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Research article

To establish the correlation between p53 and histopathological grading of glial tumors

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ABSTRACT

Glial tumors occupy approximately 70% of the spectrum of all brain tumors with astrocytoma's being the most common primary. High grade glial tumors have a poor outcome with limited survival rate. To establish the correlation between p53 status and histological grading of glial tumors. Objectives: To diagnose glial tumors on histopathological examination, to evaluate histological grade, to evaluate p53 expression and to assess the correlation between p53 expression and histological grade of gliomas. The study investigated 52 cases of gliomas. Histological grade was determined by WHO Grading System. Nuclear expression of p53 was evaluated by immunohistochemistry. A direct correlation between the histological grade and the p53 expression was observed. High grade gliomas exhibit high p53 expression. Thus, p53 as an adjunct to histological grade can provide a supportive clue to the clinicians, to predict the biological behaviour of gliomas.

Keywords: Glial tumors, p53, Immunohistochemistry

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INTRODUCTION

The incidence of brain tumors in India range from 5 to 10 per 100,000 populations. Glial tumors account for 70% of all brain tumors with astrocytoma (38.7%) being the most common primary tumor. [1,2] In the adult population majority of the tumors are high grade gliomas. In the pediatric age group the most common tumor is also astrocytoma but was low grade such as pilocytic astrocytoma and sub ependymal giant cell astrocytoma. [3]

The prognosis of high grade gliomas is very poor and has a limited overall survival rate. On top of the cancer element of the tumor various neurological symptoms accompany it, adding to the mental, physical and social suffering of the patient. Thus maintaining an acceptable quality of life for the patient is of paramount importance.

Gliomas remain one of the most difficult wounds to treat. Researchers have tried very hard to support cell physiology and genetic engineering so that we can better understand how plants grow and develop therapies to treat them. Various oncogenes and their protein products have been identified as being involved. One of these is p53, a prominent gene for suppressing the tumor.

The pressure gene, p53, is located in the short arm of chromosome 17. All cells normally have two alleles in the structure forming the wild type p53. The gene p53 is thought to be overexploited; that is, if there is only one wild type of p53, then the cell will function normally.

Type p53 is a short-lived cell cycle controller. Type p53 acts as a test point controller in phase G1 to S. When p53 activates the p21 protein, it also binds to a variety of cyclin dependent kinases (CDKs). When p21 is bound to CDKs, cyclins are activated by inhibiting their phosphorylation. Phosphorylated cyclins allow the cell to enter phase S. Thus, in the event of a burst of activity, p53 activity binds cell entry from phase G1 to phase S, leading to the formation of cell division and proliferation. [4]

In present study, the mutant type p53 was evaluated with help of Immunohistochemistry. Those cells in which p53 protein has accumulated, whether mutated or wild-type, will show positive immunostaining. [5] The present study emphasizes time correlation of p53 status with histopathological grading of glial tumors. The p53 scanning helped to evaluate the proliferative status of a glial tumor.

AIM

To establish the role of p53 (immunohistochemical) with histopathological grades of various glial tumors such as astrocytoma, oligodendroglioma and ependymoma.

MATERIAL AND METHODS

The study undertaken here is a cross-sectional and analytical study. The study was carried for a period of 2 years in Section of Histopathology and immunohistochemistry in a rural tertiary care hospital. The study protocol was drafted and was approved by the Institutional Ethics Committee. A total of 52 resected specimens were chosen from confirmed cases of Glial tumors operated were considered for this study. All the patients, diagnosed with primary glial tumors on histopathology were included in this study. All the glial tumors associated with other tumors, patients on radiotherapy or chemotherapy and cases of recurrence were excluded from the study.

The study protocol was drafted and University Ethics Committee clearance was obtained. The clinical and the demographic profiles of the patients were documented in the prepared proforma. Each case was reviewed and the final histological diagnosis was confirmed. The histopathological report of these patients were scrutinized, histological grade was given according to WHO histopathological grading of glial tumors.

The blocks of these patients were collected and slides were prepared according to the standard methods and references, p53 expression was studied by immunohistochemistry by standard procedures. The results of p53 were compared with histopathological status of Glial tumor. The comparison was also done between histopathological grading and immunophenotypes.

INTERPRETATION

Histopathological grading of Glial tumors

The results were confirmed by the nucleus of tumor cells being positive. Strong brown color of tumor cells was indicative of p53 expression in the tumor cells while blue color indicates non-expression of p53 in the tumor cells.

Histopathological grading of Glial tumors

Phenotype	Subtype	Grade
Astrocytic Tumours	Pilocytic Astrocytoma	I
	Diffuse Astrocytoma	II
	Anaplastic Astrocytoma	III
	Glioblastoma	IV
Oligodendroglial Tumours	Oligodendroglioma	II
	Anaplastic Oligodendroglioma	III
Oligoastrocytic Tumours	Oligo astrocytoma	II
	Anaplastic oligo astrocytoma	III

P53grading by Immunohistochemistry

The p53 grading for the cases was done by a single senior pathologist who was blind to the result of histological grade of the tumor to avoid any kind of bias. The p53 was determined by counting 1000 stained tumor cells. More than 10% cells were counted as positive and less than 10% cells were counted as negative.

P53 nuclear dots are divided into 1 to 3 levels, with 1 representing up to 10% cells with high nuclear capacity and 2 representing 10-30% cells with high nuclear capacity. Level 3 will be used to show high protein expression when 30-50 percent of cells show high nuclear potential. [6, 7]

Pictomicrographs

Figure 1: Low power view of pilocytic astrocytoma (10 x)

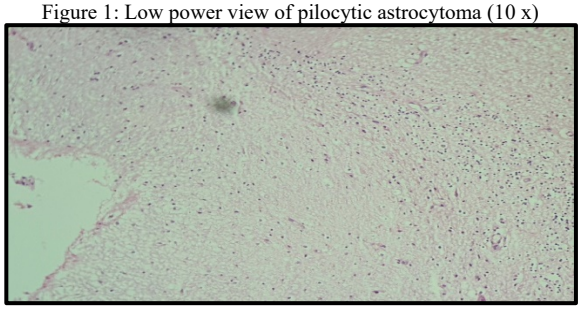


Figure 2: High power view of Pilocytic astrocytoma showing bipolar spindled cells with long hair like processes (40 x)

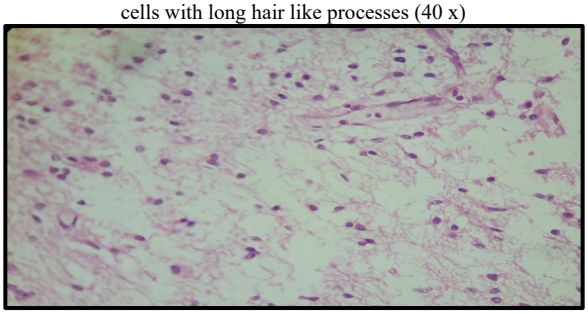


Figure 3:- Low power view of diffuse astrocytoma (10x)

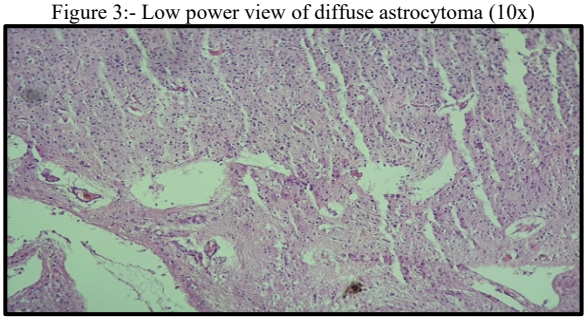


Figure 4: High power view showing nuclear atypia in a diffuse fibrillary background of diffuse astrocytoma. (40x)

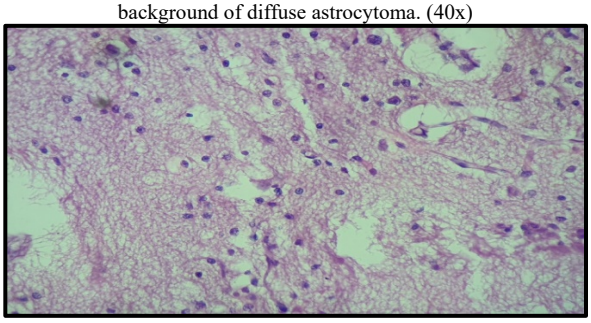


Figure 5: Low power view of anaplastic astrocytoma (10x)

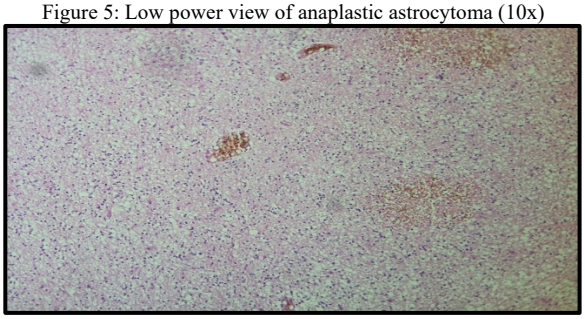


Figure 6: High power view of anaplastic astrocytoma showing nuclear atypia along with mitotic figures. (40x)

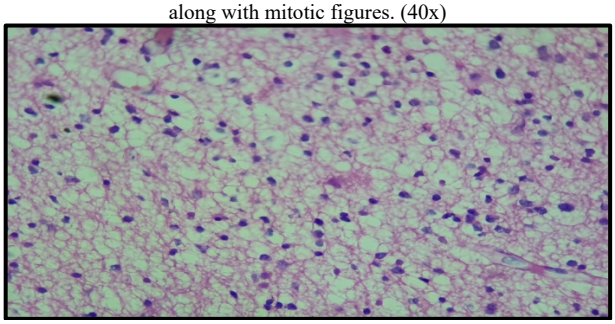


Figure 7: Low power view showing Glioblastoma multiforme (10x)

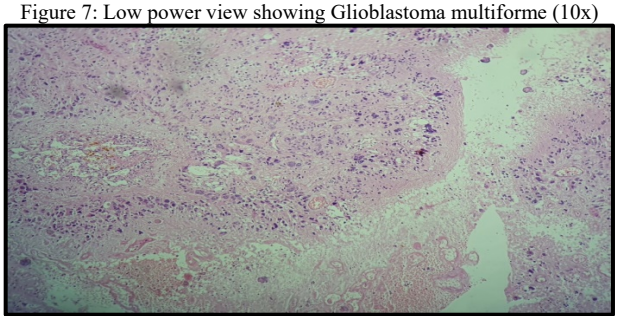


Figure 8: High power view showing highly pleomorphic cells and extensive mitosis in Glioblastoma multiforme (40x)

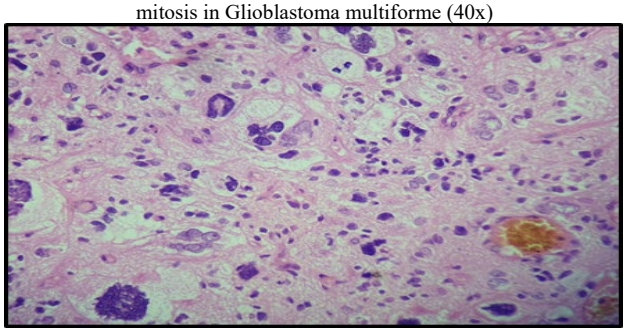


Figure 9: Low power view showing tumor cells positive for p53 (10x)

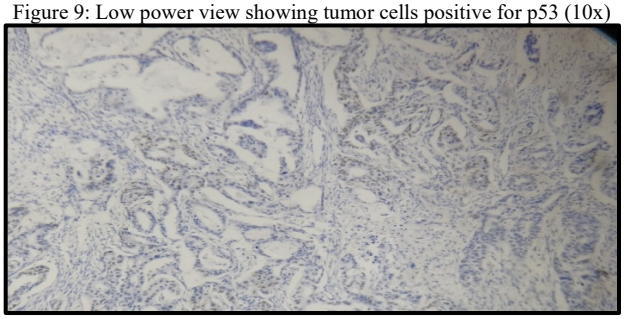
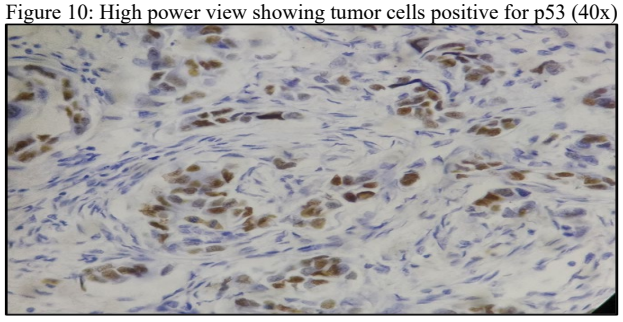


Figure 10: High power view showing tumor cells positive for p53 (40x)



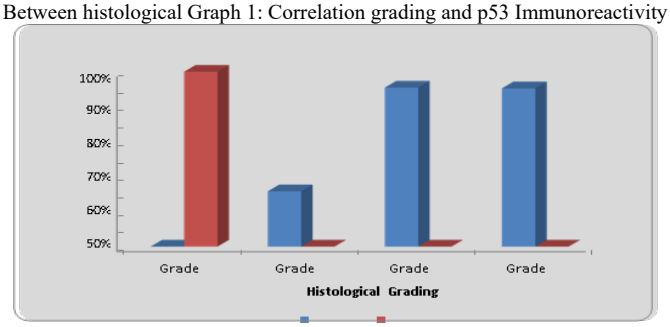
OBSERVATION AND RESULTS

The below Table 1 and Graph 1 shows the distribution of 52 cases on the basis of histological grading and p53 immunoreactivity.

Table 1: Correlation between histological grading and p53 Immunoreactivity

Grade	Positive	Negative	Total
Grade I	0(0%)	1(100%)	1(1.92%)
Grade II	6(31.58%)	13(68.42%)	19(36.54%)
Grade III	10(90.91%)	1(9.09%)	11(21.15%)
Grade IV	19(90.48%)	2(9.52%)	21(40.38%)
Total	35(67.31%)	17(32.69%)	52(100%)
χ2-value	20.98,p-value=0.0001, Significant ,p<0.001		

Between histological Graph 1: Correlation grading and p53 Immunoreactivity



On correlation with histological grading and p53 immunoreactivity, 35(67.31%) cases were p53 positive, where maximum number 19 (90.48%) cases were present in grade IV. The p value interpretation was found to be statistically significant and shows a good correlation between histological grading and p53 immunoreactivity.

DISCUSSION

Glial tumors are a very complex set of tumors having a poor prognosis especially high grade glial tumors. The diagnosis and treatment part is primarily based on histological grade of the tumor. Immunohistochemistry (IHC) is the process of making certain antigens on tissues or cells based on the recognition of antigen-antibody. In this way we can look at p53 abnormal tumor. Immunohistochemical staining is based on a longer life expectancy of p53 compared to p53. An antibody to epitopes in p53 protein is used to contaminate plant cells. Those cells where p53 protein accumulates will show good immune system.[5] P53 mutations are documented in many astrocytoma's. Transformation of p53 occurs in approximately 25 to 45% of fibrillary astrocytoma's and also has a normal frequency in both early and further stages (anaplastic and glioblastoma multiforme) astrocytoma's. This study attempted to find a correlation between p53 and histological grading of glial tumors. The study also assessed if p53 can be used as an adjunct in helping clinicians in treating glial tumors.

Correlation between histological grading and p53 Immunoreactivity

The present study showed correlation with histological grading and p53 immunoreactivity, 35(67.31%) cases were p53 positive, where maximum number 19(90.48%) cases were present in grade IV. The p value interpretation was found to be statistically significant and shows a good correlation between histological grading and p53 immunoreactivity.

Pollack et al studied 29 patients in which 48% males suffered from 11 cases of grade IV tumor and 3 cases of grade III.

51.7% of females suffered from 7 cases of grade IV and 5 cases of grade III. The p53 immunoreactivity was highest in grade IV tumors.[8]Cunningham et al studied 120 tumors in which 86 had (72%) WHO Grade 4 tumor, 19 (16%) Grade 3, and 15 (13%) Grade 2.[9]Al-Nuaimy et al studied 50 patients in which the low grade astrocytomas (grade I and II), 1 out of 11 stained positive for p53, while of high grade astrocytoma (grade III and IV), 21 out of 26 cases showed positive p53 immunoreactivity. The p53 expression has statistically significant correlation to the grade of glioma, p-value less than 0.05.[10]p53 was diagnosed in 2 of 9 cases (22.2 percent) of gliomas, 40 of 56 cases (71.4 percent) of grade II gliomas, 38 cases out of 52 (percent 73.1) of grade gliomas, and 21 35 cases (60.0 percent) of grade IV gliomas, according to Xinhua et al. Compared with the other three stages, the frequency of p53 immunopositivity was significantly lower in the grade Gliomas(P=0.0074).[11]Kyritsis et al studied 182 patients in which 57.6% males and 42.3% females were present. 122 (67%) had grade IV tumor, 48 (26%) had grade III, and 12 (7%) had grade II. P53 immunoreactivity was detected in 73 (60%) patients with grade IV, 35 (73%) patients with grade III, and 6 (50%) patients with grade II.[12] Nayak et al studied 152 patients in which , p53 immunopositivity was noted in 68 (51%) and distributed over all grades - 58.8% of grade II, 53.8% of grade III and 50% of grade IV.[13]

The findings of Cunningham et al, Pollack et al, Al-Nuaimy et al, Kyritsis et al, Nayak et al and Xinhua et al were in concordance with our study. This shows that p53 immunoreactivity is more in higher grade tumors.

CONCLUSION

The study concludes a positive correlation between p53 status and histopathological grading of glial tumors. However, the relationship of p53 immunoreactivity with age and gender was found to be statistically insignificant.

P53 immunoexpression is expressed more in high grade tumors such as anaplastic astrocytoma and glioblastoma multiforme. Therefore, p53 as an adjunct to histological grade can provide proper investigative tools to the clinicians to predict the biological behavior of gliomas so that proper and earlier management can be given to patients.

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