CLINICAL VIGNETTE

Liver Disease as a Consequence of Celiac Disease

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The patient is a 65-year-old Caucasian male who was followed at an outside facility for many years. He was told that he had stage 4 cirrhosis of unknown etiology. A liver biopsy was performed in 2004 and revealed ballooning of liver cells, eosinophils, inflammatory cells and slight portal fibrosis. No specific diagnosis was made. He sought consultation at the liver service at a large metropolitan hospital. Multiple serologies were obtained including an AMA, ANA, Hepatitis profile and hepatic panel. The serologies were all negative except for a slightly elevated ANA. He was not treated for autoimmune hepatitis and was never given steroids or azathioprine. 2003 labs included AST 103, ALT 293, alkaline phosphatase 53, GGT 35, Bili 0.75. An MRCP was normal. In October 2014 Prometheus Celiac panel, revealed deaminated gliadin peptide antibody IgG and IgA with a homozygous DQ2 genotype. Upper endoscopy and duodenal biopsy, revealed characteristic findings of Celiac Disease. He was a rare drinker and has never used illicit drugs or had exposure to toxins. He has followed a Gluten free diet since diagnosis was made and current hepatic panel is completely normal. Recent endoscopy revealed no varices and ultrasound showed echogenic changes consistent with cirrhosis with normal hepatopetal flow.

Celiac Disease or Gluten sensitive enteropathy was described in 1888 by Samuel Gee but has previously been described in the second century in Cappadocia (Modern Turkey). The cause of Celiac disease was first identified during World War II by Dr. William Dicke, a Dutch pediatrician. The Celiac duodenal lesion was described in 1954 as mucosal inflammation, crypt hyperplasia and villous atrophy. Treatment is lifetime avoidance of wheat, rye and barley and often gluten containing foods.

The incidence of Transaminitis and overt liver disease has been studied in Celiac Disease. Volta et al reviewed 600 patients with cryptogenic hypertransaminasaemia and found 55 patients with no discernible cause for their liver enzyme rise. Of these, five were positive for IgA immunofluorescence to endomysium and IgG to Gliadin. One patient was positive to IgG to Gliadin without antibodies to endomysium. All six antibody positive patients had duodenal biopsies consistent with Celiac Disease. None of these patients had any GI symptoms. Liver biopsies from five patients showed nonspecific reactive hepatitis. Transaminases reverted to normal after 6 months on a Gluten free diet. The conclusion was that about 9% of patients with cryptogenic hypertransaminasaemia had asymptomatic Celiac Disease.[1] Bardella et al evaluated 140 patients with chronic increases of serum transaminases of unknown cause and tested for anti-gliadin and antiendomysium IgA antibodies. Those with positive results were offered endoscopy and duodenal biopsies. Thirteen patients had positive antigliadin and anti-endomysial antibodies. Distal duodenal biopsies showed mild villous atrophy with increased intraepithelial lymphocytes in three biopsied cases; subtotal villous atrophy in six and total villous trophy in three. On that basis it was felt that screening for Celiac disease in patients with chronic unexplained hypertransaminasaemia was recommended.[2]

In 2002 Kaukinen reported occurrence of celiac disease in patients with severe liver failure. He described four patients with severe liver disease and untreated Celiac Disease. One had congenital liver fibrosis, one had massive hepatic steatosis, and two had progressive hepatitis without apparent cause. All had improvement in their liver disease on a Gluten free diet and all had duodenal biopsies that revealed small bowel villous atrophy with crypt hyperplasia consistent with Celiac disease.[3]

In 2007 Ludvigsson reported Celiac disease and Risk of Liver Disease in Swedish patients.[4] After eliminating patients with diabetes and other causes of liver disease they found a positive correlation between liver disease and Celiac disease, specifically with acute hepatitis, chronic hepatitis, primary sclerosing cholangitis (PSC), fatty liver, liver failure, liver fibrosis, and primary biliary cirrhosis (or cholangitis). The median duration from diagnosis of Celiac disease to the first recorded liver disease varied; Acute hepatitis, 6.7 years, PSC 10.8 years, Liver failure 7.4 years. The median age at first recorded liver disease was 54 for acute hepatitis, 66 years for PSC, and 57 years for liver failure. The study suggested that individuals with Celiac disease are at increased risk of prior and subsequent liver disease. There is increased risk of both acute and chronic hepatitis and a four-fold increase of subsequent PSC in Celiac Disease. Both Celiac Disease and PSC are immune mediated diseases. They postulate that the association between Celiac Disease and liver disease could be explained by shared autoimmunity. It is also known that a large proportion of those with Celiac Disease exhibit signs of low-grade bowel inflammation which may play a part in the increased mucosal permeability seen in active Celiac Disease. There is also prolonged transit time and an increase incidences of small intestinal bacterial overgrowth (SIBO). Aberrant lymphocyte homing mechanisms might be the key to understanding the association between Celiac Disease and liver diseases. Shared genetic predisposition between Celiac Disease and PSC may be mediated by the DQ-2 and DQ-8 genes.

In patients with celiac disease and in patients with elevation of liver enzymes investigation for the presence of Gluten enteropathy is recommended.

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