EXPANSION OF TUMOR-INFILTRATING LYMPHOCYTES FROM COLORECTAL CANCER LIVER METASTASIS; CHARACTERISTICS AND POTENTIAL HISTOLOGIC MARKER OF SUCCESSFUL CELL EXPANSION

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Background Colorectal cancer is the 3rd most common cancer worldwide. In recent years, adoptive cell therapy (ACT) of tumor-infiltrating lymphocytes (TILs) has been successful in treatment of metastatic melanoma. We cultured TILs from colorectal cancer liver metastasis. We evaluated the numbers and subsets of expanded TILs and their relationship with the original tumors' histologic findings.

Methods Fifteen samples of colorectal cancer liver metastasis were collected at a single institute. Cancer tissues were cut into 1 to 2-mm fragments and underwent initial expansion of TILs for 2 weeks. The number of the TILs per fragment was counted and checked for successful expansion at cutoff of 0.8x10^5 cells per fragment. Their characteristics were evaluated by flow cytometry. Remnant cancer tissues were made into hematoxylin and eosin-stained slides. The slides were reviewed for histologic findings including the level of stromal TILs and inflammatory cell infiltrate at the invasive margin, using the Klintup-Makinen (KM) assessment. KM score was assessed in a 4-point scale, from 0 (no increase) to 3 (florid infiltrate at invasive edge with cancer cell destructions).

Results The median number of expanded TILs per fragment after initial expansion was 1.1x10^5 cells (range: 0.16 – 8.75 x10^5) With cutoff value of 0.8x10^5 cells per fragment, successful culture rate was 66.7% (10 of 15 cases). The mean proportion of CD4+ and CD8+ T cells were 69.4% and 32.5%, respectively. The mean proportion of effector memory, effector, central memory, and naïve T cells were 73.1%, 7.8%, 1.4%, and 0.8%, respectively. Number of expanded TILs per fragment and the level of stromal TILs showed no statistical correlation (Kruskal-Wallis test, p=0.258). However, number of expanded TILs per fragment and KM score showed significant association (p=0.006). Histologically, intratumoral percentage of tumor cells, stroma, necrosis, and mucin showed no statistical correlation to expanded TILs per fragment (p=0.36, p=0.286, p=0.563, and p=0.27, respectively), and tumor size also did not show statistical correlation to expanded TILs per fragment (simple regression, p=0.122). We also reviewed patients' MSI status and history of chemotherapy after metastasis, and neither showed statistical correlation (Mann-Whitney U test, p=0.782 and p=0.661, respectively).

Conclusions Expansion of TILs from colorectal cancer liver metastasis was successfully performed, and assessment of inflammatory cell infiltrate at the invasive margin may be helpful in estimating the number of obtainable TILs before the initial expansion. Together, these data could be used for further studies to establish the effective ACT in colorectal cancer patients.