

A 17-Year-Old Girl with Chronic Intermittent Abdominal Pain

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A 17-year-old girl was admitted to our emergency department with complaints of sudden, severe, and sharp abdominal pain that began 15 days prior. On admission, she was diagnosed as having acute gastroenteritis and given metronidazole. She returned 1 week later and was diagnosed as having a urinary infection for which she was given trimethoprim. Nevertheless, she continued to experience chronic intermittent abdominal pain, vomiting,

diarrhea, and an inability to tolerate food that lasted more than 20 days before she was admitted to our hospital. She went to several different medical centers seeking treatment before being admitted to our hospital for a third time.

Her medical history was unremarkable except for the fact that her parents were first-degree cousins. She was healthy except for complaints of mild mental and motor retardation. She denied use of any prescription drugs and denied eating any unknown food or plants, and no one in her family had an inherited metabolic disease or a known gastrointestinal disease.

On follow-up in the hospital, affective symptoms such as emotional lability, psychomotor slowness, symptoms of phobia, and crying and shouting independent of pain were added to the list of her clinical symptoms. She was given olanzapine for the psychotic symptoms. Because of her mild mental retardation, sexual abuse was also considered in the differential diagnosis but there was no evidence to confirm any abuse. Upon her latest admission to the hospital she was lethargic and disoriented. Systemic examination was insignificant. Neu-

rologic examination revealed muscle weakness, especially in the proximal muscles. Deep tendon reflexes were absent. Hemogram, blood sugar, liver and kidney function tests, thyroid hormone levels, chest X-ray, electrocardiography, electroencephalography, and magnetic resonance imaging of central nervous system were all normal. Acute phase reactants were negative. Serum folate and vitamin B12 levels were normal. A computed tomography scan of her abdomen revealed cholelithiasis. Serum lead level was within normal limits. On the third day of her hospitalization she had generalized tonic-clonic seizures. Phenobarbital, diphenylhydantoin, and diazepam were prescribed to control the seizures. Analysis of cerebrospinal fluid showed neither an elevation in total protein levels nor an elevation in cell count. Subsequently, sustained high blood pressure was detected (via 24-hour blood pressure monitoring), and she was given oral calcium channel blocker for hypertension.

During a follow-up visit in the hospital, because the medical team could not exclude the diagnosis of encephalitis, antibiotics were given in addition to anti-

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Editor's note: Each month, this department features a discussion of an unusual diagnosis. A description and images are presented, followed by the diagnosis and an explanation of how the diagnosis was determined. As always, your comments are welcome via email at pedann@Healio.com.

TABLE 1.

Urine Porphyrin Concentrations in Our Patient

Porphyrin	Reference Range (mcg/24 h)	Sample from Our Patient (mcg/24 h)
Uroporphyrinogen I-III	0-25	2,672
Heptacarboxylporphyrin	0-5	2,88
Hexacarboxylporphyrin	0-2	2,00
Pentacarboxylporphyrin	0-5	1,445
Coproporphyrin I	0-25	1,234
Coproporphyrin III	0-75	8,848
Total urinary porphyrins	0-150	14,687

epileptic and antipsychotic drugs. Hyponatremia was one of the last pathological states detected. It is considered one of the indicators of inappropriate antidiuretic hormone secretion syndrome due to encephalitis, and this might have been the cause of the seizures. During the following days in the hospital, her seizures were more frequent and intravenous midazolam infusion was given to control them. The ascending paralysis progressed and she became tetraplegic and gradually lost consciousness. She was taken to our intensive care unit on mechanical ventilation with a Glasgow Coma Scale score of 3. Because intoxication or other unknown toxic causes could not be excluded, plasmapheresis and hemodialysis were conducted but had no beneficial effects.

Diagnosis:

Acute Intermittent Porphyria

Careful examination of the patient revealed a new symptom—urine that was reddish-brown in color. With the

other causes of colored urine excluded (such as hematuria, hemoglobinuria, bilirubinuria, myoglobinuria, and drug or food dye ingestion), the most probable diagnosis was acute intermittent porphyria (AIP). A Watson-Schwartz test was positive in a fresh urine sample, indicating an elevated porphobilinogen level.¹ The diagnosis of AIP was confirmed by high levels of 24-hour urinary porphyrins (Table 1). After the diagnosis of AIP, all of the potentially porphyrinogenic drugs were discontinued. She was treated with a high dosage of carbohydrates (300–400 g/day) and heme arginate (3 mg/kg per day for 4 days). Dramatic improvement was seen with the second dose of the heme arginate.

DISCUSSION

AIP is an autosomal dominant inborn error of heme metabolism caused by deficient activity of the enzyme porphobilinogen deaminase and the accumulation of its substrates, porphobilinogen and delta-aminolevulinic acid.² In cases of autosomal dominant transmission, the course of illness is typically indolent, with only 10% of individuals ever expe-

riencing an acute porphyric episode.³ Although patients often have a silent clinical outcome, women tend to have acute attacks more often than men. The most common presenting symptom among patients with AIP is severe abdominal pain.⁴ Abdominal pain is severe, diffuse, and often associated with increased bowel movements. Our patient's first complaint was severe abdominal pain mimicking acute gastroenteritis or urinary infection without a specific location.

Peripheral neuropathies secondary to axonal degeneration are also well characterized, occurring in 20% of all individuals who carry the gene defect and manifesting with proximal muscle weakness, diminution of reflexes, and dysesthesias.⁵ In our patient, muscle weakness and neuropathy progressed to tetraparalysis and mechanical ventilation was required. Autonomic neuropathy may manifest as urinary retention, paralytic ileus, restlessness, tremors, excessive sweating, tachycardia, and fluctuating blood pressure (typically labile hypertension, as seen in this case).⁶

Various combinations of psychiatric symptoms, such as psychosis, anxiety, depression, agitations, psychomotor slowness, and delirium, may be seen in the attacks of AIP.² These symptoms are often misdiagnosed, and treatment with drugs may worsen the patient's health. Acute attacks are often precipitated by exposure to certain drugs (eg, barbiturates, oral contraceptive agents, and antibiotics), cyclical hormonal changes in women, fasting or alcohol intake, and/or by infections that increase hepatic heme synthesis.⁷ In our patient, the first acute attack was initially triggered by an infection. The psychiatric signs in our patient suggested child abuse as she had mild mental-motor retardation and the symptoms began in a 2-hour period at home immediately before her admission to the hospital.

The list of medications that are contraindicated in AIP is very long and includes hormones, griseofulvin, antibiotics, metoclopramide, antiepileptics such as barbiturates, valproic acid, phenytoin, and benzodiazepines, and antihypertension drugs (including those prescribed for our patient that rapidly disturbed her clinical state).⁷ Drugs that do not have hepatic metabolism are often not porphyrinogenic. After the diagnosis of AIP, all of these drugs should be replaced with those that can be excreted by the kidneys.

Hyponatremia, which occurs in 20% of cases, is associated with the syndrome of inappropriate antidiuretic hormone secretion and also with infusion of hypotonic fluids.⁸ Electrolyte loss because of vomiting might have aggravated the hyponatremia in our patient.

CONCLUSION

Due to the variable nature of AIP, diagnosis remains difficult. Physicians should have strong clinical suspicion regarding unexplained gastrointestinal and neuropsychiatric symptoms and obtain a more detailed history and perform a careful physical examination (including the color of urine) to exclude the diagnosis of AIP and to avoid the use of harmful drugs. Suspicion, identification, discontinuation, replacement of drugs, and hemin administration during acute attacks are the main therapeutic principles of AIP.

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