Asymptomatic Autoantibodies Associate with Future Anti-glomerular Basement Membrane Disease

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ABSTRACT

The pathophysiology of anti-glomerular basement membrane (anti-GBM) disease before clinical presentation is unknown. The presence of anti-GBM, anti-protease 3 (PR3), and anti-myeloperoxidase (MPO) antibodies associate with the disease at the time of diagnosis, but little is known about the presence of these autoantibodies before diagnosis. We used serum samples from the Department of Defense Serum Repository to conduct a case-control study involving 30 patients diagnosed with anti-GBM disease and 30 healthy controls matched for the age, gender, race, and age of the serum samples. We analyzed a maximum of three samples from each subject: the most recent sample before diagnosis, the penultimate sample before diagnosis, and the oldest sample available; the average time between the most recent sample and diagnosis was 195 days (range, 4 to 1346 days). Elevated anti-GBM levels (>;0.3 U/ml) were present in four patients, all less than 1 year before diagnosis but in no controls. Detectable anti-GBM antibody levels (>;0.1 U/ml but <3 U/ml) in a single serum sample before diagnosis were more frequent in cases than controls (70% versus 17%, P < 0.001). Only study patients had detectable anti-GBM levels in multiple samples before diagnosis (50% versus 0%, P < 0.001). Almost all patients had detectable anti-PR3 and/or anti-MPO that preceded the onset of disease. Among patients with a clear antecedent antibody, anti-PR3 or anti-MPO always became detectable before the anti-GBM antibody. In summary, our data describe the subclinical formation of autoantibodies, which improves our understanding of the pathophysiology of anti-GBM disease.
Immune-Correlates Analysis of an HIV-1 Vaccine Efficacy Trial

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Abstract

BACKGROUND—In the RV144 trial, the estimated efficacy of a vaccine regimen against human immunodeficiency virus type 1 (HIV-1) was 31.2%. We performed a case–control analysis to identify antibody and cellular immune correlates of infection risk.

METHODS—In pilot studies conducted with RV144 blood samples, 17 antibody or cellular assays met prespecified criteria, of which 6 were chosen for primary analysis to determine the roles of T-cell, IgG antibody, and IgA antibody responses in the modulation of infection risk. Assays were performed on samples from 41 vaccinees who became infected and 205 uninfected vaccinees, obtained 2 weeks after final immunization, to evaluate whether immune-response variables predicted HIV-1 infection through 42 months of follow-up.

CONCLUSIONS—This immune-correlates study generated the hypotheses that V1V2 antibodies may have contributed to protection against HIV-1 infection, whereas high levels of Env-specific IgA antibodies may have mitigated the effects of protective antibodies. Vaccines that are designed to induce higher levels of V1V2 antibodies and lower levels of Env-specific IgA antibodies than are induced by the RV144 vaccine may have improved efficacy against HIV-1 infection.