GENETIC ANALYSIS AND PHENOTYPIC CORRELATION IN DUCTAL PLATE MALFORMATION

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Background and Aims Ductal plate malformation (DPM) includes polycystic liver disease (PCLD), multiple biliary hamartomas (MBH), congenital hepatic fibrosis (CHF) and Caroli disease. We sought to identify the genetic basis of a cohort of hitherto undefined DPM.

Methods 34 unrelated adults with presumed congenital liver disease underwent extended genetic analysis via a clinical exome panel (PKD1, PKD2, PKHD1, SEC63, PRKCSH, GANAB, ALG8, DNAJB11, LRPS). Clinical details and phenotypic correlation were analysed.

Results Of the 34 patients screened, genetic variants were identified in 20:

- Heterozygous variants in GANAB (n=4; 3 females, 1 male, mean age 56) were associated with a variety of mild PCLD phenotypes (with and without renal cysts, with Caroli's and with MBH). Variants were pathogenic in 2 cases and were variants of unknown significance (VUS) in 2 cases (both deleterious).

- Heterozygous variants in PRKCSH (n=2; both female, mean age 62) were associated with PCLD without renal cysts including 1 VUS (deleterious) and 1 novel pathogenic variant in a patient considered for liver transplantation.

- Heterozygous variants in the SEC63 (n=4; 3 females, 1 male, mean age 60) were associated with largely asymptomatic PCLD mostly without renal cysts including 3 pathogenic (all novel) and 1 VUS (deleterious).

- Heterozygous variants in PKD1 (n=3) and PKD2 (n=2) were identified in 4 patients with PCLD (2 with polycystic kidney and liver disease. All 5 were female (mean age 48) and with significant family history.

Conclusion Transcriptomic analysis of human HCC endothelium demonstrates a strong immunosuppressive signature. Interestingly the majority of differentially expressed genes were upregulated, suggesting that the endothelium plays an active role in immunosuppression and directly targeting these pathways could boost the efficacy of other immunotherapies.

A NOVEL NURSE-LED EARLY POST-DISCHARGE CLINIC IS ASSOCIATED WITH FEWER READMISSIONS AND LOWER MORTALITY FOLLOWING AN INDEX HOSPITALISATION WITH DECOMPENSATED CIRRHOSIS

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Background Patients hospitalised with decompensated cirrhosis (jaundice, variceal bleeding, ascites or hepatic encephalopathy) have high rates of early, unplanned readmission, associated
with increased complications and healthcare costs. Optimising preventative care reduces readmissions but many patients are readmitted before their outpatient review by hepatologists. Consequently, we established a novel care pathway with a nurse-led, early post-discharge clinic. Patients are seen within 2 weeks of discharge, with specific interventions for ascites, encephalopathy, varices, alcohol misuse and nutrition. The aim of our study was to assess impact on readmission and mortality.

Methods Following an index admission with decompensated cirrhosis, patients were seen in the nurse-led, early post-discharge clinic (intervention cohort) or received standard hepatology physician-led outpatient follow up (controls). Clinical data including demographics, liver disease aetiology, reason for admission and stage of liver disease were analysed. Outcome measures included time to first readmission, rate of readmissions and mortality up to 12 months.

Results There were 91 control patients and 78 in the intervention cohort. There were no significant differences in age, gender or aetiology of liver disease at index admission and mean MELD-Na on discharge was 18.1 and 19.8 (p=NS) in control and intervention groups respectively. Ascites was the most common decompensating event in both groups. Median time to readmission was 51 days in the control group and 98 days in the intervention group (p<0.01). The intervention cohort had significantly fewer early readmissions at 30 days (12% versus 30%, p<0.01) and 90 days (27% versus 49%, p<0.01) but not significantly at 12 months (58% versus 68%, p=0.16) with an overall reduction in bed day usage of 33%. Mortality for the control group was 4% at 30 days with no deaths in the intervention group. There were fewer deaths in the intervention group at 90 days (5% versus 15%, p<0.05) and 12 months (22% versus 41%, p<0.01).

Conclusions Following an index hospitalisation with decompensated cirrhosis, goal-directed early post-discharge care can be effectively delivered by specialist nurses, prior to outpatient review by hepatologists. This model was associated with significantly fewer unplanned readmissions, lower bed day usage and a reduced mortality. Our data suggest such nurse-led models of care deserve wider implementation and further evaluation.

O04 SERUM NUCLEAR MAGNETIC RESONANCE METABOLIC SIGNATURE CAN DISCRIMINATE IMMUNOGLOBULIN G4-RELATED SCLEROSING CHOLANGITIS AND PRIMARY SCLEROSING CHOLANGITIS

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Immunoglobulin G4-related sclerosing cholangitis (IgG4-SC) is often difficult to distinguish from primary sclerosing cholangitis (PSC) in clinical practice. Accurate, non-invasive biomarkers for discriminating IgG4-SC from PSC are required, but the diagnostic utility of global serum nuclear magnetic resonance (NMR)-based metabolomics is untested. We performed serum metabolic profiling in patients with IgG4-SC and PSC to assess for evidence of a distinctive signature that could discriminate between these conditions, predict response to therapy and provide a biomarker for disease relapse.

Stored serum samples collected prospectively from patients with IgG4-related disease (IgG4-RD; n=39 at diagnosis prior to therapy), PSC (n=100; 81 large duct; 19 small duct) and healthy controls (HC; n=16) were prepared for NMR spectroscopy using a standardised protocol. Principal component analysis (PCA) and orthogonal partial-least squares discriminant analysis (OPLS-DA) were used to identify discriminatory serum metabolites. Clinical data was obtained from review of electronic databases for correlation with metabolomics data and to adjust for confounders.

The median (range) age and gender proportion were 65 (33–83) years and 85% male for IgG4-RD, and 45 (12–84) years and 63% male for PSC. Lactate, glucose, and glutamine were increased in IgG4-RD compared to PSC (p<0.0001), whereas -CH3 lipoprotein and beta-hydroxybutyric acid resonances were decreased (p<0.001). NMR-based metabolic profiling discriminated IgG4-RD from PSC with greater accuracy (AUC 0.941, 95% CI 0.904–0.977) than upper limit normal of IgG4 titre (AUC 0.865, 95% CI 0.787–0.943).