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Role Of Diffusion Weighted Imaging And Reliability Of 'T2-Flair' Mismatch Sign In Grading And Characterization Of Astrocytomas

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ABSTRACT

Background:-
Brain tumors may show various degrees of diffusion changes related to tumor cellularity and the nucleus-cytoplasmic ratio. High-cellularity of tumors results in reduced intercellular space, which in turn results in water diffusion restriction thus causing low Apparent Diffusion Coefficient (ADC) values. Diffuse and anaplastic lower-grade astrocytomas harbour specific molecular features, such as isocitrate dehydrogenase (IDH) 1 and 2 gene mutation

Objective:-
The objective of this study is to evaluate the role of diffusion weighted imaging in grading of astrocytomas. This study also puts some light on the reliability on 'T2-FLAIR' mismatch sign in characterizing the IDH mutant and wild counterparts of anaplastic and diffuse astrocytomas.

Results:-
Out of 36 patients , 31 patients with high grade astrocytomas proven by histopathological analysis showed diffusion restriction with reduced ADC values, with a mean ADC value of 0.885 × 10−3 mm2 /s. Almost all patients who had low grade astrocytomas proven by histopathological analysis N= 5 showed no diffusion restriction with a mean ADC value of 1.157 × 10−3 mm2 /s. There is a significant decrease (p value – 0.034) in mean ADC values of high grade astrocytomas compared to low grade astrocytomas. Out of the 5 patients who were reported to have microcysts in their pathological specimens , MRI images of 4 patients showed , 'T2-FLAIR' mismatch sign.

Conclusion:
Lower ADC values suggest a malignant high-grade astrocytoma, whereas higher ADCs suggest low-grade astrocytoma. T2-FLAIR mismatch sign may reflect microcyst formation in pathological specimens , and is a useful sign in categorizing anaplastic and diffuse astrocytomas into their IDH-mutant and wild counterparts.

KEYWORDS: Patient selection: MRI protocol and Image Processing.

INTRODUCTION

Diffusion-weighted imaging (DWI) is a magnetic resonance imaging (MRI) sequence traditionally used in neuroradiology for the assessment of acute ischemia, inflammatory diseases, and evaluation of central nervous system (CNS) tumors.[1]

Brain tumors may show various degrees of diffusion changes related to tumor cellularity and the nucleus-cytoplasmic ratio. High-cellularity of tumors results in reduced intercellular space, which in turn results in water diffusion restriction thus causing low Apparent Diffusion Coefficient (ADC) values, which are useful for differentiating tumor type and grade[2].

According to World Health Organization (WHO) 2016 classification ,diffuse and anaplastic lower-grade astrocytomas harbour specific molecular features, such as isocitrate dehydrogenase (IDH) 1 and 2 gene mutation. Also, IDH-mutant-type astrocytomas show a better clinical outcome than IDH-wild-type astrocytomas with do not harbour the mutation. Therefore, preoperative identification of these molecular subtypes is useful for planning surgical procedures, devising the treatment strategy, and prognosis[3].

ACTA SCIENTIAE

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Recent studies suggest T2-FLAIR mismatch sign, which has been validated as a highly specific imaging marker of IDH-mutant astrocytomas. The definition of 'T2-FLAIR mismatch sign'comprises of 2 distinct MRI features: i) Tumor exhibits complete and homogeneous hyperintense signal on T2-WI, ii) Tumor exhibits relatively hypointense signal on the FLAIR sequence indicating partial suppression except for a hyperintense peripheral rim.[4]

Pathological analysis of IDH-mutant astrocytomas showed microcystic changes which has been attributed to T2-FLAIR mismatch sign.[5]

MATERIALS AND METHODS:

Patient selection:

We retrogradely analysed 36 patients who underwent neurosurgical procedure between August 2022 and May 2024, diagnosed as having WHO grades II–IV astrocytomas. Out of the 36 patients , 31 patients were diagnosed to have high-grade astrocytomas (23glioblastomas [WHO grade IV] and 8 anaplastic astrocytomas [WHO grade III]) and 5 low-grade astrocytomas (diffuse astrocytomas [WHO grade II]). All histopathologic diagnosis were determined on the basis of surgical specimens according to the WHO criteria.

We reviewed the preoperative MR imaging examinations all these 36 patients. The diffusion-weighted imaging (DWI) of all these patients were re-evaluated. Most of the low-grade astrocytomas displayed relatively well-defined margins, usually homogeneous tumors without any significant mass effect with minimal or no surrounding edema and little or no enhancement with contrast administration. The high-grade astrocytomas showed ill-defined margins, often heterogeneous with evidence of significant mass effect, extensive surrounding vasogenic edema and displayed heterogeneous / thick irregular ring enhancement with contrast administration.

We excluded those patients with infratentorial astrocytomas that prevented accurate ADC analysis, and those who had undergone any major surgery / chemotherapy before MR imaging.

MRI protocol and Image Processing:

DWI was performed for all patients in the axial plane using single shot echo-planar spin-echo sequence EPI [3.400/100 ms (TR/TE)], matrix 192 × 192, slice thickness 5 mm, gap 1.5 mm with a duration of 120 s, and b = 0, b = 500, and b = 1000 applied in the X, Y, and Z directions. Postprocessing of ADC maps was done using the standard software supplied on the machine console to obtain the ADC value and map; the lowest ADC values were measured using a region of interest in the center of the lesion, while preferably avoiding cystic and necrotic areas. Standard mean ADC values were calculated automatically and expressed in 10^{-3} mm^2 /s. A cut-off value of 1×10^{-3} mm^2 /s was used to differentiate restricted areas from nonrestricted areas.

DISCUSSION:

S.No	Grades of astrocytomas	N (36)	Max ADC Value (× 10^{-3} mm^2 /s)	Min ADC Value (× 10^{-3} mm^2 /s)	Mean ADC value (× 10^{-3} mm^2 /s)	SD
1.	***High grade astrocytomas***	***31***				
1a)	Glioblastomas (WHO grade IV)	23	1.3	0.5	0.873	+/- 0.274
1b)	Anaplastic astrocytomas (WHO grade III)	8	1.5	0.7	0.897	+/- 0.196
2	***Low grade astrocytomas***	***5***				

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2a)	Diffuse astrocytomas (WHO grade II)	5	1.6	0.7	1.157	+/- 1.142

Table 1. ADC values of various grades of astrocytomas.

Most of the patients who had high grade astrocytomas proven by histopathological analysis N= 31 (23 glioblastomas [WHO grade IV] and 8 anaplastic astrocytomas [WHO grade III]) showed diffusion restriction with reduced ADC values (Fig. 3) , except three patients whose ADC values were >1 × 10^{-3} mm^2 /s. The range of ADC values for high grade astrocytomas was from 0.5× 10^{-3} mm^2 /s to 1.4 × 10^{-3} mm^2 /s , with a mean ADC value of 0.885 × 10^{-3} mm^2 /s .

Almost all patients who had low grade astrocytomas proven by histopathological analysis N= 5 (diffuse astrocytomas [WHO grade II]) showed no diffusion restriction with relatively high ADC values (Fig.1) , except one patient whose ADC values was <1 × 10^{-3} mm^2 /s. The range of ADC values for low grade astrocytomas was from 0.7× 10^{-3} mm^2 /s to 1.6 × 10^{-3} mm^2 /s , with a mean ADC value of 1.157 × 10^{-3} mm^2 /s.

The findings of our study reveal that, there is a significant decrease (p value – 0.034) in mean ADC values of high grade astrocytomas (0.88 × 10^{-3} mm^2/s) compared to low grade astrocytomas (1.15 × 10^{-3} mm^2/s). Lower ADC values suggest a malignant high-grade astrocytoma, whereas higher ADCs suggest low-grade astrocytoma. This is in accordance with Yamasaki et al[6] who demonstrated that a significant negative correlation existed between ADC and astrocytic tumors of World Health Organization grades 2–4.

The grade of a tumour is related to various pathological features such as cellularity, nuclear atypia, mitosis, pleomorphism, neo-angiogenesis and necrosis[7]. Of these features, tumor cellularity is the main correlate of quantitative assessment with DWI[8]. With increasing cell density as seen with increasing grade of tumors, the impeding effects of cellular membranes and reduced intracellular and extracellular fluid are expected to result in low values of ADC in high-grade tumors and therefore high values of ADC in low-grade tumors.[9]

Maria Zulfiqar et al.[10] studied that low ADC values, independent of tumor grade, correlate with poor survival in malignant astrocytomas. Pretreatment DWI with calculation of ADC values may be helpful for planning therapy and in prognostication for patients with high-grade astrocyotomas.

Interestingly 5 patients , [3 out of 8 patients with whose histopathological analysis showed anaplastic astrocytoma (WHO grade III) & 2 out of 5 patients whose histopathological analysis showed diffuse astrocytoma (WHO grade II)] were reported to have abundant microcysts in their pathological specimens upon H&E staining.

We reviewed the T2 & FLAIR weighted images of all these 13 patients with anaplastic and diffuse astrocytomas. Out of the 5 patients who were reported to have microcysts in their pathological specimens , MRI images of 4 patients showed , tumour with homogeneously hyperintense signal in T2 weighted images , partial suppression with peripheral hyperintense rim in FLAIR images indicative of 'T2-FLAIR' mismatch sign (Fig.2). None of the patients who were categorized as anaplastic and diffuse astrocytomas , and did not display microcystic change in their pathological specimens, showed 'T2-FLAIR' mismatch sign in their MRI images. This is in accordance with Deguchi et al.[5] who demonstrated that T2-FLAIR mismatch sign may reflect microcyst formation in IDH-mutant astrocytomas and be common in IDH-mutant protoplasmic astrocytoma.

However we did not analyse the IDH-mutant status of these patients, thus posing a potential limitation to our study.

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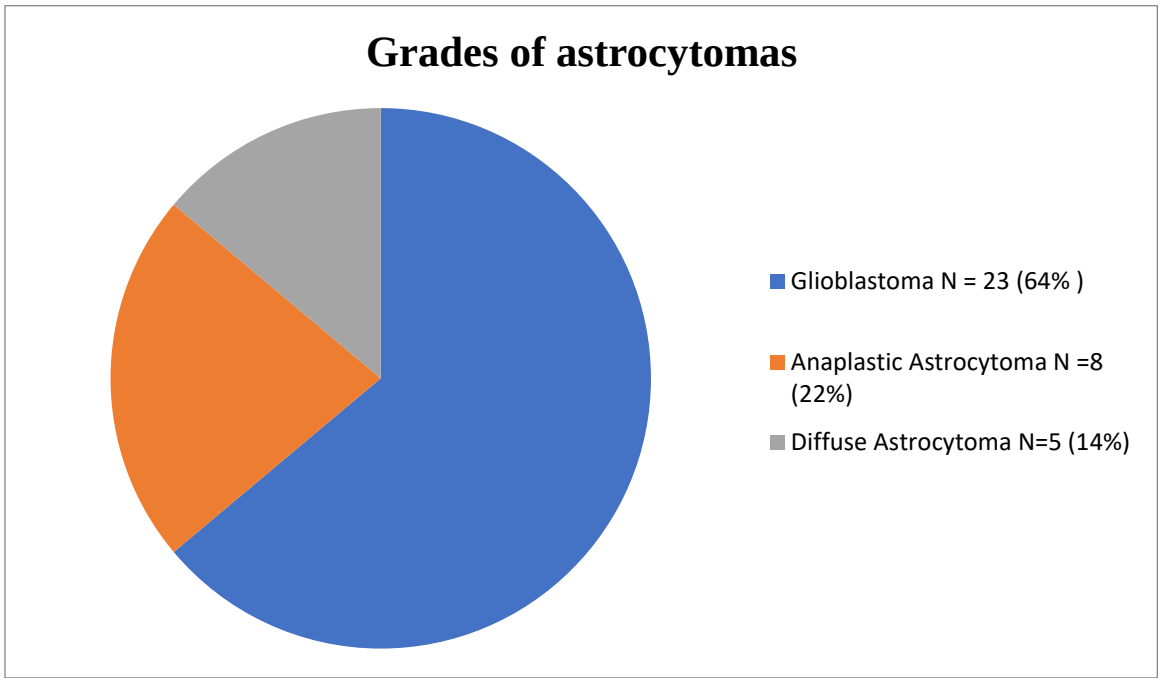

Fig 1. Pie chart showing number of patients with varying grades of astrocytomas

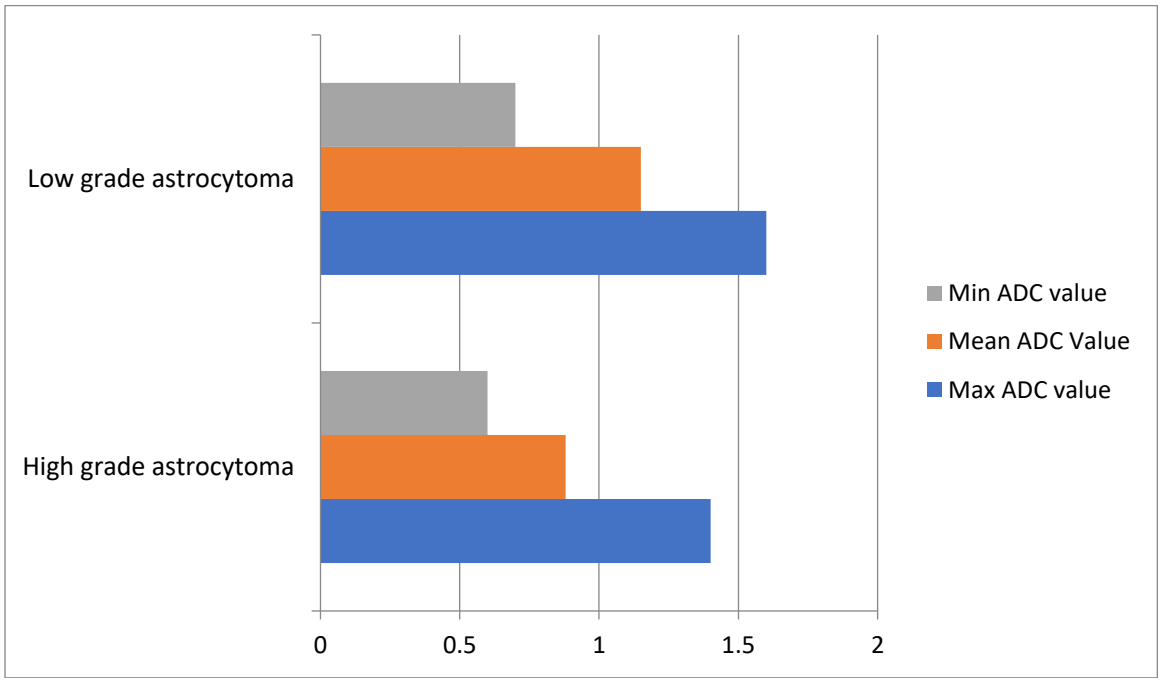

Table 1: Graph shows minimum , mean and maximum ADC values of patients with high grade & low grade astrocytomas. There is a significant decrease (p value – 0.034) in mean ADC value of high grade astrocytomas (0.88×10^{-3} mm^2/s) compared to low grade astrocytomas (1.15×10^{-3} mm^2/s).

CONCLUSION

Lower ADC values suggest a malignant high-grade astrocytoma, whereas higher ADCs suggest low-grade astrocytoma. T2-FLAIR mismatch sign may reflect microcyst formation in pathological specimens , and is a useful sign in categorizing anaplastic and diffuse astrocytomas into their IDH-mutant and wild counterparts.

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IMAGES WITH FOOT NOTES:

IMAGE-1:

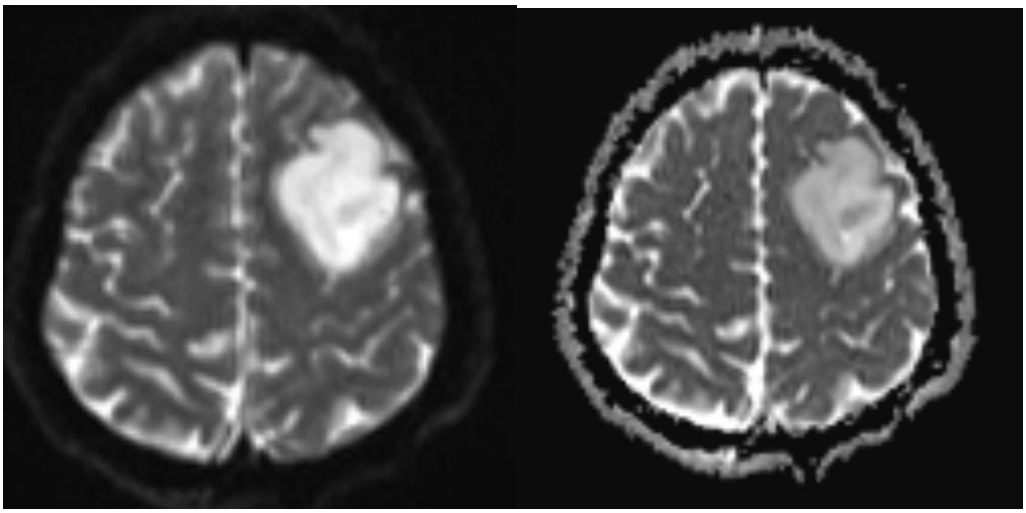

Fig-1: (right) : A patient with diffuse astrocytoma (low grade) showing a well marginated mass in the left frontal lobe, without any diffusion restriction. (left) The ADC value of this tumor was relatively high (1.21×10^{-3} mm^2/s).

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IMAGE -2:

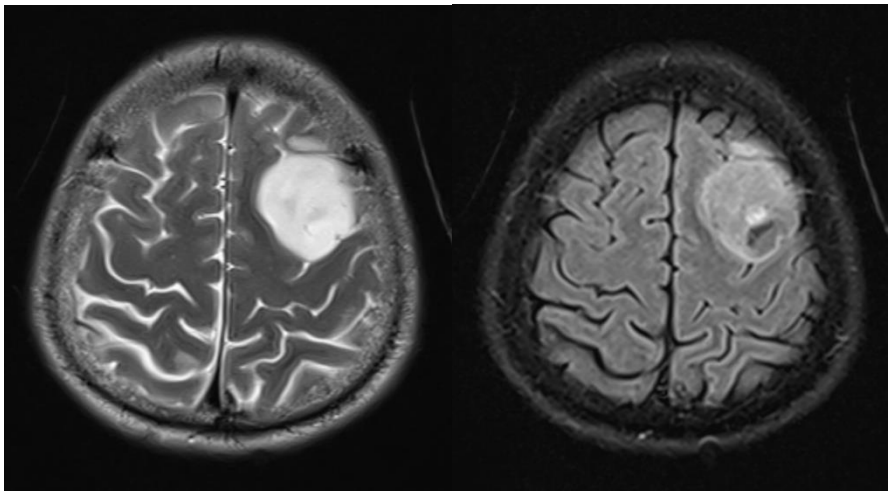

Fig 2: (right) The T2 weighted image of the same patient shows a high signal intensity mass. (left) The mass shows partial suppression in FLAIR image indicative of 'T2-FLAIR mismatch' sign. On histopathological analysis the tumor was proved to be an IDH-mutant diffuse astrocytoma

IMAGE-3:

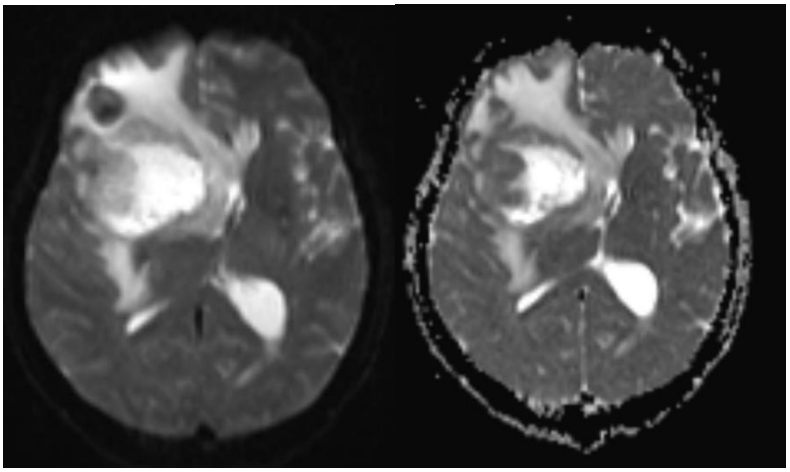

Fig-3 : (right) : A patient with glioblastoma (high grade) showing an ill-defined mass with areas of necrosis, the solid portions of the tumor showing diffusion restriction. (left) The ADC value of this tumor was relatively low (0.71 × 10^{-3} mm^2/s).