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Urinary 8-hydroxy-2'-deoxyguanosine levels are elevated in patients with IDH1-wildtype glioblastoma and are associated with tumor recurrence in gliomas

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Abstract

2021 World Health Organization (WHO) Central Nervous System (CNS) Tumor Classification includes molecular diagnostic parameters such as isocitrate dehydrogenase (IDH) mutation or 1p19q codeletion status, in addition to the classical histological classification. Several studies have revealed that patients with IDH1 mutation have a longer survival rate compared to wildtype individuals. In glioma cells, increased oxidative stress has been identified. However, till now, the relation between oxidative stress levels and IDH1 mutation status in those patients was not examined. Therefore, the aim of this study was to investigate the urinary levels of oxidatively induced DNA damage products, 8-hydroxy-2'- deoxyguanosine (8-OH-dG), (5'R) and (5'S)-8,5'-cyclo-2'-deoxyadenosines (R-cdA and S-cdA) as reliable oxidative stress markers in patients with IDH1-wildtype (n = 20) and IDH1-mutant (n = 22) glioma. Absolute quantification of 8-OH-dG, R-cdA and S-cdA was achieved by liquid chromatography-tandem mass spectrometry with isotope dilution. The levels of 8-OH-dG were significantly greater in IDH1-wildtype glioma patients than those in IDH1-mutant ones (p = 0.017). No statistically significant difference was observed for R-cdA and S-cdA levels. 8-OH-dG levels were positively correlated with patients' tumor recurrence in all patients (r = 0.382, p = 0.014). The mutation status of glioma is well correlated with oxidative stress. Examination of noninvasively measured oxidative DNA damage products along with IDH1 mutation status in glioma patients, might be particularly important in terms of evaluating and monitoring the effectiveness of treatment.

Keywords: 8,5′-cyclo-2′-deoxyadenosines; 8-hydroxy-2′-deoxyguanosine; Gliomas; Isocitrate dehydrogenase-1; Molecular diagnosis; Oxidatively induced DNA damage.

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