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Autoantibodies to PCNA in HBV and HCV

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Eugen Feist,[Aff1]

Aff1 Charite-Humboldt Universitat, Berlin, Germany

Keywords

Anti-PCNA antibodies, HBV, HCV, SLE

Context

A humoral autoimmune response against proliferating cell nuclear antigen (PCNA) was described as specific for patients with systemic lupus erythematosus (SLE) with a prevalence of about 3% to 5%. The targeted antigen is preferentially expressed during late G1 and early S phase of the cell cycle and displays a variable localization, as reflected by its typical immunofluorescence pattern. Previously, PCNA was identified as the DNA polymerase-delta auxiliary protein.

Chronic human hepatitis virus infections, especially hepatitis C virus (HCV) and hepatitis B virus (HBV), are frequently associated with several rheumatic symptoms. Moreover, different autoantibodies are detectable during hepatitis infection, such as low titer antinuclear antibodies (ANA) and rheumatoid factor.

To investigate whether an anti-PCNA antibody response is associated with chronic HCV or HBV infections.

Significant findings

Anti-recombinant rat PCNA antibodies were detectable in 6.2% of patients with SLE as well as in 12.3% of patients with HBV and in 18.7% of patients with HCV. In contrast, no reactivity against recombinant rat PCNA was detectable in the other control groups. Furthermore, preincubation with PCNA was sufficient to inhibit the reactivity of positive sera in a dose dependent manner. Anti-PCNA antibodies were detectable by immunoblotting in 3.7% of patients with SLE as well as in 5% of patients with HBV and 10.8% of patients with HCV. Anti-PCNA antibodies from patients with SLE were exclusively an immunoglobulin G (IgG) isotype, whereas sera from patients with HCV and HBV revealed an additional anti-PCNA IgM- and IgA-isotype reactivity.

Indirect immunofluorescence on lymphocytes before and after phytohaemagglutinin (PHA) stimulation revealed an enhancement of a nuclear fluorescence pattern of sera from patients with chronic HBV and HCV infections.

Comments

This study makes the exciting observation that anti-PCNA antibodies are no longer specific for SLE, because they occur more frequently in patients with chronic HCV and HBV infections. However, there seem to be some conflicting points regarding the experiments. First, using a recombinant rat PCNA as the antigen all the analyzed patients groups (and healthy controls) revealed a high background reactivity by ELISA. Second, it was not shown whether a typical PCNA pattern was observed in chronic hepatitis infections using the Hep-2 cell line in indirect immunofluorescence as the usual detection assay for anti-PCNA antibodies. Nevertheless, the results of this study highlight the fact that chronic HCV or HBV infections may not only clinically mimic a rheumatic disease. Furthermore, this completes our understanding of induction and generation of autoantibodies in states of chronic virus infection as one potential factor for the induction of an autoimmune disorder.

Methods

The recombinant full-length rat PCNA was expressed in *E. coli* and served as antigen in ELISA and immunoblotting experiments. Additionally, lysates of Chinese hamster ovary K1 cells were analyzed in immunoblotting assays. Serum samples were obtained from 243 patients with a chronic HBV infection, 379 patients with a chronic HCV infection, 80 patients with SLE, 28 patients with rheumatoid arthritis (RA), 15 patients with primary Sjogrens syndrome (pSS), 8 patients with primary biliary cirrhosis (PBC) and 8 patients with an autoimmune myositis. Absorbtion experiments were performed by preincubating sera with different concentrations of purified recombinant rat PCNA. Indirect immunofluorescence experiments were performed using Hep-2 cells (no data) and human peripheral blood lymphocyte preparations.

References

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