CA 19–9 >1000 U/l had surgery. Similarly only 3 (30%) with abnormal cytology were considered for surgery. Although most patients (n=9) who underwent surgery were symptomatic, 18/113 (16%) patients in the conservatively managed group also had symptoms related to the cystic tumours. The size of the cystic tumour in the surgical group, however, was significantly larger than that in the conservative group (4.9 cm vs 2.9 cm, p<0.01).

Conclusion Surgical decision making process in patients with pancreatic cystic lesions is complex with multiple factors influencing the choice of surgery. Our data indicate the limited role of pancreatic fluid analysis compared with symptoms and cyst size. Factors that guide and influence the need for surgical resection of pancreatic cystic tumours should be further evaluated.

Competing interests None declared.

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PMO-141 FLAGELLIN-INDUCED IL-6 PRODUCTION IS SELECTIVELY IMPAIRED IN PATIENTS WITH CIRRHOSIS

doi:10.1136/gutjnl-2012-302514b.141

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Introduction The innate immune response is an important determinant of progression in chronic inflammatory liver diseases such as alcoholic (ALD) and non-alcoholic fatty liver disease (NAFLD). Sepsis is a frequent cause of hepatic decompensation and some authors suggest a role for toll-like receptor (TLR) sensing of gut-derived pathogens (motile and gram-negative organisms) in disease progression. Paresis of the innate immune system has been described in patients with decompensated liver disease, but the function of TLRs in compensated disease has received scant attention. Our aim was to assess TLR responsiveness in patients with compensated ALD and NAFLD using a combinatorial experimental design, measuring LPS- and flagellin-induced TNFα and IL-6 production.

Methods Consenting adult outpatients with compensated ALD or NAFLD were recruited. Diagnoses were confirmed by casenote review. Exclusion criteria included alternative aetiologies, decompensated disease, other systemic immune-related illnesses, and immunosuppression (including steroids). Normal healthy volunteers without liver disease were also recruited. Monocytes isolated from peripheral blood mononuclear cells were stimulated with low dose LPS and flagellin. The production of TNF-α and IL-6 was assayed in supernatants and in patient sera by ELISA.

Results We included 28 patients and six normal controls. Patients with compensated cirrhosis have a selective defect in flagellin-induced IL-6 production (330±117 pg/ml) compared to patients with non-cirrhotic ALD or NAFLD (896±146 pg/ml; p=0.01) or healthy controls (764±96 pg/ml). There were no differences in flagellin-induced TNFα nor in LPS-induced cytokine production. There were no differences between the three groups in serum concentrations of TNF, IL-6 and RANTES.

Conclusion Paresis of the innate immune response is not universal; there is selective impairment of TLR5-mediated IL-6 production in patients with compensated cirrhosis compared to non-cirrhotic patients. These data identify potential signalling pathways that may be involved in the progression of liver disease or in the susceptibility of patients with cirrhosis to bacterial infections.

Competing interests None declared.

PMO-142 EVIDENCE REFUTING THE TROJAN-HORSE HYPOTHESIS OF BRAIN SWELLING IN ACUTE LIVER FAILURE: L-TYPE GLUTAMINASE IS EXCLUSIVELY NEURONAL

doi:10.1136/gutjnl-2012-302514b.142

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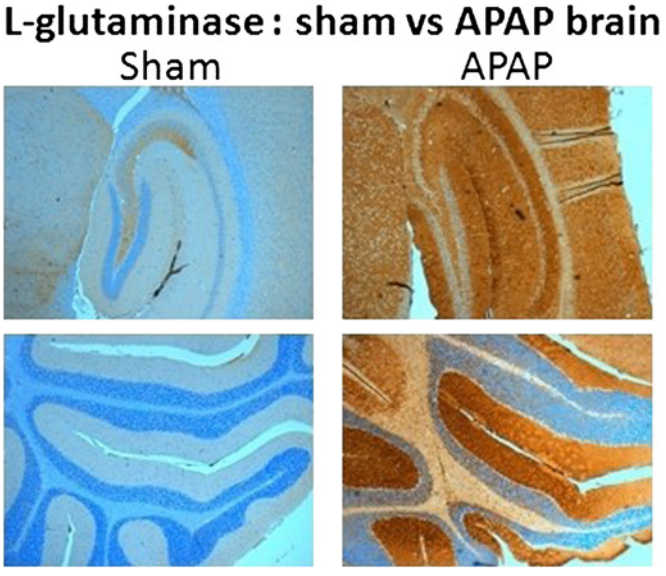
Introduction Astrocytic swelling is the characteristic feature of hyperammonemia and acute liver failure (ALF) which is thought to result from accumulation of glutamine due to the action of astrocytic glutamine synthetase (GS). It has been suggested that glutamine may not be a benign amino acid and may act as "Trojan horse" which leads to astrocytic apoptosis as it is metabolised by Glutaminase (GLN) yielding glutamate and ammonia. In vivo proof for this hypothesis is lacking. In health, GLN is mainly neuronal and generates glutamate and GABA. The aims of the study were to define the expression of the ammonia metabolising enzymes, GS and GLN in the brain of ALF animals.

Methods Two groups of CD1 mice were studied, sham: n=6; paracetamol (500 mg/kg IP): n=7. The animals were maintained normothermic and resuscitated with fluid and glucose and sacrificed at 8 h after injection of APAP or before development of coma. Arterial ammonia (COBAS) and frontal cortex brain water (dry weight technique) were measured. The brain sections were stained for GS and K and L-type GLN.

Results Arterial ammonia was significantly higher in the ALF group compared with controls (345±32 vs 132±11 p=0.002) and brain water did not reach significance (83.6±2.3 vs 76.3±2.6 p=0.05). GS protein expression was observed in the astrocytes in the dentate fascia in both groups and was not different but was also seen in the oligodendrocytes only in ALF group. L-type GLN was expressed only in the neurons and not in the astrocytes and was significantly higher in the ALF animals (++++) compared with controls (+). The most marked areas were the striatum and dentate fascia and interestingly the staining was mainly cytoplasmic. K-type GLN was not different between groups and limited to brain capillaries.

Conclusion Conclusion: The results of this study refute the Trojan-horse hypothesis and show for the first time increased protein expression of L-type GLN which is exclusively neuronal. From the pathophysiological perspective, this may function to generate excessive ammonia in the neuron thereby producing neuronal cell death.



Abstract PMO-142 Figure 1