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Radiation-induced astrogliosis and blood-brain barrier damage can be abrogated using anti-TNF treatment.

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PURPOSE: In this article, we investigate the role of tumor necrosis factor-alpha (TNF) in the initiation of acute damage to the blood-brain barrier (BBB) and brain tissue following radiotherapy (RT) for CNS tumors. **METHODS AND MATERIALS:** Intravital microscopy and a closed cranial window technique were used to measure quantitatively BBB permeability to FITC-dextran 4.4-kDa molecules, leukocyte adhesion (Rhodamine-6G) and vessel diameters before and after 20-Gy cranial radiation with and without treatment with anti-TNF. Immunohistochemistry was used to quantify astrogliosis post-RT and immunofluorescence was used to visualize protein expression of TNF and ICAM-1 post-RT. Recombinant TNF (rTNF) was used to elucidate the role of TNF in leukocyte adhesion and vessel diameter. **RESULTS:** Mice treated with anti-TNF showed significantly lower permeability and leukocyte adhesion at 24 and 48 h post-RT vs. RT-only animals. We observed a significant decrease in arteriole diameters at 48 h post-RT that was inhibited in TNF-treated animals. We also saw a significant increase in activated astrocytes following RT that was significantly lower in the anti-TNF-treated group. In addition, immunofluorescence showed protein expression of TNF and ICAM-1 in the cerebral cortex that was inhibited with anti-TNF treatment. Finally, administration of rTNF induced a decrease in arteriole diameter and a significant increase in leukocyte adhesion in venules and arterioles. **CONCLUSIONS:** TNF plays a significant role in acute changes in BBB permeability, leukocyte adhesion, arteriole diameter, and astrocyte activation following cranial radiation. Treatment with anti-TNF protects the brain's microvascular network from the acute damage following RT.

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