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In vivo tracking of superparamagnetic iron oxide nanoparticle-labeled mesenchymal stem cell tropism to malignant gliomas using magnetic resonance imaging
Laboratory investigation

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Abbreviations used in this paper: DMEM = Dulbecco modified Eagle medium; EDTA = ethylenediaminetetraacetic acid; EGFP = enhanced green fluorescent protein; FBS = fetal bovine serum; MR = magnetic resonance; MSC = mesenchymal stem cell; NSC = neural stem cell; PBS = phosphate-buffered saline; PFA = paraformaldehyde; SDF-1 = stromal cell-derived factor-1; SPIO = super-paramagnetic iron oxide nanoparticles.

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Object

Mesenchymal stem cells (MSCs) have been shown to migrate toward tumors, but their distribution pattern in gliomas has not been completely portrayed. The primary purpose of the study was to assay the tropism capacity of MSCs to gliomas, to delineate the pattern of MSC distribution in gliomas after systemic injection, and to track the migration and incorporation of magnetically labeled MSCs using 1.5-T magnetic resonance (MR) imaging.

Methods

The MSCs from Fischer 344 rats were colabeled with superparamagnetic iron oxide nanoparticles (SPIO) and enhanced green fluorescent protein (EGFP). The tropism capacity of MSCs was quantitatively assayed in vitro using the Transwell system. To track the migration of MSCs in vivo, MR imaging was performed both 7 and 14 days after systemic administration of labeled MSCs. After MR imaging, the distribution patterns of MSCs in rats with gliomas were examined using Prussian blue and fluorescence staining.

Results

The in vitro study showed that MSCs possessed significantly greater migratory capacity than fibroblast cells ($p < 0.001$) and that lysis of F98 glioma cells and cultured F98 cells showed a greater capacity to induce migration of cells than other stimuli ($p < 0.05$). Seven days after MSC transplantation, the SPIO-EGFP colabeled cells were distributed throughout the tumor, where a well-defined dark hypointense region was represented on gradient echo sequences. After 14 days, most of the colabeled MSCs were found at the border between the tumor and normal parenchyma, which was represented on gradient echo sequences as diluted amorphous dark areas at the edge of the tumors.

Conclusions

This study demonstrated that systemically transplanted MSCs migrate toward gliomas with high specificity in a temporal-spatial pattern, which can be tracked using MR imaging.

KEYWORDS: glioma; magnetic resonance imaging; mesenchymal stem cell; migration; rat; superparamagnetic iron oxide nanoparticle.

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