" High-Grade Glioma: Challenges in Diagnosis and Management" A Case Study.

Neha Ali[1]*, Raj Vishnoi[2]

Abstract:

Introduction: Gliomas are primary brain tumors arising from glial cells, categorized into low-grade and high-grade forms based on their growth characteristics. They are more prevalent in adults and are a leading cause of cancer-related deaths among young adults. Recent advancements in classification techniques, incorporating molecular features, aim to enhance survival prediction and guide treatment decisions. Diffuse gliomas, particularly glioblastoma, are the most lethal subtype of central nervous system neoplasms. Molecular and genetic indicators have significant implications for prognosis and treatment, complementing traditional histopathological assessments.

Case description: A case study of a 35-year-old woman with symptoms suggestive of a high-grade glioma is presented. Imaging revealed a mass lesion in the brain, necessitating surgical resection followed by postoperative management. The case underscores the challenges in diagnosing and managing gliomas and the importance of a multidisciplinary approach for optimal patient care.

Discussion: Highlights the aggressive nature of gliomas and the importance of complete surgical resection for improved outcomes, especially in high-grade tumors. Emerging therapies such as immunotherapy and targeted molecular treatments show promise in enhancing treatment effectiveness. Collaborative efforts among healthcare professionals are crucial for advancing the understanding and management of gliomas.

Keywords: Gliomas, primary brain tumors, glial cells, classification techniques, brain mass, surgical resection, immunotherapy, multidisciplinary approach, healthcare collaboration.

DOI Number: 10.48047/nq.2024.22.3.NQ24019 **NeuroQuantology 2024; 22(03): 173-178**

INTRODUCTION

A Glioma is a neoplasm arising from the glial cells within the brain or spinal cord. Glial cells are essential for nurturing and supporting neurons. Gliomas may occur across all age groups but are more commonly observed in adults. They are categorized as either low-grade, characterized by gradual growth, or high-grade, distinguished by rapid proliferation and aggressiveness. [1] Gliomas represent the primary cause of cancer-related mortality among adolescents and young adults. [1,2] Conventional classification techniques have constrained the efficacy of typical therapies, leading to diverse survival outcomes spanning from half a year to numerous decades. [3] Recently, there has been a transition towards a more refined categorization of diffuse gliomas. This methodology seeks to enhance the precision of survival prognostication and direct therapeutic approaches through the integration of molecular features into have progressively validated this novel classification approach as meaningful and logical, underscoring the significance of comprehending the molecular underpinnings of these neoplasms. [4.5] Tumors affecting the brain and other components of the central nervous system (CNS) rank as the eighth most prevalent form of cancer among individuals aged 40 years and above. [6]

Among CNS neoplasms, diffuse gliomas (DGs) emerge as the predominant and deadliest subtype, constituting 75% of all primary malignant brain tumors in adults. Due to their inherently aggressive nature and resistance to existing treatments, they stand as one of the most catastrophic forms of cancer. Glioblastoma, with a median diagnosis age of 46.3 years, reigns as the most prevalent (56.6%) and most aggressive form of primary brain tumors in adults, for which curative therapies are currently unavailable. [7]

***CorrespondingAuthor:-**Neha Ali
[1*]Department of Obstetrical and GynaecologicalNursing School of Nursing, Dev Bhoomi Uttarakhand University. Dehradun
[2]Department of Child Health Nursing School of Nursing, Dev Bhoomi Uttarakhand University. Dehradun

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

through histopathological assessments, including diffuse astrocytoma, oligodendrogliomas, or mixed gliomas/oligoastrocytomas. However, recent advancements have shifted towards glioma classification based on molecular and genetic indicators. These progressions offer more precise prognostic and therapeutic advantages for glioma patients. Alongside molecular and genetic markers, gliomas are graded from I to IV according to proliferation levels as indicated by the mitotic

index and the presence or absence of necrosis. [8]
There are three primary types of gliomas, differentiated by the observable characteristics of the cells they originate from: astrocytomas, ependymomas, and oligodendrogliomas. These gliomas are further categorized into low grade, atypical, and high-grade tumors based on the appearance of the cells, their rate of division, and specific molecular markers. The grading system established by the World Health Organization (WHO) relies on these molecular markers, which have demonstrated significant implications for prognosis and treatment.

Astrocytomasarise from astrocytes and can either have well-defined borders, indicating encapsulation and clear distinctions between normal and tumor cells, or they can be infiltrative, suggesting a more advanced grade. Low-grade astrocytomas are prevalent in children, while high-grade ones are more commonly found in young adults and older individuals.

Oligodendrogliomas stem from oligodendrocyte cells and tend to be less invasive compared to astrocytomas. They are more frequently diagnosed in adults.

Ependymomasoriginate from ependymal cells lining the ventricles of the brain and the central canal of the spinal cord. These tumors are commonly seen in pediatric patients. [8]

Grade / Type	WHO grade I	WHO grade II	WHO grade III	WHO grade IV
	Circumscript	Diffuse		
		Low-grade	High-grade	
Astrocytoma	Pilocytic astrocytoma	Low-grade astrocytoma	Anaplastic astrocytoma	Glioblastoma
Oligodendroglioma		Low-grade oligodendro-glioma	Anaplastic oligodendro-glioma	
Oligo-astrocytoma		Low-grade oligo-astrocytoma	Anaplastic oligo-astrocytoma	

Fig. 1 Classification of Glioma in types and WHO grades. Credit: Chemotherapy in Glioma by Walter Taal, Jacoline EC Bromberg, Martin J Van den Bent. Apr. 2015.

A notable characteristic of glial tumors is their tendency to invade nearby brain tissue. The tumor cells create an extracellular matrix which aids their migration by producing matrix proteins like tenascin, vitronectin, and fibronectin, and by expressing receptors for integrin, CD44, RHAMM, versican, and NCAM. Glial tumors also release matrix metalloproteases that break down the surrounding extracellular matrix, facilitating invasion. Intriguingly, these tumors also generate matrix metalloprotease inhibitors to regulate this behavior. [10] Radiation exposure stands as the most significant confirmed factor leading to glial tumors. Studies have shown an elevated risk of glial tumors following radiation therapy for conditions such as pituitary adenomas, craniopharyngiomas, and even low-dose radiation treatments for conditions like tinea capitis. For instance, research on children with acute lymphocytic leukemia (ALL) who underwent prophylactic cranial irradiation revealed a 2.5% occurrence of gliomas, indicating a 22-fold higher risk compared to control groups. [9]
The symptoms of gliomas can differ based on where and how large they are. Typical signs include headaches, seizures, nausea, and neurological impairments. Managing gliomas usually starts with surgically removing as much of the tumor as feasible, followed by radiation therapy and

chemotherapy. The treatment plan is tailored to the glioma's type and grade. Efficient treatment of gliomas faces challenges due to limited drug delivery through the blood-brain barrier (BBB) and the development of drug resistance. Despite a few FDA-approved combined treatments for glioblastoma, the prognosis for most patients remains unfavorable. Novel strategies to enhance anti-glioma treatment effectiveness include targeting epigenetic factors, immunotherapy, gene therapy, and various vaccine- and peptide-based approaches. With the discovery of lymphatic vessels in the central nervous system, immunotherapy emerges as a promising method capable of crossing the blood-brain barrier. [10]

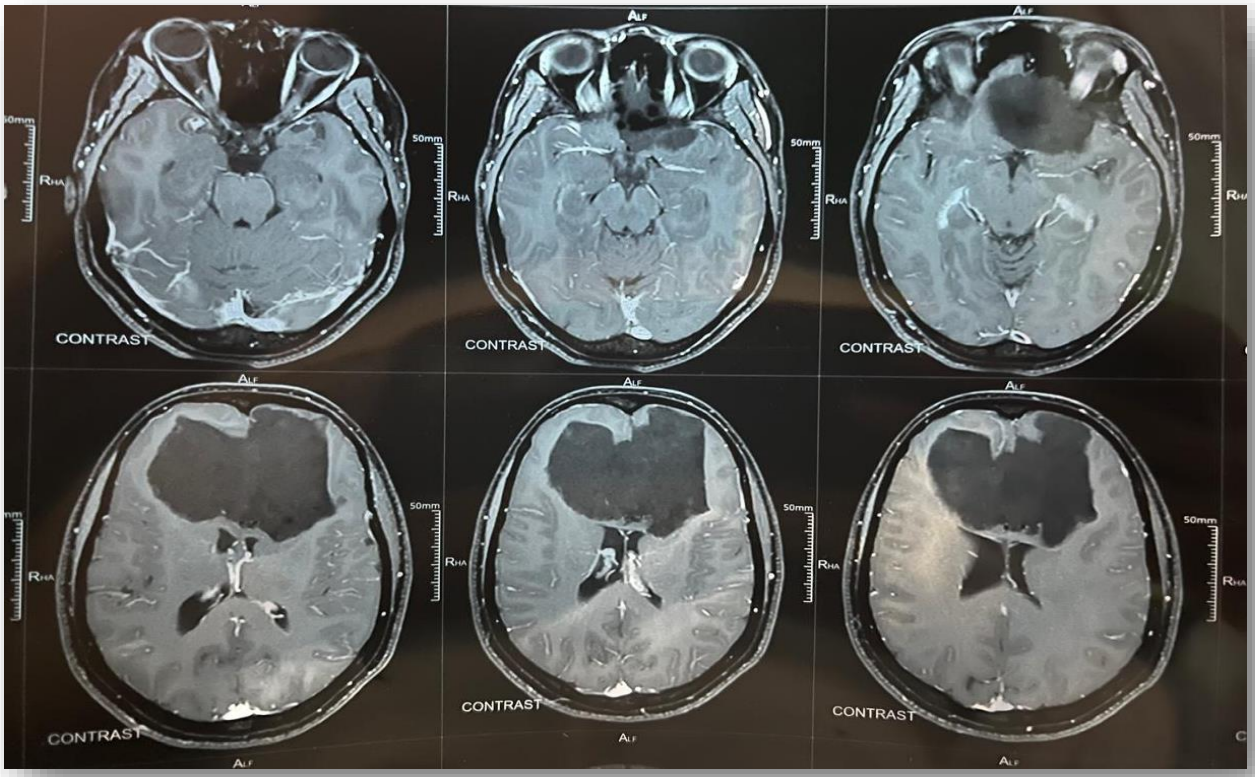
CASE DESCRIPTION

A 35-year-old woman, previously fit and well, sought medical attention at the neurosurgery department due to a three-month history of progressively worsening headaches. These headaches, ranging from moderate to severe, had become debilitating, impacting her ability to focus on her work and significantly affecting her daily life. Additionally, she reported experiencing mild visual disturbances, generalized weakness, increased drowsiness, and lethargy, which raised concerns about an underlying neurological condition. Despite consulting with several physicians and undergoing various treatments, her symptoms persisted, prompting a referral to a renowned neurosurgeon for further evaluation. A thorough examination, including a detailed medical history, was conducted, and based on her symptoms and the clinical presentation, further investigations were recommended, including a brain MRI. Following a comprehensive assessment, including a detailed medical history, various tests were recommended, including a brain MRI, to determine the cause of her symptoms and devise an appropriate treatment plan. On 10 March 2023, investigations revealed abnormal hemoglobin levels (Hb 9.4 gm/dl), TLC count (12300/cumm), RDW (21.4 CV%), and platelet count (116 per 10^3 uL).

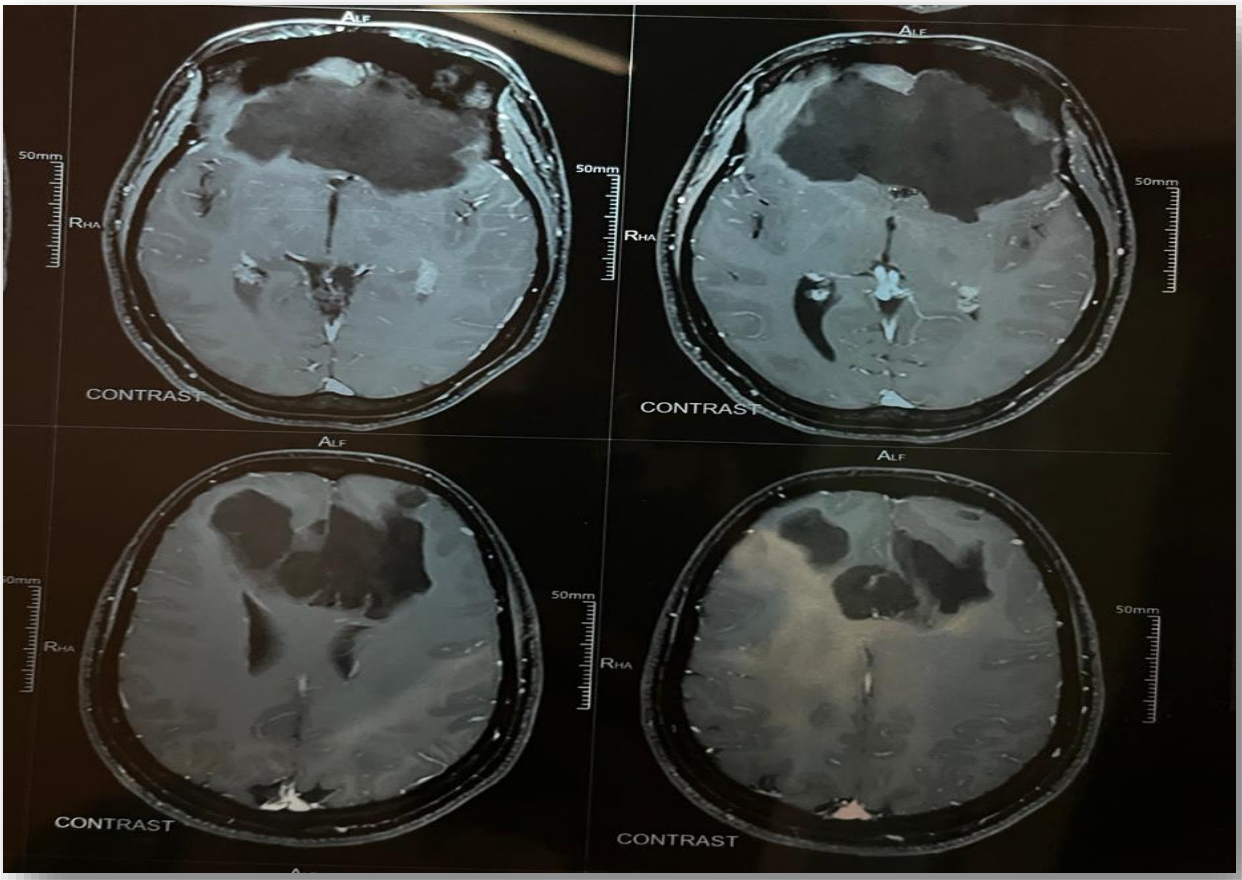
The MRI results revealed a mass lesion in the anterior corpus callosum extending into the frontal lobes, suggestive of a high-grade glioma. Gliomas are a type of brain tumor that originates from glial cells and can be aggressive in nature. The imaging characteristics of the mass, including hypointensity on T1, hyperintensity on T2, and heterogeneity on FLAIR images, were consistent with those typically seen in gliomas. The absence of blooming on SWI indicated the absence of significant hemorrhage within the mass, while the presence of diffusion restriction suggested high cellular density, which is a common feature of gliomas. Mild vasogenic edema and mass effect, along with enhancement in the post-contrast study, further supported this diagnosis. Given the nature of the tumor and its location, surgery was recommended to remove the mass and obtain tissue for histopathological examination to confirm the diagnosis. On March 23, 2023, the patient underwent surgery, which included a right temporal craniotomy with total resection of the tumor. The specimen obtained for histopathological examination consisted of multiple soft tissue pieces, which were creamy white to light brown in color and measured 11 x 9.5 x 1.5 cm in total. Microscopic examination revealed the presence of abundant lamellated keratin and keratin flakes, along with bits of tissue lined by stratified squamous epithelium showing a granular layer and adhered lamellated keratin. Some sections also showed adjacent brain tissue exhibiting focal gliosis.

Postoperatively, the patient developed a cerebrospinal fluid (CSF) leak, a common complication following brain surgery, which was managed with a second procedure under general anesthesia. A lumbar drain was placed for CSF drainage, and after a few days of discomfort, the patient's condition improved. The drain was removed once the CSF leakage was controlled. A follow-up CT scan showed a craniotomy defect with a bony flap in the bilateral frontal regions, with an ill-defined hypodense area that had mildly reduced in size compared to the previous scan, now measuring approximately 5.9 x 4.0 x 4.4 cm.

Post-surgery, the patient was managed conservatively with antibiotics to prevent infection, analgesics for pain relief, anticonvulsants to prevent seizures, and supportive measures to aid in her recovery. She is now being discharged in satisfactory condition with instructions for proper follow-up care, including regular monitoring and potential adjuvant treatment modalities such as chemotherapy and radiation therapy. This case underscores the challenges in diagnosing and managing intracranial lesions, particularly rare and aggressive tumors like high-grade gliomas. It also highlights the importance of a multidisciplinary approach involving neurosurgeons, radiologists, and oncologists to ensure optimal patient care and outcomes.


CONTRAST
CONTRAST
CONTRAST
CONTRAST
CONTRAST
CONTRAST

176


CONTRAST
CONTRAST
CONTRAST
CONTRAST

4

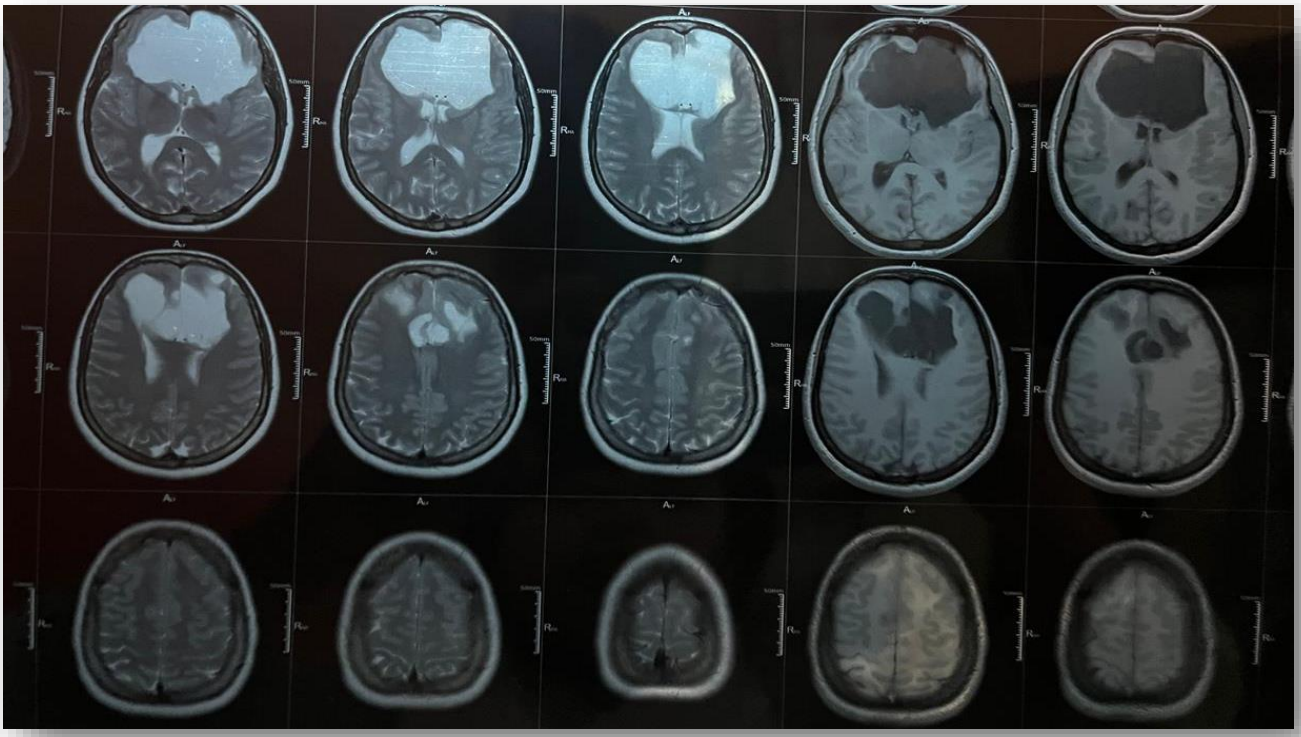


FIG: 1, "MRI Images Showing High-Grade Glioma in the Bilateral Frontal

Discussion

Gliomas, originating from glial cells in the brain or spinal cord, present significant challenges due to their aggressive behavior and resistance to treatment. They are more prevalent in adults and can be classified as low-grade, with slow growth, or high-grade, characterized by rapid proliferation. High-grade gliomas, such as glioblastomas, are particularly devastating and are a leading cause of cancer-related deaths among young adults. Conventional classification methods have been inadequate in predicting survival outcomes accurately, prompting a shift towards a more refined categorization based on molecular features. This approach aims to improve prognostication and guide treatment strategies more effectively. While the standard treatment includes surgical removal followed by radiation and chemotherapy, challenges such as limited drug delivery through the blood-brain barrier and the development of drug resistance persist [11].

Modern neurosurgical techniques have enabled the safe resection of gliomas with low morbidity and excellent long-term functional outcomes. Studies have shown that for patients with high-grade gliomas, such as glioblastoma, the extent of tumor resection significantly impacts survival and progression-free survival rates. Complete resection is crucial, as incomplete resections often lead to rapid neurological deterioration and reduced progression-free survival [12,13,14]. Emerging therapeutic approaches, including immunotherapy and targeted molecular therapies, hold promise for improving outcomes in glioma patients. Collaboration among healthcare professionals is essential for advancing the understanding and management of these complex tumors.

Summary

Gliomas are brain or spinal cord tumors originating from glial cells, commonly observed in adults and categorized as low-grade or high-grade based on their aggressiveness. High-grade gliomas, like glioblastomas, are particularly lethal. Conventional classification methods have limitations, leading to a shift towards molecular-based categorization for better prognostication and treatment planning. Treatment involves surgery, radiation, and chemotherapy, but challenges such as drug resistance and limited drug delivery through the blood-brain barrier persist. Novel therapies, including immunotherapy, show promise in improving outcomes. Collaborative efforts are crucial for advancing glioma management.

REFERENCES

1. Miller, K. D. et al. Cancer statistics for adolescents and young adults, 2020. Ca-Cancer J Clin 70, 443–459, https://doi.org/10.3322/caac.21637 (2020).
2. Jiang, T. et al. Clinical practice guidelines for the management of adult diffuse gliomas. Cancer Lett

499, 60–72, https://doi.org/10.1016/j.canlet.2020.10.050 (2021).
3. Gritsch, S., Batchelor, T. T. & Gonzalez Castro, L. N. Diagnostic, therapeutic, and prognostic implications of the 2021 World Health Organization classification of tumors of the central nervous system. Cancer 128, 47–58, https://doi.org/10.1002/cncr.33918 (2022).
4. Ostrom, Q. T., Cioffi, G., Waite, K., Kruchko, C. & Barnholtz-Sloan, J. S. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2014–2018. Neuro Oncol 23, iii1–iii105, https://doi.org/10.1093/neuonc/noab200 (2021).
5. Louis, D. N. *et al*. The 2021 WHO Classification of Tumors of the Central Nervous System: A Summary. *Neuro Oncol* **23**, 1231–1251, https://doi.org/10.1093/neuonc/noab106 (2021).
6. Ostrom QT, Patil N, Cioffi G, Waite K, Kruchko C, Barnholtz-Sloan JS. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2013–2017. Neuro-oncology. 2020;22(12 Suppl 2):iv1-iv96. Epub 2020/10/31. 10.1093/neuonc/noaa200.
7. Finch A, Solomou G, Wykes V, Pohl U, Bardella C, Watts C. Advances in Research of Adult Gliomas. Int J Mol Sci. 2021 Jan 18;22(2):924. doi: 10.3390/ijms22020924. PMID: 33477674; PMCID: PMC7831916.
8. Mesfin FB, Al-Dhahir MA. Gliomas. [Updated 2023 May 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441874/
9. W.K. Alfred Yung, Glial Tumors, Editor(s): Michael J. Aminoff, Robert B. Daroff, Encyclopedia of the Neurological Sciences, Academic Press, 2003, Pages 455-464, ISBN 9780122268700, https://doi.org/10.1016/B0-12-226870-9/00130-1.
10. Karami Fath M, Babakhaniyan K, Anjomrooz M, Jalalifar M, Alizadeh SD, Pourghasem Z, Abbasi Oshagh P, Azargoonjahromi A, Almasi F, Manzoor HZ, Khalesi B, Pourzardosht N, Khalili S, Payandeh Z. Recent Advances in Glioma Cancer Treatment: Conventional and Epigenetic Realms. Vaccines (Basel). 2022 Sep 2;10(9):1448. doi: 10.3390/vaccines10091448. PMID: 36146527; PMCID: PMC9501259.
11. Yang Z, Zhao C, Zong S, Piao J, Zhao Y, Chen X. A review on surgical treatment options in gliomas. Front Oncol. 2023 Mar 16;13:1088484. doi: 10.3389/fonc.2023.1088484. PMID: 37007123; PMCID: PMC10061125.
12. Stummer W, Pichlmeier U, Meinel T, Wiestler OD, Zanella F, Reulen H-J. Fluorescence-guided surgery with 5-aminolevulinic acid for resection of malignant glioma: A randomised controlled multicentre phase III trial. *Lancet Oncol* (2006) 7:392–401. doi: 10.1016/S1470-2045(06)70665-9.
13. 23. Stummer W, Tonn JC, Mehdorn HM, Nestler U, Franz K, Goetz C, etal. Counterbalancing risks and gains from extended resections in malignant glioma surgery: A supplemental analysis from the randomized 5-aminolevulinic acid glioma resection study. *Clin Article J Neurosurg* (2011) 114:613–23. doi: 10.3171/2010.3.JNS097.
14. 24. Stummer W, Reulen HJ, Meinel T, Pichlmeier U, Schumacher W, Tonn JC, et al. Extent of resection and survival in glioblastoma multiforme: Identification of and adjustment for bias. *Neurosurgery* (2008) 62:564–76. doi: 10.1227/01.neu.0000317304.31579.17.