IMMUNOLOGIC THERAPY (IMT)

IMT-1

A TRANSLATIONAL RESEARCH FOR PRACTICAL USE OF DENDRITIC CELL-BASED IMMUNOTHERAPY AGAINST MALIGNANT GLIOMA

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Background: Although a therapeutic effect of dendritic cell (DC)-based immunotherapy, a kind of regenerative medicine, has been recognized in various types of cancer including malignant glioma, it is still impractical because of several unsolved problems. This study is aimed to solve the problems in regenerative medicine through a clinical trial of immunotherapy using fusions of DCs and glioma cells (GCs) against malignant glioma, and to put it into practical use. Methods: Primary cultured GCs and glioma stem cells (GSCs) were generated from surgical specimens of patient. DCs were generated from PBMC of same patient, and were fused with GCs and GSCs. The entire process of cell production must be performed by pairs of two cell-culture operators in a dedicated cell processing facility. We developed a remote cell-observation system for reducing hands work of operators. As a project to establish a preservation method, cryopreservation of glioma tissues, GCs/GSCs, DCs and fusion cells followed by their viability examination. Results: The remote cell-observation system worked stable in morphological observation and cell-counting for adhesion cells. A growth curve was also automatically and accurately created. Although a morphological observation of floating cells such as GSCs and DCs was possible, there was some error in counting of those cells. A project to establish a preservation method is currently underway, including the development of storage containers and storage liquids. Conclusions: Although the remote cell-observation system required some modifications at the observation site, depth of focus, etc. for floating cells, there was no problem in accuracy for adhesion cells compared with operator's observation. This system, which can be easily installed at low cost, seemed to be helpful for practical use of regenerative medical products including this therapy. We are working on a project to establish a stable transportation and preservation method for prevalence of this treatment.

Key words: glioma | immunotherapy | dendritic cell

SURGICAL/INTRAOPERATIVE THERAPY/ MONITORING (STMO)

STMO-3

MID- TO LONG-TERM OUTCOME OF SUPRATOTAL RESECTION OF IDH1 WILD-TYPE GLIOBLASTOMA BASED ON 11C-METHIONINE PET: A RETROSPECTIVE, SINGLE-CENTER STUDY

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Purpose: Mid- to long-term outcome in glioblastoma (GBM) patients following supratotal resection (SupTR), involving complete resection both of contrast-enhancing enhanced (CE) tumors and areas of methionine (Met) uptake on ^{11}C-Met positron emission tomography (Met-PET), are not clarified. **Methods.**: A retrospective, single-center review was performed in newly diagnosed, *IDH1* wild-type GBM patients, comparing SupTR with gross total resection (GTR), in which only CE tumor tissue was completely resected. Only patients who were operated on until November 2019 were included for evaluation of mid- to long-term outcome. Following resection, all patients underwent standard radiotherapy and temozolomide treatment, and were followed for progression-free survival (PFS) and overall survival (OS). **Results:** Among the 30 patients included in this study, 7 underwent SupTR and 23 underwent GTR. Awake craniotomy with cortical and subcortical mapping was more frequently performed in the SupTR group than in the GTR group. During the follow-up period, significantly different patterns of disease progression were observed between groups. Although more than 80% of recurrences were local in the GTR group, all recurrences in the SupTR group were distant. Median PFS in the GTR and SupTR groups was 8.8 months (95% confidence interval [CI], 5.2–14.9) and 27.8 months (95% CI, 6.0-not estimable) respectively (p=0.08 by log-rank test). Median OS was 17.7 months (95% CI, 14.2–35.1) in GTR and not reached (95% CI, 30.5-not estimable) in SupTR, respectively; this difference was statistically significant (p=0.03 by log-rank test). No postoperative neurocognitive impairment was observed in SupTR patients. **Conclusion:** Compared to GTR alone, SupTR strategy with aggressive resection of both CE tumors and Met uptake area in GBM patients under awake craniotomy with functional preservation results in a survival benefit associated with better local control.

Key words: supratotal resection | Glioblastoma | positron emission tomography

STMO-5

UTILIZATION OF INTRAOPERATIVE MULTIMODAL TECHNOLOGIES [PET AND 5-ALA] FOR TREATING GLIOBLASTOMA

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Background: We can improve prognosis of glioblastoma by using positron emission tomography (PET) scans to guide them in removing tumors, and intraoperative magnetic resonance imaging (IoMRI) and 5-aminolevulinic acid (5-ALA) for identifying residual tumors. Tau proteins are reported to accumulate in glioblastomas, so we compared the efficacy of their PET tracer, THK5351, against that of ^{11}C-MET, ^{18}F-FLT, and ^{18}F-FMISO. Methods: Patients (n = 11) underwent scans between February 2020 and July 2021 for glioblastoma resection. Tumor-to-normal tissue accumulation ratio (TNR) and accumulation volumes of 4 PET tracers were evaluated. Following excisions, 5-ALA fluorescent evaluation was classified as strong, vague, or none. Residual tumor volumes and removal rates were determined using T1Gd assessments and PET tracers. IoMRI confirmed presence of residual tumors.Results: THK5351 had a TNR of 5.20, and its accumulated volume was greater than that of other tracers: 1.80 for ^{11}C-MET, 1.72 for ^{18}F-FLT, and 2.82 for ^{18}F-FMISO. 5-ALA fluorescent evaluation was vague (n = 7) or none (n = 4); respective residual tumor volumes (mL) were 2.3 and 0.2 (T1Gd), 5.7 and 0.9 (^{11}C-MET), 5.6 and 0.6 (^{18}F-FLT), 1.3 and 0.4 (^{18}F-FMISO), and 7 and 1.4 (THK5351); respective tumor removal rates (%) were 90.4 and 99.6 (T1Gd), 79.2 and 86.4 (^{11}C-MET), 84.4 and 89.2 (^{18}F-FLT), 94.3 and 94.4 (^{18}F-FMISO), and 72.3 and 83.4 (THK5351). The excised tumor tissue was found in the area where only THK5351 was accumulated.Conclusions: THK5351 accumulated in glioblastomas to a greater degree than that of other tracers, making it useful for discriminating between healthy and malignant tissues.

Key words: Glioblastoma | Positron Emission Tomograohy | 5-aminolevulinic acid

STMO-6

IMPACT OF THE EXTENT OF RESECTION ON THE SURVIVAL OF PATIENTS WITH LOWER GRADE GLIOMAS USING AWAKE BRAIN MAPPING

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Purpose: The aim of this study was to assess the effect of the extent of resection (EOR) of tumors on survival in a series of patients with lower-grade gliomas (LGGs) who underwent awake brain mapping. Methods: We retrospectively analyzed 126 patients with LGGs in the dominant and non-dominant hemisphere who underwent awake brain surgery at the same institution between December 2012 and May 2020. Results: The median progression-free survival (PFS) rate of patients with LGGs in the group with an EOR >100 %, including supratotal resection (n = 47; median survival [MS], not reached), was significantly higher than that in the group with an EOR <100% (n = 79; MS, 43.1 months; 95% CI: 37.8–48.4 months; p = 0.04). In patients with diffuse astrocytomas and anaplastic astrocytomas, the group with EOR >100 %, including supratotal resection (n = 25; MS, not reached), demonstrated a significantly better PFS rate than did the group with an EOR <100% (n = 45; MS, 35.8 months; 95% CI: 19.9–51.6 months; p = 0.03). Supratotal or gross total resection was correlated with better PFS in IDH-mutant type of diffuse astrocytomas and anaplastic astrocytomas (n = 19; MS, not reached vs. n = 35; MS, 40.6 months; 95% CI: 22.3–59.0 months; p = 0.02). By contrast, supratotal or gross total resection was not associated with longer PFS rates in patients with IDH-wild type of diffuse astrocytomas and anaplastic astrocytomas. Conclusions: It is noteworthy that supratotal or gross total resection significantly correlated with better PFS in IDH-mutant type of WHO grade II and III astrocytic tumors. In light of our finding that EOR did not correlate with PFS in patients with aggressive IDH-wild type of diffuse astrocytomas and anaplastic