Original Article

Medulloblastomas

Comparison Between Signs and Symptoms of Medulloblastomas and Desmoblastic Medulloblastomas

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ABSTRACT

Objective: To compare the signs and symptoms of Medulloblastomas and Desmoblastic Medulloblastomas.
Study Design: Retrospective study
Place and Duration of Study: This study was conducted at King Khalid University Hospital, Rayadh, Saudi Arabia from 1st January 2001 till 31st December 2010.
Materials and Methods: Total of 37 patients were included in the study. After taking written consent from all the patients or their relatives, this study was conducted. Permission was also taken from the ethical committee of the hospital. 37 patients were included in the study.
Result: Percentage of important symptoms of intracranial tumors like headache, reduced vision and hydrocephalus was comparatively higher in medulloblastomas as compare to desmoblastic medulloblastomas. None of the desmoblastic variety had metastasis on presentation, hence all of them completely excised. Unfortunately, we were able to excise only 82.14% of medulloblastomes. 14.28% were partially excised while in 3.57% of cases, surgeon was only able to take biopsy.
Conclusion: Desmoblastic variety of medulloblastoma had better prognosis as compare to Classical Medullblastoma.
Key Words: Medulloblastoma, childhood tumor, desmoblastic medulloblastomas.

INTRODUCTION

The annual incidence of tumors of the CNS ranges from 10 to 17 per 100,000 persons for intracranial tumors & 1 to 2 per 100,000 persons for intraspinal tumors; about half to three quarters are primary tumors, and the rest are metastatic .Tumors of the CNS account for 20% of all cancers of childhood. Seventy percent of childhood CNS tumors arise in the posterior fossa; a comparable number of tumors in adults arise within the cerebral hemispheres above the tentorium[1,2]. Unique characteristics of CNS tumors: first, the distinction between benign and malignant lesions is less evident in CNS than in other organs. Second, the ability to surgically resect infiltrating glial neoplasms without compromising neurologic function is limited. Third, the anatomic site of neoplasm can have lethal consequences irrespective of histologic classification. Any mass lesion within the skull is a threat to the integrity of brain function and therefore even histologically benign tumors can threaten life. Finally, the pattern of spread of primary CNS neoplasm differs from that of other tumor. The four major classes of brain tumors are, Gliomas, Neuronal tumors, poorly differentiated neoplasms and Meningiomas. In children, medulloblastomas are located in the midline of the cerebellum, but lateral locations are more often found in adults. The tumor is often well circumscribed, gray, & friable and maybe seen extending to the surface of the cerebellar folia and involving the leptomeninges. The desmoplastic variant is characterized by areas of stromal response with collagen and reticulin deposition and nodules of cells forming “pale islands” that have more neutrophil and lack the reticulin deposition. Dissemination through the CSF is a common complication, presenting as nodular masses elsewhere in the CNS, including metastases to the cauda equina that are sometimes termed “ drop” metastases because of their direct route of dissemination through the CSF[3].
Intracranial tumors can present with seizures, focal neurological deficit, raised ICP, seizure, endocrine dysfunction or can be incidental findings[4]. In the older age group (50-70) the more malignant cerebellar gliomas (anaplastic astrocytoma, glioblastoma) become more common, as do cerebral metastasis[5]. 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 medullobalstoma 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 aggressiveness[6]. Medulloblastomas are classified into

two chief histological variants, 1-"classical" and 2-desmoplastic"[7,8]. The rare variants of medulloblastoma are large cell, lipomatous, melanocytic and medullomyoblastoma[9,10].

MATERIALS AND METHODS

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

Inclusion and exclusion criteria: Only those patients were included in the study whose histopathology confirmed the diagnosis of Medulloblastoma and desmoblastic medulloblastomas. All other were excluded that 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. Out of 37 patients, 75.67% were diagnosed as classical medulloblastomas on histopathology.

Table No.1: Showing the relative percentage of two types of tumors.

Total	37	100%
Medulloblastoma	28	75.67%
Desmoblastic Medulloblastoma	9	24.32%

Table No.2: Showing signs and symptoms at presentation.

Headache	Medulloblastoma		Desmoblastic Medulloblastoma	
	Present in 26 (92.8%)	Absent in 2 (7.2%)	9 (100%)	0 (0%)
Vision	Reduced in 15 (53.57%)	Normal in 13 (46.42%)	Reduced in 3 (33.33%)	Normal in 6 (66.66%)
ICP	Raised in 27 (96.43%)	Normal in 1 (3.57%)	Raised in 8 (98.88%)	Normal in 1 (1.12%)
Cerebellar signs	Nil in 10 (35.71%)	Present in 18 (64.28%)	Nil in 3 (33.33%)	Present in 6 (66.66%)
Cranial nerve palsy	Nil in 20 (71.42%)	Present in 8 (28.57%)	Nil in 2 (22.22%)	Present in 7 (77.78%)
Hydrocephalus	Present in 27 (96.42%)	Absent in 1 (3.58%)	Present in 7 (77.77%)	Absent in 2 (22.225)

Table No.3: Neurological deficit in both types of tumors.

Neurological deficit	No deficit	Mild neurological deficit but independent	Partially dependent but can look after himself	Totally dependent
Medulloblastoma	1(3.57%)	9(32.14%)	7(25%)	11(39.28%)
Demoblastic medulloblastoma	0(0%)	5(55.55%)	2(22.22%)	2(22.22%)

In the next table, we discussed the signs and symptoms at presentation in the hospital. It is interesting to note that percentage of important symptoms of intracranial tumors like headache, reduced vision and hydrocephalus was comparatively higher in medulloblastomas as compare to desmoblastic medulloblastomas.

Similarly, desmoblastic variant present with better stage as far as neurological deficit is concerned. Desmoblastic tumors on presentation are less in percentage wise as regard to the mild, Partially dependent but can look after himself or totally dependent on other for their daily routine. More than 39% of classical medulloblastomas are totally dependant on others as compare to Demoblastic medulloblastoma tumors which are 22% on presentation.

It is interesting to note that none of the desmoblastic variant had metastasis on presentation. However medulloblastoma had 28.57% chances of metastasis according to our study. 6 out 28 patients had spinal while 2 had local spread.

Table No.4: % of Metastasis at presentation

	Nil	Local	Spinal
Medulloblastoma	20	2	6
Desmoblastic medulloblastoma	9	0	0

As discussed earlier, none of the desmoblastic variety had metastasis on presentation, hence all of them completely excised. Unfortunately, we were able to excise only 82.14% of medulloblastomes. 14.28% were partially excised while in 3.57% of cases, surgeon was only able to take biopsy.

Tumor resection

	Complete	Partial	Biopsy
Medulloblastoma	23	4	1
Desmoblastic medulloblastoma	9	0	0

DISCUSSION

In our study, majority of patients were between the ages of 6 to 12 years i.e. 40.5% (15). Out of 37 patients, Most of the studies conducted on these tumors concluded the same result. According to Remke M et al, Medulloblastoma is a rare primary brain tumor in adults, whereas it constitutes the most common malignant brain tumor in children. Integrated genomics approaches revealed at least four distinct disease variants in children. The transcriptome of adult medulloblastomas differs considerably from pediatric counterparts, both in terms of tumor biology and prognostic impact. Therefore, age-specific classification is required and must be adapted for use in clinical trials of adult medulloblastoma[11].

Similarly Yazigi-Rivard L et. al. also mentioned that it predominantly arises in the cerebellum and 4th ventricle[12]. 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 years[13]. 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 years[14]. Both these studies showed smaller age groups as compared to our study.

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%)[15]. Very similar results were shown by Stagno V[13], who calculated the male to female ratio of 59.9:40.1%.

Hydrocephalus is a very important symptom of intracranial tumors. Majority of our patients had hydrocephalus on initial presentation. Though the incidence was higher in medulloblastomas (96.42%) as compared with desmoblastic medulloblastomas where the incidence was slightly lower (77.77%). Shamji MF[16] mentioned that there was equal incidence of hydrocephalus (69%, p = 0.57). Although all the researchers agreed that it is a common symptom with very high percentage at presentation. According to Raimondi AJ and his fellows who conducted a study on 117 children with cerebellar-fourth ventricle tumors, 110 had hydrocephalus[17].

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 headaches[18]. Cannas A et. al mentioned that Medulloblastoma induces unusual headache with clinical picture of basilar-type migraine complicated by ischemic infarcts[19].

Hyperreflexia (72.5 %) and focal motor deficits (62.5 %) were the most common neurologic signs encountered in patients of infra tentorial tumors[20]. These patients represented 40% of children treated for newly diagnosed medulloblastoma[21]. 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 medulloblastoma[22].

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 Nevoid Basal Cell Carcinoma[23]. 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).[24]

Although desmoblastic medulloblastoma is a variant of medullblastoma, we try to compare and identify differences between the two. Statistically, some differences are not very important but internationally, researchers agreed that these two types are genetically different. Schroeder K, and Gururangan S[25] mentioned that the advent of deep sequencing gene technology has provided invaluable clues to the molecular makeup of this tumor and allowed neuro-oncologists to understand that medulloblastoma is an amalgamation of several distinct disease entities with unique clinical associations and behavior. This review is a concise summary of the pathology, genetic syndromes, recent advances in molecular subgrouping, and the associated gene mutations and copy number variations in medulloblastoma. According to Northcott PA et al[26], our integrative genomics approach to a large cohort of medulloblastomas has identified four disparate sub-groups with distinctdemographics, clinical presentation,

transcriptional profiles, genetic abnormalities, and clinical outcome. Medulloblastomas can be reliably assigned to subgroups through immunohisto chemistry, thereby making medulloblastoma subclassification widely available. Olson JM discussed the similar issue in his article published recently in Cancer Cell[27]. In this issue of Cancer Cell, they reveal clear genetically defined subclasses of the sonic hedgehog (SHH) subclass of medulloblastoma. This molecular dissection of the SHH subclass is not simply a cutting-edge advance; the data have profound impact on clinical trial design and decision-making. In the last, it is worth mention a very interesting research published in 2013 in Acta Neuropathol. DNA methylation profiling enables the robust subclassification of four disease subgroups in frozen and routinely collected/archival formalin-fixed biopsy material, and the incorporation of DNA methylation biomarkers can significantly improve disease-risk stratification[28].

CONCLUSION

Desmoblastic variety of medulloblastoma had better prognosis as compare to Classical Medullblastoma.

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