Radiation-induced meningiomas: the importance of continued follow up after cranial irradiation

Meningiomas induzidos por radiação: a importância do seguimento contínuo após irradiação craniana

Emerson Magno F. de Andrade1
Raphael Vicente Alves1
Mariano Ebran Fiore1
Airton Batista de Araújo Jr1
Antônio Carlos Montanaro1
Roberto Godoy1

1 - Division of Neurosurgery, Beneficência Portuguesa de São Paulo, Brazil.

INTRODUCTION

Meningiomas account nearly for 20% of all primary brain tumors and are the most common primary nonglial intracranial tumor. Many asymptomatic meningiomas are found at routine autopsy, so their occurrence is probably higher than the large series reported17. Meningiomas can occur decades after radiation therapy mainly in pediatric population treated for acute leukemia and brain tumors5,7. This long-term effects make the radiation therapy a challenge in pediatric oncology because the real risk of radiation induced tumors is unknown5,9,11,17.

We report two cases of meningioma occurring after treatment with cranial and spinal radiation for Primitive neuroectodermal tumor (PNET), illustrating the importance of continued close follow up after cranial irradiation in the pediatric population.

SINOPSE

O surgimento de tumores é uma complicação tardia após irradiiação craniana, e destes a maior parte corresponde a meningiomas intracranianos. O período de latência entre a exposição à radiação e o diagnóstico de um meningioma induzido por radiação varia com o período inicial de exposição à radiação e a dose total recebida. Os autores relatam dois casos de meningiomas resultantes de altas doses de radiação recebidas para tratamento de um PNET. Ambos os pacientes foram submetidos à reseção cirúrgica do tumor, e a análise imunohistoquímica revelou se tratar de meningioma típico. Estes casos ilustram a importância do seguimento contínuo após irradiiação craniana na população pediátrica.

Palavras-chave: Meningioma, tumor induzido por radiação, radioterapia.

ABSTRACT

A late complication following cranial irradiation is the induction of tumors, most of which are intracranial meningiomas. The latency period between radiation exposure and diagnosis of radiation-induced meningioma varies with the timing of the initial radiation exposure and total radiation dose. The authors report two cases of meningiomas as a result of high-dose irradiation received for a PNET. Both patients underwent surgical removal of the tumor and immunohistochemical examination revealed a benign meningioma. These cases illustrate the importance of continued follow up after cranial irradiation in the pediatric population.

Keywords: Meningioma, radiation-induced tumor, radiotherapy.
**CASE 1**

A 18-year-old man initially presented to another clinic at the age of 4 years with a 3-month history of seizures and headache. A magnetic resonance imaging (MRI) of the brain revealed a heterogeneous lesion in the left temporo-occipital lobe that was suggestive of brain tumor. The patient underwent surgical resection of the mass and the pathological evaluation revealed PNET. CSF cytology during that time showed no malignant cells. Craniospinal irradiation was initiated one month after surgical resection of the tumor and the patient received a total of 7200 cGy to the primary site and 3600 cGy to the remainder of the craniospinal axis. Following radiation therapy he received six cycles of PCV (procarbazine, CCNU, and vincristine) chemotherapy.

Postoperatively, the patient underwent follow-up and evolved in excellent health. MRI examinations and cerebrospinal fluid puncture were performed and revealed no evidence of leptomeningeal dissemination or recurrence of the tumor mass (Fig 1).

Fourteen years after first surgery, at age 18 years, the patient was referred to our institution experiencing headache, dizziness and memory loss. A MRI of the brain demonstrated a 3.3 x 2.6 x 2.7 cm parafalcine dural-based lesion in the right frontal lobe. The tumor was attached to the right sagittal dura, with mild mass effect, and postgadolinium T1-weighted image demonstrated homogeneous enhancement (Fig 2). The patient underwent surgical removal of the tumor via a bicoronal approach. In the postoperative period the patient evolved with good clinical and neurological recovery.

Histopathological and immunohistochemical examination revealed a benign meningothelial meningioma and there was no family history of neurofibromatosis 2 (Fig 3).

**CASE 2**

A 29-year-old woman initially presented to another clinic at the age of 7 years with a history of headache, clumsiness and ataxic gait. A MRI of the brain was performed and revealed a large, contrast-enhancing fourth ventricle tumor. The patient underwent surgical resection of the mass via suboccipital craniectomy and the pathological evaluation revealed PNET. Craniospinal irradiation was initiated and the patient received 3600 cGy to the entire craniospinal axis with an 1800 cGy boost to the tumor bed. We have no information about the particular chemotherapy drugs used.

Postoperatively, the patient underwent follow-up and evolved with progressive improvement of his neurological symptoms. MRI examinations and cerebrospinal fluid puncture were performed and revealed no evidence of leptomeningeal dissemination or recurrence of the tumor mass (Fig 4).
Relato de Caso

Figure 4. Contrast-enhanced axial T1-weighted MR images revealing no evidence of tumor, and showing surgical cavity of the PNET in posterior fossa.

Twenty-two years later, the patient was referred to our institution experiencing sporadic headache. A MRI of the brain revealed a sphenoid wing tumor that measured 2.5 x 2.5 cm and a small well-circumscribed (1.8 cm in diameter) extra-axial tumor in the right frontal convexity, both consistent with meningioma (Fig 5).

The patient underwent surgical removal of the tumor via a right pterional approach and evolved with good clinical and neurological recovery. Histopathological and immunohistochemical examination revealed a benign meningothelial meningioma and there was no family history of neurofibromatosis 2 (Fig 6).

**DISCUSSION**

The criterion to define a tumor as radiation-induced was first described by Cahan et al. in 1948 and has been modified to characterize the radio-induced meningiomas1. To define a meningioma as radio-induced, the tumor must accomplish the following criteria: 1- occur from within the treatment field, 2- differ histologically and/or radiographically from any pre-existing tumor, 3- occur after a reasonable interval after irradiation (5 years in the original description), 4- be found in a patient without a genetic predisposition for neoplasm formation1,13.

The radio-induced meningiomas (RIM) can be grouped in three categories: those who have been treated with low-dose radiation for tinea capitis (< 1000 cGy); those who have received high-dose radiation (> 2000 cGy) and a radiation exposure intermediary group (1000 – 2000 cGy). This classification, however, is quite arbitrary and variable in the literature5,9,11.

The meningiomas induced after high-dose were the first to be reported. In 1953 Mann, et al. described the case of a 4-year-old girl who received 6500 cGy to the orbit after resection of an optic nerve glioma and later developed a meningioma in the irradiated field9,14. In 1974, Modan, et al. reported meningiomas developing after low-dose irradiation in 11,000 children treated for tinea capitis with scalp irradiation and observed that the rate of meningioma formation was four times greater than that of control10. The average time interval to tumor appearance following low, moderate and high dose radiation is of 35, 26, and 19 to 24 years, respectively. This inverse relationship between increasing radiation and latency period is indicative of a dose-response and provides support for the presumed induction of meningiomas by radiation13,14. In the cases reported in this article, the latency period was 14 and 22 years, but the literature describe a much wider range of time for tumor development. Kleinsschmidt-DeMasters et al. report a case of a 68-year-old woman who received radiotherapy at 5 years of age for a presumed right cerebellar tumor and developed multiple meningiomas in the radiation portals 63 years later7, and Choudhary et al. report a child diagnosed with RIM with an unusually short latency period of 14 months4.

Radiation induced meningiomas presented at younger ages, mainly those in the high-dose group, compared with sporadic meningiomas that are predominantly tumors of the fifth and sixth decades of life. Meningiomas typically present a female predominance with an approximate female/male ratio of 2:1. This higher female/male ratio is more evident in the non-RIM compared with the RIM, although malignant meningiomas affect men and women almost equally and benign meningiomas are more commonly found in women6,9,13,15,16.

Although there are a lot of cytogenetic studies, the genetic changes that could explain the progression to meningioma after cranial irradiation have not been established. Radiation probably alters the long arm of chromosome 22 (22q), leading to mutations that affect oncogenes and tumor suppressor genes, such as p53 and NF2, in a process that is incompletely
understood. In non-RIM, the most frequent chromosomal abnormality is a deletion of 22q. Other probable genetic abnormalities in the development of RIM include chromosome 1p loss and deletions of 6p and 7p<sup>15,17</sup>.

Radiation-induced meningiomas seem to constitute a distinct entity and significant differences were described in the literature between the RIM and non-RIM. RIM have a tendency to occur along the skull base, compared to more than 30% in non-RIM<sup>10,12,15–17</sup>. Although the two cases reported in this article referred to benign meningiomas (meningothelial), the relative frequency of atypical and malignant meningiomas appears to be greater among RIM. In a large series of 253 cases, multiple meningiomas were seen in 15.8% of patients RIM but were observed in only 2.4% of patients who had not undergone radiotherapy<sup>15</sup>. Sofer et al. reported an 18.7% recurrence rate, compared with the 3% recurrence rate in their control population and the difference was statistically significant<sup>16</sup>. Comparable rates were found in the series of Sadetzki et al. (14.6%)<sup>13</sup> and in the series of Rubinstein et al. (11%)<sup>12</sup>, in contrast with the finding of only a 3% recurrence rate among sporadic cases<sup>8,11,15</sup>. A calvarial location is predominant for these tumors, where facial and parasagittal meningiomas comprise up to 95% of the neoplasm. In another series, between 4 and 19% of RIM occur along the skull base, compared to more than 30% in non-RIM<sup>10,12,15–17</sup>.

Most of RIM published in the literature were sporadic case reports, except for some series. The largest series of RIM were due to low dose radiation used to treat tinea capitis in a descriptive study of 253 cases<sup>15</sup>. In Brazilian literature there are very few publications concerning RIM<sup>2</sup>. Barboza et al. describe a case of a 50 years-old man harboring a RIM diagnosed 20 years after radiation treatment of an oligodendroglioma<sup>2</sup>. Aguiar et al. report a case of a 55-year-old woman presented with a RIM after adjuvant radiation therapy for low-grade astrocytoma, and another case of a 18-year-old man presented a RIM after craniospinal radiation therapy for PNET<sup>1</sup>. Surgical resection continues to be the treatment of choice for most RIM<sup>4,6,7,8,10,14</sup> however when tumor is located in critical areas, involve osseous structures, or is multiple, a complete removal may not be possible. In such cases, stereotactic radiosurgery may be used as primary or adjuvant management, mainly when patients have already received high doses of conventional radiotherapy<sup>3</sup>.

**REFERENCES**


**CORRESPONDING AUTHOR**

Emerson Magno F. de Andrade
Av. Umbuzeiro, 1287 / 302
Manaira, João Pessoa-PB
CEP 58038-182
E-mail: emersonmago@hotmail.com