Absence of anti-hepatitis B virus (HBV) core in HIV/HBV coinfection with advanced immunosuppression

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Hepatitis B virus (HBV) coinfection is frequent among HIV-infected patients and is associated with poorer outcomes related to monoinfection with either virus [1]. These patients may present atypical HBV serological patterns, such as nonreactive anti-HBV core (HBc) with reactive HBV surface antigen (HBsAg) [2].

We investigated the prevalence of HBsAg with nonreactive anti-HBc in a cohort of HBV/HIV-coinfected patients from an AIDS Clinic in São Paulo, Brazil. The study population was selected from a cohort of 2412 HIV-positive patients, of whom 120 were HBsAg reactive. Cases were chronically HBV-infected patients with nonreactive anti-HBc, either transiently or persistently. Controls were obtained from the same population, but had persistently reactive anti-HBc and HBsAg-reactive patients matched by age and gender in a control:case ratio of 2:1.

HIV results were obtained using two commercial enzyme immunosorbent assays (Organon Technika, Tournault, Belgium and Embrabio, São Paulo, Brazil) and confirmed using GS-HIV-1 Western Blot (Bio-Rad, Hercules, CA). HIV RNA was quantified using the Versant HIV-1 RNA 3.0 bDNA assay (Siemens Healthcare, Erlangen, Germany). CD4 T-lymphocyte counts were determined using the BD Multitest/Trucount (BD Bioscienes, San Jose, CA). A multiparticle enzyme immunoassay (AxSYM; Abbott Laboratories, North Chicago, IL) was used to detect HBV serological markers.

HBV DNA was quantified using real-time polymerase chain reaction [3] and pre-core/core and surface gene sequences were obtained for mutation detection and subgenotyping in HBV DNA-positive cases [4].

For each patient, the mean CD4 count and viral load measurement for all measurements performed 12 months prior to each HBV serological test were calculated. Opportunistic diseases and complications of chronic HBV infection were also reported. The use of HBV-active drugs (lamivudine, tenofovir, entecavir or interferon) prior to the first serological test included in the study for cases and at any time for controls was evaluated. Variables were compared using the two-sided Wilcoxon rank-sum test (for continuous variables) or the two-sided Fisher’s exact test (for categorical variables) with STATA 10.1 (Stata Corporation, College Station, TX), and a significance level of 0.05.

We identified 120 (5.0%) chronically HBV-infected patients, 12 (10.0%) of whom presented with nonreactive anti-HBc. A significantly higher proportion of cases were persistently positive for HBeAg, and cases had a lower mean CD4 count compared with controls (Table 1). Amplification of HBV DNA was achieved in three out of seven cases who were available for collection of a new sample, with a mean viral load of 5.67 log HBV DNA copies/mL. HBV subgenotype A1 was detected in all three cases. No mutations in pre-core/core and S gene sequences were identified.

In conclusion, this study revealed that anti-HBc nonreactivity occurred in 10% of HBV/HIV-coinfected patients. This finding reinforces the conclusion that isolated anti-HBc should not be used as a single screening test to detect HBV infection, as already discussed in a recent report [5]. Variables associated with anti-HBc nonreactivity were persistent HBeAg positivity and lower mean CD4 count. HBeAg positivity is related to HBV replication, and is probably associated with deficient control of the immune reaction against HBV in HBV/HIV coinfection. A lower mean CD4 count was also significantly associated with anti-HBc nonreactivity, supporting the conclusion that the host’s immunosuppression, rather than HBV mutation, is
related to the frequent finding of this pattern in HIV/HBV coinfection.

References


