

Session: P039 Viral hepatitis

Category: 1b. Viral hepatitis (incl antiviral drugs, treatment & susceptibility/resistance, diagnostics & epidemiology)

23 April 2017, 13:30 - 14:30
P0847

HBsAg mutations related to occult hepatitis B infection in HIV-1 patients result in a reduce secretion and conformational changes of HBsAg

Seyed Mohammad Jazayeri¹, Ahmad Reza Sadeghi², Frank Tacke³, Minoo Mohraz⁴, Seyed Moayed Alavian⁵, Vahdat Poortahmasebi², Elham Shirvani Dastgerdi⁶, Mansour Poorebrahim⁷

¹*Tehran University of Medical Sciences; Virology*

²*Hepatitis B Molecular Laboratory, Department of Virology, School of Public Health; Tehran University of Medical Sciences*

³*Universitätsklinikum Aachen*

⁴*Iranian Research Center for Hiv/Aids*

⁵*Middle East Liver Disease (Meld) Center*

⁶*Medical Klinik III, Universityhospital Aachen (Rwth)*

⁷*Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences*

Background: Occult hepatitis B infection (OBI) is a frequent finding among human immunodeficiency virus (HIV) infected patients. While several related mutations in the HBV genome have been reported, their distinct impact on HBsAg synthesis is largely obscure.

Material/methods: 31 (18%) out of 172 HIV-infected patients who selected from HBsAg negative patients, were positive for HBV-DNA assigned as being OBI-positive. We generated a series of expression constructs of variant HBsAg with “a” determinant amino acid substitutions at single and combined positions (P127L, P127T, S136Y and P127T + S136Y) using site-directed mutagenesis. The expression of variant HBsAg was examined by transient transfection in hepatoma cells, followed by HBsAg immunoassay and immunofluorescence staining with specific anti-HBs antibodies. The

potential impact of amino acid substitutions at different positions for conformational changes in the HBsAg was investigated using bioinformatics.

Results: All variants comprising either single or combined mutations resulted in significantly reduced HBsAg protein detection in supernatants and in cell lysates of hepatoma cells transfected with the constructs. Moreover, intracellular immunofluorescence staining of cytoblocks showed perinuclear and cytoplasmic fluorescence of HBsAg constructs with significantly diminished fluorescent intensity in comparison to wild. Altered protein conformations by predictive models, indicating an impaired detection by the host's immune response as well as by commercial antibody-based test assays

Conclusions: Mutations in the "a" determinant region of HBV as oftentimes found in OBI remarkably impair the detection of HBsAg from serum and infected cells, emphasizing the relevance of alternative methods such as HBV-DNA quantification for high-risk groups like HIV-infected individuals.