been very rarely reported in patients with AIP.[3] The pathogenesis of seizures may be implicated to hyponatremia or to the causative role of epileptogenic of some porphyrins such as ALA. Delta-aminolevulinic acid (ALA) has been describing to combine with gamma-aminobutyric acid and fusion with receptors of glutamate.[4] Further, damage to nervous system may cause following an acute attack noted as symmetric or asymmetric cortical gyriform lesions shown in MRI.[5]

Hyponatremia, as seen in our case, has been described in 50% of the literature reviewed cases. Our patient needed mechanical ventilation. This outcome suggests that irreversible or dreaded complications may occur when the irreversible PRES occurs with AIP.[6] In our case, mechanical respiratory ventilator support was required due to respiratory failure of profound motor periperal nerves involvement manifesting with quadriparesis. Bulbar muscle paralysis or respiratory muscle involvement is the most serious presentation of this disease making it fatal. This life-threatening presentation of this rare disease should be kept in mind to avoid mortality.

Current advances in magnetic resonance technology allow the differentiation between cytotoxic edema and vasogenic edema. A bright signal detected on diffusion weighted imaging (DWI) can suggest either diffusion weighting due to ischemic injury or some underlying T2 effects caused by T2 shine-through from vasogenic edema. However, apparent diffusion quotient (ADC) maps reveal to highlight free unrestricted water by removing the underlying T2 signal contribution.[7] Apparent diffusion quotient (ADC) maps revealed a bright signal in vasogenic edema in contrast to a dark signal in cytotoxic edema as in our case.

The pathophysiology of PRES is still vague and contradictory. Several theories have been hypothesized, including impairment of the blood–brain barrier, circulating toxins causing endothelial dysfunction, segmental vasospasm, and poor posterior blood vessel sympathetic innervation. Posterior reversible leukoencephalopathy syndrome PRES in AIP is indistinct and has been found to occur be due to raised blood pressure leading to autonomic nervous dysfunction.[8]

Acute intermittent porphyria (AIP) being an autosomal dominant genetic disorder, nearly 80–90% of carriers are asymptomatic because of a mutated gene.[9] Quantitative raised amount of PBG and ALA in urine are more trustworthy. Long-stored urine that turns con sun exposure is also useful in substantiating the diagnosis.

The treatment of porphyria requires two phases: acute management and prophylactic management. Intravenous hematin is an evidence-based effective therapy during acute attack.[10]

However, heme preparations are not available in our hospital so our patient was given conservative management and she improved with time certain antiepileptic medications—like barbiturates, valproate, diazepam phenytoin, and carbamazepine should be avoided in AIP patients presented with seizures as they are known to precipitate the disease.[10,11]

Orcid

Shri R Sharma https://orcid.org/0000-0003-1359-4891
Nalini Sharma https://orcid.org/0000-0001-5462-3017
Baiakmenlang Synmon https://orcid.org/0000-0001-9261-9932
Yasmeen Hynniewtaya https://orcid.org/0000-0003-0430-4987

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