RESEARCH ARTICLE

One-year Survival Rate of Patients with Primary Malignant Central Nervous System Tumors after Surgery in Kazakhstan

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Abstract

This study was conducted to evaluate the one-year survival rate of patients with primary malignant central nervous system (CNS) tumors after surgical treatment in Kazakhstan. Retrospective data of patients undergoing operations in the Department of Central Nervous System Pathology in the JSC National Centre for Neurosurgery in the period from 2009 to 2011 were used as the research material. Kaplan-Meier survival analysis was performed with the following information: gender, date of birth, place of residence, diagnosis according to ICD-10, the date of the operation, the morphological type of tumor, clinical stage, state at the end of the first year of observation, and the date of death. The study was approved by the ethical committee of the JSC National Centre for Neurosurgery. The overall one-year overall survival rate (n=152) was 56.5% (95% confidence interval (CI): 50.2-62.7), and 79.5% (95% CI 72.2-86.8) and 33.1% (95% CI: 21.0-42.3) for Grades I-II (n=76) and Grades III-IV (n=76), respectively. Significant prognostic factors which affected the survival rate were age and higher tumor grade (Grades III-IV), corresponding with results described elsewhere in the world.

Keywords: Primary malignant CNS tumors - grades I-IV - Kaplan-Meier survival rate - Kazakhstan

Asian Pac J Cancer Prev, **15 (16)**, 6973-6976

Introduction

According to the International Agency for Research on Cancer GLOBOCAN, the incidence rate of brain and central nervous system tumors worldwide in 2012 was equal to 256,213 or 3.4% per 100,000. The mortality rate was 189,394 or 2.5% per 100,000 (Ferlay et al., 2014).According to the Central Brain Tumor Registry of the United States (CBTRUS), overall incidence rate of primary brain and central nervous system tumors during 2005-2009 was 20.6 per 100,000, in which 7.3 for malignant tumors and 13.3 for non-malignant tumors. Incidence rate by gender was 22.3 in women and 18.8 in men per 100,000 (Dolecek et al., 2012). Although, primary malignant brain tumors accounted for only 2% of all cancers and were one-fifth as common as breast cancer or lung cancer, they contributed to significant morbidity, and their prognosis was very poor.

Thus, the 5-year survival rate for primary malignant brain tumors in 1999-2005 was 36% and was the sixth or the lowest among all types of cancer as pancreas, liver, esophagus, lung and stomach (American Cancer Society, 2010). The 5-year relative survival rates varied considerably according to the histological subtypes, for example 79.1% for oligodendrogliomas, 27.4% for anaplastic astrocytomas and 4.5% for glioblastomas (CBTRUS 2010). Age-specific mortality rates for brain tumors demonstrated gradual increase with each decade of age up to 55 years, after which there was a sharp increase in rates (Daroff et al., 2012). According to the SEER 2010 (Survival, Epidemiology, and End Results), primary malignant tumors of CNS (PMT CNS) incidence rate was 7.5 per 100,000 in men and 5.2 per 100,000 in women (Altekruse et al., 2010).

Histologically, according to the 2007 WHO Classification, there were many types for primary CNS tumors that significantly differed from each other in clinical behavior and prognosis, wherein each onconosologic unit was assigned a four-digit ICD/0 and gradation degree of malignancy (Louis et al., 2007; Batoroev, 2009). This gradation has 4 grades (Grade I-IV). It is based on histological criteria, such as cell density, infiltrative growth, nuclear polymorphism, mitosis, vascular proliferation and necrosis. Grade I refers to the local tumors with low proliferative capacity, they rarely transform to malignancies, and usually require only surgical treatment. In Grade II, tumors have low proliferative potential, but they are usually infiltrative and tend to recur. With time they tend to transform in a more malignant grade. Grade III has histological signs of malignancy, such as nuclear atypia and high proliferative activity. These injuries cannot be cured only by surgery

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and require radiotherapy and/or chemotherapy. Tumors of Grade IV are definitely malignant tumors with aggressive preoperative and postoperative course.

Histologically, these lesions show severe nuclear atypia, high mitotic activity, vascular proliferation and a tendency to necrosis (Huttner, 2012). The most common brain tumors are neuroepithelial tumors, and especially these cases have the most unfavorable prognosis of survival. For example, according to the population-based cancer registries of developed countries, glioblastomas which constituting up to 40% PMT CNS (Ohgaki et al., 2004; Stupp et al., 2009) have less than 10% of 5-year survival rate (Deorah et al., 2006; Sant et al., 2009). Other morphological species have slightly higher survival rate, however, usually not more than half patients live over 5 years (Ohgaki et al., 2005; Mehrazin et al., 2006; Lee et al., 2010; Jazayeri et al., 2013).

Important predictors of survival rate for PMT CNS are tumor size, age and condition of the patient, his/her socio-economic status, and the amount of surgical resection and, in cases of high malignancy of tumors, the use of radio- and chemotherapy (Sant et al., 2009; Mishra et al., 2012). According to the CBTRUS 2010, young age and a lower Grade are the most favorable prognostic factors for survival (CBTRUS 2010).

Traditional source of statistics concerning the PMT CNS in different countries are based on cancer registries or special programs. Obtained data help analyze the epidemiological situation and assess the incidence, prevalence, survival, mortality of the entire population of patients in a particular territory. Cancer registries in some countries exist for several decades, thus you can trace each patient from the onset of the disease and the method of the treatment until his/her death (Tseng et al., 2006; Altekruse et al., 2010; Baidi et al., 2011; Cancer Registry of Norway 2012). National Cancer Institute (NCI) of the United States established in 1937 is the principal U.S. federal government agency for Research on Cancer. Central Brain Tumor Registry of the United States (CBTRUS 2010) is a nonprofit corporation established in 1992 and it provides population data on the prevalence of primary malignant and non-malignant central nervous system tumors in the United States. Purpose of the CBTRUS is an accurate description of the incidence and survival rates, estimation of diagnostics and treatment, facilitation of etiologic studies, creation of awareness on the disease, and ultimately, prevention of all brain tumors (CBTRUS 2012).

National Cancer Registry in Iran was founded in 1984 when Parliament passed a law obliged all medical institutions to report each new case of cancer to the Disease Control and Prevention Center of the Ministry of Health. Offices of the National Cancer Registry get data from multiple resources, including the departments of pathologies, medical records, visual diagnosis centers, death certificates using network software (Beygi et al., 2013). In Russia, the registration of patients with malignant tumors was introduced in 1939, and Cancer Registry was created in 1996 under the order of the Ministry of Health "On the establishment of the State Cancer Registry" №420 dated 23.12.1996 (The Ministry of Health of the Russian Federation 1996; Vaktskjold et al., 2005).

As for Kazakhstan, the studies on the survival of patients with PMT CNS based on data from cancer registries have not been conducted (Igissinov et al., 2013). This is primarily due to the fact that the registry is in its infancy. In this regard, the actual problem is the creation and functioning of neuro-oncologic registry in our country. This would allow for epidemiological, medical and statistical population-based calculations in order to improve the medical care and enhance the national health system in Kazakhstan in general. This review focuses on some of the major groups of brain tumors, which can be considered as a growing problem of modern oncology.

The goal of the present research was to conduct a retrospective analysis of one-year survival rate of operated patients with PMT CNS in the Department of CNS pathology of JSC "National Centre for Neurosurgery" in 2009-2011.

Materials and Methods

Retrospective data on all operated patients with PMT CNS (C70-C72 in ICD 10) in 2009-2011 was used as research material. Materials, methods and design of the study were approved by the Ethics Committee of "National Centre for Neurosurgery" JSC which works in concordance with the Ethical Principles of the World Medical Association Declaration of Helsinki (WMA Declaration of Helsinki, 2014). JSC "National Centre for Neurosurgery" was established on July 1, 2008 and it is the largest medical, diagnostic and research institution in the Republic of Kazakhstan in the field of neurosurgery. The Centre has clinical and paraclinic units, a training center, a research library, modern equipment and 160 beds located in 7 clinical departments.

We selected 152 patients with newly diagnosed PMT CNS and operated in the Department of CNS pathology. All diagnoses of patients were morphologically verified. In the study the following information was taken into account: gender, date of birth, place of residence, diagnosis according to ICD-10, the date of the operation, the morphological type of tumor, clinical stage, state at the end of the first year of observation, and the date of death.

Further, all the studied patients were divided into 2 groups according to the morphological grading of malignancy in accordance with the classification of ICD-10 (2007). The first group consisted of patients with a diagnosis (or morphological differentiation degree) of Grades I-II in the amount of 76 people and the second group was consisted of 76 patients diagnosed with Grades III-IV. Tumor-specific survival rate for all patients and separate groups of patients was calculated by making a life tables in accordance with the Kaplan-Meier method (Glanz, 1999). Overall survival for entire study group, survival in each group in accordance with the degree of the gradation, the average age of entire study group and each of the groups, the average age of men and women in each group were determined. Statistical software such as Microsoft Office: Word, Excel, EpiInfo 7 were used in the present study for data analysis.

Results

Total number of patients was 152, of which 77 were men and 75 women. Among them: died before the year were 64 people (42%), dropped out of follow-up during the year 12 people (8%), and lived more than a year were 76 people (50%). The average age of the entire study group of Grade I-IV was 41.3±1.1 years, the average age of men was 39.1±2.4 years (95% CI: 34.4-43.9) and women was 43.6±1.6 years (95% CI: 40.5-46.8). The average age in the group of Grade I-II was 37.4±1.6 years, and the group of Grade III-IV it was 45.2±1.5 years. The average age of women in the group of Grade I-II was 41.2±2.6 years, in the group of Grade III-IV it was 45.6±2.0 years. The average age of men in the group of Grade I-II was 34.6±1.9 years, and in the group of Grade III-IV it was 45.2±2.3 years. It was determined that the average age in the group Grade I-II was significantly lower than in the group of Grade III-IV. Also average age of men was statistically significantly lower in Grade I-II, than in the group of Grade III-IV.

One-year survival rates for the analyzed period were as follows: for all patients with Grade I-IV – 56.5% (95% CI: 50.2-62.7), in the group of Grade I-II – 79.5% (95% CI: 72.2-86.8) and in the group of Grade III-IV – 33.1% (95% CI: 21.0-42.3). Table 1 shows the distribution of all the patients studied by the histology of tumors. The Table demonstrates that according to the histological type of tumor, fibrillar and protoplasmic astrocytoma prevailed in the group of Grade I-II – 48,4% (n=37), in group of Grade III-IV prevailed anaplastic astrocytoma – 39.3% (n=30) and glioblastoma – 14,41% (n=11).

Table 1. Distribution of Patients by Histology of Tumors

Histology	Code*	Grade	N	%
Group of Grades 1-2				
Pylocytic astrocytoma	9421/1	I	5	6.55
Pleomorphic xanthoastrocy	9424/3	I	3	3.93
Protoplasmatic astrocytoma	9410/3	II	6	7.86
Fibrillar and protoplasmatic astrocytoma	9420/3	II	37	48.4
Subependymal astrocytoma	9384/3	I	3	3.93
Mast cell astrocytoma	9411/3	II	4	5.24
Oligoastrocytoma	9382/3	II	1	1.31
Ganglioglioma	9505/1	I	3	3.93
Gangliocytoma	9492/0	I	2	2.62
Subependymoma	9381/1	I	1	1.31
Clear cell ependymoma	9391/3	II	3	3.93
Oligodendroglioma	9450/3	II	5	6.55
Neurocytoma	9506/1	II	1	1.31
Hemangioblastoma	9661/1	I	2	2.62
Group of Grades 3-4				
Anaplastic astrocytoma	9401/3	III	30	39.3
Anaplastic oligoastrocytoma	9382/3	III	4	5.24
Anaplastic ependymoma	9392/3	III	5	6.55
Anaplastic oligodendroglioma	9451/3	III	6	7.86
Anaplastic ganglioglioma	9505/3	III	6	7.86
Angiosarcoma	9120/3	III	1	1.31
Choroid plexus carcinoma	9390/3	III	1	1.31
Giant cell glioblastoma	9441/3	IV	5	6.55
Glioblastoma	9440/3	IV	11	14.4
Gliosarcoma	9442/3	IV	2	2.62
Desmoplastic medulloblastoma	9471/3	IV	5	6.55

* in accordance with the WHO classification

During the analyzed period only 12 patients from the entire study group took special treatments such as outpatient radio- and chemotherapy after surgical removal of a tumor (n=152). Among them 4 patients took radiotherapy, chemotherapy, and 4 patients, the combination of chemotherapy and radiotherapy. This was equal to 7.8% of the total number of patients. Therefore, more detailed study of the effect of these treatments on the prognosis of the survival rate of PMT CNS was not possible (Stewart et al., 2002; Stupp et al., 2005; 2009). We hope that in further investigations we will have more detailed patient data concerning the characteristics of their diagnosis and treatment, including the amount of surgery, specific techniques of received radio- and chemotherapy. In this regard, it is currently important to create neuro-oncologic registry in the Republic of Kazakhstan.

Discussion

Due to the high degree of grading of this nosology in histological aspects, localizations and nosology under ICD-10 C70-72, a number of diseases in our study had insufficient amount of cases for adequate statistical analysis. Along with this, it was determined that the average age in the group of Grade I-II significantly lower than in the group of Grade III-IV. Also average age of men was statistically lower in the group of Grade I-II, than in the group of Grade III-IV. These data confirm that the more mature age is one of the risk factors for malignant tumors of the CNS. One-year survival rate for the analyzed period indicates better survival in the group with a lower degree of malignancy Grade I-II – 79.5% than in the Group of Grade III-IV – 33.1%. It was statistically significant and coincided with the data of world literature. It gave evidence for the better survival in the group with a low degree of malignancy Grade I-II – 79.5% in comparison with Grade III-IV where it was equal to 33.1%. It was statistically significant and coincided with the world literature data (Ohgaki et al., 2005; Compostella et al., 2007; Smoll et al., 2012).

The data for age distribution confirm that the more mature age is one of the risk factors for malignant tumors of the CNS (Gorlia et al., 2008; American Cancer Society 2010; CBTRUS 2010; Altekruse et al., 2010; Igissinov et al., 2013; Ferlay et al., 2014).

The significant disadvantage of this study was the small number of observations for the analyzed period. Because it was very difficult to trace our patients in the outpatient period due to several reasons, the main of which was changing of address by the patient with leaving for the unknown place. Therefore, the establishment and proper functioning of the national neuro-oncologic registry is a topical issue, which would allow for the monitoring of all our patients, regardless of what kind of treatment he received and where. It will also give an opportunity to specify the tendency of tumor diseases over time associated with the territorial features, to identify specific tumor diseases in different populations and to determine

high-risk groups. It is necessary to take innovative steps for planning and evaluation of cancer control programs, set priorities for the allocation of health care resources, and forward subjects of clinical, epidemiological and medical research services in the required directions.

In conclusion, we can say that our study group with PMT CNS in JSC "National Centre for Neurosurgery" has no significant differences in survival rate compared with that in developed countries. Significant predictors of survival were age and tumor grade.

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