Diffuse astrocytic tumor and oligodendroglial tumor

The term “glioma” could technically be used to refer to all tumors of any glial lineage (i.e., from glial cells such as oligodendroglia, ependymal cells, Schwann cells, microglia…), but in its common usage, “glioma” usually refers only to astrocytic tumors.

According to the World Health Organization Classification of Tumors of the Central Nervous System 2016 diffuse astrocytic tumor and oligodendroglial tumors are differentiated by the presence of isocitrate dehydrogenase 1 or 2 (IDH1/2) mutation and the combined loss of the short arm of chromosome 1 and the long arm of chromosome 19 (1p/19q co-deletion). Diffuse astrocytoma IDH mutant often has p53 and alpha-thalassemia/mental retardation syndrome X-linked (ATRX) mutation, showing the alternative lengthening of telomeres (ALT) phenotype, while Oligodendroglioma, IDH-mutant & 1p/19q-codeleted often have wild-type p53 and telomerase reverse transcriptase (TERT) promoter mutation, showing telomerase activation. Ohba et al. analyzed IDH, ATRX, and TERT promoter mutations, and the correlation between them. Immortalized cells overcome the telomere-related crisis by activating telomerase or ALT. In glioma, telomerase is mainly activated by TERT promoter mutation, while ALT is usually associated with ATRX mutation. Although the mechanism of how ATRX mutation induces ALT remains unclear, ATRX loss alone is believed to be insufficient to induce ALT. Treatments targeting telomere maintenance are promising [1)].

Classification

see Diffuse astrocytic tumor and oligodendroglial tumor classification.

Treatment

Adults with newly diagnosed oligodendroglioma, IDH mutant, 1p/19q co-deletion CNS WHO grade II and WHO grade III should be offered radiation therapy (RT) and procarbazine, lomustine, and vincristine (PCV). Temozolomide (TMZ) is a reasonable alternative for patients who may not tolerate PCV, but no high-level evidence supports upfront TMZ in this setting. People with newly diagnosed astrocytoma, IDH-mutant, non 1p/19q co-deletion CNS WHO grade II should be offered RT with adjuvant chemotherapy (TMZ or PCV). People with astrocytoma, IDH mutant, non 1p/19q co-deletion CNS WHO grade III should be offered RT and adjuvant TMZ. People with astrocytoma, IDH mutant, CNS WHO grade IV may follow recommendations for either astrocytoma, IDH mutant, non 1p/19q co-deletion CNS WHO grade III or glioblastoma, IDH-wildtype, CNS WHO grade IV. Concurrent TMZ and RT should be offered to patients with newly diagnosed glioblastoma, IDH-wildtype, CNS WHO grade 4 followed by 6 months of adjuvant TMZ. Alternating electric field therapy, approved by the US Food and Drug Administration, should be considered for these patients. Bevacizumab is not recommended. In situations in which the benefits of 6-week RT plus TMZ may not outweigh the harms, hypofractionated RT plus TMZ is reasonable. In patients age ≥ 60 to ≥ 70 years, with poor performance status or for whom toxicity or prognosis are concerns, best supportive care alone, RT

alone (for MGMT promoter unmethylated tumors), or TMZ alone (for MGMT promoter methylated tumors) are reasonable treatment options. Additional information is available at www.asco.org/neurooncology-guidelines [2].

1)
Ohba S, Kuwahara K, Yamada S, Abe M, Hirose Y. Correlation between IDH, ATRX, and TERT promoter mutations in glioma. Brain Tumor Pathol. 2020 Mar 29. doi: 10.1007/s10014-020-00360-4. [Epub ahead of print] Review. PubMed PMID: 32227259.

2)
Mohile NA, Messersmith H, Gatson NT, Hottinger AF, Lassman A, Morton J, Ney D, Nghiemphu PL, Olar A, Olson J, Perry J, Portnow J, Schiff D, Shannon A, Shih HA, Strowd R, van den Bent M, Ziu M, Blakeley J. Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults: ASCO-SNO Guideline. J Clin Oncol. 2022 Feb 1;40(4):403-426. doi: 10.1200/JCO.21.02036. Epub 2021 Dec 13. PMID: 34898238.