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Opinion

Pathophysiological Insights into Cirrhosis and Portal Hypertension *via* the Gut Liver Axis

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ABOUT THE STUDY

Celiac Disease (CD) a chronic autoimmune disorder triggered by gluten ingestion in genetically predisposed individuals has long been recognized for its gastrointestinal manifestations. However, in the last two decades, the condition's systemic implications have received increasing attention particularly its association with other autoimmune disorders. Among these, the link between celiac disease and Autoimmune Liver Diseases (AILDs) presents a fascinating and clinically significant intersection that merits deeper exploration and awareness.

The liver often considered a silent organ until advanced dysfunction arises, can be affected by a spectrum of autoimmune conditions. These include Autoimmune Hepatitis (AIH), Primary Biliary Cholangitis (PBC), and Primary Sclerosing Cholangitis (PSC). Numerous studies have highlighted the increased prevalence of these conditions among individuals with celiac disease, suggesting shared immunological and genetic mechanisms. In my view, this association is not merely coincidental but reflective of a broader systemic autoimmune predisposition.

Shared immunogenetic pathways

A strong case can be made for the shared genetic background that underpins both CD and AILDs. Human Leukocyte Antigen (HLA) genotypes particularly HLA-DQ2 and HLA-DQ8 are central to the pathogenesis of celiac disease and are also implicated in autoimmune hepatitis. These genetic markers predispose individuals to aberrant antigen presentation, which may provoke a cascade of immune-mediated tissue damage in multiple organs, including the liver. This overlap in immune recognition and response mechanisms may explain why patients with celiac disease are at higher risk of developing hepatic autoimmunity.

Further, the gut-liver axis a bidirectional communication network between the gastrointestinal tract and liver provides another plausible explanation. Disruption of the intestinal barrier, a hallmark of active celiac disease, may allow translocation of microbial products and dietary antigens to the liver, triggering inflammatory responses and potentially initiating or exacerbating liver pathology. Therefore, the pathophysiology of these disorders is not only interconnected genetically but also anatomically and immunologically.

Clinical implications and diagnostic challenges

From a clinical perspective, recognizing the link between CD and autoimmune liver disorders is essential for timely diagnosis and management. In some cases, liver abnormalities such as elevated transaminases may be the first or only sign of celiac disease, especially in asymptomatic or atypical cases. This phenomenon, sometimes termed "celiac hepatitis," often resolves with adherence to a strict Gluten-Free Diet (GFD), underscoring the importance of considering CD in the differential diagnosis of unexplained liver enzyme elevations, particularly in children and young adults.

Conversely, in patients with known autoimmune liver disease, routine screening for celiac disease may be overlooked. Given the potential for malabsorption, nutrient deficiencies, and systemic complications, this oversight can have significant consequences. In my opinion, serological testing for CD such as Tissue Transglutaminase (tTG) IgA and endomysial antibodies should be incorporated into the workup of patients with AILDs, particularly when symptoms are non-specific or when there is a family history of autoimmune disease.

It is also crucial to differentiate between liver involvement directly attributable to celiac disease and coexisting autoimmune liver disorders. For example, while mild liver enzyme elevations may normalize with a GFD, persistent abnormalities or clinical signs of chronic liver disease warrant further evaluation for conditions like AIH, PBC, or PSC. Liver biopsy and autoimmune serology (e.g., ANA, SMA, AMA) remain essential tools in such assessments.

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Therapeutic considerations

The cornerstone of celiac disease management remains the lifelong exclusion of gluten from the diet. Interestingly, this intervention can have favorable effects on liver function as well. In cases of "celiac hepatitis," normalization of liver enzymes often occurs within 6–12 months of dietary adherence. This reinforces the importance of early identification of CD in patients with liver dysfunction.

However, the impact of a GFD on established autoimmune liver diseases is less clear. While some studies suggest modest improvements, most patients with AIH or PBC require immunosuppressive or specific pharmacologic therapy, regardless of gluten exposure. This distinction is important to prevent delays in appropriate treatment for liver disease under the assumption that a GFD alone will suffice.

Despite accumulating evidence, the association between celiac disease and autoimmune liver disorders remains under recognized in clinical practice. Greater awareness among healthcare professionals particularly gastroenterologists, hepatologists, and primary care physicians is needed to improve detection and management of this overlap.

Future research should aim to delineate the precise immunological mechanisms linking these diseases and explore whether early intervention in one condition can alter the course of the other. Additionally, longitudinal studies evaluating the long-term hepatic outcomes of CD patients on a strict GFD could provide valuable insights into the preventive potential of dietary therapy in autoimmune liver pathology.

CONCLUSION

In summary, the association between celiac disease and autoimmune liver disorders is more than an incidental finding it represents a meaningful convergence of immune-mediated pathology. Recognizing this relationship is critical for timely diagnosis, optimal treatment, and prevention of complications. As our understanding of systemic autoimmunity evolves, so too should our clinical approach, embracing a more integrative view of diseases that transcend organ boundaries. The gut and liver may be separate organs, but in the context of immune dysfunction, they are intimately connected.