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ORIGINAL PAPER

The clinical profile and histological variations of Medulloblastoma in North East India

***Bhuyan Mrinal*[1], *Haque Inamul*[2]**

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ABSTRACT

Introduction*: Medulloblastoma is the most common embryonal central nervous system (CNS) tumor of childhood. Medulloblastoma comprises up to 38% of all pediatric posterior fossa tumour.* ***Objectives****: To study the clinical presentation of medulloblastoma with regards to variables like age, sex, etc., the CT, MRI features and the various histological types, the modes of management and outcome of the patients belonging to the Northeast India.* ***Method****: This prospective study done in the Department of Neurosurgery Gauhati Medical College and Hospital from January 2010 to December 2016. A total of 65 patients were included in the study.* ***Results****: Most cases belonged to the paediatric age group with only 4.6% cases above 15 years. Male comprised 61.5% and female 38.4% with male to female ratio 1.6:1. Classical type was the most common with 51(78.4%) cases. Desmoplastic variant comprised 12(18.4%) cases and was seen in older age. Classical variants appeared as homogenous mass in CT scan while the desmoplastic and anaplastic variant appeared as heterogenous mass. Classical variants 49(75.3%) were mostly vermian in location. Heterogeneity is more common in the older age group and it is more prominent in MRI than CT. Gross total excision was done in 51(78.46%) cases and near total was done in 14(21.5%) cases. Recurrence was noted in 6 cases.* ***Conclusion****: Medulloblastoma is commonly seen in paediatric age and more common in males. Classical variant was the most common type with mostly vermian location. CT and MRI features varied in different variants of medulloblastoma. In most of the cases gross total excision was possible and surgical outcome is favorable.*

Keywords*: Posterior fossa tumor, Childhood tumour*

INTRODUCTION

Medulloblastoma is the most common embryonal central nervous system (CNS) tumor of childhood[1] and is comprised of biologically different subsets of tumors arising from stem and/or progenitor cells of the cerebellum. Although it accounts for 6%–8% of all central nervous system tumours and 12%–25% of such tumors in the pediatric age group, it constitutes only 0.4%–1% of all adult central nervous system tumors.[2, 3] Medulloblastoma comprises up to 38% of all pediatric posterior fossa tumours and represents the most common pediatric posterior fossa tumour. The term Medulloblastoma cerebelli was introduced by Bailey and Cushing in 1925 to refer a distinct, highly malignant, small cell tumour of the midline cerebellum.[4] Medulloblastoma is believed to be derived from the granule-cell progenitors which are located in the external granular layer of the cerebellum.[5,6] This is a germinal zone harboring actively proliferating progenitor cells originating from the rhombic lip during embryonic development.[7] The external granular layer eventually disappears as all cell division ceases and all post mitotic neurons move to the internal granular layer.[8] According to most accepted hypothesis medulloblastoma arise from remnants of undifferentiated neuroepithelial cells in the region of cerebellar vermis or inferior medullary vellum.[9] The cerebellum is the most common location for medulloblastomas (94.4% of cases), and most (>75%) of these arise in the midline cerebellar vermis. WHO recognizes five histological subtypes: Classic,

Address for correspondence:
[1]Associate Professor
Email: drmrinalbhuyan@gmail.com
Mobile: +919435143933
[2]Senior Resident **(Corresponding Author)**
Department of Neurosurgery, Gauhati Medical College and Hospital
Email: inamulgmc20@gmail.com
Mobile: +918011615622

anaplastic, large cells, desmoplastic/nodular, and medulloblastoma with extensive nodularity (MBEN), although majority of studies have combined large cell/anaplastic phenotypes. Classical MBs, which compromise 65% of cases, consist of sheets of undifferentiated small, round cells with characteristic high cytoplasmic-to-nuclear ratio. Anaplastic/ large cell tumors are more aggressive tumors, characterized by pleomorphic cells and high mitotic indexes compared to other types of MB. Desmoplastic/nodular MBs contain areas of more differentiated, non-proliferative cells (nodules) that are reticulin negative surrounded by areas of desmoplasia. MBEN tumors display larger and more frequent nodules than Desmoplastic/ nodular tumors. Prognosis for MBEN and desmoplastic/nodular patients is more favorable than for those with classical MB, while large cell/anaplastic tumors are associated with the worst prognosis.[10]

OBJECTIVES

In this study we will observe the clinical presentation of medulloblastoma with regards to variables like age, sex, etc., the CT, MRI features and the various histological types of medulloblastoma, the modes of management and outcome of the patients belonging to the Northeast India.

METHODS

The present study is a prospective study done in the Department of Neurosurgery, Gauhati Medical College and Hospital from January 2010 to December 2016. A total of 65 patients were included in the study. All patients were thoroughly evaluated and prepared for operative procedure and post operatively confirmed by histopathological reports. Patients there after under went radiotherapy and chemotherapy as per protocol.

Inclusion criteria: Only biopsy confirmed medulloblastoma cases were included in the study.

Exclusion criteria: The cases which were not indicative of medulloblastoma, after comprehensive summation of the history, pertinent clinical findings and pathologic characteristics associated with this tumor, were excluded from the study.

RESULTS

Age Distribution: In our study of the total 65 cases, 42(64.6%) belong to 5-15 years and constituted the most common age group.11 cases (16.9%) belong to 3-5 years group,9 cases (13.8%) in 0-3 years and 3 cases (4.6%).

Sex Distribution: Of total 65 cases, 40(61.5%) were male and 25(38.4%) were female and male to female ratio was 1.6:1

Signs and symptoms according to age distribution: In our study as shown in table 1 all cases presented with headache, vomiting was seen in 51(78.4%) cases. Anorexia with weight loss was seen in 21(32.3%) cases and lethargy in 20(30.7%) cases. Imbalance was seen in 43(66.1%) cases, papilledema was seen in 22(33.8%) and decreased vision in 16(24.6%) cases. Trance ataxia was seen in 29(44.6%) cases and appendicular ataxia in 8(12.3%) cases.

Table 1 Sign and symptoms

Symptoms and sign	Age group in years			
	0-3 years	3-5 years	5-15 years	>15 years
Headache	9	11	42	3
Vomiting	9	6	35	1
Lethargy	5	4	10	1
Anorexia /weight loss	6	5	9	1
Impaired consciousness	5	0	3	1
Trance Ataxia	7	8	13	1
Appendicular ataxia	2	0	4	2
Head tilt	4	3	7	0
Nystagmus	3	0	6	2
Impaired Vision	3	1	11	1
Papilledema	5	1	15	1
Seizure	0	0	0	0
Imbalance	7	10	25	1
Cranial nerve Palsy	3	1	11	1

Histological variations depending on age: In our study as shown in table 2 classical variant was the most common type with 51(78.4%) cases and most belong to 5-15 years with 32(49.2%) cases. Desmoplastic variant comprised 12(18.4%) cases and anaplastic variant comprised 2 cases. Figure 1, 2, 3 shows the histological slides of various types.

Table 2 Histological variant and age group

Histological Types	0-3 yr	3-5yr	5-15yr	>15yr
Classical	8	10	32	1
Desmoplastic	0	1	9	2
Anaplastic	1	0	1	0
Large Cell	0	0	0	0
MBEN	0	0	0	0

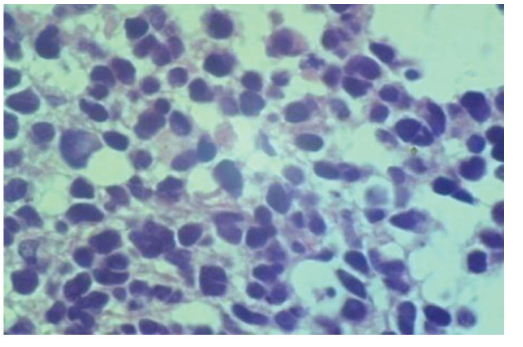

Figure 1 Classical type 100x

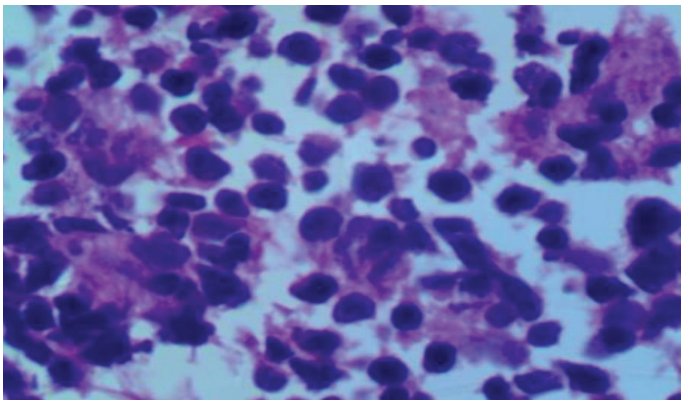

Figure 2 Desmoplastic 100x

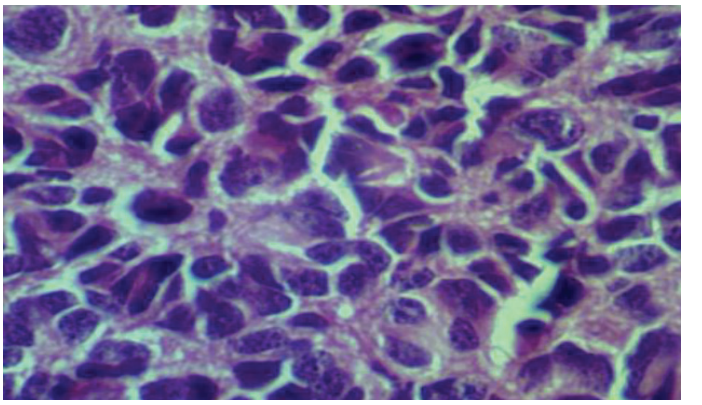

Figure 3 Anaplastic 100x

Histological variations depending on sex: In our study of 51 classical types, 33(50.7%) cases were male and 18(27.6%) cases were female. Of 12 Desmoplastic type 7(10.7%) were male and 5(7.6%) were female. Both the two cases of anaplastic variant were female.

Histological variation and tumour location: In our study of the classical variants 49(75.3%) were vermian and 2(3.07%) were paravermian in location. In the desmoplastic variety 7(10.7%) were paravermian and 5(7.6%) were lateral in location. Two anaplastic variant were paravermian in location.

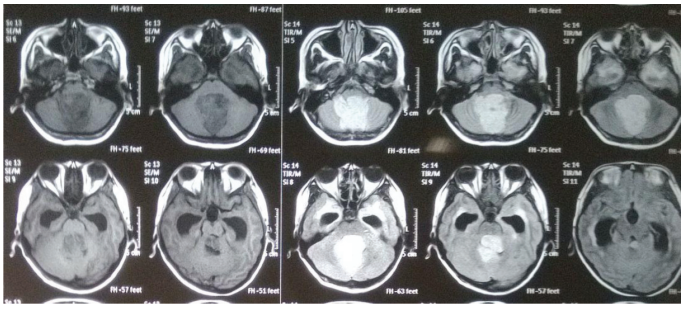

Figure 4 T1 and T2 MRI of medulloblastoma case

Histological variations and MRI signal intensity: On T1 weighted images classical variant showed hyointensity in 49(75.3%) cases and 2(3.07%) cases showed isointensity and correspondingly on T2 images 49(75.3%) cases showed hyperintensity and 2(3.07%) cases showed isointensity. In the desmoplastic variant in T1 weighted images 7(10.7%) cases showed hypointensity and 5(7.6%) cases showed isointensity while in T2 images of desmoplastic variant 2(3.07%) cases showed hyperintensity and 10(15.3%) cases showed is intensity. Of the anaplastic variant in T1 weighted images 1 showed hypointensity and 1 showed isointensity while both appeared hyperintense in T2 weighted images. Figure 4 shows the MRI features of medulloblastoma.

Histological Variations and MRI Features:

Oedema: Oedema was present in 61(93.8%) cases as shown in table 3 of which 10(15.3%) cases had marked oedema, 35(53.8%) cases had moderate oedema and 16(24.6%) cases had mild oedema. Out of the total 51 cases of classical variant 49(75.3%) had oedema and out of 12 cases of desmoplastic variant 10(15.3%) cases had oedema. Both the two cases on anaplastic variant presented with marked oedema.

Margin: Margin was well defined in 57(87.6%) cases and poorly defined in 8(12.3%) cases. In the classical variant 47(72.3%) cases had well defined margin and 4(6.15%) cases had poorly defined margin. While of 12 desmoplastic variant 10(15.3%) cases had well defined margin and 2(3.07%) had poorly defined margin. Two cases of anaplastic variant had poorly defined margin.

Hydrocephalous: In our study of the total 65 cases 54(83.07%) cases had hydrocephalous of which 45(69.2%) cases belong to classical variant,7(10.7%) cases belong to desmoplastic and 2(3.07%) belong to anaplastic variant.

Haemorrhage and Necrosis: Haemorrhage was seen in 4(6.1%) cases of desmoplastic and 2(3.07%) cases of anaplastic variant. Necrosis was seen in 4(6.1%) cases of desmoplastic and 2(3.07%) cases of anaplastic variant.

Table 3 Histological variants and MRI features

Histological type	Oedema	Margin		Hydrocephalous	Haemorrhage	Necrosis
		Well defined	Poorly defined			
Classical	49(75.3%)	47(72.3%)	4(6.15%)	45(69.2%)	0	0
Desmoplastic	10(15.3%)	10(15.3%)	2(3.07%)	7(10.7%)	4(6.15%)	4(6.15%)
Anaplastic	2(3.07%)	0	2(3.07%)	2(3.07%)	2(3.07%)	2(3.07%)
Large cell	0	0	0	0	0	0
MBEN	0	0	0	0	0	0

Histological Variations and CSF diversion and their level of Surgical Excision:

In our study as shown in table 4 of the total 65 cases 54(83.07%) had hydrocephalous and 51(78.4%) required MPVP shunt. In two cases EVD was given because of poor GCS followed by MPVP shunt placement.

All patients underwent surgical excision followed by radiotherapy. Chemotherapy was given to four cases with high grade tumour.

Gross total excision was done in 51(78.46%) cases and near total was done in 14(21.5%) cases. Out of the 14 near total excision cases 8 had extension to the brain stem. CSF collected by lumbar puncture 2 weeks following surgery had not detected any malignant cells in any patients of our series. Post-operative MRI brain showed residual tumour volume more than 1.5 cm2 in 14 (21.5%) patients.

Table 4 Surgical Treatment

Histological Types	MPVP shunt	Gross Total Excision	Near Total Excision	Subtotal Excision
Classical	42(64.61%)	41(63.07%)	10(15.3%)	0
Desmoplastic	7(10.7%)	10(15.3%)	2(3.07%)	0
Anaplastic	2(3.07%)	0	2(3.07%)	0
Large cell	0	0	0	0
MBEN	0	0	0	0

Post-operative complications: One patient who presented with poor GCS preoperatively expired 36 hours after surgery. Cerebellar ataxia was seen in 10(15.3%) cases and nystagmus in 10(15.3%) cases. Cerebellar mutism was seen in 4(6.15%) cases. Cranial nerve palsy (abducen and facial) was seen in 3(4.6%) cases. Recurrence was noted at 1year follow up in 6 cases of which two cases did not complete their radiotherapy cycles.

Follow up: Follow was done at 1 month, 3 month, 6 month, 9 month and 1 year. Recurrence was seen in 6 cases of which 4 were of classical type and 2 anaplastic type. All 6 cases had near total excision and two of them did not complete their radiotherapy cycles.

DISCUSSION

In our study majority of the cases belonged to the paediatric age group with only 4.6% cases above the age of 15 years. 64.6% cases belonged to the age group 5-15 years, 16.9% cases in 3-5 years group and 13.8% cases in 0-3 years group. Majority of cases in our study were male comprising 61.5% and female 38.4% with male to female ratio 1.6:1. Similar findings were reported by Agerlin N, Gjerris F, Brinker H,[11] with 35.5% cases in 0-4 years and 64.4% cases between 5-14 years and a male to female ratio of 2:1. In our study all cases presented with headache, vomiting was seen in 51(78.4%) cases. Anorexia with weight loss was seen in 21(32.3%) cases and lethargy in 20(30.7%) cases. Imbalance was seen in 43(66.1%) cases, papilledema was seen in 22(33.8%) and decreased vision in 16(24.6%) cases. Truncal ataxia was seen in 29(44.6%) cases and appendicular ataxia in 8(12.3%) cases. Alston RD in 2003,[12] have reported that the older child is more likely to present pressure features of headache, vomiting, and ophthalmic signs. Younger children present with non-specific features such as lethargy, behavioral disturbance, or increasing head size. Ataxia is seen in about 75% of children across the age range.

In our study classical variant was the most common type with 51(78.4%) cases and most belong to 5-15 years with 32(49.2%) cases. Desmoplastic variant comprised 12(18.4%) cases and was seen in older age group. Anaplastic variant comprised 2 cases. Of 51 classical types, 33(50.7%) cases were male and 18(27.6%) cases were female. Of 12 desmoplastic type 7(10.7%) were male and 5(7.6%) were female. Both the two cases of anaplastic variant were female. According to different literatures the age distribution of desmoplastic variety is still disputed. Mc Manamy CS, Pears J, Weston CL,[13] found classical variant in 71% cases, desmoplastic in 16% cases and anaplastic in 17% cases.

In our study of the classical variants 49(75.3%) were vermin, in the Desmoplastic variety 7(10.7%) were paravermian and 5(7.6%) were lateral in location. Two anaplastic variant were paravermian in location. Bourgouin PM,[14] Hubbard JL,[15] have reported that vermian medulloblastoma are mostly appearing as a hyper-dense mass on plain CT, and with intense homogenous enhancements with contrast. Lateral lesion is more common in older age group which appears as mixed density lesion on plain CT, and with heterogenous enhancements with contrast.

Most of the classical variant showed T1 hypointensity and T2 hyperintensity, while the desmoplastic group in T1 showed variable hypointensity and mostly is intensity in T2 MRI signal. Similar findings were reported by Bourgouin PM. Heterogeneity is more common in the older age group and it is more prominent in MRI than CT. According to them is signal intensity on T2 weighted images and more heterogeneity in older age group might be related to desmoplastic histology.

Oedema was present in 61(93.8%) cases of which 10(15.3%) cases had marked oedema, 35(53.8%) cases had moderate oedema and 16(24.6%) cases had mild oedema. Margin was well defined in 57(87.6%) cases and poorly defined in 8(12.3%) cases. Of total 65 cases 54(83.07%) cases had hydrocephalous of which

45(69.2%) cases belong to classical variant,7(10.7%) cases belong to desmoplastic and 2(3.07%) belong to anaplastic variant. Hemorrhage was seen in 4(6.1%) cases of desmoplastic and 2(3.07%) cases of anaplastic variant. Necrosis was seen in 4(6.1%) cases of desmoplastic and 2(3.07%) cases of anaplastic variant. Sandhu A,[16] had reported oedema in 90% cases and marked oedema in 1% cases; they had not reported any specific age/site distribution in their series. Bourgouin PM had reported that the vermian lesions had well defined margins and in lateral lesions had poorly defined margins. In the same study of Sandhu, they have reported haemorrhage in 1% cases only in adults.

In our study of the total 65 cases 54(83.07%) had hydrocephalous and 51(78.4%) required MPVP shunt. Gross total excision was done in 51(78.46%) cases and near total was done in 14(21.5%) cases. Out of the 14 near total excision cases 8 had extension to the brain stem. Post operatively cerebellar ataxia was seen in 10(15.3%) cases and nystagmus in 10(15.3%) cases. Cerebellar mutism was seen in 4(6.15%) cases. Cranial nerve palsy (abducen and facial) was seen in 3(4.6%) cases. Recurrence was noted in 6 cases of which two cases did not complete their radiotherapy cycles.

CONCLUSION

Our study indicates that medulloblastoma is commonly seen in paediatric age group and more common in males. Within the paediatric age group certain variants appear in younger group while others in older group. Patients usually presents with features of raised ICP, imbalance and visual disturbance. Classical variant was the most common type with mostly vermian location followed by desmoplastic variant which was paravermian to lateral in location. CT and MRI features varied in different variants of medulloblastoma. In most of the cases gross total excision was possible and surgical outcome is favourable. Post operatively radiotherapy and chemotherapy have proved very useful. Recurrence was seen to be associated with level of surgical excision and post-operative radiotherapy and chemotherapy.

Conflict of interest: There was no conflict of interest in the study.

Ethical clearance: Required ethical clearance was obtained.

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