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Occult hepatitis B virus infection: clearance or disguise?

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Occult hepatitis B virus (HBV) infection is defined as presence of HBV DNA in the liver regardless of serum HBV DNA detectability in HBsAg-negative patients.[1] Occult HBV infection is not uncommon in Korea because the prevalence of occult HBV infection depends on the HBsAg carrier rate.[2] The underlying mechanisms for occult HBV infection is not fully understood yet, but both viral and host factors are suggested to contribute to the suppressed viral replication / secretion status.[2,3]

In this issue, Kim et al reported the pattern of HBs gene mutation in Korean patients with occult HBV infection.[4] In this study, HBV S gene was PCR-amplified and sequenced from serum and/or tissue samples of chronic hepatitis B patients who lost serum HBsAg during follow-up. As a result, various patterns of mutation(s) have been identified in the major hydrophilic region of HBs protein. Quite unexpectedly, 12 out of 19 patients had HBs gene sequence similar to serotype ayw (genotype D), an unusual strain in Korea. The authors suggested two probabilities, i.e., ayw subtype being more prone to HBsAg clearance,or immune selection of HBV mutants resulting in subtype change to ayw. Considering absence of ayw in HBsAg-positive controls in this study and other reports on Korean patients,[5] it is unlikely that ayw serotype comprises significant portion of wild HBV strains in Korea. Shift of serotype from ayr (genotype C) to ayw in patient 2 also supports alternative hypothesis that immune selection favors certain type of mutants. Moreover, substitutions of particular amino acid were shown to be associated with decreased antibody reactivity by conventional ELISA. Taken together, it can be speculated that increasing levels of host immunity poses selective pressure during the natural course of chronic HBV infection. Consequently, mutants with low HBs protein antigenicity, either due to suppressed extracellular secretion or conversion to antibody-escape mutant, may selectively replicate in hepatocytes, presumably with suppressed replicative activity compared to wild type. This hypothesis is in line with previous reports that mutations in the "a" determinantare associated with inability of some but not all commercial assays to detectHBsAg.[3,6] If this is the case, assays using polyclonal antibodies would be needed for the reliable diagnosis of "a" determinant mutants.[6] At any rate, the bottom line is that HBsAg clearance by conventional method may be associated with diverse viral replication mechanisms. Thus, further studies are warranted to validate the findings of Kim's work in larger study population.

Abbreviations:

HBV, hepatitis B virus; ELISA, enzyme-linked immunosorbent assay

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Conflicts of Interest

The authors have no conflicts to disclose.

REFERENCES

1. Raimondo G, Allain JP, Brunetto MR, Buendia MA, Chen DS, Colombo M, et al. Statements from the Taormina expert meeting on occult hepatitis B virus infection. J Hepatol 2008;49:652-657.
2. Kim YS. Definition, diagnosis, and prevalence of occult hepatitis B virus infection. Korean J Gastroenterol 2013;62:143-147.
3. de la Fuente RA, Gutierrez ML, Garcia-Samaniego J, Fernandez-Rodriguez C, Lledo JL, Castellano G. Pathogenesis of occult chronic hepatitis B virus infection. World J Gastroenterol 2011;17:1543-1548.
4. Kim K-H, Chang H-Y, Park JY, Park E-S, Park YK, Han K-H, et al. Spontaneous HBsAg loss in Korean patients: relevance of viral genotypes, S gene mutations, and cccDNA copy numbers. Clin Mol Hepatol 2014;20:251-260.
5. Kim H, Jee YM, Song BC, Shin JW, Yang SH, Mun HS, et al. Molecular epidemiology of hepatitis B virus (HBV) genotypes and serotypes in patients with chronic HBV infection in Korea. Intervirology 2007;50:52-57.
6. Samal J, Kandpal M, Vivekanandan P. Molecular mechanisms underlying occult hepatitis B virus infection. Clin Microbiol Rev 2012;25:142-163.

http://dx.doi.org/10.3350/cmh.2014.20.3.249