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Abstract (oral session)

Polymorphism of IL-12p40 gene and its association with chronically high Epstein-Barr virus DNA load in paediatric liver transplant recipients

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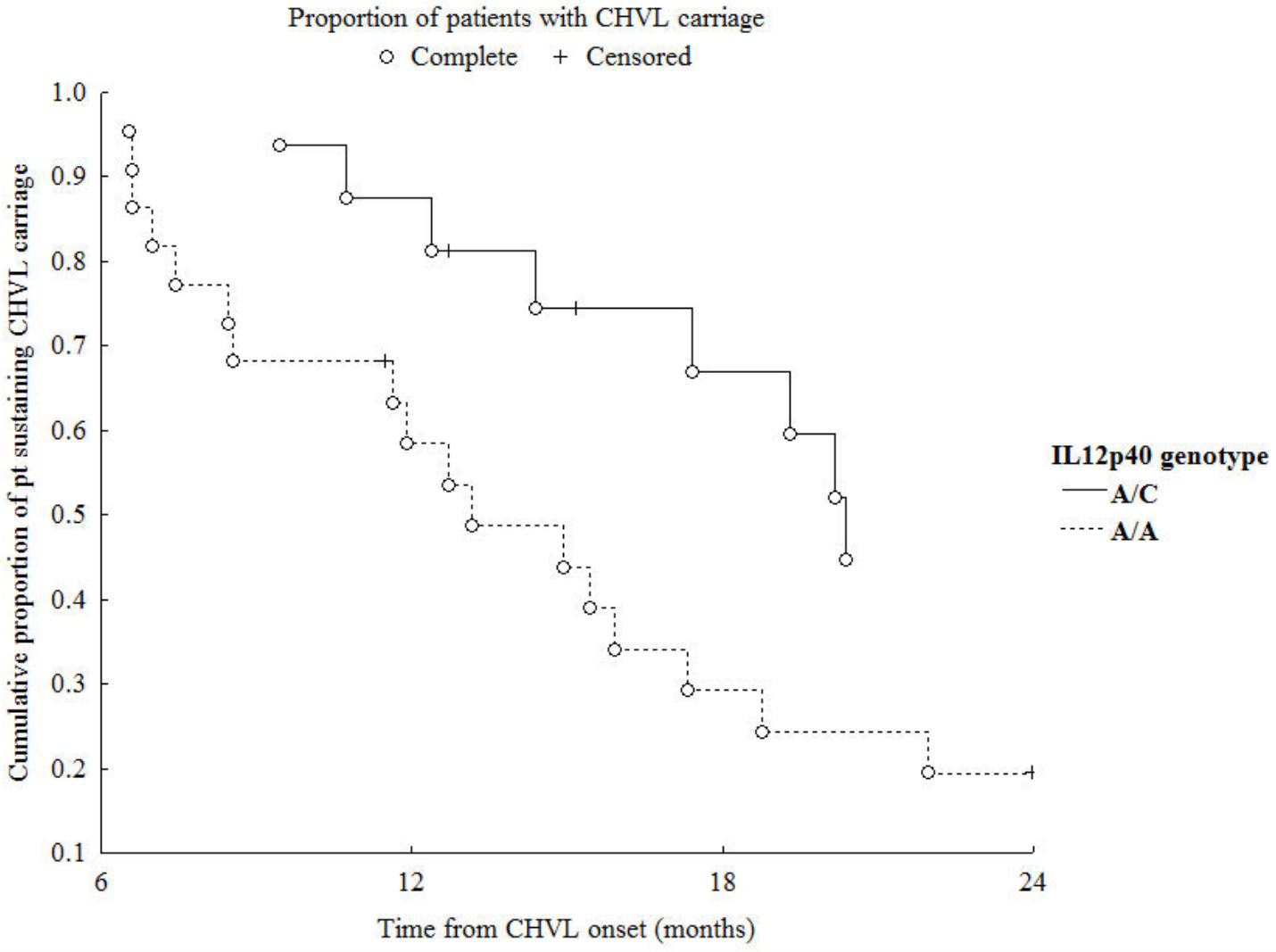
Objectives: Paediatric liver transplant (LTx) patients (pts) are at particular risk of developing EBV – related posttransplant lymphoproliferative disorders (PTLD). The risk of PTLD is higher in pts with high viremia. However, among transplant recipients is a group of pts with chronically high viral load (CHVL) who do not develop lymphoproliferations, so there is a need for new prognostic markers to define pts at risk of serious complications. Polymorphism within cytokine genes, might contribute to the pathogenesis of the disease. IL-12 plays a key role in anti-viral immune response. The A-to-C substitution within IL12B gene (SNP rs321227) affects the IL-12p40 production. The aim of the study was to analyse the polymorphism of IL-12p40 with regard to CHVL carriage in paediatric pts after LTx. Methods: One hundred seventy nine children after LTx were included in the study (median age at LTx 1.3 years, range 0.1-18). All pts were followed up for at least 12 months after LTx (median 30, range12-139). A group of 38 pts with CHVL (i.e. the presence of EBV DNA level > 4000 copies/ µg DNA in > 60% of blood samples for min. 6 months) was selected. The remaining 141 pts with moderate or undetectable viremia consisted a control group. IL12B was genotyped by RFLP-PCR. The association between IL12B genotype and CHVL was analysed by multivariate logistic regression adjusting for confounders. To analyse the impact of IL12B polymorphisms on the length of CHVL carriage (defined as the time between 1st EBV DNA level > 4000 copies and first 2 consecutive values below this level), the proportion of pts with persistent high viremia over 24-months period was assessed for each genotype. The Kaplan-Meier curves were compared using the log-rank test. The Cox proportional hazards model was adjusted for tacrolimus level. Results: Significantly increased frequency of AC genotype was found in CHVL carriers compared to controls (46.9% vs 23.2%, respectively, OR = 3.5, 95% CI:1.4 – 9.1, p = 0.002). Time-to-CHVL resolve analysis, revealed a relationship between IL-12p40 genotype and the length of CHVL-carriage. Significantly lower proportion of patients with AC genotype resolved high EBV DNA load at 24 months after the onset of CHVL carriage, when compared to dominant AA genotype, (53% vs 81%, p = 0.01; Figure). Conclusion: Polymorphism within IL-12p40 gene might contribute to high EBV DNA load persistence in paediatric pts after LTx, which in turn influence the risk of PTLD development.


Proportion of patients with CHVL carriage
Complete
Censored
Cumulative proportion of pt sustaining CHVL carriage
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
6
12
18
24
Time from CHVL onset (months)
IL12p40 genotype
A/C
A/A