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Radiation-induced meningiomas (RIM) in adults: A single-centre retrospective experience

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ABSTRACT

Introduction: Radiotherapy of central nervous system (CNS) is treatment against many paediatric cancers, even if it is a well-recognized risk factor for meningioma formation. An increased risk of developing secondary brain tumors like radiation-induced meningiomas (RIM) is related to irradiated patients.
Research question: This retrospective study aims to present RIM cases treated in a single tertiary-hospital in Greece and compare the results with international literature and cases of sporadic meningiomas.
Materials and methods: A single-centre retrospective study of all patients diagnosed between January 2012 and September 2022 with RIM after having been irradiated in CNS for paediatric cancer was undertaken through hospital's electronic record and clinical notes, identifying baseline demographics and latency period.
Results: Thirteen patients were identified with RIM diagnosis after receiving irradiation for Acute Lymphoblastic Leukaemia (69.2%), Premature Neuro-Ectodermal Tumour (23.1%), and Astrocytoma (7.7%). Median age at irradiation was 5 years old and 32 years old at RIM's presentation. The latent period from irradiation to meningioma diagnosis was 26.23 ± 5.96 years. After surgical excision, histopathologic results showed grade I meningiomas in 12 out of thirteen cases, while only one atypical meningioma was diagnosed.
Conclusion: Patients who underwent CNS-radiotherapy in childhood for any condition have an increased risk of developing secondary brain tumors such as radiation-induced meningiomas. RIMs resemble sporadic meningiomas in symptomatology, location, treatment, and histologic grade. However, long-term follow-up and regular check-ups are recommended in irradiated patients due to short latency period from irradiation to RIM development, which means younger age patients than those with sporadic meningiomas cases.

1. Introduction

Meningiomas are the most common primary brain tumors in adults and represent almost one-third of all primary tumors of the central neural system (CNS). Various risk factors have been blamed for their development, like ionizing radiation (therapeutic, diagnostic, or random exposure), hormonal factors, and genetic predilection syndromes (Wang and Osswald, 2018; Chukwueke and Wen, 2020). Indeed, the effects of ionizing radiation on intracranial meningioma growth were first studied by Munk in 1969, and since then, many researchers have linked radiation exposure with the development of different types of cerebral tumors (De Tommasi et al., 2005).

Except for malignant hematologic tumors like acute lymphoblastic leukaemia - the most common malignancy in pediatric patients - which may regress successfully with the application of contemporary therapeutic protocols of combined chemo- and radiotherapy, most malignant brain tumors in pediatric patients are aggressive, and they are generally treated with complete resection followed by adjuvant radiotherapy (Abdallah et al., 2020; Malard and Mohty, 2020; Fardell et al., 2017; Bhojwani et al., 2015). Even though no specific data exist regarding the number of paediatric patients receiving radiotherapy for malignancies yearly, Yale Medicine supports that half of the patients suffering from cancer are now treated successfully with radiotherapy, which explains the increasing numbers of cured adults and children (Medicine). The long-term side effects of neural tissue irradiation include many neurological complications such as progressive leukoencephalopathy, arteritis,

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damage to the hypothalamic pituitary axis, optic neuritis and increased risk of developing secondary lesions in the central nervous system (CNS) (Remes et al., 2019; Kawahara et al., 2007; Yamanaka et al., 2017; Marosi et al., 2008). The majority of these tumors are benign and mainly belong to the category of meningiomas, which are the most common brain neoplasm caused by ionizing radiation (Al-Mefty et al., 2004; Sadetzki et al., 2000).

In the international bibliography, meningiomas occurring within a previously radiated field after a defined latency period are being called "Radiation-Induced Meningiomas (RIM)" (Yamanaka et al., 2017; Godlewski et al., 2012). The most current World Health Organization (WHO) classification of CNS tumors in 2021 does not recognize them as a separate entity, but ionizing radiation is regarded as a well defined causing factor of meningiomas' formation (WHO Classification of Tumours Editorial Board, 2021). It is widely accepted that a meningioma to be considered as a result of radiation must meet specific conditions as they are described in Table 1 (Wiemels et al., 2010; Morgenstern et al., 2016; Co et al., 2019). However, some studies suggest that RIMs have their own clinical, histological, immunohistochemical, and biological behavior (Godlewski et al., 2012; Rubinstein et al., 1984; Caroli et al., 2006).

The development of such meningiomas seem to be related with several factors like the patient's age of being irradiated, the amount of the administrated radiation (Gy), and the targeted area (Kok et al., 2019). Data have shown that patients being treated with radiation for glioma, leukaemia or lymphoma have increased risk for having meningioma in the affected area in a period of less than 24 years. It has been observed that radiation-induced meningiomas are usually formed 20-15 years after irradiation, while the risk of developing such meningioma after radiotherapy is about 30% for the next 30 years (Wiemels et al., 2010). Many scientists have also considered that irradiated patients have 2% chance of developing meningioma at 5 years, and 8,9% at 10 years after the treatment (Yamanaka et al., 2017). Regarding the amount of received radiation, many researchers state that 1–2 Gy of radiation during childhood is associated with 9.5 further risk of forming meningioma (Yamanaka et al., 2017). Moreover, patients who have received approximately 8 Gy of radiation for scalp treatment have greater risk of developing meningiomatosis over a 35-year period.

Despite these epidemiologic numbers, still RIMs belong to the category of meningiomas. Both their clinical appearance and treatment does not differentiate from the one of de novo meningiomas. Similarly, the histologic types of RIMs remain the same with the known ones of the meningiomas which based on the most recent classification by the World Health Organization (WHO), in 2021, are divided into three histological grades described in Table 2 (Chukwueke and Wen, 2020; Marosi et al., 2008; WHO Classification of Tumours Editorial Board, 2021). Most of them are benign (Grade I), and 5–7% are atypic (Grade II) meningiomas. Only a very small percentage of meningiomas will eventually be developed into malignancy (Grade III) and it is calculated to be 0,17/100.000 meningiomas per year (Chukwueke and Wen, 2020; Marosi et al., 2008).

To date, hundreds of studies have reported meningiomas in patients who have been irradiated in their childhood for neoplasms either of CNS or for hematologic diseases. However, the appearance of radiation-induced meningiomas still concerns many scientists who try to examine the appropriate time for follow-up of irradiated patients and the differences from sporadic meningiomas cases.

Therefore, this paper includes a retrospective study of radiation-induced meningiomas cases treated in the Department of Neurosurgery of 'Attikon' General University Hospital in Greece. Examining the characteristics of included patients and meningiomas, this study aims.

- to recognize the latent period between irradiation and meningioma formation,
- to compare the results with the international bibliography,
- to compare the RIMs characteristics, and the age at diagnosis with the sporadic meningiomas cases.

Table 1
Characteristics of radiation-induced meningiomas (Wiemels et al., 2010; Morgenstern et al., 2016; Co et al., 2019).

Characteristics of Radiation-Induced Meningiomas:
a) to be formed within the irradiated field
b) to appear with different histological characteristics from other previous tumors
c) at least five years should have elapsed between irradiation and meningioma's appearance
d) it should have been absent during irradiation
e) patient should not have a metastatic tumor
f) the incidence of neurofibromatosis type II should be excluded

Table 2
Histological classification of meningiomas by World Health Organization (WHO) (WHO Classification of Tumours Editorial Board, 2021).

Grade I (benign):	Meningiomas with very low mitotic activity, in which total removal equates to complete cure.
Grade II (atypical):	Meningiomas with atypical cells, increased cellularity, nucleus with characteristic necrotic areas, and increased mitotic activity. Recurrency is often in such tumors and additional radiotherapy is required after surgery.
Grade III (anaplastic or malignant):	Meningiomas with characteristic nuclear atypia, intense mitotic activity and malignant tumor behavior and may give extracranial metastases.

2. Material and methods

A single centre, retrospective study was undertaken to investigate the association of CNS irradiation during childhood with the development of meningioma in adult patients, managed at the Department of Neurosurgery of 'Attikon' General University Hospital, from January 2012 to September 2022. For the purposes of this analysis, the neurosurgical database was searched to identify patients diagnosed with radiation-induced meningioma after having been treated with radiotherapy of CNS for managing paediatric cancer in the timeframe of the last decade. As a purely retrospective, single-centre, non-interventional study, formal ethical approval was not required.

2.1. Inclusion and exclusion criteria

From this dataset, patients were deemed eligible for inclusion if aged over 18 years and having previously been irradiated in their Central Nervous System (CNS) due to a paediatric cancer based on the provided documents of their medical history. Patients who developed meningioma without previous radiotherapy of CNS, were excluded from this study. Patients with two or more meningiomas in different places will be included as well and will be considered that suffer from multiple meningiomatosis due to radiation.

2.2. Patient demographics

The collected data were then reviewed to identify information on patient's gender, age at diagnosis of meningioma, age at irradiation, reason for irradiation, site of received radiation, the time between meningioma diagnosis and irradiation, the location of meningioma, the neurosurgical management of meningioma and the meningioma's histopathologic grade based on the classification by the World Health Organization (WHO). As the clinical presentation of meningiomas is not typical, and the diagnosis of a lesion like meningiomas is based on radiological findings (head CT scan or brain MRI) rather than symptomatology, this study did not focus on the patient's clinical symptoms. However, it should be referred that all included patients had neurological signs which combined with the radiological findings led to the decision of surgical approach to their lesions within a trimester from the

diagnosis. No data were collected on the radiology centre or hospital where patients had been irradiated as well as the meningioma diagnosis during a regular follow-up or only due to the patient's neurological deterioration. All information was supplemented from hospital's electronic patient record (MEDIS), as well as paper-based patient notes.

2.3. Outcome measures

The primary outcome measure was the elapsed time between radiotherapy and meningioma's diagnosis. Secondary outcome measures were the histopathologic grade of meningioma, the age at diagnosis, and the site of meningioma.

2.4. Statistical analysis

Statistical analysis was done using simple biostatistical apps for statistic calculations and comparisons. Because of the small size of population, special statistic tools are not possible to be utilized to avoid any possible small-size bias. A p value of 0.05 was statistically significant. Frequencies were generally reported in percentages. Medians are reported with a 95% confidence interval (CI) and a range. The results of this study will be compared with the ones of international literature.

3. Results

Of the 96 patients yielded by the search of the 'Attikon' General University Hospital electronic patient record (MEDIS) between January 2012 and September 2022, 83 were excluded for failing to meet the inclusion criteria; hence, this retrospective cohort study reported outcomes for 13 patients. Fig. 1 displays the patient selection process and demonstrates the exclusion reasons.

Therefore, this retrospective study examined the cases of thirteen patients with radiation-induced meningioma (RIM) who were diagnosed and treated in our neurosurgical department. These patients had been irradiated during their childhood for paediatric cancer. Their demographic characteristics are presented in Table 3.

Median age at irradiation was 5 years old with a small preponderance of female gender (F:M 7:6), while the median age of RIM presentation was 32 years old with a distribution from 20 to 46 years old as described in Table 4. From the thirteen patients, 9 cases of patients having undergone radiotherapy due to Acute Lymphoblastic Leukaemia were recorded, 3 patients had been irradiated for Premature Neuro-Ectodermal Tumour (PNET), and only one patient received radiation for astrocytoma. Irradiation was covering the entire skull in 53.9% of patients and it was targeting the whole CNS in 46.2% of the studied cases.

All the studied patients were treated surgically for the meningioma and the calculated latent period of meningioma development after irradiation was 26.23 ± 5.96 years with 95% confidence interval to be 22.99–29.47 years. In Fig. 2, there is illustrated a box plot showing the time between irradiation and meningioma's development, which is positively skewed meaning that the majority of patients had shorter latent period than 26 years (median value).

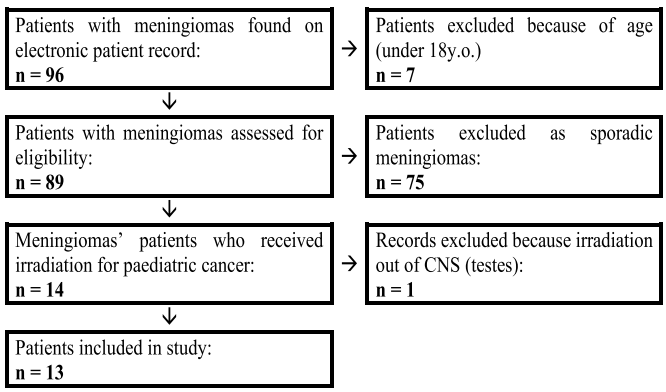

Fig. 1. 'Patients' selection process.'

Fig. 3 illustrates a pie-chart showing the frequencies of meningiomas' locations. Most patients -five out of thirteen-had formed a parasagittal RIM. Convexity's meningiomas come next with 23.1% frequency and temporal meningiomas follow at 15.4% percentage. One patient presented with meningioma at sphenoid wing and one with intraventricular meningioma. Also, one out of thirteen patients, a 31-year-old man developed multiple meningiomatosis having two lesions, one parasagittal and one on left temporal lobe.

The extent of brain meningiomas surgical resection is traditionally described by Simpson's classification – a scale associating the extent of visual surgical excision with the risk of recurrence (Table 5) (Operative Neurosurgery; Simpson, 1957). In our series, except from the intraventricular meningioma case, all other meningiomas were completely excised – Simpson grade I – with the appropriate surgical technique based on their location, size, and morphology, including resection of any dural attachment or underlying abnormal bone. The 34-year-old woman with the intraventricular lesion underwent an endoscopic approach and therefore the excision grade is regarded as Simpson grade II. Table 3 includes a summarized description of the main surgical techniques used in each case. On our surgical results, no complications were reported intra- or post-operatively during the five years follow up, but the size of cases is not indicative, as patients with such medical history often tend to be related to surgical and systemic complications. Finally, the surgical excision of the meningiomas resulted in grade I RIM in 12 out of 13 patients. Only one case of a 33-year-old woman having been irradiated for acute lymphoblastic leukaemia formed a meningioma in sphenoid wing which was surgically removed resulting in a grade II meningioma based on histopathological report.

4. Discussion

It is generally accepted by the literature that patients who had been irradiated in CNS during childhood prophylactically for malignancy of hematopoietic system or had been accidently exposed to high doses of ionizing radiation have an increased chance of developing CNS meningiomas in adulthood (Godlewski et al., 2012). In a study by British Pediatric Cancer Center examining the development of secondary brain tumor in 17890 patients who had been irradiated in their childhood, found that 137 patients developed meningioma, 73 people had glioma and, 37 developed other types of CNS tumors (Fujii et al., 2020). Fujii et al. in a study of 77 patients, showed that 21% of the studied population was diagnosed with brain tumor after irradiation in childhood. From this subgroup, 10% had cavernoma, 6% meningioma, 3% skull osteoma, and one patient was found with anaplastic astrocytoma (Fujii et al., 2020). However, the current study examined only radiation-induced meningiomas cases.

4.1. Reason for irradiation

As many pediatric cancer patients nowadays achieve long-term survival, there are increasingly cases of adult-onset long-term complications including secondary brain tumors. In the study of Yamanaka et al. in 2017, patients received radiotherapy for primary tumors such as hematologic malignancies (54 patients –21,5%), low-grade gliomas (45 patients -17,9%), medulloblastoma (37 patients –14,7%), pituitary adenomas (20 patients -7,9%), pineoblastoma/neuroectodermal tumors/spongioblastoma/neuroblastoma (5 patients –1,9%), embryonic stem cell tumors (4 patients -1,5%), craniopharyngiomas (3 patients –1,1%), head and neck cancer (16 patients -6,3%), cranial angioma (11 patients –4,3%), scalp lesions/cranial lesions (51 patients –20,3%), and other tumor types (5 patients –1,9%). The mean age of irradiation in these patients was 13 ± 13,5 years with the 95% confidence interval to be 11,3–14,8 (Yamanaka et al., 2017). The results of the current study

Table 3
Demographic data of included patients.

Serial No.	Gender	Age at meningioma diagnosis (years)	Age at irradiation (years)	Reason for irradiation	Site of Radiation	Time from irradiation to meningioma presentation (in years)	Meningioma's location	Meningioma management	Histologic grade
1	M	20	1	ALL	Skull	19	Parasagittal	Bifrontal craniotomy - removal of dural attachment - ligation of 1st 1/3 of sagittal sinus - total resection - without bone involvement	I
2	M	23	6	PNET	Skull	17	Parasagittal	Bifrontal craniotomy - removal of dural attachment - ligation of 1st 1/3 of sagittal sinus - total resection - bone drilling	I
3	F	23	5	ALL	Skull	18	Left convexity	Parietal craniotomy - total resection of tumour and dura - without bone involvement	I
4	F	27	1	ALL	CNS	26	Parasagittal	Bifrontal craniotomy - removal of dural attachment - ligation of 1st 1/3 of sagittal sinus - total resection - without bone involvement	I
5	M	29	4	ALL	CNS	25	Right convexity	Frontoparietal craniectomy - debulking - total resection of tumour -dura -bone	I
6	M	31	4	PNET	CNS	27	Mult. Meningiomatosis (parasagittal, L. temporal lobe)	Two surgical procedures: -1st bifrontal craniotomy for parasagittal meningioma - removal of dural attachment - ligation of 1st 1/3 of sagittal sinus - total resection - bone drilling - 2nd pterional craniotomy for temporal meningioma with total excision of tumour and dura - without bone involvement	I
7	M	32	6	ALL	Skull	26	Right convexity	Parietal craniotomy - total resection of tumour and dura - without bone involvement	I
8	F	33	3	ALL	Skull	30	Sphenoid wing	Pterional craniectomy - debulking - total resection of tumour -dura -bone	II
9	F	34	7	Astrocytoma	Skull	27	Intraventricular	Endoscopic approach - tumor resection grade Simpson II	I
10	F	38	7	PNET	CNS	31	Parasagittal	Bifrontal craniotomy - removal of dural attachment - ligation of 1st 1/3 of sagittal sinus - total resection - without bone involvement	I
11	M	38	14	ALL	CNS	24	Left temporal	Extended pterional craniotomy - total resection of tumour and dura - without bone involvement	I
12	F	41	4	ALL	CNS	37	Right temporal	Temporal craniotomy - debulking - total resection of tumur and dura - without bone involvement	I
13	F	46	12	ALL	Skull	34	Parasagittal	Bifrontal craniotomy - removal of dural attachment	I

(*continued on next page*)

Table 3 (*continued*)

Serial No.	Gender	Age at meningioma diagnosis (years)	Age at irradiation (years)	Reason for irradiation	Site of Radiation	Time from irradiation to meningioma presentation (in years)	Meningioma's location	Meningioma management	Histologic grade
								- ligation of 1st 1/3 of sagittal sinus - total resection - without bone involvement	

*M (Male), F (Female), ALL (Acute Lymphoblastic Leukaemia), PNET (premature neuro-ectodermal tumour), Mult. Meningiomatosis (Multiple Meningiomatosis), CNS (Central Nervous System).

Table 4
Statistics of patients' demographics.

Patient Demographics (n = 10)	
Males (n, %)	6 - 46.2%
Females (n, %)	7 - 53.9%
Age at meningioma diagnosis (median age, range)	32y.o. – 20-46y.o.
Age at irradiation (median age, range)	5y.o. – 1-14y.o.
Elapsed time (mean, median, range, 95% confidence interval)	26.23y. – 26y. – 17-37y. – 22.99–29.47y.
Reason for irradiation (n, %)	ALL(9, 69.2%), PNET(3, 23.1%), Astrocytoma (1, 7.7%)
Site of radiation (n, %)	Skull(7, 53.9%), CNS(6, 46.2%)
Histopathologic grade (n, %)	Grade I(12, 92.3%), Grade II(1, 7.7%)

*n(number of size), ALL (Acute Lymphoblastic Leukaemia), PNET (premature neuro-ectodermal tumour).

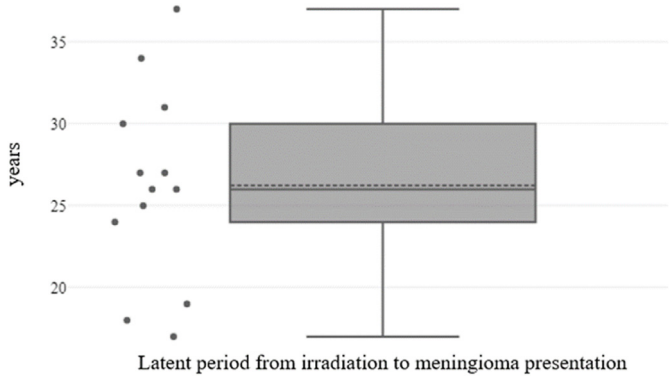

Fig. 2. 'Box-plot presenting the time from irradiation to meningioma's presentation.'

showed that from the 13 irradiated patients, 9 received radiotherapy for acute lymphoblastic leukaemia, 3 for PNET, and only 1 patient was irradiated adjunctively for astrocytoma. The median age of patients needing irradiation was 5 years old in our study.

4.2. Dose and site of radiation

One of the main causing factors of meningiomas is radiation, hence the amount of radiation and the site of it play a significant role in the side-effects of it, like the formation of meningiomas (Remes et al., 2019; Yamanaka et al., 2017; Kok et al., 2019; Fujii et al., 2020; Chester et al., 2020; You et al., 2013). The most common dose spectrum of radiation that could cause secondary brain tumors was considered to be a medium dose which means approximately between 20 and 36 Gy based on the studies of Galloway et al. and Vinchon et al. (Galloway et al., 2011; Vinchon et al., 2011). In the studies of Yamanaka et al. and Bowers et al., the amount of irradiated dose was 38.8 ± 16.8 Gy and 20–29.9 Gy respectively (Yamanaka et al., 2017; Bowers et al., 2017). Many researchers state that 1–2 Gy of radiation during childhood is associated with 9.5 further risk of forming meningioma (Kawahara et al., 2007). Moreover, patients who have received approximately 8 Gy of radiation for scalp treatment have greater risk of developing meningiomatosis over a 35-year period. In the current retrospective study there were not enough data to examine the dose (Gy) of radiation in included patients, however, it is reported that radiation was covering the entire skull in 53.85% of patients and it was targeting the whole CNS in 46.15% of the studied cases.

4.3. Latent period between irradiation and meningioma diagnosis

While the prophylactic radiotherapy of CNS in patients with acute lymphoblastic leukaemia (ALL) increases the survival rate by 85%, it is reported that the mean time until RIM appearance – the latent period – is about 25 years after irradiation (Kawahara et al., 2007). Yamanaka et al. in their study in 2017 showed that the latent period for RIM formation was 22,9 ± 11,4 years with the 95% confidence interval to be 21,4–24,3 years. More specifically, the elapsed time between radiotherapy and meningioma development for Grade I tumors was 24,8 years with the 95% confidence interval to be 22,8–26,7 years. Respectively, for Grade II meningiomas, latent period was 21,9 years with the 95% confidence interval to be 18,4–25,4 years, and for Grade III meningiomas, it was 12,9 years with the 95% confidence interval to be 7,9–17,8 years (Yamanaka et al., 2017). Benerjee et al. in a retrospective study of 60 patients who had been irradiated to skull for acute lymphoblastic leukaemia at the age of 1–8 years old, found that latent time was 25 years after radiotherapy (Banerjee et al., 2009). Another study by Bowers et al. in 2017 resulted in an elapsed time of 22 years from cranial radiotherapy until meningiomas formation (Bowers et al., 2017). In our study, the calculated latent period of meningioma development after irradiation was 26.23 ± 5.96 years with 95% confidence interval to be 22.99–29.47 years.

4.4. RIM location

Yamanaka et al., in their study, reported that secondary meningioma in dome of the skull was developed in 138 patients (51,3%), in 96 people (35,6%) a skull base meningioma was found, intraventricular meningioma was recorded in one patient (0,3%), and 4 cases (1,4%) had meningioma in spinal cord. Moreover, in the same study, 184 patients (73,3%) appeared with a single lesion, while 30 of the studied people (11,9%) had multiple lesions (Yamanaka et al., 2017). Bowers et al. refer to one of the biggest retrospective studies of 4221 patients resulting in 85,2% single-lesion RIM and 14,2% multiple meningiomas (Bowers et al., 2017). In literature, there has been reported even a case of meningioma within the orbit after irradiation for ALL (Char and Shiel, 2008). In the current study, all of the 13 patients formed secondary skull meningiomas. Five out of 13 people (38.5%) developed a parasagittal meningioma, 23.1% of the included patients had a meningioma of the convexity of the skull, 15.4% formed the meningioma in temporal lobe, one patient presented with meningioma at sphenoid wing and one with intraventricular meningioma. Also, one out of thirteen patients, a

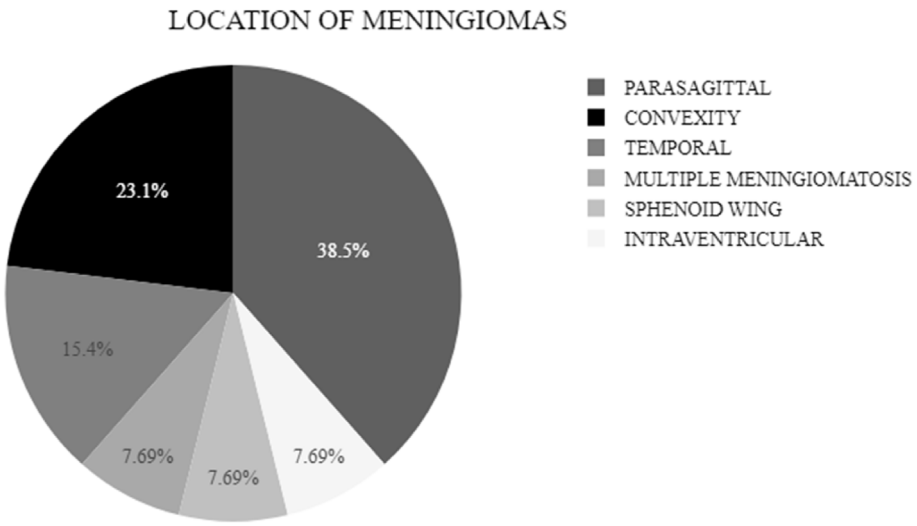

Fig. 3. 'Frequencies of radiation-induced meningiomas locations.'

Table 5
Simpson classification on meningioma resection (Operative Neurosurgery; Simpson, 1957).

Grade I:	Complete tumor excision – resection of dural attachment – removal of underlying bone or sinus.
Grade II:	Complete tumor excision – coagulation of dural attachment – removal of underlying bone or sinus.
Grade III:	Complete tumor excision – without removal of dural attachment or underlying bone or sinus.
Grade IV:	Partial tumor excision
Grade V:	Biopsy

31-year-old man developed multiple meningiomatosis having two lesions, one parasagittal and one on left temporal lobe.

4.5. Histologic grade

Yamanaka et al. referred that within the patients having RIM, 140 were diagnosed with grade I meningioma, 55 had grade II and 10 cases of grade III meningioma were found (Yamanaka et al., 2017). In one of the biggest multicentered retrospective studies in America and Canada in which 26 centers with 4221 patients had been participated, showed that from those children who survived a pediatric cancer, 169 developed meningioma and 97% of these were benign, in contrast with the 3% of the malignant cases (Bowers et al., 2017). The results of our study showed that 12 out of 13 patients were diagnosed with Grade I meningioma based on the histopathologic exam and only one patient had atypic meningioma (Grade II). Lastly, it should be noted that the 3 histological grades of sporadic meningiomas do not differentiate significantly in the case of RIMs. The majority are benign (Grade I), and there are only rare cases of malignant meningiomas (Grade III).

4.6. Relation to sporadic meningiomas

As it has been reported RIM belong to meningiomas' category, hence they mostly have same characteristics.

However, the median age of RIM presentation was 32 years old in our study with a distribution from 20 to 46 years old, and similar results have been published in literature, while it is known that sporadic meningiomas are commonly presented between the 6th and the 7th decade of life (Chukwueke and Wen, 2020; Marosi et al., 2008). This means that patients who have been irradiated in CNS during childhood, should have follow-up earlier than it should be expected for a sporadic meningioma.

On the other hand, clinical appearance of both sporadic meningiomas and RIMs is related to a wide spectrum of symptoms which variate from totally asymptomatic patients to serious neurologic deficits. An important percentage of meningiomas are being diagnosed as incidental finding on imaging for other reasons. Usually, when intracranial meningiomas are symptomatic, patients appear with mild neurologic symptoms which progressively deteriorate in different timeframes. The most common symptom, at about 36% of meningiomas' patients, is headache without any specific characteristics. Other symptoms that have recorded with increased frequency include seizures, behavioral disorders, personality disorders, level of consciousness disorders, visual disturbances, anosmia, olfactory disturbances, tinnitus or hearing impairment (Chukwueke and Wen, 2020).

In addition, the frequency of RIM locations is also the same as that of sporadic meningiomas with most common sites in descending percentage order to be: parasagittal-falx, convexity, sphenoid wing, olfactory groove, suprasellar, posterior fossa, intraventricular, and finally in other brain regions (Marosi et al., 2008; Godlewski et al., 2012; Morgenstern et al., 2016; Co et al., 2019). Similar were the data found in our study and international literature regarding RIMs.

It should also be noted that the management protocol of RIM does not differentiate from the one of de novo meningiomas. The majority of symptomatic patients with meningioma require treatment and the treatment of choice is surgical excision for meningiomas larger than 2 cm in diameter. The therapeutic decisions are usually taken depending on meningioma's size, location, relation with adjacent structures, patient's neurologic condition, age, general health status, and desire. Asymptomatic patients whose meningioma was an incident finding, usually are managed conservatively with repeated imaging studies until they present with neurological symptoms (Wang and Osswald, 2018). Radiosurgery is another possible treatment for small meningiomas.

5. Conclusion

Patients who undergo CNS radiation therapy in childhood for any condition have an increased risk of developing in adulthood secondary brain tumors -benign or malignant-such as radiation-induced meningiomas. RIMs resemble to sporadic meningiomas in symptomatology, location, treatment, and histological grade. However, long-term follow-up and regular check-ups are recommended in irradiated patients due to the short latency period from irradiation to RIM development, which means younger age patients than those with sporadic meningiomas cases. Further research is needed to identify the regular manner in which follow-up should be suggested in such patients.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

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