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Cancer Lett. 2009 Nov 26. [Epub ahead of print]

Therapeutic effect of genetically engineered mesenchymal stem cells in rat experimental leptomeningeal glioma model.

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Disseminating disease of high grade gliomas is difficult to treat. We examined the therapeutic effect of intrathecal administration of mesenchymal stem cells transduced with herpes simplex virus-thymidine kinase gene (MSCtk) followed by systemic ganciclovir (GCV) administration in rat experimental leptomeningeal glioma model. First, to examine in vivo bystander effect, rats were intrathecally co-injected with a mixture of MSCtk and C6 cells and then, intraperitoneally administered with GCV or saline for 10days (co-injection model). Next, to examine the therapeutic effect of MSCtk/GCV therapy, MSCtk cells were intrathecally administered 1day after C6 injection and then, GCV or saline was administered (treatment model). GCV administration significantly reduced tumor size on day 14 both in the co-injection model (0.41 ± 0.22 vs. 3.10 ± 0.97 mm², $p < 0.01$) and in the treatment model (0.73 ± 0.29 vs. 2.84 ± 0.82 mm², $p < 0.01$). Survival was also significantly prolonged in GCV group both in the co-injection model (29.2 ± 3.3 vs. 18.8 ± 0.8 days, $p < 0.001$) and in the treatment model (21.5 ± 1.5 vs. 17.2 ± 0.5 days, $p < 0.001$). This study provided a novel treatment strategy for leptomeningeal glioma dissemination using intrathecal MSCtk injection followed by systemic GCV administration.

PMID: 19945214 [PubMed - as supplied by publisher]

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