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Virological Characteristics of Hepatitis B Genotype G/A2 Recombination Virus in Japan

ABSTRACT

Aim: We identified four cases of infection with hepatitis B virus genotype G and A2 recombinant (HBV/G/A2) strains, which were initially overlooked by enzyme immunoassay-based genotyping. The patients were all men who have sex with men (MSM) and inhabited several metropolitan areas of Japan, suggesting the recombinant strains might be circulating among high-risk groups such as MSM. Here, we investigated the genomic structure and virological properties of the HBV/G/A2 strains.

Methods: Complete genome sequences of the isolates were determined and phylogenetically analyzed (Tanaka Y et al., Hepatology 2007 & Virology 2008). Replication efficiency of HBV/G/A2 was investigated by transfecting plasmids containing 1.24-fold viral genome (Sugiyama M et al., Hepatology 2006). The *in vivo* viral kinetics of HBV/G/A2 were investigated using chimeric mice with humanized livers (Tanaka Y et al., Hepatology 2007 & Virology 2008).

Results: Phylogenetic analysis revealed that the four strains were almost identical (>99.7% homologous). The preS2/S region of these strains was highly homologous to that of genotype A2 and the remaining region was almost identical to that of genotype G, reflecting inter-genotypic recombination. Interestingly, in all four cases, genotype A was co-infected as a minor population. *In vitro* analysis revealed that HBV/G/A2 had a low replication rate. Although detectable viremia was not measurable following the inoculation of HBV/G/A2 into chimeric mice, subsequent superinfection of HBV genotype A greatly enhanced HBV/G/A2 replication and viral spread.

Conclusions: We found that four cases of HBV/G/A2 recombinant among MSM

patients in the metropolitan areas of Japan, and HBV/A co-infections are required for its efficient replication. High-risk groups such as MSM should be carefully tested for infection of genotype G-derived variants.