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Frequency and clinical relevance of high human herpesvirus 6B DNAemia following liver transplantation in children

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Background: The impact of HHV-6B DNA*emia* in paediatric solid organ transplant recipients remains largely unknown. It has been suggested that HHV-6B may be implicated in a febrile syndrome, bone marrow suppression, an acute graft rejection/dysfunction and a risk of subsequent opportunistic infection including cytomegalovirus (CMV) disease. The aim of the study was to investigate the frequency and significance of high HHV-6B DNA*emia* in relation to clinical outcomes in paediatric liver transplant (LTx) recipients.

Material/methods: Sixty-eight children who underwent LTx between February 2011 and December 2014 were included in this study. Serial quantifications of HHV-6B DNA were performed in blood samples collected over a course of first 12 months post-LTx (total number of 804 samples; median 11 per patient). All patients received universal anti-CMV prophylaxis ((val)ganciclovir for up to 3-6 months, then acyclovir for up to 12 months). No intervention was directed specifically for HHV-6B DNAemia. Clinical, virological (EBV-, CMV-, HHV-7 DNAemia) data and through tacrolimus levels were collected. High HHV-6B loads were defined as >3 $\log_{10}$ copies/mL. Patients with high HHV-6B loads were compared with those with undetectable or low viraemia.

Results: High HHV-6B DNA loads were found in 18 (26.5%) patients. Median peak HHV-6B DNA*emia* was 3.52 $\log_{10}$ copies/mL (interquartile range, IQR: 3.3 - 4.4 $\log_{10}$ copies/mL). Children with high HHV-6B DNA*emia* were younger and had higher peak EBV DNA loads then those with undetectable or low HHV-6B loads (Table). No differences with regard to CMV - and HHV-7 co-infection were found. In

addition no significant differences in immunosupression levels and occurrence of acute rejection episodes were observed.

Conclusions: High HHV-6B DNA*emia* occurs frequently among paediatric LTx patients and is associated with higher EBV DNA loads but not with CMV or HHV-7 co-infection or episodes of acute graft rejection.

Characteristics	High HHV-6B DNA*emia* (n = 18)	Low/undetectable HHV-6B DNA*emia* (n = 50)	P-value
Age at LTx, years, median (IQR)	0.98 (0.79 - 1.24)	3.20 (1.6 - 9.4)	**0.000015**
Male, n (%)	9 (50)	28 (56)	0.66
Peak EBV load (log_{10} copies/mL)	4.39 (3.97 - 4.93)	3.92 (2.86 - 4.39)	**0.034**
CMV DNA*emia*, n (%)	11 (61.1)	25 (50)	0.42
HHV-7 DNA*emia*, n (%)	15 (83.3)	44 (88)	0.62
Rejection episodes, n (%):	7 (38.9)	17 (34)	0.71
Through levels of tacrolimus, ng/mL; median (IQR):			
1 month after LTx	7.92 (7.61 - 8.50)	8.13 (7.18 - 8.90)	0.68
6 months after LTx	7.25 (5.81 - 9.08)	7.9 (6.55 - 8.92)	0.55
12 months after LTx	6.34 (5.16 - 7.16)	7.68 (5.63 - 4.39)	0.05