

The Distinct Phenotype of Autoimmune Sclerosing Cholangitis in Pediatric Patients is Associated with Prominent Hepatic Type 17 and B-lymphocyte Immune Responses

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Introduction

Primary Sclerosing Cholangitis (PSC) is a rare autoimmune liver disease (AILD) leading to the sclerosis of the intra- and extrahepatic bile ducts. Up to 30% of pediatric PSC patients have an overlap with symptoms of Autoimmune Hepatitis (AIH), referred to as Autoimmune Sclerosing Cholangitis (ASC).

Hypothesis

Composition of liver infiltrating inflammatory cells differ between the subtypes of AILD.

Methods

30 subjects with the clinical diagnosis of AIH, PSC or ASC were selected from a retrospective cohort (n=10 in each group). Clinical data was obtained by chart review. Archived formalin-fixed, paraffin-embedded liver biopsies were subjected to immunohistochemistry for the markers (n=3-4 per group): interleukin (IL)-17a, CD79a, panCK, CD4, and CD8. Immunoreactivity was semi-quantitatively analyzed by applying a four-point scale: 0-absent, 1-mild, 2-moderate, 3-severe.

Results

The mean ages for the PSC, ASC, and AIH groups at the time of liver biopsy were 14.2±1.5, 13.2±2.6, and 9.7±2.8 years, respectively, with female predominance in all subgroups. Concomitant Inflammatory Bowel Disease (IBD) was present in 50-60% of subjects with PSC or ASC, but only in 20% with AIH. Liver serum biochemistry values at the time of liver biopsy showed significantly higher levels of Alkaline Phosphatase (ALP) in ASC patients (mean of 885 vs 269 vs 243 in ASC vs PSC vs AIH, respectively with p<0.05 in One-Way ANOVA). Serum aminotransferase levels did not significantly differ between the three groups. Analysis of immunohistochemistry revealed a higher prevalence of IL17a positive cells in the portal tracts of patients with ASC (mean activity score: 2.5 vs 1 vs 1 for ASC vs PSC vs AIH, respectively with p<0.005 in ANOVA). Periductal accumulation of IL17a positive cells was accompanied by portal tract infiltration with CD79a+ B-lymphocytes in ASC subjects, but not the other groups. While CD8 infiltration was similar among all three groups, high prevalence of portal CD4+ cells was restricted to the ASC and AIH groups.

Conclusions

Biochemical evidence of bile duct injury in ASC subjects is associated with periductal accumulation of IL17a+ and CD79a+ lymphocytes, indicating a role of Th17 and B lymphocytes in orchestrating bile duct epithelial injury in ASC. We are currently aiming to validate our findings in a larger cohort.

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