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Study Of Evaluation Of Role Of Ki67 And p53 Markers In Central Nervous System Tumors.

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ABSTRACT

Our study conducted explores the role of Ki67 and p53 markers in Central Nervous System (CNS) tumors. A cohort of 50 cases underwent comprehensive evaluation, revealing noteworthy patterns in age distribution, gender predominance, clinical symptoms, and site-specific occurrences. Results indicated a higher prevalence of CNS tumors in the 41-60 age group, with a male predominance in glioblastoma multiforme, glioma, and astrocytoma, and a female predilection in ependymoma and pituitary adenoma cases. Clinical presentations were diverse, with headache emerging as the most common symptom. Frontal and parietal lobes were the most frequently affected sites. Ki67 immunohistochemical staining facilitated an assessment of proliferative activity, revealing a predominance of cases with less than 5% positivity. Correlation with histopathological diagnoses showcased higher Ki67 expression in aggressive tumors like glioblastoma multiforme and lower expression in benign meningiomas. The study contributes valuable insights into the complex landscape of CNS tumors, emphasizing the utility of Ki67 as a prognostic marker.

Keywords: Central Nervous System tumors, Ki67, p53, Immunohistochemistry, Histopathology.

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INTRODUCTION

The intricate landscape of Central Nervous System (CNS) tumors presents a formidable challenge in diagnosis and treatment [1]. In the quest for more precise prognostic indicators, the investigation into molecular markers has gained substantial momentum. Among these, Ki67 and p53 have emerged as pivotal players, offering valuable insights into the proliferative and genetic characteristics of CNS tumors [2, 3]. Ki67, a marker of cellular proliferation, provides crucial information about the growth fraction of neoplastic cells, aiding in the assessment of tumor aggressiveness. On the other hand, p53, a tumor suppressor gene, is pivotal in the regulation of cell cycle and apoptosis [4]. Dysregulation of p53 is commonly associated with malignancy, making it a promising marker for evaluating the genetic aberrations underlying CNS tumors [5-7]. Our study aims to comprehensively evaluate the role of Ki67 and p53 markers, shedding light on their potential as reliable indicators for prognosis and therapeutic stratification in the complex realm of CNS tumors.

METHODOLOGY

This descriptive cross-sectional design study to investigate the prognosis and behaviour of central nervous system (CNS) tumours based on Ki-67 and p53 indices.

The sample size, calculated using the formula $N=(Z\alpha+Z\beta \text{ error})^2 \times PQ/E^2$, revealed a low prevalence of CNS tumors (10/100,000), leading to a small expected sample size. However, due to the tertiary care nature of the institute and the availability of approximately 100 CNS tumour samples, a sample size of 50 was chosen for the study. Selection criteria included histopathologically confirmed cases of CNS tumors obtained from neurosurgical specimens, while cases with neoadjuvant therapy or inadequate/hemolyzed/autolyzed specimens were excluded.

Tissue samples from primary tumors, obtained between January 2020 and June 2021, were processed by slicing at 5mm thickness and fixing in 10% formalin for 24 hours. Formalin-fixed paraffin-embedded sections, 4-5µm thick, were stained with Hematoxylin and eosin for histopathological evaluation, focusing on assessing histological type and tumor grade according to the WHO classification of CNS tumors 2016. Immunohistochemical examination, using Ki-67 and p53 markers, was conducted on representative tumor paraffin blocks. The slides were examined for nuclear staining, with materials including well-fixed sections, APES/Poly-L-Lysine coated slides, a microwave (EZ-Retriever System), antigen retrieval solution, phosphate buffer saline, primary antibody ready-to-use, polymer detection kit, hematoxylin stain, and mounting media. The examination aimed to elucidate the correlation between these markers and the clinical outcomes of CNS tumors.

RESULTS

The study is conducted in Department of Pathology of tertiary care centre and all the samples are received in the histopathology section. Proper data is obtained from the requisition letter and the clinical history, MRI findings as well as other required information is obtained from the form. All the biopsy and excision samples received were processed and then IHC stain was applied on all the 50 samples collected. Total of 50 cases were studied in our institute, and the following findings were noted in all of the cases.

Out of 50 cases, maximum number of cases were found in 41-60 years of age group which was followed by 21-40 years of age group.

Individual male and female ratio was calculated from all the histopathological diagnosis and it showed male predominance in glioblastoma multiforme, glioma and astrocytoma cases. Ependymoma and pituitary adenoma showed female predominance.

The most common symptom found in all the cases was headache followed by giddiness, weakness and loss of consciousness.

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Table 1: Comparison of Ki67 with the diagnosis:

Diagnosis	Ki67			Total
	≤ 5	5.01 - 10.0	> 10	
Astrocytoma	2	7	0	9
Ependymoma	3	0	0	3
Extra ventricular neurocytoma	1	0	0	1
Glioblastoma Multiforme	2	5	4	11
Glioma	3	3	0	6
Gliosarcoma	0	1	0	1
Medulloblastoma	0	1	0	1
Meningioma	8	4	0	12
Oligodendroglioma	1	1	0	2
Papillary Adenocarcinoma	1	0	0	1
Pituitary adenoma	2	0	0	2
Schwanomma of CP Angle	1	0	0	1
Total	24	22	4	50

Ki67 was applied to all the cases of the CNS tumors including meningioma, glioblastoma multiforme, ependymoma, astrocytoma, etc. Maximum cases included were grade II WHO followed by grade IV and grade I. After the application of the IHC marker, it was interpretated that most of the cases showed less than 5% positivity of.

Table 2: Site wise distribution of CNS tumor cases

Site	Frequency	Percentage
Cerebellar Hemisphere	1	2.0
Cerebellum	2	4.0
CP angle	1	2.0
Extramedullary	1	2.0
Frontal	24	48.0
Parietal	11	22.0
Posterior fossa	1	2.0
Sellar mass	2	4.0
Spinal region	1	2.0
Suprasagittal	1	2.0
Temporal	4	8.0
Thalamus	1	2.0
Total	50	100.0

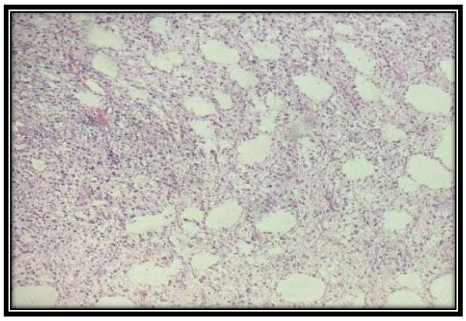

Figure 1: Fibrillary Astrocytoma

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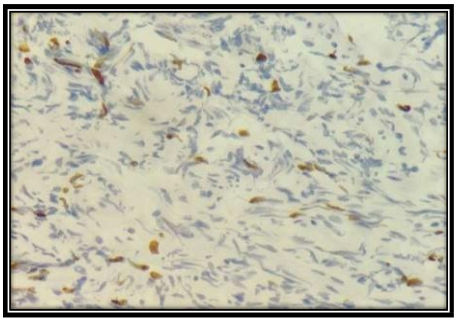

Figure 2: Ki67 in astrocytoma (Ki67=4%)

DISCUSSION

Our study focused on the evaluation of Ki67 and p53 markers in Central Nervous System (CNS) tumors. The comprehensive analysis of 50 cases revealed intriguing patterns in age distribution, gender predominance, clinical symptoms, and site-specific occurrences of CNS tumors. Additionally, the study investigated the correlation between Ki67 expression and various histopathological diagnoses. The following discussion delves into the key findings and their implications [8-10].

Age and Gender Distribution

The study identified a predominant occurrence of CNS tumors in the 41-60 age group, followed by the 21-40 age group. This age distribution aligns with existing literature, highlighting the susceptibility of individuals in the middle and later stages of life to develop CNS tumors. Moreover, a gender-based analysis revealed a male predominance in cases of glioblastoma multiforme, glioma, and astrocytoma, while ependymoma and pituitary adenoma exhibited a female predilection. These findings underscore the complex interplay of genetic, hormonal, and environmental factors contributing to the development of CNS tumors.

Clinical Symptoms

The most common presenting symptom across all cases was headache, followed by giddiness, weakness, and loss of consciousness. These symptoms are consistent with the diverse manifestations of CNS tumors, reflecting the intricate relationship between tumor location, size, and associated neurological deficits. The study's findings emphasize the importance of recognizing these clinical symptoms for early detection and intervention, ultimately improving patient outcomes [11].

Site-wise Distribution

The distribution of CNS tumors across different anatomical sites revealed a preponderance of cases in the frontal lobe (48.0%), followed by the parietal lobe (22.0%). This site-wise distribution aligns with the diverse functional and structural characteristics of the brain regions, influencing the clinical presentation and prognosis of CNS tumors. Understanding the site-specific distribution aids in refining diagnostic and therapeutic approaches tailored to the distinct challenges posed by tumors in different regions of the CNS.

Ki67 Expression and Histopathological Diagnoses

The application of Ki67 immunohistochemical staining allowed for a detailed assessment of proliferative activity in various CNS tumors. We found distribution of Ki67 expression across different diagnoses. Notably, the majority of cases demonstrated less than 5% positivity for Ki67, indicating a relatively lower proliferative index in the studied samples.

The comparison of Ki67 expression with histopathological diagnoses elucidates valuable insights into the correlation between proliferative activity and tumor types. For instance, glioblastoma multiforme exhibited a higher proportion of cases with Ki67 expression greater than 10%, signifying its aggressive

nature. In contrast, meningioma, a typically benign tumor, displayed predominantly low Ki67 expression, consistent with its indolent behavior.

Grade-wise Distribution

Further classification based on the World Health Organization (WHO) grading system revealed that most cases belonged to grade II, followed by grade IV and grade I. This distribution aligns with the known hierarchy of tumor grades, where higher grades generally indicate increased malignancy and aggressiveness. The study's findings corroborate existing knowledge regarding the grading of CNS tumors and emphasize the relevance of incorporating molecular markers like Ki67 for a more nuanced classification.

Limitations and Future Directions

While the study provides valuable insights, it is essential to acknowledge certain limitations. The sample size of 50 cases, though representative, may not capture the entire spectrum of CNS tumors. Additionally, the study predominantly focused on Ki67 and did not explore the combined impact of multiple molecular markers. Future research endeavors could expand the scope by incorporating larger sample sizes, exploring additional markers, and correlating molecular findings with patient outcomes.

CONCLUSION

In conclusion, the study's comprehensive analysis sheds light on the intricate landscape of CNS tumors, emphasizing the role of Ki67 as a valuable marker for assessing proliferative activity. The age and gender distribution, clinical symptoms, and site-specific occurrences provide a holistic understanding of the diverse nature of CNS tumors. The correlation between Ki67 expression and histopathological diagnoses underscores the potential of molecular markers in refining diagnostic accuracy and prognostication. These findings contribute to the ongoing efforts in unraveling the complexities of CNS tumors, guiding clinicians toward more informed decision-making and personalized treatment strategies.

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