Evaluation of Graft Fibrosis, Inflammation, and Donor-specific Antibodies at Protocol Liver Biopsies in Pediatric Liver Transplant Patients: A Single-center Experience

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Background and objectives: The impact of graft fibrosis and inflammation on the natural history of pediatric liver transplants is still debated. Our objectives were to evaluate the evolution of posttransplant fibrosis and inflammation over time at protocol liver biopsies (PLBs), risk factors for fibrosis, presence of donor-specific antibodies (DSAs), and/or their correlation with graft and recipient factors

Materials and Methods: A single-center, retrospective (2000-2019) cross-sectional study on pediatric liver transplant recipients who had at least 1 PLB, followed by a longitudinal evaluation in those who had at least 2 PLBs, was conducted. Fibrosis was assessed by the Liver Allograft Fibrosis Semiquantitative score, inflammation by the rejection activity index, DSAs by Luminex

Results : A total of 134 PLBs from 94 patients were included. Fibrosis was detected in 87% (30% mild, 45% moderate, and 12% severe), 80% in the portal tracts. There was an increase in fibrosis between the 1-3 and the 4-6 y group (P = 0.01), then it was stable. Inflammation was observed in 44% (30% mild, 13% moderate, and 1% severe), 90% in the portal tracts. Anti-HLA II (IgG) DSAs were detected in 14 of 40 (35%). Portal fibrosis was associated with portal inflammation in the 1-3 y group (P = 0.04). Low immunosuppression levels were correlated with sinusoidal fibrosis (P = 0.04) and DSA positivity (P = 0.006). There was no statistically significant correlation between DSA positivity and the presence of graft fibrosis or inflammation

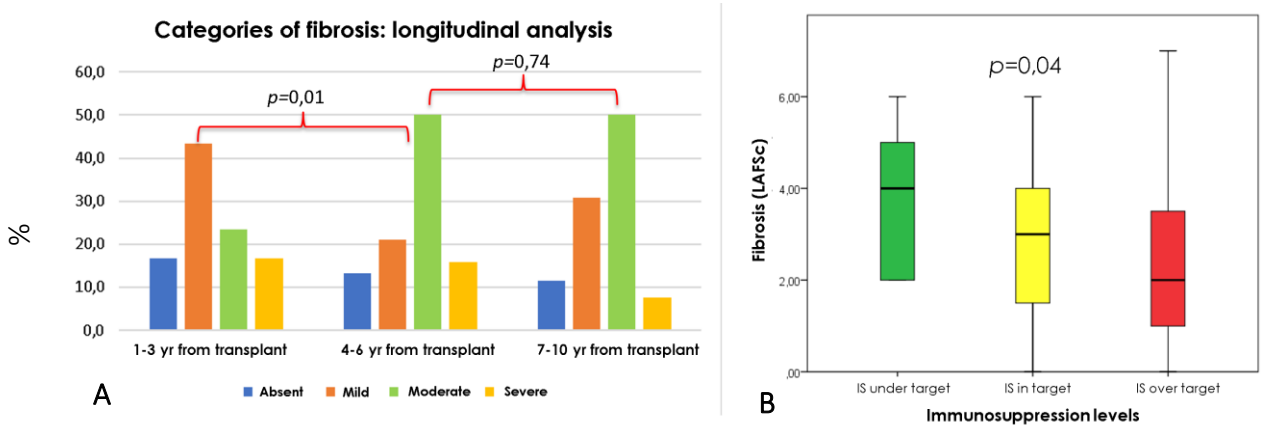

Fig 1: A) progression of fibrosis: longitudinal analysis, B) correlation between fibrosis and immunosuppression, boxplot graph

	DSA+ (n=14)	DSA- (n=26)	Significance
EBVDNA			
• +/-	5/9	9/16	p=0,63
Rejection episodes	2	7	p=0,3
Fibrosis (LAFSc,mean)			
• Total	3,29	3,54	p=0,67
• Portal	1,57	1,65	p=0,72
• Sinusoidal	0,79	0,73	p=0,63
• Centrolobular	0,93	0,92	p=0,54
Infiammation (RAI, mean)			
• Total	1,14	0,88	p=0,29
• Portal	0,93	0,69	p=0,1
Age at transplant, mean	2,9	3,8	p=0,47
Immunosuppression levels			
• Categories			
Under target	4	1	
In target	6	4	p=0,049
Over target	4	11	
• FK, mean	2,3	4,7	p=0,006
Gender, M (%)	10 (71%)	11 (42%)	p=0,079

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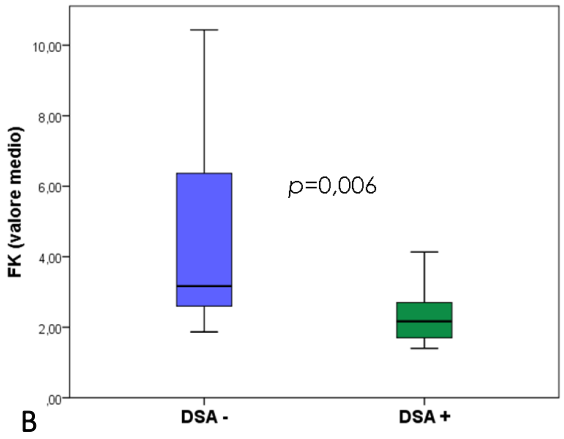

Figure 2: A) Correlations between the presence of DSAs and different patient and graft factors B) Correlation between the presence of DSAs and immunosuppression, boxplot graph

Conclusions

- History of transplanted liver, in our cohort, evolves to mild/moderate fibrosis through time, mostly within 6 years from transplantation;
- Low immunosuppressive regimen and inflammation were correlated to the presence and grade of fibrosis;
- The causal link between fibrosis and inflammation remains uncertain and we believe that other factors may well contribute to the development of fibrosis.
- Suboptimal immunosuppression may play a role in the development of fibrosis and DSAs.