jaundice to encephalopathy (<7 days), 8 Subacute/Acute Liver Failure (S/ALF: jaundice to encephalopathy >7 days), and 18 healthy controls (HC). Flow cytometry was performed to investigate monocyte phenotype (CD14, CD16, HLA-DR, CD54, CD163, CD11b and CCR5).

**Results** Compared to HC, total monocyte count was elevated in S/ALF, but reduced in hyperALF (<0.001), while CD14hi/CD16+ monocytes were expanded in percentage of total monocytes and absolute numbers in S/ALF (17.4%; 0.14) compared to HC (4%; 0.014) (<0.001). Although the percentage of CD14hi/CD16+ monocytes in hyperALF was higher (5.6%; <0.01), the absolute number (0.013) was similar to HC. Though all CD14hi/CD16+ monocytes expressed HLA-DR, the Mean Fluorescence Intensity (MFI) was reduced compared to HC (<0.001). HyperALF CD14hi/CD16+ monocytes had lower HLA-DR MFI compared to S/ALF (<0.001). A similar pattern was seen for CD86 expression (<0.01). CD14hi/CD16+ monocytes showed increased expression of CD163 in hyperALF but not in S/ALF compared to HC (<0.01). Compared to HC, CD11b and CCR5 were up-regulated in all ALF groups (<0.001).

**Conclusion** We have demonstrated an expansion of CD14hi/CD16+ monocytes in ALF with an activated phenotype for adhesion and migration. CD14hi/CD16+ macrophages in S/ALF possibly reflecting a pathogenic role in the perpetuation of liver injury, while they resemble M2 in hyperALF and may be instrumental to the resolution of liver injury. This distinction requires further investigation should therapeutic strategies to target monocyte migration be attempted.

**Competing interests** None declared.

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**Abstract PTU-016**

**ALBUMIN RESTORES RENAL BLOOD FLOW (RBF) AUTOREGULATION IN PATIENTS WITH REFRACTORY ASCITES AND ACUTE-ON-CHRONIC LIVER FAILURE (ACLF) THROUGH STABILISATION OF ENDOTHELIAL FUNCTION**

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**Introduction** Haemodynamic alterations in liver failure are associated with endothelial dysfunction, a pro-inflammatory state and sympathetic activation which lead to disturbed RBF autoregulation and renal failure. Albumin is a multifunctional protein that has been shown in several studies to prevent and treat renal dysfunction in patients with advanced cirrhosis and liver failure. We hypothesised that the beneficial effects of albumin in cirrhosis is likely to be through mechanisms in addition to volume expansion. The aims of the study were to investigate the effects of albumin on systemic and renal haemodynamics, inflammation and endothelial dysfunction in refractory ascites and patients with acute kidney injury (AKI) in the setting of ACLF.

**Methods** Twenty-two patients were recruited [Group 1, n=12, refractory ascites; Group 2, n=10 patients with AKI admitted with an acute deterioration of their liver function due to either alcoholic refractory ascites; Group 2, n=10 patients with AKI admitted with an acute deterioration of their liver function due to either alcoholic refractory ascites]. Both groups were treated with Albumin 60 g/d over 3–4 days. cardiac output (CO) and renal blood flow (RBF) haemodynamics were measured. Endothelial dysfunction was assessed through measurement of von Willebrand factor (vWF) and serum nitrite (NO) levels. F2α isoprostanes (F2α), resting neutrophil burst and Interleukin (IL)-6 were quantified as markers of oxidative stress, endothoxemia and inflammation respectively.

**Results** Albumin therapy was associated with significant improvements in haemodynamic parameters (increased RBF, MAP, decreased CO, HR; p<0.05) which resulted in a shift in the RBF autoregulation curve towards normalisation (Abstract PTU-016 figure 1). In parallel, improvement of renal dysfunction (creatinine, creatinine clearance and Na+ excretion; p<0.05 each), sympathetic activation (noradrenaline levels; p<0.01), inflammation/oxidative stress (F2α and neutrophil burst; p<0.05), endothelial dysfunction (vWF and NO metabolism p<0.05) and the functional capacity of albumin (IMAR p<0.005) was observed. Restoration of RBF correlated inversely with change in vWF (r²=0.55, p<0.001).

**Conclusion** This study suggests that albumin infusion improves albumin function which has pleiotropic effects and results in a reduction in inflammation and improvement in endothelial function leading to improved systemic haemodynamics and renal blood flow autoregulation.

**Competing interests** None declared.
NHS was undertaken on archived liver tissue specimens. Three chemical analysis via application of a monoclonal antibody to IgG4 without pancreatitis or sclerosing cholangitis. Immuno-histo-ve plasma cells are observed in a cohort of patients with AIH.

We set out to establish the frequency with which IgG4 was noted did the proportion of IgG4 +ve plasma cells equate to none of the seven cases in which 10 IgG4 +ve plasma cells/HPF in no individual did this represent >40% of the total hepatic plasma cell infiltrate. Consequently, significant IgG4 +ve plasma cell infiltrates are not observed among non-Asian patients with AIH presenting to our institution.

Competing interests None declared.

RESULTS

Sixty-three liver tissue specimens underwent immunohistochemical analysis. These specimens derived from 53 Caucasian and 10 Afro-Caribbean patients. All patients met the revised International Autoimmune Hepatitis Group diagnostic criteria for probable or definite AIH. The median age of patients at diagnosis was 31 years and 78% were female. Among this cohort 44 patients presented with chronic disease and histological evidence of chronic active hepatitis while 19 presented with acute disease in whom histology demonstrated hepatic collapse in 16 and severe lobular hepatitis in three patients. Only 7 of 65 samples (11%) demonstrated >10 IgG4 +ve cells/HPF. While there was a greater number of biopsy specimens with >10 IgG4 +ve plasma cells/HPF in acute vs chronic presentations this did not reach statistical significance (16% vs 9%, p=0.44). Additionally, there was no difference in the frequency of this finding between males and females (males 21% females 8% p=0.4) or between different ethnic groups (11% in Caucasians vs 10% in Afro-Caribbeans, p=0.99).

Importantly, in none of the seven cases in which >10 IgG4 +ve plasma cells/HPF were noted did the proportion of IgG4 +ve plasma cells equate to >40% of the total plasma cell infiltrate.

Conclusion While a small proportion of non-Asian AIH patients demonstrate >10 IgG4 +ve plasma cells/HPF in no individual did this represent >40% of the total hepatic plasma cell infiltrate. Consequently, significant IgG4 +ve plasma cell infiltrates are not observed among non-Asian patients with AIH presenting to our institution.

Competing interests None declared.

REFERENCES


Abstract PTU-016a Figure 1

Conclusion It appears that there are a number of functional defects in circulating monocytes in patients with AH. The marked impairment of phagocytosis and intracellular killing may contribute to the increased susceptibility to infection in this group of patients.

Competing interests None declared.

General Liver

PTU-017 IGG4 +VE AUTOIMMUNE HEPATITIS IS NOT OBSERVED AMONG PATIENTS OF NON-ASIAN ORIGIN

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Introduction IgG4 mediated autoimmune disease has recently been described in relation to pancreatitis and sclerosing cholangitis. Furthermore recent reports, mainly from Japan, have also identified cases of autoimmune hepatitis (AIH) in which an IgG4 positive hepatic inflammatory infiltrate predominates.

Methods We set out to establish the frequency with which IgG4 +ve plasma cells are observed in a cohort of patients with AIH without pancreatitis or sclerosing cholangitis. Immunohistochemical analysis via application of a monoclonal antibody to IgG4 was undertaken on archived liver tissue specimens. Three fields per biopsy specimen were analysed and the number of IgG4 +ve plasma cells per high powered field (HPF) and the proportion of these as a total of the plasma cell infiltrate were recorded. As per recent publications a biopsy specimen was determined to be IgG4 +ve if more than 10 IgG4 +ve plasma cells were seen per high powered filed (HPF) AND where this number equated to >40% of the total plasma cell infiltrate. Immunohistochemical and histopathological analysis was undertaken by a single, experienced, hepato-pathologist (YZ).

Results Sixty-three liver tissue specimens underwent immunohistochemical analysis. These specimens derived from 53 Caucasian and 10 Afro-Caribbean patients. All patients met the revised International Autoimmune Hepatitis Group diagnostic criteria for probable or definite AIH. The median age of patients at diagnosis was 31 years and 78% were female. Among this cohort 44 patients presented with chronic disease and histological evidence of chronic active hepatitis while 19 presented with acute disease in whom histology demonstrated hepatic collapse in 16 and severe lobular hepatitis in three patients. Only 7 of 65 samples (11%) demonstrated >10 IgG4 +ve cells/HPF. While there was a greater number of biopsy specimens with >10 IgG4 +ve plasma cells/HPF in acute vs chronic presentations this did not reach statistical significance (16% vs 9%, p=0.44). Additionally, there was no difference in the frequency of this finding between males and females (males 21% females 8% p=0.4) or between different ethnic groups (11% in Caucasians vs 10% in Afro-Caribbeans, p=0.99).

Importantly, in none of the seven cases in which >10 IgG4 +ve plasma cells/HPF were noted did the proportion of IgG4 +ve plasma cells equate to >40% of the total plasma cell infiltrate. Consequently, significant IgG4 +ve plasma cell infiltrates are not observed among non-Asian patients with AIH presenting to our institution.

Competing interests None declared.

REFERENCES