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ORIGINAL PAPER

Morphological pattern and frequency of intracranial tumors in children

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Abstract
Background Brain tumors are the second most common neoplasm in children. Pattern of primary brain tumors in children has not been reported in Iran. Brain tumors have been the subject of controversy both with respect to pattern of occurrence and to potential causes.
Objective To determine the age, sex, location, and histologic diagnosis of intracranial tumors in children less than 15 years of age.
Materials and methods A retrospective study of 619 children who were admitted to the neurosurgical center between 1978 and 2003 was performed. Charts were reviewed to extract information about demographics, location, and histopathological diagnosis of tumors. All patients entered into this study had pathologically proven brain tumor. The frequency distribution of brain tumors by age and sex, location, and histopathology was calculated.
Results The male–female ratio, 58.1 to 41.9%, vary significantly ($p<0.05$). The mean age of the patients at time of diagnosis was 8.8 years (SD=3.9). Fifty-one percent of brain tumors were located in supratentorial, and 49.0% in the infratentorial region. In supratentorial region, 57.0% of the tumors were in the hemispheric. In infratentorial region, 68% of the tumors were in the midline. The mixed five most common histological diagnoses in patients were astrocytoma (40.4%), followed by medulloblastoma (18.4%), ependymoma (10.5%), craniopharyngioma (8.8%), and meningioma (4.2%). Most of the brain tumor types (85%) occurred in children between 5 to 15 years of age. Astrocytoma occurred mostly in children aged 5–15 years (87%).
Conclusion Males were affected more than females. A significant male predominance was observed in craniopharyngioma and medulloblastoma. Astrocytoma was the first most common brain tumor in all age groups. Certain tumor types show a predilection for the certain period of life.

Keywords Epidemiology · Brain tumors · Children · Location · Histopathology

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Introduction

Brain tumors are the most common solid tumors of childhood. Malignant brain tumors are the leading cause of death among children and the second most common type of pediatric cancer [2, 8]. Approximately, 872 (22% of all primary brain tumors) individuals under 20 years of age are diagnosed with a brain tumor in Iran each year [17, 20]. These cancers continue to have poorer survival rates than the other most common childhood cancers, leukemia, and lymphomas [3]. Brain tumors have been the subject of controversy both with respect to patterns of occurrence and to potential causes [7].

To determine the age, gender, histologic diagnosis, and tumor location in pediatric patients, we reviewed 619 patients who were operated on at the Department of Neurosurgery, Tehran University Hospital during the period from 1978 to 2003. All patients who entered into this study had pathologically proven brain tumor. The results of this

study carry important implications for future health planning strategies and provide a baseline for further studies on evaluation of malignancies in Iran.

Materials and methods

Medical records of 619 children age less than 15 years old with primary brain tumors who presented to the Department of Neurosurgery at the Sharitee Hospital University of Tehran for primary treatment of their tumors between 1978–2003 were reviewed. The patients' charts were retrospectively reviewed to extract information about age at the time of admission to hospital, sex, histologic diagnosis, and location of the tumors. All patients who entered into this study had pathologically proven brain tumor. The frequency distribution of brain tumors by age, sex, location, and histopathology was calculated. For age, the mean, standard deviation, and 95% confidence intervals were presented. *T* test and Chi-squared tests with $p<0.05$ were used, depending on the variable to be analyzed, using the SSPS statistical package. Demographic and the histopathological data of primary brain tumors of all the patients were reviewed and compared with those of other countries.

Results

An analysis of total series has resulted in the general conclusion that cases almost were not equally distributed between males and females. The male–female ratio was 58.1 to 41.9%, vary significantly ($p<0.05$). The mean age of the patients at time of diagnosis was 8.8 years (SD=3.9) with median of 9 years and the ages ranged from 0.5 to 15 years. The mean age for males was 8.9 years (SD=3.8) with median of 9 years. The mean age for females was 8.5 years (SD=4.0) with median of 8 years. The mean age of females was not significantly different compared to that of males.

The five most common histologic tumor types in both sexes among patients were astrocytoma in 250 cases (40.4%), followed by medulloblastoma in 114 cases (18.4%), ependymoma in 65 cases (10.5%), craniopharyngioma in 55 cases (8.8%), and meningioma in 26 cases (4.2%). These account for 82.3% of all brain tumor cases. A significant ($p<0.05$) male predominance was observed in the craniopharyngioma (male/female ratio of 2.1) and medulloblastoma (male/female ratio of 1.8).

Fifty-one percent of brain tumors were located in supratentorial and 49.0% in the infratentorial region. The mean ages of patients with tumors at diagnosis of supratentorial and infratentorial tumors were 9.0 and 8.5 years, respectively. The ratio of male to female occurrence was 1.47 for supratentorial and 1.33 for infratentorial tumors.

Hemispheric (cerebral) tumors occurred in 180 patients. They accounted for 57.0% of the tumors located in supratentorial region. This group accounted for 29.1% of the total tumor series. The five most common histologic tumor types among hemispheric tumors were astrocytoma (32.7%), meningioma (13.8%), lymphoma (13.3%), ependymoma (11.6%), and glioblastoma (10.5%) (Table 1). These accounted for 81.9% of all brain tumors in cerebral region. The mean age at diagnosis for patients with this group of tumors was 8.8 years. The male–female ratio was 1.5.

Supratentorial midline (axial) tumors occurred in 136 patients. They accounted for 43.0% of tumors located in the supratentorial region and accounted for 22.0% of the total tumor group. The frequency of histologic tumor types was as follows: craniopharyngioma (40.4%), optic-hypothalamic astrocytoma (39.0%), pituitary adenoma (8.8%), germinoma (5.9%), teratoma (3.7%), and chordoma (2.2%) (Table 1). The mean age at diagnosis for patients with this group of tumors was 9.4 years. The male–female ratio was 1.4.

Cerebellar tumors occurred in 98 patients. They accounted for 32.3% of tumors located in the infratentorial region and accounted for 15.8% of the total tumor group. The frequency of tumors based on histologic diagnosis occurring in this region was as follows: astrocytoma (77.6%), medulloblastoma (10.2%), glioblastoma (5.1%), lymphoma, schwannoma, and hemangioblastoma (2.0%

Table 1 Anatomical locations and histological tumor types of supratentorial brain tumors

Anatomic location	Histologic tumor type	Number (%)
Midline (axial)	Craniopharyngioma	55 (40.4)
	Optic-hypothalamic Astrocytoma	53 (39.0)
	Chordoma	3 (2.2)
	Pitutary Adenoma	12 (8.8)
	Teratoma	5 (3.7)
	Germinoma	8 (5.9)
	Total	136
Hemispheric (cerebral)	Astrocytoma	59 (32.7)
	Ependymoma	21 (11.6)
	Meningioma	25 (13.8)
	Lymphoma	24 (13.3)
	Glioblastoma	19 (10.5)
	Hemangiopericytoma	12 (6.6)
	Ganglioma	4 (2.2)
	Neuroblastoma	3 (1.7)
	Schwannoma	4 (2.2)
	Choroid plexus papiloma	3 (1.6)
	Teratocarcinoma	1 (0.05)
	Intraventricular astrocytoma	5 (2.7)
	Total	180

Table 2 Anatomical locations and histological tumor types of infratentorial brain tumors

Anatomic location	Histologic tumor type	No. (%)
Midline (axial)	Brainstem astrocytoma	50 (24.4)
	Astrocytoma of vermis	7 (3.4)
	Medulloblastoma	104 (50.7)
	Ependymoma	44 (21.5)
	Total	205
Hemispheric (cerebellar)	Astrocytoma	76 (77.6)
	Medulloblastoma	10 (10.2)
	Meningioma	1 (1.0)
	Lymphoma	2 (2.0)
	Glioblastoma	5 (5.1)
	Schwannoma	2 (2.0)
	Hemangioblastoma	2 (2.0)
	Total	98

each) (Table 2). The mean age at diagnosis for patients with this group of tumors was 8.5 years. The male–female ratio was 1.2.

Infrantentorial midline (axial) tumors occurred in 205 patients. They accounted for 67.7% of tumors located in the infratentorial region and accounted for 33.0% of the total tumor group. The distribution of histologic tumor types in this region was medulloblastoma (50.7%), brainstem astrocytoma (24.4%), ependymoma (21.5%), and astrocytoma of vermis (3.4%) (Table 2). The mean age at diagnosis for patients with this group of tumors was 8.5 years. The male–female ratio was 1.4.

Patients with malignant tumors had a mean age at time of diagnosis of 8.7 years. The mean age at diagnosis of patients with malignant supratentorial tumors was 9.4 years compared to 8.5 years for infratentorial tumors.

When the data were examined for the age differences, 6.2% of tumors occurred in patients younger than 2 years of age; 9.2% occurred in patients between the ages of 2–5 years; 40% of the tumors occurred in patients 5–10 years of age; and 44.7% in patients 10–15 years of age. Most of brain tumor types occurred in children between 5 to 15 years of age and these account for about 85% of tumors.

In children between 0–2 years of age, 57.5% of tumors were located in the infratentorial region. The breakdown of histological diagnosis was as follows: astrocytoma (23.1%), ependymoma (23.1%), medulloblastoma (15.4%), glioblastoma (7.7%), meningioma (7.7%), hemangioma (5.1%), lymphoma (5.1%), chordoma, craniopharyngioma, and neuroblastoma (2.6% each) (Table 3).

Tumors (59.5%) occurring in patients between the ages of 2–5 years were located in the infratentorial region. The distribution of histological tumor types was as follows; astrocytom (32.8%), ependymoma (25.9%), medulloblastoma (22.4%), glioblastoma, lymphoma, craniopharyngioma, and schwannoma (3.4% each), meningioma, pituitary adenoma, and teratoma (1.7% each) (Table 3).

Tumors (49.0%) occurring in patients between the ages of 5–10 years were located in the infratentorial region. The frequency of histological tumor types was as follows: astrocytom (41.9%), medulloblastoma (19.4%), craniopharyngioma (11.1%), ependymoma (7.9%), meningioma (5.9%), lymphoma (5.1%), glioblastoma (3.2%), hemangioma (2.0%), schwannoma, and ganglioma (1.2% each) (Table 3).

In children between 10–15 years old, 45.3% of the tumors were infratentorial tumors. The frequency of various tumors based on histological diagnosis was as follows: astrocytom (41%), medulloblastoma (16.3%), craniopharyngioma (8.5%), ependymoma (7.4%), lymphoma (6.4%), meningioma (6.0%), glioblastoma (3.9%), schwannoma (3.5%), hemangioma (2.0%), and pituitary adenoma (1.8%) (Table 3).

Comparing the most frequent tumors types by age groups (Table 3), we observed that astrocytoma was the first most common brain tumor in all age groups and

Table 3 Ten most frequent brain tumor types by age group

Age <2		Age 2–5		Age 5–10		Age 10–15	
Brain tumor type	(%)	Brain tumor type	(%)	Brain tumor type	(%)	Brain tumor type	(%)
Astrocytoma	23.1	Astrocytoma	32.8	Astrocytoma	41.9	Astrocytoma	41.0
Ependymoma	23.1	Ependymoma	25.9	Medulloblastoma	19.4	Medulloblastoma	16.3
Medulloblastoma	15.4	Medulloblastoma	22.4	Craniopharyngioma	11.1	Craniopharyngioma	8.5
Glioblastoma	7.7	Glioblastoma	3.4	Ependymoma	7.9	Ependymoma	7.4
Lymphoma	7.7	Meningioma	3.4	Lymphoma	5.9	Meningioma	6.4
Craniopharyngioma	5.1	Hemangioma	3.4	Meningioma	5.1	Lymphoma	6.0
Schwannoma	5.1	Lymphoma	3.4	Glioblastoma	3.2	Glioblastoma	3.9
Meningioma	2.6	Chordoma	1.7	Schwannoma	2.0	Hemangioma	3.5
Pituitary adenoma	2.6	Craniopharyngioma	1.7	Hemangioma	1.2	Schwannoma	1.8
Teratoma	2.6	Neuroblastoma	1.7	Pituitary adenoma	1.2	Ganglioma	1.8
Others	5.0	Others	0.2	Others	1.1	Others	3.4

astrocytoma occurred mostly in children aged 5–15 years (87%). Ependymoma was the second most common brain tumor in children less than 2 years of age and age 2–5 years, and it was the fourth most common brain tumor in children aged 5–10 and 10–15 years. While medulloblastoma ranked the second most common brain tumor in children aged between 5–10 and 10–15 years, it was the third in children less than 5 years. Craniopharyngioma occurred mostly in children aged 5–15 years and it was ranked the third most common brain tumor in age group of less than 2 and 5–10 years.

Discussion

The histopathological data of 619 brain tumors of all the patients less than 15 years was collected and compared with the findings reported from countries of the region and in the West.

The mean age of 619 patients in our study population was 8.8 years. This is comparable to those reported by authors from Seoul, Spain, and Canada [5, 14, 19]. Sex distribution and the discovery of a clear sex predilection of certain tumor types have proved to be statistically significant [13]. An analysis of our total series has resulted in the general conclusion that there is a preponderance of males over females (58.1 to 41.9%), which is comparable to results previously mentioned in the literatures [5, 6, 11, 12, 14, 18, 19]. It was interesting that this general sex preponderance of patients with a given tumor was even more pronounced in a particular tumor type. A significant ($p<0.05$) male predominance was observed in the craniopharyngioma and medulloblastoma with a male/female ratio of 2.1 and 1.9, respectively. The male predominance of craniopharyngiomas was noted within the first two decades of life with a male–female ratio of 1.5 [11, 13].

The results showed that the most common histological diagnosis were astrocytoma, medulloblastoma, ependymoma, and craniopharyngioma, accounted for slightly more than two thirds (76.2%) of all admitted cases with brain tumors. The frequency rate for intracranial tumors in children less than 15 years old observed in this study has similarities to previously reported series of childhood brain tumors in Germany by Kaatsch et al. [10] and Rickert and Paulus [6]. Also, the frequency distribution of children brain tumors were similar to those reported by authors from Korea, Syria, Pakistan, Hungary, and United States [2, 5, 9, 11, 15].

An analysis of our total series has resulted that there is a preponderance of supratentorial tumors over infratentorial tumors. This is comparable to the previously reported series of brain tumors [6, 14] but more than that reported by authors from Syria and Lahore [9, 11]. The frequency distribution of histopathologic tumors between the infratentorial and supratentorial regions were similar to those previously reported [6, 9, 11, 14].

Certain tumor types show a predilection for the certain periods of life [13]. In this study, when the data were examined for age differences, the frequency rates for intracranial tumors in patients younger than 2 and 2–5 years were 6.2 and 9.2%, respectively. This is lower compared to the previously reported by Westernized countries such as Canada [14], that the 11.5% of cases occurred in patients younger than 2 years of age and 20.5% in 2–5 years of age. According to the present study, about 85.0% of cases occurred in patients aged 5–15 years. This rate is higher compared to the above-mentioned study [14].

According to the present study, astrocytomas with the frequency of 39.5% were the first most common brain tumors among patients accounting for more than one third of all brain tumors. It was the first most common brain tumor in all age groups for both sexes in children. The rate is comparable to the Westernized countries such as Canada [14], and discrepancies were found in the percentage of astrocytomas, as pointed out by authors in the region and Westernized countries [9, 11, 16, 19]. The frequency rates in existing reports are about 19–44%. Medulloblastoma usually occurs in children particularly between the ages of 3 and 8 and they make up about 20% of all childhood brain tumors [21]. The tumor is more common in males than in females. In this study, medulloblastoma was the second most common brain tumor among Iranian patients under 15 years of age accounting for 18.4% of all brain tumors in that age group with a male prediction (sex ratio of 1.9). According to the present study, medulloblastoma has an age pattern, i.e., 16.7% in patients less than 5 years and 83.4% in patients of 5 years of age to 15 years. Medulloblastoma ranked the third most common brain tumor among patients under 5 years of age and the second for those older than 5 to 15 years of age. In our study population, the frequency distribution of medulloblastoma was somehow different than those previously reported series of brain tumors in the age by group under study. The frequency rates in existing report ranged 15–53% [9, 11, 16, 19].

Ependymomas represents 5–10% of intracranial neoplasm in children [1]. In this study, ependymoma account for 10.5% of all primary brain tumors, and it was the second most common brain tumor in children less than 5 years of age, and it was the fourth most common brain tumor in children aged 5–15 years old. The relative frequency of ependymoma and ranking is not comparable to the report by Keene et al. [14], but the frequency is comparable relatively to other reports ranged 8–17 [9, 11, 19].

Craniopharyngioma tumors account for about 10% of all pediatric brain tumors; they make up slightly less than 1 in 10 of the brain tumors in children under the age of

15, and most often seen in children between the ages 8–12 years [4, 21]. In this study, craniopharyngioma account for approximately 9.0% of all primary intracranial tumors: 67.3% in males and 32.7% in females mainly in children aged 5–15 years. Craniopharyngioma tumor was ranked the third most common brain tumor in age group of less than 2 and 5–10 years. This relative frequency of craniopharyngioma tumors is relatively comparable to the countries in the West and the region, ranged about 8–14% [11, 14].

The frequency rate of children brain tumors in the country of the region such as Syria, Pakistan and the rate in Westernize countries is somehow different. The distribution of brain tumors were different than those reported by authors from Syria [11], that the most common tumor found in Syrian children population was medulloblastoma (27.5%), followed by astrocytoma 25.8%), then craniopharyngioma (14.1%) [11]. Our data are similar to those reported from the neighboring countries, such as Lahore Pakistan [9], in which astrocytomas (44.8%) were the commonest of all brain tumors followed by medulloblastoma (15.5%) and ependymoma (10.3%). Comparing our figures to those in Spain [19], the predominant histological types were medulloblastoma (33.9%) and astrocytoma (19.6%). Discrepancies were found in percentage of tumors in various studies related to methods of collecting statistical material which differ substantially from one country and or to another and region or race.

Conclusion

The results of our study present an important epidemiological understanding of pediatric patients with brain tumors. Gender plays an important role in the frequency of primary intracranial tumors. Primary brain tumors had preponderance in the male sex. In this study, we emphasized sex difference in some types of tumors. Pediatric brain tumors were more common in the supratentorial region and astrocytomas were the most common tumors. We noted that certain tumor types show a predilection for the certain periods of life. In our children patient population, the frequency and distribution of certain tumors were somehow different than those reported by authors from the Western and Far Eastern countries. Whether these results are unique to Iran, or reflect a regional difference in the disease distribution between the Middle East region and the rest of the world, remain to be determined. The difference may be attributed to both environmental exposures and infectious agents that are suspected of playing a role in the development of childhood brain tumors, and also due to the different methodological approach in collecting data. Epidemiologic research will lead to a more understanding of children brain tumor etiology. Because of the rarity of CBT and their apparent etiologic complexity and diversity, future studies must be large and include patients and collaborations from several disciplines and numerous geographic areas to incorporate extensive genetic exploration and molecular epidemiology. The present data provide a baseline for further studies on the evaluation of brain tumors in Iran and encourage further, wider epidemiological studies of a prospective nature.

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