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A High Grade Gliomatosis Cerebri Case Report; MR, Diffusion MR and MR Spectroscopy Findings

Yüksek Greydli Gliomatozis Serebri Olgusu; MR, Diffüzyon MR ve MR Spektroskopi Bulguları

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Summary

Gliomatosis cerebri is a rare primary diffuse cerebral malignity. ''It is characterized by the diffuse proliferation of neoplastic glial cells that involve more than two cerebral lobes. For a definitive diagnosis histopathological examination is required. Advanced magnetic resonance imaging techniques are very useful in the pretreatment diagnosis-staging and post-treatment follow-up. In this report a patient with gliomatozis cerebri was presented with magnetic resonance, diffusion weighted imaging and magnetic resonance spectroscopy findings. In addition, the importance and the role of magnetic resonance spectroscopy in the diagnosis and staging of gliomatosis cerebri is discussed. *(Turkish Journal of Neurology 2014; 20:16-19)*
Key Words: Gliomatosis cerebri, anaplasia, diffusion weighted imaging, MR spectroscopy

Özet

Gliomatozis serebri, nadir görülen bir primer diffüz beyin tümörüdür. Beynin ikiden fazla lobunu tutan neoplastik glial hücrelerin diffüz proliferasyonu ile karakterizedir. Kesin tanı için histopatolojik inceleme gereklidir. Gelişmiş manyetik rezonans görüntüleme yöntemleri tümörün preoperatif tanısında, evrelendirilmesinde ve tedavi sonrası takiplerinde oldukça faydalıdır. Bu makalede anaplazi gösteren bir gliomatozis serebri olgusu manyetik rezonans görüntüleme, difüzyon ağırlıklı görüntüleme ve manyetik rezonans spektroskopi bulguları eşliğinde sunulmuştur. Ayrıca manyetik rezonans spektroskopinin gliomatozis serebri tanı ve evrelemesindeki, rolü ve önemi değerlendirilmiştir. (Türk Nöroloji Dergisi 2014; 20:16-19)
Anahtar Kelimeler: Gliomatozis serebri, anaplazi, difüzyon ağırlıklı görüntüleme, MR spektroskopi

Introduction

Gliomatosis cerebri (GC) is a rare, diffuse primary brain tumor. It was first described in 1938 by Nevin (1). It is characterized by the diffuse proliferation of neoplastic glial cells involving more than two lobes of the brain. Infratentorial structures and spinal cord can also be involved (2,3). According to the central nervous system (CNS) classification of World Health Organization, it is categorized under neuroepithelial tumors of unknown origin. Its histopathology is not fully known but most of the histological findings indicate that the pathology is of diffuse, infiltrative, and early stage astrocytoma origin (1,4).

Advanced magnetic resonance (MR) imaging methods can be used in the diagnosis, differential diagnosis, staging and post-treatment follow-up of GC (3). The aim of the present paper is to present the findings from routine MR sequences, diffusion-weighted MR imaging and MR spectroscopy of a case with malign-transforming GC and its post-treatment control images. The roles of diffusion-weighted MR and MR spectroscopy in the staging of the tumor are also evaluated.

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Case

30-years-old female patient consulted in our neurology policlinic with numbness in her left arm and leg. Her complaints were going on for 3 months and had recently got worse. She also experienced attentional deficit and impaired mental functions. Her family and medical history was unremarkable. She showed right central type facial paralysis in her neurological examination. The muscle strength in her upper left and lower left extremities were assessed as 3/5. She did not show any other neurological findings. Her routine hemogram and biochemical tests were normal.

Her MRI showed vaguely outlined infiltrative lesions in her frontal and parietal lobes bilaterally, in the splenium of the corpus callosum, right temporal lobe, right thalamus and basal ganglia, appearing hypointense in the fluid-attenuated inversion recovery (FLAIR) and T2-weighted images and iso-hypointense in the T1-weighted images. Right thalamus and right lateral ventricle were compressed due to the mass effect of the lesion on the right side and the midline was shifted towards left. Right frontal and parietal cerebral sulci and fissures were narrowed. A mild contrasting was detected in the lesioned areas on both parietal lobes following intravenous contrasting agent administration (Figure 1). Secondary to the diffusion restriction, an increased signal intensity in the b: 1000 images and a decreased signal intensity in the apparent diffusion coefficient (ADC) images were seen in these areas observed in the diffusion-weighted imaging (Figure 2). In the multivoxel MR spectroscopy examination using long echo time (TE: 135 ms), maximum choline/creatine (Cho/Cr), choline/N-acetylaspartate (Cho/NAA) and NAA/Cr ratios were obtained from the spectrum of the right parietal tumor region. These measurements were Cho/Cr: 5.68, Cho/NAA: 20.34 and NAA/Cr: 0.27. On the contralateral normal brain parenchyma, these values were Cho/Cr: 0.99, Cho/NAA: 0.32 and NAA/Cr:

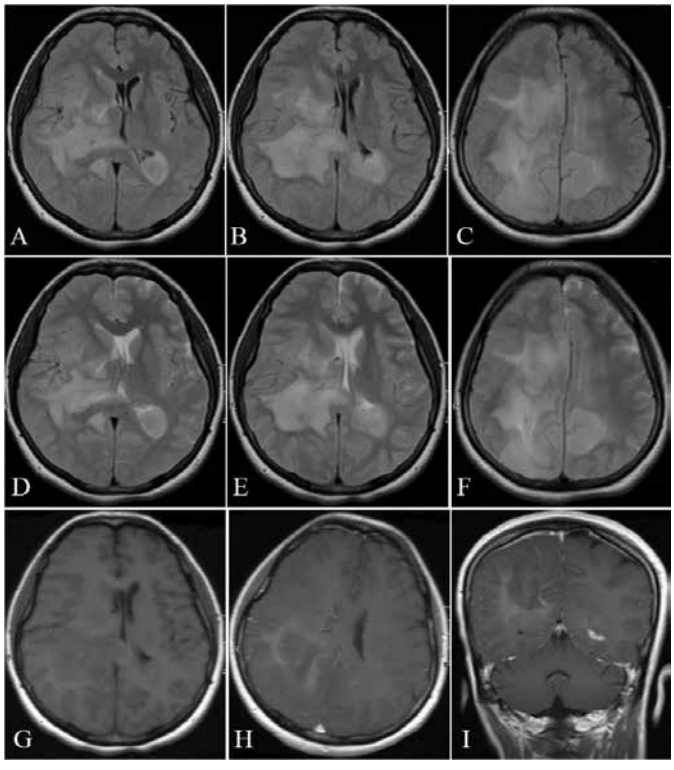

Figure 1. MRI showing vaguely outlined infiltrative lesions in her bilateral frontal and parietal lobes, splenium of the corpus callosum, right temporal lobe, right thalamus and basal ganglia, appearing hypointense in the axial FLAIR (A, B, C) and T2-weighted (D, E, F) slices and iso-hypointense in the T1-weighted (G) slice. Secondary to the mass effect, right ventricle is compressed and there's a shift towards left. There is mild contrast in the lesion areas on the parietal lobes seen in the post-contrast T1-weighted axial (H) and coronal (I) images.

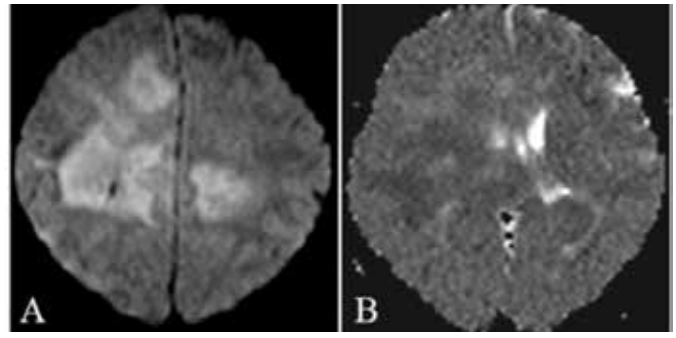

Figure 2. Secondary to the diffusion restriction, increased signal intensity in b: 1000 images (A) and decreased intensity in ADC (B) in the diffusion-weighted images.

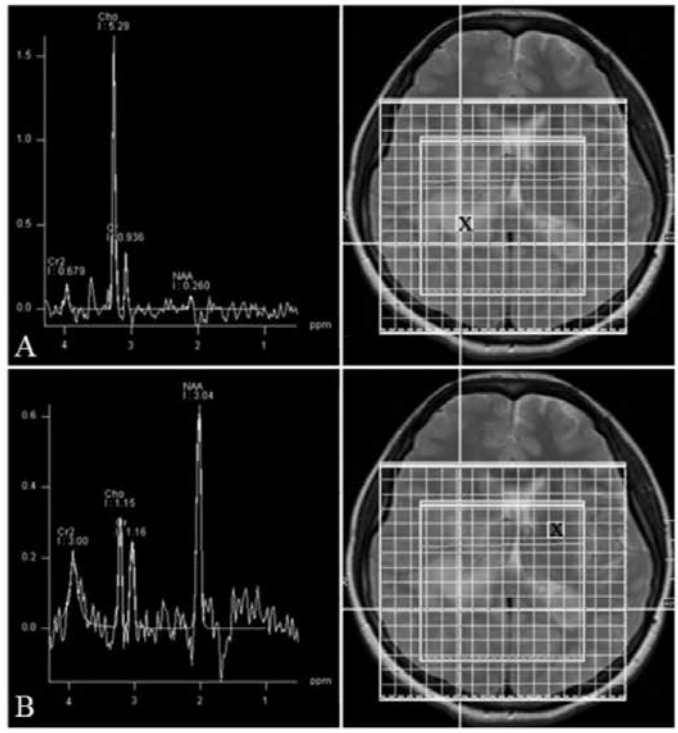

Figure 3. In the MR spectroscopy, increase in Cho level (A) and decrease in NAA and Cr levels in the right parietal lesion areas. Normal brain parenchyma values for Cho, NAA and Cr are seen on the left cerebral hemisphere (B).

2.62 (Figure 3). The apparent increase in Cho/NAA and Cho/Cr ratios and the decrease in NAA/Cr suggested that the tumor was at the advanced stage. The stereotactic biopsy made on the right parietal lobe suggested it to be a advanced stage glial tumor of astrocyte origin. Based on these radiological and histopathological findings, the case was diagnosed as GC.

The patient was given 5000 centigray external radiotherapy concurrent with 75 mg/m^{2}' temozolomide. Anti-edema treatment was also started but then gradually tapered off. In the 6th month follow-up MR after the treatment, the mass effect of the lesion on the right side was completely gone. Right lateral ventricle compression and leftward shift were not observed. The lesion areas seen as increased signal intensity in the T2 and FLAIR sequences were slightly reduced. Intravenous contrast agent administration did not cause any contrast in the lesion areas. In addition, signal increase was observed in the FLAIR, T2 and T1-weighted images of the left parietal area, possibly due to the bleeding accompanying radiation necrosis (Figure 4).

The patient missed the follow-up controls and died after 6 months.

Discussion

Gliomatosis cerebri is a rare tumor. It is seen in almost all age groups but more prevalent between 40-50 years of age (1,3). It is more frequent in males than in females (5).

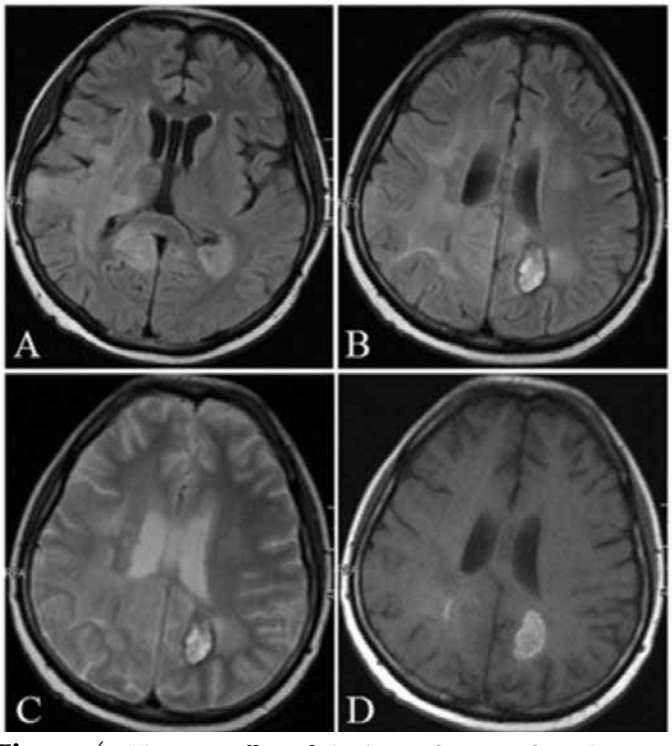

Figure 4. The mass effect of the lesion disappeared in the post-treatment. There is no right ventricle pressure or leftward shift. There is a mild improvement in the lesion areas seen as increased signal in the axial FLAIR (A, B) and T2-weighted (C) images. On the left parietal, signal increase possibly due to the bleeding caused by radiation necrosis can be seen in FLAIR, T2 and T1 images.

In GC, the diffuse infiltration of the neoplastic glial cells into nerve bundles does not cause apparent necrosis, cystic and hemorrhagic changes. The neurons are relatively preserved. Subsequently, the clinical profile is non-specific and varied, and also uncorrelated with MR findings (3). In a study evaluating 160 cases retrospectively, the most common neurological symptoms were corticospinal tract findings with 58% and personality changes with 48%. Also in this study, 39% reported headaches, 38% seizures, 37% cranial neuropathy, 34% intracranial pressure increase and 33% reported spinocerebellar deficit (1). The literature also includes cases that consulted in dementia clinics (6). Our case also had corticospinal tract involvement, consciousness changes, impaired mental functions and facial paralysis.

The tumor can develop as primary or as secondary to the proliferation of existing cerebral neoplasm (7).

Gliomatosis cerebri is characterized by the involvement of at least two brain lobes but it can involve the entire CNS. It was reported that outside of cerebral hemispheres, 75% of thalamic nuclei, 50% of corpus callosum, 10%-15% of brainstem and spinal cord and 10% of cerebellum could be involved (5).

Often of astrocyte origin, neoplastic proliferation can be either oligodendrocyte or mixed type (2). In a study including 296 patients, the most frequent type was seen to be of astrocytic origin with 108 patients. In this study, 54 of the tumors were of oligodendrocyte origin, 17 were of mixed type and 117 were undifferentiated (8).

Cranial CT findings are non-specific and therefore insufficient for the diagnosis. Magnetic resonance imaging is much more sensitive compared to cranial CT and superior in terms of visualizing the areas of involvement. The lesion areas are seen hyperintense in T2 and FLAIR, and hypointense in T1-weighted images. The signal increase in T2-weighted sequence indicates tumoral cell infiltration and therefore myelin break down. Contrast involvement can be observed as a result of blood-brain barrier destruction due to tumoral cell infiltration. This is meaningful for anaplasia (3,9,10). Ware et al.'s study reported that the contrast involvement in the lesion is the strongest determinant in the negative prognosis (11).

The literature includes studies where the advanced stage brain tumors are differentiated from the early stage ones using diffusion-weighted MRI. In a study by Kang et al., it was shown that the ADC values obtained from the tumors in the diffusion-weighted imaging can be used in staging the tumor. In this study, stage IV tumors had lower ADC values and there was a statistically significant difference between stage II and IV, and stage II and IV tumors (12). In our study as well, a restricted diffusion and low ADC values were obtained much like advanced stage tumors.

Magnetic resonance spectroscopy is a valuable noo-invasive tool in the diagnosis and staging of brain tumors. In the case of GC, the reduced peak of NAA is the most commonly observed finding. Choline/creatinine and Cho/NAA ratios increase. The choline levels are generally elevated but they can also remain at the normal ranges. It is indicated that the high myo-inositol and glycine ratio in the absence of choline peak is characteristic for gliomatosis cerebri. Choline/N-acetyl asparate ratio is related to the tumor's stage and prognosis (9,10,13). In a study, patients with early stage (stage II) lesions showed a mild increase up to 1.3 in Cho/NAA while this ratio was 2.5 in anaplastic lesions and 8.9 in advanced and stage IV tumors (14). Even though the increase

of lactate is regarded as an indicator of bad prognosis, this issue is still under debate. While a lactate peak could be found in advanced stage tumors, the studies caution that it should not be taken as a reliable determinant of malignity or bad prognosis. The area where choline/N-acetyl asparate ratio is the highest is used for staging the tumor. In addition, it allows the determination of the area for open or stereotactic biopsy (10). In our study, the stereotactic biopsy on the right parietal lobe, which was the area with the highest choline/NAA ratio in the multi-voxel MR spectroscopy, determined the tumor as advanced stage glial tumor.

Differential diagnosis between GC and other neurological diseases with prominent white matter involvement should be made. Such diseases may include progressive multifocal leukoencephalopathy, multiple sclerosis, acute disseminated encephalomyelitis, viral encephalitis, CNS vasculitis, Behçet disease, cerebrovascular diseases and venous sinus thrombosis. Magnetic resonance spectroscopy contributes to the differential diagnosis (5). An increase in acute ischemia and infarction peak is observed. In the chronic stage, NAA, Cho, Cr and lactate peaks decrease (15,16). In the demyelinating lesions, lactate peak is observed as a function of the inflammation during the acute stage. Due to the myelin destruction, Cho and lipid increase can be seen. In the chronic stage, reduced Cho and NAA peaks are noteworthy (17,18). The glutamine/glutamate ratio in the tumefactive demyelinating lesions was found to be high in a study. It was reported that this finding, which is not observed in intraaxial brain tumors, can be used in the diagnosis of demyelinating lesions (19). The aminoacid, acetate and succinate peaks in the infectious brain lesions can be used in the differential diagnosis of neoplastic lesions (20). However, in a meta-analysis of 26 studies on MR spectroscopy concluded that there is not enough evidence showing that MR spectroscopy provides adequate information for the differential diagnosis between neoplastic and non-neoplastic lesions (21).

The optimum treatment method for GC is not currently known. Radiotherapy and chemotherapy are generally used in conjunction. Surgical treatment is only used for decompression in cases where intracranial pressure is increased. The survival durations after the treatment range between 13 and 22 months (2). One study reports that the prognosis for men, young people and for oligodendrocyte-origin tumors is more favorable (8).

In conclusion, advanced imaging techniques such as diffusion-weighted MR and MR spectroscopy are complementary to the routine MR sequences in the evaluation of GC. It should be remembered that diffusion-weighted MR and MR spectroscopy can be used as non-invasive methods in staging GC.

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