

Medulloblastomas, Presentation at tertiary care hospital

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ABSTRACT

Aim: To assess the most common age group of patients of medulloblastoma and their symptoms at presentation in a tertiary care hospital.

Methods: This retrospective cross sectional study was conducted at King Khalid University Hospital, Rayadh, Saudi Arabia from 1st January 2001 till 31st December 2010. 37 patients were included in the study.

Result: Majority of the patients presented between the ages of 6 to 12 years. 67.5% were males and headache was present in 94.6% patients. Cerebellar and long tract signs were present in 64.9%.

Conclusion: All the male patients between the ages of 6 to 12 years who presented with headache in combination with cerebellar and long tract signs should be seen by a neurosurgeon in order to exclude the infra tentorial tumor.

Keywords: Medulloblastoma, infra tentorial tumor, pediatric brain tumors.

INTRODUCTION

Any mass lesion within the skull is a threat to the integrity of brain function and therefore even histologically benign tumors can threaten life. Brain tumors were described in old ages by Greek and Egyptian historians. In the 18th and 19th centuries, signs and symptoms were described by Theodor Schwann (1810-1882. Professor of Anatomy, Liege, Belgium), Harvey Williams Cushing (1869-1939. Professor of Surgery, Harvard University Medical School, Boston, USA) and John a Wada (20th century Japanese neurologist)¹ while first of all Virchow systematically classified the brain tumors in 1826².

The majority of the brain tumors are sporadic. Various possible environmental risk factors such as smoking, diet, occupation and mobile phone use have been studied with no causative link proven. Intracranial tumors can present with seizures, focal neurological deficit, raised ICP, endocrine dysfunction or can be incidental findings¹. The incidence of tumors of nervous system is approximately 10-15/100,000. Nervous system tumors occur more commonly with increasing age, with a peak incidence in childhood at 5-9 years and second peak at 50-55 years. Medulloblastoma is the commonest tumor of infancy and childhood. In the older age group (50-70) the more malignant cerebellar gliomas (anaplastic astrocytoma,

glioblastoma) become more common, as do cerebral metastasis².

Comparative studies on markers of biological aggressiveness of classical and desmoplastic medulloblastomas (MBs) are rare in literature. Regarding age distribution and location of tumours, the differences between classical and desmoplastic were documented. The classical medulloblastoma occurred predominantly in children and 80% were midline in location. The tumours of desmoplastic histology were located laterally in majority of cases. These tumours were in an almost equal distribution in children (56%) and adults (44%). Both histological variants of medulloblastoma are not different with regard to biological parameters of aggressiveness³. Medulloblastomas are classified into two chief histological variants, 1-“classical” and 2-“desmoplastic”^{4,5}. The rare variants of medulloblastoma are large cell, lipomatous, melanocytic and medulloblastoma^{6,7}.

The treatment-related side effects as well as predictive outcome still remain as a major challenge. The improved understanding of the disease and advances in molecular biology is changing the treatment paradigms from Chang's staging system to molecular risk stratification. However, surgery still remains as an important mainstay of therapy and is formidable. The role of radical surgery has always been a crucial factor in the outcome of these patients, the best survival being reported in patients who had total excision of the tumor and with no metastasis.

The objective of the study was to assess the most common age group of patients of medulloblastoma and their symptoms at presentation in the tertiary care hospital.

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MATERIAL AND METHODS

After taking written consent from all the patients or their relatives, this retrospective cross sectional study was conducted at King Khalid University Hospital, Rayadh, Saudi Arabia from 1st January 2001 till 31st December 2010. Convenient sampling technique was employed for selection of patients. Permission was also taken from the ethical committee of the hospital. 37 patients were included in the study.

Limitations and delimitation: The major limitation of the study was that it was conducted in only one city of Saudi Arabia. The current study is a single institution study and needs cautious interpretation. Population-based studies are required to determine the cancer burden due to pediatric malignancies of the brain in this population and for the morphological categorization of brain tumors in Pakistan. The major delimitation was few patients or their attendants refused to give consent.

Inclusion and exclusion criteria: Only those patients were included in the study whose histopathology confirmed the diagnosis of Medulloblastoma. Only those patients were excluded from the study who refused to give consent or histopathology was in doubt to confirm the type of tumor.

RESULTS

Total of 37 patients were included in the study. Age ranges from 6 months to 54 years with majority of patients were between the ages of 6 to 12 years i.e. 40.5% (15). Out of 37 patients, 25 were males and 12 were females with male to female ratio of 67.5:32.4. Maximum number of patients presented with headache. Next common signs were cerebellar and long tract signs.

Table1: Signs and symptoms at first presentation.

Sign & symptoms	Present	Absent	%age
Headache	35	2	94.6
Cerebellar signs	24	13	64.9
Long tract signs	24	13	64.9
Cranial nerve palsy	15	22	40.5

As far as the vision is concerned, 49.6% (18 out of 37) of patients had reduced vision. So patients with infra tentorial tumors can present with normal or reduced vision with equal chances. 51.4% i.e., 19 patients had normal vision. Usually some type of neurological deficit is present in patients of infratentorial tumors. Only 1 patient had no neurological deficit in our group of patients. 14 patients had mild whereas 9 had moderate neurological deficit. In 13 patients, disease progress

to such an extent that they were totally dependent upon other people in everyday life.

Table 2: Neurological deficit.

Neurological deficit	n	%age
No deficit	1	2.7
Mild neurological deficit but independent	14	37.8
Partially dependent but can look after himself	9	24.3
Totally dependent	13	35.1

Another important feature of these patients is raised intracranial pressure on examination. Raised intracranial pressure may result in hydrocephalus, headache, reduced vision or cranial nerve palsy. 94.6% of our patients had raised intracranial pressure. It seems to be very unlikely that a patient of intracranial tumor present with normal pressure.

Table 3: Ratio of intracranial pressure.

Normal	2	5.4%
Increased	35	94.6%
Total	37	100%

One of the important point which is worth mentioning is 91% of the patients had hydrocephalus on examination. Only 3 patients are without this important finding.

Table 4: Presence of hydrocephalus

Hydrocephalus	n	%age
Without hydrocephalus	3	8.1
With hydrocephalus	34	91
Total	37	100

Table 5: ICP

ICP	n	%age
Normal	2	5.4%
Increased	35	94.6%

We concluded that it is very unlikely for infratentorial tumors to present with systemic metastasis. If they ever, metastasis can be local or spinal. One of the most important route is flow of CSF which can carry the tumor cells.

Table 6: Tendency of metastasis.

Metastasis	n	%age
Nil	29	78.4
local	2	5.4
Spinal	6	16.2

DISCUSSION

Out of 37 patients in our study, majority were males (25) with male to female ratio of 67.5:32.4. Similar result was concluded by Saima Nasir and her colleagues in a study conducted at PIMS Islamabad

between 1998 till 2010⁸. Other studies conducted by Memon et al in Jamshoro and Rehman et al, King Edward Medical University^{9,10}. All showed the similar results.

In our study, majority of the patients are between the ages of 6 to 12 years. All the authors agreed that medulloblastoma is the commonest intracranial tumor of childhood¹¹. Yazigi-Rivard L et. al. also mentioned that it predominantly arises in the cerebellum and 4th ventricle¹². While Stagno V and his colleagues conducted a similar study in Uganda and showed a slightly lower age group. He concluded that the mean age in his country was 6.5 years¹³. Similarly Kulkarni AV and his colleagues conducted a study in the Hospital for Sick Children in Ontario, Canada. He also showed median age at tumor diagnosis was 4.9 years¹⁴. Both these studies showed smaller age groups as compared to our study. Ahmed et. al. conducted a study in Karachi in which he reported mean age as 8.8 years¹⁵.

Majority of our patients were male with the 2/3rd majority (67.5:32.4). Same conclusion was drawn by Rickert CH who conducted a study in Gerhard-Domagk-Institute of Pathology and Institute of Neuropathology, University Hospital Münster, Germany. According to him, 60.7% of these tumors occurred in boys and the most common entities leading to extraneural metastases were medulloblastomas (56.3%), germinomas (9.8%), glioblastomas (6.9%), ependymomas (3.7%) and pilocytic astrocytomas (2.9%)^{16,17}. Very similar results were shown by Stagno V¹³, who calculated the male to female ratio of 59.9:40.1%.

Headache, a very important presenting complaint, can be due to multiple reasons like muscle spasm, decrease vision, frontal sinusitis, hypertension and so on. It is present in 94.6% of our patients. According to *Muzumdar D* from *Department of Neurosurgery, Seth Gordhandas Sunderdas Medical College and King Edward VII Memorial Hospital, Mumbai, India*, 75.3% presented with headaches¹⁸. *Cannas A et. al* mentioned that Medulloblastoma induces unusual headache with clinical picture of basilar-type migraine complicated by ischemic infarcts¹⁹.

Hyperreflexia (72.5 %) and focal motor deficits (62.5 %) were the most common neurologic signs encountered in patients of infra tentorial tumors¹⁷. These patients represented 40% of children treated for newly diagnosed medulloblastoma²⁰. Authors of this article calculated long tract and cerebellar signs present in 64.9% of our patients which is very near to these two above mentioned studies. We also mentioned that 15 out of 37 patients had involvement of cranial nerves (40.5%). Abducent nerve palsy is

another common initial presentation in patients with medulloblastoma²¹.

Decrease vision is present in 49.6% of patients. Pribila JT from Department of Ophthalmology, University of Michigan, USA mentioned that multiple intracranial meningiomas causing papilledema and visual loss in a patient with Nevroid Basal Cell Carcinoma²². Besides typical signs and symptoms of increased intracranial pressure, cranial nerve palsies or visual problems were frequently found (in 70% and 30% of the patients, respectively)²³.

Survivors of pediatric medulloblastoma are at risk for neurocognitive dysfunction. Reduced white matter integrity has been correlated with lower intelligence in child survivors, yet associations between specific cognitive processes and white matter have not been examined in long-term adult survivors²⁴. Only one patient out of 37 was without any neural deficit in our study group patients. Rest of them had some sort of motor or sensory deficit.

Similarly only 3 patients (8.1%) were without hydrocephalus on initial examination. On reviewing international literature, it was noted that symptomatic hydrocephalus predominated at presentation²⁵ (66.9%). Shamji MF and his colleagues mentioned 69% incidence of hydrocephalus in his patients ($p=0.57$)²⁶. Raimondi AJ calculated an even higher incidence of hydrocephalus. In his study of 117 children with cerebellar-fourth ventricle tumors, 110 had hydrocephalus²⁷. These results are same as we concluded regarding hydrocephalus.

There are other symptoms worth mentioning in patients of infratentorial tumors. There are patients who present with short history of nausea and vomiting and later on diagnosed as medulloblastoma²⁸.

Fortunately, none of our patient had extra neural metastasis on presentation. Though 8 out of 37 patients had spinal or local metastasis, extraneural metastasis (ENM) in patients with medulloblastoma is a rare but a well-described phenomenon, both in children and adults²⁹. Medulloblastoma has one of the highest rates of metastasis outside the central nervous system (CNS). Bone metastases are the most common lesions, although lymph node and visceral spread have also been reported²⁹. A survey of published cases of extraneural metastases of primary brain tumours in children under the age of 18 years revealed 245 cases; 60.7% occurred in boys and 27.3% were directly related to the placing of a shunt. Metastases were encountered equally often in bone (56.3%) and visceral organs (55.5%) but were markedly rarer in lymph nodes (25.3%). Medulloblastomas showed a preference for bones (88.3% of cases), germinomas for bones (77.8%) and visceral organs (66.7%), whereas ependymomas and

ependymoblastomas were more frequently found in lymph nodes and visceral organs (71.5-100%)³⁰.

CONCLUSION

In the light of above mentioned studies, it is recommended that all the male children between the age of 4 to 12 years who present with headache, cerebellar or long tract signs and had hydrocephalus should be immediately referred to neurosurgeon for exclusion of space occupying lesion in the brain.

REFERENCES

1. John Leach and Richard Kerr. Elective neurosurgery. In: Norman S Williams, Christopher J.K. Bulstrode, & P. Ronan. Editors. Bailey & Love's Short Practice of Surgery. 25th Edition. London: 2008. Edward Arnold Publisher; P. 623-644
2. D.G.T. Thomas and M.F.Pell. Tumors of the Nervous System. 711-729. in; A Cusher, G R Giles, A R Moosa. Editors. Essential Surgical Practice. 3rd Edition, 1995. P 979-995
3. Pramanik P, Sharma MC, Mukhopadhyay P, Singh VP, Sarkar C. A comparative study of classical vs. desmoplastic medulloblastomas. *Neurol India* 2003;51:27-34
4. Rubinstein LJ, Northfield DW. The medulloblastoma and so-called "arachnoidal cerebellar sarcoma". A critical re-examination of a neurological problem. *Brain* 1964;87:379-412.
5. 3-Herpens MJHM, Budka H. Primitive neuroectodermal tumors including the medulloblastoma: glial differentiation signalled by immunoreactivity for GFAP is restricted to the pure desmoplastic medulloblastomas ("arachnoidal sarcoma of the cerebellum") *Clin Neuropathol* 2011;4:12-8.
6. Kleihues P, Burger PC, Scheithauer BW. Histological typing of tumors of the central nervous system. WHO series. New York: Berlin, Springer-Verlag; 2012.
7. Giangaspero F, Bigner SH, Kleihues P, Pietsch T, Trojanowski JQ. Medulloblastoma. In: Kleihues P, Cavenee WK, eds. Pathology and Genetics of Tumors of the Nervous System. Lyon: IARC Press; 2010. pp. 129-37.
8. Saima Nasir, Bibi Jamila, Samina Khaleeq. A Retrospective Study of Primary Brain Tumors in Children under 14 Years of Age at PIMS, Islamabad. *Asian Pacific J Cancer. Asian Pacific Journal of Cancer Prevention*, Vol 11, 2010. P 1225-1227.
9. Memon F, Rathi SL, Memon MH (2007). Pattern of solid paediatric malignant neoplasm at LUMHS, Jamshoro, Pakistan. *J Ayub Med Coll Abbottabad*, 19, 55-7.
10. Rehman AU, Lodhi S, Murad S (2009). Morphological pattern of posterior cranial fossa tumors. *Ann KEMU*, 15, 57-9.
11. Sengupta S, Chatterjee U, Banerjee U, Ghosh S, Chatterjee S, Ghosh AK. A study of histopathological spectrum and expression of Ki-67, TP53 in primary brain tumors of pediatric age group. *Indian J Med Paediatr Oncol*. 2012 Jan;33(1):25-31.
12. Yazigi-Rivard L, Masserot C, Lachenaud J, Diebold-Pressac I, Aprahamian A, Avran D, Doz F. Childhood medulloblastoma. *Arch Pediatr*. 2008 Dec;15(12):1794-804.
13. Stagno V, Mugamba J, Ssenyonga P, Kaaya BN, Warf BC. Presentation, pathology, and treatment outcome of brain tumors in 172 consecutive children at CURE Children's Hospital of Uganda. The predominance of the visible diagnosis and the uncertainties of epidemiology in sub-Saharan Africa. *Childs Nerv Syst*. 2013 Oct 17.
14. Kulkarni AV, Piscione J, Shams I, Bouffet E. Long-term quality of life in children treated for posterior fossa brain tumors. *J Neurosurg Pediatr*. 2013 Sep;12(3):235-40.
15. Ahmed N, Bhurgri Y, Sadiq S, et al (2007). Pediatric brain tumours at a tertiary care hospital in Karachi. *Asian Pac J Cancer Prev*, 8, 399-404.
16. Rickert CH. Extraneural metastases of paediatric brain tumours. *Acta Neuropathol*. 2003 Apr;105(4):309-27
17. Muzumdar D, Deshpande A, Kumar R, Sharma A, Goel N, Dange N, Shah A, Goel A. Medulloblastoma in childhood-King Edward Memorial hospital surgical experience and review: Comparative analysis of the case series of 365 patients. *J Pediatr Neurosci*. 2011 Oct;6(Suppl 1):S78-85.
18. Cannas A, Solla P, Mascia MM, Floris GL, Tacconi P, Uselli S, Ambu R, Marrosu MG. Dipartimento di Scienze Cardiovascolari e Neurologiche, Sez. Neurologia, University of Cagliari, Cagliari, Italy. *J Neuroophthalmol*. 2008 Mar; 28(1):41-6.
19. Uche EO, Shokunbi MT, Malomo AO, Akang EE, Lagunju I, Amanor-Boadu SD. Pediatric brain tumors in Nigeria: clinical profile, management strategies, and outcome. *Childs Nerv Syst*. 2013 Apr 18.
20. Gajjar A, Sanford RA, Bhargava R, Heideman R, Walter A, Li Y, Langston JW, Jenkins JJ, Muhlbauer M, Boyett J, Kun LE. Medulloblastoma with brain stem involvement: the impact of gross total resection on outcome. *Pediatr Neurosurg*. 1996 Oct;25(4):182-7.
21. Baldawa S, Gopalakrishnan CV. Bilateral abducent nerve palsy as the initial clinical manifestation of medulloblastoma. *Acta Neurochir (Wien)*. 2010 Nov; 152(11):1947-8.
22. Pribila JT, Ronan SM, Trobe JD. Multiple intracranial meningiomas causing papilledema and visual loss in a patient with neuroendocrine carcinoma syndrome. *Cephalalgia*. 2006 Oct;26(10):1238-41.
23. Mazzucco A, von der Weid N, Godoy N. Brain tumors of the posterior fossa in childhood. An overview of the patients of the medical university hospital's pediatric department Berne in the years 1990-1994. *Praxis (Bern 1994)*. 1996 Aug 20;85(34):1001-4.
24. Brinkman TM, Reddick WE, Luxton J, Glass JO, Sabin ND, Srivastava DK, Robison LL, Hudson MM, Krull KR. Cerebral white matter integrity and executive function in adult survivors of childhood medulloblastoma. *Neuro Oncol*. 2012 Sep;14 Suppl 4:iv25-36.
25. Stagno V, Mugamba J, Ssenyonga P, Kaaya BN, Warf BC. Presentation, pathology, and treatment outcome of brain tumors in 172 consecutive children at CURE Children's Hospital of Uganda. The predominance of the visible diagnosis and the uncertainties of epidemiology in sub-Saharan Africa. *Childs Nerv Syst*. 2014 Jan;30(1):137-46.
26. Shamji MF, Vassilyadi M, Lam CH, Montes JL, Farmer JP. Congenital tumors of the central nervous system: the MCH experience. *Pediatr Neurosurg*. 2009; 45(5): 368-74.
27. Raimondi AJ, Tomita T. Hydrocephalus and intratentorial tumors. Incidence, clinical picture, and treatment. *J Neurosurg*. 1981 Aug;55(2):174-82.
28. Stefanits H, Ebetsberger-Dachs G, Weis S, Haberler C. Medulloblastoma with multi-lineage differentiation including myogenic and melanotic elements: a case report with molecular data. *Clin Neuropathol*. 2013 Oct 16.
29. Maiti T, Sabharwal P, Pandey P, Devi BI. Sub-cutaneous metastasis in medulloblastoma: A case report and review of literature. *J Pediatr Neurosci*. 2013 May;8(2):168-70
30. Nikitović M, Bokun J, Paripović L, Golubičić I, Grujičić D, Sopta J. Bone metastases in medulloblastoma--single institution experience. *Pediatr Hematol Oncol*. 2013 Mar;30(2):80-91.