

Short latency period of Radiation Induced Meningioma in Adult Patient following High Dose Irradiation: A Case Report

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Abstract

Introduction: We present a case of adult onset Radiation-Induced Meningioma (RIM) following resection of astrocytoma with short latency period of only 18 months.

Case Report: A 44-year old man who had high dose irradiation following astrocytoma resection came to our institution due to the appearance of intracranial tumor in the field of radiation in the follow-up MRI. Observation was done and a head CT scan was done 6 months later, where intracranial tumor was doubled in size. Surgical resection was done and histopathological result of high-grade meningioma confirming the diagnosis of RIM. Most RIM are usually presenting in children receiving high dose radiotherapy with mean latency period of 26.2 ± 9.3 years.

Result: Our patient is older at presentation; he underwent astrocytoma resection previously and was receiving high dose irradiation of 46 Gy.

Conclusion: In astrocytoma patients receiving adjuvant radiotherapy, physician must be aware of RIM; in addition to the recurrence of the high-grade gliomas.

Keyword: High Dose Irradiation, Radiation Induced Meningioma, Radiation Therapy, Short Latency Period

Introduction

Radiotherapy has been used as therapeutic tools for many pathologies, however several evidence have reported an association between radiotherapy and the occurrence of secondary tumors.[1] In a longitudinal study by Vincon et al., 42 out of 552 children (7.2%) who received cranial irradiation developed radiation-induced tumor, with cumulative risks after 5 years and 10 years were 1.0% and 8.9% respectively. [2] Meningiomas has been found to be the most common radiation-induced tumor after brain irradiation. [1][3] Radiation-induced meningioma (RIM) has been largely documented in patients who received irradiation in their childhood. [4] A study conducted by Ron et al. showed that pediatric patient who received low dose irradiation (1-2 Gy) had a 9.5-fold risk of developing RIM. [5] The mean latency time from primary malignancy to the meningioma diagnosis was 26.2 ± 9.3 years. [3] Meanwhile, cases on short latency period for RIM were very scarce, where the shortest latency reported was 7 months. [6] The latency period is related to the age at irradiation, and

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directly proportional with the secondary tumor's aggressiveness. [7][8][9] The pediatric population has a higher chance of developing RIM since their developing meninges is particularly sensitive to irradiation. [9]

Widely defined criteria of the radiation induced brain tumor are as follows: 1) tumor occurred in the irradiated area; 2) sufficient latency period (i.e., usually >5 years); 3) radiotherapy-induced tumor has different histological type than the primary neoplasm; 4) patient do not have pathologies favoring development of the tumor. [10] [11] [12] RIM has been classified into three groups based on the irradiation dosage: (1) low-dose (<10 Gy); (2) moderate dose (10-20 Gy) and (3) high dose (>20 Gy). [12] In this report, we present a case of 44-year-old man with short latency radiation-induced meningioma following high dose irradiation.

Case Report

A 40-year-old man went to Karyadi Hospital in October 2015 due to the bulging mass behind his right eye. He was unable to see from his right eye and complaining of persistent headache. The physical examination showed he had proptosis and optic nerve atrophy in the right eye. A head CT scan with contrast revealed a contrast-enhancing mass in the temporal region, behind the right eye, extending through the orbital wall and pushing the right eyeball (Figure 1). The mass was caseating in the centre, with an ill-defined border. Eyeball exenteration and tumor biopsy were conducted. The pathological anatomy result showed proliferation of meningeal cells arranged hypercellular, with pleomorphic and hyperchromatic nuclei, 5 to 10 mitosis in high power field; consistent with pathological findings of atypical meningioma (WHO Grade II).

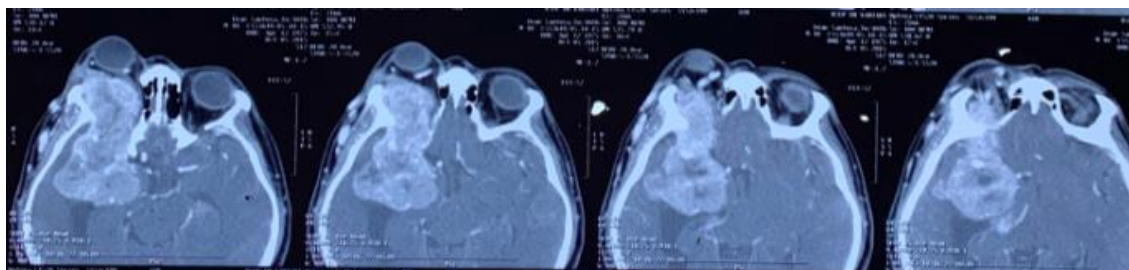


Figure 1. Head CT Scan showed a contrast enhancing mass behind the right eye, extending through the right temporal lobe. The size is 9 cm x 4.5 cm x 5 cm, with significant mass effect and minimal midline shift.

Fourteen months after the first surgery in December 2016, the patient had fat-like tissue coming out from the right orbit. The patient thus was referred to Soedjono Hospital. A pre-operative head CT scan was done in Soedjono Hospital, and contrast enhancing large intracranial mass in the right temporal lobe was found (Figure 2A.).

Surgery was planned to remove the intracranial mass. Intraoperatively, the tumor was found to be highly vascularized, and only part of the tumor was able to be resected. A histopathological examination showed glial tumor cells consisting of rounded and oval cells with hyperchromatic nuclei; this finding was concluded as anaplastic astrocytoma (WHO Grade III) (Figure 2B). Consequently, adjuvant radiotherapy was planned.

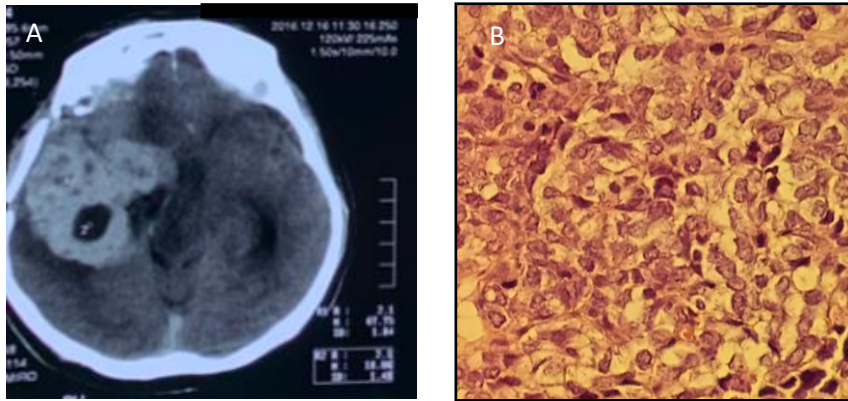


Figure 2. CT Scan with contrast showed intracranial mass in the right temporal lobe with massive edema. Multiple hypodensities intratumorally was found. Profound midline shift can also be seen in this image (A). Histopathological findings with hematoxylin and eosin (HE) staining (x400) of the lesion showed rounded and oval glial cells which were hyperchromatic with moderate mitosis, concluded as anaplastic astrocytoma (B).

Due to the patient's unstable condition, the irradiation was initiated in January 2018, 18 months after the astrocytoma removal surgery. The irradiation given was 4,600 cGy with booster up to 6,000 cGy in 4 weeks period. The patient was asymptomatic during the irradiation and underwent a close observation. No adjuvant chemotherapy was given to this patient. There was no tumor left in the right temporal lobe (Figure 3A, B.)

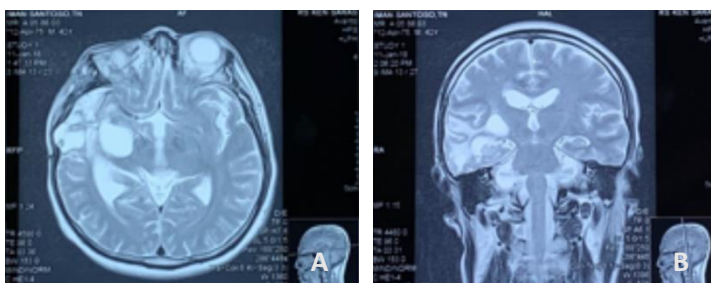


Figure 3. Last T2 weighted MRI post irradiation. The intracranial mass was not found in the right temporal lobe, axial cut (A) and sagittal cut (B).

Since the patient wanted to get an artificial eyeball, he underwent a follow-up MRI in July 2019. MRI Scan was done, and a rounded homogenous contrast-enhancing intracranial mass was found (Figure 4A, B). He was then referred to Soedjono hospital for further management. The patient was observed for six months, and a follow-up Head

CT scan was done. The intracranial mass in the field of radiation increased in size to 4.2 cm x 4.0 cm x 5 cm (Figure 4C, D). Surgical resection was performed, resulting in Simpson Grade IV (i.e., subtotal resection with a remaining mass in the base due to tumor's strong attachment to the surrounding tissue). A histopathological result showed proliferating rounded and oval cells with hyperchromatic and pleomorphic nuclei; mitosis was easily found with atypical tumor cells (Figure 5A, B). This finding was consistent with papillary meningioma (WHO grade III).

Follow-up MRI two months after the surgery showed remaining mass in the right temporal base. A close observation and follow-up MRI 9 months later showed no progression, and the remaining mass appeared smaller. The patient had no complaints and agreed to do close monitoring.

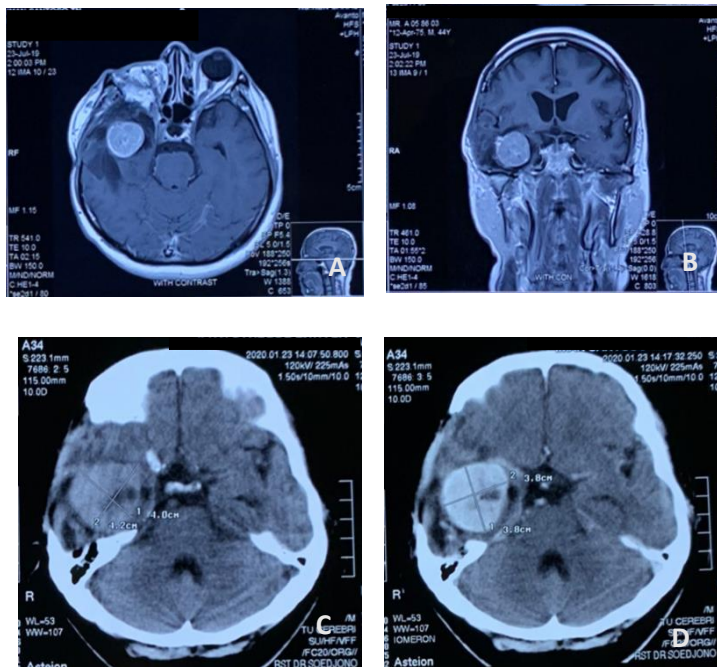


Figure 4. T1 weighted MRI with contrast 18 months after the last irradiation, a rounded homogenous and contrast enhancing intracranial mass was found, axial cut (A) sagittal cut (B). Pre-operative CT scan; pre contrast (C) and post contrast (D) showed rounded contrast enhancing lesion, homogenous, and well-defined border mass in the right temporal lobe.

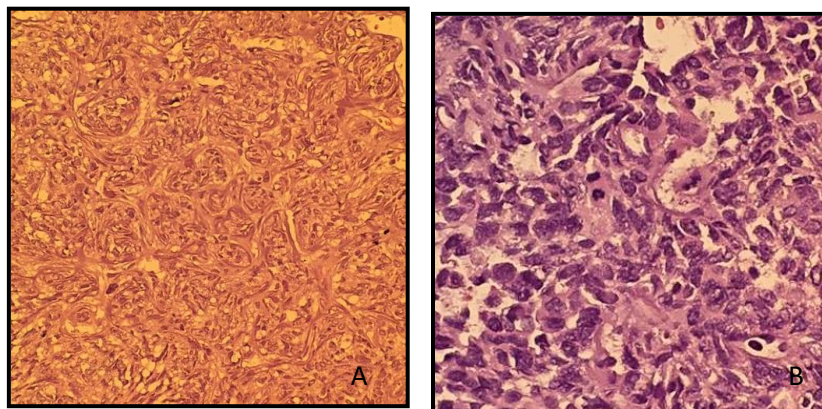


Figure 5. Histopathological findings with HE staining showed proliferation of rounded and oval pleomorphic cells, with hyperchromatic nucleus forming whorls formation. Tumor cells proliferation at the edge of the blood vessels creating a papillary structure (x40) (A), with frequent prominent mitosis with atypical cells (x400) (B).

Discussion

RIM is known as the most common secondary tumor caused by cranial irradiation. Radiation is able to induce meningeal reaction due to inflammatory adhesions between the brain and dura mater, stromal proliferation, and leptomeningeal thickening. [4]

As previously mentioned, younger age at irradiation was found to be significantly correlated with the development of RIM. [13] A study conducted by Shuryak et al. hypothesized that many cases of RIM in childhood are due to process of initiation tumorigenesis (i.e., a process where mutations of normal stem cell shift the cells into a pre-malignant state; which potentially becomes fully malignant). [14] These pre-malignant cells in children have longer times to exploit their growth and have more rapid cellular proliferation rates. However, few documented cases explain the increased risks of RIM in older patients. [15] One possibility included promotion tumorigenesis; where irradiation increases the number of already existing pre-malignant cells; thus, increasing the acceleration of the cell's proliferation.[16] A case report by Hu et al described that short latency period in an adult can be caused by the presence of brain tumor stem cell (BTSC). This can be identified by using CD133⁺ marker, since it can exhibit stem cell properties in vitro and capable for initiating tumor in vivo. [6] These mechanisms may explain the incidence of short-latency RIM in our middle age patient.

Our patient received 46 Gy of irradiation dose, which was classified as high dose irradiation.[12] This was one of the documented risk factors for RIM development, since the higher dose of radiation caused more rapid loss of cellular control mechanism and earlier expression of neoplastic phenotype. [11][17] The average latency period of high dose irradiation was 19.5 years compared with 35.2 years after low dose irradiation. [18]

In radiation therapy, tumorigenesis was restricted to the normal cells that were not killed by radiation; eventually these cells mutated into neoplasia. [19] Therefore, the highest incidence of radiation-induced tumors occurs in the peripheries, where the tissues were exposed with a lower irradiation dose. [20] These findings were similar to our case, where the RIM occurred in the field with a lower irradiation dose.

Several studies compared the characteristics of RIM with typical meningiomas. RIM was found to occur at an earlier age than spontaneous meningiomas, which usually occurred in the 5th or 6th decade of life), had a more aggressive nature, multiple, and higher recurrence after treatment. [21]

Papillary meningioma (WHO Grade III) which was aggressive in our case was thought to be one of RIM characteristics after high dose irradiation. Higher proliferative

activity of high-grade tumor was associated with a shorter latency period of RIM. In a study conducted by Wilson et al., it was found that the more malignant the meningioma, the latency will be shorter. [22] Determination of mitotic labeling index also provides a dependable basis for planning further treatment for aggressive RIM.[9]

The widely chosen approach in managing RIM is by completely removing the tumor surgically.[9][11] However, due to RIM's aggressive nature, difficult locations, and multiplicity, complete surgical removal is challenging to achieve. Due to its high recurrence, wider bone resection and more extensive dural margin excision are recommended.[18] Another challenge that needs to be addressed is that surgical approach through the previously irradiated field can lead to poor wound healing, CSF leakage, and a higher chance of infection. [11][12] Pre-operative investigation of RIM should be done more thoroughly since large-vessel occlusive vasculopathy is known to be one of the side effects of high dose irradiation. Adjuvantive treatment for RIM following radical surgery was stereotactic radiosurgery, radiosurgery, and brachytherapy. Adjuvant chemotherapy or interferon management can also be one of the treatment options. [23]

Several limitations in case management deserve mention. Firstly, we were unable to obtain the histopathological specimen from the first surgical procedure since the craniotomy was performed in a different hospital. Consequently, we could not re-assess the pathological result from the previous hospital.

RIM, which commonly presents in the adult who received cranial irradiation as a child, may hinder us from making a correct diagnosis in those receiving cranial irradiation as an adult. The possibility of RIM with short latency in adult prompt us to conduct a close regular follow up in patients receiving high dose cranial irradiation.

Conclusion

RIM has been known to be one of the consequences of radiotherapy and usually occurs in patients with a history of childhood radiotherapy. However, RIM which appears in adult receiving cranial irradiation is quite rare. Promotion tumorigenesis, where exposure to radiotherapy was causing increased proliferation of pre-existing malignant cells, might be the underlying pathomechanisms of this phenomenon, and high dose irradiation was one of the risk factors for the development of RIM. Therefore, regular follow-up should be warranted in an adult patient who received cranial irradiation, especially in those who received high-dose radiation.

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