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Reversible Cerebral Vasospasm in Acute Intermittent Porphyria: A Case Report and Review of the Literature

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ABSTRACT

The porphyrias are rare inherited diseases of heme biosynthesis which can involve the nervous system. The most common neurological manifestations of acute intermittent porphyria are autonomic visceral neuropathy, peripheral motor neuropathy, and central nervous system dysfunction. In rare cases, patients with acute intermittent porphyria have presented with cerebral infarction, suggested to be due to vasospasm in cerebral arteries. We report a case of reversible vasospasm in porphyric encephalopathy demonstrated by both magnetic resonance and conventional angiography. Unexplained abdominal pain occurred before the onset of neurological symptoms.

LEARNING POINTS

- Acute intermittent porphyria can affect the central nervous system.
- Abdominal pain with neurological symptoms should prompt consideration of porphyria.
- Cerebral vasospasm is implicated in the pathogenesis of cerebral infarction.
- Heme arginate is the treatment of choice for central nervous system injury.

KEYWORDS

Porphyria, cerebral infarction, vasospasm

INTRODUCTION

Acute intermittent porphyria (AIP) is an autosomal dominant disorder of heme biosynthesis that can affect the autonomic, peripheral and central nervous systems. Transient and permanent MRI abnormalities have been rarely described in instances where the central nervous system (CNS) is affected. Recent studies have proposed cerebral vasospasm as a cause of reversible ischaemia. Heme arginate is the treatment of choice and very effective if given early in the course of illness [1].

CASE DESCRIPTION

A 28-year-old Caucasian woman was admitted to hospital with abdominal pain and vomiting. She had no family history of porphyria and no known exposure to porphyrinogenic drugs. She did not smoke. Her general physical examination was normal. At the time of admission, her blood pressure (BP) was 120/75 mmHg, and her heart rate was 80/min. There were no focal neurological deficits or visual disturbance. Except for a low serum sodium level (130 mmol/l), all biochemistry tests were within normal limits. She was not pregnant. A series of tests including an abdominal CT scan, ultrasound and colonoscopy was normal.

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One week later, the patient developed right-sided hemiparesis without gait disturbance. At this time, her BP was 130/70 mmHg and her heart rate was 85/min. She was apyretic and did not complain of headache.

There was no epileptiform activity on an electroencephalogram. The cerebrospinal fluid was normal. MRI of the brain showed large regions of signal in the left fronto-parietal cortex on T2-weighted images. These areas of signal abnormality did not greatly enhance after intravenous contrast infusion and were thought to be ischaemic in origin. Cerebral angiography revealed diffuse narrowing of the A1 segments of the anterior cerebral arteries and the posterior cerebral arteries bilaterally. All usual causes of cerebral vasospasm were excluded: drugs, migraine, vasculitis and phaeochromocytoma. Atypical posterior reversible encephalopathy syndrome (PRES) was the initial diagnosis. Tests for connective tissue disorders, viral infection, heavy metal poisoning, thyroid function and antithyroid antibodies were all negative.

The diagnostic of porphyria was suspected because urine turned red when exposed to light. Urinary δ-aminolevulinic acid (ALA), porphobilinogen (PBG) and porphyrin levels were markedly increased, confirming an acute attack of AIP. Red cell (RBC) PBG deaminase activity was normal. Following treatment with heme arginate and a high carbohydrate diet, the patient's hemiparesis markedly improved. MR angiography revealed almost complete resolution of the vasospasm.

At discharge, the patient was given a long list of the porphyria contraindicated drugs. Four years later, the patient is living normally.

DISCUSSION

The porphyrias are a heterogeneous group of inherited disorders of heme biosynthesis. There are seven main types of porphyria, which are broadly classified according to clinical features into neuropsychiatric, dermatological and mixed forms. These disorders are due to a specific alteration in the pattern of accumulation of porphyrin and porphyrin precursors. AIP is the commonest of the acute porphyrias. The most common symptom is severe abdominal pain, which may be complicated by neuropsychiatric symptoms. The acute attacks are often triggered by exposure to exogenous precipitating factors, including a wide range of commonly prescribed drugs. Most difficulties in the diagnosis of an acute attack arise in patients who do not have a family history of porphyria, particularly if the combination of symptoms is atypical [1].

The most common neurological manifestations of AIP are autonomic visceral neuropathy, peripheral motor neuropathy, muscular weakness, and central nervous system (CNS) dysfunction. CNS involvement is common and may present as behavioural changes, irritability, psychosis, hallucinations and seizures. Organic brain syndrome is rare and often develops if an attack progresses. The mechanism of AIP is unknown. The pathogenetic mechanisms which lead to the neurological dysfunction have remained poorly understood, partly due to the lack of a suitable animal model of these rare disorders [1, 2]. Recent studies have proposed vasculopathy as a cause of reversible ischaemia [2–6].

King et al. [2] suggested vasospasm as a cause of the neurological manifestations of AIP. In May 1994, Aggarwal et al. [3] demonstrated transient cerebral cortical changes on MRI, which resolved on follow-up imaging. In 1995, Kuperschmidt reported on transient bioccipital lesions in two patients with AIP and suspected vasospasm [4]. Black et al. describe angiographic demonstration of reversible cerebral vasospasm in porphyric encephalopathy [5]. Vasculopathy is also implicated in the pathogenesis of abdominal pain during AIP attacks [6]. During an acute attack, vasospasm may be due to the presence of excessive amounts of porphyrin metabolites causing cytotoxic or vasospastic cerebral lesions. In 2017, Olivier et al. performed a systematic review by searching in PubMed for published studies of vasospasm in AIP and identified a total of nine case reports [7].

Meyer et al. have proposed heme deficiency in nervous tissue as a cause of the neurological complications of AIP [8].

The findings in our patient document reversible arterial narrowing, which results in ischaemia and cerebral infarction. The initial cerebral angiogram showed diffuse vasospasm. The follow-up MR angiogram, performed 1 month later, showed complete resolution of these findings. This observation supports the concept that cerebral infarct, possibly resulting from porphyria-induced vasospasms, may be an important cause of cerebral dysfunction during acute AIP attacks.

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