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Epidemiology of pediatric primary malignant central nervous system tumors in Iran: A 10 year report of National Cancer Registry

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ABSTRACT

Background: CNS tumors are the leading cause of cancer related deaths among children and adolescents. Nonetheless, the incidence of pediatric CNS tumors in developing countries is poorly understood. We aimed to provide epidemiologic features of primary malignant CNS tumors in Iranian children 0–19 years of age using National Cancer Registry (NCR) data bank.
Methods: The data recorded by NCR over a 10 year period (2000–2010) were reviewed.
Results: Of 1948 tumor cases, 93.3% were located in brain, 5.1% were found in the spinal cord & cauda equina, and 1.6% affected cranial nerves and other parts of the nervous system. The overall average annual age specific incidence rate was 1.43 per 100,000. Males were more likely to develop CNS tumors (1.65 per 100,000) compared to females (1.21 per 100,000, $p < 0.01$). Children under 5 years of age had the highest age specific incidence rate (1.86 per 100,000). Astrocytic tumors with the incidence rate of 0.61 per 100,000 were the most frequent specific histology followed by embryonal (0.38 per 100,000), and ependymal tumors (0.10 per 100,000). With regard to the histological distribution of tumors, some unique features including the high proportion of unspecified malignant neoplasms (7.6%) were noted.
Conclusion: The overall incidence rate was markedly lower than western findings. Major differences were also observed in incidence rates of specific histologies. Although the discrepancies may be attributable to diversity in classification schemes and registration practices, a real ethnic and geographical variation in predisposition to development of pediatric CNS cancers is strongly suggested.

1. Introduction

CNS tumors have long been recognized as the most frequent solid tumors of children and adolescents [1]. These tumors are not only the leading cause of cancer related deaths in childhood period, but also leave survivors with a wide range of serious physical and neurological morbidities resulting from the disease itself or the required treatments [2].

Despite all worthwhile efforts to describe the incidence and distribution patterns of pediatric CNS tumors in developing countries [3–8], there is still a serious paucity of nationwide registry-based information in this area. In fact, lack of rigorous disease surveillance systems in developing countries may present some serious challenges to nationwide epidemiologic research. In Iran, the descriptive investigation of the frequency of pediatric CNS tumors has been limited to a few local institution-based studies which were mostly unable to produce incidence rates [9–11].

The National Cancer Registry (NCR) in Iran was established in 1984 when the parliament passed a legislation mandating all health care facilities to report every newly diagnosed case of malignant tumor to the center for disease control at the health ministry according to International Classification of Diseases for Oncology (ICD-O) [12]. The NCR-related offices receive the data from multiple resources including pathology departments, medical documents, imaging centers, and death certificates using a network-based registration software. The raw data is scanned for duplicates and analyzed in order to release annual reports, though with a lag time of 4 years.

To our knowledge, since the establishment of Iran NCR, its data bank has never been used to provide detailed descriptive statistics on primary malignant CNS tumors among children. In this regard,

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we aimed to investigate the data recorded by NCR over a 10 year period between 2000 and 2010 to estimate the incidence and distribution of primary malignant CNS tumors for Iranian pediatric population and compare them to those of other nations.

2. Methods

2.1. Data collection

The NCR raw data recorded during a 10 year period from March 21, 2000, to March 20, 2010, were reviewed for primary malignant CNS tumors in patients under 20 years of age according to ICD-O-3 topographic codes for CNS tumors including C71.0–C71.9 (brain), C70.0–C70.9 (meninges), and C72.0–C72.9 (spinal cord, cauda equina, cranial nerves and undetermined parts of CNS) with the exclusion of metastatic lesions. The search was conducted both manually and in a computerized manner using SPSS 17.0 statistical software. In general, from a total of 464,701 malignant tumors documented during the entire period of study, 2052 cases were found to meet our inclusion criteria.

2.2. Measurements and analysis

The tumors were histologically classified according to WHO 2007 classification of CNS tumors [13]. This classification scheme provides a very elaborate histological stratification of tumors which allows for comparisons in statistics of individual tumor histologies between different reports. Table 1 illustrates major tumor categories that will be discussed here and their corresponding ICD-O 3 morphologic codes. The tumor histologies that could not be incorporated into WHO categories of CNS tumors including those with ICD-O morphologic codes: 8000–8005 (unspecified malignant neoplasms), 9380 (glioma malignant not otherwise specified (NOS)), and 9680 (diffuse large B-cell lymphoma) as well as rare histologies with total counts less than 10, including tumors with ICD-O morphologic codes 9530 (anaplastic meningioma), 9364 (Ewing sarcoma), 9540 (Malignant peripheral nerve sheath tumor (MPNST)), and 9430 (astroblastoma) were classified as the "others" group. It is important to note that pilocytic astrocytoma had been classified as a malignant tumor with behavior code "3" by ICD-O-2 guidelines while, ICD-O3 downgraded the tumor's behavior code to "1" and recommended to treat it as a tumor with uncertain behavior [14]. Although the world's most reputable cancer registries including the Surveillance, Epidemiology, and End Results (SEER) and National Program of Cancer Registries (NPCR) continue to collect pilocytic astrocytomas, NCR in Iran revoked the registration of this tumor since 2005. Therefore, in order to prevent underestimating the frequency of the tumor, all cases of pilocytic astrocytomas were excluded from the current study.

For comparison purposes we chose to provide standard age categories compatible with those used by SEER [15] and Central Brain Tumor Registry of United States (CBTRUS) [16]. Therefore, the age groups were defined as 0–4 years (early childhood), 5–9 years (middle childhood), 10–14 years (late childhood), and 15–19 years (adolescence). In order to assess the anatomical distribution, tumors were disaggregated according to ICD-O topographic codes corresponding to brain (C 71.0–71.9, C70.0 (cerebral meninges)) and spinal cord & cauda equina (C72.0–C72.1, C70.1 (spinal meninges)). Since the process of last year's data was not yet completed by NCR at the time of inquiry, the detailed information regarding the anatomical localization of CNS tumors was not available. Thus, last year's data were excluded from site-specific analysis.

According to the annual reports released by the Cancer Control Office at the Center for Disease Control, the coverage provided by the NCR on the whole population grew significantly from 20% in 2000 to 93% in 2008 [17]. The estimated coverage is calculated through dividing the number of cancer incident cases by the predicted number of malignant cases. The predicted incidence of malignancies for earlier years of registration was 100 per 100,000 based on WHO estimates of cancer incidence in developing countries. However, through further analysis of the NCR data and more recent cohorts in Iran, a higher incidence of 113 per 100,000 has recently been used as the predicted annual rate of malignant cases. In order to ensure the accuracy of the findings, only cases registered during the last 2 years (2008–2010) were considered for rate calculations. Age specific incidence rates were computed and expressed as per 100,000 person-years for total population as well as each individual age group. The reference populations used for denominators were combined estimates of 2008–2009 and 2009–2010 populations according to the 2006–2007 and 2011–2012 census records (available at http://www.amar.org.ir/). All the counts and relative frequencies were determined using SPSS 17.0 statistical software. STATA 12 was also utilized to provide incidence rates with 95% confidence intervals (95% CI).

Table 1
ICD-O-3 morphology coding for major histology groups according to 2007 WHO classification of CNS tumors.

Tumor histologies	ICD-O morphology code
Astrocytic tumors	
Pilocytic astrocytoma	9421/1[a], 9425/3
Diffuse astrocytoma	9400/3, 9410/3,9411/3, 9420/3
Anaplastic astrocytoma	9401/3
Unique astrocytoma variants	9381/3[b], 9424/3[c]
Glioblastoma	9440/3, 9441/3, 9442/3
Oligodendroglial tumors	9450/3, 9451/3
Oligoastrocytic tumors	9382/3
Ependymal tumors	9391/3, 9392/3, 9393/3, 9394/3
Choroid plexus tumors	9390/3
Embryonal tumors	
Medulloblastoma	9470/3, 9471/3, 9474/3
CNS primitive neuroectodermal tumor(PNET)	9473/3
CNS neuroblastoma	9500/3, 9490/3
Other embryonal tumors	9501/3, 9392/3, 9508/3
Lymphomas & hematopoietic neoplasms	9590/3, 9731/3, 9930/3
Germ cell tumors	9064/3,9070/3,9071/3,9100/3, 9080/3,9084/3,9085/3

[a] Pilocytic astrocytoma was classified as a malignant tumor with the behavior code "3" according to ICD-O-2 guidelines. While in ICD-O-3, the tumor is assigned the behavior code "1" and is treated as a tumor with uncertain behavior.
[b] Gliomatosis cerebri.
[c] Pleomorphic xanthoastrocytoma.

3. Results

3.1. Overall findings

A total of 2052 newly diagnosed primary malignant CNS tumors including 104 cases of pilocytic astrocytoma were documented during the 10 year period of data registration. After the exclusion of pilocytic astrocytomas, the remaining 1948 cases were enrolled in the study. Although the children were almost evenly distributed across different age groups, the adolescents (15–19 years) were slightly predominant (29.7%) (Table 2). The overall average annual incidence rate for primary malignant CNS tumors was 1.43 per 100,000 person-years (Table 3). The age specific incidence rates declined with advancing age. Accordingly, children under 5 years of age were more likely (1.86 per 100,000) to develop malignant CNS tumors than their older counterparts. The male to female ratio was 1.3 and males had a significantly higher incidence rate of tumors (1.65 per 100,000) compared to females (1.21 per 100,000, $p < 0.01$) (Table 3).

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