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CASE REPORT OF AUTOIMMUNE HEPATITIS AND CONCOMITANT PRIMARY BILIARY CHOLANGITIS

RELATO DE CASO DE HEPATITE AUTOIMUNE E COLANGITE BILIAR PRIMÁRIA CONCOMITANTE

REPORTE DE CASO HEPATITIS AUTOINMUNE Y COLANGITIS BILIAR PRIMARIA CONCOMITANTE

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ABSTRACT

Autoimmune hepatitis with concomitant primary biliary cholangitis has rarely been reported. In this case, we describe a 57-year-old woman who had criteria for this diagnosis based on a liver biopsy that showed a mixed infiltrate of lymphocytes associated with interface hepatitis, rosettes, emperipolesis, plasma cells, and over 50% of the portal ducts did not have a central biliary duct. The treatment provided was Azathioprine, prednisone, and omeprazole, which led to a remarkable complete normalization of her liver enzymes after four weeks. This successful treatment outcome underscores the importance of early identification and treatment for improving long-term outcomes.

Keywords: Autoimmune Hepatitis. Primary Biliary Colangitis. Autoantibodies.

RESUMO

Hepatite autoimune com colangite biliar primária concomitante foi raramente descrita. Apresentamos o caso de uma mulher de 57 anos que preencheu os critérios para esse diagnóstico com base em uma biópsia hepática que mostrou um infiltrado misto de linfócitos associado à hepatite de interface, rosetas, emperipolese, células plasmáticas e mais de 50% dos ductos portais sem ducto biliar central. O tratamento administrado foi azatioprina, prednisona e omeprazol, o que levou a uma notável normalização completa de suas enzimas hepáticas após quatro semanas. Este resultado terapêutico bem-sucedido ressalta a importância da identificação e do tratamento precoces para melhorar os resultados a longo prazo.

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Palavras-chave: Hepatite Autoimune. Colangite Biliar Primária. Autoanticorpos.

RESUMEN
Raramente se ha descrito una hepatitis autoinmune con colangitis biliar primaria concomitante. Se presenta una mujer de 57 años que tenía criterios para este diagnóstico basado en una biopsia hepática que mostraba un infiltrado mixto de linfocitos asociados a hepatitis de interfase, rosetas, emperipolesis, células plasmáticas, y más del 50% de los conductos portales no tenían un conducto biliar central. El tratamiento administrado fue azatioprina, prednisona y omeprazol, lo que condujo a una notable normalización completa de sus enzimas hepáticas al cabo de cuatro semanas. Este resultado terapéutico satisfactorio subraya la importancia de la identificación y el tratamiento precoz para mejorar los resultados a largo plazo.

Palabras clave: Hepatitis Autoinmune. Colangitis Biliar Primaria. Autoanticuerpos.

1 INTRODUCTION

Autoimmune Hepatitis (AIH) is an inflammatory disease of the liver mediated by circulating antibodies. The most likely cause is a loss of tolerance to hepatocyte antigens due to an interaction between a genetic predisposition and environmental factors. (1,2)

It has been reported that the estimated global incidence of autoimmune hepatitis was 1.28 cases per 100,000 population, and the pooled global prevalence was 15.65 cases per 100,000 population. (3)

Presentation can range from asymptomatic patients with a slight increase in liver function tests to acute liver failure. Elevated transaminases characterize laboratory results, detection of autoantibodies such as antinuclear antibodies (ANA) or anti-smooth muscle antibodies (SMA), increased levels of immunoglobulin G (IgG) in the blood, and the presence of interphase hepatitis or infiltration of plasma cells into liver tissue. (1)

The most common subtype is autoimmune hepatitis type 1, which presents with positive ANA and anti-smooth muscle antibodies. Diagnosis can be difficult, as shown in this case, in which lab results showed negative ANA on initial tests. (2)

This study aims to highlight an atypical presentation of autoimmune hepatitis with negative antinuclear antibodies and discuss the most appropriate tests to diagnose it.

2 CASE REPORT

A 57-year-old woman with a personal history of nephrolithiasis seven years ago, episodes of migraines, two miscarriages, one of them due to polyhydramnios, and a family history of alcoholic cirrhosis, was admitted to the emergency room with nausea, jaundice, malaise, dark urine and pruritus. Six days after admission, she presented with mild epigastric pain. On physical examination, she presented jaundiced skin, sclera, and mucous membranes; their vital signs were unchanged (BP: 120/80 mmHg, HR: 74 bpm, SatO2: 94%, FiO2: 21% Tº: 36.8 ºC).

Liver function studies on admission revealed Total Bilirubin: 9.7, Direct Bilirubin: 8.9, Indirect Bilirubin: 0.84, AST: 1213, and ALT: 1643 (Table 1). An abdominal ultrasound revealed multiple lithiasis images, with liver and bile ducts preserved. Initially, he received intravenous fluid therapy and a liquid diet that evolved into a soft diet. Five days later, an abdominal CT scan with contrast showed an increase in liver size, a highly distended gallbladder with thickened walls and heterogeneous contents, and a diameter of the common bile duct of approximately 4 mm. Laboratory tests revealed negative ANA, IgG:

2194, IgE: 29.35, negative c-ANCA, negative ANCA and positive anti-smooth muscle antibodies (SMA) with a titer of 1:320 (Table 2). An ultrasound-guided liver biopsy showed a mixed infiltrate of lymphocytes and eosinophils associated with grade 4 interface hepatitis. The presence of rosettes, emperipolesis and plasma cells was observed. There was mild leukocytic infiltration in the bile ducts, metaplasia of the ductal plate, and more than 50% of the portal ducts did not have a central bile duct. The patient's Simplified Diagnostic Criteria (SCD) score was 7, confirming the diagnosis of autoimmune hepatitis. The final diagnosis was autoimmune hepatitis with concomitant primary biliary cholangitis.

The patient was treated with azathioprine, prednisone, and omeprazole. Subsequently, his liver enzymes began to improve, and they were completely normalized within 4 weeks. After showing a good response to treatment, the patient was discharged.

2.1 ETHICAL CONSIDERATIONS

All the procedures carried out in this study were in accordance with the ethical standards of institutional and/or national research committees and the Declaration of Helsinki (revised in 2013). Written informed consent was obtained from the patient for the publication of this case report. The study was approved by the ethics committee of the Catholic University of Santa Maria.

3 DISCUSSION

AIH is a chronic autoimmune inflammatory disease of the liver, mainly divided into type 1 AIH and type 2 AIH. AIH type 1 is the most common form (95%) and frequently associated with the presence of ANA and SMA. While AIH type 2 is less frequent (5%) and is related to Antimicrosomal Liver/Kidney Antibodies type 1 (LKM-1). (1,2)

Recent literature highlights that up to 20% of patients with AIH may be negative for ANA, focusing on the presence of SMA. This seronegativity can delay diagnosis in advanced stages of the disease. The latter is consistent with the patient's findings, which were ANA negative and SMA positive. On the other hand, the exclusion of other etiologies of hepatic impairment and the favorable response to immunosuppressive treatment with corticosteroids are also compatible with AIH. (4) (2,5)

The exact etiopathogenesis of AIH is unknown, however, the role of cell-mediated immunity and antibody-dependent mechanism as agents that can cause liver damage

has been described, both attributed to exposure to an autoantigen. It is important to recognize possible inducers of the disease, especially in contexts in which there is a high prevalence of AIH and infections, these generate a cross-reaction by epitopes and can favor the appearance of AIH in patients with an acute infection. (6) (7)

On the other hand, it is considered that AIH is a polygenic disease, within the genetic factors associations with molecules of the major histocompatibility complex type II, such as DR3 and DR4, have been described. The presence of mononuclear cells, such as B and T lymphocytes, are involved in the production of autoantibodies, as well as pro-inflammatory components. Polymorphonuclear cells have been of special interest in AIH, especially low-density granulocytes and those expressing the enzyme myeloperoxidase (MPO), involved in the production of neutrophil extracellular traps (NETs) that are activated by pathogenic microorganisms or other cytokines. Their overactivation has been related to autoimmunity and organ damage, which is why they have been considered objective indicators for the diagnosis and course of AIH. Its usefulness lies in reducing the number of biopsies and the risks that come with it. (6,8) (9) (10) (10)

The clinical presentation is usually asymptomatic; most patients do not present manifestations of hepatobiliary disease, presenting an elevation of AST and ALT with a greater frequency of presentation in the female sex. In the present case, a significant elevation of AST and ALT was found, which was indicative of liver damage and cell lysis. (1)

It is recommended that diagnostic review criteria (CRDs) and CDS be used to establish the diagnosis of AIH. In the present case, the CDS criteria were used because they have an advantage in the diagnosis of individual patients, taking into account autoantibodies, immunoglobulin levels, liver histopathology and ruling out viral hepatitis. The patient had a score of 7, confirming the diagnosis of HAI. (5)

The coexistence of hepatitis A, B, C, or E, Epstein-Barr virus (EBV), Human Herpes virus (HHV) should be ruled out. It has also been linked to the presence of vitamin D deficiency and gut barrier dysfunction with or without bacterial translocation. Drug-induced Autoimmune Hepatitis has also been described, however, it is also unknown how exactly it occurs, it is considered idiopathic. The interaction of these and other factors has yet to be studied in the pathophysiology of HAI. This case did not present the presence of hepatitis A, B, or C viruses as evidenced by laboratory results, however, a limitation of

our study is that no tests were performed for EBV, HHV, or hepatitis E virus. (7,8) (11) (6,8,11)

Timely and appropriate treatment is crucial to prevent progression to cirrhosis and irreversible liver failure, improving long-term outcomes. The patient responded favorably to treatment with azathioprine and prednisone, consistent with current guidelines recommending immunosuppressants as the first line of treatment in AIH. This case underscores the need for a comprehensive diagnostic approach that includes clinical, biochemical, and histological evaluation, especially in patients who have atypical autoantibodies or who are seronegative for the most common autoantibodies. (4,12) (13) (14)

4 CONCLUSION

In conclusion, the diagnosis of AIH is based on a combination of clinical, serological, and histological findings. The importance of considering AIH in patients with hepatic impairment, even in the absence of ANA, is highlighted. It is recommended that more research be carried out that seeks to better understand the immune mechanisms that lead to the development of this disease and to apply more precise diagnostic criteria.

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