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Early impairment of spatial cognition after local brain irradiation with carbon ions

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Cerebral dysfunction is one of the major concerns associated with radiotherapy of brain tumors and acute lymphoblastic leukemia. Side effects such as learning impairment and cognitive dysfunction are reported on the central nervous system (CNS) tissue after exposure to radiation during cancer therapy. This study investigated early effects on the cognitive function and microvessel density (MVD) after local brain irradiation with carbon ions using mice. Irradiation was carried out a 290 MeV/u 5 mm SOBP (Spread out Bragg Peak) carbon beam with 7.6 cm diameter produced by the Heavy Ions Medical Accelerator in Chiba (HIMAC) at the National Institute of Radiological Sciences, Japan. The irradiation dose was set at level known to produce vascular change followed by necrosis, which appeared the late period after irradiation with 30 Gy. The whole of brain was irradiated, excluding eyes and brain stem. The mice irradiated with single dose of 30 Gy showed deficit in short-term working memory assessed at 36 hr after irradiation, whereas mice receiving carbon irradiation showed no deficit in long-term reference memory. At 16 weeks after irradiation, the irradiated mice showed marked learning impairment compared with age-matched controls and the irradiated mice showed substantial impairment of working memory.

Histopathological observation revealed no abnormal finding in the irradiated brain at 1 week after irradiation, although irradiated mice showed marked neuronal degeneration at the hippocampus within CA1 to CA3 layers at 16 weeks after irradiation. In the irradiated group, neuronal cells in the hippocampal CA1-3 areas were reduced by 30-49%. However, MVD of the hippocampus decreased rapidly from 1 week after irradiation. The cerebral MVD also declined from 1 to 12 weeks and radiation vasculopathy generally was dose and time dependent.

It is possibility that radiation-induced degeneration of neuronal cells caused by same mechanism as the ischemia follow vasculature breakdown. These results furthermore suggested that high LET beam with carbon-ions have severely induce neuronal degeneration by vasculature breakdown.

Primary author: Dr TAKAI, Nobuhiko (Pharmaceutical Sciences, Nagasaki International University)

Co-authors: Mrs UZAWA, Akiko (Research Center for Charged Particle Therapy, National Institute of Radiological Sciences); Dr HIRAYAMA, Ryoichi (Research Center for Charged Particle Therapy, National Institute of Radiological Sciences); Dr NAKAMURA, Saori (Pharmaceutical Sciences, Nagasaki International University); Prof. OHBA, Yoshihito (Pharmaceutical Sciences, Nagasaki International University); Dr MATSUMOTO, Yoshitaka (Research Center for Charged Particle Therapy, National Institute of Radiological Sciences); Dr FURUSAWA, Yoshiya (Research Center for Charged Particle Therapy, National Institute of Radiological Sciences)

Presenter: Dr TAKAI, Nobuhiko (Pharmaceutical Sciences, Nagasaki International University)

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