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Recurrent Tumor or Radionecrosis

Rekürrent Tümör yada Radyonekroz

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ABSTRACT

It is important to distinguish tumor recurrence from radionecrosis because subsequent therapy and prognosis are guided by the cause of progression. Necrosis is an important histological feature of glial tumors. Tumor necrosis is due to an insufficient blood supply and is ischemic in nature. Differentiating tumor recurrence from radiation necrosis can be difficult. We report a case and discuss the importance of differentiating tumor necrosis from radiation necrosis in patients with irradiated glioma.

KEY WORDS: brain tumor, magnetic resonance imaging, radionecrosis, radiotherapy.

ÖZ

Tümör rekürrensi ve radyonekroz ayırımını yapmak uygun tedaviyi planlamak ve prognoz açısından önemlidir. Nekroz glial tümörlerin önemli histolojik özelliklerindendir. Tümör nekrozu yetersiz kan desteği ve iskemi sonucudur ve radyasyon nekrozundan ayırımı zor olabilir. Biz burada radyoterapi gören hastalarda tümör nekrozu ve radyasyon nekrozu ayırıcı tanısının önemini bir olgu eşliğinde tartışıyoruz.

ANAHTAR SÖZCÜKLER: Beyin tümörü, manyetik rezonans görüntüleme, radyonekroz, radyoterapi.

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INTRODUCTION

Various pathological changes can occur in response to radiation therapy administered to or near the central nervous system. Necrosis is an important histological feature of glial tumors. Tumor necrosis is due to insufficient blood supply and is ischemic in nature. Differentiation from radiation necrosis can be difficult. In fact, both are coagulative necrosis types. After optimum surgical and radiation treatments in a patient with glioma, clinical or radiographic evidence of progression may develop because of tumor recurrence, radiation necrosis or both. Radiation-induced neoplasms have been reported on rare occasions (2,3). The differential diagnosis of tumor necrosis and radiation necrosis in patients with irradiated glioma is discussed.

CASE REPORT

This 46-year-old male patient underwent right frontoparietal craniotomy on December 29, 1999 for a mass which proved to be glioblastoma multiforme. Total gross resection of the tumor was followed by radiotherapy and chemotherapy.

The patient was neurologically intact and functional until February 2002 when he developed moderate left hemiparesis. Cranial magnetic resonance imaging (MRI) disclosed recurrence of the tumor. The patient was reoperated on February 28, 2002. Subtotal resection of the tumor was performed along with duraplasty. The histopathological diagnosis was the same as previously.

The patient was rehabilitated postoperatively but the left hemiparesis subsequently worsened and the cranial MRI showed regrowth of the tumor. MR images showed postoperative changes in the right frontopariteal region. Multifocal, patchy contrast enhancement was seen in the wall of cavity in the anterior part of the operation zone (Figure 1). T2-weighted and FLAIR images demonstrated irregular, shaggy, hyperintense signal changes in the white matter close to the operation zone (Figure 2). A solid mass lesion, showing homogenous contrast enhancement and which progressed in the follow-up was detected in the posterior part. The patient was operated again on November 11, 2002. At surgery, the tumor was grossly totally removed using ultrasonic aspiration. An encephalomalasic area, anterior to the tumor site but completely separated from it by normal brain tissue was also removed for histopathological evaluation. Histopathologically,

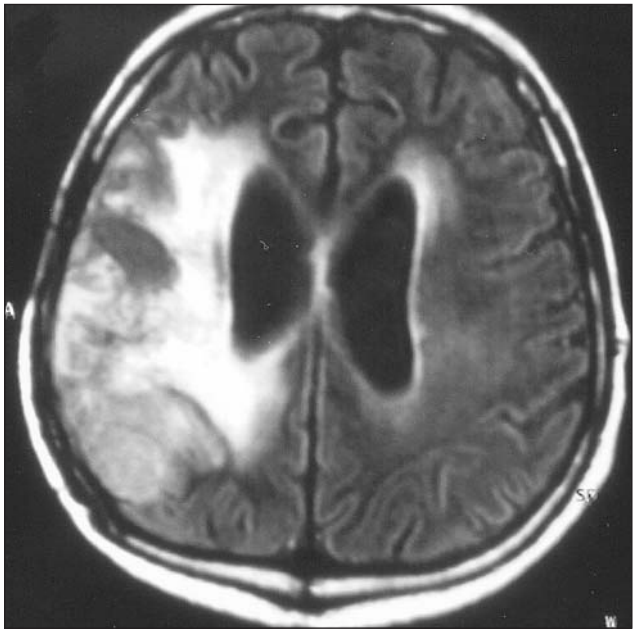

Figure 1: Axial FLAIR weighted image shows irregular, shaggy hyperintense signal changes in the white matter close to the operation zone and in the posterior part of this area a solid mass lesion.

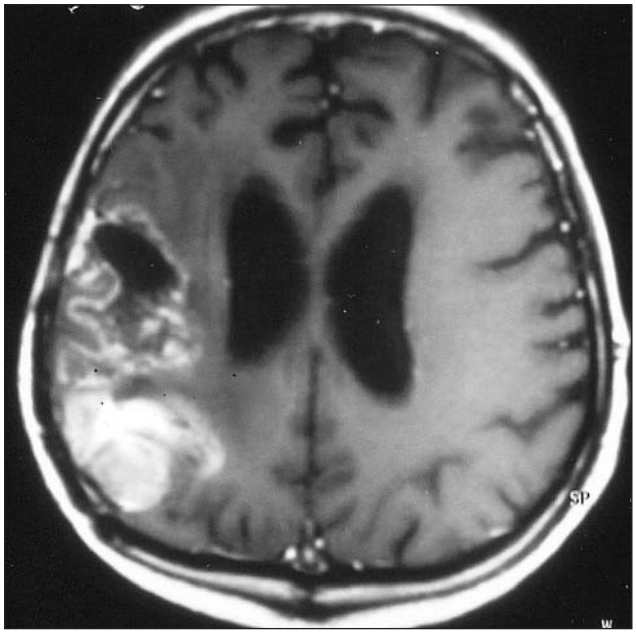

Figure 2 : Axial T1 weighted contrast enhanced image demonstrates irregular contrast enhancement in the wall of operation cavity and solid mass lesion enhancing heterogenously.

areas of radionecrosis were observed as poorly delimited zones of eosinophilic necrosis, often patchy in distribution and unassociated with pseudopalisading. Necrotic, thrombosed vessels with hyalinised walls were noted in the center of

necrosis (Figure 3). Areas of radionecrosis were observed in approximately 30-40% of the tumoral specimens. Necrosis, endothelial proliferation and atypical glial cells were noted in the tumor tissue (Figure 4). There were also prominent cellular pleomorphism, nuclear atypia, bizarre cells and mitotic figures in the tumor (Figure 5).

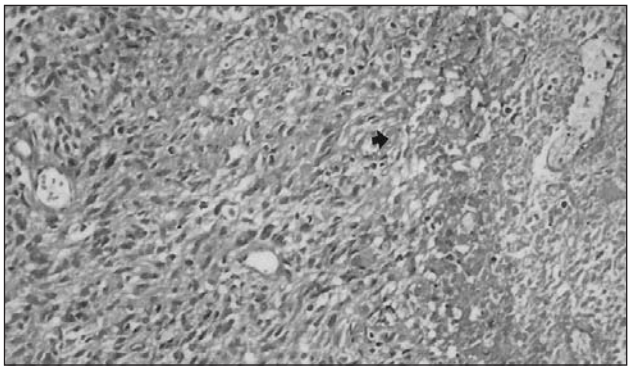

Figure 3: Higher magnification of necrosis areas (arrow) in GBM (H&E X 200).

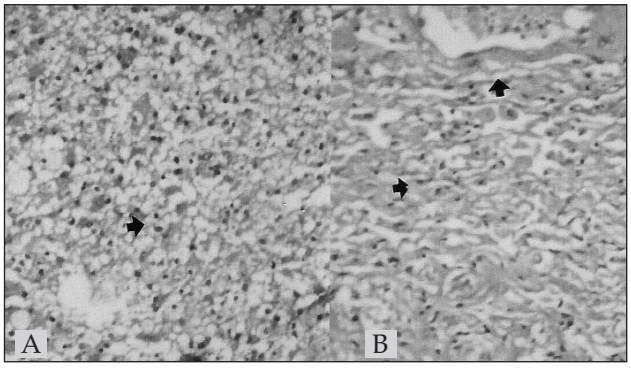

Figure 4: Photomicrograph showing late delayed reaction, **A**: necrosis (small arrows), lack of pseudopalisading were seen (H&E X200) and **B**: fibrinoid necrosis of blood vessel (arrow)

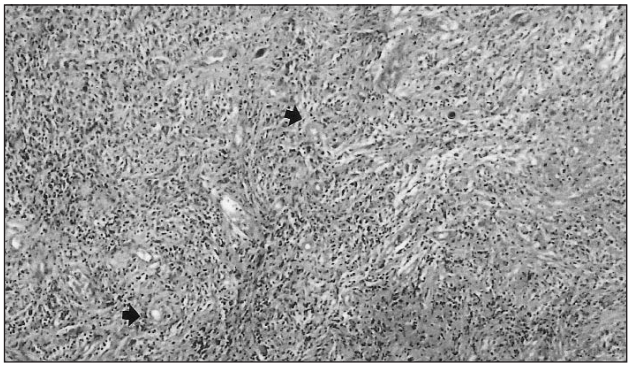

Figure 5: Residual tumor (GBM): Peripheral palisading of malignant cells around areas of necrosis (pseudopalisading) and endothelial cell proliferation (arrows) in GBM are seen at low power. (H&E X40).

DISCUSSION

It is important to differentiate tumor recurrence from radionecrosis because subsequent therapy and prognosis are guided by the cause of progression. The different types of radiation injury to the central nervous system include focal radiation necrosis, diffuse white matter injury (i.e. nonnecrotizing leukoencephalopathy), and necrotizing leukoencephalopathy (6). Damage to the cerebral vasculature is believed to be the underlying etiology of radiation necrosis. Vascular alterations include heterogeneous endothelial hyperplasia, fibrinoid necrosis of the penetrating arterials, vascular occlusions, and morphologic changes as seen in large vessel atherosclerosis. There is disruption of the blood-brain barrier, which causes the vasogenic edema seen on the CT scan as well as the increased signal seen on the T2 weighted images (1, 4, 6).

There appears to be an increased likelihood of radiation necrosis when patients receive a standard regimen versus the hyperfractionated doses. Patients receiving the standard treatment also develop radiation necrosis sooner than patients receiving hyperfractionated doses. Patients receiving methotrexate therapy in combination with central nervous system (CNS) radiation also have increased risk (1,6).

On MRI, the abnormal brain areas are is hypointense in unenhanced T1weighted and hyperintense on T2-weighted images. After administration of contrast material, no enhancement is seen on non-necrotizing leukoencephalopathy areas and nothing in necrotizing leucoencephalopathy areas. On the other hand, enhancement is observed at the gray-white matter junction in the acute phase of necrotizing leucoencephalopathy . Patients with radiation necrosis may have focal or multifocal areas of enhancement in the periphery of the usually central necrotic process. (5,6)

The differential diagnosis includes CNS infection and recurrent neoplasm. Serial MRIs of the brain may show an absence of progression, which would strongly suggest radiation necrosis. However, a tumor cannot be excluded when the radiation necrosis is progressive. There is evidence that positron emission tomography (PET) would help in differentiating radiation necrosis from metastatic

disease or recurrence of tumor. PET mainly detects glucose uptake and consumption of tumor cells, and its main limitation is its low spatial resolution. There is evidence that PET scanning would help in differentiating radiation necrosis from metastatic disease or recurrence of the tumor, but this technique is not widely available and may be uninformative if the lesion is hypometabolic (5-7).

Besides PET, MR Spectroscopy (MRS) and MR perfusion may demonstrate viable tumor tissue. They can be effectively be used for the differential diagnosis of these two entities and they are now widely available in most of MR units. MR Spectroscopy is a useful in vivo examination for analyzing the metabolites of the human brain in small concentrations. High choline and low N-acetyl aspartate levels are detected in recurrent tumors, while decrease or absence of major metabolites is usually seen in radiation necrosis. However, there are shortcomings with the practical application of MRS in the reliable assessment of the metabolic composition of the brain, because of inaccuracies in quantification caused by magnetic inhomogeneities and because of degradation of the spectral resolution from the overlapping of peaks from unwanted metabolites (8, 9). MRS data obtained from our patient was not useful for the same reasons.

Perfusion MR imaging used to to noninvasively measure cerebral perfusion via assessment of various hemodynamic measurements such as cerebral blood volume, cerebral blood flow, and mean transit time. Potential applications of perfusion MR imaging include noninvasive histological assessment of tumors as well as differentiation radiation necrosis from recurrent tumor by assessing regional blood flow and volume (10-11). We could not performed perfusion MR imaging in our patient since it was not available in our institution.

Radiation effects on the CNS are often delayed and can be divided into three categories. Acute reactions are associated with impaired blood-brain barrier function and lead to edema. Early delayed reactions occur several weeks following radiotherapy. Damaged white matter and mild vascular hyalinization are observed in this phase. The late delayed reactions are the most common postirradiation changes seen in autopsy material. They consist of coagulative tissue necrosis with glial reaction and fibrinoid or hyaline changes of blood vessels with abnormal endothelial cells and perivascular fibrosis. These changes are not specific (3).

Necrosis is an important histological feature of glial tumors. Necrosis of the tumor is due to insufficient blood supply and is ischemic in nature but its differentiation from radiation necrosis can be difficult. Radiation necrosis is often patchy, ill defined, calcified, and extends into the surrounding brain. Radiation necrosis is not associated with pseudopalisading. A distinctive feature is thickened vessels, which may show hyalinization or fibrinoid necrosis indicative of radiation damage (2, 3).

This case serves as a reminder of the importance of the differentiating tumor necrosis from radiation necrosis in patients with irradiated glioma. Survival time is known to be short in patients with recurrent glioma while it is variable and may be longer if there is little mass effect with radionecrosis.

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