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A RARE CAUSE OF CHRONIC HEPATITIS: CELIAC DISEASE

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Abstract

Introduction. *Celiac disease is a chronic bowel disease with a prevalence of 1% in the general population. This condition, immune-mediated, may exhibit multiple extra-intestinal changes, including the liver.*

Case presentation. *We present the case of a 43-year-old patient presenting in our clinic for fatigue, associated with cytolytic and cholestatic hepatic syndrome with an onset of 10 years. During this time, the patient performed multiple investigations with the exclusion of viral, autoimmune etiology, primitive biliary cirrhosis and Wilson's disease. An abdominal ultrasound recorded an elongated, with an infundibular septum gallbladder. Abdominal computer tomography did not detect any changes. The final diagnosis is chronic alithiasic cholecystitis receiving hepatoprotective treatment with symptom relief and improved hepatic disorders. Over the past 2 years, the patient was diagnosed with osteoporosis (T score = -2.7 followed by treatment with Calcium and Vitamin D and improvement in T score to -2.1), and an iron deficiency anemia corrected with oral iron treatment. Upon resuming the anamnesis, we notice the presence of an intermittent bloating associated with diarrhea. Positive anti-transglutaminase antibodies required upper endoscopy with biopsy witch confirmed celiac disease.*

Conclusion. *Despite the rather low prevalence of celiac disease in the etiology of hepatocytolysis, it is important to investigate its presence in the context of hepatic changes with uncertain etiology. This case motivates us to be rigorous in looking for secondary causes of hepatic impairment even in patients with apparently benign changes.*

Keywords: *celiac disease, chronic hepatitis, hepatic cytolisys.*

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Rezumat

Introducere. *Boala celiacă este o afecțiune cronică a intestinului subțire, cu o prevalență de 1% în populația generală. Această condiție, mediată imun, poate prezenta afectări extraintestinale multiple, inclusiv hepatice.*

Prezentare caz. *Prezentăm cazul unei paciente în vârstă de 43 de ani care se prezintă în serviciul nostru pentru fatigabilitate, asociind citoliză și colestază hepatică cu debut de aproximativ 10 ani. În această perioadă, pacienta a efectuat multiple investigații, cu excluderea etiologiei virale, autoimune, a cirozei biliare primitive și a bolii Wilson. Ecografic abdominal se decelează un colecist alungit, septat infundibular. Tomografia computerizată abdominală nu evidențiază modificări patologice. Diagnosticul final este de colecistită cronică alitiazică pentru care primește tratament hepatoprotector cu ameliorarea simptomatologiei și reducerea colestazei hepatice. În ultimii 2 ani se adaugă diagnosticul de osteoporoză (scor T= -2,7 pentru care a urmat tratament cu Calciu și Vitamina D rezultând ameliorarea scorului T pâna la o valoare de -2,1). Sindromul anemic feripriv s-a corectat sub tratament cu fier oral. La reluarea anamnezei, pacienta declară prezența unui meteorism abdominal intermitent asociat cu scaune diareice. Prezența anticorpilor anti transglutaminază pozitivi a impus efectuarea endoscopiei digestive superioare cu biopsie, care confirmă boala celiacă.*

Concluzie. *În ciuda prevalenței destul de reduse a bolii celiace în etiologia hepatocitolizei, este important să investigăm prezența acesteia în contextul unor modificări hepatice cu etiologie incertă. Acest caz ne motivează să fim riguroși în căutarea unor cauze secundare de afectare hepatică, chiar și la pacienții cu modificări aparent benigne.*

Cuvinte cheie: *boală celiacă, hepatită cronică, hepatocitoliză*

We presented the case of a 43 years female patient who was admitted to our clinic in order to investigate the etiology of a persistent hepato-cytolytic and cholestatic syndrome, expressing no symptoms except a moderate fatigability.

For the etiology of these disorders, a large number of investigations were performed in the last 10 years. The patient declared no alcohol consumption and other etiology were excluded: viral hepatitis (Antibody to hepatitis C virus and hepatitis B surface antigen negative), autoimmune hepatitis (Antinuclear antibodies, Anti-smooth muscle antibody, Liver-kidney microsomal type 1 antibody normal range), primary biliary cholangitis (Antinuclear antibodies and antimitochondrial antibodies normal range), Wilson disease (ceruloplasmin and copper concentration normal). Abdominal ultrasound detected an elongated gallbladder with an infundibular septum with no additional information added by abdominal computer tomography.

The upper endoscopy showed an esophageal diverticulum and antral gastritis. In this context, the final diagnosis was chronic alithiasic cholecystytis and the patient received hepatoprotective treatment with an amelioration of symptoms and improvements of biochemical tests. In the last 2 years, she was diagnosed with autoimmune thyroiditis with normal thyroid status and osteoporosis (T score =-2,7). The T score improved (-2,1) under the treatment with vitamin D and Calcium. Also, an iron deficiency anemic syndrome was detected and corrected by oral iron administration.

After understanding the whole history, we insisted with anamnesis and the patient declare intermittent bloating associated with diarrhea, considered irrelevant before by the patient. The objective exam at admission was normal with a body constitution: BMI=19.5 kg/m^2. Blood pressure: 120/80mmHg; Heart rate: 85/min. Laboratory results are presented in Table 1. We perform an Anti-tissue transglutaminase antibody test for the suspicion of celiac diseases in the context of the digestive symptoms, malabsorption (anemia, osteoporosis) and modified liver tests.

Abdominal ultrasound showed normal dimensions and echogenicity of the liver, portal vein and biliary ducts with normal dimensions, gallbladder without stones, but a hyperechogenic image at the caudal wall suggesting a polyp (Image 1). There were no other changes seen in the ultrasound of the abdomen. In the context of elevated levels of anti-tissue transglutaminase antibody, we perform an upper endoscopy with biopsy that showed no changes on the esophagus and duodenum but a mild antral inflammation (Image 2). Histopathologic results of the biopsy showed a duodenal mucosal fragment with edema, congestion and moderately inflamed lympho-plasmococcal infiltrate in the corium. There is an increase in intraepithelial lymphocytes and cryptal hyperplasia without alteration of villous architecture. The diagnosis of celiac disease was made in the context of clinical (bloating associated with diarrhea, fatigability), biological (anemia, osteoporosis, elevated anti-tissue transglutaminase antibody) and histological specific changes.

We explain to the patient the importance of the diet for treating this disease and the connection between elevated liver enzyme and celiac disease. After 6 month of diet the patient came for evaluation and we found normal hepatic function.

Discussions

The presented case is an example that we, as practitioners, have to insist in looking for the

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right diagnosis and the essential role of a thorough history. Even if the most frequent diseases that are responsible for the biological changes were excluded, the details given by the patient were able to lead us to the right diagnosis.

Celiac disease is the most common food intolerance in the world and affects nearly 1% of the world's population, reaching 10-15% in patients with first degree relatives with this disease[1]. It is a chronic autoimmune enteropathy, induced in genetically susceptible individuals after ingestion of wheat gluten that resolves with gluten free diet. It was initially considered that gluten hypersensitivity is limited to the intestine and all other features are secondary to malabsorption, but now is established that many of these findings may not be explain by malabsorption alone. Celiac disease is therefore a multi-systemic disease that can affect other organs such skin, brain, bones and the liver[2].

In the absence of other causes, celiac disease is present in up to 9% of the patients with elevated liver enzyme levels[3]. Hypertransaminasemia is found in about 40% of adults with a classical presentation of the celiac disease. In these patients, the clinical manifestation of the disease could not be visible[4]. Liver dysfunction in celiac disease include asymptomatic rise in serum transaminases, autoimmune hepatitis, primary biliary cirrhosis and primary sclerosing cholangitis.

A study that included 158 consecutive adults with celiac disease show that mean range of ALT was 61 (25-470) IU and AST 47 (30-190) IU[5]. Another conclusion of this research is that the two groups of patients (with or without liver changes) had no differences in anthropomorphic, epidemiological and histological data[5]. Alkaline phosphatase (ALK) could be abnormal in 4-20% of the cases and may reflect metabolic bone disease[6]. Studies that included liver biopsy to characterize the associated liver pathology have reported: no abnormality, non-specific hepatitis or occasional severe changes like cirrhosis or fibrosis[7].

An interesting finding is that the mean age of the celiac patients (28 years range 19-37) with cryptogenic hypertransaminemia was lower than in patients with celiac diseases but without hypertransaminemia (39 years range 18-79). This finding suggests that elevated liver enzyme are an early sign of celiac disease[8].

The mechanism of these changes is not fully understood, but there are some certain functional abnormalities proved to be involved. The first is represented by increase intestinal permeability that could be responsible for the arrival of toxins and antigens to the liver trough the portal circulation. These can trigger the release of pro-inflammatory mediators, hepatic

LABORATORY RESULTS:					
Hemoblobin	12.4g/dl	ALT	27U/L	FT4	1.2 ng/dl
Iron	81mg/dl	AST	63U/L	Total Ca	9,7mg/dl
Ferritin	30ng/ml	GGT	148U/L	Vitamin D	33,6ng/ml
Cholesterol	266mg/dl	ALK	209U/L	Total proteins	8.03g/dl
LDL c	161mg/dl	Total Bilirubin	0.55mg/dl	Albumin	4.15 g/dl
TSH	1.31uIU/ml	Direct Bilirubin	0.23mg/dl	Anti-tissue transglutaminase antibody	22,72U/ml

Table 1. *Laboratory result at admission*

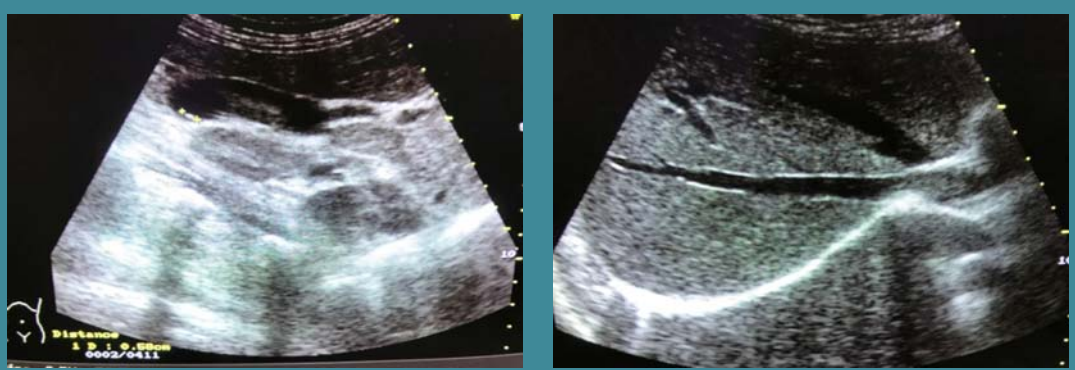

Image 1. *Ultrasound of the liver and gallbladder that showed normal structure of the liver with a possible polyp on the gallbladder wall*

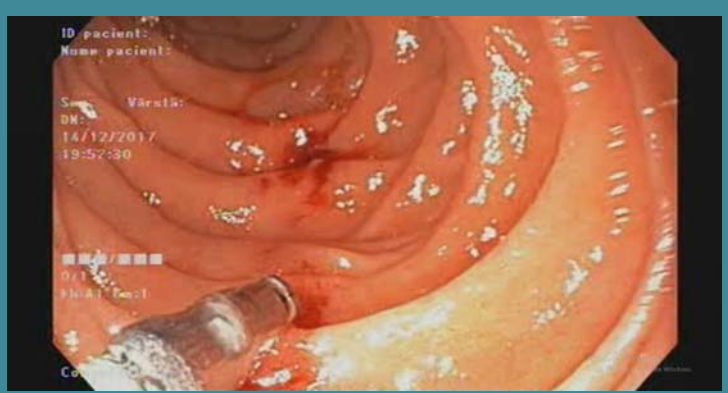

Image 2. *Upper endoscopy with biopsy showing no changes in the duodenum*

inflammation and increased liver enzymes[9]. Other malfunctions may be: chronic intestinal inflammation, malabsorption and malnutrition with its metabolic effects, small intestine bacterial overgrowth and genetic predisposition to autoimmunity. Nevertheless, the published researches tend to imply that all these mechanisms may coexist[10].

The treatment for the hepatic disorders is gluten free diet. A study that included 158 consecutive adults with celiac disease showed that after diagnosis 67 patients had changes in the liver enzymes. After 1 year of strictly gluten free diet, 95 % of these patients had normal transaminase levels[5]. Our patient normalized the liver function in 6 months of gluten free diet.

An important lesson from this case is underlining that in patients with elevated liver enzyme without a known cause, blood test to diagnose celiac disease need to be performed, since celiac disease is the most frequent cause of elevated transaminase of unknown origin. We also propose to perform screening for celiac disease in patients with autoimmune hepatitis, primary biliary cirrhosis and primary sclerosing cholangitis. The symptoms improve or reverses after gluten free diet in short time making the early recognition of the disease extremely important for the rest of patient's life. The particularity of the case is represented by the lack of classical symptoms for celiac disease and long history of abnormal liver tests with a correct diagnosis after 10 years.

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