Epidemiology of central nervous system tumors

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Primary central nervous system (CNS) tumors are relatively infrequent in comparison with other malignant tumors. However, CNS tumors are the most frequent solid tumors in childhood and adolescence, accounting for approximately 20% of all malignant diseases in this age (1). There are many differences between childhood and adult CNS tumors according to frequency of some histologic types, biology, treatment, and prognosis.

Epidemiological analysis of the histologic features of CNS tumors in different ages showed that in childhood, medulloblastoma ranks first among all tumors with participation of 24%, but it is not among the most common intracranial neoplasms in adults. Astrocytoma is second in children, whereas it is third in adults. Glioblastoma ranks third in children, but it makes up more than half of the CNS tumors in adults. Meningioma, which ranks second in adults, is relatively rare in children (2).

According to epidemiological literature, incidence of primary CNS tumors in a defined population varies from 4.9 to above 16/100 000 per year, while higher rates are generally found in societies with available and competent medical care, and with good organized cancer registries. Also, incidence rates are influenced by frequency of autopsy and improvement of case ascertainment with brain imaging technology such as CT and NMR (1,3). The American Cancer Society estimates that 16,800 new intracranial tumors were diagnosed in 1999, and the primary cancer of the CNS was the cause of death in 13 100 people in the same year (4). Some investigators report that the incidence of primary CNS tumors, especially in the elderly has substantially increased during the past two decades (3).

Despite variations among the different data sources in reporting and diagnostic practices, a general pattern of age-specific incidence was found: smaller peak in childhood can be seen, followed by a higher peak, reaching a maximum between 50 and 70 years of age, and then decline after those ages (2,4). Some authors stated that this decline is likely to be an artifact due to chance and bias. Elderly patients may be less likely to present themselves to a doctor due to symptoms of CNS tumor, may also be less likely to be referred for CT, or to have a necropsy if they are dead. The diagnostic bias may also be present in the very elderly people (5).

Mortality rates within each European area do not vary much, with the
majority of countries within the range of 4-10/100 000 (6). In the Belgrade population, during the period 1983-1997, age-adjusted mortality rate for primary CNS tumors was 4.8/100 000 (5.6/100 000 for male, and 4/100 000 for female population (7). The shape of age-specific incidence curve resembles of the age-specific mortality curve (8). It means that age-specific mortality rates of CNS tumors also increase exponentially with increasing age up to 65 years, and then decline. Riggs suggests that observed biphasic pattern of age-specific mortality rates can be explained by the existence of a primary CNS tumor-susceptible population subset in which the risk of CNS tumor mortality increases exponentially with age and population subset depletion occurs (8).

The primary CNS tumors occur at almost equal rate in both sexes, except meningiomas, which are more frequent in women (2).

In childhood population, incidence rate of CNS tumors very from 2.5/100 000 to >5/100 000, while mortality rate reaches the value of about 1/100 000 (9).

The etiology of primary CNS tumors remains largely unknown. Numerous epidemiological, genetic and other studies have been carried out to clarify the role of environmental and genetic factors in etiology of CNS tumors. Few definite risk factors have been found for these malignancies.

Ionizing radiation was widely regarded as one of established environmental risk factors for CNS tumors for a long period of time, but more recent studies could not confirm this finding. This is in accordance with the fact that doses of ionizing radiation used in today’s diagnostics are low so that no association with the primary CNS tumors can be observed (10).

With traditional epidemiological research designs, few environmental risk factors for malignant brain tumors have been revealed, and although syndromes exist where CNS tumors occur frequently, these explain a small proportion of the overall incidence. Inherited syndromes, such as neurofibromatosis types I and II, tuberous sclerosis, Gorlin syndrome, Turcot syndrome, and nevoid basal-cell carcinoma syndrome are established as being associated with tumors of the CNS. However, they are present in only a small fraction (~5%) of patients (9).

In a similar way, the search for genetic causes has been thwarted by the rarity of families with multiple affected relatives, inhibiting genetic linkage, sib-pair, or even population-based association studies. In several genetic epidemiologic studies, familial aggregation of CNS tumors was seen. There is an increased risk of cancer in sibs, but the evidence regarding the occurrence of cancer in other relatives is inconsistent.

Molecular genetic studies generally involve searching for candidate proto-oncogenes and tumor suppressor genes by comparing DNA from tumor material with constitutional (germ line) DNA.

Several recent epidemiological studies have investigated relations between CNS tumors and maternal diet. These studies based on hypothesis that transplacental exposure to N-nitroso compounds increases the risk of childhood CNS tumors. Although the evidence is far from being conclusive, they found an increasing risk with increasing frequency of processed meats, particularly for mothers who took no vitamin (10). At the opposite, some recent epidemiological studies provided indication that prenatal vitamin supplementation might be related with reduction of brain tumor risk (11).

Early reports suggest that an association between CNS tumors and residential exposure to electromagnetic fields have not been confirmed. Also, no consistent association between these tumors and inferred parental occupational exposure to electromagnetic fields has been observed (9).

Other suggested risk factors for which the evidence is inconsistent or merits further investigation are previous head injuries, family history of epilepsy, high birth weight, maternal passive smoking and use of antiepileptic drugs and barbiturates during pregnancy, etc (10).

Having in mind all mentioned findings relating to frequency, distribution and etiology of primary CNS tumors, prospective regional studies of incidence patterns and up to date epidemiological appraisal are necessary. Also, there is need for current estimation of geographical and secular variation of occurrence of CNS tumors. Further analytic epidemiological investigations are required to confirm associations suggested in the few previous studies and to identify other currently unknown associations.

REFERENCES