

Frontal Meningioma After Postoperative Cranial Irradiation for Posterior Fossa Medulloblastoma

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✓ The development of cranial neoplasms subsequent to therapeutic radiation therapy (RT) is a rare entity but a serious complication. Radiation induced meningiomas are late complications in patients who have received high dose irradiation for brain tumors and the most common form of radiation-induced neoplasm. Radiation-induced meningiomas occurring after treatment of a medulloblastoma are rarely seen. We present a case of a 21-year-old male with frontal meningioma developed after 13 years from neuroaxis radiation therapy for medulloblastoma. Surgical resection and RT was applied for our patient at the age of 8 due to medulloblastoma. At age 21, the patient noted gradual onset of frontal headaches. A neurological examination at that time did not reveal any focal neurologic deficits. Magnetic resonance imaging demonstrated a left frontal mass. The patient underwent left frontal craniotomy and the mass removed totally. Histopathological examination revealed a meningotheliomatous meningioma.

Key words: Medulloblastoma, meningioma, radiation therapy

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Medulloblastom İçin Yapılan Postoperatif Kranyal Işınlama Sonrası Frontal Meningiom

✓ Tedavi edici radyasyon terapisi sonrasında kranyal tümör gelişimi enderdir, ancak ciddi bir komplikasyondur. Radyasyonun indüklediği meningiomlar, beyin tümörleri için yüksek doz radyasyon alan hastalarda görülen geç bir komplikasyondur ve radyasyonun indüklediği tümörlerin en sık görülen formudur. Posterior fossa medulloblastom tedavisinden sonra radyasyonun indüklediği meningiom gelişmesi nadirdir. Biz posterior fossa medulloblastom için nöroaksis radyasyon terapi uygulandıktan 13 yıl sonra frontal meningiom gelişen 21 yaşındaki erkek hastamızı sunuyoruz. Hastamıza 8 yaşında medulloblastom nedeniyle cerrahi kitle rezeksiyonu ve radyoterapi uygulanmış. 21 yaşında gittikçe artan frontal baş ağrısı gelişmiş. Nörolojik muayenede herhangi bir fokal nörolojik defisit saptanmadı. Kranyal magnetik rezonans görüntüleme sol frontal kitle saptandı. Hastada sol frontal kranyotomi yapıldı ve total kitle rezeksiyonu yapıldı. Histopatolojik incelemede meningotelyomatöz meningiom saptandı.

Anahtar kelimeler: Kranyal radyasyon, kromozom analizi, medulloblastom, meningioma

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The survival rates in cases with intracranial tumors have been improved owing to combined treatment modalities which consisted of surgery, radiation therapy (RT) with/without chemotherapy^(6,7,10). However, emergence of complications in the long term especially dependent on RT were started to be

seen^(6,7). The development of a new primary cranial neoplasm has long been recognized as a possible late effect of curative therapy for an original childhood cancer.

Radiation-induced brain tumors (RIBT) have been also reported after benign scalp lesions,

benign and malignant intracranial tumors, and hematologic malignancies^(12,15). The radiation-induced meningioma (RIM) was first reported in 1953, when Mann, et al. described a 4-year-old girl who was treated with 65 Gy for an optic nerve glioma and later developed a meningioma in the irradiated field which eventually became malignant. Meningioma has been reported to be the most common form of the RIBT in the literature^(1,15).

Our patient to whom surgical resection and RT were applied at the age of 8 due to medulloblastoma, had no stigmata of neurofibromatosis or any other hereditary neoplastic diseases. Meningioma in frontal region has developed after 13 years from medulloblastoma treatment. We did chromosome analysis in our case and determined deletion of chromosome 1p and 6q.

CASE REPORT

A 8 year-old male was admitted to another hospital with month-history of occipital headaches. Physical exam at the time of admission demonstrated papilledema and neck stiffness. Computed

tomography (CT) of the head demonstrated a large, solid and enhancing midline posterior fossa lesion with mass effect and obstructive hydrocephalus (Figure 1). The patient underwent midline suboccipital craniectomy. The mass was removed totally. Histopathological examination demonstrated medulloblastoma. The patient was treated with postoperative RT directed at the whole brain (40 Gy), and the posterior fossa as a focal boost (15 Gy). The patient tolerated RT well and did not have any short-term complications. Patient follow-up registry in radiation oncology was available for the next 12 years. Magnetic resonance imaging (MRI) in October 2006 showed no tumor recurrence in posterior fossa and new lesion in the cerebrum. In 2007, at age 21, the patient noted onset of gradual frontal headaches. A neurological examination at that time did not reveal any focal neurologic deficits. MRI demonstrated a left frontal mass (Figure 2). The mass was localized in the frontal dura with a wide base which spread homogeneously by a contrast medium. The patient underwent left frontal craniotomy and the mass removed totally (Simpson Grade 1) (Figure 3). Histopathological examination revealed a menin-



Figure 1. Brain CT in 1998 showed a midline posterior fossa lesion with obliteration of fourth ventricle.



Figure 2. Brain MRI with contrast enhancement examined in 2007 showing a homogeneously enhanced round mass in the left frontal region.

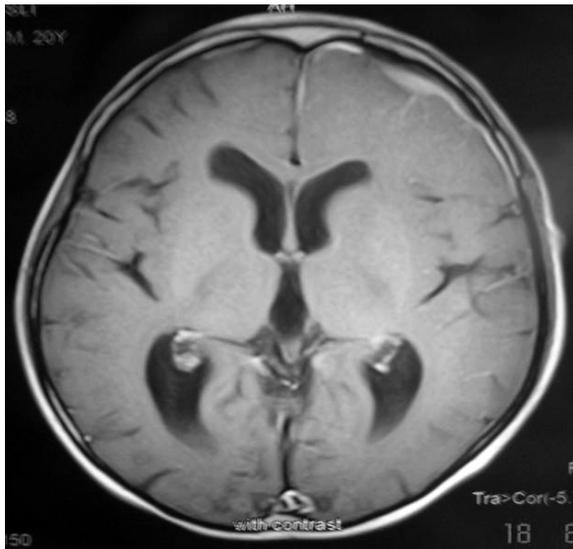


Figure 3. The patient underwent left frontal craniotomy and the mass removed totally. Histopathological examination revealed a meningotheliomatous meningioma

gotherliomatous meningioma (WHO grade I). We did molecular analysis with fluorescence in situ hybridization test (FISH) for our case. Molecular analysis determined deletion of chromosome 6q and 1p. Thereafter, the patient has been on follow-up for the last 21 months with normal neurological examination findings.

DISCUSSION

Dose-response relationships were apparent for meningioma. Most RIMs are induced by low-dose external cranial irradiation (700-1,500 rad) applied to treat scalp and face lesions and include meningiomas developing after treatment of tinea capitis. High-dose radiation RIMs (3,000-6,000 rad) might develop following high-dose radiation therapy applied to the skull to treat other primitive brain tumors, such as optic nerve gliomas, medulloblastomas, pituitary adenomas, and gliomas. For doses in excess of 30 Gy, relative risks were of the order of 50-100 Gy for meningioma⁽¹⁾. RIM following high dose radiation has been reported following a latency period ranging from 1 to 58 years^(2,12,15). The relatively shorter latency period with increasing dose is indicative of a dose response relationship

and leads additional support for the presumed induction of meningioma by radiation⁽⁵⁾. RIMs with high dose developed more rapidly (mean 24.6 years) compared with the low dose group (mean 40 years)⁽¹⁾.

It's quite difficult to differentiate between radiation-induced, and other types of meningiomas. The RIM cases studied revealed features that are similar to common meningioma: a slight female preponderance, middle-aged to elderly predominance, and histologically WHO grade I and II tumors with a low to medium recurrence risk and aggressive behavior^(1,5,13). RIMs have a number of characteristic features: irradiation of the primary condition occurs during childhood, and girls are more susceptible than boys to tumor induction^(1,13). The meningiomas induced are often aggressive or malignant, they are likely to be multiple, and have a high recurrence rate following treatment. Those with a more malignant histology have a shorter latency.

According to Cahan, a meningioma can be considered radiation-induced: if it (1) did not exist before the irradiation, (2) developed in the previously irradiated area, (3) was confirmed by histological studies, and (4) had a latency period of at least 5 years from irradiation (3). To explain the relationship between the irradiation and the induced meningiomas as well as possible pathogenesis of these tumors, it is necessary to consider the high sensitivity of the meningeal tissue to irradiation. It may be hypothesized that meninges might be affected by exposure to very low doses of radiation, such as those produced by diagnostic x-ray studies and CT scanning, as these are the most frequent forms of ionizing radiation exposure of the head⁽⁸⁾. Furthermore, it must be remembered that the meninges of the children are extremely sensitive and, presumably more vulnerable to the adverse effects of radiation and that mesodermal tissues are likewise sensitive to oncogenetic stimulus⁽¹⁵⁾.

Sporadic meningiomas show multiple complex chromosome aberrations. Abnormalities in the 22q locus have been identified as the most frequent finding. Approximately 50 % of sporadic meningiomas exhibit a chromosome 22q abnormality^(13,15,16). The development of RIMs seems to be related to the alteration of the inhibitory effect of the region located near the c-sis gene on the long arm of chromosome 22. Deletions of the short arm of chromosome 1 are the second most frequently detected abnormality during cytogenetic analysis of sporadic meningiomas^(13,15,16). Chromosome 1 abnormalities have been implicated in tumor progression and higher grade meningiomas. The existence of tumor suppressor genes on 1p suggests that detection of the allelic status of chromosome 1p may predict the clinical prognosis of patients affected by this type of brain tumor. Mutations in the neurofibromatosis 2 (NF2) gene have been described in 30 % to 60 % of sporadic meningiomas⁽¹⁴⁾. Unlike sporadic meningiomas, NF2 gene inactivation in RIM group and loss of chromosome 22 are less frequent^(13,14). The pathogenesis of radiation-induced meningiomas seems to be more complex than that of spontaneous meningiomas, and the difference between two types of meningiomas is difficult to explain only with cytogenetic results. We did chromosome analysis in our case and determined loss of chromosome 1p and 6q. These findings have shown a correlation with the result of RIMs reported in the literature.

Medulloblastoma is a primitive neuronal tumor, usually arising in childhood. Treatment is surgical resection followed by craniospinal RT. The prognosis of treated medulloblastoma in children and adolescents has improved during the last 40 years. For patients with localized disease, 5- and 10-year overall survival rates were 59 % and 31 %, respectively⁽¹⁰⁾. As the treatment of medulloblastoma improves, increased numbers of long-term survivors will be exposed to the risk of secondary neoplasms. Only 0.4 % of sec-

ondary tumors which develop from medulloblastoma settle in the brain and CNS⁽⁶⁾. As secondary tumours, meningioma, astrocytoma, oligodendroglioma, and glioblastoma were reported in patients with medulloblastoma^(6,7,10). All of the reported meningiomas that are secondary to medulloblastoma have developed because of high-dose radiation^(1,2,4,5,7,15). After high-dose radiation for medulloblastoma, RIMs were described following latency periods ranging from 2.2 to 36 years^(2,5,15). In a patient with medulloblastoma, only 36 % of meningiomas emerging after a long latency period settle in posterior fossa⁽¹⁵⁾. The reason might be application of the whole brain irradiation apart from focal boost in the treatment of medulloblastoma.

In conclusion, RIM at children with medulloblastoma is increasing recently, probably in relation to the increased long-term survival rates in patients with medulloblastoma. When RT is indicated, use of the minimally effective dose may reduce the risk of secondary CNS neoplasms emerging many years later. The RT given may have influenced the subsequent cytological changes of tumor cells. Chromosomal analyses in tumors which develop secondary to medulloblastomas will be useful in understanding the relevant pathology. Prolonged follow-up of all pediatric cancer survivors, particularly those exposed to radiation, is crucial to the early detection of these tumors and should be considered part of the effective therapy of the primary disease.

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