IJBC 2012;1: 19-23

Epidemiological features of Central Nervous System tumors at MAHAK Pediatric Cancer Treatment and Research Center

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Submitted: 07-05-2011 , Accepted: 18-07-2011

Abstract

Background: In this study, we examined the epidemiologic characteristics of childhood brain tumors in patients referred to MAHAK Pediatric Cancer Treatment and Research Center (one of the main national referral centers for childhood malignancies in Iran) for treatment.

Materials and Methods: This cohort (simple sampling) study consisted of 198 children less than 15 year old with CNS tumor referred to MAHAK Pediatric Cancer Treatment and Research Center from 2007 to 2010. The unique checklist contained epidemiological features filled for each individual. Results: Out of studied patients 125(63.1%) were male and 73(36.9%) were female. The mean age of patients was 6.11±3.65 years. Tumors were located in supratentorial (N=60, 30.3%), infratentorial (N=134, 67.7%) and spinal (N=4, 2%) regions. High-grade glioma and medulloblastoma were the most common tumors in supratentorial and infratentorial locations respectively. The majority of patientin medulloblastoma group had T2M0 (N=44, 22.2%) stage. Thirty-one (15.7%) patients had arelapse. There were 38.4% treatment and 41.4% death. The five years survival rate among patients was 28%.

Conclusion: The same frequency of CNS tumors in children less than 15 years old referred to MPCTRC was observed compared to other studies. The sex incidence, the mean age at presentation, tumor sites, brain tumor's pathologies, signs and symptoms, metastases and relapses were also in line with other studies. There were significant differences in terms of high consanguinity rate and high incidence of familial cancer history as compared to reports from others.

Keywords: Brain, tumor, infratentorial, supratentorial, spinal, treatment, childhood.

Introduction

The second most common childhood malignancies after leukemia are central nervous system (CNS) tumors [1-3]. These tumors comprise nearly 15-20% of all childhood neoplasms which affect children of all ages, ethnicities and races [4-9]. Childhood CNS tumors accounts for approximately 2000 cases less than 20 years old in the United States[7]. In 2007, there were 20,500 individuals (11,170 males and 9,330 females) with CNS tumor in the USA[10].

The worldwide age-standardized incidence of CNS tumor is 3.7 for males and 2.6 for females per 100,000 annually[11]. The embryonal type of CNS tumor occurs in 33% of patients less than 3 years old[12]. It is clear that Medulloblastoma, glioma and ependymoma are the most common types of childhood brain tumors,[13] while primitive neuroectodermalembriogenictumorislesscommon

in children age 8 to 15 years old[14]. Approximately 3-5% of children with Medulloblastoma may suffer systemic metastases [15,16].

As the childhood neoplasms are the second most common cause of death beyond the neonatal age group [6,9], improvements in diagnosis and managment of pediatric CNS tumors can increase the number of long-term survivors and their quality of life [4,8]. The worldwide age-standardized mortality for primary malignant brain tumors is about 2.8 for males and 2.0 for females per 100,000 1.

Studying the treatment patterns can be a powerful prognostic tooland improve the outcome of childhood CNS tumors[9]. The objective of this study was to evaluate the epidemiological features of childhood CNS tumors in patients referred to MPCTRC (MAHAK's Pediatric Cancer Treatment and Research Center) for treatment and follow-up.

Patients and Methods

This was a simple sampling study, which comprised of 198 eligible patients with CNS tumor who were registered at MPCTRC from 2007 to 2010 for treatment or consult. The total number of admitted patients in that time span was 1517and 198 (13.05%) had CNS tumors.

A checklist was assigned to each individual that included epidemiological information including sex, age at diagnosis, signs and symptoms, tumor location, prior malignancy, family history of cancer (type of cancer diagnosed in patient's parents) and consanguinity (parental familial marriage). All patients were categorized into four groups according to their age at diagnosis: less than one year, 1-5 years, 5-10 years and 10-15 years old. The patients took multimodality treatments according to their pathology. MPCTRC provides financial supports for all admitted patients. We also evaluated the socio-economic status of patients based on data compiled at the welfare services of this center.

Data were analyzed by SPSS version 19, with confidence intervals of 95%. Kolmogorov-Smirnov test was used to check the normal distribution of variables, Chi-square for parametric and Spearman method for non-parametric data respectively. We also used t-test to compare means.

Results

Out of 198 enrolled patients 125 (63.1%) were males and 73 (36.9%) were females. The Male/ Female ratio was 1.71/1. The tumor location in our patients was supratentorial in 60 patients (30.3%), infratentorial in 134 patients (67.7%) and spinal in 4 patients (2%). Male predominance was observed in all age groups except in patients with infratentorial tumor who were less than one year old and children with supratentorial tumor who were aged between 10 to 15 years (Table 1).

The mean age was 6.11 ± 3.65 years (range 1 to 14 years). According to analysis the mean age of patients in different tumor location categories was as supratentorial 6.33 ± 4.08 years (range 1-14 years), infratentorial 5.96 ± 3.41 years (range 1-14 years) and spinal 7.75 ± 4.99 years (range 1-12 years).

Glioma (n=36, 59.99%) and medulloblastoma (n=65, 48.51%) were the most common tumor types in supratentorial and infratentorial locations respectively (Table 2). According to our data medulloblastoma (n=65, 33.51%), glioma (n=61, 31.44%) and Astrocytoma (n=27, 13.93%) were the most common tumors in patients.

According to our findings, 100 patients (50.5%) had specific signs and symptoms from 1 to 6 months before their diagnosis. The most common

Table1: distribution of sex and age in each tumor location category

Age	< 1 year			1 – 5 years			5 – 10 years			10 – 15 years			
Tumor location	Supra	Infra	Spinal	Supra	Infra	Spinal	Supra	Infra	Spinal	Supra	Infra	Spinal	Total of sex groups
Male	3(60%)	2(40%)	0	10(62.5%)	29(63%)	1(100%)	15(62.5%)	40(67.8%)	1(100%)	7(46.7%)	15(62.5%)	2(100%)	125(63.1%)
Female	2(40%)	3(60%)	0	6(37.5%)	17(37%)	0	9(37.5%)	19(32.2%)	0	8(53.3%)	9(37.5%)	0	73(36.9%)
Column total	5(100%)	5(100%)	0	16(100%)	46(100%)	1(100%)	24(100%)	59(100%)	1(100%)	15(100%)	24(100%)	2(100%)	
Total of age group	10 (5.1%)			63 (31.8%)			84 (42.4%)			41 (20.7%)			198(100%)

clinical presentations according to frequency were vomiting (n=106, 53.5%), headache (n=102, 51.5%), disturbance of gait and balance (n=51, 25.8%), strabismus (n=27, 13.6%), impaired vision (n=24, 12.1%), seizure (n=19, 9.6%), hemi parasia (n=18, 9.1%), diplopia (n=16, 8.1%), papilledema (n=15, 7.6%) and vertigo (n=14, 7.1%) respectively. The majority of children with infratentorial tumors had vomiting (n=72, 53.7%), headache (n=65, 48.5%) and disturbance of gait and balance (n=37, 27.6%), while in patients with supratentorial tumors headache (n=36, 60.3%) and vomiting (n=33, 55%) where the most common signs respectively. A significant correlation between vomiting and sex (p =0.037), diplopia and sex (p =0.027) and between age and nystagmus (p =0.002) was observed.

The family history of cancer was seen in 19 patients (9.6%) as CNS malignancies and 31 patients (15.7%) as other malignancies respectively. The underline disease and comorbidities in four patients (2%) was neurofibromatosis type1 and one patient had tuberous sclerosis (0.5%). The parental familial marriage was in 77 patients (38.9%). Most study patients had low socio-economic status (n=102, 51.5%) according to data compiled at welfare services of MPCTRC. The ethnicity of enrolled patients was Caucasians (Iranians n=167, Azerbaijani n=3, Afghans n=10and Iraqis n=18).

Forty-seven patients (23.7%) had metastasis with 41 patients (20.7%) having CSF and 1 patient having spleen metastasis. Thirty-one patients (15.7%) had a relapse during their treatment: supratentorial 13 patients (41.9%), infratentorial 16 patients (51.6%), and spinal 2 patients (6.5%). There was significant correlation between relapse and tumor sites (p =0.037). The mean age of relapse in enrolled patients was 1.9 ± 2.38 years. The mean age of relapse time according to tumor sites was 2.1 ± 2.67 among patients with supratentorial, 1.5 ± 1.89 in patients with infratentoria, and 4 ± 4.24 in patients with spinal tumor.

The statistical analysis showed that 76 patients (38.4%) completely received protocol regiments and out of 198 patients, 82 (41.4%) died during or after the treatment. The frequency of death according to the tumor site was 24 patients (29.3%) with supratentorial tumors and 58 patients (70.7%) with infratentorial tumors. The five-year survival rate was 28% and the median survival time was 3.36 years.

Discussion

The aim of this study was to evaluate the epidemiological features of CNS tumors in patients admitted to MPCTRC for diagnostic procedures, treatment and consecutive follow-up. MAHAK as a NGO to support children suffering from cancer commenced its activity in early 1991and has expanded within a few years. It is a primarily social and supportive center in Tehran, to provide hostel facilities for patients and accompanying parents coming from rural areas. From early on the need for

Table2: Tumor histology types in supratentorial and infratentorial sites among enrolled patients

Tumor histology	Tumor location		Total
	Supratentorial	Infratentorial	
Medulloblastoma	----------	65 (48.51%)	65 (33.51)
Glioma	36(59.99%)	25 (18.66%)	61 (31.44)
Astrocytoma	----------	27 (20.15%)	27 (13.93)
Ependymoma	6 (10%)	14 (10.43%)	20 (10.31)
PNET	8 (13.33%)	1 (0.75%)	9 (4.64)
Optic nerve glioma	4 (6.67%)	----------	4 (2.06)
AT/RT (Atypical Teratoid Rhabdoid Tumor)	2 (3.33%)	1 (0.75%)	3 (1.55)
Germ cell tumor	1 (1.67%)	1 (0.75%)	2 (1.03)
Craniopharyngioma	1 (1.67%)	----------	1 (0.51)
Primary CNS malignant lymphoma	1 (1.67%)	----------	1 (0.51)
Histiocytosis	1 (1.67%)	----------	1 (0.51)
Total	60(100%)	134 (100%)	194 (100%)

a comprehensive center was recognized and with generous public help and support MPCTRC became a reality in 2007. In line with its activities, MAHAK has set up a comprehensive cancers registry, which has been the source of current information. The estimated annual cancer incidence in Iran is 150 per 100,000 in children aged 0-15 years old, meaning 3,000-3,500 new cancers per annum, which is higher than other reports from developed countries, although recent reports indicates an increasing cancer incidence trend in these countries[15].

Central Nervous System tumors are the second most frequent malignancy of childhood in most parts of the world with a prevalence of 15-20% of all childhood malignancies [2,6]. At MPCTRC the number of eligible patients with childhood CNS tumors is lower than expected (198 out of 1517 patients), thus indicating a lower frequency (13.05%).A probable reason for this disparity is the selective patient admission at other centers and referring the difficult to handle malignancies for instance leukemia, soft tissue sarcomas, bone sarcomas and others to MPCTRC.

Reports have demonstrated a predominant male incidence in childhood CNS tumors, which is approximately twice as common in males as in females [4,7,8]. According to the present data, males comprised 63.1% and females 36.9% of CNS tumors, with 1.7 time higher incidence in males than females. However, patients younger than one year had equal sex distribution. In this study, low grade or high-grade glioma had a higher incidence in females compared to males. As this is a hospital-based research, we could not generalize its findings.

The histological type of CNS tumors can affect the age patterns of patients[13]. Annually about 2,200 CNS tumors are diagnosed in US children less than 20 years4. Childhood CNS tumors are more common in children younger than 8 years old [2,4,9,12]. Analysis showed that CNS tumor among our patients had age related frequencies and the mean age was 6.11±3.65 years old, which is in concordance with other reports.

According to previous studies, infratentorial tumors (64.1%), have a higher frequency than supratentorial (35.9%) tumors among children[13]. One of the most common CNS tumors in children is medulloblastoma [2,5,9]. Infratentorial astrocytoma is also prevalent among children [8]. Packer et al. [2] and Sievert et al.3 reported that glioma could account as 10-25% of childhood CNS tumors and ependymoma comprises 5-10% of childhood brain tumors[2]. In Sweden, medulloblastoma and glioma where the most common types of childhood brain tumors[1]. In a report by Ahmed et al. [8], they concluded that astrocytoma, medulloblastoma and ependymoma where the most common types of CNS tumors in children. In our hospital based study, infratentorial tumors were more common than supratentorial tumors. The commonest types of CNS tumors were in ordermedulloblastoma, astrocytoma, glioma and ependymoma.

The prevalent signs in childhood CNS tumors are headache, nausea, vomiting and lethargy while endocrinopathies, papilledema, ataxia and diplopia are less common [6,8,11,12]. The prevalent signs in children with CNS tumors who referred to MPCTRC were vomiting, headache and disturbance of gait and balance while the les common signs were diplopia, papilledema and vertigo.

Systemic metastases in childhood CNS tumors occur in 3-5% of cases in medulloblastoma5. The frequency of metastasis and relapse according to other reports are 23-64% and 10-60% respectively[16]. The occurrence of metastasis and relapse in our patients were 25.3% and 15.7% respectively which is in concordance with other reports.

Stevenson et al.[8] suggested that inherited genetic conditions and some diseases like neurofibromatosis, tuberous sclerosis and Li-Fraumeni syndrome could account as known risk factors in suffering childhood CNS tumors. In our study, 50 patients (25.3%) of participants revealed a familial history of cancer and four patients had neurofibromatosis type 1 and one patient had tuberous sclerosis. Consanguine marriage in Iran is as high as in other Middle Eastern countries with mean frequency of 30 % in urban and up to 64 % in rural areas. Consanguine mating may be consider as a critical public health issue in terms of other inheritable malignant disorders that impact on social welfare. Out of 198 patients, 38.9% were the result of consanguine mating. Certainly, there should be more investigation to conclude that this parameter could be considered as a risk factor of CNS tumors. Our results imply the need for surveillance of family members of cancer victims.

CNS tumors are the leading cause of mortality and morbidity in children suffering from childhood

malignancies [4,13]. In our study, the mortality rate of CNS tumor in children was 41.4%.

Conclusion

The same frequency of CNS tumors in children less than 15 years old referred to MPCTRC was observed compared to other studies. The sex incidence, the mean age at presentation, tumor sites, brain tumor's pathologies, signs and symptoms, metastases and relapses were also in line with other studies. There were significant differences in terms of high consanguinity rate and high incidence of familial cancer history as compared to reports from others.

Acknowledgment

This study has been supported by MAHAK Pediatric Cancer Treatment and Research Center. Authors wish to thank staff in the department of medical records as well as department of oncology and hematology for their assistance in data generation and collection.

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