Extrahepatic causes of transaminase elevation are often overlooked when evaluating patients with chronic liver disease. A 54-year-old woman was referred for the management of chronic hepatitis B (HBV). Serologic testing showed a pattern of chronic hepatitis B infection with mild transaminase elevation. Further diagnostic testing suggested a pattern of quiescent HBV disease. Additional testing revealed no other explanation of the abnormal transaminase level and liver biopsy showed no significant pathologic change. She subsequently returned with malabsorption complaints and tested positive for celiac disease antibodies. Duodenal biopsies confirmed the presence of villous atrophy. The celiac disease was therefore the cause of the elevated transaminases concealed by the finding of a positive HBsAg. Elevated liver enzymes may be the only presenting sign of celiac disease; clinicians should include screening tests for celiac disease in the standard evaluation of patients with chronic liver disease as well as asymptomatic elevated liver enzymes.

**INTRODUCTION**

Celiac disease has long been associated with hepatic diseases including primary sclerosing cholangitis (1), primary biliary cirrhosis (2), hepatitis C (3), autoimmune hepatitis (4), and acute fatty liver (5). Its association with simple elevations in serum transaminases is much more common with prevalences of up to 54% in untreated cases (6,7). Hypertransaminasemia has also been reported as the presenting feature of otherwise asymptomatic celiac disease in several cases (8).

We report the case of celiac disease discovered in the evaluation of a patient with a positive HBsAg. This case emphasizes the importance of screening for celiac disease as a cause of hypertransaminasemia in asymptomatic individuals as well as those with chronic liver disease.
CASE REPORT
A 54-year-old Caucasian woman was referred for the management of suspected chronic HBV. She had been diagnosed with chronic HBV after presenting with mildly elevated transaminases found on routine evaluation. She reported no hepatitis risk factors or prior episodes of acute hepatitis. Medication history was equally unremarkable. Further complaints included rare loose stools and a bloating sensation but no obvious symptoms of malabsorption or weight loss. Past medical history was significant only for an unknown thyroid tumor necessitating thyroidecomy 30 years prior. Family history was significant for a sister with autoimmune vasculitis but no gastrointestinal or liver diseases.

Physical examination was unremarkable. There were no signs of chronic liver disease or nutritional deficiencies.

Laboratory data revealed an alanine transaminase (ALT) of 84 U/L (normal 30–65) and an aspartate transaminase (AST) of 58 U/L (normal 15–37). The bilirubin, albumin, alkaline phosphatase, hematocrit, and prothrombin time levels were within normal limits. The HBsAg and HBcAb were positive while the HBeAg was negative suggesting either an inactive carrier state versus active disease with an HBV precore mutant strain. HBV DNA by PCR was undetectable supporting the diagnosis of an inactive carrier state. Further testing for other chronic viral infection, autoimmune disease, hemochromatosis, Wilson's disease, and alpha-1-antitrypsin deficiency were all negative.

A liver biopsy was obtained due to the unexplained elevated liver enzymes which showed essentially normal findings. Specifically there was no substantial evidence of inflammation, fibrosis, or steatosis.

Subsequently the patient returned to clinic with complaints of worsening diarrhea and weight loss of 10 pounds over a two month period. At this time a malabsorption evaluation was pursued revealing 42 grams of fecal fat/day and positive titers for Ig-A antigliadin, antiendomysial, and tissue transglutaminase antibodies.

Enteroscopy with small bowel biopsy revealed severe villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis consistent with the diagnosis of celiac disease. The patient was subsequently started on a gluten-free diet with symptomatic improvement and normalization of the transaminases.

DISCUSSION
Celiac disease represents an important cause of elevated liver enzymes. While some patients present with the classic signs of diarrhea and malabsorption, many asymptomatic celiac cases may only present with hypertransaminasemia. Bardella, et al reported on 140 patients with unexplained elevations in transaminases and found 9.3% to be positive for IgA anti-endomysial and antigliadin antibodies (9). The prevalence of celiac disease greatly exceeds that of more commonly screened disorders such as Wilson's disease or alpha-1-antitrypsin deficiency yet is routinely ignored as a potential cause of asymptomatic elevations in liver enzymes.

The etiology of hypertransaminasemia in celiac disease is unclear. Proposed mechanisms include the relation of celiac disease to malnutrition and bacterial overgrowth however these seem to be only minor contributors (7). Liver enzyme abnormalities probably result due to increased intestinal permeability (10) and chronic intestinal inflammation (7). When the disease is treated with a gluten-free diet liver enzymes levels almost universally normalize within six months.

Liver biopsy of confirmed celiac patients with elevated liver enzymes is only recommended if there is persistent transaminase elevation despite several months of treatment with a gluten-free diet or if elevations in serum bilirubin are present (7,8). Liver test abnormalities in celiac disease generally include mild elevations in AST and ALT values with normal alkaline phosphatase and bilirubin levels. Liver biopsy findings are nonspecific and not helpful in the diagnosis or treatment of the disease (8,11). In our case the biopsy was performed for the confounding factor of HBsAg positivity coupled with elevated enzymes and undetectable HBV DNA.

We feel the association of HBV in this case was coincidental and effectively delayed the diagnosis of celiac disease. Celiac disease has been associated with primary biliary cirrhosis (2), primary sclerosing cholangitis (1), hepatitis C (3), autoimmune hepatitis (4), and fatty liver (5) but the association with HBV is less clear. Volta, et al found no increased prevalence of IgA antigliadin antibodies in 30 HBsAg positive

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# Celiac Disease

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patients (4). However in the Bardella series of 158 patients with small intestinal biopsy proven celiac disease, twice the normal prevalence of HBsAg was found although the authors admitted the association could merely be due to chance (7).

Given the importance of early treatment of celiac disease to prevent complications such as loss of bone mineral density, clinicians should be aware of celiac disease as a cause of elevated liver enzymes. Screening for celiac disease should be part of the evaluation of patients with known chronic liver disease as well as those with unexplained elevations in liver enzymes.

## References


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