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Epidemiology of central nervous system tumors

Malignant tumors are one of the most frequent death causes in developed countries. Many countries keep cancer registries to obtain an accurate estimate of the epidemiological situation. In Poland these data are collected and statistically worked out by the Polish National Cancer Registry. Since 1998, the European Network of Cancer Registries (ENCR), whose aim is to create data base for monitoring cancer incidence and mortality in the European Union has been in full operation. In 1973 the Surveillance, Epidemiology, and End Results Program (SEER) started to register epidemiological information about cancers in the USA. Besides, there is the Central Brain Tumor Registry of the United States (CBTRUS), which deals with CNS tumors only. Worldwide data concerning cancer diseases are registered by The International Agency for Research on Cancer (IARC). These registries facilitate access to information and comparison of data from different countries.

CNS neoplasms are diagnosed in 9% of cases of malignant tumors in adults, but, in the pediatric population, they are found in about 20% of cases (4). According to the IARC data worldwide incidence of primary CNS malignancies accounts for 3.6/100 th/year in men, and 2.5/100 th/year in women. In developed countries these incidence rates are about twofold higher than in developing countries (9).

According to data from the Oncology Center, 2695 CNS malignancies were registered in Poland in 2002. Males were insignificantly more often diagnosed with malignant CNS tumors (52.5%) than females (47.5%).

INCIDENCE

In 2002 in Poland CNS cancer incidence by sex was estimated at 6.5/100 th/year for men and 4.7/100 th/year for women. In comparison with Western European countries these rates are insignificantly lower. According to the ENCR data for 1998, CNS incidence in the European Union countries was 7.7/100 th/year, the rates were higher for men (8.2/100 th/year) than for women (6.64/100 th/year).

The highest incidence in Europe was noted in Sweden (14.5/100 th/year), Greece (14.27), and the lowest in the Netherlands (5.93), France (6.51), Austria (6.18) and Ireland (6.84). In these countries the incidence among men is higher than among women (M:F ratio 1.4:1) (9).

In the USA the detection of cancers is very high. According to data from the SEER program, CNS malignancies incidence between 1998 and 2002 was 6.4/100 th people/year, and the risk of detection of CNS malignant tumor for the whole population was estimated at 0.58%, (0.68% for males and 0.5% for females) (10). In the same years, based on the CBTRUS data the CNS cancer (malignant and benign) incidence was estimated at 14.1/100 th/year. Malignancies represented more

than half of all CNS tumor cases (malignant and benign cancer incidence for the same period was 7.3/100 th/year and 6.8/100 th/year respectively).

According to the CBTRUS data the overall CNS tumor incidence (malignant and benign) was insignificantly higher for females (14.3/100 th/year), than for males (13.9/100 th/year) (8). Table 1 presents a percentage distribution of CNS malignances in individual age groups in the USA in the 5-year period of 1998–2002. The highest percentage of persons with CNS malignant tumor was found among patients between 65 and 74 years (17.1%). A relatively high percentage of persons with CNS tumor were children and adolescents below 20 years (13.8%). The average age of CNS tumor diagnosis was estimated at 55 years (8).

Table 1. Percentage distribution of CNS malignant tumors in individual age groups in USA in the 5-year period (1998–2002). The data come from CBTRUS

Patient's age at the moment of diagnosing CNS cancer	Percentage of patients with CNS tumor
below 20	13.8
20–35	10.0
35–44	11.7
45–54	14.4
55–64	15.4
65–74	17.1
75–84	14.2
85+	3.6

On the basis of the SEER program data, Legler and all assessed CNS malignancies incidence in different age groups in the two 5-year periods: i.e. 1975–1979 and 1991–1995. No significant increase in incidence rate was found for people aged 15–69 years. However, a substantial increase in CNS malignancies incidence was noted among people over 70 years between 1991–1995, as compared to 1975–1979. The highest, almost threefold increase concerned persons over 85. However, in the population below 15 years of age the mean incidence rate in the period of 1975–1985 remained at the level about 2.4/100 th/year. In the years 1984–1986 the incidence rate jumped to about 3/100 th children /year, to remain in the following years at approximately the same level. This incidence jump was mainly explained by easier access to MRI in the USA at this time and was associated with marked improvement in CNS tumors detection (5).

MORTALITY

In 2002 in Poland 24.4% of deaths were caused by neoplastic diseases, 2.6% of these deaths were caused by CNS tumors (Polish Central Statistical Office data) (11). The mortality from CNS tumors was 5.4/100 th/year for males and 3.7/100 th/year for females. Similar mortality rates were recorded for the United States and European Union populations. Based on data coming from the SEER study the annual CNS malignant tumors mortality for 1998–2002 was estimated at 4.5/100 th/year (5.6/100 th/year for males and 3.7/100 th/year for females). These values have not significantly changed over the last three decades (10).

In Europe CNS tumors mortality rates are comparable to those for Poland and the USA. In 1998 the overall CNS tumors mortality in the EU countries was 5.78/100 th/year (ENCR). However, mortality rates varied considerably in individual European Union countries. The highest mortality rates were noted in Greece (9.97/100 th/year), Luxemburg (9.38) and Belgium (8.36), whereas the lowest were recorded in France (4.97), followed by Portugal (5.04) and Italy (5.07) (9).

PROGNOSTIC FACTORS

Survival prognoses for persons with CNS tumor diagnosed during the last 30 years have greatly improved, but they are still unfavourable. According to the SEER data for the USA a 5-year survival was achieved by 30.8% of patients during the period of 1989–1996 compared to only 22.5% in 1974–1976 (3, 10).

The survival length in persons diagnosed with CNS malignancy depends on the histological type and progression degree of the tumor but also on the patient's age and sex (better prognosis in young adults and females), localization of the tumor, first symptoms and possibility of complete resection of the tumor (6).

The patient's age at the moment of diagnosis is an important prognostic factor. The more advanced the patient's age the worse the prognosis. A 5-year survival in persons below 45 was achieved by 58.7% of patients, while among those aged 45–54 years, 55–64, 65–74, 75 and older – by 23%, 10.2%, 6.5%, 3.6%, respectively (SEER, USA 1988-1996). In children population and persons below 19 years, the 5-year survival is significantly higher, and it is estimated at 65%. Sex does not significantly affect the prognosis. The prognosis for females is slightly more favourable (10).

The histological type of CNS tumor is another significant prognostic factor. The most common type of CNS tumors are gliomas – they make up 42% of all tumors and 77% of malignancies (8). Among gliomas the most frequent histological type is glioblastoma, which is followed by astrocytomas. The prognosis in the case of glioblastoma is poor. Only 10% of the patients survive 2 years and a longtime survival is achieved by less than 5% of treated patients. Moreover, 95% of untreated patients die within 3 months of the diagnosis (4).

Astrocytomas are not a uniform group as regards the prognosis. Anaplastic and diffuse astrocytomas prognosticate poorly and significant percentage undergoes transformation to glioblastoma. The patients with anaplastic astrocytoma after surgical treatment combined with radiotherapy prognosticate better – a 5-year survival is achieved by 50% of patients, in comparison to 21% of those after surgical treatment only. However, astrocytomas of limited growth secure a longer survival (4).

Meningiomas are relatively common CNS neoplasms – they are diagnosed in about 30% of patients with primary CNS tumors, and in most cases they are benign. The prognosis for patients from younger age groups, in whom meningiomas tend to grow faster, is poor unless surgical treatment is undertaken on time (1).

EPIDEMIOLOGY OF THE MOST FREQUENT TYPES OF CNS TUMORS

Gliomas are stated in 42% of primary CNS tumors, 29% of which derive from cerebrospinal meninges. Basing on the CBTRUS registry it was estimated, that during the 5-year period between 1997 and 2001 glioblastoma was the most frequent glioma type, according for 50.5% of gliomas, apart from astrocytomas (24.9%), among which the most common was anaplastic astrocytoma. Thus about 75% of all gliomas are glioblastomas and astrocytomas (8).

Glioblastoma is the most malignant glioma of astrocytic origin, and most frequently noted primary CNS neoplasm (21%) (8). This type of tumor occurs threefold more frequently in males than in females and can appear at any age with its incidence peak following between 45–65 years. Its typical localization is the white matter of the cerebral hemispheres, most frequently the frontal lobes. It is rarely localized in the posterior cranial cavity. In children it usually occurs in the brain stem. An early diagnosis and properly performed surgery gives a chance for survival at least 12 months after the operation.

Astrocytomas constitute about 10% of CNS tumors (8). The incidence peak occurs in the fifth decade of life, males are affected almost twofold more frequently than females (M:F 1.8:1). Most frequently astrocytomas are localized in the frontal and temporal lobes of the cerebral hemispheres.

Meningiomas are the most common benign intracranial neoplasms. Malignancies occur in about 7% of cases. Meningiomas appear usually in middle and older age groups. The older the age group the higher the tumor incidence. Females are diagnosed twofold more frequently. Children are rarely diagnosed with meningiomas. The prognosis in most cases is favourable.

Among other primary CNS tumors neurinomas (7.9%), pituitary tumors (5.9%), lymphomas (3.3%) and craniopharyngiomas (0.7%) are registered relatively frequently (CBTRUS 1997–2001) (8).

Metastases represent about 40% of all CNS neoplasms. The most common sources of metastases in CNS in adults are: lung cancer, breast cancer, digestive system cancer, urinary system cancer and melanoma. In younger age groups metastases to CNS most frequently originate from sarcomas and germinal tumors. Eighty percent of brain metastases are localized subtentorially, 15% in the cerebellum, 5% in the brain stem. Typically the metastases are found in the border zone of the grey and white matter and in terminal vascularisation regions. Digestive system neoplasms and minor pelvis tumors often metastasize to cranial posterior cavity. Frontal, temporal lobes and frontal-temporal-parietal and temporal-parietal-occipital regions are most frequently affected by metastatic tumors.

About 35% of patients suffering from organ tumors develop metastases to the CNS. About 20–40% of persons with malignancies die because of intracranial metastases. Untreated patients die within 4 weeks of the diagnosis. The recommended treatment in most cases is radiotherapy, which prolongs the patient's life by about 3–6 months (2, 7).

RISK FACTORS

Nowadays there are three proven risk factors for CNS tumors: genetic predisposition, ionizing radiation and sex. Brain tumors coexist as one of the components in many congenital genetic syndromes. They include e.g. type 1 and 2 of neurofibromatosis, Turcot syndrome, Hippel-Landau syndrome, Gardner syndrome, tuberus sclerosis and others. A population-based study performed in Sweden showed a significantly increased risk for astrocytoma incidence among first-grade relatives of patients with this type of tumor.

The second well known risk factor for CNS tumors is exposure to high, curative doses of ionizing radiation, which were earlier used in the treatment of benign tumors, but are currently confined to neoplastic tumors radiotherapy only. Besides, sex can determine an increased risk for developing certain types of neoplasms. Meningioma, acoustic schwannoma, pituitary adenoma are more frequently observed in females while medulloblastoma, high-grade gliomas show an increased incidence in males (2, 3).

Other potential risk factors have also been considered in the literature, but their influence on CNS tumors incidence has not been established conclusively. They include: occupational exposure involving electromagnetic radiation and action of toxic substances such as vinyl chloride, organic solvents, pesticides, nitro compounds, cadmium, tin and lead. Also a diet rich in nitroso compounds, some medications, coexisting diseases (epilepsy, multiple sclerosis, tuberculosis, head injuries), viruses (SV40, JC, BU, HIV) and other infectious agents (e.g. *Toxoplasma gondii*), blood group A are considered to be potential risk factors for CNS tumors. Up to now the influence of these factors on the increase of CNS tumor incidence has not been fully documented (1, 3).

CONCLUSIONS

1. CNS malignances represent about 9% of all malignant tumors in adults, and about 20% in children.

2. The highest percentage of CNS malignancies is observed in the age group of 65–74 years.

3. The highest CNS tumors incidence is detected in males.

4. The 5-year survival in persons with CNS malignancies deteriorates with age. The highest percentage of 5-year survivals is found in children and adolescents below 19 years of age.

5. Prognosis in persons with CNS tumors depends on the histological type of the tumor, its localization, the patient's sex and age at the moment of diagnosis.

6. The established risk factors for CNS tumors are: genetic predisposition, ionizing radiation exposure and sex.

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SUMMARY

The aim of this paper is a presentation of the current epidemiological situation concerning cancer diseases of the CNS in Poland, Europe and the United States. In the last years the fast development of diagnostic methods and increased access to CT and MRI has significantly improved the detection of CNS neoplasms. The establishment of cancer registries has made it possible to extend and systematize knowledge in this field. The epidemiological data included in the paper concerning incidence, mortality, surveillance and prognostic and risk factors come from international and domestic cancer registries.

Epidemiologia nowotworów ośrodkowego układu nerwowego

Celem pracy jest przedstawienie sytuacji epidemiologicznej dotyczącej chorób nowotworowych ośrodkowego układu nerwowego w Polsce, Europie i Stanach Zjednoczonych. W ostatnich latach, dzięki szybkiemu rozwojowi metod diagnostycznych i upowszechnieniu się dostępu do CT i MRI, znacznie poprawiła się wykrywalność nowotworów ośrodkowego układu nerwowego, a wprowadzenie rejestrów chorób nowotworowych pozwoliło na poszerzenie i usystematyzowanie wiedzy w tym zakresie. Zawarte w pracy dane epidemiologiczne na temat zapadalności, umieralności, przeżywalności oraz czynników rokowniczych i czynników ryzyka pochodzą z międzynarodowych i krajowych rejestrów chorób nowotworowych.