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CASE REPORT | LIVER

Hemolysis in Acute Alcoholic Hepatitis: Zieve's Syndrome

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Abstract

A 45-year-old man presented with acute alcoholic hepatitis, jaundice, and anemia on admission. There was no history of bleeding or any evidence of gastrointestinal blood loss. Lab studies revealed hemolysis as the cause of anemia. The patient was diagnosed with Zieve's syndrome and managed with supportive measures. He recovered well and was discharged to a detoxification unit in a stable condition. Zieve's syndrome has been described in literature, mostly in non-English language case studies, but is largely under-recognized and under-reported. Diagnosis should be made quickly to avoid unnecessary invasive diagnostic interventions.

Introduction

Zieve's syndrome is an uncommonly recognized form of acute hemolytic anemia that manifests as a triad of jaundice, hyperlipidemia, and alcoholic steatohepatitis.[1] The syndrome was first described in 1957 by Dr. Leslie Zieve. While there are many etiologies of anemia in alcoholics, Zieve's syndrome is distinct in that it is an acute hemolytic anemia.[1,2]

Case Report

A 45-year-old man presented for voluntary admission to the alcohol detoxification unit. His alcohol history included consuming 4 hard lemonades in the morning, at least 1 pint of vodka during the day, and a "few" beers at night. He started consuming alcohol at about age 20 years, and since then, had been drinking heavily every day. At presentation, he complained of nausea, vomiting, weakness, and dark urine over the prior 2 weeks. He denied abdominal pain, fevers, chills, hematemesis, coffee ground vomitus, or melena. His past medical history was significant for hypertension and alcoholic liver disease. There was no history of any illicit drug use.

Physical examination was remarkable for scleral icterus, conjunctival pallor, and a dry oral mucosa. Laboratory tests showed hemoglobin 6.5 g/dL, hematocrit 19%, mean corpuscular volume 115 fL, red cell distribution width 17%, total bilirubin 16 mg/dL, direct bilirubin 6.3 mg/dL, alkaline phosphatase 97 U/L, aspartate aminotransferase 47 U/L, alanine aminotransferase 23 U/L, lactate dehydrogenase 326 U/L, albumin 3.5, and an international normalized ratio of 1:1. The patient's peripheral smear showed polychromasia, macrocytosis, tear drop cells, ovalocytes, spur cells, and schistocytes (Figure 1). A stool occult blood test was negative. Upper endoscopy was normal with no varices. Additional laboratory tests were consistent with hemolytic anemia, including reticulocytosis (12%), elevated LDH level, and an undetectable haptoglobin level. The patient was diagnosed with Zieve's syndrome, and was provided supportive management with intravenous hydration, supplementation of thiamine and folate, and management of alcohol withdrawal. He recovered rapidly during his short stay. His bilirubin trended down within a few days and hemoglobin remained stable 2 weeks after initial transfusion at 9.7 g/dL. He was discharged to a detoxification unit in a stable condition.

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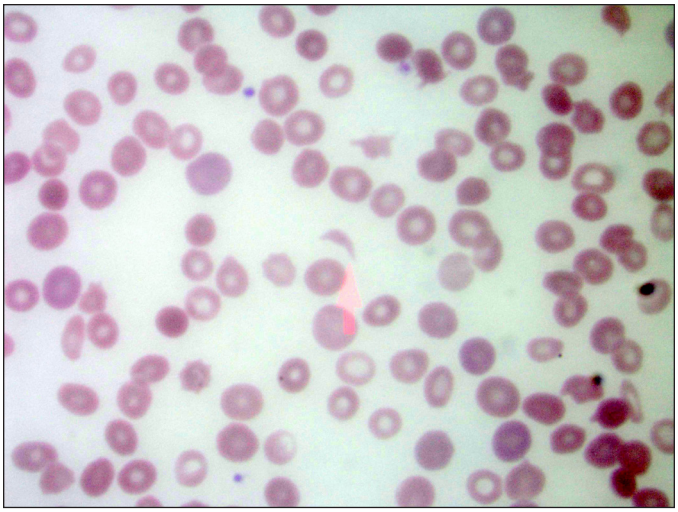

Figure 1. Peripheral smear from patient showing schistocytes and spur cells.

Discussion

The mechanism of hemolysis in Zieve's syndrome is not entirely understood, but alterations in red cell metabolism such as pyruvate kinase instability leave erythrocytes susceptible to circulating hemolysins, such as lysolecithin.[2] Changes in membrane lipid composition, as indicated by increased cholesterol and polyunsaturated fatty acids (PUFA), have been documented in patients with Zieve's syndrome during the hemolytic phase[3]; however, up to 50% of patients may have a normal lipid profile.[1] There have been about 200 cases of Zieve's syndrome published in the last 57 years, mostly in the non-English language literature.

It is important to recognize this syndrome for several reasons. It is more common than previously thought, with some estimates of 1 in 1,600 admissions to the general medicine ward.[4] Timely recognition can prevent unnecessary diagnostic or therapeutic interventions. Cases of Zieve's syndrome have been described in patients who were referred to surgery for exploratory laparotomy or cholecystectomy due to clinical presentation mimicking acute cholecystitis or a surgical abdomen.[5,6] In the setting of alcoholic hepatitis, calculation of discriminant function may lead to misrepresentation of the level of liver injury (since much of the bilirubin may be from hemolysis rather than liver inflammation). This may change the decision for initiation of glucocorticosteroids.

Zieve's syndrome may be recurrent, and the definitive treatment is alcohol cessation.[7,8] Patients with Zieve's syndrome may have other associations that need timely recognition and treatment, such as intracranial hemorrhage, acute renal failure, and myalgias.[9-11] The challenging task remains identification of the syndrome to prevent unnecessary invasive testing or referrals and provide definitive therapy such as alcohol cessation counseling and enrollment into programs that would prevent relapse of alcoholism. Zieve's syndrome should be suspected whenever there is anemia and elevation of unconjugated bilirubin in the setting of acute alcohol intake with no obvious sign of gastrointestinal bleeding.

Disclosures

Author contributions: S. Shukla obtained the clinical data, wrote the manuscript, and is the article guarantor. M. Sitrin reviewed the manuscript.

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