

P0504 HBsAg mutations related to occult hepatitis B virus infection in HIV-positive patients resulted in a reduced secretion of HBsAg

Seyed Mohammad Jazayeri*¹, Ahmadreza Sadeghi¹, Frank Tacke², Mino Mohraz¹, Vahdat Poortahmasebi¹, Mansour Poorebrahim¹

¹Tehran University of Medical Science, Tehran, Iran, ²University Hospital Aachen

Background: Occult hepatitis B infection (OBI) is a frequent finding in human immunodeficiency virus (HIV)-infected patients. The aims of this study were to find out the prevalence of OBI in HIV-1 patients and to analyze mutational patterns in OBI-positive subjects and investigate the distinct impact of mutations on HBsAg synthesis.

Materials/methods: 172 HBsAg-negative, HIV-1-positive patients were selected. HBV serologic and molecular assays were performed. After direct sequencing analysis, a series of expression constructs of variant HBsAg with “a” determinant amino acid substitutions was generated using site-directed mutagenesis. The expression of variant HBsAg was examined by transient transfection in hepatoma cells, followed by HBsAg immunoassay and immunofluorescence stained with specific anti-HBs antibodies.

Results: Thirty-one samples (18%) were OBI positive. Among 24 available OBI-positive samples, 17 (71%) contained at least one mutation only within the ‘a’ determinant region of HBsAg. A stretch of mutations was found between amino acid positions 121 and 136. All variants comprising either single or combined mutations resulted in significantly reduced HBsAg detection in supernatants and in cell lysates. Intracellular immunofluorescence staining of cytoblocks showed perinuclear and cytoplasmic fluorescence of HBsAg constructs with significantly diminished fluorescent intensity in comparison to the wild type.

Conclusions: Mutations in the “a” determinant region of HBV as often found in OBI remarkably impair the detection of HBsAg from serum and infected cells. HBV serologic assays are not reliable markers to exclude occult HBV infection in HIV-positive patients, emphasizing the relevance of alternative methods such as HBV-DNA quantification for HIV-infected individuals.