Original Article

Evaluation of Radiographic, Neuropathological, and Demographic Findings in Children Aged 1 To 18 Years with Brain Tumor

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Abstract

Background: Brain tumors in children can involve different parts of the brain and cause high mortality. These tumors have different types, and they cause different conflicts and complications. So far, limited studies have been conducted in Iran on children's brain tumors. This study aimed to evaluate radiographic, neuropathological, and demographic findings in children aged 1 to 18 years with brain tumors.

Materials and Methods: In this descriptive study, which was conducted for children aged 1 to 18 years with brain tumors admitted to the children's ward of Shohada Hospital (Iran-Tehran) in 2012-2018, 64 children were evaluated. Patient information was extracted from patients' files, including basic data radiological and clinical findings. A significance level was considered less than 0.05.

Results: Twenty-six patients (40.6%) were girls, and 38 (59.4%) were boys. 96.9% of the children were term, and the mortality rate was 40.6%. 57.8% were diagnosed in less than one month from the onset of symptoms. 47.6% of patients had a positive family history, and none of them had a history of brain infection. The most common clinical complaint was N/V. The most common location of the tumor was the fourth ventricle (31.3%), and acute hydrocephalus was also seen in 19 patients (29.7%). The most common tumor was medulloblastoma (93.8%), and the most common stage was grade 4 (98.4%). Desmoplastic medulloblastoma was the most common form of medulloblastoma. 9.4% of patients were positive for tumor marker P53. None of the patients were positive for Beta-Catenin.

Conclusion: The findings have shown that being a boy, involvement of the fourth ventricle and medulloblastoma are the most common characteristics of brain tumor involvement in Iranian children.

Keywords: Brain tumor, Pediatric, Medulloblastoma

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Introduction

Brain tumors are the most common cause of death among malignancies and are the second most common brain

disorders after stroke. Brain tumors are associated with decreased performance and quality of life in children[1]. According to studies in Canada, brain tumor is the second cause of cancer in people under the age of 20[2]. Each year, approximately 11,000 to 13,000 Americans are dying from primary tumors of the central nervous system (CNS)[3]. Primary tumors of the central nervous system account for approximately 20% of childhood cancers and 25% of all childhood cancer mortality[4,5]. The causes of primary brain tumors are still unknown in most cases[6].

Even though brain tumors comprise a small percentage of all malignancies, their high prevalence, especially in children and adolescents, is associated with impaired normal growth and development, academic failure, performance loss, increased disability in various aspects of life, and ultimately a significant decrease in quality of life and due to low life expectancy and survival and loss of many years of life, it is one of the main causes of death in this age group[6,7]. Finding preventable factors in brain tumors can help in preventing this disorder or at least inappropriate management of patients[8].

P53 is the most common tumor suppressor protein in humans. Mutation in this protein is the main cause of cell formation in cancerous cells[9]. P53 mutations are seen in about 12% of brain tumors in Li-Fraumeni syndrome, including adult astrocytomas and children's medulloblastoma[10]. P53 mutations are seen in 30% and 65% of primary glioblastoma multiforme (GBM) and secondary GBM, respectively[11].

There is limited data about the cause, prognosis, and risk factors for brain tumors[12]. Due to the different prevalence, etiology, type, and clinical manifestations of brain tumors in children and adolescents compared to adults, it is important to investigate this disorder separately in this age group[2]. This study aimed to evaluate radiographic, neuropathological, and demographic findings in children aged 1 to 18 years with brain tumors.

Methods

This research received the ethics code from the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1402.585). This descriptive study was conducted on children admitted to Tajrish Shahada-e-Hospital (Iran-Tehran) between 2012 and 2018.

In this study, the files of all children more than one year and below 18 years' old who were diagnosed with a medulloblastoma brain tumor in Shohada Tajrish Hospital (the only referral hospital in the country equipped with the stereotaxic system) were assessed. Patients who had the diagnosis of brain tumor medulloblastoma based on the World Health Organization indicators and patients who were given a possible diagnosis based on imaging and based on the pathology of a definite diagnosis of brain tumor were included in the study. This research used the World Health Organization (WHO) diagnostic criteria for medulloblastoma. The exclusion criteria were not confirmed medulloblastoma and not having a biopsy specimen. Information was extracted from patients' files and analyzed.

Age, sex, time of diagnosis, symptoms and clinical findings, duration of symptoms until definitive diagnosis, underlying disease, first complaint, history of brain infection, and head trauma were recorded. Also, the imaging results, tumor location, postoperative mortality up to one month, and complications after tumor resection (tumor removal) were extracted from the files based on WHO diagnostic classification.

The normality of the distribution of the study variables was checked using the One-Sample Kolmogorov-Smirnov Test. Normal quantitative variables are shown as mean (standard deviation), quantitative variables with abnormal distribution are shown as median (range between 25-75 percentiles), and qualitative variables are shown as numbers (percentage). All statistical analyses were performed using SPSS software version 22. A statistically significant level was considered 0.05 in all the performed analyses.

Results

In this study, 64 children were examined; 38 (59.4%) were boys. 96.9% of the examined children were term, and the mortality rate was 40.6%. The data about gender, birth, and mortality of patients are seen in Table 1.

Table 2 shows the mean time of diagnosis to death was 14.44±14.96 months, and the mean time of surgery to relapse was 14.90±8.94 months.

Table 3 shows the radiological information of the patients. Based on our findings, it was seen that the

Table 1: Data on gender, birth, and mortality.

		n (%)
Gender	Girl	26 (40.6)
	Boy	38 (59.4)
Birth	Term	62 (96.9)
	Preterm	2 (3.1)
Mortality	No	38 (59.4)
	Yes	26 (40.6)

most common location of the tumor was the fourth ventricle (31.3%), and acute hydrocephalus was also seen in 19 patients (29.7%). The pathological data of the patients were assessed, and the findings are reported in Table 4. The data on different types of treatment and post-surgery complications are seen in Table 5.

Discussion

In this study, which was conducted to evaluate radiographic, neuropathological, and demographic findings of brain tumors in children aged 1 to 18 years, 64 children were assessed, of which 59.4% were boys. 96.9% of the children were term, and the mortality rate was 40.6%. 47.6% of patients had a family history, and none had a history of brain infection. The most common clinical complaint of the patients was N/V. The most common location of the tumor was the fourth ventricle (31.3%), and acute hydrocephalus was also seen in 19 patients (29.7%). The most common tumor was medulloblastoma (93.8%), and the most common disease stage was grade 4 (98.4%). Desmoplastic medulloblastoma was also the most common form of medulloblastoma. 9.4% of patients were positive for tumor marker P53. None of the patients were positive for Beta-Catenin.

Beta-catenin expression is directly associated with neural stem cell proliferation and self-renewal[13]. It seems that any mutation in this factor may induce brain cancer14, but we have not found such a result.

Based on a systematic review, pesticide exposures, various genetic variants, farming or hairdressing jobs, personal hair dye, and cured meat consumption may be associated with an increased risk of brain tumor onset in adults. M1B-1 antigen was shown to increase the risk of progression. Pesticide exposure, high birth weight, and maternal cured meat consumption during pregnancy may increase the risk of brain tumor onset in childhood. However, maternal consumption of supplements such as folic acid may decrease the risk in children[15].

Shah et al.'s study evaluated the demographic and histopathological characteristics of pediatric brain

Table 2: clinical information of the patients.

		n (%)
Time to diagnose	<1 month	37 (57.8)
	1-2 months	11 (17.7)
	2-3 months	3 (4.8)
	3-6 months	6 (9.7)
	6-12 months	3 (4.8)
	12-24 months	1 (1.6)
	>24 months	1 (1.6)
Underlying disease	Yes	9 (14.1)
	No	55 (85.9)
Positive familial history	Yes	30 (47.6)
	No	33 (52.4)
History of brain infection	Yes	0 (0.0)
	No	64 (100)
History of head trauma	Yes	17 (26.6)
	No	47 (73.4)
Chief complaint	N/V	51 (79.7)
	Diplopia	8 (12.5)
	Headache	25 (39.1)
	Gait disturbance	36 (56.3)
	Ataxia	12 (18.8)
	Seizure	3 (4.7)
	Macrocephaly	5 (7.8)
	Dizziness	2 (3.1)
	Developmental Regression	2 (3.1)
	Paresis	2 (3.1)
	CN Palsy	10 (15.6)
	Lethargy	1 (1.6)
	Involuntary Neck Movement	1 (1.6)
	Tremor	1 (1.6)
	torticollis	1 (1.6)
	opsomyoclonus	1 (1.6)
	Blurred vision	1 (1.6)

Table 3: The radiological information of patients.

		n (%)
Tumor location	Fourth ventricle	20 (31.3)
	Vermis	4 (6.3)
	Left cerebellar hemisphere	3 (4.7)
	Right cerebellar hemisphere	1 (1.6)
Macroscopic hemorrhage within the tumor		5 (7.8)
Acute hydrocephalus		19 (29.7)
Brain stem compression		6 (9..4)
Enhancement		5 (7.8)
Brainstem involvement		3 (4.7)
Middle cerebellar peduncle involvement		0 (0.0)
Roof of the fourth ventricle involvement		0 (0.0)

Table 4: The pathological data of the patients.

		n (%)
Anaplastic/large medulloblastoma		6 (9.4)
Desmoplastic medulloblastoma		10 (15.6)
Medulloblastoma with extensive nodularity		6 (9.4)
Type of tumor	Medulloblastoma	60 (93.8)
	Medulloblastoma/PNET	1 (1.6)
	Embryonal	1 (1.6)
	ETMR	1 (1.6)
	Cavernoma	1 (1.6)
Stage of tumor	1	1 (1.6)
	4	61 (98.4)
Tumor marker		
P 53	Positive	6 (9.4)
	Negative	24 (37.5)
Beta-Catenin	Positive	0 (0.0)
	Negative	26 (40.6)

tumors (PBT) based on the World Health Organization classification in India and reported that PBTs in boys (55.3%) were higher compared to girls (44.7%). The most common anatomical location was the cerebellum (39.5%), followed by the hemisphere (22.4%). Supratentorial tumors (52.6%) were more dominant than subtentorial tumors (47.4%). Astrocytomas (40.8%) and embryonal tumors (29.0%) were the most common histological types, accounting for approximately more than two-thirds of all tumors. Craniopharyngioma (11.8%) and ependymoma (6.6%) were the third and fourth most common tumors, respectively[16]. In the current study, it was seen that 59.4% of the patients were boys. The most common location of the tumor was the fourth ventricle, which was seen in 31.3% of patients, followed by the cerebellum. The most common type of tumor was medulloblastoma. Our study's findings differed from the study of Shah et al. The gender distribution in the two studies was almost similar, but the type and location of the tumors were different in the two studies. This difference could be due to the genetic difference between the two populations, as our study was conducted on Iranian children. However, the study by Shah et al. was conducted on Indian children. Genetics can be effective in the incidence and prevalence of brain tumors in children, although there is still a need for more studies in this respect[6].

The study of Ogun et al. investigated central nervous system tumors in children in Ibadan, Nigeria. Seventy-seven tumors, 44 in boys, were included in the study. Astrocytic tumors included 20 cases, embryonal tumors 15, ependymal tumors 15, germ cell tumors 6, sellar tumors (all craniopharyngiomas) 9, and other histological types 12 cases. Thirty-seven neoplasms were WHO grade 1, eleven grade 2, ten grade 3, and nineteen grade 4. The most common tumors in this series were pilocytic astrocytomas, medulloblastoma, craniopharyngioma, and ependymoma, respectively[17]. In the current study, it was also seen that brain tumors were more common in boys, and in this sense, these two studies are similar. In our study, the most common type of tumor was medulloblastoma, and most of the patients in our study were grade 4, which was different from Ogun et al.'s study. The differences in the genetics of the investigated patients can cause these differences between the two studies.

Jaiswal et al. reviewed the spectrum of primary intracranial tumors in a tertiary neurological institution in India. Among children, astrocytoma tumors (25.1%), embryonal tumors (20.6%), and ependymal tumors (14.8%) were the most commonly reported histologies. Glioblastoma and all other tumors showed a male tendency, while meningiomas were more common in females. A significant difference in the mean age of some tumor subtypes was observed compared to the Central Brain Tumor Registry of the United States (CBTRUS)[18]. In our study, it was seen that brain tumors

Table 5: Post-surgery complications and different types of treatment.

	n (%)
Surgical Excision	62 (96.9)
Adjuvant Chemotherapy	56 (87.5)
Craniospinal irradiation if>3 years	55 (86.0)
Post-surgery complications	**n (%)**
Infection	1 (1.6)
Hydrocephalus	0 (0.0)
Metastasis	16 (25.0)
Secondary malignancy	0 (0.0)
Paralysis	4 (6.3)

had a male tendency; in this respect, these two studies were similar, but there was a difference between the most common cancer types between the two studies, as in the study of Shah et al. of course, among the differences between this study and the current study, the population studied was more in the study of Jaiswal et al.

Mohammad et al. described the histopathological types and basic demographic parameters of brain tumors in Madinah province of Saudi Arabia. The most common histopathological diagnosis in this study was meningioma (30.8%), astrocytic tumors (29.1%), metastatic tumors (7.7%), and embryonal tumors (6.6%), respectively. Meningothelial meningioma was the most common type of meningioma (48.5%). The majority of astrocytic tumors (52%) were classified as WHO grade IV[19]. The findings of this study differed in the type of tumor, but in this study, like our study, most of the patients were grade 4. Of course, this difference in the type of cancer can be due to the different designs of the two studies because the current study was conducted on children. However, the study by Mohammad et al. was conducted on adults and children, and more than 80% of the subjects in this study were adults.

Rajendran et al. evaluated the incidence of supratentorial tumors and different histopathological characteristics in children under 18. The most commonly reported tumors were astrocytoma and craniopharyngioma, followed by ependymoma[20]. The findings of this study were different from our study. Based on the studies conducted, such as the study by Rajendran et al., it seems that the most common tumor in children in India is astrocytoma. However, so far, no studies have been conducted in Iran, which clarifies the need to conduct these studies in the future in Iran.

Conclusion

It is concluded that the gender difference in the occurrence of brain tumors in children is not statistically significant, but clinically, these tumors have a male tendency. The mortality rate was 40.6%. The most common location of the tumor was the fourth ventricle (31.3%), and the acute hydrocephalus rate was 29.7%. The most common brain tumor In Iranian children is medulloblastoma, with a rate of 93.8%, and the most common tumor stage was grade 4, which was seen in 98.4%.

Acknowledgment

None.

Conflict of interest

The authors further declare that they have no conflict of interest.

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