ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 12 | December - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A CROSS-SECTIONAL STUDY OF HISTOPATHOLOGICAL SPECTRUM OF GLIAL TUMORS AND EXPRESSION OF CD117 IN GLIAL TUMORS IN A TERTIARY CARE HOSPITAL

Pathology

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ABSTRACT

Glial tumors constitute the majority of primary central nervous system (CNS) neoplasms. Despite aggressive multimodal treatment, high-grade gliomas have a poor prognosis. CD117 (c-kit), a transmembrane tyrosine kinase receptor, is a potential target for selective inhibitors like imatinib. This study aimed to evaluate the histopathological spectrum of glial tumors and correlate CD117 expression with tumor grade and histological subtypes. A cross-sectional observational study was conducted on 60 histologically confirmed cases of glial tumors over two years (April 2023–March 2025) at a tertiary care hospital in Hyderabad. Immunohistochemistry (IHC) for CD117 was performed. Expression was scored semi-quantitatively based on the percentage of positive cells (0 to 3+). The study included 60 patients with a mean age of 35.1 years and a male preponderance (60%). Glioblastoma Multiforme (WHO Grade 4) was the most common subtype (30%). Overall, CD117 positivity was observed in 53.3% of cases. There was a statistically significant association between CD117 expression and higher WHO grades (p=0.025). High-grade gliomas showed 65.6% positivity compared to 39.3% in low-grade gliomas (p=0.041). Significant correlations were also found between CD117 expression and nuclear pleomorphism (p=0.005), mitosis (p=0.009), and necrosis (p=0.002). CD117 expression is significantly upregulated in high-grade gliomas and tumors exhibiting aggressive histological features. This suggests that CD117 may serve as a potential therapeutic target for tyrosine kinase inhibitors in malignant glial tumors.

KEYWORDS

Glial tumors, CD117, c-kit, Glioblastoma, Immunohistochemistry.

INTRODUCTION

Central Nervous System (CNS) tumors represent a substantial burden of morbidity and mortality. Among these, glial neoplasms are the most common primary CNS tumors, accounting for approximately 30-40% of all primary CNS tumors and 80% of malignant brain tumors.[1] The prognosis for these tumors, particularly high-grade variants like Glioblastoma Multiforme (GBM), remains poor despite advances in neuroimaging and standard therapies including surgery, radiation, and chemotherapy.

Recent research has focused on molecular markers to refine diagnosis and identify therapeutic targets. CD117, the protein product of the *c-KIT* proto-oncogene, is a type III receptor tyrosine kinase. It plays a critical role in cell survival, proliferation, and differentiation. CD117 is well-established as a diagnostic and therapeutic target in Gastrointestinal Stromal Tumors (GIST), where overexpression is effectively targeted by tyrosine kinase inhibitors (TKIs) such as imatinib mesylate.[2][3]

Evidence suggests the CD117/SCF signaling pathway is operative in the developing brain and may be deregulated in glial neoplasms. However, reports on the frequency of CD117 expression in gliomas vary significantly across literature, ranging from 15% to 76%. This study aims to analyze the histopathological spectrum of glial tumors in a tertiary care setting and evaluate the expression of CD117, correlating it with tumor grade and histological hallmarks of aggression to assess its potential as a therapeutic target.

MATERIAL AND METHODS

This cross-sectional observational study was conducted in the Upgraded Department of Pathology at Osmania General Hospital, Hyderabad, Telangana. The study duration was two years, from 2023 to 2024. The study included 60 cases of central nervous system neoplasms. Inclusion criteria were histologically confirmed glial tumors with adequate tissue for Immunohistochemistry (IHC). Exclusion criteria included mixed gliomas, autolyzed samples, and insufficient tissue. Routine hematoxylin and eosin (H&E) stained sections were evaluated, and tumors were classified and graded according to the 2021 WHO Classification of Tumors of the Central Nervous System (5th Edition).[4]

Selected formalin-fixed paraffin-embedded (FFPE) blocks were subjected to IHC. Sections (4µm) were antigen-retrieved using citrate buffer (pH 6.0) in a microwave, followed by incubation with rabbit monoclonal antibody to CD117. A polymer-based detection system (HRP-DAB) was used.

Scoring Of CD117 CD117 expression was defined by cytoplasmic/membranous staining and scored semi-quantitatively:

- **Score 0:** No staining
- **Score 1+:** 1–10% positive cells
- **Score 2+:** 11–50% positive cells
- **Score 3+:** >50% positive cells Scores 1+, 2+, and 3+ were considered positive.

Data were analyzed using SPSS version 22.0. The Chi-square test was used to evaluate associations between categorical variables. A p-value of <0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS

Demographic And Clinical Profile In the cohort of 60 patients, the age ranged from 2 to 77 years, with a mean age of 35.10 ± 22.91 years. The incidence was highest in the ≤20 years age group (35%), followed by the 41–50 years group (21.7%). Males comprised 60% (*n*=36) and females 40% (*n*=24) of the study population. The most common clinical presentation was headache (60%), followed by vomiting (40%). Midline tumors were the most frequent (43.3%), followed by right-sided (33.3%) lesions.

Histopathological Spectrum Glioblastoma Multiforme (WHO Grade 4) was the most frequent histological subtype, accounting for 30% (*n*=18) of cases, followed by Pilocytic Astrocytoma (10%, *n*=6)

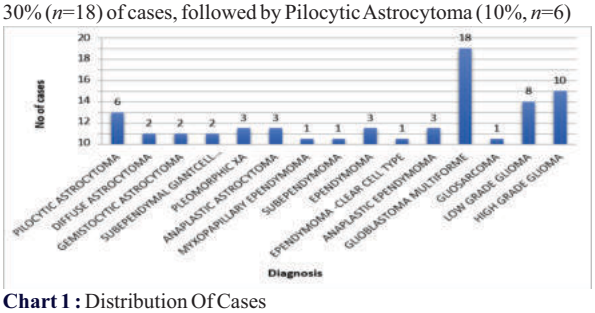

Chart 1 : Distribution Of Cases

CD117 Expression Overall, CD117 positivity was observed in 32 out of 60 cases (53.3%). Among the positive cases, 25 showed 1+ staining, 6 showed 2+ staining, and 1 showed 3+ staining. 15 out of 18 cases of Glioblastoma multiforme were positive (83.3%). 4 cases of Pilocytic astrocytoma and high grade glioma, 3 cases of Pleomorphic xanthoastrocytoma, and 2 cases each for Subependymal giant cell astrocytoma, Anaplastic astrocytoma and Ependymoma were positive.

Correlation with WHO Grade There was a statistically significant correlation between CD117 expression and tumor grade (p=0.025). Grade 4 tumors showed the highest positivity (80%), while Grade 1 tumors showed 33.3% positivity. When grouped into Low Grade (I & II) and High Grade (III & IV), high-grade gliomas showed significantly higher CD117 expression (65.6%) compared to low-grade gliomas (39.3%), with a p-value of 0.041 (Table 1).

Table 1: Correlation Of CD117 Expression With Tumor Grade

WHO Grade	Total Cases	CD117 Negative n (%)	CD117 Positive n (%)
Grade I	18	12 (66.7%)	6 (33.3%)
Grade II	10	5 (50.0%)	5 (50.0%)
Grade III	12	7 (58.3%)	5 (41.7%)
Grade IV	20	4 (20.0%)	16 (80.0%)
Total	**60**	**28**	**32**
P value 0.025*			
Grouped Analysis			
Low Grade (I & II)	28	17 (60.7%)	11 (39.3%)
High Grade (III & IV)	32	11 (34.4%)	21 (65.6%)
P value 0.041*			

*Significant at p<0.05

Correlation with Histological Parameters CD117 expression was strongly associated with histological markers of aggression. Tumors with marked nuclear pleomorphism, presence of mitosis, and necrosis showed significantly higher CD117 positivity compared to those without these features. There was no statistically significant association between CD117 expression and patient age (p=0.216), sex (p=0.672), or tumor laterality (p=0.316).

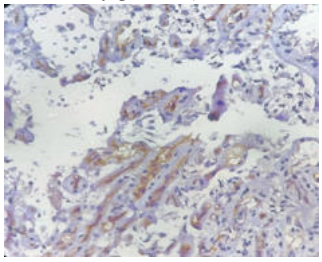

Figure 1: Glioblastoma multiforme showing CD117 positivity (400x)

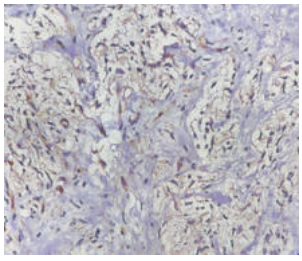

Figure 2: Anaplastic astrocytoma showing CD117 positivity (400x)

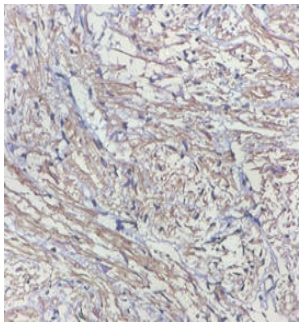

Figure 3: Pilocytic Astrocytoma showing CD117 positivity (400x)

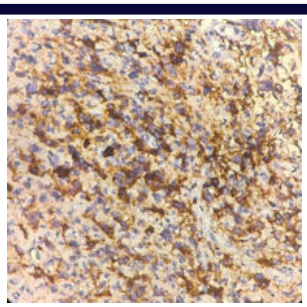

Figure 4: Glioblastoma multiforme showing CD117 positivity (400x)

DISCUSSION

This study analyzed the expression of CD117 in 60 glial tumors. The overall positivity rate of 53.3% in our study aligns with findings by Jayanandhini et al. [5] (54%) and Abdel Rhman et al. [6] (57.7%) . However, it differs from Cetin et al.[7] (75%) and Gomes et al. [8] (15.6%), likely due to variations in antibody clones, scoring criteria, and sample sizes.

The most significant finding of this study is the strong correlation between CD117 expression and high-grade histology. We observed 80% positivity in glioblastomas (Grade 4) versus 33.3% in Grade 1 tumors. This is consistent with Cetin et al.[7], who reported significantly higher CD117 immunoreactivity in high-grade gliomas, and Dehghan et al.[9], who found 61.1% positivity in high-grade versus 21.2% in low-grade tumors (p=0.001). These findings support the hypothesis that *c-KIT* upregulation is involved in the progression and malignant transformation of glial tumors.

Furthermore, our data revealed a significant association between CD117 expression and hallmarks of anaplasia: marked nuclear pleomorphism (p=0.005), mitotic activity (p=0.009), and necrosis (p=0.002). This reinforces the concept that CD117 is an indicator of aggressive biological behavior in gliomas. The lack of correlation with age or gender suggests that CD117 overexpression is a tumor-intrinsic property rather than a demographic feature.

The high expression of CD117 in glioblastomas (83.3% of cases in our subtypes analysis) is clinically relevant. Since small molecule inhibitors like imatinib and sunitinib target KIT tyrosine kinase activity, CD117-positive high-grade gliomas represent a potential subset of tumors that might benefit from targeted therapy, similar to GISTs.

CONCLUSION

The present study demonstrates that CD117 expression is common in glial tumors, particularly in high-grade malignancies like Glioblastoma Multiforme. A significant correlation exists between CD117 positivity and higher WHO grade, as well as with aggressive histological features such as necrosis and mitosis. These findings suggest that CD117 may serve as a potential target for tyrosine kinase inhibitor therapy in patients with high-grade gliomas, warranting further investigation through clinical trials.

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