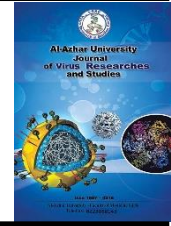




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Role of MR Spectroscopy in Evaluation of Posterior Fossa Tumors in Children

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Abstract

This study aims to go over the most common tumors of posterior fossa affecting children, with emphasis on their Magnetic Resonance Imaging “MRI” findings and Magnetic Resonance “MR” Spectroscopy, to improve histological approach in imaging, helping the management and approach for surgeons in providing information to the patients’ parents. It was a prospective study carried out on 20 patients with posterior fossa tumors. The patients were referred to Radiology Department of AL-Zahraa University Hospital for MRI and MR Spectroscopy examination after getting approval from ethical committee. A written informed consent was taken from parents. This study was conducted for a period of six months from May 2021 to October 2021. 20 patients ages ranged 3-14 years. Eight were males and twelve were females. Incidence of pilocytic astrocytoma 8 cases (40%), ependymoma 6 cases (30%), medulloblastoma 4 cases (20%) and atypical teratoid rhabdoid tumor 2 cases (10%). Their distribution in the posterior cranial fossa was 2 cases at the pons (10%), 4 cases at the cerebellum (20%), 10 cases at the fourth ventricle (50%), 2 cases at the midline posterior fossa (10%) and 2 cases at the CPA (10%). Different metabolite peaks were evaluated from resulting MR spectra, including choline, NAA, creatine, lipid, lactate, myoinositol and taurine peaks. Metabolite ratios, such as Cho/Cr and Cho/NAA ratios, were used for diagnosis and differentiation of different tumor types. We concluded MR spectroscopy is a powerful tool in diagnosis of posterior fossa tumors in pediatric patients and determination of tumor grades because it enables biochemical assessment of tumor dynamics.

Keywords: MR Spectroscopy, Posterior fossa, Tumors, Children.

1. Introduction

Brain tumors represent the most common solid neoplasm in children and second most

common pediatric malignancy following leukemia [1]. Approximately 65% of all

brain pediatric tumors arise in posterior cranial fossa. Tumor localization is cerebellar hemispheres, fourth ventricle, midbrain, pons, medulla oblongata and CPA. Common posterior fossa brain tumors in children include juvenile pilocytic astrocytoma (commonest), medulloblastoma (MB), ependymoma, and brainstem glioma. Less frequently, atypical rhabdoid/teratoid tumor (ATRT), hemangioblastoma, dermoids, meningioma, high grade glioma, and metastatic lesions [2]. Children with posterior fossa tumors present with signs and symptoms of increased intracranial pressure, gait disturbances and cranial nerve deficit depending on the size, type and location of the tumor [1]. Advanced MR neuroimaging techniques allow assessment of the physiologic features of brain tumors, resulting in better preoperative characterization and better outcomes [3]. Imaging findings on CT and conventional magnetic resonance imaging provide important clues to the most likely diagnosis. Moreover, information obtained from advanced MR imaging techniques, such as DWI, MR Spectroscopy, perfusion-weighted imaging and dynamic contrast studies, increase diagnostic accuracy [4]. Aim of study to go over the most common tumors of posterior fossa affecting children, with emphasis on their MRI findings and MR Spectroscopy, to improve histological approach in imaging, helping the management and approach for surgeons in providing information to the patients' parents.

2. Patients and Methods

It was a prospective study carried out on 20 patients with posterior fossa tumors. The patients were referred to Radiology Department of AL-Zahraa University Hospital for MRI and MR Spectroscopy examination after getting approval from ethical committee. A written informed consent was taken from parents of the parents after proper explanation of the

study. This study was conducted for a period of six months from May 2021 to October 2021.

2.1. Inclusion criteria of the participants

Patients included in this study were pediatric patients less than 15 years old and Children were diagnosed with posterior fossa tumors (Primitive neuro-ectodermal tumor, Medulloblastomas, Pilocytic Astrocytomas and Ependymomas).

2.2. Exclusion Criteria

Previous history of hypertension, thyroid disease, blood disease, renal disease, hepatic disease, any associated disorders like urinary tract infections.

2.3. Magnetic Resonance Imaging Technique

MR imaging were performed on a 1.5-T MR imaging unit (Achieva Philips medical system). All the patients were imaged in the supine position using a circular polarized head coil and were asked to remove any metallics and asked about any hypersensitivity to MRI contrast medium. Children \leq 10 years old were given sedative syrup 20 to 30 minutes before the examination. Meanwhile, children $>$ 10 years were informed about the duration of examination (total examination time did not exceed 40 minutes).

Multiple pulse sequences were used to obtain:

- Routine fast spin echo (FSE) and T1WI in axial, coronal and sagittal planes.
- FLAIR.
- Post contrast study in axial, sagittal and coronal planes. The contrast media used was Magnivest (Gd DPTA) {Gadolinium (Diethelene Triamine Penta acidic acid)}, it was

administrated intravenously in a dose of 0.1-0.2 mmol/kg body weight. T1-WIs was obtained immediately after the end of contrast injection.

- DWI (b = 0, 500, 1000) in axial plane and post processing ADC maps.
- Post contrast MRI study of the spine was made as in case of suspected drop-down metastasis from posterior cranial fossa malignancy.
- (MRS): Axial T1 with contrast to locate the multivoxels for 1H-MRS studies. We selected the voxels in the estimated center of the lesion. Measurement parameters were 1700/180/2 (TR/TE/excitations), 16x16 phase-encoding steps, 160x160 mm field of view, 14 mm section thickness and 1024 data points, a spectral width of 2500 Hz. In all patients, MR spectra were obtained with a TE of 144 msec with additional TE of 35 msec. Water suppression by CHESS technique, outer volume fat suppression as well as magnetic shimming were performed automatically with post processing of the spectroscopic data. Metabolic peaks used were NAA at

2.02 ppm, Cho at 3.22 ppm, Cr at 3.01 ppm, lipid containing compounds in the range of 0.9-1.3 ppm, lactate at 1.33 ppm, myoinositol peak at 3.6 ppm and taurine peak at 3.4 ppm. Cho/NAA, Cho/Cr, NAA/Cho and NAA/Cr were calculated automatically.

2.4. Analysis of MR Spectroscopy findings

Fetal MRS findings were correlated with the histopathological results either by biopsy or operative resection. The histopathology results were used as the Gold Standard for diagnosis. Final diagnosis was concluded from MRI findings, histopathological results and/or follow up. Statistical methods were used to deduce the sensitivity and specificity of MR Spectroscopy in the diagnosis.

3. Results

A total number of 20 patients 8 males (40%) & 12 females (60%) as shown in figure (1), with age ranged from (3 - 14) years.

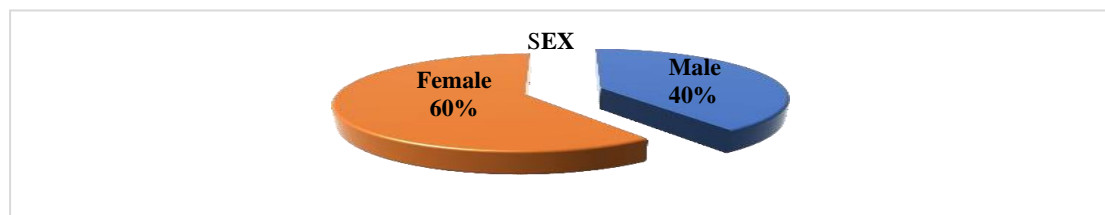


Figure (1): Pie chart showing sex distribution among study cases with female predominance 60%.

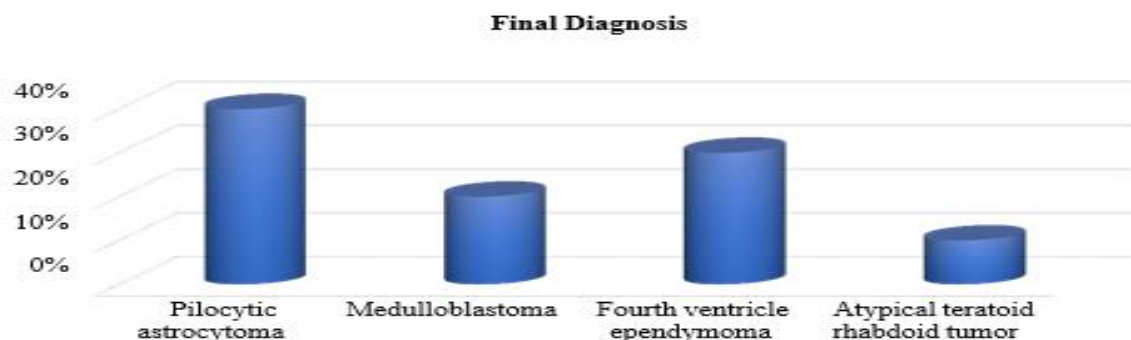


Figure (2): Bar chart showing Final diagnosis by histopathology with predominance of pilocytic astrocytoma (40%).

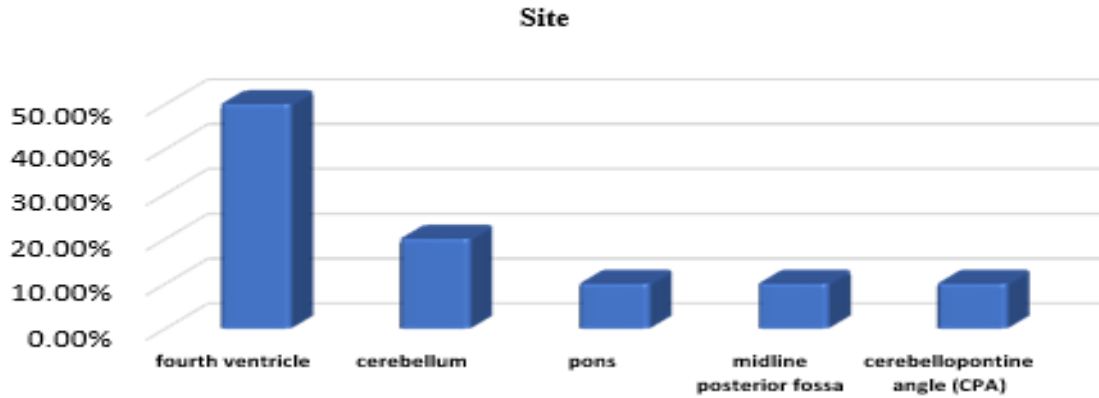


Figure (3): Column chart showing distribution of the studied tumors in the posterior fossa structures with predominance in the fourth ventricle (50%)

Table (1): Distribution of MRI signal intensity on T1WI in 20 patients.

T1WI	Number=20	Percentage%
Hypointense signal intensity	20	100%
Isointense signal intensity	0	0%
Hyperintense signal intensity	0	0%

Table (2): Distribution of MRI signal intensity on T2WI in 20 patients.

T2WI	Number=20	Percentage%
Hyperintense signal intensity	20	100%
Hypointense signal intensity	0	0%
Isointense signal intensity	0	0%

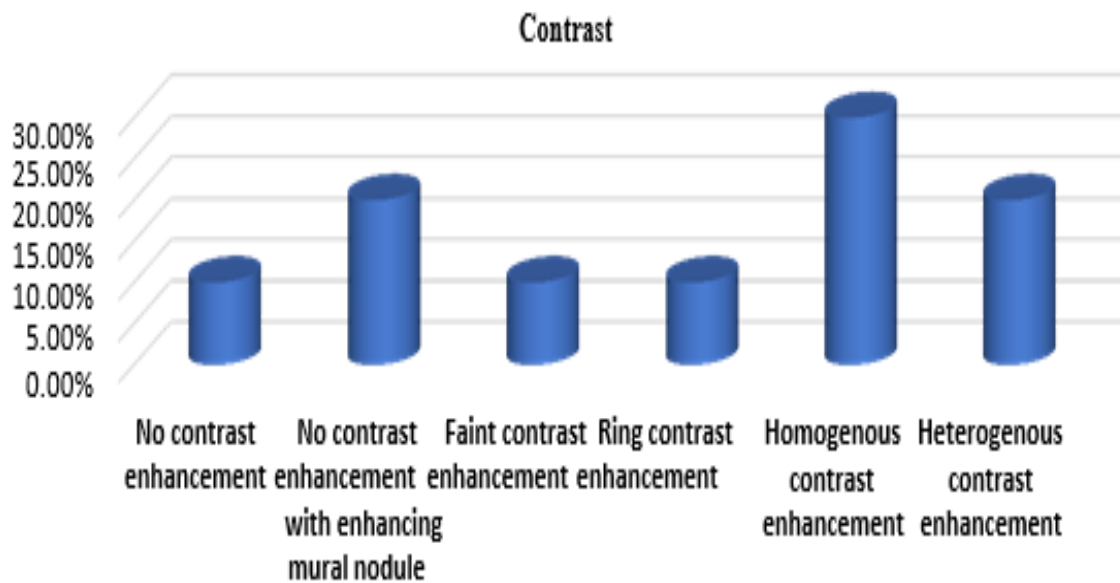


Figure (4): Bar chart showing contrast enhancement with predominance of homogenous contrast enhancement (30%).

3.1. Cases Presentation

3.1.1 Case 1:

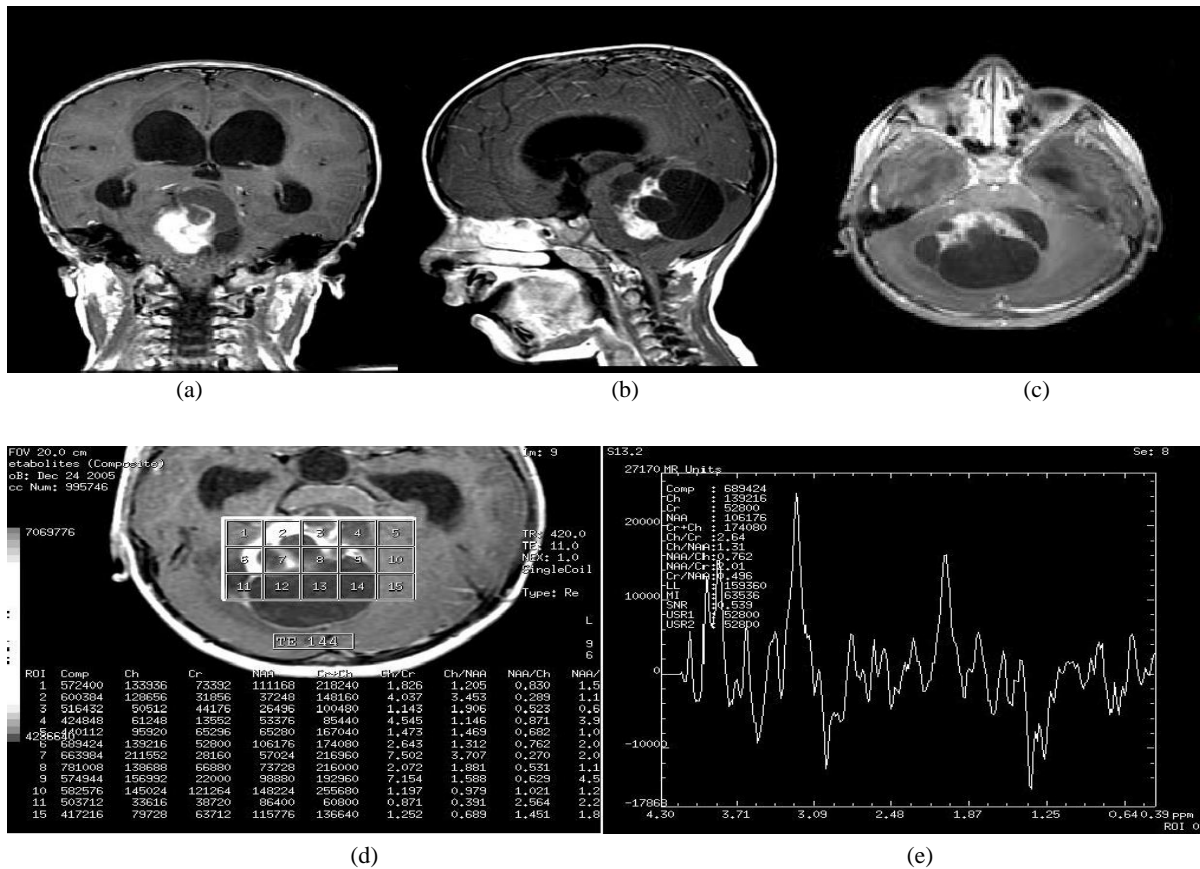
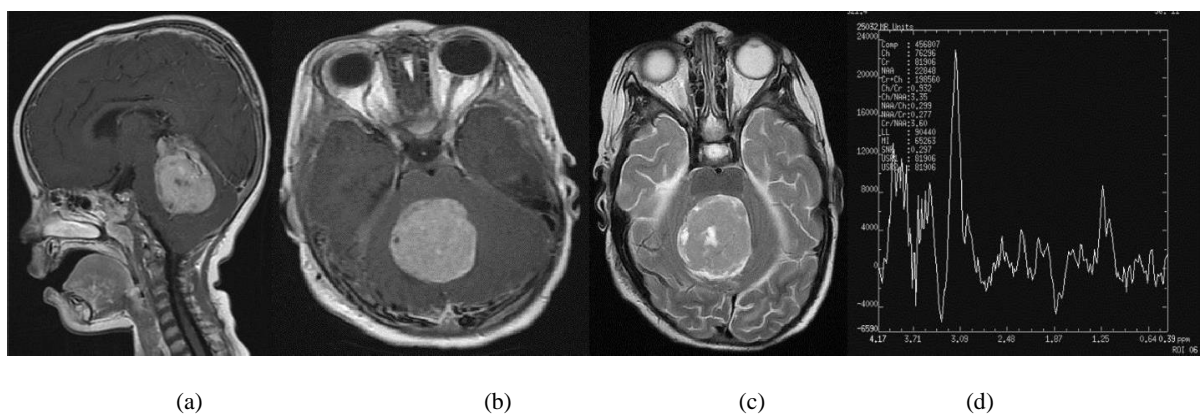


Figure (5): MRI and MRS of a case of infratentorial pilocytic astrocytoma in male patient 6 years with manifestation of increased ICT showing cystic mass with solid enhancing nodule in the region of the 4th ventricle, (a) Coronal T1WI+C, (b) sagittal T1WI+C, (c) Axial T1WI+C views, (d) and (e) showing Multi voxel MRS (TE = 144ms) with elevated choline peak (3.2 ppm), very small creatine peak (3 ppm), relatively small NAA peak (2.2 ppm), elevated myoinositol level and prominent Lactate peak (Inverted Lactate doublet at 1.3 ppm).

3.1.2 Case 2:



4. Discussion

WHO classifies those tumors according to histopathological subtypes into pilocytic astrocytoma (WHO grade I), medulloblastoma (WHO grade IV), brainstem glioma (WHO grade II) and ependymoma (WHO grade II) (WHO grade IV) [5]. Our study included 20 pediatric patients under 15 years old who were suspected to have posterior cranial fossa tumors. Pediatric posterior fossa tumors are common among males than females but in our study eight out of 20 patients were males (40%) and twelve were females (60%) with ratio equals 3:2 (F:M). Karatag et al, [6] stated that pilocytic astrocytomas were the most common posterior cranial fossa tumor, followed by brainstem glioma then medulloblastoma. In our study we also found that pilocytic astrocytoma has the highest incidence rate (8 cases of 20) (40%), followed by fourth ventricle ependymoma (6 cases of 20) (30%), followed by Medulloblastoma (4 cases of 20) (20%). Two cases of ATRR (10%) in a 3 years and 4 years old children. Astrocytomas account for 60% of all intracranial neoplasms in pediatrics and includes pilocytic astrocytoma, diffuse astrocytoma, subependymal giant cell astrocytoma, anaplastic astrocytoma and GBM. Low-grade astrocytomas (WHO grade I and II) are more common than high-grade astrocytomas [3]. In our study, there were 8 cases of cerebellar astrocytoma among 20 cases (40%). This percentage was in agreement with Koeller & Rushing [7]. MRS performed on the solid portion of pilocytic astrocytomas shows elevated choline/NAA ratio and elevated lactate level, which is an aggressive metabolite pattern [3]. In our work, there was elevated Cho/NAA ratio in all cases and this result was in agreement with all authors. Elevated lactate peak was present in 4 of 8 cases of pilocytic astrocytoma (50%), and this was in agreement with Plaza et al, [3]. According to Oz et al [8] Cr/Cho was low and was the most significant differentiator

from all other posterior fossa tumors. This was observed in our cases where creatine peaks were very small in MRS, and Cho/Cr ratio was high. Panigraphy et al, [9] stated that the most significant differentiators of pilocytic astrocytoma were low creatine and myoinositol. Yet, in our study, myoinositol peak was prominent in 6 cases out of 8 cases (75%). Anaplastic astrocytoma represents 25% of all gliomas and is the consequence of progression from low-grade astrocytomas showing high choline and low NAA and myoinositol levels. They can occur in patients of all ages and should be suspected when rapid clinical deterioration is seen. Borja et al, [3] and Chong et al [10]. In agreement with these authors, in our study there were 2 of 8 cases of anaplastic astrocytoma (25%). Grading of glioma: MRS distinguishes between low and high-grade gliomas with an accuracy of 78–96%. The measurement of choline can aid in grading gliomas. High-grade gliomas show higher Cho/Cr and Cho/NAA ratios than low grade gliomas [11]. Metwally LIA et al [12] revealed significant differences between low and high-grade gliomas. Significantly higher values for Cho/NAA and Cho/Cr and lower values for NAA/Cr were found in patients with high-grade gliomas compared with low-grade gliomas patients. In our study, no significant difference could be observed between Cho/NAA and Cho/Cr ratios of low-grade glioma and those of anaplastic astrocytoma. This observation was in agreement with Borja et al, [3] who stated that high levels of choline have also been reported in some low-grade tumors, so false positives may occur with the use of MRS. Ependymoma is the third most common primary brain tumor in children and show a peak in the 0 to 4 age group and occur more in males [13]. In Our study, 6 out of all 20 cases were ependymomas representing 30% and all cases show decreased NAA and elevated choline and lactate levels and that agrees with Plaza et al, [3]. Ependymoma and pilocytic astrocytoma were best separated

by creatine and NAA/Cho ratio [9]. In our study, we found that no significant difference of Cho/Cr ratio between ependymoma and pilocytic astrocytoma, this may be explained by marked increase of choline in ependymoma and marked decrease of creatine in pilocytic astrocytoma. Ependymomas have higher myoinositol than medulloblastoma or pilocytic astrocytoma Panigraphy et al, [9]. In agreement with this study, we found high myoinositol peaks in all grades II and III ependymomas. In our study, we had 6 cases of ependymoma, 2 of them looked more aggressive and infiltrative on conventional MRI examination. These ependymomas proved to be of anaplastic type on histopathological examination. On MRS study, Cho level was 3.2 in both grade II and grade III ependymoma so to our knowledge, no reported studies in literature discussed this difference in metabolic features between grade II and grade III ependymoma.

Medulloblastoma is the most common malignant pediatric brain tumor consisting of 20% -30% of all childhood CNS malignancies. Medulloblastoma occurs with a median age of 4 years and a male predominance [14]. In agreement with these studies, the mean age of medulloblastoma cases in our study was 3 years. However, the percentage of medulloblastoma cases was 20% of posterior fossa tumors in which is less than what reported. Medulloblastomas have characteristic spectroscopic signature with high taurine, depleted NAA, and prominent choline and lipid peaks [3]. Prominent signal intensity from taurine was observed in all medulloblastoma spectra. Of all posterior fossa tumors studied, mean Cho and lipid were highest in medulloblastoma. In agreement with these studies, in our study, we observed elevated choline peak in all medulloblastoma cases with high Cho/Cr, Cho/NAA ratio and prominent lipid and lactate peaks. In our study, small taurine peak was found in one case of medulloblastoma, this was in agreement

with Panigraphy et al, [9] who stated that taurine levels are low in some desmoplastic/nodular medulloblastoma, a variant of medulloblastoma. ATRTs are highly malignant tumor accounting for 1% - 2% of pediatric brain tumors. They are the most common malignant CNS tumor of children below 1 year of age Chiang et al , [15] MRS shows aggressive metabolites with elevated choline, decreased NAA, and prominent lipid and lactate peaks. Also, there was no evidence for taurine in cases studied Plaza et al, [3]. In agreement with these studies, one case of ATRT in our study shows prominent lipid/lactate peak, no detected taurine peak. Cho/Cr ratio was found to be 3.8 and Cho/NAA ratio was 8.

5 .Conclusion

Posterior fossa tumors are commoner in children than in adults and the major cause of death from cancer in children. Proton MRS is considered an important tool that can improve the noninvasive categorization and provides important information on tumor activity that cannot be obtained by MRI alone. Further information could be provided to surgeons and oncologists to improve care and information given to the parents at the time of diagnosis. Distribution of the lesions in our study was: eight cases pilocytic astrocytoma (40%), six cases fourth ventricle ependymoma (30%), four cases of medulloblastoma (20%) and two cases of ATRT.(%10) Prominent MRS features of each of the studied tumor types were as follows: The prominent feature of JPA is very low creatine and increased lactate. Low grade astrocytoma has similar features and is characterized by prominent myoinositol peak. Anaplastic astrocytoma is characterized by high lipid and lactate and higher metabolic ratios than low grade astrocytoma. However, no statistically significant difference of metabolite ratios could be found between both tumors. The prominent metabolic feature of ependymoma is high myoinositol level.

Moreover, it was found that anaplastic ependymoma had significantly higher metabolite ratios than grade II ependymoma. Both medulloblastoma and PNET proved to have similar metabolic features with characteristic high taurine peak which was not found in other tumors. ATRT appeared to have aggressive malignant metabolic pattern. But no specific metabolites increase, or decrease was found.

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