A Case of Gliomatosis Cerebri Mimicking Limbic Encephalitis: Malignant Transformation to Glioblastoma

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Abstract

Gliomatosis cerebri (GC) is a specific entity defined as diffuse infiltration of neoplastic glial cells into at least three cerebral lobes and preservation of the surrounding neuronal architecture. We report a patient with secondary GC that mimicked clinicoradiological features of limbic encephalitis (LE). A 72-year-old man had developed headache and disorientation insidiously 2 weeks previously. On admission, neurological examination showed confusion and hyperreflexia in the right extremities. Brain magnetic resonance imaging (MRI) revealed T2-hyperintensity in bilateral frontal, the left parietal, the left temporal lobes and bilateral posterior periventricular zones. Slight enhancement existed in the left lower temporal region. Cerebral angiography exhibited no tumor stains. Repeated cerebrospinal fluid studies showed mild pleocytosis and cytology of class I. There were no infectious pathogenic agents. His neurological symptoms were ameliorated at 7 days after treatment with dexamethasone and glycerol. Follow-up MRI showed no pathognomonic changes. Mild memory dysfunction remained. He was diagnosed as LE of unknown cause. Three months later he became disoriented. Brain CT revealed a hemorrhagic mass with surrounding edema in the left temporal, frontal and parietal lobes. MRI displayed marked enhancement in these regions. Urgent neurosurgery was performed and glioblastoma multiforme (GM) was confirmed pathologically. The early clinicoradiological course of this patient suggested similarities to LE. At 3 months after clinical onset, the neuroradiological features reflected rapid transformation from secondary GC to massive GM. Thus, it is important to pay more attention to the differential diagnoses of GC and LE in patients who have memory deficits and widespread MRI lesions.

Key words: gliomatosis cerebri, secondary type, limbic encephalitis, glioblastoma multiforme

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Introduction

Gliomatosis cerebri (GC) is a rare form of glioma described by Nevin (1) in 1938. According to the World Health Organization (WHO) classification of brain tumors GC is identified as a clinicopathological entity. In the fourth edition of the WHO classification of tumors of the central nervous system, published in 2007, GC (code 9381/3) is defined as diffuse infiltration of neoplastic glial cells into at least three lobes and preservation of the surrounding neuronal architecture (2). Neuroradiological profiles have been described in reports of pathology-proven GC patients (3-6). Here, we report a patient who had secondary GC which mimicked the clinicoradiological course of limbic encephalitis (LE).

Case Report

A 72-year-old man had developed headache, fever and disorientation insidiously 2 weeks previously, and was admitted to our department. Physical examination showed blood pressure of 148/90 mmHg and body temperature of 37.8°C. Japan coma scale was 2 with confusion. Muscle stretch reflexes were brisk in the right upper and lower extremities without Babinski’s sign. The remaining neurological examination was normal. On routine laboratory testing, white cell count was increased to 17,000/mm³ (neutrophilic
leukocytes of 94.5%) and C-reactive protein was 1.1 mg/dL. Brain CT disclosed obscure cerebral gyri in the left frontal and temporal regions (Fig. 1A and 1B). Fluid-attenuated inversion recovery (FLAIR) imaging revealed hyperintensity signal areas in bilateral frontal, the left parietal and the left temporal lobes. Hyperintense signal areas were also found around the posterior regions of bilateral lateral ventricles (Fig. 2A and 2B). Hyperintense lesions spread to the left cerebral hemisphere, predominantly in the white matter (Fig. 2C). Slight enhancement was found in the left lower temporal region (Fig. 2D-2F). Cerebral angiography exhibited no tumor stains. Repeated cerebrospinal fluid studies showed mild pleocytosis of 11-20 cells/mm$^3$, increased protein levels of 74-84 mg/dL, cytology of class I and negative results of infectious pathogenic tests, including herpes simplex, bacteria and fungus. Gallium scintigraphy of whole body revealed no abnormal accumulation. Intravenous administration of dexamethasone and glycerol was performed. At 7 days after admission, his consciousness state became normal. A mild degree of short-term memory impairment remained at 2 months after clinical onset. Follow-up magnetic resonance imaging (MRI) showed no remarkable changes. The clinical and neuroradiological courses suggested LE of unknown origin. One month later, his disorientation was exacerbated. Brain CT showed a high density mass surrounded by low density areas in the left frontal, parietal and temporal lobes (Fig. 1C and 1D). FLAIR imaging disclosed hypointense and hyperintense signal massive lesions with surrounding hyperintense signal areas in the left temporal, frontal and parietal lobes. Hyperintense signal areas were not changed in the right frontal and the right periventricular regions (Fig. 3A and 3B). Remarkable and irregular enhancement was seen in the left temporal, frontal and parietal lobes (Fig. 3C-3E). Urgent neurosurgery was performed and the neuropathological diagnosis of glioblastoma multiforme (GM) was confirmed.

Discussion

We report a patient with secondary GC mimicking LE at two months after clinical onset. One month later, our patient showed malignant transformation to massive GM, together with exacerbation of disorientation.

GC is divided into primary and the secondary types. Primary GC is considered as de novo formation of glioma. Secondary GC results from the spreading of a focal glioma. In general, neuroradiological features of GC are known to reveal extensive lesions into the corpus callosum. MRI appearances of typical GC show widespread T2-hyperintensity in the cerebral white matter without enhancement (3, 4). The initial MRI of the present patient displayed white matter-predominant and infiltrative lesions in at least three lobes of the left cerebral hemisphere. Focal enhancement or mass effects have been described in several GC patients when malignant transformation was generated from a part of GC (5-8). Therefore, the neuroradiological hallmarks of the
Figure 2. (A, B) Axial FLAIR imaging shows hyperintensity signal areas in bilateral frontal, the left parietal and temporal lobes. Ill-defined hyperintensity areas are shown in bilateral posterior periventricular regions. (C) Sagittal FLAIR imaging shows continuous hyperintense signal areas in the left temporal, frontal and parietal lobes. (D-F) Gadolinium-enhanced T1-weighted imaging shows faint enhancement in the left lower temporal lobe.

Figure 3. (A, B) Three months later FLAIR imaging shows a mixed signal intense mass and surrounding hyperintense signal areas in the left temporal, frontal and parietal lobes. Hyperintense signal areas are not altered in the right frontal and right periventricular regions. (C-E) Gadolinium-enhanced T1-weighted imaging shows marked enhancement in the left temporal, frontal and parietal lobes.
present patient were compatible with secondary GC. It would be of pathological importance to determine how often GC transforms to GM or malignant astrocytoma. Recent studies highlight somatic mutations of isocitrate dehydrogenases 1 and 2 genes in a majority of malignant gliomas (9, 10). Thus, genetic and neuropathological analyses are needed to elucidate the frequency of malignant transformation in GC patients.

In general, the differential diagnosis of GC includes multiple sclerosis, viral encephalitis, adrenoleukodystrophy, metachromatic leukodystrophy and subacute sclerosing panencephalitis because cerebral lesions are confluent and extensive on CT and MRI. LE is characterized by infectious or autoimmune inflammation in the limbic system. The most cardinal sign is short-term memory impairment. Neurological symptoms typically develop over a few weeks. In the present case, despite the widespread MRI lesions, he had only a mild degree of short-term memory dysfunction at 2 months after clinical onset. This clinicoradiological profile led to the initial misdiagnosis of LE. The following month, massive lesions were revealed on CT and MRI. Thus, physicians should pay more attention to the differential diagnoses of GC and LE in patients who have minor memory deficits and diffuse infiltrative MRI lesions. A brain biopsy is recommended for an early diagnosis of GC when MRI lesions are not attenuated on follow-up MRI.

References


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