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Title: When to Search for the Zebra of Hematology: A Case of Acute Intermittent Porphyria Treated with Givosiran

Introduction

Acute intermittent porphyria (AIP) is the most common of the rare group of diseases known as acute porphyria. AIP is an autosomal dominant disease of heme synthesis enzymes of the liver. The resultant pathologic levels of porphyrins induce neurovisceral attacks, often with abdominal pain, nausea, vomiting, and wide variety of neuropsychiatric symptoms. Patients are often misdiagnosed given the association of the symptoms with more common etiologies. Reducing the AIP patient's morbidity depends on the clinician's ability to suspect and recognize the findings of this rare disease and administer its appropriate treatments in a timely manner.

Case Description

An 18-year-old woman was admitted to the hospital for the second time in two months for abdominal pain and intractable nausea and vomiting. Her vitals were unremarkable, and exam elicited abdominal tenderness diffusely. Initial laboratory studies only found an abnormality of low ferritin of 26 ng/mL signifying iron deficiency without anemia. Computed tomography and magnetic resonance imaging of the abdomen were without any disease findings. The patient underwent esophagogastroduodenoscopy and colonoscopy which revealed mild chronic duodenitis with negative celiac disease testing. A functional gastrointestinal disorder was suspected and antimotility and antiacid agents were prescribed. Following discharge, a hematology evaluation was sought when serum and urine porphyrin studies sent during the hospitalization returned elevated. Further interview revealed that patient had been experiencing abdominal pains, worst mid-menstrual cycle, along with paresthesia at fingers. She was empirically treated for AIP with hemin and carbohydrate loading while confirmatory gene testing was sent. Symptoms were improved and a pathogenetic variant of the hydroxymethylbilane synthase gene was found, consistent with AIP. In the six months that followed, she required three more hemin treatments for exacerbations. Due to persistence of disease, she was initiated on the novel givosiran, a heme synthesis gene interference agent, which she tolerated well.

Discussion

Unexplained and refractory abdominal and neuropsychiatric symptoms in a young female should prompt consideration of checking serum and urine porphyrin levels. In the case of AIP, treatment with hemin and carbohydrate loading may alleviate attacks while more frequent manifestations may necessitate trial of novel gene modulating therapies such as givosiran.

Key terms: Acute, intermittent, porphyria, porphyrin, givosiran