INTRAHEPATIC CXCR3 AND CXCL10 ARE ASSOCIATED WITH LIVER DISEASE IN HIV-HBV CO-INFECTION

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Background: HIV infection significantly alters the natural history of chronic hepatitis B (HBV). Compared to HBV mono-infection, HIV-HBV infected individuals experience accelerated progression of liver disease and increased liver-related mortality that persists on HBV-active antiretroviral therapy (ART). We investigated the hypothesis that increased microbial translocation (MT) and chronic immune activation (IA) secondary to HIV infection was a driver forliver fibrosis in HIV-HBV co-infected individuals.

Methods: Liver biopsies and plasma were collected from a HIV-HBV coinfected individuals (n=37) naïve to ART. Liver fibrosis was assessed using transient elastrography (TE) and liver biopsy. Lipopolysaccharide (LPS), soluble (s) CD14, CCL2 andCXCL10 were measured in plasma. Liver biopsies were analysed by immunohistochemistry (IHC) for HIV RNA and CXCL10 and qPCR for CXCL10 with its receptor CXCR3, interferons α, β and γ.

Results: The cohort was young, predominantly male, HBeAg positive with median CD4+ T cell count of 360 (210-470) cells/microL. Liver disease at baseline was mild with >80% classified as $\leq$2 by TE. HIV RNA was detected in liver but was infrequent and largely localized to T-cells. Intrahepatic CXCR3 and CXCL10 were strongly correlated and significantly associated with histological and TE measures of liver fibrosis and ALT, AST and GGT (Spearman rho 0.3-0.61). AST was significantly associated with all plasma markers except plasma LPS and IFN-γ. Plasma LPS and sCD14 were not associated with liver fibrosis.

Conclusion: Markers of MT were not associated with liver disease in HIV- HBV co-infected individuals. However, CXCR3 and CXCL10 were significantly associated with fibrosis and liver enzyme elevation consistent with infiltration of CXCR3+ cells such as activated T-cells driving liver disease. CXCR3 and CXCL10 should be investigated as novel targets to minimize liver disease in HIV-HBV co-infection