



Celiac Disease and Liver Abnormalities: What Relationships?

D Tagzout* and A Tebaibia

Algiers Faculty of Medicine, Algiers University, El-Biar Hospital, Algeria

***Corresponding author:** D Tagzout, Algiers Faculty of Medicine, Algiers University, El-Biar hospital, Algiers, Algeria.

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Introduction

Celiac disease (CD) may be associated with liver abnormalities (LA) and these abnormalities are often liver blood tests abnormalities corresponding to cryptogenic hypertransaminasemia or celiac hepatitis (CH) which is reversible after strict gluten free diet (GFD). CH may be the only manifestation of unrecognized CD. Other LA may be associated, especially those of dysimmune origin or overload. The mechanisms of these associations are unclear and the role of the GFD is uncertain.

Keywords: Celiac disease; Hypertransaminasemia; Dysimmune liver disorders; Cirrhosis

Introduction

CD is an autoimmune enteropathy secondary to gluten ingestion in genetically predisposed individuals. Although its main target organ is the small intestine, CD is currently considered as a multi-systemic disease, where the injury may affect different organs, particularly the liver. The GFD strict adherence, is so far the only effective treatment whose role on liver damage seems positive. A number of studies have shown that LA occurs at a higher frequency in patients with CD, and these are often non-specific abnormalities of liver bioassays corresponding to CH. Specific chronic LA may associate with CD. A cautious diagnostic approach will not ignore the different associations.

Celiac Hepatitis

CH is the most common LA during CD, observed in 13 to 60% of cases of untreated CD, with reversibility in more than 2 thirds of cases after 6 to 12 months of strict GFD [1]. This response to the GFD confirms this diagnosis. CH is asymptomatic and may be the only sign of previously unrecognized CD. The elevation of

transaminase levels is moderate, between 3 and 5 times the upper limit of the normal rate, and it has been shown that ALAT elevation in celiac children is correlated with the severity of villous atrophy and poor growth [2]. The hypothesis explaining this abnormality is an intestinal hyperpermeability with a massive passage of toxins and intra-luminal antigens through the portal circulation, and it has been shown that the intestinal permeability as well as the level of transaminases are corrected by a GFD [3].

Celiac Disease and Liver Abnormalities

Primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH) may be associated with CD. The frequency of CD during PBC ranges from 1% to 7% and the frequency of PBC during CD varies from 0.1% to 3% depending on the studies [4]. CD is present in 4 to 6% of patients with type 1 or type 2 AIH. Cases of primary sclerosing cholangitis associated with CD have been described in the literature. The mechanism of these associations remains unknown but it may be a genetic susceptibility to immune disorders involving several

antigenic targets (enterocytes, cholangiocytes, hepatocytes). The effect of GFD seems very weak without significant improvement in liver signs.

Celiac Disease and Non Alcoholic Fatty Liver Disease

CD is seen in 3 to 7% of patients with non alcoholic fatty liver disease (NAFLD) [5]. CD screening is indicated for NAFLD associated with unexplained anemia, nutritional deficiency, or repeated abdominal pain. It should be noted that there is a risk of NAFLD after follow-up of the GFD, it is therefore necessary to ensure a strict monitoring of the weight after follow-up of the GFD in order to avoid the overweight related to the correction of the intestinal absorption.

Celiac Disease and Virus Hepatitis

The treatment of C hepatitis by the old regimen: interferon and ribavirin resulted in reactivation of some latent CD [6]. Currently, this risk is zero with treatment with direct antivirals. Immunization after vaccination against B hepatitis is reduced during CD and corrected under GFD.

Advanced Liver Injury During Celiac Disease

It has been shown that the risk of developing hepatic cirrhosis is multiplied by 2.23 in celiac patients compared to non-celiac patients [6]. CD can be associated with different types of liver disorders so serological screening of CD should be made during the evaluation of patients with cirrhosis. The mortality rate from hepatic cirrhosis is high during CD compared to the general population [7]. In some studies, it has been reported that well followed GFD, in hepatic cirrhotic patients candidates for liver transplantation, allowed improvement of liver function with removal of patients from the waiting list.

Practical Recommendations

According to the 2019 recommendations of the European Society for the Study of Celiac Disease (ESsCD) [8], screening for CD is indicated for unexplained hypertransaminasemia, and liver assessment is recommended for newly diagnosed CD. The elevation of transaminases generally does not exceed five times the upper limit of normal. A significant elevation exceeding five times the upper limit of normal in a celiac patient requires etiological research. In the absence of liver enzyme normalization after a strict year of GFD, histological evaluation of liver injury should be performed [9]. Cryptogenic hypertransaminemia is asymptomatic.

In case of association with signs suggestive of chronic liver disease: jaundice, ascites, splenomegaly, signs of portal hypertension or liver failure, liver investigations should be performed for chronic liver disease associated with CD [9].

Conclusion

Liver abnormalities in celiac disease are dominated by celiac hepatitis which may be the only sign of celiac disease and with responds to the gluten free diet. More specific liver abnormalities may be associated with celiac disease with an uncertain response to the gluten-free diet. Hepatic cirrhosis is more common in the celiac population compared to the general population and the effect of the gluten-free diet seems beneficial.

Acknowledgement

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Conflict of Interest

No conflict of interest.

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