Acute intermittent porphyria with psychiatric manifestations: A case report

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KEYWORDS

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The porphyrias are a group of eight genetic disorders of heme biosynthesis that result from the deficient activity of a certain enzyme in the biosynthesis pathway. These disorders are separated by symptom manifestation and classified as acute porphyrias and cutaneous porphyrias. One of the acute porphyrias, acute intermittent porphyria (AIP), is caused by a prophobilinogen deaminase deficiency and usually presents as abdominal pain, nausea, constipation, and confusion.[1]

CASE

Mr. G is a 55 year old Caucasian male with a past medical history significant for acute intermittent porphyria (AIP), chronic back pain, renal insufficiency, hypertension, and nicotine dependence. The patient has presented to the hospital with multiple AIP exacerbations since diagnosed eleven year prior to the current case. As with previous admissions, the patient's initial symptoms upon presentation included severe gastrointestinal pain and non-bloody emesis.

Initial laboratory values, including amylase, lipase, and liver function tests were within normal limits with the exception of a slightly elevated serum creatinine of 1.5 mg/dl (0.5-1.2 mg/dl). Thyroid-stimulating hormone (TSH) was normal. Urine drug screen was positive for cannabinoids, which he admitted to frequent marijuana use. He denied alcohol or other illicit drug use. A bowel obstruction was ruled out with an acute abdominal series. Computed tomography scan with contrast 3 months previous was normal. His family history is significant for two brothers with AIP; he does not have a family history of mental illness. He is unemployed, and enjoys photography and traveling with music groups. He is coherent and functioning outside of the hospital. Home medications included alendronate 70 mg weekly, calcium/vitamin D supplementation daily, promethazine 25 mg three times daily, gabapentin 300 mg three times daily (TID), propranolol LA 120 mg daily, and tramadol 50 mg every 4 hours as needed for pain.

Similar to previous treatment courses, the patient was initiated on intravenous (IV) panhematin therapy at 4 mg/kg/day. Panhematin transiently replenishes the depleted heme pool that regulates the overproduction of enzymes involved in heme synthesis. He was also initiated on symptomatic management including IV promethazine and IV hydromorphone. He was initiated on pantoprazole 40 mg IV daily for stress ulcer prophylaxis. Serum creatinine decreased to 1.2 mg/dl with IV fluid hydration.

Two days into his hospital admission, he began to display symptoms of delirium, including decreased cognition and disorientation. Upon interview by the psychiatric consult team, the patient was able to state his correct name; however, he believed he was in another state and displayed carphologia, picking at objects in the air. Much of his speech was incomprehensible and he was having visual hallucinations of bugs, chipmunks, and squirrels. At the time of the interview, he was cooperative, but other reported symptoms included aggressive and wandering behavior requiring redirection and attempts to pull out his IV line. He was requiring a constant one-to-one patient assistant (safety sitter). His sleep pattern was also disturbed and he would remain awake for 24-36 hours and then sleep for 12-18 hours. He certainly displayed a delirium picture as described by disturbance of consciousness, change in cognition, and fluctuating presentation. Differential diagnosis included delirium due to AIP, opiate use, other medications, cannabinoid use, or infectious process.

The attending gastroenterologist initiated chlorpromazine 50 mg scheduled three times daily and as needed oral or intramuscular (IM) haloperidol 5 mg every 8 hours. At the time of psychiatric consult he had received 2 doses of IM haloperidol within 24 hours. After evaluating the patient, the psychiatric team initiated a new regimen including perphenazine 4 mg in the morning and 8 mg in the evening, and olanzapine orally disintegrating tablet 5 mg every 8 hours as needed for

psychotic agitation. The team also altered his gabapentin to 300 mg in the morning and 600 mg at bedtime (previously was 300mg TID) to assist with normal sleep pattern. Within 48 hours of the new antipsychotic regimen and only one use of the as needed olanzapine, the patient's cognition normalized and he presented with normal orientation and functioning. The decision was made to discontinue antipsychotics prior to patient discharge from the hospital, with the understanding that these medications be reinitiated if he presents with similar delirium symptoms in the future.

DISCUSSION

Mr. G experienced a common presentation for AIP exacerbations, including severe abdominal pain, nausea and electrolyte imbalances. Seizures are also a potential manifestation. AIP exacerbations are often precipitated by an increased demand for heme synthesis or direct induction of the enzymes in the biosynthesis pathway. Porphyrinogenic events can include hormonal fluctuations during menstrual cycle, fasting or dieting, smoking, infections and surgery. Medications are also a common cause of an exacerbation because all cytochrome P450 enzymes increase hepatic heme turnover. Acute attacks are usually more common in premenopausal women and have a peak occurrence in patients 30-40 years old.[1,3] Exacerbations usually last 1-2 weeks and mostly involve an uncomplicated recovery; however, rarely life-threatening symptoms may include neurologic complications that progress into respiratory and bulbar paralysis, and death.[1] Our patient already had a long history of AIP diagnosis; however, it is worth noting that AIP exacerbations are commonly misdiagnosed because of non-specificity of symptoms and rarity of the disorder. Several tests exist for rapid detection of increased levels of urinary prophobilinogen, a porphyrin precursor to heme. These rapid tests are followed by biochemical confirmation of the type of acute porphyria.[3]

Treatment of an acute exacerbation includes symptomatic management and potential use of IV panhematin. Symptomatic management may include opiate pain control, antiemetics, fluid replacement, and correction of electrolyte imbalances and sympathetic overactivity.[4,5] Psychiatric manifestations of AIP are well documented in the literature and the incidence of neuropsychiatric presentation during an exacerbation is estimated to be as much as 19-58 percent. The pathogenesis of neuropsychiatric manifestations is unknown but theories such as free radical damage and oxidative stress are suggested.[2] Common symptoms include anxiety, depression, disorientation, hallucinations or paranoia. In our case, Mr. G's psychiatric manifestations were managed as a delirium presentation with perphenazine and olanzapine. There is no preferred antipsychotic for management of neuropsychiatric symptoms; however, there are non-preferred medications that are known to cause an exacerbation of AIP, including but not limited to quetiapine, ziprasidone, clonazepam, diazepam, and valproic acid.[6] In general, phenothiazines are considered safe in AIP and older (first generation) antipsychotics have more evidence for safe utilization. Perphenazine is an inexpensive choice if necessary for long-term therapy and is commonly used in this institution. The medications were well-tolerated and did not appear to exacerbate physical symptoms of AIP. Several references that group medications into varying classes of tolerability in patients with AIP are available and these sources were utilized in the management of the patient.[6] Because Mr. G's mental status returned to baseline, the antipsychotics were discontinued prior to his discharge from the hospital. It is unclear if Mr. G. may benefit, now or in the future, from maintenance antipsychotic management. There is the possibility that AIP is more common in patients with psychiatric illnesses although limited evidence exists, and it is unknown if maintenance medication therapy may prevent or decrease the severity of neuropsychiatric manifestations during an exacerbation.[5,7] Finally, patient education and identification of precipitating factors in order to avoid future exacerbations must be a part of the overall treatment plan.[3]

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