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Mitigation of Acute Radiation-Induced Brain Injury by Anlotinib: A Meaningful Study

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Radiation therapy is one of the most commonly used treatments for primary and metastatic cranial tumors [1,2], it plays an important role in the radical and palliative treatment of brain tumor patients. With the continuous development of radiotherapy technology, the problem of radiation-induced brain injury (RBI) has received increasing attention. RBI is categorized into acute injury, early delayed injury, and late delayed injury [3]. RBI can cause central nervous system damage, resulting in some degree of cognitive impairment [4-6].

In recent years, many scholars have conducted a series of studies on the prevention and treatment of RBI. Studies have found that the Nerve growth factor (NGF) and Shenqi Fuzheng Injection (SFI) can alleviate RBI [7,8]. Moreover, numerous studies have shown that Bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor, can reduce vascular permeability, normalize the blood-brain barrier, and reduce vasogenic brain edema, thereby effectively inhibiting the progression of RBI [9-13]. However, the anti-VEGFR antibody anlotinib has not attracted attention.

Previously, GAO et al.'s animal experiments on the mitigation of RBI by anlotinib were of great interest [14]. The authors evaluated changes in demyelination, glial cell activation, hypoxia, and microvascular permeability after anlotinib treatment by establishing a mouse model of RBI. The experiments showed that anlotinib, a small-molecule inhibitor of multireceptor tyrosine kinases, improved intra-tumor oxygenation and caused downregulation of hypoxia-inducible factor-1α (HIF-1α) by inhibiting the VEGF/VEGFR2 pathway. Inhibition of HIF-1α reduces the development of RBI in an animal model [15]. Although, anlotinib failed to inhibit the development of demyelination, anlotinib treatment significantly attenuated the adverse effects of acute RBI in a dose-dependent manner by down-regulating astrocyte activation, ameliorating cerebral hypoxia, and alleviating cerebral edema[14].

GAO et al.'s [14] study elucidated the palliative effect of anlotinib on acute RBI at the molecular level, which clearly

pointed the way to new ideas for deeper mechanistic studies to follow. In the future, the prevention and treatment of RBI is still a subject to be investigated. In the next phase of the experiment, it can be further explored whether anlotinib has a mitigating effect on delayed-phase RBI. And imaging studies can be added to analyze and record the location, morphology, signal manifestation, edema extent, and enhancement characteristics of the lesions after enhancement of the radiation injury lesions. Three non-invasive techniques: MRI, PET, and MRS can be biomarkers to identify the onset and progression of radiation-induced cognitive deficits [16]. Therefore, further observation of the effect of anlotinib on the mitigation of RBI by combined MRI, MRS and PET imaging means is important for the judgment of the degree of RBI, the selection of drug dosage, and the determination of the time of drug administration.

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