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Autoantibodies in Hepatitis C: Red Flag or Bystander Effect?

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Autoantibody reactivity is a common occurrence in liver diseases. As in other liver diseases, chronic hepatitis C is associated with the presence of various autoimmune markers and autoimmune disease. This autoantibody reactivity in turn may be a reflection of immune system activation. Molecular mimicry of viral antigens by self antigens, chronic stimulation of B cells, and a bystander effect are some proposed mechanisms for the development of autoimmune phenomena in hepatitis C.¹

The development of autoantibodies and autoimmune diseases is a recognized side effect of interferon therapy in adults.² However, it is unclear whether interferon unmasks previously unrecognized autoimmune disease or causes de novo autoimmune disease. Interestingly, some studies report an association between baseline autoantibody levels and HCV treatment response in adults.³

In this issue of JPGN, Molleston and colleagues analyzed autoantibodies in stored serum from the PEDS-C trial.⁴ Autoantibodies were present in 19% of the children at baseline, with a non-significant upward trend in prevalence over the course of treatment. These autoantibodies were not predictive of treatment outcome, treatment side effects, or ALT elevations during treatment.

Since the PEDS-C trial excluded children with evidence of preexisting autoimmune diseases, we cannot determine if interferon worsened pre-existing autoimmune disorders. However, the PEDS-C population was well suited for the assessment of de novo development of autoimmune disease. This occurred in 3 out of the 114 children, two of whom developed autoantibodies while on peginterferon.

The scant data that is available suggests the presence of a positive ANA in approximately 6–15% of healthy controls.⁵ This is comparable to the ANA positivity rate in the PEDS-C cohort prior to treatment.

The current study sheds light on an aspect of pediatric hepatitis C that has been largely unexplored until present. Molleston et al. were able to measure changes in autoantibodies over the course of HCV therapy in a well-characterized cohort of children. They determined that autoantibodies did not correlate with ALT, and probably are not mere markers of inflammation. They also did not find a relationship between autoantibodies and response to therapy, showing that the prognostic value reported in adults did not hold in this population.

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In addition, the authors determined the incidence of de novo autoimmune disease with HCV treatment.

Furthermore, these findings are particularly timely. With the advent of new directly-acting antivirals, the end of the interferon era may be imminent, making it less feasible to study the effect of exogenous interferon on autoantibody reactivity. Thus, the present study adds to our understanding at an opportune moment in pediatric hepatology.

For the practitioner, this article shows that if preexisting autoimmune disease has been excluded, one need not routinely check for autoantibodies during therapy in the absence of symptoms.

The findings reported in this issue of JPGN are a major contribution, and the area of autoimmunity in pediatric HCV is in its nascent stages. Additional data from large cohorts, advances in immunology, and improved autoantibody tests will enhance our understanding of chronic hepatitis C and its myriad manifestations.

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Abbreviations

HCV	hepatitis C virus
ALT	alanine aminotransferase
ANA	antinuclear antibody

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