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Opinion Article

A Review of Extrahepatic Manifestations in Chronic Hepatitis B and C Infections

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DESCRIPTION

When most clinicians think of chronic Hepatitis B (HBV) and Hepatitis C (HCV) infections, the focus tends to remain fixed on their hepatocellular consequences fibrosis, cirrhosis and hepatocellular carcinoma. However, as we deepen our understanding of viral hepatitis as a systemic disease, it is increasingly clear that the extrahepatic manifestations of HBV and HCV are not peripheral curiosities, but central clinical features with substantial impact on patient morbidity and quality of life. As a hepatologist practicing in a high-income healthcare environment, I am often struck by how underrecognized and undertreated these systemic complications remain, even in specialized settings. Despite widespread availability of diagnostic tools and antiviral therapies, many patients suffer years of misdiagnosis and mismanagement of symptoms that, if attributed early to chronic viral hepatitis, could have prompted curative or life-altering interventions.

Chronic hepatitis C is especially notorious for its immunologically driven extrahepatic manifestations. Up to 70% of patients with HCV may develop at least one such condition during the course of their illness. Chief among them is mixed cryoglobulinemia, a small-vessel vasculitis resulting from immune complex deposition. This condition can present subtly with fatigue, arthralgia, or purpura or more aggressively with renal involvement (membranoproliferative glomerulonephritis) and neuropathy. In many cases, patients may consult rheumatology or nephrology services multiple times before the underlying HCV is addressed as the root cause. Similarly, HCV has been strongly linked to B-cell non-Hodgkin lymphoma, particularly marginal zone lymphomas. In fact, in some cases, antiviral therapy alone can induce remission of the malignancy, highlighting the causative role of chronic viral stimulation. Other recognized associations include thyroid dysfunction, Sjogren's-like syndrome, porphyria cutanea tarda and lichen planus a wide array of conditions that span dermatology, endocrinology and neurology.

The eradication of HCV with Direct-Acting Antivirals (DAAs) has revolutionized care, offering not only hepatic benefits but also resolution of many extrahepatic symptoms. Yet, in high-income countries, where DAA availability is widespread, the medical community must be vigilant in using these therapies not just for liver disease prevention but for systemic symptom control and quality-of-life restoration. Chronic hepatitis B presents a different but equally significant extrahepatic profile. While less commonly associated with cryoglobulinemia, HBV has been implicated in PolyArteritis Nodosa (PAN) a necrotizing vasculitis of medium-sized arteries. Though rare in the post-antiviral era, PAN was historically a feared complication of HBV and still occasionally presents in endemic populations or in patients with poor viral control.

In addition, glomerulonephritis, particularly membranous nephropathy, has been linked to chronic HBV infection. In children, spontaneous resolution may occur; however, in adults, antiviral therapy plays a key role in halting disease progression. HBV has also been associated with neurological syndromes such as Guillain-Barre and mononeuritis multiplex, though causal relationships remain under investigation. The broader concern is that systemic manifestations are often siloed into their respective specialties, with little cross-disciplinary dialogue. A patient with HCV-related vasculitis may be seen by dermatology for years without referral to hepatology. Likewise, a patient with HBV and renal dysfunction may undergo extensive nephrologic workup without viral serologies being repeated or reassessed. This compartmentalization leads to diagnostic delays and therapeutic inertia.

In high-income countries with advanced health infrastructure, there is no excuse for this fragmentation. Electronic medical records, multidisciplinary case conferences, and patient registries should be leveraged to flag potential extrahepatic manifestations early. Clinician education across all specialties must emphasize that chronic hepatitis B and C are multisystem diseases, not just hepatocellular conditions. Another concern is post-cure complacency in HCV management. While DAAs effectively clear the virus, patients often remain at risk for persistent or irreversible extrahepatic sequelae, particularly if the diagnosis was delayed. Surveillance and long-term follow-up should not be discontinued simply because viral load is undetectable. Likewise,

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HBV suppression with nucleos(t)ide analogues may not fully reverse immune-mediated damage, requiring coordinated care plans even in virally controlled patients.

CONCLUSION

The extrahepatic manifestations of chronic hepatitis B and C infections are clinically significant, frequently overlooked and often treatable. In high-income settings, where diagnostic resources and antiviral therapies are readily available, there is a moral and clinical imperative to shift from a liver-centric to a patient-centric model of care. By improving interdisciplinary communication, investing in clinician education and incorporating extrahepatic screening into routine hepatitis care, we can radically improve outcomes for patients with chronic viral hepatitis. These infections are no longer incurable, but their full systemic burden must be acknowledged and addressed if we are to provide truly comprehensive care.