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Primary Biliary Cholangitis Associated with Autoimmune Hemolytic Anemia: Case Report

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ABSTRACT
Primary biliary cholangitis (PBC), formerly known as primary biliary cirrhosis, and autoimmune hemolytic anemia (AIHA) are autoimmune diseases. Although the association of several autoimmune diseases is common, however the association between primary biliary cholangitis (PBC) and autoimmune hemolytic anemia (AIHA) is rare. We report a case of (AIHA) confirmed by direct Coombs test in a patient followed in our unit for a year for PBC under ursodesoxycholic acid (UDCA) well conducted.

Introduction

Primary biliary cholangitis (PBC) is a chronic liver disease characterized clinically by intrahepatic cholestasis syndrome and pathologically by progressive destruction of the small bile ducts. In the absence of treatment, liver disease progresses to cirrhosis and its complications (portal hypertension (PHT), liver failure). [1]. Autoimmune hemolytic anemia (AIHA) is linked to the presence of autoantibodies directed against one or more antigens of erythrocyte membrane causing their accelerated destruction [2]. The association between PBC and other autoimmune diseases is often described (autoimmune hepatitis, thyroiditis, diabetes, celiac disease...), however, the association with AIHA is exceptional [3]. We describe a case of primary biliary cholangitis associated with autoimmune hemolytic anemia.

Case report

A 42-year-old woman followed for PBC under ursodesoxycholic acid (UDCA) at a rate of 13 mg / kg / d consulted for asthenia and cutaneous mucosal jaundice evolving for a month. She was also followed for a hyperlipidemia diagnosed for 2 years untreated. The physical examination showed a frank cutaneous mucosal jaundice without hepatosplenomegaly.

Biological data revealed anemia at 5.5 g / dL (normal rate 12-16 g / dL) normochromic normocytic regenerative with a reticulocyte rate 200 g / l (normal value 20-120 g / l) Associated with cholestasis without cytolysis: a total bilirubin high at 39 mg / l (normal value 2-12 mg / l) predominantly indirect BID at 27 mg / l (normal value 0-3 mg / l), an alkaline phosphatase (PAL) at 307 IU / l (normal value 40-150 U / l), a gamma glutamyl transferase (GGT) at 224 IU / l (normal value 9-36 IU / l); normal transaminases ASAT at 33 IU / l (normal value 4-34UI / l) and ALAT at 40 IU / l (normal value 0-55UI / l). A hemolysis assessment was carried out**:** a collapsed Haptoglobin at 0.08 g / l (normal value 0.14-2.73g / l), LDH 275 IU / l (normal value 125-243 IU / l). The blood smear showed spherocytes and the direct Coombs test was positive. The results of medullogram with immunohistochemically study objectified a reaction marrow,entering into the framework of a dysimunitary disease. Given these data, we concluded at primary biliary cholangitis associated with Coombs-positive hemolytic anemia. The patient initially received boluses of Solumedrol 5 mg / kg / day for 3 days then relay to oral prednisone at a dose of 1 mg / kg / day, the UDCA was maintained at the same dose. This allowed after a month of treatment, disappearance of jaundice and normalization of the hemoglobin to 12g / dl as well as the liver function tests. Corticosteroid therapy was stopped gradually, the patient remained on UDCA alone at a dose of 13 mg / kg / day.

Discussion

Primary biliary cholangitis (PBC) mainly affects middle-aged women [3]. It is an autoimmune disease associated with the presence of anti-mitochondrial antibodies of the M2 type [4] and is characterized by appearance of cholestasis often associated with pruritus, in the absence of treatment the progression is towards cirrhosis.

PBC is frequently associated with other autoimmune pathologies,mainly autoimmune hepatitis [5] , defining an overlapping syndrome, insulin-dependent diabetes [6], autoimmune thyroiditis [7] Collagenosis, in particular rheumatoid arthritis (RA), [8] mixed connective tissue and systemic lupus erythematosus [9]. However, an unusual association with PBC have been reported, including interstitial lung disease, [10] ulcerative colitis [11], membranoproliferative glomerulonephritis [12], celiac disease, [13] and autoimmune thrombocytopenia [14]. The association between PBC and AIHA is rare [15]. Autoimmune hemolytic anemia results from the production of autoantibodies to red blood cell antigens that cause the destruction of erythrocytes. It can be primary (idiopathic) or

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secondary to other autoimmune disorders, malignancies or infections [16]. Direct Coombs test (direct antiglobulin test) is the cornerstone of the diagnosis of AIHA [17] associated with signs of hemolysis, including anemia, reticulocytosis, increased lactate dehydrogenase and indirect bilirubin. The current case is about a patient presenting an acute clinical and biological hemolysis counted by a regenerative AHAI confirmed by direct Coombs test. At present, it is not certain that the combination of the two diseases occur by chance or they reflect a common immunological basis. [18]. According to a study by (Brack Stone and Ghent 2000) 50% of patients with PBC have hemolysis, this may be due to damage of red blood cells (RBCs) membrane by the increased plasma concentration of endogenous bile salts secondary to cholestasis, and which may at the same time expose the antigens "hidden" in the membranes of (RBCs), [19] witch explaining the remission of AIHA in certain patients only after starting UDCA [20]. On the other hand, these patients are likely to develop autoantibodies against erythrocyte as part of immune deregulation [21]. In a review of the literature, 23 cases of association of PBC and AIHA were studied. There were no cases of AIHA diagnosed before the onset of PBC. This suggests a possible causal relationship between these two pathologies. In our case, despite treatment well conducted by the UDCA, the patient suffered of hemolysis which only improved after starting corticosteroid therapy, this being in favor of an autoimmune origin.

The recommended treatment for AIHA associated with PBC includes corticosteroids (1mg / kg / day) to control hemolysis in the acute phase, and an immunosuppressant (ciclosporin-A or cyclophosphamide), or UDCA (13-15mg / kg / j) in maintenance treatment. [22] Some patients with PBC with mild AIHA have been successfully treated only with ursodeoxycholic acid [23], indeed corticosteroid therapy is contraindicated in cirrhotic patients due increasing risk of metabolic, bone complications and portal vein thrombosis. Finally, in some patients who do not respond to corticosteroids after three months of well conducted treatment [20], a splenectomy may be indicated [24] [25].

Conclusion

The combination of PBC and AIHA should be mentioned in the recent appearance of anemia without externalized bleeding associated with hyper bilirubinemia for an early diagnosis of hemolysis.

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