www.jkns.or.kr http://dx.doi.org/10.3340/jkns.2011.50.2.119
Print ISSN 2005-3711 On-line ISSN 1598-7876
J Korean Neurosurg Soc 50 : 119-122, 2011

Case Report

Glioblastoma Mimicking Herpes Simplex Encephalitis

Tai-Seung Nam, M.D.,[1,2] Kang-Ho Choi, M.D.,[1,2] Myeong-Kyu Kim, M.D.,[2] Ki-Hyun Cho, M.D.[2]
Department of Neurology,[1] Chonnam National University Hwasun Hospital, Hwasun, Korea
Department of Neurology,[2] Chonnam National University Medical School, Gwangju, Korea

We report a case of 70-year-old man with glioblastoma presenting as acute encephalitic illness. The patient exhibited sudden onset of cognitive impairment and headache for 2 days. Initial brain MRI showed left temporal lobe hyperintensity, and cerebrospinal fluid cytology revealed a mild pleocytosis. The patient had initially improved after medical treatment with a presumptive diagnosis of herpes simplex encephalitis (HSE). After 8 months, the patient complained of recurrent seizures. A follow-up brain MRI revealed marked increases in size and surrounding perilesional edema in the left temporal lesion on T2-weighted images and a new contrast-enhancing lesion on gadolinium-enhanced T1-weighted images. Stereotactic brain biopsy revealed a glioblastoma. The atypical encephalitic presentation of glioblastoma should be considered if definitive evidence for the diagnosis of HSE cannot be obtained.

Key Words : Glioblastoma · Herpes simplex encephalitis.

INTRODUCTION

Glioblastoma is the most common and most malignant primary brain tumor in adults, and in fact, comprises approximately 50% of the cases occurring in patients aged greater than 65 years[7]. The diagnosis of glioblastoma bestows a poor prognosis for patients in all age groups; however, elderly patients seem to be affected the greatest exhibiting poorer survival rates than younger patients[5].

It is not difficult to identify brain tumors upon clinical presentations, brain MRI, and Fluorine-18 fluorodeoxyglucose positron emission tomography (^{18}F-FDG-PET) scans. However, it can often be hard to distinguish temporal lobe tumors from herpes simplex encephalitis (HSE), if they are presented as the temporal lobe lesion with acute encephalitic illness. Here we describe a case of a man with acute encephalitic symptoms who was initially misdiagnosed with HSE, but was finally diagnosed as glioblastoma.

CASE REPORT

A 70-year-old man was admitted to our hospital due to cognitive impairment, mild fever, and headache for 2 days. On neurological examination at the time of admission, memory impairment was observed, while cranial nerve dysfunction, limbs weakness, or sensory loss were not. Initial brain MRI showed a hyperintense lesion without enhancement in the left medial temporal lobe (Fig. 1A-E). Electroencephalography (EEG) revealed a slowing on the left temporal derivations. ^{18}F-FDG-PET scans revealed a well-circumscribed area of increased uptake of FDG in agreement with the involved lesion seen on brain MRI (Fig. 1F). Examination of CSF revealed white blood cell of 9/mm^3 (0-5/mm^3), protein levels of 45 mg/dL (15-50 mg/dL) and glucose levels of 65 mg/dL (45-80 mg/dL). Herpes simplex virus-Polymerase chain reaction (HSV-PCR) assay in the CSF was negative. CSF cytospin analysis for the detection of malignant cells and viral cultures were also negative. Seoul Neuropsychological Screening Battery revealed prominent cognitive impairment (Table 1). After treatment with intravenous acyclovir (30 mg/kg/day for 14 days) and methylprednisolone (1 mg/day for 5 days) under the diagnosis of HSE, his cognitive function was improved. After being discharged from hospital, the patient was lost to follow-up for several months.

Eight months after being discharged, the patient revisited due to repetitive seizures and drowsy mentality. A follow-up brain MRI revealed a marked increase in the size of the left temporal lesion on T2-weighted image (Fig. 2A, B, C). A gadolinium-enhanced T1-weighted image showed a new contrast-enhancing lesion (Fig. 2D, E). EEG revealed focal or lateralized sharp-and/or slow-wave complexes over the left temporal derivations. The patient was taken to the operating room, and subsequently underwent a stereotactic brain biopsy and left temporal lobecto-

• Received : October 26, 2010 • Revised : March 3, 2011
• Accepted : August 8, 2011
• Address for reprints : Tai-Seung Nam, M.D.
Department of Neurology, Chonnam National University Hwasun Hospital,
322 Seoyang-ro, Hwasun-eup, Hwasun 519-763, Korea
Tel : +82-62-220-6175, Fax : +82-62-228-3461
E-mail : nts0022@hanmail.net

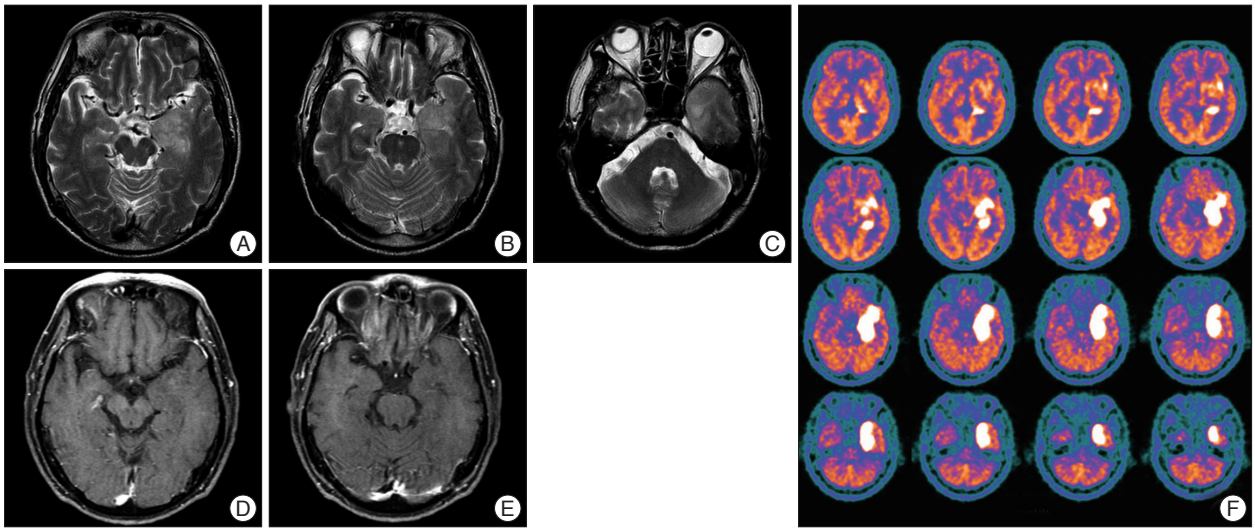

Fig. 1. Brain MRI and Fluorine-18 fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) scan at admission. Axial T2-weighted image shows a hyperintense lesion with mild swelling in the left medial temporal lobe (A, B and C). Gadolinium-enhanced T1-weighted image shows normal findings (D and E). Transaxial PET scan reveals a well-defined region of increased uptake of ^{18}F-FDG in the left medial temporal lobe (F).

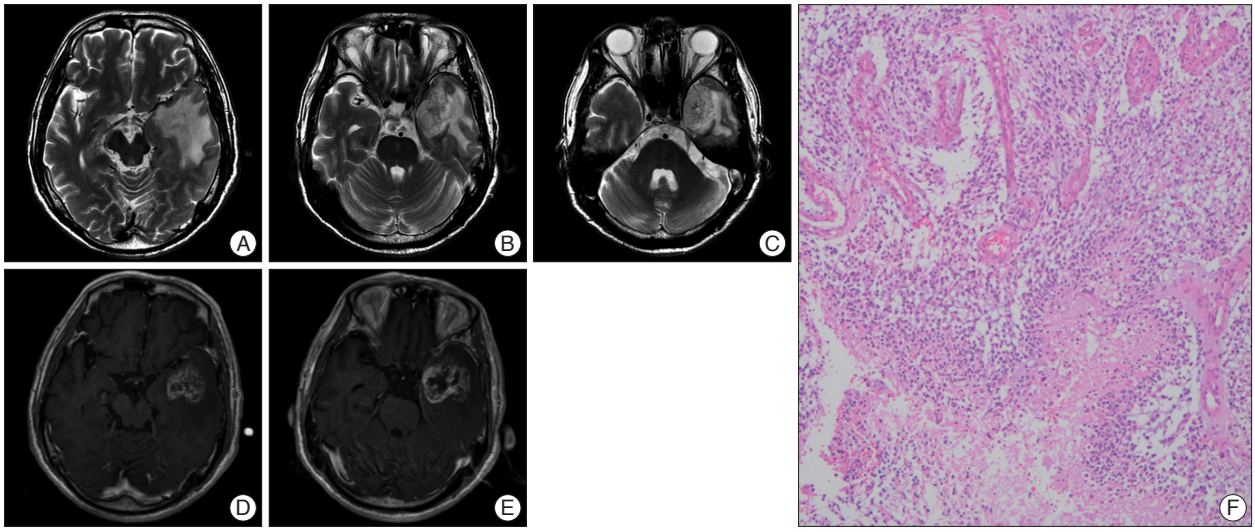

Fig. 2. Brain MRI and pathologic examination at an 8-month follow-up. Axial T2-weighted image shows an extensively diffuse hyperintense lesion with central necrosis, marked perilesional edema in the left temporal lobe and compression of the left cerebral peduncle (A, B and C). Gadolinium-enhanced T1-weighted image shows an irregular peripheral rim-enhancement with central necrosis and surrounding perilesional edema (D and E). Pathologic examination reveals an increased cellularity, tumor necrosis, and endothelial cell proliferation (hematoxylin and eosin stain, ×100) (F).

my, followed by postoperative radiotherapy. The histopathologic finding of the lesion revealed an increased cellularity, tumor necrosis, and endothelial cell proliferation (Fig. 2F). Further, the tumor cells had an immunoreactivity for glial fibrillary acidic protein. Immunohistochemical staining for Ki-67 revealed a high proliferation index. These findings were compatible with the diagnosis of glioblastoma.

DISCUSSION

This case highlights unusual central nervous system (CNS) manifestations in a patient with temporal lobe glioblastoma. The presenting encephalitic symptoms, CSF findings, brain MRI, and ^{18}F-FDG-PET scans are suggestive of HSE. However, similar clinicoradiological findings for glioblastoma and HSE, can lead to delays in the diagnosis of glioblastoma and treatment of patients, and thus resulting in significant cerebral morbidity and poor prognosis.

HSE is the major cause of serious sporadic encephalitis with a predilection for the temporal lobe[8]. Therefore, intravenous acyclovir should be continued until the temporal lesion is diagnosed as any other diseases except HSE, because failure to consider the possibility of HSE can lead to a delay in accurate diagnosis and proper treatment, with a significant risk of mortality and morbidity[3]. The HSV-PCR assay of the CSF is an invaluable test in the diagnosis of a patient with suspected HSE. However, it sometimes tends to remain false-negative in the acute phase of HSE because the intensity of the PCR product

band of an earlier CSF sample is weak[1]. For this reason, the negative result of the HSV-PCR assay in our case was overlooked and acyclovir continued to be intravenously administrated. The patient improved at the time of discharge. In retrospect, it may have been due to the corticosteroid effect but not acyclovir administration.

Primary and metastatic brain tumors, including glioblastoma, can present as acute encephalitis or encephalopathy, although the frequency is very low. Ginsberg and Compston[6] reported that 1 (1.5%) out of 65 patients with acute encephalitis actually had a brain tumor (oligodendroglioma). Whitley et al.[12] reported that 5 (5.3%) of 95 patients who were biopsy-negative for HSE had brain tumors, of whom 3 had primary CNS tumors (2 patients with glioblastomas and 1 patient with primary CNS lymphoma) and 2 had metastatic colon adenocarcinoma. Further, Rees and Howard[11] reported 3 patients with high grade gliomas mimicking acute viral encephalitis. They suggested that stereotactic brain biopsy should be considered in patients with temporal lobe masses if a definitive diagnosis using PCR assays for common viruses is unavailable. If we had performed stereotactic brain biopsy on our patient based on the initial CNS manifestations, functional deficits would have been much less severe.

MRI, ^{18}F-FDG-PET, and Proton-MR spectroscopy (MRS) scans of the brain are commonly done in the work-up of patients who appear clinically to have had a brain tumor. First, MRI is more sensitive than computerized tomography (CT) in the detection of brain tumors. However, it has been occasionally encountered the patients whose initial MRI were negative or had mild abnormalities, and soon thereafter had high grade glioma[2]. Second, ^{18}F-FDG uptake is generally high in high-grade tumors or in anaplastic transformation of previously known low-grade tumors[7]. However, Lee et al.[10] reported that ^{18}F-FDG-PET hypermetabolism can be observed in the acute phase of encephalitis due to active inflammation[9]. Third, MRS features of glioblastoma tend to have elevated lipid signal, whereas those of acute encephalitis tend to have elevated myoinositol signal and gradual normalization after the initial acute phase of encephalitis. However, encephalitis tends to resemble low-grade glioma or gliomatosis cerebri with reduced N-acetylaspartate signal and elevated choline and myoinositol[4]. After all, in suspected tumors, serial brain imaging studies are needed to document the evolution of brain tumor and to rule out underlying encephalitis. In our case, additional brain MRI could not be performed in our case due to loss of follow-up. If we had performed short repeat brain imaging after being discharged, early surgical removal for temporal lobe glioblastoma would have been sufficiently available.

Table 1. Results of neuropsychological tests

Tests	Response
Attention	
Digit span : forward/backward	5/3
Letter cancellation	NL
Language and related functions	
Spontaneous speech	Fluent
Contents	NL
Comprehension	NL
Repetition	15/15
S-K-BNT	5/15
Reading	NL
Writing	NL
Praxis	NL
Finger naming	NL
Right-left orientation	AB
Calculation	AB
Body part identification	NL
Visuospatial Functions	
Interlocking pentagon	NL
RCFT	22/36
Memory	
SVLT 1st/2nd/3rd	2/3/2
Delayed recall	0
Recognition score	12
RCFT immediate recall	6.5/36
RCFT delayed recall	4/36
RCFT recognition score	16
Frontal executive functions	
Motor impersistence	NL
Contrasting program	NA
Go-no-go test	NA
Fist-edge-palm	AB
Alternating hand movement	B
Alternating square and triangle	NL
Luria loop	NL
K-MMSE	21/30
CDR	1
GDS	23/30
B-ADL	20/20

S-K-BNT : short form of Korean version of the Boston Naming Test, RCFT : Rey complex figure copy test, SVLT : Seoul verbal learning test, K-CWST : Korean-color word stroop test, K-MMSE : Korean version of minimental status examination, CDR : Clinical dementia rating scale, GDS : Geriatric depression scale, B-ADL : Barthel activities of daily living, AB : abnormal, NL : normal, B : borderline, D : deformed, NA : not available

CONCLUSION

High-grade brain tumors may present as acute encephalopathy with temporal lobe involvement by brain imaging. Therefore, an intensive follow-up with short repeat brain imaging as well as stereotactic biopsy is necessary in patients with temporal lobe masses if definite evidence for the diagnosis of HSE cannot be obtained.

References

1. Al-Okaili RN, Krejza J, Wang S, Woo JH, Melhem ER : Advanced MR imaging techniques in the diagnosis of intraaxial brain tumors in adults.

Radiographics 26 Suppl 1 : S173-S189, 2006
2. Aurelius E, Johansson B, Sköldenberg B, Staland A, Forsgren M : Rapid diagnosis of herpes simplex encephalitis by nested polymerase chain reaction assay of cerebrospinal fluid. **Lancet 337** : 189-192, 1991
3. Chen W : Clinical applications of PET in brain tumors. **J Nucl Med 48** : 1468-1481, 2007
4. Demaerel P, Wilms G, Robberecht W, Johannik K, Van Hecke P, Carton H, et al. : MRI of herpes simplex encephalitis. **Neuroradiology 34** : 490-493, 1992
5. Fisher JL, Schwartzbaum JA, Wrensch M, Wiemels JL : Epidemiology of brain tumors. **Neurol Clin 25** : 867-890, vii, 2007
6. Ginsberg L, Compston DA : Acute encephalopathy : diagnosis and outcome in patients at a regional neurological unit. **Q J Med 87** : 169-180, 1994
7. Iwamoto FM, Cooper AR, Reiner AS, Nayak L, Abrey LE : Glioblastoma in the elderly : the Memorial Sloan-Kettering Cancer Center Experience (1997-2007). **Cancer 115** : 3758-3766, 2009
8. Kimberlin DW : Management of HSV encephalitis in adults and neonates : diagnosis, prognosis and treatment. **Herpes 14** : 11-16, 2007
9. Landy HJ, Lee TT, Potter P, Feun L, Markoe A : Early MRI findings in high grade glioma. **J Neurooncol 47** : 65-72, 2000
10. Lee BY, Newberg AB, Liebeskind DS, Kung J, Alavi A : FDG-PET findings in patients with suspected encephalitis. **Clin Nucl Med 29** : 620-625, 2004
11. Rees JH, Howard RS : High-grade glioma mimicking acute viral encephalitis-three case reports. **Postgrad Med J 75** : 727-730, 1999
12. Whitley RJ, Cobbs CG, Alford CA Jr, Soong SJ, Hirsch MS, Connor JD, et al. : Diseases that mimic herpes simplex encephalitis. Diagnosis, presentation, and outcome. NIAD Collaborative Antiviral Study Group. **JAMA 262** : 234-239, 1989