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Original Article

Usefulness of apparent diffusion coefficient value and proton magnetic resonance spectroscopy as a noninvasive techniques in recurrent cerebral gliomas

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ABSTRACT

Objective: Conventional MRI does not provide sufficient information to differentiate post-radiotherapy necrosis from brain tumor recurrence, recent studies have investigated the use of more advanced imaging modalities that are able to differentiate between the two entities.
Aim of the study: To assess the usefulness of combined apparent diffusion coefficient (ADC) value and single voxel spectroscopy (SVS) in the differentiation between recurrent brain gliomas and post-radiotherapy necrosis.
Methods: Twenty-two patients with suspected tumor recurrence after surgical resection and radiotherapy treatment were included in our study. MRI with contrast, diffusion weighted MRI with ADC value and MR spectroscopy were done to all patients.
Results: ADC values were $\leq 1.150 \times 10^{-3}$ mm^2/sec for recurrent high grade gliomas, >1.150–$\leq 1.370 \times 10^{-3}$ mm^2/sec for recurrent low grade gliomas and $>1.370 \times 10^{-3}$ mm^2/sec for post radiation necrosis. NAA/Cr ratio could significantly differentiate between recurrent gliomas and post radiation necrosis (p value = .019), also Cho/Cr was significant p value = .006. Also NAA/Cr and Cho/Cr were statistically significant in differentiating recurrent high grade from low grade gliomas (p value < .001).
Conclusion: Combination of calculated ADC value and MR spectroscopy added more information and increase the accuracy of conventional MR imaging in the differentiation of patients with suspected recurrent brain glioma from post-radiotherapy necrosis.

1. Introduction

In adults, gliomas are the most common type primary brain tumor. Grade of these lesions is based on their degree of aggressiveness [1]. In brain gliomas, contrast-enhanced magnetic resonance imaging (CE-MRI) is still representing the main tool for evaluating the treatment response, and it is based on the size of the lesions, and pattern of enhancement, which are estimating bad prognosis and failure of treatment [2]. It is unfortunate that, radiotherapy of gliomas can induce changes on CE-MRI mimicking tumor recurrence, it is called post-treatment radiation effect (PTRE). Pseudoprogression has been primarily reported in patients who underwent radiotherapy for GBM [3]. In high grade brain glioma, multiple studies showed later disappearance of the abnormal enhancement lesions following radiation treatment [4,5].

In the era of more belligerent management of brain tumors, including recent new adjuvant strategies such as gamma-knife and stereotactic radiosurgery, the clinical manifestation and imaging pattern of post-radiotherapy necrosis and tumor recurrence can be confusingly similar. Because the treatment choices and prognosis are different completely, differentiation between radiation necrosis and tumor recurrence is considered a challenging task. Re-operation with surgical biopsy is often required to be sure of the diagnosis before further management can be arranged [6].

Because of this, current studies have investigated the use of more advanced imaging techniques that are skillful to study physiological and metabolic properties of tumor. These functional imaging techniques include CT/MR perfusion, diffusion weighted

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imaging (DWI), MR spectroscopy, single-photon emission computed tomography (SPECT), and positron emission tomography (PET) [7–9].

Because of conventional MRI does not provide sufficient data to differentiate delayed radiation therapy effects from tumor recurrence [10], diffusion-weighted (DW) imaging and calculation of apparent diffusion coefficient (ADC) have been used to discriminate the normal white matter areas from necrosis, cyst formation, brain edema, and enhanced solid tumor. DWI and ADC values are considering very effective in the grading and differentiation of brain tumor types depending on molecular diffusion [11].

MR spectroscopy (MRS) shows the abnormal data in nearly 100% of cerebral tumors, it is beneficial in the differentiation of cerebral tumors and in characterization of metabolic changes related to tumor progression and treatment response [11].

MR spectroscopy is used to assess infiltrating brain tumors since choline elevation can extend to areas without contrast enhancement or to tissue that looks normal on conventional MRI. An elevation of myoinositol indicates zones of active glial activation due to a reaction toward infiltrating tumor cells. Lactate and lipids can be used as indicators for higher tumor grades, as does increased choline [12].

MR spectroscopy, including single and multivoxel spectroscopic imaging. Multivoxel spectroscopic imaging methods are useful and more adequate to identify glioma grade and allow selective evaluation of different parts of the target volume. Although single-voxel spectroscopy (SVS) is a reliable technique for analysis of tumor grade with a short acquisition time, the voxel placement is considering critical to the examination and may affects the data obtained [12].

On the other hand, the end point of radiation injury is radionecrosis which considers the worst adverse effect of the radiotherapy. Generally, Radionecrosis occurs 3–12 months after radiotherapy but can occur up to years or even decades later on. The developed radionecrosis process depends on irradiated brain volume, radiotherapy dose and chemotherapy association. The radionecrosis incidence is higher in patients, who treated with radiochemotherapy than those treated with radiotherapy alone. Conventional MR techniques frequently cannot differentiate between radionecrosis and tumor recurrence, further advanced MRI techniques help in the analysis of original tumor or necrotic tissue properties and also, providing more accurate data on its nature [13].

The aim of our study was to assess the usefulness of calculating ADC value and SVS in the differentiation between possibly recurrent brain gliomas from post-radiotherapy necrosis (radionecrosis).

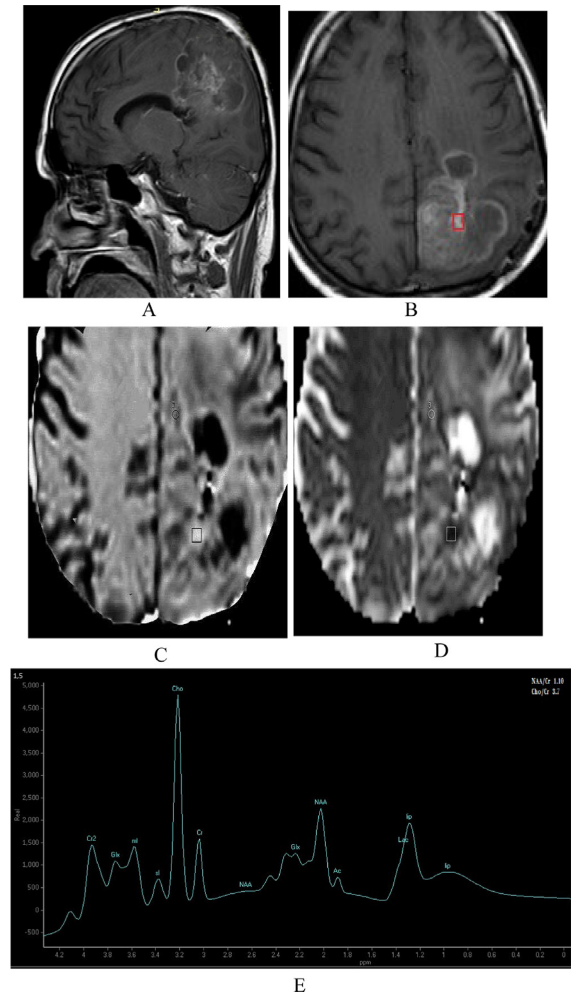

Fig. 1. A case of recurrent high grade glioma in 55 years old male post resection of left parietal tumor (histopathologically proved as glioblastoma multiforme. The patient had completed radiotherapy since 6 months and was presented with headache and vomiting. (A) & (B) *Sagittal and axial post contrast T1WIs:* demonstrate a heterogeneously enhanced lesion with cystic component in the Left parafalcine parietal region. (c) Diffusion weighted image and (D) Corresponding *ADC map:* ADC value = 0.1.1 $\times 10^{-3}$ mm^2/s. (E) *Single voxel MR spectroscopy with voxel placed on the focal enhancing lesion at (B). The spectra reveals:* increased Cho peak, decreased NAA peak, with Cho/Cr ratio = 3.7, and NAA/Cr ratio = 1.1.

2. Patients and methods

Twenty-two patients (13 males and 9 females) were included in our study, all patients were suspected to have a tumor recurrence. They all had surgical resection and radiotherapy treatment of histopathologically proved cerebral gliomas. All patients completed radiotherapy treatment by at least 6 months, with no other inclusion or exclusion criteria required. Through, stereotactic biopsy histopathological specimens were obtained then grading was done according to World Health Organization (WHO) II criteria [14]. All patient gave written consent after explaining the aim of study to them. Our MRI results were collected and correlated with the final diagnosis obtained by the biopsy.

2.1. MRI examination

All examinations were performed on a 1.5-T MR imaging and spectroscopic scanner (Achiva Philips medical system) using a dedicated standard head coil (see Figs. 1–3).

Conventional MRI was performed for all patients. The examination was sequenced as follow: axial T1 weighted spin-echo (SE), axial T2 weighted fast SE, and axial FLAIR (fluid-attenuated inversion-recovery). DWI was acquired by using an axial echo-planar SE sequence (5000/65), ms repetition time/echo time [TR/TE]; 5-mm section thickness; diffusion gradient encoding in three orthogonal directions-diffusion sensitization factor [*b*-value] at 500 and 1000 s/mm^2, 240 mm field of view; 160 $\times$ 160 matrix in one minute. Then, contrast enhanced T1 weighted SE sequence was acquired in axial, sagittal and coronal planes after intravenous administration of Gadopentetate Di Meglumine (Magnevist®; Bayer Schering Pharma AG, Berlin, Germany), the used dose was 0.1 mmol/kg of body weight.

In 3 orthogonal directions, diffusion gradient encoding was obtained at; b = 1000 s/mm^2; FOV, 220 mm; matrix pixels = 128 $\times$ 64; 5 mm section thickness; also, section gap = 0.2 mm; and NSA, 1. When DWI data acquisition was obtained, a post – processing ADC maps with automatic calculation of the ADC values were performed immediately using the standard provided software.