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Case Report

Underrecognized Zieve's syndrome, A case report

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ABSTRACT

Zieve's syndrome (ZS) is a triad of hemolytic anemia, cholestatic jaundice and hyperlipidemia that presents in the setting of alcohol abuse and liver disease. ZS is not well known and remains underdiagnosed. We present a case of ZS in a 38-year-old female with a history of chronic alcohol abuse and pancreatitis to raise awareness of ZS. It is important for ZS to be recognized promptly to avoid unnecessary and possibly harmful interventions.

1. Introduction

Zieve's syndrome (ZS) was first described in 1958 as a triad of hemolytic anemia, cholestatic jaundice and hyperlipidemia seen in the setting of alcohol abuse and liver disease [1]. It is an underdiagnosed syndrome due to its lack of awareness within the medical community thus the prevalence among alcoholics is unknown. It is important for ZS to be recognized promptly to avoid unnecessary and possibly harmful interventions.

1.1. Case presentation

A 38-year-old female with a history of chronic alcohol abuse and recurrent alcoholic pancreatitis presented with two days of altered mentation, right upper quadrant (RUQ) abdominal pain, gait instability and hematemesis. She denied fevers, chills, diaphoresis, or melena. She was on no medications and previously drank one pint of vodka daily but was now drinking two to three shots of liquor daily.

Physical examination revealed stable vital signs. She appeared lethargic with generalized jaundice of the skin, diffuse abdominal distention, RUQ tenderness and asterixis. On admission, labs were notable for hemoglobin of 6.9 g/dL, platelet count of 64, lactate dehydrogenase was 381 U/L, haptoglobin was undetectable and reticulocyte count was 5.7% consistent with hemolytic anemia. Total bilirubin was 11.2 mg/dL with an indirect bilirubin of 9.2 mg/dL, AST of 204 U/L, ALT of 62 U/L and alkaline phosphatase was 70 U/L. The prothrombin and activated partial prothrombin times were normal however the international normalized ratio was 2.04. Direct antiglobulin test (DAT) was negative. Triglycerides were elevated at 172 mg/dL with total cholesterol of 359 mg/dL. Screening for hepatitis A, B, and C was negative. RUQ ultrasound revealed hepatic steatosis. Peripheral smear showed macrocytosis and thrombocytopenia without schistocytes. Computed tomography (CT) of head was negative.

Patient was treated conservatively with lactulose and intravenous fluids with improvement in mentation. She received one unit of packed red blood cells after which her hemoglobin remained stable. Her upper endoscopy showed portal hypertensive gastropathy and a proton pump inhibitor was started. At discharge, total bilirubin, indirect bilirubin, liver enzymes, lipid levels and LDH were down trending. Patient was lost to follow up thus we were unable to assess whether she continued to use alcohol or if symptoms recurred.

2. Discussion

Alcohol use causes conditions such as macrocytic anemia, alcoholic hepatitis and liver cirrhosis. We are presenting a lesser known complication of chronic alcoholism known as Zieve Syndrome (ZS), found in heavy alcohol users with a triad of hemolysis, jaundice and hyperlipidemia. Hyperlipidemia is commonly missed due to the fluctuating levels that resolve within one to two weeks after an acute episode [2]. It has been noted that there is an atypical presentation of ZS in which patients have normal lipid levels.

Pathogenesis of ZS is unknown however theories regarding hyperlipidemia and hemolytic anemia have been proposed. It is thought that the mobilization of fat to and from a fatty liver, dysregulation of serum lipids due to damaged pancreatic alpha cells, along with postulated lipoprotein lipase deficiency leads to transient hyperlipidemia that is seen in these patients [3]. The fluctuations in lipid levels can also cause

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pancreatitis amongst these patients, it is possible that our patient's prior episodes of pancreatitis could have been related to prior undiagnosed ZS. The source of hemolysis in ZS may be related to the hyperlipidemia as high levels of lysolecithin and lysocephalin can aggravate the hemolytic process [4]. Hemolysis can lead to hyperbilirubinemia however the elevation in direct bilirubin is also seen with liver disease [3]. Patients who present with a history of alcohol abuse in combination with laboratory findings can sometimes be diagnosed and treated with glucocorticoids for alcoholic hepatitis. The Maddrey discriminant function is used to assess prognosis of the disease course however it can be falsely elevated in this patient population as bilirubin is expected to be elevated in ZS. The use of glucocorticoids in ZS is linked to increased morbidity and mortality in critically ill patients and an increased incidence of infection [5]. Recognizing hemolytic anemia rather than macrocytic anemia will help to differentiate ZS from alcoholic hepatitis [6].

Symptoms typically resolve in 4–6 weeks with alcohol abstinence and conservative therapy. Plasmapheresis is indicated in high-risk patients with severely elevated lipid level, a history of pancreatitis, and intracerebral hemorrhage due to increased risk for complication from the hypertriglyceridemia [7]. The diagnosis of ZS in our patient was made based on a history of heavy drinking, the clinical triad and pertinent physical and laboratory examination findings. Our patient's elevated LDH and indirect bilirubin along with low serum haptoglobin and negative DAT were consistent with hemolytic anemia. These findings combined with elevated triglyceride level in setting of heavy alcohol use were indications to evaluate for ZS.

3. Conclusion

With little known data on ZS, it is important to contribute adequate patient cases and literature to prospectively reduce extraneous interventions. In patient's presenting with chronic alcohol use and unexplained hemolytic anemia, clinicians should consider ZS prior to treatment to improve patient safety and promote cost effective care. From the few cases available, alcohol cessation is the most important aspect of supportive care. With more information about ZS we can continue to learn about treatment and prevention.

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Registration of Research Studies

Name of the registry: Not applicable
Unique Identifying number or registration ID:
Hyperlink to your specific registration (must be publicly accessible and will be checked):

Consent

Exhaustive attempts have been made by the medical team to contact the patient's family to obtain informed written consent. However, in the absence of the above-mentioned, this paper has been sufficiently anonymized in order to avoid harm to the patient and their family.

Guarantor

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Declaration of competing interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102464.

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