# Acute 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

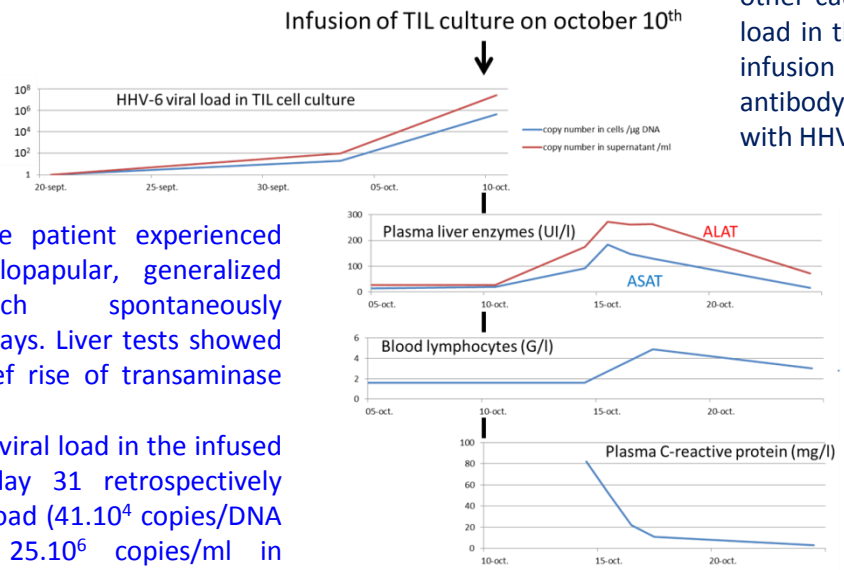
Infusion of **ex vivo expanded autologous T lymphocytes** is a promising adjuvant **anti-tumor strategy**. During the process, cell cultures are thoroughly tested for infectious pathogens before re-infusion, but viral dynamics may be rapid. We report a case where HHV-6 has been reactivated in a T cell 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%) **on october 10th**.

*Fig.1 – events before and after TIL infusion*

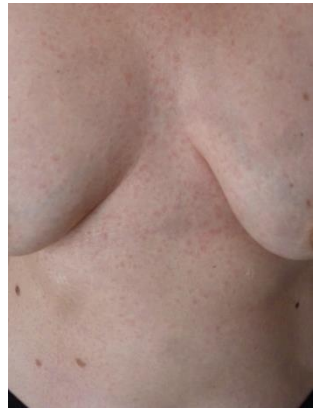



**Four days later**, the patient experienced fever and a maculopapular, generalized exanthema which spontaneously disappeared in few days. Liver tests showed a moderate and brief rise of transaminase level (fig. 1 and 2).

Results of the HHV-6 viral load in the infused T cell culture at day 31 retrospectively showed a high viral load ($41.10^4$ copies/DNA µg in cells, and $25.10^6$ 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.

*Fig.2 – roseola-like exanthema*



## 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 involvement.

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 expanded T lymphocytes must be closely monitored for T Lymphotropic latent viral infection before reinfusion.