CIRCULATING LEVELS OF INTERLEUKIN-18 CORRELATE WITH SEVERITY FOLLOWING HUMAN ACUTE LIVER INJURY

Methods Analysis of SF levels in acute liver injury patients admitted to a tertiary liver center, with western blotting and immunohistochemistry for ferritin isoforms.

Results Retrospective database analysis revealed elevated admission SF (>300 μg/l) in 109/124 (87.9%) of acute liver injury patients. Extreme SF elevations (>10000 μg/l) were more common in POD (36/71, 50.7%) compared with non-POD patients (5/53, 9.4%, p<0.001). Extremely elevated admission SF was confirmed in a prospective cohort of 47 POD cases (22/47, 46.8%). In both POD cohorts, admission SF was significantly higher in patients who died/ were transplanted compared with spontaneous survivors (p=0.001, AUC 0.772 (95% CI 0.614 to 0.831) and in patients who developed hepatic encephalopathy (p=0.038) or the systemic inflammatory response syndrome (SIRS, p=0.006).

CIRCULATING LEVELS OF NEOPTERIN ARE ASSOCIATED WITH ADVERSE OUTCOMES FOLLOWING PARACETAMOL-INDUCED ACUTE LIVER INJURY

Methods Macrophage activation is implicated in the pathogenesis of multiorgan failure following paracetamol overdose (POD). Simple biomarkers of macrophage activation could aid earlier identification of high-risk POD patients. Neopterin is synthesised from macrophages and monocytes upon stimulation by interferon-γ and serum levels reflect the intensity of monocyte/macrophage activation.

Results A total of 24/35 (72.7%) PODs developed hepatic encephalopathy (HE), and therefore acute liver failure. Neopterin levels were significantly higher in patients who died/ were transplanted compared with spontaneous survivors (p<0.001, AUC 0.722 (95% CI 0.614 to 0.831)) and in patients who developed hepatic encephalopathy (p=0.038) or the systemic inflammatory response syndrome (SIRS, p=0.006). Hyperferritinemia correlated with proinflammatory (IL-6, Spearman’s r=0.442, p=0.006; IL-8, r=0.502, p=0.001) and antiinflammatory (IL-10; r=0.349, p=0.030) cytokine release following POD, and with organ dysfunction (SOFA; r=0.529, p=0.001), but not with serum ALT (r=0.113, p=0.227). The ferritin/ALT ratio did not improve prognostic accuracy in PODs (AUC 0.706 (95% CI 0.595 to 0.817)). Immunohistochemistry confirmed H and light (L) ferritin isoform expression in both normal liver tissue and explanted tissue from ALF patients. Immunoblotting of serum from POD patients with elevated SF revealed significant amounts of circulating H-ferritin, with no circulating H-ferritin observed in healthy controls.

Conclusion Extreme elevations of SF are common following POD, and are associated with adverse outcomes. SF is a widely available biomarker that may have prognostic value in patients with POD-ALF and merits further evaluation in larger, prospective studies. The correlation with SIRS, organ failure and cytokinaemia and the observation of circulating H ferritin also suggests that SF may be a mediator of adverse outcome.

Competing interests None declared.

EXTREME HYPERFERRITINAEMIA FOLLOWING PARACETAMOL-INDUCED HUMAN ACUTE LIVER INJURY

Introduction Activated macrophages may play a critical role in the pathogenesis of acute liver failure (ALF). Serum ferritin (SF) is a circulating marker of macrophage activation, and heavy (H) isoforms of ferritin may have immunostimulatory effects. However, ferritin may be released from necrotic liver, confounding SF interpretation in ALF. The SF/ALT ratio may have prognostic value in non-paracetamol ALF, but has not been examined in patients with paracetamol (POD)-ALF.

Methods Analysis of SF levels in acute liver injury patients admitted to a tertiary liver center, with western blotting and immunohistochemistry for ferritin isoforms.

Results Retrospective database analysis revealed elevated admission SF (>300 μg/l) in 109/124 (87.9%) of acute liver injury patients. Extreme SF elevations (>10000 μg/l) were more common in POD (36/71, 50.7%) compared with non-POD patients (5/53, 9.4%, p<0.001). Extremely elevated admission SF was confirmed in a prospective cohort of 47 POD cases (22/47, 46.8%). In both POD cohorts, admission SF was significantly higher in patients who died/ were transplanted compared with spontaneous survivors (p=0.001, AUC 0.772 (95% CI 0.614 to 0.831) and in patients who developed hepatic encephalopathy (p=0.038) or the systemic inflammatory response syndrome (SIRS, p=0.006).

Conclusion Extreme elevations of SF are common following POD, and are associated with adverse outcomes. SF is a widely available biomarker that may have prognostic value in patients with POD-ALF and merits further evaluation in larger, prospective studies. The correlation with SIRS, organ failure and cytokinaemia and the observation of circulating H ferritin also suggests that SF may be a mediator of adverse outcome.

Competing interests None declared.