Zieve’s Syndrome Presenting With Severe Hypertriglyceridemia

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ABSTRACT

Zieve’s syndrome (ZS) is a rare disease characterized by a triad of hemolytic anemia, cholestatic jaundice, and transient hyperlipidemia seen in patients with alcoholic steatohepatitis. We report a case of ZS with severe hypertriglyceridemia. Among the reported cases of ZS in English literature, we believe this is the first case of the syndrome presenting with severe hypertriglyceridemia requiring plasmapheresis.

INTRODUCTION

The triad of hemolytic anemia, cholestatic jaundice, and hyperlipidemia seen in the setting of alcohol abuse and liver disease was first described by Zieve in 1958.¹ It is an underreported syndrome due to the lack of awareness within the medical community. It is speculated that it might not be as rare of a syndrome as previously thought, and its frequency in a general medical ward has been estimated at 1 in 1,600 admissions.² However, due to underdiagnosis, its true prevalence among alcoholics is unknown. There are approximately 200 reported cases of Zieve’s syndrome (ZS), mostly in non-English literature.

CASE REPORT

A 46-year-old white man presented with dyspnea and right upper quadrant abdominal pain of 2-month duration. His medical history was significant for chronic emphysema, alcohol and tobacco dependence, hepatic steatosis, hyperlipidemia, and transient ischemic attack. He was seen earlier in the day by his primary care physician for dyspnea and noted to be hypoxic with oxygen desaturation down to 91%. He was sent to the emergency department and admitted for chronic obstructive pulmonary disease exacerbation. Other associated symptoms included dizziness, chest pressure, fatigue, dark urine, and decreased appetite. He denied fever, chills, diaphoresis, hematemesis, melena, or tremors. The patient had been a heavy drinker for the past 20 years, consuming 56–84 g of alcohol per day. He admitted to drinking before coming to the hospital. Physical examination revealed stable vital signs. Generalized jaundice of the skin and palate was noted, with no other stigmata of end-stage liver disease. His lung examination was significant for right upper quadrant tenderness with mild hepatomegaly. There was no abdominal distention, ascites, splenomegaly, or caput medusa noted. Rectal examination revealed guaiac-negative stool. The chest radiograph was significant for chronically elevated right hemidiaphragm but no acute process. Electrocardiogram was unremarkable.

On admission, laboratory examination was notable for white blood cell count of 3.2 K/µL, red blood cell count of 4.09 million/µL, hemoglobin of 12.6 g/dL (baseline average hemoglobin noted to be 16 g/dL), hematocrit of 36.8% with mean corpuscular volume of 90 fl, absolute reticulocyte count of 31,595 cells/mm³, a red cell distribution width of 15.5%, sodium of 122 mmol/L, total bilirubin of 2.9 mg/dL, direct bilirubin of 2.0 mg/dL, albumin of 3.3 g/dL, lactate dehydrogenase of 544 U/L, aspartate aminotransferase of 184 U/L, alanine aminotransferase of 90 U/L, and lactic acid of 5.2 mmol/L. The prothrombin and activated partial prothrombin times and international normalized ratio were normal. Per the phlebotomist, the patient’s blood was very lipemic on several draws and was described as “strawberry milk-like” in color and consistency. A hemolysis workup and lipid panel revealed haptoglobin to be severely

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follow-up with his primary care physician. Omega-3-acid ethyl esters, with an uneventful subsequent mission with supportive care. His hemoglobin remained stable, symptoms improved over the course of the 4-day hospital admission. The patient’s triglycerides improved significantly to 638 and 369 mg/dL, respectively, after 2 plasma exchanges. The patient’s symptoms improved over the course of the 4-day hospital admission with supportive care. His hemoglobin remained stable, and he was discharged home on a statin, feno.

DISCUSSION

The diagnosis of ZS in our patient was made based on a history of heavy drinking, the clinical triad, and other pertinent physical and laboratory examination findings. The degree of hypertriglyceridemia observed in this case makes it a unique presentation of ZS among the reported cases in English literature to date. A PubMed and Google Scholar literature search revealed no case reports of reported triglyceride levels of more than 500 mg/dL. Because the hypertriglyceridemia was not severe in those cases, no aggressive measures were taken in addressing the hypertriglyceridemia such as plasmapheresis or intravenous insulin therapy.

The exact pathogenesis of ZS is not known. However, different theories have been proposed to explain the mechanism behind hyperlipidemia and hemolytic anemia. Massive mobilization of fat to or from a fatty liver and dysregulation of blood lipids due to damaged pancreatic alpha cells lead to transient hyperlipidemia. It is postulated that the deficiency of lipoprotein lipase, the protein that removes lipids from the plasma, also contributes to hyperlipidemia. Fluctuations in lipid levels observed in ZS can also lead to acute pancreatitis. Some reports have considered pancreatitis as an essential feature of ZS. Our patient had an episode of pancreatitis 2 years ago and could have had an episode of ZS at that time which may have gone undiagnosed.

Hyperlipidemia is suspected to be the source of hemolysis in patients presenting with ZS. Furthermore, high levels of lysolecithin and lysocephalin can also aggravate the process of hemolysis that manifest as a decrease in hemoglobin levels, as seen in our patient. While hemolysis leads to hyperbilirubinemia, most of the direct bilirubin elevation observed is secondary to hepatocyte injury due to alcoholism. Several acquired intracellular defects predispose the red blood cell membrane to hemolysis. Pyruvate kinase instability has been observed in red blood cells in patients with ZS. Acetaldehyde, a highly reactive metabolite of ethanol, is known to bind and inhibit red blood cells enzymes, leading to hemolytic anemia. Moreover, alterations in lipid composition of red blood cell membranes during the acute phase of the syndrome can lead to hemolysis as well. Reduction in polyunsaturated fatty acid levels and oxidation of reduced erythrocyte glutathione caused by alcohol-induced vitamin E deficiency have also been proposed to cause hemolysis. Because the vitamin E levels were within normal limits in our patient, this seems unlikely to be the etiology of hemolysis in this case.

Patients most often recover in 4–6 weeks after alcohol abstinence. Alcohol cessation leads to a shift of enormous amounts of lipids from the plasma and liver to adipose tissue as lipases become excessively activated, leading to a decrease in plasma triglycerides. Plasmapheresis is not necessary in all patients for hypertriglyceridemia, as alcohol cessation should lead to the resolution of lipemia in few days. However, high-risk patients with a history of pancreatitis and intracerebral hemorrhage should be evaluated for possible plasmapheresis due to increased risk of complications from hypertriglyceridemia. ZS can also manifest as surgical abdomen, leading to unnecessary invasive procedures in the setting of hyperbilirubinemia and transaminitis. In addition, given the history of alcohol abuse and laboratory findings likely suggesting alcoholic hepatitis, long courses of glucocorticoids are often ordered due to the use of scoring systems, such as Maddrey discriminant function, to prognosticate the disease course in patients with alcoholic hepatitis. Many of these scoring systems incorporate bilirubin levels in their calculation. As previously noted, bilirubin levels are expected to be elevated in patients with ZS, causing superficially elevated Maddrey discriminant function scores and unnecessary glucocorticoid use. The use of glucocorticoids has been linked to increased morbidity and mortality in critically ill patients along with increased incidence of hospital-acquired bacterial and fungal infections. A previous report highlights this issue and stresses the importance of recognizing ZS, along with hemolytic anemias in general, to improve patient safety and promote cost-effective care. Hence, it is of paramount importance to consider ZS in patients with unexplained hypertriglyceridemia and hemolytic anemia.
importance that clinicians are aware of ZS and its manifestation in alcoholics as well as its management.

DISCLOSURES

Author contributions: F. Choudhry, J. Kathawa, and K. Kerton wrote the manuscript. S. Farshadsefat and M. Piper revised the manuscript. M. Piper is the article guarantor.

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