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Intra-lesion injection of activated Natural Killer (NK) cells in recurrent malignant brain tumors

Niloufar Shayan Asl¹, Maryam Behfar², Rouzbeh Shams Amiri³, Rashin Mohseni⁴, Masoumeh Azimi¹, Javad Firouzi¹, Mohammad Faranoush⁵, Amirhossein Izadpanah¹, Monireh Mohammad¹, Amir Ali Hamidieh⁶, Zohreh Habibi⁷, Marzieh Ebrahimi⁸

Affiliations

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Abstract

Despite multi-modal therapies for patients with malignant brain tumors, their median survival is < 2 years. Recently, NK cells have provided cancer immune surveillance through their direct natural cytotoxicity and by modulating dendritic cells to enhance the presentation of tumor antigens and regulate T-cell-mediated antitumor responses. However, the success of this treatment modality in brain tumors is unclear. The main reasons are; the brain tumor microenvironment, the NK cell preparations and administration, and the donor selection. Our previous study showed that intracranial injection of activated haploidentical NK cells resulted in the eradication of glioblastoma tumor mass in the animal model without any evidence of tumor recurrence. Therefore, in the present study, we evaluated the safety of intra-surgical cavity or intra cerebrospinal fluid (CSF) Injection of ex vivo activated haploidentical NK cells in six patients with recurrent glioblastoma multiform (GBM) and malignant brain tumors resistance to chemo/radiotherapy. Our results indicated that activated haploidentical NK cells express activator and inhibitor markers and can kill the tumor cells. However, their cytotoxic potential on patient-derived GBM (PD-GBM) was more than that of its cell line. Also, their infusion increased the overall disease control rate by about 33.3%, with a mean survival of 400 days. Moreover, we showed that local administration of the activated haploidentical NK cells in malignant brain tumors is safe, feasible, tolerated at higher doses, and cost-effective.

Keywords: Haploidentical NK cells; NK Cell Therapy; Recurrent Glioblastoma multiform.

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