Comment: Chemoradiotherapy for glioblastoma patients—The double-edged sword

It has been a decade since the Stupp regimen supplanted other treatments for glioblastoma, increasing 2-year survival from 10% to 26%.[1] As our patients are living longer, they are beginning to experience more neurotoxicity. An interesting, small longitudinal MRI study, performed at Massachusetts General Hospital, involved 14 patients, ages 35–70 years, with glioblastoma treated with radiotherapy plus concomitant and adjuvant temozolomide.[2] As testimony to the difficulty of studying this population, death, clinical decline, or transfer to other trials left only 3 patients remaining at 35 weeks.

To control for tissue distortion caused by mass effect and midline shift, eligible patients had tumor confined to one hemisphere, with the comparative volumetric data taken from the contralateral hemisphere. Using quantitative neuroimaging, the authors showed volumetric decreases in whole brain and gray matter, surprisingly without substantial white matter change. Diffusion tensor imaging measures included apparent diffusion coefficient, which was significantly increased in the subventricular zone (SVZ). As neural progenitor cells reside in the SVZ and are particularly vulnerable to the neurotoxic effects of radiation and chemotherapy, the authors suggest the possibility of microvascular disruption specific to this site.

A limitation of this study is that neurocognitive assessments were not performed. Others[3] have found that changes in white matter fractional anisotropy correlate with decreases in verbal memory, attention, and digit span in young patients with breast cancer treated with chemotherapy. It is possible that early changes in brain volume might serve as an early warning system for potential worse cognitive outcome, allowing us to truncate additional chemotherapy. As the Stupp regimen is also used for younger patients with oligodendroglioma, who also survive longer, the weighing of the benefits and harms of treatment become even more important.

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2. Prust MJ, Jafari-Khouzani K, Kalpathy-Cramer J, et al. Standard chemoradiation for glioblastoma results in progressive brain volume loss. Neurology 2015;85:xxx–xxx.
3. Deprez S, Amant F, Smeets A, et al. Longitudinal assessment of chemotherapy-induced structural changes in cerebral white matter and its correlation with impaired cognitive functioning. J Clin Oncol 2012;30:274–281.

Lynne P. Taylor, MD

From Virginia Mason Medical Center, Seattle, WA; University of Washington, Seattle; and Tufts University School of Medicine, Boston, MA.

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