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Abstract (poster session)

Acute human herpesvirus-6 (HHV-6) reinfection following infusion of ex vivo expanded tumor-infiltrating autologous T lymphocytes due to intense HHV-6 replication in cell culture

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Objectives: Infusion of ex vivo expanded autologous T lymphocytes is a promising adjuvant anti-tumor strategy. During the process, cell cultures are thoroughly tested for infectious pathogens before re-infusion, but viral dynamics may be rapid. We report a case where HHV-6 has been reactived in a T cell culture and was responsible for a roseola-like syndrome after reinfusion. Case report: A 39 year old female patient presented with a relapsing melanoma featuring only a metastatic axillary lymph node, and was included after informed consent in the clinical trial “Tumor Infiltrating Lymphocytes Adjuvant Therapy of Melanoma (TIL)” (NCT00200577). The axillary lymph node was excised, and T cells were sorted and cultivated with IL-2. Tests at day 24 of culture detected low HHV-6 viral load (21 copies/DNA µg in cells, and 100 copies/ml in supernatant) and were negative for other pathogens. Intravenous infusion was performed after 31 days of culture (CD4: 86%). Four days later, the patient experienced fever and a maculopapular, generalized exanthema which spontaneously disappeared in few days. Liver tests showed a moderate and brief rise of transaminase level. Results of the HHV-6 viral load in the infused T cell culture at day 31 retrospectively showed a high viral load (41.10e4 copies/DNA µg in cells, and 25.10e6 copies/ml in supernatant). During the follow-up of the patient, anti-HHV-6 IgG titers rose from 40 (before the infusion) to 640 (2 weeks after the infusion). On the day of infusion, PBMC collected from the patient was negative for HHV-6 DNA; unfortunately, HHV6 viral load has not been performed thereafter. Comments: This case illustrates that ex vivo amplification of T lymphocytes may lead to reactivation of the T lymphotropic HHV-6. Even if this roseola-like syndrome could be attributed to other cause (allergy), the rise of HHV-6 viral load in the T lymphocytes culture before re-infusion and the increase of HHV-6 IgG antibody after re-infusion were consistent with HHV-6 involvment. To our knowledge this is the first report of an HHV-6 reinfection after infusion of an autologous cell culture; this case stresses the need for close monitoring of such culture because of potentially rapid viral replication. Moreover, HHV-6 known properties of immunomodulation of immune system probably altered and anti-tumor efficiency of HHV-6 infected TIL. Conclusion: Ex-vivo expansion of T lymphocytes must be closely monitored for T Lymphotropic latent viral infection before reinfusion.