Meningiomas Related to the Chernobyl Irradiation Disaster in North-Eastern Romania Between 1990 and 2015

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Even if meningiomas are the most common radio-induced tumors that occur in the adult population, the epidemiology of these types of tumors after Chernobyl nuclear accident, is still unclear. This paper aims to determine the tumoral behavior of intracranial meningiomas in North-Eastern Romania, affected by the radioactive cloud from Chernobyl nuclear accident , over a period of 25 years, namely between 1990 and 2015. Our research consists of an analytical, observational, cohort-based and retrospective study, conducted in Prof. Dr. N. Oblu Clinical Emergency Hospital of Iasi, Romania, on a group of 1287 patients diagnosed with intracranial meningiomas and operated between 1990 and 2015. In these period there was an increased number of intracranial meningiomas, with first peak between 1993-1996 and the second peak between 2007-2015, corresponding to 7-10 years and 21-30 years, after the Chernobyl accident. Regarding the annual frequency of histopathologic grading, for grade I meningiomas there were no trend or cyclicity of the cases diagnosed each year, but for grade II and III meningiomas there were an ascending trend in the period 1996-2000, that corresponds to the 10-14 years from the Chernobyl accident.

Keywords: meningiomas, atypical meningioma, Chernobyl, radio-induced meningiomas

More than 30 years have passed since the Chernobyl nuclear accident, and the literature on the consequences of the catastrophe, which includes more than 30.000 publications, most of them in Slavic languages [1], has not yet fully understood the magnitude of the consequences. As for the incidence of brain tumors, especially intracranial meningiomas after the disaster, it is still unclear.

Following the explosion of the fourth reactor of the Chernobyl nuclear power plant on April 26, 1986, the radioactive cloud covered the entire Northern Hemisphere, and the emissions exceeded 100 times the radioactive contamination of the Hiroshima and Nagasaki bombs [2]. Radioactive contamination from Chernobyl has spread over 40% of Europe (France, Italy, Germany, Greece, Austria, Switzerland, Slovenia, Scandinavia, Iceland) and in Asia (Turkey, Georgia, Armenia, China), North Africa and North America [3]. As far as Romania is concerned, Chernobyl radiation maps have shown that all of Romania was affected by the radioactive cloud, with the highest concentrations in the eastern part of the country and in the southern area[4].

At different time periods, the greatest sources of radiation dose were intake of short-lived radioactive iodines (^{131}I), external exposure from radionuclides particularly ruthenium (^{103}Ru, ^{106}Ru), lanthanum (^{140}La), cerium (^{141}Ce, ^{144}Ce), zirconium (^{95}Zr), niobium (^{95}Nb), tellurium (^{132}Te), barium (^{140}Ba) and ingestion of radioactive caesiums (^{141}Cs, ^{144}Cs).

Nevertheless, the most significant radioactive substances in the emissions were iodine, strontium, caesium and plutonium, each with different half-lives and with its own set of problems [5].

Meningioma is the most common radio-induced tumor that occurs in the adult population, literature describing over 150 individuals with radio-induced meningiomas [6]. Several hypotheses have suggested the role of high doses of radiation in the development of meningiomas, a study in 1999 reporting an increased incidence of meningiomas in survivors of the Hiroshima atomic bombing, even finding a significant correlation between tumor incidence and the dose of radiation, and with a higher incidence of meningiomas in hypocenter areas [7].

This paper aims to determine the tumoral behavior of intracranial meningiomas in North-Eastern Romania, affected by the radioactive cloud, over a period of 25 years, namely between 1990 and 2015.

Experimental part

Material and methods

Our research consists of an analytical, observational, cohort-based and retrospective study, conducted in Prof. Dr. N. Oblu Clinical Emergency Hospital of Iasi, Romania on a group of 1287 patients diagnosed with intracranial meningioma and operated, between 1990 and 2015. Inclusion criteria were: grade I, II and III intracranial meningiomas, and exclusion criteria were: age under 18

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years old and association of meningiomas with genetic syndromes (e.g. neurofibromatosis).

Results and discussions

1287 patients with meningiomas underwent surgery at Prof. Dr. N. Oblu Clinical Emergency Hospital of Iasi, 64.65% (832 cases) of whom were female and 35.35% (455 cases) were male. As concerns patient distribution on 10-year age groups, meningiomas are predominant in the 50-59 years age groups (30.30% of all patients), immediately followed by the 60-69 years age group (28.36% of all patients) (fig. 1).

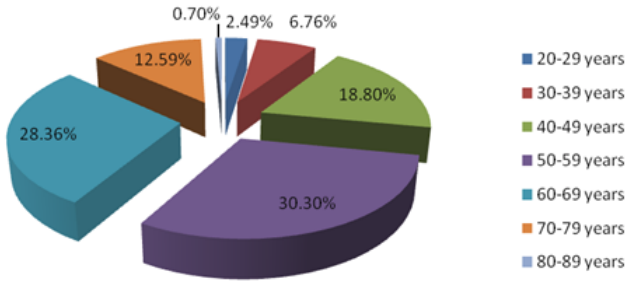

Fig. 1. Distribution of Cases of meningioma on age groups (1990-2015)

Of all 1287 meningiomas, 79.80% (1027 cases) were grade I meningiomas and 20.20% (260 cases) were grade II and III meningiomas. In each age group, there are more patients diagnosed with grade I tumors than patients with grade II and III tumors. The only exception is the 80-89 years age group, where 44.44% of the patients were diagnosed with grade I meningioma and 55.56% with grade II and III (fig. 2). 51.20% of all 1287 cases were diagnosed during the first 12 years of 1995-2006, and the remaining 48.74 % were diagnosed and operated during the following 9 years.

Unfortunately, very few studies have been conducted on the correlation between radiation from Chernobyl and the occurrence of brain tumors. However, the link between ionizing radiation and cancer is not new, and the carcinogenic potential of ionizing radiation was observed in early X-ray workers [8], in patients with high-dose irradiation used in the treatment of other brain tumors or cancers and in studies on animal models [9-12], but also in the survivors of the Hiroshima [7] and Nagasaki [13] attacks, who exhibited an increased risk of meningioma. Thus, thorough long-term studies on the atomic bomb survivors in Japan were the first to make a major contribution to the estimation of the radiation dose and the risk of developing brain tumors [7,13-15].

Seyama *et al.*(1981) reported a five-fold increase in brain tumor incidence among the male atomic survivors of Hiroshima and Nagasaki, exposed to radiation levels above 1 Gy between 1961 and 1975 [16].

The high incidence of nervous system tumors was noticed in childhood cancer patients who received extremely high-dose cranial radiotherapy, most frequently 10 Gy [17-20], and further literature studies reported a significant dose-response relationship between the occurrence of brain tumors and external radiation receiving for different diseases [17,21-23].

Regarding the influence of radiation from the Chernobyl accident on the development of brain tumors, further studies have shown a significant correlation. Thus, Orlov *et al.*(2001,2006) [24,25] proved that between 1987 and 2004, in Ukraine, the incidence of Central Nervous System (CNS) tumors in children up to 3 years of age doubled, and in infants increased by 7.5 times [24,25]. Also, a study conducted by the Ukrainian Institute of Neurosurgery in Kiev showed that the number of children with brain tumors increased by 63.7% between 1987 and 1991 compared to the period before Chernobyl, i.e. 1981-1985[26-28].

Regarding brain damage *in utero* after Chernobyl accident, there is a huge amount of new evidence for brain effects following exposure of ionizing radiation and for radiation-induced cellular and molecular basis: changes in the gene expression profile [29,30], neurosignaling alterations, neuroinflammatory response, apoptotic cell death, cell death and injury mediated by secondary damage [31].

Another study conducted on a cohort of Latvian and Estonian liquidators (5.546 and 4.786 men, respectively), followed from 1986-1998, showed an increase in the incidence of brain cancers [32] and a report on the North-Eastern population of Romania showed the increase in the incidence of oligoastrocytoma cases after the accident [33].

Between 1990 and 2015, there was an increase in the number of intracranial meningiomas in the periods 1993-1996 and 2007-2015, i.e. 7-10 years and 21-30 years after the accident, respectively (fig. 3).

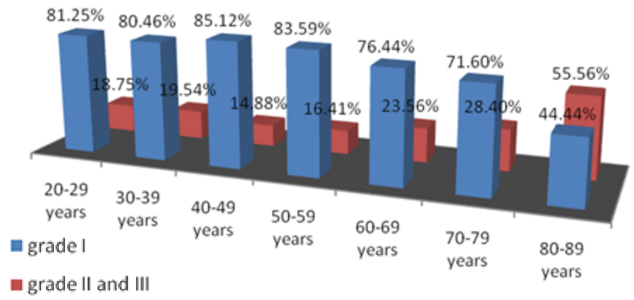

Fig. 2. Distribution of Cases by the degree of malignancy, according to Age group (1990-2015)

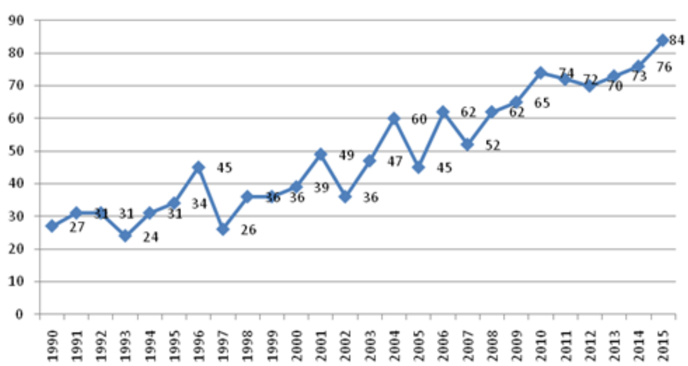

Fig. 3. Evolution of the annual frequency of the case reported between 1995 and 2015

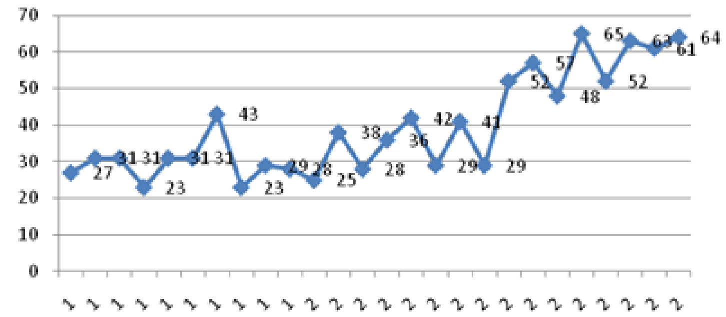

Fig. 4
Evolution of the annual frenquency of grade I Meningiomas

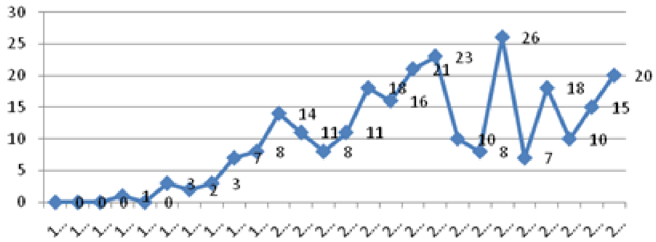

Fig. 5
Evolution of the annual frequency of grade II and III meningiomas

Regarding the latency period between the initial exposure to radiation and the occurrence of the tumor, the data collected from the victims of the atomic bombings of Hiroshima and Nagasaki proved that radiation-induced malignancies become clinically apparent: within 5 years for leukemia and various blood cancers, within 10 years for thyroid cancer, in 20 years for breast and lung cancers and, in 30 years in skin, stomach and rectal cancer [34]. Data obtained from the regions near Cernobyl showed an increase of the incidence of the thyroid cancer, but no increased risk of other types of malignancy: leukaemia, Hodgkin's and non Hodgkin's lymphoma [35,36].

Surprisingly, very few cutaneous malignancies have been detected so far in Cernobyl areas in the individuals that received large radiation exposures and that developed keratoses. However, two patients first presented in 1999 with basal cell carcinomas on the nape of the neck and the right lower eyelid, areas that received lower exposures [37] also, there were a lot of cases of dry eye syndrome and radiation cataracte [37,38]. All patients with such eye diseases need cataract and eyelid surgery to improve visual acuity and quality of life [39-41]. However the largest public health problem caused by the accident was the mental health impact [38].

In our study, time series chart (1995-2015) shows the variation of the number of patients diagnosed and treated each year, with a relatively ascending trend after 2008 (fig. 3). As the Chernobyl fallout is more recent (1986), it did not allow the determination of this latency period so well, the different views in literature being sometimes contradictory. Thus, with regard to the latency period for brain tumors, some studies have found a latency period of 10 years [42], others argued that solid tumors occur only decades after the incident [43], while studies have even found an average period of 20 years [44,45].

As for the demographic distribution of meningiomas in our study, they predominate in women (64.65%) compared to men (35.35%), and they occur especially in the 50-59 age group (fig. 1), in line with the literature data [46].

A recent review conducted on all the radiation-induced meningiomas between 1953 and 2015 identified 251 cases of radiation-induced meningiomas of whom 109 were men, 133 women and 9 unknown, the average irradiation dose delivered to primary lesion being 38.8 +/- 16.8 Gy. Secondary meningiomas were located in the calvaria, skull base and intraventricular region. Secondary meningiomas were classified in grade I (140), grade II(55) and grade III(10), and the radiation doses delivered to the primary lesion were 39.2, 37.3 and 43.0 Gy for grade I, II and III meningiomas [47].

Regarding the correlations between the degree of irradiation and the histopathological degree of the meningiomas, the views in literature are sometimes contradictory. Thus, a 1958-1995 study among 80.160 atomic bomb survivors from Hiroshima and Nagasaki proved that among 467 primary nervous system tumors, the most common tumors were meningiomas (88 tumors), and among them, 78% (69 cases) were largely calvarial, of which only 3 malignant meningiomas [48], while Shoshan et al.(2000), Soffer et al. (1983), Rubinstein et al. (1984) reported that radiation-induced meningiomas are more frequently atypical or anaplastic and have a higher recurrence rate [49-51].

Regarding the findings of our study, the time series chart (1995-2015) for grade I meningiomas indicates the variation in the number of patients, but it does not show a trend or cyclicity of the cases diagnosed each year. In contrast, for grade II and III meningiomas, the chart shows their relative absence until 1995, with an ascending trend in the period 1996-2000 (10-14 years after the accident), followed by the variation of these cases after 2000, with irregular ups and downs in the number of diagnosed patients (figs.4 and 5).

Conclusions

Between 1990-2015 there were an increase in the number of intracranial meningiomas, with first peak in the period 1993-1996 and the second peak between 2007-2015 corresponding to 7-10 years and 21-30 years after the Chernobyl accident. Regarding the distribution of cases by the degree of malignancy, according to age group, there were more patients diagnosed with grade I meningiomas, than patients with grade II and III, with the only exception on the 80-89 years age group. Regarding the annual frequency of histopathologic grading, for grade I meningiomas there is no trend or cyclicity of the cases diagnosed each year, but for grade II and III meningiomas there is an ascending trend in the period 1996-2000, that corresponds to the 10-14 years from the Chernobyl accident.

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