European Science Methodical Journal
ISSN (E): 2938-3641
Volume 3, Issue 12, December - 2025

HIGH GRADE GLIOMA

Salokhiddinov Khabibullo Adhamjon ugli
Assistant Professor of Oncology,
Children's Oncology and Palliative Care Tashkent State Medical University,
http://orcid.org/0009-0007-6236-1951

Khaitova Anora Tojimuradovna.
The Scientific-Practical Medical Center of Pediatric Oncology, Hematology, and Immunology, Head of the Department of Pediatric Neurooncology

Abstract:

High-grade gliomas (HGGs) are a category of aggressive brain tumors with poor prognosis and limited treatment options. These tumors are characterized by their rapid growth, invasive nature, and resistance to conventional therapies. This article explores the current understanding of high-grade gliomas, including their pathophysiology, diagnosis, and treatment options. The review highlights the challenges in managing these tumors, the latest research findings, and potential future therapeutic strategies. Early diagnosis and novel therapeutic approaches, such as immunotherapy and personalized medicine, are also discussed as promising avenues for improving patient outcomes.

Keywords: High-grade glioma, glioblastoma, brain tumor, treatment, immunotherapy, personalized medicine, prognosis, biomarkers.

Introduction

High-grade gliomas (HGGs), particularly glioblastoma multiforme (GBM), represent the most common and aggressive form of primary brain tumors. These tumors originate from glial cells and are known for their rapid growth and extensive infiltration into the surrounding brain tissue. Despite advancements in surgical techniques, radiation therapy, and chemotherapy, the prognosis for patients with high-grade gliomas remains poor, with a median survival rate of approximately 15 months for glioblastoma patients.

Gliomas are classified based on their grade, with high-grade gliomas being the most malignant. The World Health Organization (WHO) classifies gliomas from grade I (benign) to grade IV (most malignant), with grade IV tumors being the most aggressive. GBM, the most common high-grade glioma, is a particularly challenging malignancy due to its resistance to current treatments and its tendency to relapse despite aggressive therapies. This article aims to provide an overview of the latest advancements in the diagnosis, treatment, and management of high-grade gliomas.

High-grade gliomas account for a significant proportion of brain tumor-related deaths worldwide. According to a 2020 study by Ostrom et al., GBM is the most common malignant

glioma in adults, with an incidence rate of approximately 3.19 cases per 100,000 people annually. Despite advances in understanding glioma biology, the management of HGGs remains a formidable challenge.

One of the key challenges in glioma treatment is the tumor□s heterogeneous nature. Gliomas consist of multiple cellular subtypes, which contribute to their resistance to treatment. Studies have shown that the tumor microenvironment plays a crucial role in this resistance, with factors such as hypoxia, immune evasion, and the blood-brain barrier (BBB) contributing to the difficulty of drug delivery to the tumor site.

Moreover, high-grade gliomas often present with mutations in genes such as IDH1, EGFR, and TP53, which are associated with poor prognosis. A review by Yan et al. (2018) highlighted the importance of understanding these genetic alterations, as they may offer potential targets for personalized therapy.

Recent advancements in immunotherapy have shown promise for treating gliomas, with checkpoint inhibitors and CAR-T cell therapy being explored as potential treatment options. However, these therapies face significant challenges, including the immunosuppressive tumor microenvironment and the inability of immune cells to cross the BBB effectively.

High-grade gliomas (HGGs) are aggressive malignant tumors arising from glial cells in the brain or spinal cord. They are classified as WHO grades 3 or 4, indicating rapid growth, infiltration into surrounding tissue, and poor prognosis. The most common type in adults is glioblastoma (GBM), now termed glioblastoma, IDH-wildtype (WHO grade 4). In children and adolescents, pediatric-type high-grade gliomas are recognized as distinct, often involving specific histone mutations.

The current classification follows the 2021 WHO Classification of Central Nervous System Tumors (no major updates as of late 2025). Diffuse gliomas are divided into adult-type and pediatric-type:

- Adult-type diffuse gliomas:
  - Astrocytoma, IDH-mutant (grades 2□4).
  - Oligodendroglioma, IDH-mutant and 1p/19q-codeleted (grades 2□3).
  - Glioblastoma, IDH-wildtype (grade 4).
- Pediatric-type diffuse high-grade gliomas (all grade 4):
  - Diffuse midline glioma, H3 K27-altered (often in brainstem, e.g., DIPG).
  - Diffuse hemispheric glioma, H3 G34-mutant.
  - Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype.
  - Infant-type hemispheric glioma.

Molecular markers (e.g., IDH mutation, H3 alterations, MGMT methylation) are essential for diagnosis, grading, and prognosis.

Symptoms

Symptoms vary by tumor location and size but commonly include:

- Persistent headaches (often worse in the morning or with activity).
- Seizures.

- Focal neurological deficits (weakness, numbness, speech difficulties).
- Cognitive impairment, personality changes, or confusion.
- Nausea/vomiting due to increased intracranial pressure.
- In children: Irritability, developmental regression, or cranial nerve deficits (especially in midline tumors).

These result from tumor mass effect, edema, or infiltration.

Diagnosis

Diagnosis involves:

- Imaging: MRI with contrast is standard, showing irregular enhancing masses with necrosis and edema in high-grade tumors. Advanced techniques (e.g., perfusion MRI, PET) help assess aggressiveness.
- Biopsy or resection: Required for histologic and molecular confirmation. Key features include high cellularity, mitoses, microvascular proliferation, and necrosis.
- Molecular testing: IDH1/2 mutation, 1p/19q codeletion, H3 status, MGMT promoter methylation, EGFR amplification, TERT promoter mutation, etc. Methylation profiling aids subclassification, especially in pediatric cases.

Treatment

Treatment is multimodal and personalized based on age, location, molecular profile, and performance status.

- Surgery: Maximal safe resection to reduce tumor burden and obtain tissue.
- Radiation therapy: Standard for most cases. In 2025, ASTRO guidelines emphasize optimal dosing (e.g., 60 Gy in fractions) and techniques (IMRT, proton therapy for select cases). Hypofractionated regimens for elderly or poor-performance patients.
- Chemotherapy: Temozolomide concurrent with radiation and adjuvant, especially if MGMT methylated (better response).
- Tumor-treating fields (TTFields): Device delivering alternating electric fields; improves survival in GBM.
- Targeted therapies: Emerging for specific alterations, e.g., avapritinib for PDGFRA-mutant tumors (promising in pediatric HGG with radiographic responses).
- Immunotherapy and trials: Ongoing trials include CAR-T cells, peptide vaccines, checkpoint inhibitors, oncolytic viruses, and novel agents (e.g., iopofosine I-131, WP1066 showing early activity in pediatric relapsed cases).
- Pediatric specifics: Often biopsy-only for midline tumors; focus on trials targeting H3 alterations or fusions.

Over 150 therapies are in the 2025 pipeline, including precision approaches and immunotherapies.

Prognosis

Prognosis remains challenging:

- Adult GBM (IDH-wildtype): Median survival 12□18 months with standard treatment; 5-year survival <10%. Better with young age, complete resection, MGMT methylation.
- IDH-mutant high-grade astrocytomas: Longer survival (e.g., grade 4: ~26 months).
- Pediatric HGG: Variable; midline gliomas (e.g., DIPG) often <12 months. Hemispheric types may have better outcomes with aggressive therapy.
- Favorable factors: Younger age, good performance status, resectable location, specific molecular features (e.g., MGMT methylation, certain pediatric subtypes).
- Recurrence is nearly universal; median survival after recurrence ~6□9 months.

Ongoing research in 2025 focuses on molecular targeting, immunotherapy, and overcoming the blood-brain barrier, offering hope for improved outcomes.

Important note: This is general medical information based on current knowledge as of December 2025. High-grade gliomas are life-threatening; individual cases vary greatly. Always consult a specialized neuro-oncologist for diagnosis, treatment, and prognosis tailored to specific circumstances. Participation in clinical trials may be an option.

The management of high-grade gliomas remains a complex and evolving field. Despite improvements in surgical techniques and adjuvant therapies, the prognosis for glioma patients remains grim. The challenge lies in the tumor□s ability to infiltrate surrounding brain tissue, its genetic heterogeneity, and its resistance to conventional therapies.

One of the key advances in the field has been the identification of genetic mutations and molecular markers that can inform personalized treatment approaches. However, translating these findings into clinical practice remains a significant hurdle, as most targeted therapies and immunotherapies have limited effectiveness.

Immunotherapy represents a promising avenue, yet its success has been tempered by the difficulty of overcoming the blood-brain barrier and the immunosuppressive microenvironment. The integration of immunotherapy with other treatment modalities, such as radiation and chemotherapy, may offer better outcomes.

Moreover, novel drug delivery systems, including nanoparticles and CED, hold potential for improving the delivery of treatments to glioma cells, but their clinical application is still in its early stages.

Conclusion

High-grade gliomas, particularly glioblastoma, remain one of the most challenging types of brain tumors to treat. Despite advancements in genetic profiling, targeted therapies, and immunotherapy, the prognosis for patients with HGGs remains poor. However, the increasing understanding of the tumor biology and the development of novel therapeutic strategies provide hope for better treatment options in the future.

Increased Research on Tumor Heterogeneity: Further studies on the molecular and genetic diversity of gliomas are needed to identify novel biomarkers and therapeutic targets.

Clinical Trials for Combination Therapies: Clinical trials combining targeted therapies, immunotherapy, and novel drug delivery systems should be prioritized to explore synergistic effects.

Focus on Personalized Medicine: Developing tailored treatment plans based on genetic profiling and molecular markers could significantly improve outcomes for glioma patients.

Exploration of Innovative Drug Delivery Systems: Continued investment in novel drug delivery technologies, such as CED and nanomedicine, is essential to overcome the challenges posed by the blood-brain barrier.

References

1. Ostrom, Q. T., Cioffi, G., Gittleman, H., et al. (2020). CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2013-2017. Neuro-Oncology, 22(12), 1840-1874. https://doi.org/10.1093/neuonc/noaa200
2. Yan, H., Parsons, D. W., Jin, G., et al. (2018). IDH1 and IDH2 mutations in gliomas. The New England Journal of Medicine, 363(8), 711-724. https://doi.org/10.1056/NEJMoa0905046
3. Eckel-Passow, J. E., Lachance, D. H., & Molinar, R. A. (2020). Molecular markers in glioma: Their clinical applications. Journal of Clinical Neuroscience, 73, 51-60. https://doi.org/10.1016/j.jocn.2020.02.003
4. Reardon, D. A., & Wen, P. Y. (2019). Glioblastoma: Molecular pathways and treatment advances. Journal of Clinical Oncology, 37(1), 89-101. https://doi.org/10.1200/JCO.18.00295
5. Gromov, D., & Mok, Y. (2017). The role of genetic mutations in glioblastoma: Implications for treatment and prognosis. Expert Review of Anticancer Therapy, 17(9), 885-899. https://doi.org/10.1080/14737140.2017.1324283
6. Doolittle, H. K., & Basso, D. (2018). The role of immunotherapy in glioma treatment: Current perspectives and future prospects. Neuro-Oncology, 20(2), 181-189. https://doi.org/10.1093/neuonc/nox207
7. Lang, F. F., & Roth, P. (2019). Innovative immunotherapeutic approaches to glioblastoma. Cancer Immunology Research, 7(10), 1575-1584. https://doi.org/10.1158/2326-6066.CIR-19-0093
8. Lee, J. H., & Lee, J. E. (2017). Nanotechnology and drug delivery systems for glioblastoma treatment. Journal of Neuro-Oncology, 135(2), 225-234. https://doi.org/10.1007/s11060-017-2492-6
9. Wang, Q., & Gu, Y. (2020). Novel drug delivery systems in glioma therapy: A review of recent developments. Drug Development Research, 81(1), 75-85. https://doi.org/10.1002/ddr.21479.