Hepatitis B Virus (HBV) Coinfection Accelerates Immunologic Progression in Patients With Primary HIV Infection in an Area of Hyperendemicity for HBV Infection

To The Editor—We read with interest the article by Chun et al [1]. They demonstrated the negative impact of chronic hepatitis B virus (HBV) coinfection on HIV progression by increasing the risk for AIDS-defining illness and death (adjusted hazard ratio [aHR], 1.80; 95% confidence interval [CI], 1.20–2.69) among 2352 HIV-infected active duty military personnel and other beneficiaries in whom the HIV diagnosis seroconversion window was estimated at ≤3 years and the prevalence of chronic HBV infection was 3%. The negative impact, we believe, would be also observed by using immunologic progression as a study end point in patients with primary HIV infection in areas of higher endemicity for HBV infection.

Between January 1997 and December 2011, we conducted a prospective observational study in patients with primary HIV infection at 2 major medical centers for HIV care in Taiwan where HIV care, including combination antiretroviral therapy (cART) and HIV monitoring, is provided free of charge. In Taiwan, most HBV infections occurred in the perinatal period and childhood, and the prevalence of chronic HBV infection was 18%–20% among adults born before nationwide HBV vaccination was implemented in 1986 [2]. We identified patients aged ≥18 years who did not start antiretroviral treatment during the first 3 months after the diagnosis of primary HIV infection.

Primary HIV infection was defined as an interval of ≤6 months between negative and positive HIV serologic tests with enzyme-linked immunosorbent assay; an incomplete Western blot finding; or a negative HIV serologic test in the presence of HIV viremia demonstrated by real-time polymerase chain reaction (PCR). Immunologic progression was defined as the occurrence of a CD4 count <350 cells/μL ≥3 months after diagnosis of primary HIV infection.

We performed HIV-1 V3 genotyping testing to determine the HIV tropism of the HIV-1 strains in the study subjects [3]. In brief, viral RNA was extracted using the QIAamp Viral RNA Mini Kit (Qiagen). The purified RNA was subjected to 1-step reverse-transcription PCR. The partial HIV-1 env gene containing the V3 fragment was PCR amplified, sequenced, and analyzed. Population-based nucleotide sequence analysis of the PCR fragments was conducted by using an automatic sequencer (3100 Avent Genetic Analyzer; ABI). The geno2pheno
was used to determine the HIV-1 tropism. We identified clinical and virologic predictors of immunologic progression by using Kaplan-Meier curves and proportional hazards models.

During the 15-year study period, 143 eligible patients with primary HIV infection who had not started cART were included for analysis, including 15 (10.5%) with chronic HBV infection. During the study period, 84 patients (58.7%) experienced immunologic progression. In a Cox proportional hazards model, a lower baseline CD4 count (aHR, 1.55 per 100-cell/µL decrease; 95% CI, 1.26–1.90), infection with dual/mixed- or C-X-C chemokine receptor type 4 (CXCR4)-tropic virus (aHR, 2.90 compared with CCR5-tropic virus; 95% CI, 1.16–6.62) and HBV coinfection (aHR, 3.46; 95% CI, 1.16–10.32) were independent predictors of immunologic progression (Figure 1).

Our findings that HIV-infected patients with chronic HBV infection who presented with primary HIV infection had accelerated immunologic progression, compared with patients without chronic HBV infection, support the findings of Chun et al, in which the negative impact of chronic HBV infection on HIV progression had faster progression of hepatic fibrosis and a higher risk of cirrhosis, end-stage liver disease, and hepatocellular carcinoma than HBV-monoinfected patients [4, 5]. The findings of these studies [1, 4, 5] indeed provide a strong impetus to accelerate prevention and treatment efforts for HBV infection in HIV-infected populations in the era of cART, when long-term survival has become possible [6]. To minimize the influence of HBV infection, immunization of all susceptible individuals is a crucial step [7], and early initiation of cART including antiretroviral drugs active against both HIV and HBV should be recommended to prevent coinfected individuals from subsequent disease progression [8].

Notes

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Figure 1. Product-limit survival estimates with 95% confidence intervals of immunologic-progression-free survival according to the status of chronic hepatitis B virus (HBV) infection in HIV-infected patients with primary HIV infection who did not initiate combination antiretroviral therapy.

References


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