Zieve syndrome in acute alcoholic hepatitis

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ABSTRACT

A 31-year-old woman presented with acute alcoholic hepatitis, jaundice, anemia, and hypertriglyceridemia following ethylene glycol poisoning. She had no previous history of anemia or gastrointestinal bleeding. Laboratory findings were consistent with acute hemolytic anemia. She was diagnosed with Zieve syndrome and was managed with supportive measures. Zieve syndrome is a rare occurrence with only a handful of published case reports. Although rare, the diagnosis should be on the differential in this subgroup of patients to avoid unnecessary and invasive diagnostic interventions.

KEYWORDS Bilirubin; hemolytic anemia; pancreatitis; triglycerides; Zieve syndrome

Zieve syndrome presents with a triad of jaundice, hemolytic anemia, and hyperlipidemia that develops secondary to alcohol-induced liver injury. The first case was described by Dr. Leslie Zieve in 1957. Patients affected by Zieve syndrome typically present with abdominal pain, nausea, and other nonspecific symptoms. Anemia is a common finding in chronic liver disease; however, Zieve syndrome is the only related problem that can cause hemolytic anemia. Treatment of Zieve syndrome includes supportive management with blood transfusion and abstinence from alcohol.¹ Even though it is considered rare, its true prevalence among alcoholics is unknown due to underdiagnosis.

CASE REPORT

A 31-year-old white female alcoholic with resultant cirrhosis, gastroesophageal reflux disease, and depression presented after suspected cocaine overdose and witnessed seizure. She had an extensive history of alcohol abuse and drank a pint of vodka daily. She was intubated for airway protection, started on a lorazepam drip for status epilepticus, and admitted to the intensive care unit. On admission, laboratory results were concerning for severe metabolic acidosis with a pH of 7.1 and lactic acidosis of 13. She was also found to have an elevated osmolar gap. Urine toxicology was positive for cocaine, with an ethyl alcohol level of 0.04 g/dL. She was found to have hemolytic anemia with a low haptoglobin, elevated lactate dehydrogenase, and 2+

schistocytes noted on a manual count. Complete blood count showed a hemoglobin level of 8.1 g/dL (baseline 13 g/dL) with a mean corpuscular volume of 101 fL and a platelet count of 59,000/mm³. The metabolic panel was significant for elevated creatinine at 2.0 mg/dL. Lipase was elevated at 308 U/L, and liver function tests were remarkable for aspartate aminotransferase of 230 U/L, alanine aminotransferase of 92 U/L, total bilirubin of 19.1 mg/dL, and direct bilirubin of 8.7 mg/dL. The lipid panel showed a triglyceride level of 8890 mg/dL requiring plasmapheresis. She was also found to be coagulopathic with an international normalized ratio of 3.14.

The hematology service was consulted, as there was initial concern for thrombotic thrombocytopenic purpura. Given her low plasmonic score which predicts ADAMTS13 deficiency, thrombotic thrombocytopenic purpura was ruled out. She was diagnosed with Zieve syndrome in the setting of chronic liver disease and acute alcoholic hepatitis. She ultimately required dialysis due to worsening renal function likely caused by the direct cytotoxic effect of glycolic acid. She was provided supportive management with intravenous hydration, supplementation of thiamine and folate, and management of alcohol hepatitis with a 4-week course of prednisolone following a negative septic workup. Her symptoms improved slowly over the course of a prolonged hospitalization. Her hemoglobin levels remained stable with a subsequent decrease in bilirubin levels following improvement in renal function. She was discharged home 4 weeks

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Received January 22, 2020; Revised February 18, 2020; Accepted February 24, 2020.

Figure 1. Peripheral blood smear showing schistocytes suggestive of hemolysis (black arrow) and acanthocytes seen in chronic liver disease (red arrow).

after admission in stable condition after completing physical therapy and inpatient rehabilitation.

DISCUSSION

Zieve syndrome is considered a rare sequelae of chronic liver disease. The mechanism behind the hemolysis is not entirely understood, but it is hypothesized that pyruvate kinase instability leaves red blood cells susceptible to hemolysis by circulating hemolysins. A shift in membrane lipid composition, including elevated cholesterol and polyunsaturated fatty acid levels, has been documented in the hemolysis phase of Zieve syndrome. However, it's important to note that almost 50% of patients with Zieve syndrome have been found to have normal lipid profiles.² It is hypothesized that deficiency of lipoprotein lipase leads to the transient hyperlipidemia seen in this particular disease. Also, it is not unusual for patients to present with concomitant acute pancreatitis as a result of the hyperlipidemia, which was also present in our patient. Review of the literature suggests that some consider pancreatitis to be an essential feature of Zieve syndrome.³ Another proposed mechanism behind the hemolysis is vitamin E deficiency, commonly seen in alcoholics, which in turn leads to erythrocyte glutathione deficiency.^{2,4}

Although Zieve syndrome is considered rare, many believe that it is more common than previously reported. Some studies estimate the incidence to be 1 in 1600 admissions.^{1,5} The disease is often misdiagnosed in favor of acute abdomen, as symptoms and laboratory results often overlap, leading to unnecessary surgical procedures. The diagnosis in this case was established based on a history of alcohol abuse and other pertinent physical examination and laboratory

findings. This patient had an extensive history of alcohol abuse and displayed the triad of anemia, jaundice, and hyperlipidemia. Her lab work also supported the diagnosis. The peripheral blood smear showed evidence of hemolysis with schistocytes, and the bone marrow biopsy demonstrated reticulocytosis (Figure 1). Furthermore, the combination of transient hyperlipidemia and a negative Coombs test supported the diagnosis of Coombs test–negative hemolytic anemia. Based on these findings, the diagnosis of Zieve syndrome was established.

Timely recognition of Zieve syndrome is crucial in avoiding unnecessary and potentially harmful treatment. Often, patients admitted with Zieve syndrome are incorrectly treated with corticosteroids. High bilirubin levels in the setting of hemolysis along with elevated scoring systems (Maddrey discriminant function) often lead clinicians to presume underlying alcoholic hepatitis. Data have shown that treating critically ill patients with steroids often leads to adverse outcomes along with an increased incidence of hospital-acquired infections.^{2,6} Other associations seen in Zieve syndrome, although less common, include acute renal failure and myalgias, commonly mistaken for polymyalgia rheumatica due to elevated plasma viscosity.⁷ Most documented cases have shown that patients often recover within 5 to 6 weeks following alcohol cessation. It is presumed that abstinence causes decreased serum lipid levels as a result of movement of lipids from plasma and liver to adipose tissue. The challenge for clinicians remains the timely recognition of Zieve syndrome in order to improve patient care and avoid unnecessary and costly treatment. This case illustrates the importance of considering Zieve syndrome in those who present with acute anemia in the setting of chronic liver disease.

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