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Malignant Meningioma; Tumor Recurrence or Radiation Necrosis? Can Magnetic Resonance Spectroscopy-Perfusion İmaging Help?

Malignant Meningioma; Tümör Rekurrensi veya Radyasyon Nekrozu? Manyetik Rezonans Spektroskopi-Perfüzyon Görüntüleme Yardım Edebilir mi?

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To the Editor,

Meningioma is the most common primary brain tumor in adults. Most meningiomas (90%) are benign, 6% are atypical and a small proportion (2%) are malignant (1, 2). Rarely, they show an aggressive course with an increased recurrence rate and dissemination to intracranial sites or outside the central nervous system (CNS). These tumors may cause focal or generalized seizures or focal neurological deficits by compression of adjacent neurological tissues with progressive increase in size (3).

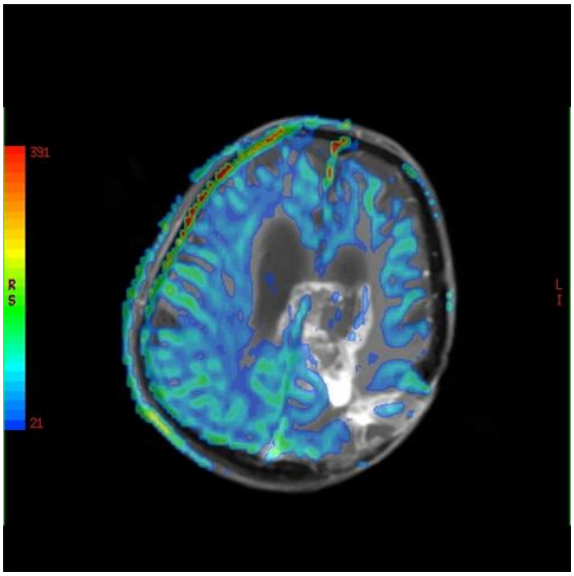

Figure 1. In the perfusion analysis the mass showed any perfusion

Primary choice of treatment is surgery and complete surgical resection is often curative. For most incompletely resected or recurrent tumors not previously irradiated, radiotherapy is the treatment of choice. Radiotherapy may be administered as either conventional external beam irradiation or stereotactically by linear accelerator, gamma knife or cyber knife radiosurgery (1, 3). Stereotactic radio surgery (SRS) is a common approach for patients with meningioma and is an effective, efficient and generally well-tolerated form of treatment for these patients. Unfortunately, SRS leads to radio necrosis in ~10% of patients which can potentially result in progressive neurologic deficit (4, 5). Radiation-induced neurotoxicity in CNS can occur in three ways. Acute toxicity occurs during or immediately after radiation treatment; early delayed neurotoxicity occurs within up to 12 weeks following treatment; and delayed neurotoxicity develops and progresses within 3 months to a few years following treatment. Other forms of delayed radiation neurotoxicity include radiation leukoencephalopathy, radiation myelopathy and, in the peripheral nervous system, plexus or nerve root lesions. It can lead to a mass effect, cranial nerve paralyses, hypothalamo-hypophyseal deficiency and deterioration in mental functions of patients (6).

We aimed to present a case with malignant meningioma that developed recurrent disease which was treated with radiotherapy following surgical excision of the recurrent disease. During follow up a mass lesion at the site of the prior disease radiological consistent with radiation necrosis was detected. The differentiation between a tumor recurrence or radiation necrosis was not histopathologically confirmed in this patient since the patient

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refused the procedure. Differential diagnosis of these conditions is discussed in the light of current literature.

A 64-year-old male patient admitted to the hospital with headache which started and progressed in the last three months. His physical examination and history was not peculiar. His complete blood count and biochemical tests were in normal ranges. Cranial computerized tomography (CT) revealed 2x3 cm mass at the left parietal region of brain. The mass was excised surgically. Histopathological diagnosis was malignant meningioma, WHO grade 3. The patient was followed without any complaints until he began to have headache 3 years after surgery. Repeated cranial CT scan showed 3x4.5 cm recurrent mass at the site of prior surgery. Patient was treated with 14 Gy gamma knife radio surgery targeting enhancing gross tumor volumes without margin.

About seven months after gamma knife, he had deterioration in his mental status. Repeated cranial CT showed a 3x5.5 cm mass with peripheral edema in left parietal region. He was treated with dexamethasone at a dose of 10 mg intravenous bolus and 4x4mg intravenous maintenance. To distinguish tumor recurrence from radiation necrosis biopsy was planned but the patient refused the procedure so, magnetic resonance imaging (MRI) of the brain was applied. It showed a 3×5.5 cm left parietal mass, at the level of vertex, confounding with a field of surrounding edema, which was hypo-intense at T1 weighted sequences, relatively hyper-intense at T2 weighted sequences, and showed a peripheral contrast enhancement after administration of intravenous contrast agent (ICA). Magnetic resonance spectroscopy (MRS) and magnetic resonance perfusion imaging (MRPI) were performed since radiation necrosis was suspected because of the presence of hyper-intense areas at T2 weighted and FLAIR sequences at pons, left cerebellar hemisphere, and bilateral peri-ventricular white matter areas. In the MRPI analysis the mass showed any perfusion (Figure 1). An evident decrease in choline, creatine, and N-acetyl aspartate (NAA) peaks were found compared with the normal brain parenchyma at MRS study (Figure 2). Necrosis due to radiation was diagnosed rather than tumor recurrence as a result of these tests. Dexamethasone treatment was continued in decreasing doses. Simultaneously, hyperbaric oxygen therapy (HBOT) was administered. HBOT was comprised of 20 sessions at 2.0 atmospheres, for 90 minutes. Patient's mental status meliorated dramatically.

The degree of effects of radiation on CNS is dependent on various factors including the total radiation dose administered, fractionation dose, total treatment duration, radiotherapy administered tumor volume and type of radiation treatment. Additional factors include whether concomitant chemotherapy is administered or not, and the existence of co-morbidities as hypertension, diabetes mellitus and vascular diseases (7). Necrosis develops usually at the site exposed to the highest dose; in other words, the site adjacent to the tumor. It is thought that cerebral edema increases the sensitivity to radiation because the majority of the radiation related lesions occur at the white matter surrounding the tumor tissue (4).

Pathological examination of the tissue specimen is necessary for the exact diagnosis of radiation necrosis. Coagulation necrosis at white matter, fibrinoid necrosis at vascular walls and telangiectasia's are the main pathological findings of radiation necrosis (7, 8).

Differential diagnosis of tumor recurrence after radiotherapy and radiotherapy related tissue injury is very important for making efficient treatment planning in patients with meningioma who have a history of surgery and radiotherapy. Although histopathological examination is necessary for the diagnosis (9), Radiological procedures such as cranial CT and MRI can also be useful. MRS-MRPI results show a high correlation with histopathological findings of radiation necrosis and tumor recurrence. MRS can detect possible sites of radiation necrosis and MRPI shows decreased NAA and choline peaks at these areas compared to normal tissues. Although low choline levels might be seen at both tumor

tissue and necrosis decreased NAA peaks are seen at areas of necrosis but not at tumor tissue (6, 10). In the presented case, radiation necrosis was suspected rather than tumor recurrence regarding the findings at imaging study and clinical status of the patient. Choline and NAA peaks were clearly decreased when compared with normal brain parenchyma at MRS-MRPI study of this case.

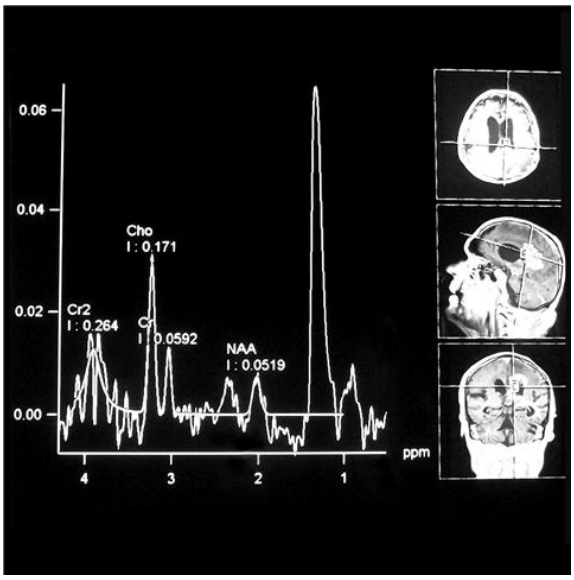

Figure 2. MR spectroscopy shows a decrease intensity N acetyl aspartate, choline and creatin and increase lactate peak in 1.2ppm

Steroids are generally the first line treatment to control symptoms and signs related to edema and mass effect. But efficiency of corticosteroids in treatment of brain edema related to radiation necrosis is limited (11). They inhibit the pro-inflammatory response seen in the radio necrotic mass. One of the most commonly chosen agent, dexamethasone, also acts through transcriptional and post-transcriptional mechanisms to reduce the radiation-induced cytokine response along with enhancement of normal brain function (6, 11). HBOT reduces cerebral edema, normalizes brain water content and limits brain infarct in the treatment of such patients. It decreases the risk of seizures, prevents the occurrence of motor deficits, and recurrent cerebral circulation disturbances. HBOT stops the progression of necrosis due to radiation and provides a survival improvement. Cognitive function recovery was observed when HBOT is used in patients with brain radiation necrosis (12). HBOT stimulates angiogenesis, fibroblast and osteoblast proliferation as well as collagen formation in irradiated tissues, and increases cellular levels of oxygen (6). In our case dexamethasone and HPOT provided a recovery in mental functions of the patient. So, this treatment regimen may be conceivable in patients similar to ours. In the present case, patient and primary relatives of the patient denied invasive procedures and radiation necrosis was diagnosed on the basis of radiological imaging techniques (brain MRI, MRS and MRPI studies) in the absence of histopathological diagnosis. Addition of MRS-MRPI studies to the routine radiological procedures might be useful for the differential diagnosis of tumor recurrence or radiotherapy associated tissue injury in patients who refuse invasive testing. Such patients may also benefit from dexamethasone and HBOT treatment.

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