

A Retrospective Study to Evaluate the Role of Diffusion MRI in Differentiating Pediatric Posterior Fossa Tumors

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Received: 11-01-2024 / Revised: 22-02-2024 / Accepted: 10-03-2024

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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to evaluate the role of diffusion MRI in differentiating pediatric posterior fossa tumors.

Methods: This study was a retrospective study and conducted in the Department of Radiodiagnosis. The inclusion criteria were pediatric patients less than 20 years of age with posterior fossa tumor who had performed MRI and DWI/ADC prior to any treatment. The study period was of one year. During the study period, there were 100 patients with posterior fossa tumors.

Results: There were 52% male as compared to females. 70% had high grade tumor and 30% had low grade tumor. In high grade tumor, 25 had medulloblastoma and in low grade tumor, 15 had Pilocytic astrocytoma. The ADC ratio cut-off level for differentiation medulloblastoma from ependymoma, medulloblastoma from ATRT, medulloblastoma from pilocytic astrocytoma and medulloblastoma from diffuse midline glioma were noted. The ADC ratio of medulloblastoma was significantly lower than ependymoma, pilocytic astrocytoma and DIPG. The ADC cut-off ratio of ≤ 1.115 allowed discrimination medulloblastoma from other posterior fossa tumors with sensitivity, specificity, PPV and NPV of 94.6%, 82%, 68.4% and 96.8%, respectively.

Conclusion: In Conclusion, diffusion MRI has a significant role in diagnosis of various types of pediatric posterior fossa tumors. ADC ratio can be used to differentiate medulloblastoma from other posterior fossa tumor in pediatric patients with good level of diagnostic performance.

Keywords: Pediatrics, posterior fossa, brain neoplasms, medulloblastoma, diffusion MRI.

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Introduction

The posterior fossa is situated between the tentorium cerebelli above and the foramen magnum below. Anteriorly the clivus, anterolaterally the petrous ridge of the temporal bones, laterally the mastoid part of the temporal bones, and posterior-inferiorly the occipital bone form the bony landmark of the posterior fossa. The cerebellum, the pons, and the medulla are situated within it. [1] Children are more likely to develop posterior fossa tumors than adults. However, the distribution changes with age. [2] One of the leading causes of cancer-related deaths in the pediatric population is due to malignant tumors of the central nervous system (CNS). [3]

Age determines the location of tumors. Supratentorial tumors predominate in neonates, but infratentorial tumors are more prevalent in children over one year of age. [4] Among the different types of childhood brain tumors, their incidence ranges from 1 to 3 per 100,000. [5] Childhood neoplasms occur in the infratentorial region in about 54% to 70% of pediatric brain tumors, whereas in the adult population, it is about 15% to 20%. [5] Common posterior fossa brain tumors in children include juvenile pilocytic astrocytoma (JPA), medulloblastoma, ependymoma, and brainstem glioma. Less frequently, atypical rhabdoid/teratoid tumor, hemangioblastoma, dermoids, schwannoma of the eighth cranial nerve, cerebellar

gangliocytoma, meningioma, high-grade glioma, and metastatic lesions are encountered. [5] About 15-20% of brain tumors in adults occur in the posterior fossa. Subacute strokes are the most prevalent overall lesion of the posterior fossa in adults, while vestibular schwannoma among the extra-axial and cerebellar metastases among the intra-axial lesions are the most frequent neoplastic lesions within it. [1]

The commonest malignancy in the pediatric age group is leukemia, followed by brain tumors. [6] Pediatric brain tumors are usually seen in children below 10 years. [7] The incidence ranges from 1 to 3 per 100,000 cases. [8,9] Primary intracranial tumors most commonly occur in the posterior fossa in children. [10] The location of the tumors is age dependent. In infants, supratentorial tumors are more common, while infratentorial tumors are predominant in children over 4 years. Infratentorial tumors are more common overall, accounting for 45-60% of all cases. [11,12] Even histopathology remains the gold standard for definite diagnosis, but there are some limitations of sampling errors during biopsy from tumor heterogeneity where tumor under grading can occur. It has been reported [13] as diffusion MRI is the non-invasive tool to measure water diffusion within the lesion which could demonstrate whether the lesion has high or low cellularity. Diffusion weighted imaging (DWI) has been explored as a rapid method for grading of brain tumors, either by visual assessment of signal characteristics or quantitative analysis of apparent diffusion coefficient (ADC) values. [14,15]

The aim of the present study was to evaluate the role of diffusion MRI in differentiating pediatric posterior fossa tumors.

Materials and Methods

This study was a retrospective study and conducted in the Department of Radiodiagnosis, PMCH, Patna, Bihar, India. The inclusion criteria were pediatric patients less than 20 years of age with posterior fossa tumor who had performed MRI and DWI/ADC prior to any treatment. The study period was of one year. During the study period, there were 100 patients with posterior fossa tumors.

Imaging Technique

Using a routine brain protocol (Sagittal 3D TFE T1W imaging, Ax TSE T2W and 3D FLAIR imaging, Coronal T2W gradient/Ax SWI and post contrast axial, coronal and sagittal imaging); 3D TFE T1W images (8.6/4.1; number of signal acquired, 1 mm; section thickness, 5 mm; intersection gap, 1 mm; matrix, 26x256; field of view [FOV], 23 x 23 cm), TSE T2W images (4,500/96; number of signal acquired, 1; section thickness, 5 mm; intersection gap, 1 mm; matrix, 400x270; FOV, 23 x 20 cm). T1-weighted fat-

suppressed gradient echo sequences after administration of gadolinium contrast 0.1 mmol/kg (Gadobutrol, Gadovist; Bayer Healthcare Pharmaceuticals) was also performed as part of the routine protocol.

All patients underwent DWI/ADC with either a 1.5T (Siemens Magnetom aera; Siemens Healthcare, Erlangen, Germany) or 3T MR (Phillips Achieva dStream; Philips, Best, the Netherlands) scanners. A single shot echo-planar diffusion-weighted imaging sequence was performed. Imaging parameters of DWI were as followings: 3,000-45,00/89-95 (TR/TE) with diffusion sensitivities $b=0$ and $b=1,000$ s/mm² for both scanners. The diffusion gradients were applied sequentially in three orthogonal directions to generate 2 sets of axial DW images. The ADC maps were automatically generated from the datasets of DWI images using the operating console and ADC were calculated.

Post-Processing

DWI data were transferred to a Synapse 3D workstation (Fujifilm Medical Systems, USA, Inc.) and ADC maps were generated.

Imaging Analysis

MRI were reviewed by two experienced neuroradiologists who were blinded to the patient's pathological diagnosis on Picture Archiving and Communication System (PACS) by consensus manner, as the following details.

i. Conventional MRI Characteristics

All of the imaging were analyzed in conventional MRI characteristics on T1W, T2W, FLAIR, Gradient/SWI and post contrast study. The score of signal intensity on T1W and T2W images were classified into 5 scales (for T1W score; score 1: Higher than white matter, score 2: Isointense to white matter, score 3: As low as gray matter, score 4: Higher than CSF, lower than gray matter, score 5: As low as CSF, and for T2W score; score 1: Lower than white matter, score 2: As low as white matter, score 3: Isointense to gray matter, score 4: Lower than CSF, higher than gray matter, score 5: As high as CSF).

The location of the tumors was classified as midline and lateral location. Cystic component was the area within the tumor that show water signal intensity with smooth border and no rim enhancement and was classified into macrocystic (more than or equal to 1 cm in size) and microcystic (less than 1 cm in size). Necrotic area was the non-cystic and non-enhancing tissue within the tumor which was distinguished from cystic area by its irregular border and lack of rim enhancement and then was classified into presence and absence. Enhancement was graded by the percent of area

enhancement (Moderated to marked: more than 25 percent of the tumor, minimal: less than 25 percent of the tumor, absent: no enhancement, peripheral: rim enhancement only). Grading area of high signal intensity on T2w/FLAIR images of the peritumoral structure (None, mild, extensive) was also performed by using visual scale. Calcification or blood components containing within the tumor was defined by the present area of very low signal intensity on T1W, T2W, FLAIR images and susceptibility artifact on gradient images/SWI (present, absent).

ii. Diffusion Imaging

The ADC value obtained at the solid part with greatest restricted diffusion on ADC mapping by avoiding the area of necrosis, bleeding and calcification. The regions of interests were placed in three different locations, the mean ADC value was calculated. Ratio between the mean lowest ADC value within the solid tumor to normal cerebellar white matter was calculated. Visual scale on DWI images was grading by signal intensity on DWI images of the highest b-value at the highest restricted diffusion area within tumor by comparison to adjacent normal gray matter of cerebellum using five-point scale (-2: markedly

hypointense, -1: hypointense, 0: isointense, 1: hyperintense, 2: markedly hyperintense).

Statistical Analysis

All data were analyzed using SPSS statistics Version 19.0.2. Descriptive statistics was used to describe the demographic data and conventional MRI findings, also with T1W and T2W signal intensity score. Categorical data was demonstrated as number and percentage, continuous data was demonstrated as mean, standard deviation, range, and median.

Comparison of the ADC ratio in different types of tumor was compared by Kruskal-Wallis test with Bonferroni corrected significant level at p-value < 0.00139. Comparison of the ADC ratio and DWI visual scale between high- and low-grade tumors were compared by Mann-Whitney U test with significant level at p-value < 0.05. The optimal cut-off level of ADC ratio and DWI visual scale to differentiate medulloblastoma from other posterior fossa tumors and to differentiate high grade tumor from low grade tumor were analyzed by using logistic regression analysis and ROC curves.

Results

Table 1: Demographic Data

	Overall (n=10)	High Grade (n=70)		Low Grade (n=30)
		Medulloblastoma (n=25)	Other high-grade tumor (n=45)	
Age (years)				
Median (min-max)	7.6 (1 - 19)	8 (1 - 19)	6.6 (1 - 17)	9 (1 - 18)
Median (IQR)	7.4 (3 - 11)	8 (5 - 12)	6.5 (4 - 11)	9 (3 - 11)
Mean	7.92 (4.99)	8.64 (5.11)	7.70 (4.9)	7.73 (5.17)
Sex				
Male	52	20	20	12
Female	48	5	25	18

There were 52% male as compared to females. 70% had high grade tumor and 30% had low grade tumor.

Table 2: Types of Posterior Fossa Tumor

Tumor	Number
High grade tumor	
Medulloblastoma	25
Diffuse midline glioma	32
Anaplastic ependymoma	5
ATRT	4
Anaplastic astrocytoma	1
High grade, unclassified astrocytoma	1
Glioblastoma	2
Low grade tumor	
Ependymoma	10
Pilocytic astrocytoma	15
Diffuse Astrocytoma	3
Low grade glioma	1

In high grade tumor, 25 had medulloblastoma and in low grade tumor, 15 had Pilocytic astrocytoma.

Table 3: ADC Ratio and DWI Visual Scale of Tumors

	ADC Ratio			DWI visual Scale [number of tumor(percentage)]				
	Mean \pm SD	Min	Max	1	2	3	4	5
1- Medulloblastoma	0.91 \pm 0.17	0.64	1.45	0	0	0	7	18
2- ATRT	0.86 \pm 0.16	0.63	1	0	0	0	0	4
3- Ependymoma (grade II-III)	1.3 \pm 0.35	0.86	1.87	0	0	2	4	4
4- DIPG	1.57 \pm 0.32	0.97	2.14	1	7	12	11	1
5- Pilocytic astrocytoma	2.11 \pm 0.51	1.24	2.77	0	8	6	1	0
6- Glioblastoma WHO IV	0.75 \pm 0.1	0.68	0.82	0	0	1	0	1
7- High grade astrocytoma	2.17 \pm 0.8	1.6	2.73	0	1	0	0	0
8- Diffuse Astrocytoma WHO II	1.66 \pm 0.33	1.33	1.98	0	0	1	2	0
9- Low grade glioma WHO I	1.92	1.92	1.92	0	0	1	0	0

The ADC ratio cut-off level for differentiation medulloblastoma from ependymoma, medulloblastoma from ATRT, medulloblastoma from pilocytic astrocytoma and medulloblastoma from diffuse midline glioma were noted.

Table 4: ADC Ratio Cut-Off Level

	ADC ratio	Sensitivity	Specificity	PPV	NPV
Med Vs others	≤ 1.115	94.6	82	68.4	96.8
Med Vs Epen	≤ 0.995	78.3	82.8	91.6	65.5
Med Vs ATRT	≤ 0.935	65.5	51	87.8	21
Med Vs PA	≤ 1.17	94.7	100	100	93.7
Med Vs DIPG	≤ 1.195	95.7	90	87.3	95.5

The ADC ratio of medulloblastoma was significantly lower than ependymoma, pilocytic astrocytoma and DIPG. The ADC cut-off ratio of ≤ 1.115 allowed discrimination medulloblastoma from other posterior fossa tumors with sensitivity, specificity, PPV and NPV of 94.6%, 82%, 68.4% and 96.8%, respectively.

Discussion

Central nervous system tumor account for 20% of all tumors among pediatric patients and posterior fossa is the most frequent location in populations older than 1 year of age, but cerebral hemispheres is the common location for adult patients. [16] Variety of tumor types arising in posterior fossa are classified by WHO grading according to histologic subtype and degree of anaplasia [16,17] and also these gradings indicate the prognostic factor of the patients. [17] The common pediatric posterior fossa tumors are comprised of pilocytic astrocytoma, medulloblastoma, ependymoma, diffuse intrinsic pontine glioma (DIPG) and a rare disease, atypical teratoidrhabdoid tumor (ATRT). The highest WHO grading and the most common malignant tumor is medulloblastoma as Aquilina (2013) [18] reported which the treatment should be more aggressive for the best outcome as Bergman (2019) [19] reported in their previous works.

In the present study, results showed a significant difference between ADC ratio in different tumor grades, histological subgroups including the common three pediatric posterior fossa tumors: pilocytic astrocytoma, ependymoma,

medulloblastoma. ADC ratio between high grade and low-grade groups were significantly different. This corresponded with previous study. [20] This might be explained by the information that restricted diffusion from limited water molecular diffusivity representing high cellularity of the tumor. As highest WHO grade of ATRT, medulloblastoma and glioblastoma (WHO IV), ADC ratio showed the lowest value. Ependymoma as WHO grade II and III tumor had higher ADC ratio than medulloblastoma. Pilocytic astrocytoma as WHO grade I tumor had higher ADC ratio than ependymoma and medulloblastoma. There were 52% male as compared to females. 70% had high grade tumor and 30% had low grade tumor. In high grade tumor, 25 had medulloblastoma and in low grade tumor, 15 had Pilocytic astrocytoma. The ADC ratio cut-off level for differentiation medulloblastoma from ependymoma, medulloblastoma from ATRT, medulloblastoma from pilocytic astrocytoma and medulloblastoma from diffuse midline glioma were noted. The ADC ratio of medulloblastoma was significantly lower than ependymoma, pilocytic astrocytoma and DIPG.

The ADC cut-off ratio of ≤ 1.115 allowed discrimination medulloblastoma from other posterior fossa tumors with sensitivity, specificity, PPV and NPV of 94.6%, 82%, 68.4% and 96.8%, respectively. The result from our study showed that ADC ratio range of ependymoma was lower than as reported by Zitouni S et al., (2017) [21] which could be from the different number of cases of

different grades of ependymoma as in our study (4 anaplastic ependymoma WHO grade III and 7 ependymoma WHO grade II, but they did not mention). ADC cut-off level at ≤ 1.17 could be differentiate medulloblastoma from pilocytic astrocytoma with excellent level of diagnostic performance from area under the curve (AUC) being 0.9936 in ROC curve. This corresponded with the study by Ahmed et al., (2018). [20] ADC cut-off level at ≤ 1.195 also differentiated medulloblastoma from DIPG with very good level of diagnostic performance from AUC being 0.9681 in ROC curve.

Conclusion

In Conclusion, diffusion MRI has a significant role in diagnosis of various types of pediatric posterior fossa tumors. ADC ratio can be used to differentiate medulloblastoma from other posterior fossa tumor in pediatric patients with good level of diagnostic performance.

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