The anti-tumor effect of the fibrin glue mixed with temozolomide againstmalignant glioma, an in vivomodel.

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Abstract:

BACKGROUND: Temozolomide (TMZ) is the most common chemotherapeutic drug for glioblastoma (GBM) and malignant brain tumor. Previous studies showed that the treatment with TMZ induced autophagy, apoptosis and senescence in cancer cells. In this study, we focused on fibrin glue as drug delivery system (DDS) for administering a high concentration of TMZ in glioma cells. MATERIALS AND METHODS: We used 3 malignant glioma cell lines (U87MG, two established cell lines). These cell suspensions were injected into the back of nude mice to make the subcutaneous tumor. After a few days, the various condition fibrin glue sheets were placed in contact with subcutaneous tumor (4groups, n = 6/group). We measured the tumor size in the certain period and performed immunohistochemical staining to evaluate the effect of fibrin glue mixedTMZ(F.G-TMZ) against the subcutaneous tumor. Further, the purpose of investigating the effect on the normal brain, we placed F.G-TMZ on the surface of mice brain. After 48hours and 2weeks, brains were removed and the slices were immunohistochemically stained (H.E, GFAP, COX2, etc.) to evaluate the effect of fibrin glue mixed TMZ against normal brain. RESULTS: The observation periods of sucutaneous tumor were 26-28days. All mice didn't die and no significant adverse effects were observed during the period. In all cell lines, F.G-TMZsignificantly suppressed the growth of subcutaneous tumor size than the other conditions. Immunohistochemical study showed that F.G-TMZ induced autophagy, apoptosis, senescence to the subcutaneous tumor. Further, severe inflammation, edema and demyelination caused by F.G-TMZ didn't occur in the normal mice brain at acute phase and chronic phase. CONCLUSIONS: F.G-TMZ would be a new tool of drug delivery system against malignant

brain tumor.