11 patients survived spontaneously (PALF-S) and nine died or required liver transplantation (PALF-NS). PALF-NS had higher peak INR (13.9 vs 7.4, p<0.001), SOFA score (13 vs 6, p<0.001), MELD (46 vs 35, p<0.05) and APACHE II score (20 vs 6.5, p<0.001). There were no differences in the total monocyte counts between PALF-NS and PALF-S (0.2 vs 0.43 X10 000 cells/dl). However, a significant reduction in the proportion of CD14lo/CD16hi MØ was observed in PALF-NS compared to PALF-S (0.5% vs 2.7%, p=0.01) and this was predictive of outcome (AUROC 0.838; values greater than 2% giving a sensitivity of 81%, specificity 89% for survival with medical management).

Conclusion These are the first reported data defining the relative proportions of MØ subsets in PALF. They show that the proportion of CD14lo/CD16hi MØ is significantly reduced in PALF, the degree of which is predictive for outcome. This reduction may be due to early sequestration of these MØ within the liver or other organs through CCR2 independent pathways.

OP23 BACTERIAL TRANSLOCATION AND REGULATORY T LYMPHOCYTES IN PATIENTS WITH LIVER CIRRHOSIS

doi:10.1136/gut.2010.223362.23

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Introduction Increased prevalence of bacterial infectious diseases has been observed in cirrhotic patients, classically attributed to immunosuppression-associated liver cirrhosis. Conversely, advanced states of liver cirrhosis predispose to increased antigenic load. A possible role has been ascribed to the translocation of bacteria and endotoxins (lypopolysaccharide, LPS) from the gut. LPS increases the plasma levels of LPS-binding protein (LBP), the principal plasma protein responsible for transporting LPS to immune effector cells. High serum LBP has been proposed to identify a subset of cirrhotic patients with ascitis characterised by an activation of the immune cells to producer proinflammatory cytokines. Moreover, raised levels of circulating LBP or proinflammatory cytokines have been implicated in the endothelial activation and haemodynamic derangement observed in cirrhosis. A chronic antigenic stimulus will induce a monocyte and lymphocyte activation.

Aim Intestinal permeability and bacterial translocation and their influence on T lymphocytes activation and differentiation in T reg were analysed in patients with compensated and decompensated liver cirrhosis. In particular, the regulation of T cell activation, mediated by co-stimulatory molecules, the expression of activation markers and the proportion of T CD4+ regulatory cells, as a function of bacterial translocation, were studied.

Method 40 patients with liver cirrhosis, 20 of them without previous decompensation (CC) and 20 with ascetic decompensation (DC), and 20 healthy controls (HC) were studied. Bacterial translocation was analysed by serum concentrations of lypopolysacharide-binding protein (LBP). Membrane expression of co-stimulatory molecules (CD28), activation markers (CD25 and CD122) and proportion of T regulatory cells (defined as those CD4+CD25highintracellular FoxP3+) were studied by flow cytometry with specific antibodies. Values of the variables were expressed as median (interquartile range). Comparisons between variables were made by the Mann–Whitney U test. Associations between variables were analysed by the Pearson's correlation coefficient.

Results Serum concentrations of LBP were significantly elevated in patients with compensated (7.7 (5.7–9.1 microg/ml) and decompensated (28.2 (10.7–40.6)) cirrhosis when compared with healthy controls (3.4 (2.7–4.2)) (p<0.001). Significantly higher concentrations of LBP were detected in those patients with higher portal hypertension. Those patients with decompensated cirrhosis shows an activation state characterised by increased percentages of CD25+ and CD122+ expression on CD4+ T cells. A decrease of CD28 expression was detected in T CD4+ lymphocytes from patients with decompensated cirrhosis (DC, 94% (89–98%); CC, 97% (92–98%); HC, 98 (96–99), DC vs HC: p=0.010). Moreover, T reg lymphocytes, expressed as a proportion of global T CD4+ cells, were significantly increased in patients with compensated and decompensated cirrhosis (DC, 14.7% (13.3–16.1%); CC, 10.3 (10.1–11.2); HC, 8.4 (7.2–8.7), p<0.001 in each case). A significant and positive correlation was detected between serum LBP concentration and percentage of CD4+ T reg (r=0.787, p<0.001).

Conclusion Patients with liver cirrhosis, fundamentally those with previous decompensation, shows increased intestinal permeability and chronic systemic antigenic stimuli. As a response to those, T lymphocyte activation is detected. Probably as a mean to decrease the continuous antigenic stimuli, a diminution of co-stimulation and an expansion of suppressor populations are observed in them.

Viral hepatitis

OP24 VASCULAR ENDOTHELIAL GROWTH FACTOR ACTIVATION OF LIVER SINUSOIDAL ENDOTHELIAL CELLS VIA VASCULAR ENDOTHELIAL GROWTH FACTOR RECEPTOR-2 REGULATES HEPATOCELLULAR HEPATITIS C VIRUS REPLICATION

doi:10.1136/gut.2010.223362.24

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Introduction Hepatitis C virus (HCV) is a major concern for human health, with an estimated 180 million people infected worldwide. HCV primarily infects hepatocytes in the liver and the majority of infected subjects develop progressive liver disease. Treatment options remain limited and hence, there is an urgent need for new therapies that target viral and host cell pathways. Vascular endothelial growth factor (VEGF) is a multifunctional cytokine that is produced by a variety of cell types in response to low oxygen and viral infections. VEGF targets vascular endothelial cells that are present in many tissues, including liver sinusoidal endothelial cells (LSEC). LSEC are in close apposition to hepatocytes in the liver and VEGF is known to regulate LSEC proliferation and function.

Aim We recently demonstrated that HCV promotes VEGF expression in hepatocytes (Mee et al, 2010 *Gastroenterology*) and the aim of this study was to investigate the role of VEGF in LSEC-hepatocyte interactions in HCV infection.

Method Using primary human LSEC we established direct LSEC-hepatocyte co-culture models to recapitulate the hepatic microenvironment. The effects of VEGF on LSEC and hepatocytes were analysed in both monoculture and co-culture.

Results Initial studies demonstrated that LSEC do not express the full complement of HCV receptors or entry factors and fail to support HCV replication. However, in vitro co-culture of LSEC and hepatocytes to model the hepatic epithelial-endothelial cell environment demonstrated that LSEC significantly reduce the permissivity of hepatocytes to support HCV replication. Interestingly, this effect was abrogated by inclusion of a neutralising antibody or a drug antagonist targeting VEGF receptor-2 (VEGFR-2). Importantly, recombinant VEGF had no effect on HCV replication in hepatocyte monocultures, suggesting that VEGF stimulates endothelial cells to modulate expression of molecules