Extended Abstract

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3rd International Conference on Radiology and Imaging, August 24-26, 2015, Toronto, Canada - Irradiation in central nervous system tumors

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Historically the treatment of brain metastases is viewed with skepticism. The hospitalization by itself prolongs life by one - two months. Treatments with steroids reduce symptoms, but effect is short. Whole Brain Radiotherapy (WBRT) have been made mainstay for several decades, increasing survival up to six months, but it has been associated with neurocognitive impairment. Several experimental strategies of radiation-induced central nervous system toxicity prevention have recently resulted in encouraging data. The present review summarizes the background for this research and the treatment results. It extends to the perspectives of tissue regeneration strategies, based for example on stem and progenitor cells. Preliminary data suggest a scenario with individually tailored strategies where patients with certain types of comorbidity, resulting in impaired regeneration reserve capacity, might be considered for toxicity prevention, while others might be “salvaged” by delayed interventions that circumvent the problem of normal tissue specificity. Given the complexity of radiation-induced changes, single target interventions might not suffice. Future interventions might vary with patient age, elapsed time from radiotherapy and toxicity type. Potential components include several drugs that interact with neurodegeneration, cell transplantation (into the CNS itself, the blood stream, or both) and creation of reparative signals and a permissive microenvironment, e.g., for cell homing. Without manipulation of the stem cell niche either by cell transfection or addition of appropriate chemokines and growth factors and by providing normal perfusion of the affected region, durable success of such cell-based approaches is hard to imagine. The risk of permanent central nervous system (CNS) toxicity, which typically becomes detectable after an asymptomatic latency period, continues to influence clinical treatment decisions. Interindividual differences in sensitivity result in a certain variability of the threshold dose and preclude administration of a guaranteed safe dose, even in the current era of high-precision image-guided radiotherapy. There were 285 CNS tumors (67 gliomas, 107 meningiomas, 49 schwannomas, and 64 other/NOS tumors) among 105,444 individuals with radiation dose estimates to the brain contributing 3.1 million person-years of observation. Based on a simple linear model without effect modification, ERR/Gy was 1.67 (95% confidence interval, CI: 0.12 to 5.26) for glioma, 1.82 (95% CI: 0.51 to 4.30) for meningioma, 1.45 (95% CI: - 0.01 to 4.97) for schwannoma, and 1.40 (95% CI: 0.61 to 2.57) for all CNS tumors as a group. For each tumor type, the dose-response was according to linearity and seemed to be stronger among males than among females, particularly for meningioma (P = 0.045). There was also evidence that the ERR/Gy for schwannoma decreased with attained age (P = 0.002). Elevated risks for brain/CNS tumors were consistently observed in reference to radiation exposure, but the strength of this association varied across cohorts. The easiest and most effective way of avoiding CNS side effects is to minimize the dose of radiation. This does, however, not solve the problem of normal tissue present within the target volume, for example due to diffuse microscopic spread, which escapes current imaging technology. For certain groups of patients, further progress can only be expected from efforts directed at widening the therapeutic window between tumor and normal tissue through specific modulation of their responses to ra-

Note: This work is partly presented at Euroscicon conference on Advanced Nanotechnology, April on 18-19, 2019 held at Paris, France

diotherapy (e.g., toxicity prevention) or from delayed intervention such as tissue regeneration strategies. Both prevention and treatment of side effects have their specific advantages and disadvantages. Importantly, they are not standard clinical options at this time. To exploit potential targets for intervention, we will discuss the pathogenesis of radiation-induced CNS toxicity and review preclinical data on prevention and tissue regeneration. We focus on two types of damage, i.e. neurocognitive decline and radiation necrosis. The latter is relevant to treatment of the brain and the spinal cord. On the other hand, when possible surgery is is the gold standard indication in a single or with significant mass effect lesions. In the past decade radiosurgery has become a very popular alternative, with high efficiency and few side effects, but until now 3D conformal radiotherapy or IMRT continue to be most employee techniques, including WBRT with hippocampal sparing

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