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Distinguishing inflammation from tumor and peritumoral edema by myeloperoxidase magnetic resonance imaging.

Kleijn A, Chen JW, Buhrman JS, Wojtkiewicz GR, Iwamoto Y, Lamfers ML, Stemmer-Rachamimov AO, Rabkin SD, Weissleder R, Martuza RL, Fulci G.

Brain Tumor Research Center, Massachusetts General Hospital, Boston, Massachusetts, USA.

Abstract

PURPOSE: Inflammation occurs routinely when managing gliomas and is not easily distinguishable from tumor regrowth by current MRI methods. The lack of noninvasive technologies that monitor inflammation prevents us to understand whether it is beneficial or detrimental for the patient, and current therapies do not take this host response in consideration. We aim to establish whether a gadolinium (Gd)-based agent targeting the inflammatory enzyme myeloperoxidase (MPO) can selectively detect intra- and peritumoral inflammation as well as glioma response to treatment by MRI. **Methods:** We carried out serial Gd-bis-5-HT-DTPA (MPO-Gd) MRI before and after treating rodent gliomas with different doses of oncolytic virus (OV) and analyzed animal survival. The imaging results were compared with histopathologic and molecular analyses of the tumors for macrophage/microglia infiltration, virus persistence, and MPO levels.

RESULTS: Elevated MPO activity was observed by MRI inside the tumor and in the peritumoral cerebrum at day 1 post-OV injection, which corresponded with activation/infiltration of myeloid cells inhibiting OV intratumoral persistence. MPO activity decreased, whereas tumor size increased, as the virus and the immune cells were cleared (days 1-7 post-OV injection). A 10-fold increase in viral dose temporally decreased tumor size, but augmented MPO activity, thus preventing extension of viral intratumoral persistence.

CONCLUSIONS: MPO-Gd MRI can distinguish enhancement patterns that reflect treatment-induced spatiotemporal changes of intratumoral and intracerebral inflammation from those indicating tumor and peritumoral edema. This technology improves the posttreatment diagnosis of gliomas and will increase our understanding of the role of inflammation in cancer therapy.

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