Congeintal porto-systemic shunts – who is at risk of developing hepatic tumours?

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Background

Congenital porto-systemic shunts (CPS) were first described by John Abernethy, a St Bartholomew's surgeon in 1793. There is a spectrum of anatomical shunts between the portal venous system and the systemic circulation with varying degree of intra-hepatic portal vein hypoplasia. Complications of CPSs include pulmonary hypertension, heptopulmonary syndrome, encephalopathy, and hepatic tumours.

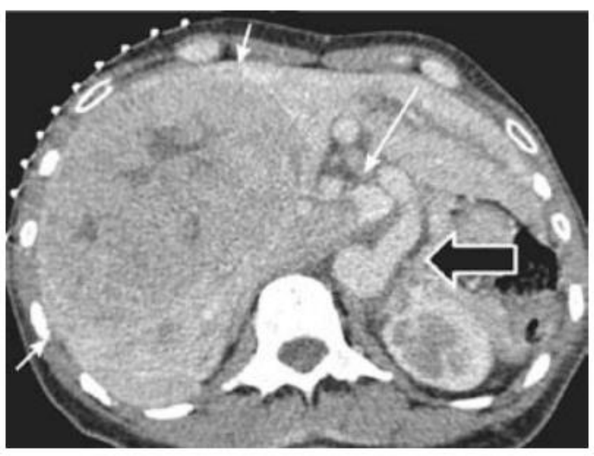


Figure 1. CT demonstrating large HCC in the right lobe of the liver, porto–systemic shunt (long arrow), hypertrophied coeliac axis (black arrow)

Aim

In patients with CPS we aimed to compare the subgroup of patients with hepatic tumours to those who did not form tumours.

Methods

Single-centre retrospective cohort study of all patients with CPS referred from 1990 to 2016. Data are quoted as median (IQR). Categorical data were compared using a two-tailed Chi-squared test, and continuous data using a two tailed Mann-Whitney test. A P value of 0.05 was considered significant.

Next generation sequencing was performed on available liver tumour specimens from FFPE tissue blocks for a panel of genes associated with hepatocellular carcinomas.

Ethics and disclosures

This study was supported by the joint BSPGHAN and CLDF start up grant. Ethical approval was obtained for this study (REC reference number: 16/EM/0342)

Results

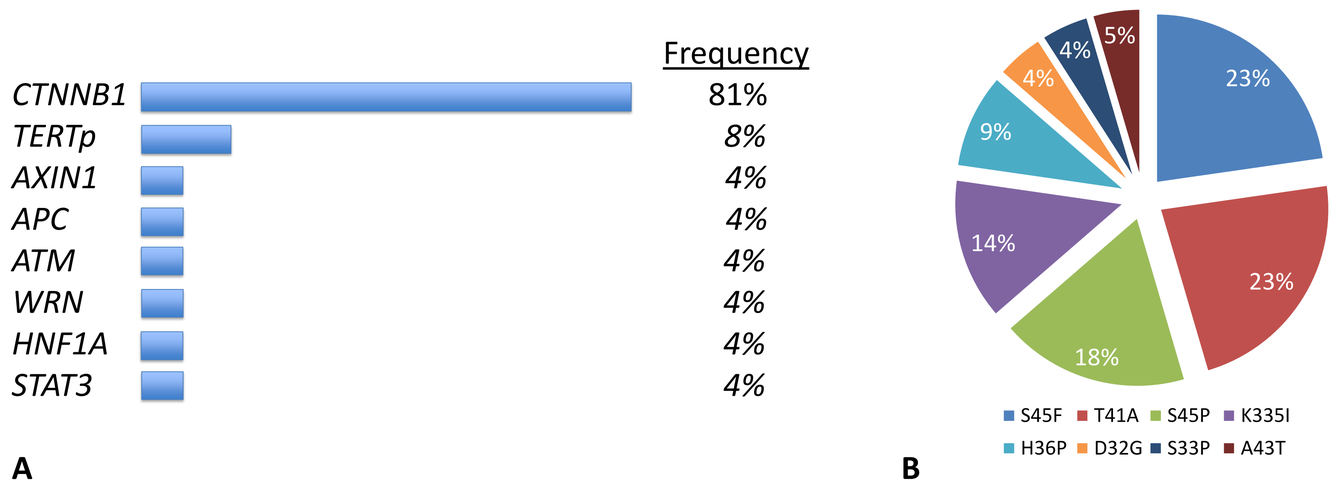
	Tumour (n=21)	No Tumour (n=25)	P value
Age at presentation IQR (years)	12 0.7 - 17	0.1 0 - 2.3	**<0.001**
Sex (M:F)	13 : 8	14 : 11	0.77
Perinatal presentation	5 (24%)	16 (64%)	**0.009**
Absent hepatic portal veins on radiology	11 (53%)	1 (4%)	**<0.001**
Classification Type 1 Type 2	 11 10	 1 24	**<0.001**
Operative closure Age at operation IQR	14 (67%) 8.4 5.1 - 14.1	13 (52%) 3.1 2.9 – 4.4	0.38 0.53

Table 1. Showing radiological and demographic data of patients with and without liver tumours.

46 patients were investigated for CPS at a median age of 8 months (1m– 14y). The group with tumours presented at a significantly higher age compared to those without (P <0.001). There was a significantly higher proportion of patients with tumours in the group who did not have identifiable intrahepatic portal veins on imaging (P <0.001). Congenital cardiac anomalies found in 17 patients (8 of those with tumours and 11 of those without). A total of 8 patients had associated cutaneous haemangiomata (3 in the tumour and 5 in the non-tumour group). 3 patients developed pulmonary hypertension (1 of which had a tumour), and 4 developed hepatopulmonary syndrome (2 of which had a tumour). There were no significant differences in the ammonia levels between the two groups. Of the 14 intrahepatic shunts, 8 closed spontaneously by 2 year of life.

Genetic sequencing

21/46 cases had tumours of which 26 had samples available for sequencing. 9 different *CTNNB1* mutations were found in 17 separate tumours with a predisposition for Exon 3.



A **B**

Figure 2. A Genes and their frequency of mutation in tumour samples. **B** Different amino acid changes coded for by the mutations

Conclusions

Lack of intrahepatic portal veins on imaging, and presenting later in life are associated with the development of liver tumours in patients with CPS. Associated respiratory complications are not related to the formation of liver tumours

Benign and Malignant tumours in patients with CPS are predisposed to mutations, especially in Exon 3 of the *CTNNB1* gene.

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BSPGHAN working for children with digestive and liver disorders
British Society of Paediatric Gastroenterology Hepatology and Nutrition

Children's Liver Disease Foundation
fighting childhood liver disease