Spontaneous Regression and Regrowth of Central Nervous System Lymphomatoid Granulomatosis
—Case Report—

Go TAKEISHI,1 Kouichi MOROKI,2 Takuma KAWASOE,3 Tsuyoshi FUKUSHIMA,4 Kiyotaka YOKOGAMI,1 Kazuki NABESHIMA,5 and Hideo TAKESHIMA1

1Division of Neurosurgery, Department of Clinical Neuroscience, and 4Department of Pathology, Faculty of Medicine, University of Miyazaki, Miyazaki, Miyazaki; 2Tokuda Neurosurgical Hospital, Kanoya, Kagoshima; 3Department of Neurosurgery, Prefectural Nichinan Hospital, Nichinan, Miyazaki; 5Department of Pathology, Fukuoka University Hospital and School of Medicine, Fukuoka, Fukuoka

Abstract

A 74-year-old woman presented with central nervous system (CNS) lymphomatoid granulomatosis (LYG) that spontaneously regressed and then regrew shortly thereafter. Initial magnetic resonance imaging studies showed a well demarcated, round, enhanced lesion with perifocal edema in the left temporal lobe. The enhanced lesion and perifocal edema had drastically regressed without treatment at follow-up examination. Two months later, the lesion reappeared and was larger, so was completely removed via left fronto-temporal craniotomy. The histological diagnosis was CNS LYG. CNS LYG should be considered in the differential diagnosis of spontaneously regressing brain tumors.

Key words: lymphomatoid granulomatosis, central nervous system, spontaneous regression

Introduction

Lymphomatoid granulomatosis (LYG) is a rare low-grade malignant angiocentric, angiodestructive, lymphoproliferative disorder, which commonly involves the lungs6,11) but rarely the central nervous system (CNS), kidneys, liver, or skin. CNS LYG accounts for approximately 30% of all LYG cases.8) Characteristic histological findings are infiltration of scattered Epstein-Barr virus (EBV)-positive atypical B-cells in a predominantly T-cell background. CNS LYG is histologically scored on a scale of grades 1–3, and may progress to diffuse large B-cell lymphoma.7) The clinical course is variable and no standard treatments have been established.2) We report a rare case of CNS LYG with spontaneous regression and regrowth during a short clinical course.

Case Report

A 74-year-old woman presented at a local hospital in July 2006 complaining of headache. Magnetic resonance (MR) imaging revealed a slightly high intensity area without mass effect in the left medial temporal lobe (Fig. 1). T1-weighted MR imaging with gadolinium-diethylenetriaminepenta-acetic acid (Gd-DTPA) showed a well demarcated, round, enhanced small mass lesion in the same area (Fig. 2A), and T2-weighted imaging showed the lesion surrounded by perifocal edema (Fig. 2B) at follow up in March 2007. Fluorine-18 fluorodeoxyglucose-positron emission tomography (FDG-PET) showed equivalent uptake in the lesion and the normal surrounding parenchyma (Fig. 3A). The maximum standardized uptake value (SUVmax) of the lesion was 5.82. Similarly, the SUVmax of
the contralateral normal brain tissue was 5.04. Whole-body FDG-PET detected no abnormal high uptake except in the brain lesion (Fig. 3B). One month later, enhanced lesion and the perifocal hyperintense area had spontaneously regressed without treatment (Fig. 2C, D). However, the lesion size had drastically increased with marked perifocal edema in May 2007 (Fig. 2E, F), and she was referred to our hospital.

On admission, she was slightly disoriented and manifested left homonymous hemianopsia. T1-weighted MR imaging with Gd-DTPA disclosed ring enhancement (Fig. 2G) and T2-weighted imaging showed marked perifocal hyperintensity (Fig. 2H). Diffusion-weighted imaging revealed a hypointense lesion (Fig. 4). Blood tests yielded the following results: lactate dehydrogenase 363 IU/l (normal 119–229 IU/l), C-reactive protein 0.11 mg/dl (normal 0–0.3 mg/dl), soluble interleukin-2 receptor 2050 U/ml (normal 220–530 U/ml), and β2-microglobulin 3.3 μg/ml (normal 1.3–2.2 μg/ml). The mass lesion was surgically removed via a left fronto-temporal craniotomy. The resected tumor was solid, well demarcated, and hard-elastic (Fig. 5A).

Histological examination revealed perivascular invasion by many medium to large atypical lymphoid cells (Fig. 5B, C). The MIB-1 labeling index was 31% (Fig. 5D). Immunohistochemical staining found the infiltrated atypical lymphoid cells were positive for CD3 (Fig. 5E) accompanied by medium to large CD20-positive lymphoid B-cells (Fig. 5F). The infiltrated cells were also positive for EBV-encoded small ribonucleic acid (Fig. 5G) and latent membrane protein (Fig. 5H), indicative of EBV infection. The final diagnosis was grade 3 CNS LYG. We planned to administer high-dose methotrexate therapy, but her general and cognitive status deteriorated and her family had her transferred to a hospital in her hometown where she died one week later of tumor progression, within 14 months of first detection of the radiological abnormality.

**Discussion**

At least 18 cases of CNS LYG have been reported.12) The 2001 World Health Organization definition of CNS LYG is B-cell proliferation of uncertain malignant potential associated with T-cell infiltration.7) As in our patient, the histological findings of CNS LYG resemble those of T-cell-rich B-cell lymphoma.

A clinical diagnosis of CNS LYG based on neuroimaging studies is difficult, but MR imaging is the best diagnostic technique.5) Multiple punctate and linear enhancements appear to be a specific finding because CNS LYG most likely affects the perivascular tissues and vessel walls.14,15) With time, these lesions evolve and show ring-like enhancement in the periphery and a non-enhanced center.14) In our case, the solid enhanced mass lesion changed to a ring-like enhanced lesion within one month. Diffusion-weighted imaging is also useful for differentiation.
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Fig. 3 A: Fluorine-18 fluorodeoxyglucose-positron emission tomography (FDG-PET) images acquired before admission showing iso-uptake in the lesion. The maximum standardized uptake value of the lesion and contralateral normal brain were 5.82 and 5.04, respectively. B: Whole-body FDG-PET image showing no abnormal high uptake except for the brain lesion.

Fig. 4 Diffusion-weighted magnetic resonance image showing a hypointense lesion.

Fig. 5 A: Photograph of the solid and hard-elastic tumor. B–H: Photomicrographs showing perivascular lymphoid cell infiltration with nuclear atypia (hematoxylin and eosin stain, original magnifications B: ×200, C: ×400). The MIB-1 labeling index was 31% (D: original magnification ×400). Immunohistochemical staining showing the infiltrated lymphoid T-cells positive for CD3 (E: original magnification ×400), with CD20-positive B-cells (F: original magnification ×400), and the lymphoid cells positive for Epstein-Barr virus (EBV) (original magnifications G: ×400, EBV-encoded small ribonucleic acid; H: ×400, latent membrane protein).

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...ing CNS LYG from malignant lymphoma, as the signal intensity of CNS LYG is relatively lower than that of malignant lymphoma. FDG-PET may be useful and the low or iso-uptake of FDG by low grade tumors like CNS LYG was observed in ours and a previous case. Ultimately, the histological findings are the most important for accurate diagnosis of CNS LYG. Predominant polyclonal T-lymphocytic invasion is usually observed in the perivascular area, and the presence of atypical B-cells is suggestive of EBV infection.

The prognosis of CNS LYG is usually poor because of the potential for transformation to malignant lymphoma. Although the prognosis of grade 3 CNS LYG is similar to that of diffuse large B-cell lymphoma, isolated brain involvement, in the absence of other systemic localizations, may be associated with good life expectancy. Unfortunately, the diagnosis of our patient was grade 3 CNS LYG and she had very poor outcome. The treatment
of CNS LYG is a matter of debate, but is primarily based on steroid administration and radiotherapy. Grade 3 CNS LYG responded to chemotherapy with rituximab.5) The CNS LYG in the left temporal lobe of our patient regressed spontaneously within a month without therapy but regrew rapidly and showed ring enhancement on follow-up imaging studies. No spontaneous regression was observed in a patient with cutaneous LYG.1) Such spontaneous regression is extremely unusual in a patient with CNS LYG.

CNS LYG is associated with EBV infection, and EBV is associated with different types of aggressive non-Hodgkin’s lymphoma.4) We speculate that the conditions and grades of CNS LYG are associated with immunoreactions against EBV. In fact, EBV-associated lymphoproliferative diseases such as LYG are seen in individuals with congenital or acquired immunodeficiency, such as patients with human immunodeficiency virus infection or post-transplant. If host immunoreactivity increases against EBV, the CNS LYG lesion may regress, as happened in our case. Based on our experience, we suggest that CNS LYG should be considered in the differential diagnosis of spontaneously regressing brain tumors.

References


Address reprint requests to: Go Takeishi, MD, Division of Neurosurgery, Department of Clinical Neuroscience, Faculty of Medicine, University of Miyazaki, 5200 Kihara, Kiyotake-cho, Miyazaki 889-1692, Japan.
e-mail: gentama@e-mail.jp