

**Zieve's Syndrome: a case report****Síndrome de Zieve: um relato de caso**

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**ABSTRACT**

Alcoholism is prevalent throughout the Americas, it affects an average of 10% of the population, therefore it can be considered a public health problem. Alcohol abuse can cause several injuries to the metabolism, being responsible for causing liver damage and other complications. Zieve's syndrome (ZS) is considered an example of these insults, it represents a rare condition and is generally underdiagnosed in clinical practice. The rarity of this syndrome means that patients are often submitted to unnecessary exams due to the lack of knowledge of this possible diagnosis by the medical team. It should be suspected whenever there is anemia, elevation of indirect bilirubin and secondary hyperlipidemia in the context of acute and abusive alcohol intake, without any obvious sign of gastrointestinal bleeding. In this article we discuss a case report about ZS of a patient attended at a metropolitan hospital in Belo Horizonte.

**Keywords:** zieve's syndrome, alcohol, Hemolysis, Jaundice.

**RESUMO**

Alcoolismo é predominante em toda a América, afecta uma média de 10% da população, pelo que pode ser considerado um problema de saúde pública. O abuso do álcool pode causar várias lesões ao metabolismo, sendo responsável por causar danos hepáticos e outras complicações. A síndrome de Zieve (ZS) é considerada um exemplo destes insultos, representa uma condição rara e é geralmente subdiagnosticada na prática clínica. A raridade desta síndrome significa que os pacientes são frequentemente submetidos a exames desnecessários devido à falta de conhecimento deste possível diagnóstico pela equipa médica. Deve ser suspeito sempre que haja anemia, elevação da bilirrubina indirecta e hiperlipidemia secundária no contexto de ingestão aguda e abusiva de álcool, sem qualquer sinal óbvio de hemorragia gastrointestinal. Neste artigo discutimos um relato de caso sobre ZS de um paciente atendido num hospital metropolitano em Belo Horizonte.

**Palavras-chave:** síndrome de zieve, álcool, hemólise, icterícia.

**1 INTRODUCTION**

Alcoholism is prevalent throughout the Americas, it affects an average of 10% of the population, so it can be considered a public health problem. Alcohol abuse can cause

several injuries to the metabolism, being responsible for causing mainly liver damage and other complications. It usually resolves with alcohol withdrawal with a resolution of 4 to 6 weeks.

The condition is currently underreported because the findings of the syndrome are common in alcoholic patients and are generally self-limited. The ZS as a differential diagnosis in these cases is important because it avoids unnecessary treatments and invasive tests. In this context, we report a patient with ZS diagnosed without invasive procedures and with resolution of the condition only with maintenance of abstinence.

## **2 CLINICAL CASE**

A 40-year-old male patient was attended at the emergency department with a complaint of holocranial headache, tremors and dark urine. Reports two previous syncope events at home without memory or sphincter loss. Past history of alcoholism for over 20 years with consumption of at least 1 liter of sugarcane liquor per day. He denies fever, abdominal pain, melena vomiting or changes in bowel habits.

On physical examination, jaundice ectoscopy was +3 / +4 and mucosal skin pallor were noted. There were no cardiopulmonary changes, no pain or palpable visceromegalies in the abdomen.

Laboratory tests showed hemoglobin 7.9, hematocrit 25.4%, mean corpuscular volume (MCV) 122, creatinine 0.85, urea 9, amylase 39, lipase 42, aspartate aminotransferase (AST) 257, alanine aminotransferase 69, lactate dehydrogenase (LDH) 669, international normalized ratio (INR) 0.97, B12 vitamin 389, folic acid 10.6, ferritin 1269, serum iron 145. In hematology, he observed polychromasia and poikilocytosis. Abdominal ultrasound (US) showed a liver with preserved dimensions and contours, without dilation of the bile ducts.

There were no signs of bleeding in the gastrointestinal tract. Laboratory tests that investigated anemia were consistent with hemolytic anemia with significant reticulocytosis (25.6%), high LDH levels, increased levels of indirect bilirubin. The diagnosis of Zieve syndrome was established. Supportive treatment was performed with intravenous hydration, thiamine and maintenance of alcohol withdrawal. The patient showed a significant improvement in the condition in a few days, as well as hemoglobin levels (9g / dl in 3 days). He was discharged with outpatient follow-up.

**3 DISCUSSION**

The etiology of anemia in elitist patients can have multifactorial causes, such as liver dysfunction, ineffective erythropoiesis, malabsorptive syndrome or hemolysis. Patients may have nutritional deficiencies (such as vitamin B12, folic acid and iron), signs of bleeding or liver disorders, high LDH value, significant reticulocytosis and low haptoglobin. However, not all of these changes must always be present in Zieve Syndrome (SHUKLA, S.; SISITRIN, M., 2015).

Zieve's syndrome was first described in 1957 when Dr. Zieve studied about twenty (20) alcoholic patients with acute hemolytic anemia. It is characterized by a classic triad of jaundice, hyperlipidemia and hemolytic anemia. (HOUDHRY , F., 2019)

The diagnosis of ZS in the patient of this clinical case was determined based on the history of alcohol abuse, in addition to jaundice, hemolytic anemia and hyperlipidemia not explained by other causes (TWOHIG, A. P., et al., 2020). Presented in this way, the classic diagnostic triad. However, it is important to note that ZS may present with symptoms other than those previously mentioned.

The mechanism of hemolysis of this syndrome is not fully understood in the literature, but they believe it is related to a change in the metabolism of red blood cells, so that erythrocytes are more susceptible to circulating hemolysins (SHUKLA, S.; SISITRIN, M., 2015). In addition, vitamin E deficiency, induced by alcohol, can decrease the levels of polyunsaturated fatty acids and cause oxidation of erythrocyte glutathione, which leads to instability of this enzyme and erythrocyte hemolysis (ABUGHANIMEH, K., et al., 2019).

Current studies have shown that ZS is underreported and it is not often known and diagnosed by medical staff. Patients with this syndrome may have a higher alcoholic hepatitis score, thus contributing to excessive treatment with the use of corticosteroids and the possibility of inducing immunosuppression and promoting unnecessary additional complications. It can be seen, then, that the lack of knowledge of this pathology at first is one of the challenges faced in the management of these patients (ABUGHANIMEH, K., et al., 2019).

Despite the absence of nutritional deficiency (such as vitamin B12, folic acid and iron), lack of signs of bleeding or liver abnormality on ultrasound, in the aforementioned clinical case, laboratory tests showed high LDH, significant reticulocytosis and low haptoglobin, signs suggestive of alcoholic hepatitis and hemolysis. In view of the social

history of alcoholism associated with the alterations presented, the hypothesis of hemolytic anemia secondary to ZS was raised.

After hospitalization and, consequently, alcohol withdrawal, it was possible to notice an improvement in the hemoglobin level curve. The patient remained with a good evolution and improvement of anemia, despite not having undergone vitamin and mineral replacement. The recognition and early diagnosis of ZS avoided invasive tests such as myelogram, which are unnecessary for the diagnosis of the syndrome. In addition, it saved the health care network from spending on high-cost exams and carrying out inappropriate treatments.

After the diagnosis of ZS, most patients recover within four (4) to six (6) weeks after alcohol withdrawal. However, maintaining the ethyl habit can aggravate the disease and potentially evolve to death (TWOHIG, A. P., et al., 2020). In addition, these patients are often associated with other diseases such as: intracranial hemorrhages, renal failure and myalgia. Because of this, they must be monitored longitudinally for possible treatment (SHUKLA, S., 2015).

The persistence of alcohol abuse can aggravate Zieve's syndrome and evolve to death. Thus, the treatment of SZ constitutes support and, mainly, alcohol abstinence.

#### **4 CONCLUSION**

Zieve's syndrome is a rare and generally underdiagnosed condition. It should be suspected whenever there is anemia, elevation of indirect bilirubin and secondary hyperlipidemia in the context of acute and abusive alcohol intake, without any obvious sign of gastrointestinal bleeding.

In clinical practice, ZS needs to be readily recognized by doctors and the scientific community in general. This recognition can be achieved by increasing the dissemination of clinical reports in the literature and in medical education, allowing professionals to make a correct diagnosis and perform the appropriate follow-up.

In addition, early diagnosis prevents invasive tests and the use of unnecessary medications, which can worsen the clinical condition. Currently, no specific treatment is recommended for patients with transient hemolytic anemia due to Zieve's syndrome and the therapy is supportive with the encouragement of the cessation of alcoholism.

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