Outcome in Cystic Fibrosis Liver Disease

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Evidence suggests that cystic fibrosis liver disease (CFLD) does not impact on mortality or morbidity in CF. The aim of this study was to review children enrolled in a study of CFLD in 1999–2000.

Methods: Participants were reviewed clinically and radiologically. 3 participants (2 cases, 1 control) were lost to follow-up, 1 control refused, and 8 participants(5 cases) were excluded.

Results: There was no difference in age, (mean 19.9±3.2 yrs) duration of follow-up (76.9±20.2mths), gender(63%) male between cases and controls. 7 patients with CFLD died (5 liver failure) 1 liver transplant, and 3 controls died. Crude mortality for patients with CFLD was 11.3/1000 person yrs of age (95%CI 3.5–19.0) compared to 4.1/1000 (95% CI 0.6–8.9) for controls. Patients with liver disease died younger (median 17.5 yrs V 21.5 (p=0.06). There was no difference in height, weight or BMI between the groups. Nutritional parameters (sum skin fold thickness 30.1±17.4 V 38.1±21.2 p=0.03), Slowachman score (49.1±11.4 V 55.4±12.5 p=0.02) were poorer in patients with CFLD. They had a higher proportion of CF Diabetes Mellitus (40.7% V 15.2% p=0.02). 9 children with evidence (clinical/radiological) of liver disease at baseline, had no evidence of portal hypertension as adults.

Conclusion: Patients with CFLD may have a higher mortality and die younger than CF patients without liver disease. However some children with CFLD will not manifest clinically significant liver disease as adults.

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Hepatic tissue TGF-β and SMAD proteins as markers of the fibrosing process in cystic fibrosis: a pilot study

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TGF-β are cytokines that regulate proliferation and differentiation of cells. Dysregulation of the TGF-β pathway may modulate the development of severe disease groups including hepatic fibrosis. TGF-β signals through the transmembrane receptor serine/threonine kinase to activate SMAD proteins, which modulate the transcription of target genes. The aim of this study was to investigate the correlation of hepatic tissue TGF-β1, TGF-β3, ALK5 and Smad 2, 3, 4 with the degree of liver involvement in cystic fibrosis (CF).

Methods: Eleven CF patients underwent percutaneous liver biopsy. The biopsy needle was directed to the site of the lesion under CT scan. Fibrosis was graded as 0 (normal), 1, 2 and 3 (mild to moderate). Two groups were studied: Group A: 6 CF patients having normal liver (fibrosis 0) and mean age of 11.2 years, and Group B: 5 CF patients having mild to moderate fibrosis (1, 2, 3) and mean age of 15.0 years.

Results: The mean rank of TGF-β1, TGF-β3, ALK5 5, SMAD 2, 3, 4 was 6.40, 7.80, 7.40, 7.60, 7.20, 7.60, respectively, in group B as opposed to 5.67, 5.17, 4.33, 4.83, 4.67, 4.67 in group A. Hepatic tissue mean cytokine values tended to be higher in the fibrotic liver as compared to normal liver.

Conclusion: Hepatic fibrosis increased with age in CF. TGF-β and SMAD proteins were increased in the presence of fibrosis at histology. The differences did not reach statistical significance, probably, due to the small number of individuals. These cytokines may be involved in the reactive fibrogenic process of the liver.

9. Gastrointestinal and liver disease

Fibrosis blood tests to detect liver disease in patients with cystic fibrosis

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Objectives: Liver disease is a major complication of cystic fibrosis and is generally seen within the first ten years of life. The aim of this study was to evaluate a blood test, the FibroMeter, to detect liver fibrosis or cirrhosis in children with cystic fibrosis.

Population and Methods: Fifty-one children with ages ranging from 1 to 18 years were included in this study between September 2007 and September 2008. All were followed by the Cystic Fibrosis Center at the University Hospital in Angers, France. The children were staged into one of four groups on the basis of their biological and ultrasound results. The results of liver biology, ultrasonography, the FibroMeter test, and transient elastometry were compared.

Results: The FibroMeter results in the children without liver disease or elevated γ-glutamyltransferase and without abnormal ultrasound were significantly better than those with clear cirrhosis or an abnormal ultrasound. Of the 33 children that had transient elastometry, only two had results above 7 kPa, whereas eight had an abnormal ultrasound.

Conclusion: The FibroMeter could be useful in detecting children at risk of developing fibrosis or cirrhosis. Transient elastometry assesses the degree of fibrosis in patients but does not seem to be an effective tool to detect liver fibrosis. These results will have to be confirmed by longitudinal study of these children.

Immunity in CF associated liver disease

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It seems that immunity play an important role in CF-related liver disease’s outcome. If the immune deficiencies or autoimmunity are the causes remain to be demonstrated.

Aim study was to assess the influence of humoral immunity on liver disease of CF patients. Material and method: 27 patients, age 3–21 years, with cystic fibrosis associated liver disease (CFLD) and normal liver function, were considered for study. Inclusion criteria: A.F508 homozygous genotype, good respiratory and nutrition status; patients with immunodeficiency, hypoalbuminemia, pulmonary chronic infection, hepatotoxic treatment history or hepatitis were excluded. Serum levels of immunoglobulin A, M, G, MBL (mannose binding lectine) and protein electrophoresis were evaluated. Results: Combined Ig deficiency was registered in 26% CFLD patients, 14.8% had selective deficit in IgA. Only 8 patients (29.6%) had normal immunoglobulin values, but 3 of them MBL deficient. Low MBL level were found in 44.4%-12 pts (8 with other immunodeficiency); protein electrophoresis showed increase γglobulin level in 41.6% (3 pts) of MBL deficient patients. Only 18% had normal immunoglobulin and MBL levels.

Conclusion: Large percentage of immunoglobulin and MBL deficit among patients with CFLD sustain the association between immune deficiencies and occurrence of associated liver disease in cystic fibrosis patients. In which way the diseases influence each other remain to be documented by more studies.