

Role of MRI in Diagnosis of Medulloblastoma

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ABSTRACT

Background: Brain tumors represent the most common solid neoplasm in children and second most common pediatric malignancy overall. The majority of primary childhood brain tumors occurs in the infratentorial compartment and includes: medulloblastoma, juvenile pilocytic astrocytoma (JPA), ependymoma, brainstem/pontine glioma, and atypical teratoid rhabdoid tumor (ATRT) which is an additional rare but important primary brain tumor of early childhood.

Objective: This study aims to provide an overview of the imaging features and appearances of the most common primary posterior fossa brain tumors in children and the diagnosis of medulloblastoma.

Patients and Methods: The pool of our study was 25 patients (12 males and 13 females) who presented to diagnostic radiology departments at EL Demerdash Teaching Hospital and National Cancer Institute. They had been diagnosed to have posterior fossa lesions. Patients' age ranged from 1 to 17 year with mean age of 4.73 years. **Results:** statistically significant difference between medulloblastoma and other posterior fossa tumors according to location and diffusion. Medulloblastoma is 4th ventricular in location and shows restriction in diffusion weighted images. **Conclusion:** Medulloblastoma is predominately 4th ventricular in location, Medulloblastoma is restricted in diffusion weighted images.

Keywords: Magnetic resonance imaging, diffusion weighted images, medulloblastoma, posterior fossa tumors.

INTRODUCTION

Posterior fossa tumors are more common in children than adults. Central nervous system tumors are the most common solid tumors in children; between 54% and 70% of all childhood brain tumors originate in the posterior fossa ⁽¹⁾.

Certain types of posterior fossa tumors, such as medulloblastoma, ependymomas, primitive neuroectodermal tumors (PNETs), and astrocytomas of the cerebellum and brain stem, occur more frequently in children. Some glial tumors, such as mixed gliomas, are unique to children; they are located more frequently in the cerebellum (67%) and are usually benign ⁽²⁾.

Hydrocephalus is common in children with posterior fossa tumors, occurring in 71% to 90% of pediatric patients; approximately 10% to 40% demonstrate persistent hydrocephalus after posterior fossa tumor resection ⁽²⁾. Medulloblastomas are highly malignant tumors; they are the most common malignant posterior fossa tumor in the pediatric population. They are characterized by their tendency to seed along the neuraxis, following cerebrospinal fluid (CSF) pathways, and they represent one of the few brain tumors, including ependymoma, pinealoblastoma, and lymphoma, to metastasize to extraneural tissues. Originally classified as a glioma, medulloblastoma is now referred to as a primitive neuroectodermal tumor (PNET) ⁽³⁾.

Of medulloblastoma patients, 10-30% demonstrate CSF dissemination at diagnosis, mandating evaluation of the entire neuraxis with contrast-enhanced studies. Extra-axial metastases account for 5% of cases; most metastases are to the bone; less frequently, metastases are to the liver and

lymph nodes ⁽⁴⁾. Children with non-disseminated medulloblastoma have a high likelihood of long-term survival, with a 5-year survival rate of 80%. Intensified therapy has been shown to increase survival in children with disseminated disease. However, the quality of life in long-term survivors remains an important issue, because most survivors have neurologic and cognitive deficits ⁽⁴⁾.

Signaling pathways that regulate medulloblastoma tumor formation have been discovered. Advances in the molecular biology of medulloblastoma indicate that better understanding of the growth control mechanisms in medulloblastoma may lead to the development of new therapies for the disease ⁽⁵⁾.

Although medulloblastoma has a highly characteristic appearance on computed tomography (CT) scanning, magnetic resonance imaging (MRI) is the preferred tool. The multiplanar capability of MRI provides better 3-dimensional visualization of the extent of the tumor, as well as better visualization of edema and herniation, when present. MRI also is better for evaluating the remainder of the neuraxis for metastasis. In addition, MRI spectroscopy may help better delineate the tumor's boundaries ⁽⁶⁾. With CT scanning, only axial images can be obtained; by contrast, with MRI, any plane can be used for imaging. On CT scans, posterior fossa images often are degraded by beam-hardening artifacts ⁽⁷⁾.

AIM OF WORK

To describe findings of different posterior fossa lesions and the diagnosis of medulloblastoma.

PATIENTS AND METHODS

This study was conducted on 25 patients with ages ranged from 1 to 17 year old with mean age of 4.73 years at MRI unit of the diagnostic radiology departments at El Demerdash Teaching Hospital and National Cancer Institute.

Inclusion criteria: Pediatric age group. Both sexes were included. Patients with clinical findings suggestive of posterior fossa lesions.

Exclusion criteria: Patients over the age of 18 year old. Patients known to had contraindications for MRI, e.g. an implanted magnetic device, pacemakers or claustrophobic patients.

Ethical Considerations: Oral consents were obtained from all patient’s guardians prior to inclusion in the study. The study was conducted according to the stipulations of the ASU (Ain Shams University) ethical and scientific committee.

Study tools: Full history taking. Clinical examination. The selected patients with suspected posterior fossa lesion were imaged by MRI using the following sequences: T2WI (axial). Fluid attenuation inversion recovery (FLAIR) (axial & sagittal). T1WI (axial & sagittal). Diffusion weighted images (DWI)

& apparent diffusion coefficient (ADC) maps. Post-contrast sequence (axial CE T1WI).

Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric. Also qualitative variables were presented as number and percentages.

The comparison between groups regarding qualitative data was done by using *Chi-square test*.

The comparison between more than two independent groups with quantitative data and parametric distribution was done by using *One Way ANOVA test*.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P-value > 0.05: Non significant (NS). P-value < 0.05: Significant (S). P-value < 0.01: Highly significant (HS)

RESULTS

Table (1): Comparison between different posterior fossa lesions as regard location.

Location	Medulloblastoma		Ependymoma		Pilocytic astrocytoma		Brain stem glioma		Test value*	P-value
	No.	%	No.	%	No.	%	No.	%		
Left cerebellar hemisphere	3	37.5%	0	0.0%	1	50.0%	0	0.0%	7.329	0.062
Right cerebellar hemisphere	0	0.0%	3	42.9%	0	0.0%	1	12.5%	5.734	0.125
Vermis	1	12.5%	0	0.0%	0	0.0%	0	0.0%	2.214	0.529
4 th ventricle	6	75.0%	6	85.7%	0	0.0%	0	0.0%	15.556	0.001
Tectal plate of midbrain	0	0.0%	0	0.0%	0	0.0%	2	25.0%	4.620	0.202
Midbrain	0	0.0%	0	0.0%	0	0.0%	3	37.5%	7.244	0.065
Pons	0	0.0%	0	0.0%	0	0.0%	5	62.5%	13.281	0.004
Medulla oblongata	0	0.0%	0	0.0%	0	0.0%	2	25.0%	4.620	0.202
Right cerebello-pontine angle	0	0.0%	1	14.3%	0	0.0%	0	0.0%	2.679	0.444
Right middle cerebellar peduncle	0	0.0%	0	0.0%	1	50.0%	0	0.0%	11.979	0.007

P-value >0.05: Non-significant; P-value <0.05: Significant; P-value <0.01: highly significant

*Chi-square test; •: One way ANOVA test

From **table (1)** we notice that there was statistically high significance difference between medulloblastoma and ependymoma as regard their location in the 4th ventricle highly significance difference between brainstem gliomas and their location in the pons and also high significance difference between pilocytic astrocytoma and its location in the right middle cerebellar peduncle.

Table (2): Comparison between different types of posterior fossa tumors criteria.

		Medulloblastoma	Ependymoma	Pilocytic astrocytoma	Brain stem glioma	Test value	P-value
		(n=8)	(n=7)	(n=2)	(n=8)		
Size	Mean±SD Range	3.75 ± 0.46 3 – 4	5.04 ± 2.98 0.5 – 10	4.00 ± 1.41 3 – 5	4.88 ± 1.73 3 – 7	0.738•	0.541
Enhancement	Enhancing mural nodule	1/8 (12.5%)	0/7 (0.0%)	1/2 (50.0%)	0/8 (0.0%)	12.852*	0.169
	Heterogeneous	4/8 (50.0%)	6/7 (85.7%)	1/2 (50.0%)	5/8 (62.5%)		
	Homogenous	3/8 (37.5%)	1/7 (14.3%)	0/2 (0.0%)	1/8 (12.5%)		
	Non-enhancing	0/8 (0.0%)	0/7 (0.0%)	0/2 (0.0%)	2/8 (25.0%)		
Nature	Solid	6/8 (75.0%)	4/7 (57.1%)	1/2 (50.0%)	6/8 (75.0%)	1.037*	0.792
	Solid/Cystic	2/8 (25.0%)	3/7 (42.9%)	1/2 (50.0%)	2/8 (25.0%)		
Diffusion	Facilitated	4/8 (50.0%)	7/7 (100.0%)	2/2 (100.0%)	8/8 (100.0%)	10.119*	0.018
	Restricted	4/8 (50.0%)	0/7 (0.0%)	0/2 (0.0%)	0/8 (0.0%)		
Hydrocephalus	No	6/8 (75.0%)	6/7 (85.7%)	1/2 (50.0%)	3/8 (37.5%)	4.461*	0.216
	Yes	2/8 (25.0%)	1/7 (14.3%)	1/2 (50.0%)	5/8 (62.5%)		
CSF permeation	No	1/2 (50.0%)	1/1 (100.0%)	1/1 (100.0%)	2/5 (40.0%)	2.115*	0.549
	Yes	1/2 (50.0%)	0/1 (0.0%)	0/1 (0.0%)	3/5 (60.0%)		
Brain leptomeningeal deposits	No	6/8 (75.0%)	6/7 (85.7%)	2/2 (100.0%)	8/8 (100.0%)	2.679*	0.444
	Yes	2/8 (25.0%)	1/7 (14.3%)	0/2 (0.0%)	0/8 (0.0%)		
CSF seeding	No	4/7 (57.1%)	3/3 (100.0%)	0/2 (0.0%)	1/1 (100.0%)	2.357*	0.308
	Yes	3/7 (42.9%)	0/3 (0.0%)	0/2 (0.0%)	0/1 (0.0%)		

P-value >0.05: Non-significant; P-value <0.05: Significant; P-value <0.01: highly significant

*Chi-square test; •: One way ANOVA test

From **table (2)** we notice that there is statistically significance difference between medulloblastoma and being restricted in diffusion.

Illustrated Cases

A male patient of 12 year old known to had posterior fossa medulloblastoma that was surgically removed. For follow up conventional MRI with contrast of the brain and spine was done.

MRI findings:

A cystic space occupying lesion (SOL) was found in the vermis partially encroaching upon the 4th ventricle measuring 3.6×3.4×2 cm in its widest diameter. The lesion was partially solid and partially cystic due to areas of cystic degeneration, it exhibits low signal intensity in T1WI and high signal intensity in T2WI with heterogeneously enhanced solid part in T1 post-contrast images and the lesion showed facilitated diffusion in DWI, no supratentorial hydrocephalic changes, images of the spine are unremarkable with no evidence of CSF seeding.

MRI diagnosis: Recurrent medulloblastoma.

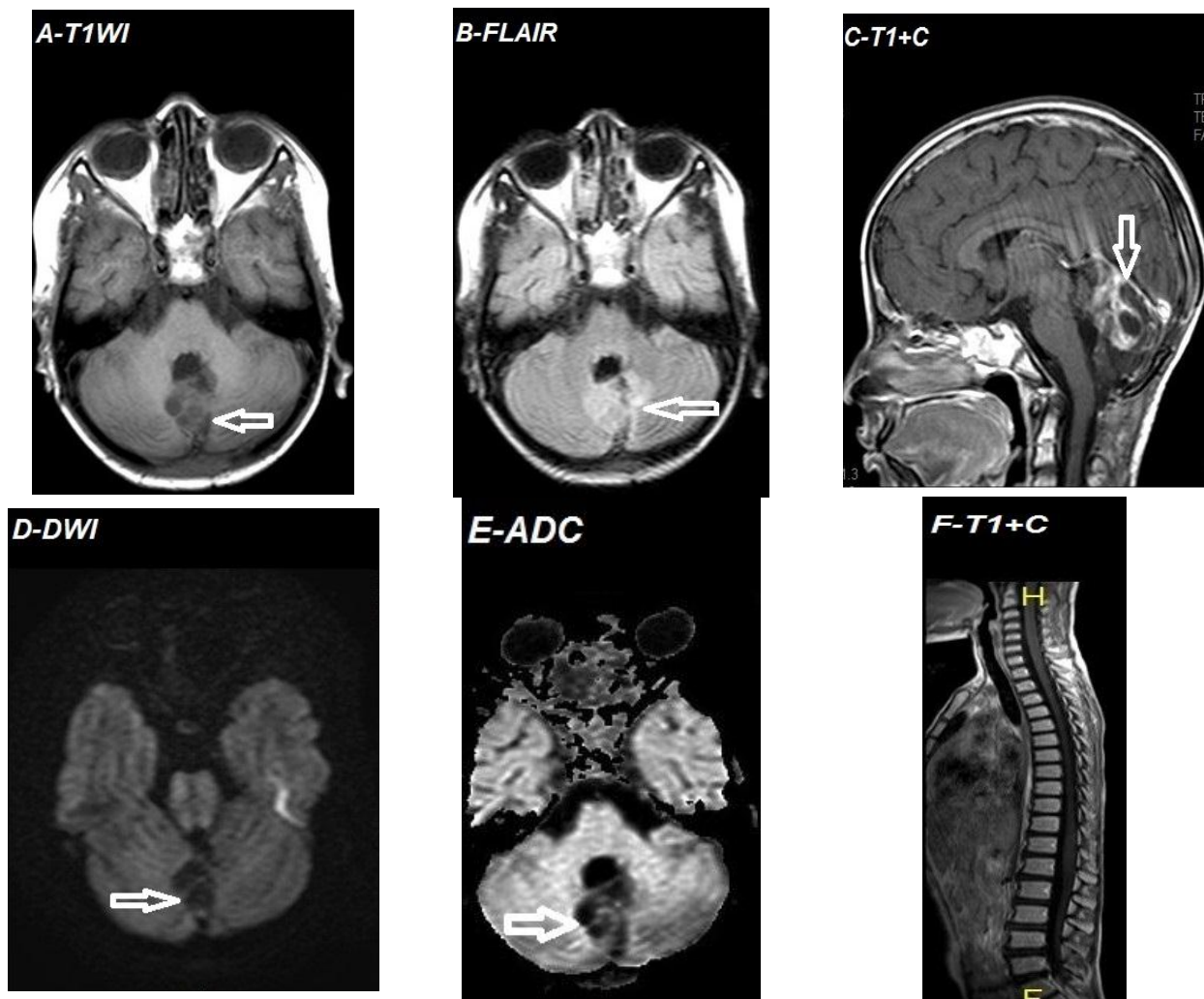


Fig. (Error! No text of specified style in document.1): Recurrent medulloblastoma (A) Axial T1WI hypointense SOL in the vermis encroaching into the 4th ventricle (B) Axial FLAIR showing the lesion is hyperintense (C) Sagittal T1 post-contrast image showing the lesion is heterogeneously enhanced with areas of cystic degeneration (D &E) DWI and ADC map showing the lesion facilitated in diffusion (F) Sagittal T1 post contrast image showing normal spine.

DISCUSSION

Currently there is a widespread use of MRI to determine the tumor extent for surgical and radiotherapy planning, as well as for post-therapy monitoring of tumor recurrence or progression. MRI provides an initial diagnosis of an intracranial mass lesion with a success rate of 30–90% depending on tumor types⁽⁸⁾.

Conventional MRI (CMRI) is the cornerstone in the initial evaluation of brain tumors. However, in some instances, CMRI is not effective for the differentiation of tumor type or for detection of tumor grade. DWI can increase both the sensitivity and specificity of MR imaging in the evaluation of brain tumors by providing information about tumor cellularity, which may in turn improve the prediction of tumor grade⁽⁸⁾.

Infratentorial tumors account for 45– 60% of all pediatric brain tumors and the most common infratentorial tumors include juvenile pilocytic astrocytoma (JPA), medulloblastoma, ependymoma, and brainstem glioma. Less commonly, we encounter atypical teratoid-rhabdoid tumor (ATRT) and hemangioblastoma, but they are important to be recognized and discussed because they mimic the most common tumors radiologically. An accurate diagnosis has important clinical implications related to prognosis and treatment⁽⁹⁾.

According to *Dörner et al.*⁽¹⁰⁾, 46% of posterior fossa tumors in their study were located in the cerebellum, 22% in the 4th ventricle, 24% in the brainstem and 8% in the cerebello-pontine angle, and there is discrepancy with our study where 40%

of the lesions were placed in the cerebellum, 48% were located in the fourth ventricle, 32 % in the brain stem and 4% in the cerebello-pontine angle and we have 20% overlapping lesions arising from both 4th ventricle and cerebellum and 4% overlapping lesions arising from both brainstem and cerebellum and they were calculated twice.

Children with posterior fossa tumors frequently present with severe headache and vomiting, which are usually the result of obstructive hydrocephalus, at the time of diagnosis, hydrocephalus is present in approximately 70% to 80% of patients with posterior fossa tumors. In one study conducted in India, hydrocephalus was noted in all cases with posterior fossa tumors *El-Gaidi et al.* ⁽¹¹⁾ which is to a lesser extent closes to our study where 64% of all our cases (16/25 cases) are associated with hydrocephalus. Collectively, in posterior fossa lesions, hydrocephalus is depending on the tumor size and the degree of compression on the 4th ventricle.

In our study; medulloblastoma accounts for 32% of all cases which close to what *Zimmerman et al.* ⁽¹²⁾ reported; medulloblastoma accounts for 36% of all posterior fossa tumors in children

In our study, 75% of medulloblastoma arise from the 4th ventricle and midline in location and 37.5% arise off midline in the Lt cerebellar hemisphere with one case overlapping arising from both left cerebellar hemisphere and 4th ventricle and median age approximately 6 years and this partially comes in line with *Fruehwald-pallamar et al.* ⁽¹³⁾ who reported that cases arise from the 4th ventricle and is midline in location in 78% of all medulloblastoma cases and there is contradiction in that those arising off midline in the cerebellar hemispheres account for 22% of the cases and the median age of occurrence was 9.1 year.

As regard enhancement in our study: 100% of medulloblastoma cases showed different patterns of enhancement with 50% of which showed heterogeneous pattern of enhancement and 37.5% showed homogenous enhancement and only one case (12.5%) shows enhancing mural nodule due to cystic degeneration, this is partially came in line with *Yeom et al.* ⁽¹⁴⁾ who said 100% of medulloblastomas in their study enhance and there is discrepancy in the patterns of enhancement where 11% showed homogenous enhancement, 39% showed heterogeneous enhancement and 50% showed multiple aggregates of ring like enhancement which reflects multiple foci of tumor necrosis.

In our study: the only lesion that shows truly restricted diffusion in DWI is medulloblastoma with a percentage of 50%. This came in line with *Jaremko et al.* ⁽¹⁵⁾ who said that

increased cellularity of medulloblastoma led to increased signal intensity on diffusion weighted sequences; although helpful, this finding had some overlap with other posterior fossa tumors, however absence of this criterion was a misleading as in case number one where without the past history of surgically removed medulloblastoma we could not reach the diagnosis of recurrent medulloblastoma as the lesion was facilitated in DWI and ADC map.

Only 25% of medulloblastomas in this study were associated with hydrocephalus of which 50% shows CSF permeation and there was discrepancy with *Koral et al.* ⁽¹⁶⁾ who said that as the lesions grow, there is anterior displacement and compression of the fourth ventricle, which often leads to obstructive hydrocephalus in approximately 90% of cases if uncompensated, transependymal flow of CSF may be seen along the margins of the lateral ventricles this is may be attributed to that the lesions were causing partial obstruction of the 4th ventricle.

In our study, we had 25 cases of posterior fossa lesions of which 11 cases performed MRI spine with contrast (7 of which were medulloblastomas, 3 were ependymomas and one case was brainstem glioma).

Medulloblastomas mostly disseminated through CSF seeding with a percentage of 42.9% (3 cases of all 7 cases who performed MRI spine) and brain leptomeningeal deposits represent 25% of all medulloblastomas in our study; our results were near to the results of *Packer et al.* ⁽¹⁷⁾ which was 50.8 % of medulloblastoma cases showed leptomeningeal dissemination at time of diagnosis.

Ependymomas account for 28% of all our cases with median age of occurrence approximately 5 year and predominately occurred in males (71%) and there was discrepancy with *Tortori-Donati et al.* ⁽¹⁸⁾, *Nazar et al.* ⁽¹⁹⁾ who said that they constitute 15% of the neoplasms with the median age of occurrence at 5.8 year, and there was a slightly increased preponderance in males (51%).

Ependymomas were mainly 4th ventricular lesion in our study with a percentage of 85.7% (6 cases of all 7 ependymoma cases) this comes in line with what *Tortori-Donati et al.* ⁽¹⁸⁾ reported as they may arise anywhere in the ventricular system, but the fourth ventricle, especially the caudal part of its floor was the commonest site. They also said the solid portion of the tumor showed marked, homogeneous contrast enhancement, but non-enhancing tumors were described which differed from what we found in our study as majority of the cases show heterogeneous enhancement pattern (85.7%).

Jaremko et al. ⁽¹⁵⁾ reported that 50% of classic ependymomas in their study showed restricted diffusion but in our study all ependymomas exhibit facilitated pattern of diffusion. This may be due to the decreased number of classic ependymoma in that study (2 cases).

With ependymoma, hydrocephalus was less evident criterion in our study with a percentage of 14.3% (just 1 case) that did not cause any transependymal permeation, and there was discrepancy with **Tortori-Donati et al.** ⁽¹⁸⁾ who reported that hydrocephalus was present in all cases in their study. This is mostly due to partial obstruction of the 4th ventricle by the tumor in our study.

Brain stem gliomas accounted for 32% of all our cases with mean age of occurrence is approximately 10 year which partially came in line with **Kwon et al.** ⁽²⁰⁾ who reported that brainstem tumors constituted 25% of all posterior fossa tumors in childhood they also stated that most tumors (75%) occur before the age of 10 year, predominantly males were affected which was different with our study where females are more affected (6 females from all 8 cases), they also reported that brainstem gliomas most commonly originate in or involve the pons (54%) followed by the medulla (32%); infrequently they involve the midbrain which partially agreed with our study where the most affected was the pons with percentage of 62% but followed by the midbrain (37.5%) not the medulla oblongata.

Mauffrey ⁽²¹⁾ reported in his study that 37% of all brainstem gliomas showed enhancement in T1 post-contrast images and 22.2% of which showed heterogeneous enhancement and 14.8% of them showed homogenous enhancement where there was discrepancy with our study in which 75% of all brainstem gliomas showed different pattern of enhancement and 62.5% of which show heterogeneous pattern and 12.5% show homogenous pattern of enhancement.

Juvenile pilocytic astrocytomas accounted for 20% of the cases as reported by **Zimmerman et al.** ⁽¹²⁾ and there was discrepancy with our study where it accounted only for 8% of our cases mostly this was because the low number of cases in our study and very low number of pilocytic astrocytoma included (only 2 cases) in comparison to the comparative study where the number of cases were 115 cases of which 23 pilocytic astrocytoma were diagnosed. However in the same study all pilocytic astrocytoma cases were located in the cerebellum which came in line with our study where 100% of juvenile pilocytic astrocytomas were located in the cerebellum.

Pilocytic astrocytoma is enhanced lesion in our study where all of our lesions showed different patterns of enhancement which comes in line with **Zimmerman et al.** ⁽¹²⁾ where they reported that 100% of juvenile pilocytic astrocytoma in their study show enhancement on T1 post-contrast images.

In our study, diffusion restriction was not a feature of pilocytic astrocytoma which came in line with **Rumboldt et al.** ⁽²²⁾ who said because of the relatively sparse cellularity of these lesions, pilocytic astrocytoma were hypointense on DWI and hyperintense in ADC map relative to these other histopathologies.

Leptomeningeal metastatic dissemination from PA had been previously regarded as rare, however, with the advent of MRI, there had been an increase in number of cases detected as **Kumar et al.** ⁽²³⁾ said. In one recent review **Figueiredo et al.** ⁽²⁴⁾ were able to identify 8 reported cases of pilocytic astrocytoma of cerebellar origin causing leptomeningeal tumor spread, and this contradictory with our study where pilocytic astrocytoma didn't disseminate by CSF seeding or brain leptomeningeal deposition which came in line with the consideration of the low grade of the tumor.

CONCLUSION

Medulloblastoma is 4th ventricular in location, restricted in diffusion weighted images and metastasizes via CSF seeding differentiating it from ependymoma which spread mainly via foraminal extension.

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