A Case of Primary Central Nervous System Lymphoma Mimicking Acute Disseminated Encephalomyelitis

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Background: In recent years, the frequency of primary central nervous system lymphoma (PCNSL) has increased, even among immunocompetent patients. In order to treat the disease optimally, early diagnosis is important. Case Report: We describe a 44-year-old woman presented with visual disturbance. Clinical symptoms of patient were progressively worsening despite steroid treatment. Brain MRI lesions seemed like acute disseminated encephalomyelitis, but stereotactic biopsy revealed PCNSL. Conclusion: Atypical clinical signs and symptoms could delay diagnosis of PCNSL. If patient would be worsened despite steroid therapy, early brain biopsy may lead to exact diagnosis and then optimal treatment.

KEY WORDS: Acute disseminated encephalomyelitis · Primary central nervous system lymphoma.

Introduction

Primary central nervous system lymphoma (PCNSL) is an aggressive form of non-hodgkin’s lymphoma of lymphocytic origin that arises within the brain parenchyma, leptomeninges, spinal cord, or rarely, the eye.1 Within the last two decades, the incidence of PCNSL has increased dramatically in immunocompetent as well as in immunocompromised individuals.2 PCNSL produces a variety of neurological symptoms and brain imaging findings, and focal involvement of the central nervous system (CNS) without systemic lymphomatosis can make diagnosis difficult without a brain biopsy. Because of its diffuse infiltrative growth pattern, clinical symptom are dominated by cognitive dysfunction, psychomotor slowing, personality changes, and disorientation. Because PCNSL could cause rapid brain damage and may lead to death within several months, early diagnosis is very important. Herein, we describe a patient who initially presented with visual disturbances and revealed demyelinating like lesions in the brain MRI.

Case

A 44-year-old woman developed rapid-onset bilateral visual disturbances, which had persisted for 10 days. Visual disturbances began from the left eye, and then progressed to the contralateral eye at approximately 1 week from symptom onset. There was no past medical and family history except for a human papilloma virus vaccination 3 months prior to symptom onset.

Neurological examination showed no focal neurologic deficits except bilateral visual disturbance. Laboratory tests were normal at admission (white blood cell: 5950/mm³, red blood cell: 3.98 × 10⁶/mm³, hemoglobin: 12.4 g/dL, hematocrit: 36.5%, platelet: 291000/mm³, erythrocyte sedimentation rate: 7 mm/h), as was blood chemistry (protein: 7.8 mg/dL, albumin: 4.4 mg/dL, alanine aminotransferase: 19 U/L, aspartate aminotransferase: 30 U/L, lactate dehydrogenase: 221 U/L). The anti-nuclear antibody test for autoimmune disease was negative, as were rheumatoid factor, antineutrophil cytoplasm antibody, antiSm, anti-Ro, anti-La, and systemic lupus erythematosus screening tests. Tests for hepatitis B virus, human immunodeficiency virus, cytomegalovirus, measles, mumps and rubella were all negative, and there was no abnormal finding on chest radiography. Cerebrospinal fluid was also normal (pressure: 90 mm Hg, WBC: 5/mm³, protein: 43 mg/dL, glucose: 64 mg/dL). Cytological examination of cerebrospinal fluid showed no malignant cells and all virus tests were negative.

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Initial brain MRI revealed diffuse abnormal high signal intensity and multifocal enhancement along the subcortical white matter of both cerebral hemispheres, the splenium of the corpus callosum, the left optic nerve, left thalamus, left cerebral peduncle, left basal ganglia, left cerebellar peduncle, and left pons (Fig. 1). Electroencephalogram showed diffuse slow waves.

These findings suggested multiple sclerosis or acute disseminated encephalomyelitis (ADEM). Methylprednisolone treatment was initiated at 1000 mg/day for 5 days. Visual acuity had got worse, and we decided immunoglobulin therapy. Brain MRI T2-weighted images at 30 days after first symptom onset showed that previous lesions of high signal intensity was largely unchanged, except for a slight increase in intensity. At 40 days after development of initial symptom, the patient developed right hemiparesis while undergoing treatment. On neurologic examination, the right limbs showed muscle weakness with medical research council grade III and a positive toe sign at right side. Follow-up third brain MRI revealed enhancement of the left basal ganglia and a pathological diagnosis of PCNSL was made following a stereotactic brain biopsy (Fig. 2). Histopathological characteristics of PCNSL were confirmed by brain biopsy. Highly cellular tumor composed predominantly of large centroblast-like cells on hematoxylin and eosin staining and there was positivity in anti-CD20 immunostaining. The mitotic activity is generally high in PCNSL. A high proliferative activity is evidenced by the expression of the Ki-67 antigen by the majority of the tumor cells (Fig. 2).

**Discussion**

The median age at diagnosis of PCNSL in immunocompetent patients is usually 60 years, but the typical age at presentation among patients with acquired immunodeficiency syndrome is younger, especially the mean age is 31 to 36 years. As with all masses in the central nervous system, the location of PCNSL lesions determines the clinical presentation.
presenting symptoms and signs in one large case series of 248 immunocompetent patients with PCNSL included the following: focal neurological deficits in 70% of patients; neuro-psychiatric symptoms in 43%; headache/nausea/vomiting suggestive of increased intracranial pressure in 33%; seizures in 14%; and ocular symptoms in 4%. Common focal deficits include aphasia, hemiparesis, and ataxia due to discrete intracerebral lesions as well as less common cranial nerve palsies secondary to leptomeningeal deposits. Neuropsychiatric changes such as apathy, depression, slowed thinking, and confusion have been attributed to the infiltration of white matter tracts by PCNSL that involve the periventricular regions or corpus callosum.1

On physical examination, tumor formation or peripheral lymph node enlargement are rare. There are no characteristic blood chemistry findings. CSF protein can also increase, but other CSF parameters are usually unremarkable. As such, PCNSL is difficult to diagnose with peripheral blood tests and physical examination alone. In this case, there was no remarkable findings in blood chemistry. The high intensity signals were observed in the deep white matter using MRI which can lead to PCNSL being misdiagnosed such as stroke, vasculitis, or encephalitis. Furthermore, vascular dementia, Creutzfeldt-Jacob disease, progressive multifocal leukoencephalopathy, demyelinating diseases, infectious diseases, and neoplastic diseases should be differentially diagnosed by brain MRI.

Treatment options for PCNSL include chemotherapy, radiation therapy, corticosteroid treatment, and plasma exchange. Current treatment for PCNSL is chemotherapy with methotrexate-based regimens, with or without adjuvant radiation therapy.2,3 However, prognosis of PCNSL is generally very poor. PCNSL cells also show a poor response to the treatments described above including chemotherapy. Without treatment, the average survival time is 3-5 months; even with treatment, the average survival time is only about 40 months.4

This case has a number of unique aspects. For approximately 40 days following symptom onset, other than visual disturbance, no focal neurological sign was observed, and there were no change in consciousness. The patient was initially diagnosed as a demyelinating, because brain MRI showed white matter involvement only and a recent report described ADEM associated with human papilloma virus vaccination.5

This case was challenging to diagnose because there was no response to either steroids or immunoglobulin therapy in the early stages and disease progression was very fast. Thus, even when neuroinflammatory disorders like ADEM are suspected, early biopsy for diagnosis should be considered, particularly when the patient’s condition is deteriorating rapidly despite of steroids or immunoglobulin therapy.

REFERENCES