Original Research Article

A single-centre observational study of 124 surgically managed glioma patients: molecular subtyping and its correlation with clinico-radiological profile

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ABSTRACT

Background: The World Health Organization (WHO) 2016 classification incorporated molecular subtyping in glioma, highlighting the diagnostic and prognostic significance. The study aims to determine the isocitrate dehydrogenase (IDH-1) gene, α-thalassemia/mental retardation syndrome X-linked (ATRX) gene, and tumor suppressor gene-53 (p53) mutation in glioma and their correlation with various clinical and radiological parameters.
Methods: In this prospective observational study, histopathological slides of glioma (2017-2018), were analyzed for IDH-1, ATRX and p53 mutations and their correlation with various clinical and radiological parameters.
Results: IDH-1 mutation was found in 48 (38.7%), ATRX loss in 38 (30.6%) and p53 mutation in 40 (32.5%) patients. The expression of IDH-1 was significantly higher (43.7%) in adults; however, no significant difference was seen with gender. Also 51.2% of patients, who presented with seizures, showed IDH-1 expression; and 27.7% of patients, who had neurological deficit also showed IDH-1 expression. IDH-1 expression was high in glioma located at insula (73.3%) and parietal lobe (71.4%); while ATRX loss was seen in glioma located at insula (80%). Intraventricular glioma characteristically lacks all three markers: IDH-1 expression, p53 overexpression and ATRX loss. IDH-1 expression and p53 overexpression was seen mainly in diffuse fibrillary astrocytoma, oligodendroglioma, anaplastic astrocytoma and glioblastoma.
Conclusions: Molecular subtyping is of paramount importance in glioma management. IDH-1 mutation is commonly observed in adults and patients presenting with seizures. The duration of symptoms correlates with IDH-1 and ATRX mutations. Hypothalamic tumors lack all three mutations.

Keywords: Isocitrate dehydrogenase-1 mutation, Glioma, Immunohistochemistry, α-thalassemia/mental retardation syndrome X-linked gene, Tumor suppressor gene-53, Astrocytic tumors

INTRODUCTION

Glioma constitutes nearly three-fourth of all the primary brain tumors, out of which, majority are glioblastoma.[1] Bailey and Cushing introduced a naming convention for glioma and proposed a classification system based on morphological characteristics.[2] Later on, the morphology based classification was modified by the 'first edition' of the World Health Organization (WHO) guidelines (1979).[3]

Thereafter, the classification for the central nervous system tumors were amended and published in 1993, 2000, 2007, and 2016. The molecular subtyping is gaining worldwide acceptance and recognition as a paramount factor governing surgical decision making.[3] The molecular profiling helps the surgeon to decide whether aggressive surgical debulking in needed or not, or if adjuvant chemotherapy or target therapy is required or not. In our study, we have prospectively analyzed the correlation of clinical and radiological profile of the histopathologically proven glioma patients. The aims of our study was to determine the protein expression signatures of important growth-control genes, i.e., isocitrate dehydrogenase-1 (IDH-1), α-thalassemia/mental retardation syndrome X-linked (ATRX) gene, and tumor suppressor gene-53 (p53) mutation, in the cohort of glioma, and to analyze clinico-radiological patterns and differences among these.

METHODS

Study design

In this single-centre observational study, histopathological slides of all the operated patients of glioma, from 2017 to 2018, were analyzed for IDH-1, ATRX and p53 mutations. The patients with inadequate tumor tissue and/or incomplete medical records were excluded. Institutional ethical clearance and individual consent to use clinical, radiological and histopathological details of patients were taken as per our departmental protocol.

Study parameters

The patient's details were noted from the hospital information system (HIS) and patient record files from the departments of Neurosurgery and Pathology. Their clinical details in form of age, sex, duration of symptom, clinical features, radiological findings and operative details were noted. The slides were reviewed and the histological diagnosis was established.

Immuno-histochemical examination

Expression of IDH-1 protein, ATRX mutation and p53 expression were determined by the standard streptavidin biotin peroxidase immunohistochemical method. We used H09 (mouse monoclonal) clone of IDH-1 antibody at dilutions 1:30 (category number DIAH09, Dianova), DO-7 (rabbit polyclonal) clone of ATRX antibody at 1:200 dilutions (category number HP A001906, sigma aldrich),

and Mo a Hu clone of p53 antibody at dilutions 1:80 (category number M700101, Dako).

For interpretation, number of the immune-reactive tumor cells were expressed as a percentage. In cases with heterogeneous immunoreactivity, areas with the strongest staining were scored. For interpretation of ATRX in immunohistochemistry (IHC) only nuclear staining was considered. Vascular endothelial cells, and infiltrating lymphocytes and reactive astrocyte nuclei served as positive internal controls. More than 50% loss of nuclear staining was considered as ATRX loss. Similarly, for the interpretation of p53, more than 50% of tumor cells showing strong nuclear reactivity was labelled as p53 overexpression/mutation. For IDH-1 interpretation, diffuse cytoplasmic staining was interpreted as IHC-positive. It was interpreted as IHC-negative, if no cytoplasmic positivity was seen in tumor cells. DNA based analysis (direct DNA Sangers's sequencing) was further performed in IDH-1 IHC-negative cases, wherein, DNA from the formalin fixed paraffin embedded (FFPE) tumor sections using the QIAamp DNA FFPE Tissue Kit (QIAgen, Valencia, California 56404) were interpreted.

Primer sequences used were forward 5′AATGAGCTCTATATGCCATCACTG3′ and reverse 5′ TTCATACCTTGCTTAATGGGTGT3′. Polymerase chain reaction (PCR) amplification was performed in a total of 10 mL reaction mixture having 1 mL of 10×PCR buffer, 0.8 mL of 10 mM 2′-deoxynucleoside 5′-triphosphate (dNTPs), 0.25 mL of each forward and reverse primers, and 0.2 mL of AmpliTaq gold PCR master mix (applied biosystems, Inc Foster City, California) and 50 ng of tumor DN. Initial denaturation was performed at 95°C for 5 min. This was followed by 37 cycles of amplification consisting of denaturation at 95°C for 30 sec, annealing at 60°C for 45 sec, and extension at 72°C for 1 min and final extension at 72°C for 2 minutes. Bidirectional sequencing was performed using ABI (Applied Biosystems) 3730 sequencer.

Statistical analysis

Statistical package for social sciences, version 23.0 (SPSS-23) was used for data analysis. A P-value of less than 0.05 is considered as statistically significant. To test the association/difference in proportions between two categorical variables, Pearson chi-square test was used. In case, the expected frequency in any cell was reported was less than 5, Fisher exact test was used in place of chi-square test for the same objective.

RESULTS

Clinico-radiological profile of patients

A total of 202 glioma cases were operated during 2017-2018 at our department; out of which 124 cases (male:female=81:43) were included and analyzed subsequently for molecular subtyping IHC. Seventy-eight

cases were excluded on grounds of inadequate sample or staining. Mean age of patients was 35.9 years (range from 3 to 75); with 21 patients in pediatric age (less than 18-years).

The duration of symptoms before admission ranges from a less than 1-month (n=27), 1-6 months (n=48) and more than 6 months (n=49). Most common clinical presentation was raised intracranial pressure (n=56) followed by sensory-motor deficits (n=47) and seizure (n=41). Most common location of glioma was frontal lobe (n=36) followed by insular (n=15) and temporal lobe (n=15). Radiologically, the tumor showed contrast enhancement in 44 (35.5%) patients, intra-tumoral calcification was present in 27 (21.7%) patients and cystic degeneration was seen in 27 (21.7%) patients.

The most common histopathology was astrocytic tumors (n=77) followed by oligodendroglial tumors (n=22), ependymal tumor (n=18) and mixed glial tumor (n=7) (Figure 1 and 2). The most common astrocytic tumor was glioblastoma (n=33) followed by diffuse fibrillary astrocytoma (n=25) and pilocytic astrocytoma (n=12). Overall, the most common WHO grade of tumor was grade II (n=62), followed by grade IV (n=33), grade I (n=15) and grade III (n=14). Summary of the clinical, radiological and molecular profile details of this study is given in Table 1.

Molecular subtyping and its clinico-radiological correlation

IDH-1 mutation was found in 48 (38.7%) patients while 76 (61.3%) patients were labelled as IDH-1 wild type. The expression of IDH-1 was significantly higher (43.7%) in adults as compared to that in children (P=0.01). Similarly, the expression was higher in females (41.9%), though the difference was statistically not significant. The ATRX mutation (ATRX loss) was found in 38 (30.6%) patients and p53 mutation was found in 40 (32.5%) patients; however, no significant difference was seen with age or gender.

The expression of IDH-1 and p53 overexpression showed a trend that the longer is the duration of symptoms, the more is expression of IDH-1. IDH-1 expression was noted in 51.2% of patients, who presented with seizures (P=0.04); and 27.7% of patients, who had neurological deficit at time of admission, showed IDH-1 expression (P=0.04). No similar correlation was found with ATRX loss and p53 overexpression.

IDH-1 expression was high in glioma located at insula (73.3%), parietal lobe (71.4%) and corpus callosum (100%; all three patients). ATRX loss was seen in glioma located at insula (80%), thalamus (50%) and brainstem (50%). On analyzing the radiological characteristics, no significant correlation was seen with IDH-1 expression or ATRX loss. Hypothalamic glioma characteristically lacks all three markers; IDH-1 expression, p53 overexpression and ATRX loss.

Table 1: Summary of glioma cases (n=124).

Clinical parameters	Number of cases
Age (years)	
Mean	35.9
Range	3-75
<18 year (children)	21
>18 year (adult)	103
Sex	
Male	81
Female	43
Duration of symptoms	
< 1 month	27
1-6 months	48
> 6 months	49
Clinical features	
Raised intracranial pressure	56
Motor deficit	47
Seizure	41
Location of tumor	
Frontal lobe	36
Temporal lobe	15
Insular lobe	15
Temporo-parietal lobe	3
Parietal lobe	7
Intraventricular	11
Thalamus	4
Corpus callosum	3
Brain stem	2
Posterior fossa	9
Spine	13
Others	6
Radiological features	
Contrast enhancement	44
Intratumoral calcification	27
Cystic degeneration	27
Histopathology	
Astrocytic tumors	77
Glioblastoma	33
Diffuse fibrillary astrocytoma	25
Pilocytic astrocytoma	12
Pleomorphic xanthoastrocytoma	1
Anaplastic astrocytoma	6
Oligodendroglial tumors	22
Oligodendroglioma	19
Anaplastic Oligodendroglioma	3
Ependymoma	18
WHO Grade I and II ependymoma	13
Anaplastic ependymoma	5
Molecular profile	
IDH-1 mutation	48
ATRX loss	38
p53 overexpression	40

The relation of these molecular markers with histopathological grades and types were also studied. IDH-1 expression was seen mostly in diffuse fibrillary astrocytoma (60%) followed by oligodendroglioma (57.9%), anaplastic astrocytoma (50%) and least common in glioblastoma (36.4%). Similar trend was seen for p53 overexpression also. ATRX loss was seen mostly in anaplastic astrocytoma (66.6%) followed by diffuse fibrillary astrocytoma (50%). Interestingly, ATRX was significantly retained in pilocytic astrocytoma, oligodendroglioma and glioblastoma. Summary of the molecular profile of glioma cases is given in the Table 2.
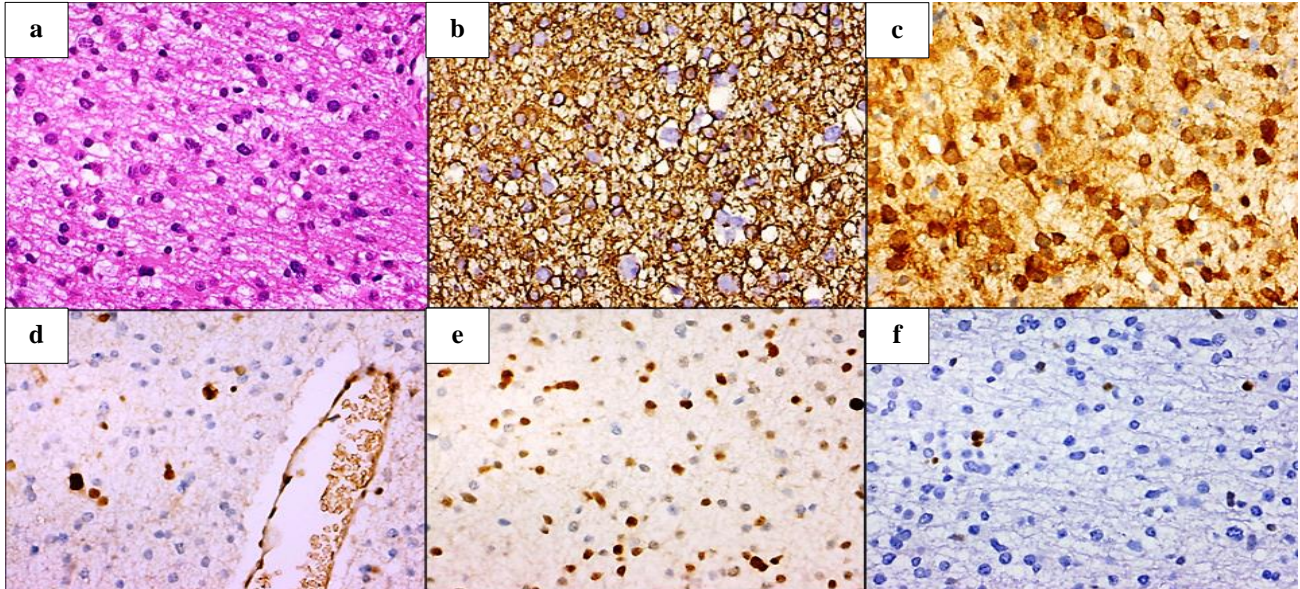

Figure 1: (a) H and E stained section shows diffuse astrocytoma WHO grade II (X400), (b) on immunohistochemistry tumor cells are positive for GFAP (X400), (c) cytoplasmic positivity of IDH-1 (X 400), (d) loss of nuclear expression of ATRX (X400), (e) overexpression of p53 nuclear positivity (X400) and (f) Ki 67 is <1% (X400).
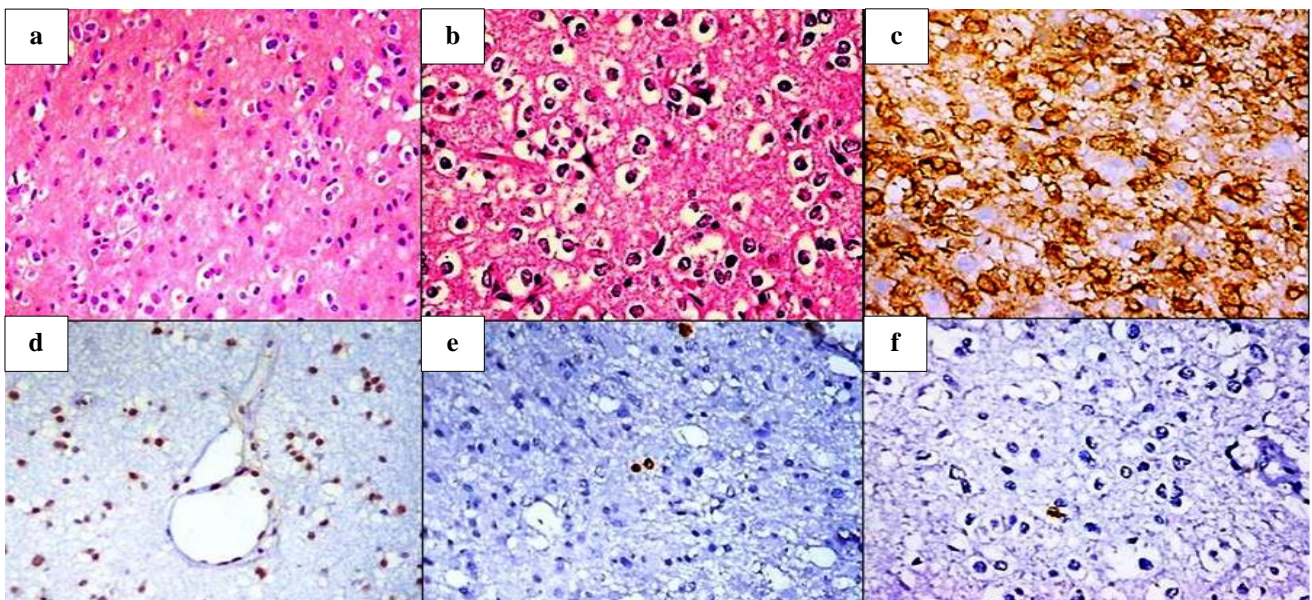

Figure 2: H and E stained section shows oligodendroglioma WHO grade II (X200), (b) tumor cells show perinuclear clearing and chicken wire appearance (X400), (c) on immunohistochemistry tumor cells are show cytoplasmic positivity of IDH-1 (X 400), (d) retention of nuclear expression of ATRX (X400), (e) overexpression of p53 nuclear positivity in <1% (X400) and (f) Ki 67 is <1% (X400).

Table 2: Molecular profile of glioma patients included in the study.

Study parameter		IDH Expression (n=48)	ATRX Loss (n=38)	p53 overexpression (n=40)
Age (in years)	<18	3 (14.3)	04 (19)	4 (19)
	≥18	45 (43.7)	34 (32)	36 (35)
Gender	Male	30 (37)	25 (30.9)	26 (32)
	Female	18 (41.9)	13 (30.2)	14 (32.5)
Duration of symptoms	< 1 month	09 (33.3)	08 (30.8)	07(25.9)
	1-6 months	18 (37.5)	10 (20.4)	17 (35.4)
	>6 months	21 (42.8)	20 (40.8)	16 (32.7)
Clinical symptom	Seizure	21 (51.2)	16 (39)	16 (39)
	Raised ICP	21 (37.5)	21 (37.5)	21 (37.5)
	Motor deficit	13 (27.7)	10 (21.3)	13 (27.7)
Radiological pattern	Contrast enhancement	14 (31.8)	12 (27.3)	20 (45.4)
	Calcification	07 (25.9)	09 (27)	06 (22.2)
	Cystic changes	11 (40.7)	10 (37.0)	09 (33.3)
Histopathology	Pilocytic astrocytoma	00 (0)	02 (16.7)	01 (8.3)
	Ependymoma	00 (00)	01 (50)	00 (0)
	Diffuse fibrillary astrocytoma	15 (60)	13 (52)	13 (56)
	Ependymoma	00 (00)	00 (0)	02 (18.1)
	Oligoastrocytoma	05 (71.4)	03 (42.9)	02 (28.6)
	Oligodendroglioma	11 (57.9)	04 (21.0)	00 (0)
	Glioblastoma	12 (36.4)	09 (25)	15 (45.4)
Tumor location#	Frontal	17 (47.2)	11 (30.6)	14 (38.9)
	Insular	11 (73.3)	12 (80)	08 (50)
	Temporal	07 (46.7)	04 (26.7)	04 (26.7)
	Temporo-parietal	01 (33.3)	00 (0)	02 (66.7)
	Parietal	05 (71.4)	01 (14.3)	04 (57.1)
	Occipital lobe	01 (100)	00 (0)	00 (0)
	Parieto-occipital	00 (0)	01 (100)	00 (0)
	Spine	01 (7.7)	03 (23)	03 (23)
	Orbit	00 (0)	00 (0)	01 (50)
	Intraventricular	02 (18.2)	02 (18.2)	01 (9.1)
	Thalamus	00 (0)	02 (50)	02 (50)
	Hypothalamus	00 (0)	00 (0)	00 (0)
	Corpus callosum	03 (100)	00 (0)	00 (0)
	Brainstem	00 (0)	01 (50)	00 (0)
	Posterior fossa	00 (0)	01 (11.1)	01 (11.1)

number in bracket represent percentage of patients positive for that specific location.

DISCUSSION

Since the amendments of WHO 2016 classification, the insights into the molecular pathology of glioma have significantly improved both the understanding of gliomagenesis as well as their prognosis and likelihood of response to specific adjuvant therapies. It would not be a surprise, if one day, the primary treatment option of glioma would be molecular target therapy. Therefore, understanding the role of these mutations in the natural course of glioma, is of paramount importance. Accumulation of the genetic alterations are thought to initiate the glioma pathogenesis and then further progression of the tumor.[2-5] The molecular signature of glioma is of diagnostic and prognostic significance.[6-8] Various genetic alterations described in the literature are 1p/19q deletions for oligodendrogliomas, O6-methylguanine-DNA methyltransferase (MGMT) promoter hypermethylation, and epidermal growth factor receptor (EGFR) alterations. These molecular profiling allows more accurate classification and better prediction or prognostication of the clinical outcome. The identification of the IDH-1 gene mutation, as well as ATRX gene became the turning point in the history of glioma research. Tumor suppressor gene p53 inactivation is a key event in human oncogenesis.[7]

Considering the importance of these molecular markers in gliomagenesis and their prognostic and therapeutic role, present study was outlined to evaluate the expression of these molecular markers (IDH-1, ATRX and p53 expression) in various grades of glioma and correlate the expression of these markers with clinico-radiological features.

Role of IDH mutation in gliomagenesis

IDH genes encodes two types of proteins predominantly: IDH-1, cytoplasmic form, and the IDH-2, mitochondrial form.[8] In case there is mutation of above gene, the amino acid is substituted at the active site, resulting in weird form of protein production. Among 90% of cases, mutation effects the codon 132 of IDH-1, while in 10% cases, the mutation effects the codon 172 of IDH-2. Physiologically, the IDH-1 (in cytoplasm) and IDH-2 (in mitochondria) converts isocitrate to α-ketoglutarate (α-KG). However, the mutated IDH produces stereotype alternate of α-KG, and the new product is D-enantiomer of 2-hydroxyglutarate (D-2HG), that in turn accumulates within tumor cells.[9,10] The D-2HG is supposed to be the main driver of gliomagenesis. The enzymatic blockade induced by the accumulation of D-2HG results in increased levels of histone H3 lysine methylation levels and in global DNA hypermethylation.[9-11] The IDH mutation is followed by 'epigenetic remodelling', that acts as a fertile substrate in which, over time, the occurrence of new "lineage-defining" alterations (i.e., 1p/19q codeletion, CIC, FUBP1 and pTERT mutations in oligodendrogliomas; p53 and ATRX mutations in astrocytomas) lead to gliomagenesis.[9-12] Succeeding "tertiary" alterations (activating mutations of intracellular signaling pathways or amplification/activation of receptor tyrosine kinases) may then occur and lead to tumor progression to higher grades.[11,12] It is interesting to note that these IDH mutations are no longer needed, once tumor has progressed. Nonetheless, some authors propose that there is an advantage of losing mutant IDH, once the tumor has progressed.[10-13] The D-2HG not only effects intracellular micro-environment, but also alters the functioning of surrounding neurons. The presence of IDH mutation has been shown to correlate with the risk of seizure. Additionally, the IDH mutation has been shown to decrease immunity or antitumor immune response.[9-13]

There are three importance of IDH mutation: classifying diffuse glioma into IDH mutant-1p/19q codeleted gliomas (corresponding to oligodendrogliomas), IDH mutant 1p/19q non-codeleted gliomas (corresponding to grade II and III astrocytomas and secondary glioblastomas) and IDH-wildtype gliomas (primary glioblastomas and a minority of diffuse grade II and III astrocytomas); prognosticating patients as the IDH mutant, 1p/19q codeleted gliomas has a median survival of 15 years, the IDH mutant, non codeleted gliomas have a median survival of 7-9 years for grade II and 5-6 years for grade III, while the IDH wild type lower grade gliomas has median survival of 2 years for grade III and 3.5 years for

grade II gliomas and; response to chemotherapy and radiotherapy as the IDH mutant gliomas have reduced levels of nicotinamide adenine dinucleotide (NADH) and nicotinamide adenine dinucleotide phosphate (NADPH) and inhibition of IDH restores their levels, therefore reduces the cytotoxic effect of ionizing radiations on tumor cells.[10-13]

Role of ATRX and p53

Physiologically, ATRX protein is ubiquitously expressed in cell nuclei (e.g., endothelial cells, pre-existing glial cells which serve as a positive internal control). Mutation in the ATRX gene results in a loss of nuclear protein expression in tumor cells.[14,15] The p53 gene is located on human chromosome 17p13.1 and encodes p53 protein, which is a homotetramer that adapts a dimer-of-dimers topology.[16] The protein is positioned at the center of a regulatory network that controls cell proliferation, survival, genome integrity and other functions, thereby governs transcription activity of a cell.[16,17] Under normal conditions, p53 activity is low and checked by MDM2 and MDM4 through ubiquitination and degradation. The interaction between p53 and MDM2 is disrupted in response to stress signals such as DNA damage, further leading to p53 induction.[18] p53 integrates stress signals and promotes cell cycle arrest, senescence and apoptosis to prevent damaged cells from propagation.

The latest iteration of The Cancer Genome Atlas (TCGA) glioblastoma project shows that the p53 pathway was deregulated in nearly 85% of glioma.[19] The mutational status of p53 is associated with glioblastoma progression and p53 inactivation is correlated with a more invasive, less apoptotic, more proliferative, and more stem-like phenotype.[20,21]

Correlation of IDH1, ATRX and p53 mutations with clinico-radiological profile

In this study, a higher degree of IDH-1 expression was seen in adults (53%) and similar observations were also noted by Pollack et al and Bleeker et al.[22,23] This differential expression of IDH-1 among different age group suggests existence of various age related pathways of tumorigenesis. Despite of the fact that many studies have described that IDH-1 mutation is more common in glioma located in frontal lobe, IDH-1 mutation was common in tumors located at the insular region (73.3%), in the present study.[24] This difference may be because of the referral pattern in our country, as being a tertiary institute, insular glioma came across more frequently, compared to other hospitals. Similar age or gender correlation was not found for p53 overexpression. This study showed p53 overexpression in 19% of pediatric patients and 33.3% of adult patients. Rasheed et al in their study of 72 adults and 48 childhood glioma, found that 22% adult and 2.1% pediatric patients with p53 gene alterations.[25] The p53 mutation was equally expressed in males and females in the present study, however, this

association was not statistically significant. Cunningham et al in their study of 120 cases, found that p53 overexpression was more in males as compared to females (46% versus 27 %).[26]

As highlighted in present study that longer the duration of symptoms, higher the degree of IDH-1 expression and patients with duration of symptoms more than 6 months showed the maximum IDH-1 expression (42.8%), though statistically insignificant. Thus, the present study supports that IDH-1 mutated glioma has longer history and are slow growing. ATRX retained status was significantly associated with duration of symptom in group of <1 month and 1-6 month (P≤0.05) while ATRX loss status was noted maximum in patients with duration of symptoms more than 6 months, however, this association was not found statistically significant.

Ikemura et al studied ATRX status in 193 cases of glioma and found that glioblastoma patients with ATRX loss tumors were much younger than those with ATRX retained tumors.[27] The present study also noted similar finding, however, it was not statistically significant.

It was also noted that history of seizure and absence of neurological deficit were significantly associated with IDH-1 expression. These findings correlate with data from other studies also, like Stockhammer et al observed similar result and postulated that it may be due to altered metabolic profile of IDH-1 mutated cells which have become epileptogenic.[24] On comparing IDH-1 expression with the radiological findings of glioma in the present study, no statistical significant association was noted between the radiological findings (contrast enhancement, calcification and cystic changes) and IDH-1 mutation. However, Carrillo et al reported that absence of contrast enhancement has statistically significant association with IDH-1 expression.[28]

The present study showed that most of the oligoastrocytoma tumors (71.4%) had IDH-1 expression followed by oligodendroglial tumors (54.6%) and astrocytic tumor (42.2%). None of the ependymal tumor had IDH-1 positivity. This finding was in concordance with the various other studies.[24-29] Glioblastoma with ATRX loss occurred more frequently in locations other than the cerebral hemispheres (5/15 versus 9/103, p=0.006) in one of the study described in the literature.[29] Similar finding was also observed in the present study (4/9 versus 6/24 P=0.008). In this study, the astrocytic tumors (42.9%) had more expression of p53 overexpression than oligodenroglial tumors (4.5%). This finding is concordant with other reported studies.[20-24]

Sarkar et al in their study of 62 patients, found p53 overexpression in 50% glioblastoma.[30] It was found that 45.4% cases of glioblastoma showed p53 overexpression.

The present study showed that there was an increase in the prevalence of ATRX loss from low grade to high grade i.e.

I to III (20, 32.5 and 42.9% respectively), while in grade IV, it has further increased to 66.6%. It was statistically significant only in grade I and grade IV tumors. This finding is similar to the study by Liu et al who suggested that this loss is a marker of progression.[29]

Is IDH-1 mutation related to ATRX or p53 expression?

IDH-1 mutation was observed in 48/124 (38%) of the glial tumors. Moreover, patients with 'IDH1R132H mutation and ATRX loss' were young (19-49 years), however this was not statistically significant. Also, IDH-1 mutation was much more common in astrocytic tumors with ATRX retained (60%) than expressing ATRX loss (50%) (P<0.0001, χ2 test). The ATRX loss was more common in astrocytic tumors with p53 overexpression (45.4%) than in astrocytoma without p53 alteration (29.5%).

Are hypothalamic glioma or insular region glioma different?

An interesting finding was observed that glioma located at hypothalamic zone did not show IDH-1 mutation, p53 overexpression and ATRX loss. Mistry et studied molecular markers from the 254 glioblastoma patients and concluded that the glioma in ventricular zone do not display a distinct molecular signatures.[31]

Similarly, Eseonu et al analyzed 74 patients of insular glioma found that the IDH-1 mutation and 1p/19q codeletion is well correlated with survival of these patients.[32] Leeuw et al in their systemic review, found frontal lobe as the most common location for IDH-1 and 1p/19q codeletion glioma, however, insula being the second or third common; and again ventricle being the least common location.[33] Tang et al studied the molecular characteristics of insular glioma and found that purely insular grade-II glioma displayed a high frequency of IDH1 mutations with favorable outcome.[34]

CONCLUSION

The present study in single institutional analyzed a large-scale descriptive database, focusing on glioma, which models population-based prevalence from northern India and adds substantial data on status of IDH-1, ATRX and p53 mutation in glioma. Immune-histological/genetic study for each glioma patient is recommended, henceforth, the management is individualized. The duration of symptoms and location of glioma correlates with IDH-1, ATRX or p53 mutation. IDH-1 expression and ATRX loss is seen in diffuse fibrillary astrocytoma. It is advisable to maintain an institutional/departmental tumor bank, wherein, all tumor tissue should be stored for any future research and routine molecular analysis as and when required.

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