Lack of anti-hepatitis B core antibodies in patients infected with hepatitis B virus

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Background and aims

Diagnosis of hepatitis B virus (HBV) on-going infection is based on the detection of HB surface antigen (HBsAg) and anti-HB core antibodies (anti-HBcAb) in the serum. Anti-HBcAb presence indicates HBV exposure and therefore past or on-going infection. They are known very robust serological markers with, usually, life-long persistence in case of hepatitis B. From 1920 to 1983 we diagnosed HBV chronic infection in five patients lacking detectable anti-HBcAb. We analysed here the epidemiological, clinical and virological features of these infections.

Patients and Methods

Routine HBV testing was performed between 06/2013 and 01/2017 (43 months) in Marseille university hospitals, southeastern France. HBV serologies were performed using Architect Abbott assays. HBsAg-positivity was confirmed by seroneutralisation. Serum HBV DNA detection/quantification was performed using the RealTime HBV viral load Abbott assay or the VERIS/Mdx System HBV assay. Direct population sequencing of the HBsAg/reverse transcriptase (RT) coding-region and the pre-core/core region of the HBV genome were performed using in-house protocols. HBV sequences were analysed using the geno2pheno HBV tool, sequence comparisons and phylogenic analysis.

Results

We observed this lack of anti-HBcAb in five HBV-chronically-infected patients out of 65,910 patients in whom a HBV serology was performed. This serological profile was observed in 0.56% of the 889 patients diagnosed as HBsAg-positive. These five patients had an age mean of 55±15 years, and 4 (80%) were male. Three patients were HIV-infected, with a low CD4 cell count, below 200/mm3. Two of them were HIV-Hepatitis C virus co-infected. Mean alanine aminotransferase level was 32±25 IU/L, liver cytolysis being only found in one case. HBV replication was quantified in three cases, HBV DNA load being above 2 log10 IU/mL. HBV genotype was D3 in two cases, A2 and B2 in one case each, and unknown in one case due to the absence of detectable HBV DNA. Core gene sequences (799-nucleotide-long) did not show particular deletion or insertion.

Conclusion

Even if this HBV serological profile is rare, it could appear in few patients, particularly in immunocompromised. This has to be considered because it may impair chronic HBV infection diagnosis in absence of HBsAg testing.

References


Table 1. Epidemiological, clinical and virological features of patients chronically-infected with HBV and anti-HBc-negative

Fig1. Phylogenetic tree based on the hepatitis B surface antigen/reverse transcriptase (Fig 1.a) and pre-core/core (Fig 1.b) encoding regions of the hepatitis B virus genome. The HBV sequences obtained from cases diagnosed in our laboratory are indicated in a dark blue font. The sequences with the highest BLAST score recovered from the NCBI GenBank nucleotide sequence database (http://www.ncbi.nlm.nih.gov/genbank/) are indicated by a light blue font and were incorporated in the phylogeny reconstruction. In addition to reference sequences for HBV genotypes, nucleotide alignments were performed using the MUSCLE software (http://www.ebi.ac.uk/Tools/muscle/index.html). The evolutionary history was inferred in the MEGA6 software (http://www.megasoftware.net) using the neighbour-joining method and the Kimura 2-parameter method. The percentage of replicate trees in which the associated taxa clustered together in the bootstrap test (100 replicates) is shown next to the branches. The tree is drawn to scale, branch lengths in the same units as those of the evolutionary distances used to infer the phylogenetic tree; the scale bars indicate the number of nucleotide substitutions per site. Bootstrap values >50% are shown on the branch.