Antitumor effect of fibrin glue containing temozolomide against malignant glioma.

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Abstract:

Temozolomide (TMZ), used to treat glioblastoma and malignant glioma, induces autophagy, apoptosis and senescence in cancer cells. We investigated fibrin glue (FG) as a drug delivery system for the local administration of high-concentration TMZ aimed at preventing glioma recurrence. Our high-power liquid chromatography studies indicated that FG containing TMZ (TMZ-FG) manifested a sustained drug release potential. We prepared a subcutaneous tumor model by injecting groups of mice with three malignant glioma cell lines and examined the antitumor effect of TMZ-FG. We estimated the tumor volume and performed immunostaining and immunoblotting using antibodies to Ki-67, cleaved caspase 3, LC3 and p16. When FG sheets containing TMZ (TMZ-FGS) were inserted beneath the tumors, their growth was significantly suppressed. In mice treated with peroral TMZ plus TMZ-FGS the tumors tended to be smaller than in mice whose tumors were treated with TMZ-FGS or peroral TMZ alone. The TMZ-FGS induced autophagy, apoptosis and senescence in subcutaneous glioma tumor cells. To assess the safety of TMZ-FG for normal brain, we placed it directly on the brain of living mice and stained tissue sections obtained in the acute and chronic phase immunohistochemically. In both phases, TMZ-FG failed to severely damage normal brain tissue. TMZ-FG may represent a safe new drug delivery system with sustained drug release potential to treat malignant glioma.