Frontal Lobe Radionecrosis Following Radiotherapy of an Extracranial Tumor

Ekstrakraniyal Bir Tümörün Radyoterapisi Sonrasında Oluşan Frontal Lob Radyonekrozu

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Abstract: Cerebral radionecrosis is uncommon but important complication of radiation therapy of extracranial and intracranial tumors. In this report we present a case who operated for squamous cell carcinoma of left eyelid and received radiotherapy a total dose of 5250cGy after operation 18 months before admission. She admitted to our clinic with headache and generalized seizures which started in last month. Cranial MRI showed a dense lesion about 4x4 cm. in the left frontal lobe. The patient was operated and mass was removed totally. Histopathological findings were regarded as vascular changes secondary to radiotherapy and coagulative necrosis. Based on a review of the literature a possible mechanism of necrosis, treatment methods and clinical outcome are discussed.

Key Words: Radionecrosis, brain tumor, extracranial tumor, radiotherapy

Introduction

Cerebral radionecrosis is a rare but well known complication of radiotherapy for intracranial or extracranial tumors (4,11,12,15,17). It may develop as a result of irradiation of nasopharenx, orbita, paranasal sinuses and parotis (1,5,10,15,16). Vedly varying frequency of occurrence (0.5%-25%) has been reported (4,11,17).

Radiation induced brain injury may develop as; an acute reaction to irradiation during the radiotherapy, a temporary post-radiation necrosis occurring several months after receiving radiation or a delayed radiation necrosis occurring many months even years after radiation therapy. Most delayed radiation necrosis may appear as intracranial mass lesions. They are life threatening in most cases and need to be surgically removed.
Although there are different views on the risky doses, irradiation above 60Gy is generally believed to cause necrosis in the brain (4,8,9,17). The occurrence of radiation therapy related central nervous system injuries are dependent on both treatment factors such as fraction size, total radiation dose, treatment volume, and host factors such as tissue sensitivity, sublethal damage repair time, concurrent diseases like diabetes mellitus, hypertension according to Normal Tissue Complication Probability Theory. When conventional fraction size used, TD 5/5 which represents the dose of radiation that could cause no more than a 5% severe complication rate for whole brain irradiation is 45 Gy, 1/3 brain irradiation is 60 Gy and TD 50/5 which represents the dose of radiation that could cause no more than a 50% severe complication rate for whole brain irradiation is 60 Gy, 1/3 brain irradiation is 75 Gy.

It is important to note that most frequent cerebral necrosis have been reported in recent years than before. Reasons for this include; relatively higher doses with unconventional external beams fraction size and techniques such as interstitial brachytherapy, stereotactic radiosurgery, concomitant use of radiosensitizers, to increase survival rate.

CASE REPORT

A 56 year old female patient was admitted to our clinic with acute headache started about a month ago. She also experienced epileptic seizures twice during that period. The patient had a history of squamous cell carcinoma located on left eyelid with invasion to extraocular muscles.

She had undergone enucleation with eyelid excision and a course of postoperative radiotherapy with daily 250cGy fractions to a total dose of 5250cGy (250x21 fraction) using anteroposterior and left lateral fields to cover left orbital region, Co 60 teletherapy machine in a private center. Two 45 degree wedge filters was applied to achieve homogenous dose distribution. There was no information regarding selected planning target volume, obtained isodose distribution, the amount and the region of the brain volume exposed to irradiation. Neurological examination of the patient indicated intact functions except enucleated left eye.

Cranial magnetic resonance imaging (MRI) demonstrated a dense lesion of about 4 cm. in length in the frontal white matter. MRI revealed a diffuse swelling appearance characterized by T2 flair hyperintensity at a lesion site. The mass showed heterogenous peripheral opaqueness after contrast injection (Figure 1).

![Figure 1: Cranial MRI demonstrated a dense lesion compressed the left ventricle](image1)

With these findings, the patient was operated and left frontal craniotomy was performed. The gray and relatively necrotic mass was completely removed. Histopathologic features of the specimen showed inflammation and gliosis in the brain parenchyma, vascular hyalinization, infiltrating lymphocytes and coagulative tissue necrosis. These findings were regarded as vascular changes secondary to radiotherapy and coagulative necrosis (Figure 2).

![Figure 2: Histopathologic features of the specimen; vascular hyalinisation and infiltrating lymphocytes was seen.](image2)
Postoperative period was complication free and the patient discharged from hospital in one week. She expressed no further complaints during her last examinations 3 months after operation.

DISCUSSION

Radiation induced necrosis in brain parenchyma can be caused by either vascular damage or a direct damage to parenchymal cells although vascular damage is accused to be the causative agent in most cases (11,12). The histopathological evaluation of our case confirmed the hypothesis of vascular damage as vascular hyalinisation, coagulative necrosis and infiltrative lymphocytes were the dominant changes.

Total radiotherapy dose, fraction dose, volume and radiotherapy techniques, are the important factors for development of radiation induced complications in brain. Complication probability can be estimate using fraction size, total radiation dose, treatment volume, sublethal damage repair time. Increased fraction size, total dose and treatment volume increased the complication rate. Tolerance doses are defined considering percent irradiated whole organ volume. Treatment dose and volume description is administered using the estimated probability rate. Among these, fraction size is considered as the most critical factor followed by others. In the present case, fraction dose was 2.5 Gy which is not in conventional fraction dose (1.8 -2 Gy) range and rather higher. To find out equivalent conventional fractionation schedule of used unconventional fractionation schedule of this case, Linear Quadratic Formula was used.

Formula: BED: n.d(1+d: a/b)

n: Fraction number, d: Fraction dose, BED : Biologic equivalent dose

a/b: Suggested values were 1.5, 2, 3 Gy therefore all three values were used in calculations.

Calculated fraction numbers (n) are 30 in all three namely 1.5, 2, 3 Gy a/b values. This means equivalent conventional fractionation total dose is approximately 60 Gy with conventional fraction size 1.8 -2 Gy. Occurrence of severe complication probability in this dose level is negligible. Therefore we assume that large fraction size could responsible of the radiation damage in the present case. The use of larger dose than conventional fraction size must be approached cautiously. Furthermore, the rate of irradiated volume to whole brain should be considered.

Oppenhaimer and colleagues (9) have reported cases of delayed radiation necrosis following a wide range of 20-69 Gy therapeutic doses. Rubin and colleagues (12) report an approximate 5% occurrence of radionecrosis above total doses of 5000cGy. In a report including findings from 68 patients, Glass and collaborators (4) suggested the risky dose as above 4500cGy. In summary; total doses below 5000cGy are generally considered less risky in terms of the formation of radionecrosis. However daily doses and the fractions are considered as critical in reducing the risk for necrosis, as the total dose applied (2,7,17). A daily dose of 200cGy is considered safe. In this regard, the daily dose of 250cGy given to our patient during radiotherapy was most likely a major factor in the formation of cerebral necrosis.

Although the radiation induced necrosis is a well documented complication, serious challenges exist in diagnosis using radiological techniques or MRI. It is often difficult to differentiate a necrosis from a tumor by computerized tomography (CT) or MRI(3). Positron emission tomography (PET) is suggested as one of the most powerful techniques in diagnosis (11,14). In addition 18f-PET and dynamic CT and magnetic resonance spectroscopy are also valuable tools in diagnosis of radionecrosis(6,13,14). During the diagnostic process of our case, the histopathology observed in the left frontal lobe was thought as a tumor, at first, since a tumor in the left eyelid had already been removed. However, it was identified as radionecrosis based on postoperative examination of the tissue (which would otherwise be difficult using CT or MRI).

There are no different opinions about the treatment of radionecrosis. If there is notable
increase in intracranial pressure, surgical remove of the necrotic tissue seems to be the most appropriate treatment.

As a conclusion, it is demonstrated in our case that presence of an intracranial mass in patients treated for extra/intracranial pathologies using radiotherapy could be an indication of radionecrosis. Thus the possibility of radionecrosis, in addition to the possibilities of recurrence or metastasis need to be seriously considered in diagnosis.

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REFERENCES:

10) Ostwald PM, Cooper SG, Denham JV, Hamilton CS. Dosimetry of high energy electron therapy to the parotid region. Radiotherapy and Oncology;33:148-156, 1994