recipients with high EBV loads showing low activity of specific $CD8^+$ T were at high risk for PTLD, using an enzyme-linked immunospot assay in pediatric solid-organ transplant recipients. Such a functional impairment may be present and influence the chronic high EBV load state.

Analyzing the expression profile of EBV-related genes is useful in clarifying the pathogenesis of EBV-associated diseases [16]. In each chronic high EBV load carrier, EBER1 and BARTs were abundantly detected, and LMP2 was found in half of the carriers. The mean expression level of LMP2 was low, compared with those of EBER1 and BARTs. No transcript specific for latency type 3 was detected in chronic high EBV load carriers. This restricted pattern is latency type 0, which is found in EBV-infected memory B cells [8, 29, 30], suggesting that the pattern of infected B cells in those with chronic high EBV loads may be the same as that in healthy EBV carriers. Qu et al [31] reported that peripheral blood lymphocytes in those with chronic high EBV loads after solid-organ transplant were divided into 2 types of infected cells: lymphocytes expressing LMP2 and carrying a low number of copies of EBV, and others coexpressing LMP1 and LMP2 and having a high number of copies of EBV. In the present study, expression of LMP1 was not observed in all chronic high EBV load carriers. Quantification in the blood sample may not have been sufficiently sensitive to detect a small population of infected cells expressing the LMP1 gene. Additionally, the expression pattern may vary with the time at which the blood sample is obtained. Transcripts specific for latency type 3 were detected in some samples from chronic high EBV load carriers obtained within 4 months after EBV infection (data not shown), and the pattern of EBV gene expression subsequently changed to latency type 0. Dynamic changes in the immune response, such as an increased precursor frequency of EBV-specific $CD8^+$ T cells after reduced immune suppression, may influence expression patterns in chronic high EBV load carriers; however, this change was not evaluated in the present study.

After primary infection, EBV persists as a latent infection in memory B cells. Then, memory B cells occasionally differentiate into plasma cells that undergo lytic infection and produce new virus. Newly infected naive B cells become transformed but are controlled by $CD8^+$ T cells specific for EBV. This cycle is necessary to maintain a latent infection in vivo [21, 32]. Thus, we suggest a novel mechanism for the maintenance of high viral loads in the blood of chronic high EBV load carriers. First, a large number of memory B cells latently infected with EBV survive after the primary or reactivated EBV infection occurring after transplant. Second, the latently infected memory B cells readily differentiate into plasma cells to produce the virus. Immunosuppression may influence these processes. Treatment with acyclovir or ganciclovir for a relatively prolonged period may modulate the chronic high EBV load state. However, our results did not provide mechanistic or therapeutic information.

Acknowledgments

We thank the following people for providing samples from patients with infectious mononucleosis or posttransplant lymphoproliferative disorder: Naoko Nishimura and Takao Ozaki (Konan Kosei Hospital); Masayuki Hasegawa and Kazue Ito (Nagoya Ekisaikai Hospital); Masanori Yamada (Chubu Rosai Hospital); and Yasuko Abe (Shizuoka Children's Hospital). We also thank Fumiyo Ando for secretarial assistance.

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