Primary Central Nervous System T-cell Lymphoma
—Case Report—

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Abstract
A 46-year-old male presented with a rare primary non-Hodgkin's lymphoma of the central nervous system of T-cell lineage, localized primarily in the right parietal region. There was no evidence of acquired immunodeficiency syndrome. Biopsy of the tumor allowed immunohistochemical confirmation of the diagnosis. Irradiation and chemotherapy were given, and the patient has remained well for 24 months. The clinical manifestations, management, and outcome of T-cell lymphoma are very similar to those of B-cell lymphoma.

Key words: T-cell lymphoma, immunohistochemistry, central nervous system

Introduction
Primary central nervous system (CNS) lymphomas account for less than 2% of all cases of malignant lymphomas, which have recently increased in frequency, and less than 2.5% of cases of intracranial tumors. They are observed with increased frequency in patients with hereditary or acquired immune deficiency status, particularly those receiving organ transplants or suffering from the acquired immune deficiency syndrome (AIDS). Among the large number of primary lymphomas of the CNS subjected to marker studies, the majority are of B-cell origin which generally have a poor prognosis, with primary T-cell non-Hodgkin's lymphoma of the CNS being extremely rare. Few primary parenchymatous CNS lymphomas of T-cell origin have been reported.

Case Report
A 46-year-old male was in good health until late November 1996 when he had a generalized convulsive seizure episode following left extremity numbness. On admission the patient was well orientated and responsive. General examination was unremarkable. There was no lymphadenopathy or hepatosplenomegaly. Extensive clinical examination including thorax and abdomen computed tomography (CT) and ophthalmological examination found no systemic evidence of lymphoma. Neurological examination showed the visual fields were normal. The patient was slightly unsteady on moving when turning rapidly, and also had left extremity motor weakness. His medical history was unremarkable, with no evidence of immunodeficiency. The human immunodeficiency virus (HIV) test was negative. The cerebrospinal fluid (CSF) protein content was 120 mg/dl and cytology was insignificant. No evidence of viral or other infectious disease was present and the CSF β2-microglobulin level was normal (1.21 mg/dl).

CT and magnetic resonance imaging of the brain disclosed a densely enhanced mass lesion in the right medial parietal cortical region (Figs. 1 and 2). A full workup failed to detect any evidence of systemic neoplastic processes. Right cerebral angiography demonstrated an avascular mass in the right medial parietal region without evidence of ne-
On the 10th hospital day, right craniotomy with ultrasound guidance was performed. The leptomeninges appeared normal. The identifiable tumor was biopsied. The frozen-section diagnosis was malignant non-Hodgkin's lymphoma, subsequently confirmed by histological and immunohistochemical examinations.

The surgical specimen consisted of fragments of granular and pinkish tissue. Histological examination revealed perivascular aggregates of large lymphocytes and intra-adventitial cellular collections that spread out from fairly large sheet-like masses. Large lymphocytes with scant cytoplasm and dark nuclei involving cerebral parenchyma without necrosis were found. The cells had bizarre, pleomorphic nuclei (Fig. 3A). The cells identified as lymphocytes were positive to common leukocyte antigen staining and antibodies against T cells (Fig. 3B) but not for antibodies directed against B cells (Fig. 3C). Over 30% of the cells were positive for MIB-1, indicating a high degree of malignancy (Fig. 3D).

The patient did well postoperatively, but left extremity motor weakness remained. The patient was treated with chemotherapy (predonisolone, cyclophosphamide, pirarubicin, and vincristine) and radiotherapy (40 Gy whole brain and 10 Gy to the site of the tumor). He remains well at 24 months after the operation.

**Discussion**

Primary lymphomas in the CNS commonly occur after the fifth decade in immunocompetent hosts. They account for less than 2.5% of all intracranial tumors. Primary CNS lymphomas, which present solitary or multiple lesions adjacent to the ventricle, are usually supratentorial and the majority of primary CNS lymphomas are non-Hodgkin's lymphomas of B-cell origin.

The first case of primary intracranial parenchymatous T-cell lymphoma was reported in 1981. Primary parenchymatous CNS lymphoma of T-cell origin non-associated with HIV is a rare lesion, with only occasional cases reported in the literature. Cases, however, are being recognized more frequently as a result of increased use of immunohistochemistry. The present case of primary T-cell lymphoma of the right parietal region was confirmed by histological and immunohistochemical studies. The etiology of primary CNS T-cell
lymphoma remains unclear. Recent studies in CNS T-cell lymphoma patients have demonstrated the presence of Epstein-Barr virus (EBV) or elevated EBV antibody titer in the CSF. However, an etiological role for the virus in patients with CNS lymphoma is speculative.

Primary CNS lymphomas of T-cell origin may manifest clinically with diffuse or focal symptomatology, like CNS lymphomas of B-cell origin. Clinically, patients with primary T-cell lymphomas of the CNS usually present symptoms and signs of increased intracranial pressure, impairment of higher cortical function, and focal neurological deficit related to the site of space-occupying lesions. Villegas et al. reported that immunosuppression is not far more commonly associated with primary CNS T-cell lymphomas. In our review of the literature, it has been suggested that primary CNS lymphomas of T-cell lineage demonstrated some different characteristics regarding location of the tumor, age of presentation, gender, and survival as compared with primary B-cell lymphoma in the CNS. Primary CNS T-cell lymphomas non-associated with HIV have been frequently described in the posterior fossa (44.8%) when compared with primary CNS B-cell lymphomas. Previous reports manifested that infratentorial primary CNS B-cell lymphomas represented 12.5-29% of all primary CNS B-cell lymphomas. Of the infratentorial presentations of primary T-cell lymphomas in the CNS, cerebellum was the most common localization.

Primary parenchymatous T-cell lymphomas in the CNS may manifest at any age and at a somewhat younger age than patients with primary B-cell CNS lymphomas, although the peak of this incidence remains in the sixth decade of life, with a median age of 43 years (range 2-67). Similarly, primary CNS B-cell lymphomas demonstrate an average age at diagnosis of 56-59 years, and the peak of occurrence endures in the sixth and seventh decades.

Review of primary parenchymatous T-cell lymphoma non-associated with AIDS in the CNS found a clearly male predominance with a proportional
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Author (Year)</th>
<th>Age, Sex</th>
<th>Initial symptom</th>
<th>Location of tumor</th>
<th>Operation</th>
<th>Radiation</th>
<th>Chemotherapy</th>
<th>Corticosteroid therapy</th>
<th>Survival period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Suzuki et al. (1981)</td>
<td>43, M</td>
<td>headache</td>
<td>lt parietal</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>done</td>
<td>20 mos</td>
</tr>
<tr>
<td>2</td>
<td>Marsh et al. (1983)</td>
<td>20, M</td>
<td>headache, diplopia growth retardation</td>
<td>rt frontal, cerebellum</td>
<td>biopsy, gross total</td>
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<td>not mentioned</td>
</tr>
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<td>3</td>
<td>Bogdahn et al. (1986)</td>
<td>2, F</td>
<td>seizure</td>
<td>lt frontal</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>not mentioned</td>
<td>≥ 24 mos</td>
</tr>
<tr>
<td>4</td>
<td>Grant et al. (1986)</td>
<td>51, M</td>
<td>dystarhria, hemiparesis</td>
<td>lt frontal</td>
<td>biopsy</td>
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<td>not mentioned</td>
<td>≥ 16 mos</td>
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<tr>
<td>5</td>
<td>Kuwata et al. (1987)</td>
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<td>aphasia, amnesia</td>
<td>lt temporal</td>
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<td>done</td>
<td>not mentioned</td>
<td>≥ 14 mos</td>
</tr>
<tr>
<td>6</td>
<td>O’Neill et al. (1987)</td>
<td>38, F</td>
<td>headache</td>
<td>lt thalamus</td>
<td>biopsy</td>
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<td>not mentioned</td>
<td>not mentioned</td>
<td>not mentioned</td>
</tr>
<tr>
<td>7</td>
<td>Provincial et al. (1988)</td>
<td>54, M</td>
<td>speech disturbance</td>
<td>rt frontoparietal, cerebellum</td>
<td>biopsy, hemiparesis</td>
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<td>not mentioned</td>
<td>not mentioned</td>
<td>not mentioned</td>
</tr>
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<td>8</td>
<td>Provincial et al. (1988)</td>
<td>16, M</td>
<td>confusion</td>
<td>rt parietal</td>
<td>biopsy</td>
<td>done</td>
<td>not done</td>
<td>done</td>
<td>1 mo</td>
</tr>
<tr>
<td>9</td>
<td>Ng et al. (1988)</td>
<td>40, M</td>
<td>abnormal behavior</td>
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<td>not mentioned</td>
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<td>10</td>
<td>Yoshino et al. (1989)</td>
<td>30, M</td>
<td>seizure</td>
<td>rt frontal</td>
<td>biopsy</td>
<td>done</td>
<td>not done</td>
<td>done</td>
<td>≥ 14 mos</td>
</tr>
<tr>
<td>11</td>
<td>Morgella et al. (1989)</td>
<td>28, M</td>
<td>hypotalamic dysfunction</td>
<td>bil temporal, brain stem</td>
<td>biopsy</td>
<td>done</td>
<td>not done</td>
<td>done</td>
<td>20 mos</td>
</tr>
<tr>
<td>12</td>
<td>Grant and von Dethling (1990)</td>
<td>60, F</td>
<td>hemiparesis, amnesia</td>
<td>cerebellum</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>not mentioned</td>
<td>≥ 17 mos</td>
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<tr>
<td>13</td>
<td>Hardwidge et al. (1990)</td>
<td>32, M</td>
<td>headache, dystarhria</td>
<td>cerebellum</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>done</td>
<td>21 mos</td>
</tr>
<tr>
<td>14</td>
<td>Bednar et al. (1991)</td>
<td>48, F</td>
<td>hypotalamic dysfunction</td>
<td>cerebellum</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>not mentioned</td>
<td>≥ 36 mos</td>
</tr>
<tr>
<td>15</td>
<td>Knorr et al. (1992)</td>
<td>20, M</td>
<td>seizure</td>
<td>cerebellum</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>not mentioned</td>
<td>not mentioned</td>
</tr>
<tr>
<td>16</td>
<td>Feldges et al. (1993)</td>
<td>21, M</td>
<td>hypopituitarism</td>
<td>cerebellum</td>
<td>biopsy</td>
<td>done</td>
<td>not done</td>
<td>done</td>
<td>≥ 24 mos</td>
</tr>
<tr>
<td>17</td>
<td>Matsuno et al. (1993)</td>
<td>60, M</td>
<td>dystarhria, ataxia</td>
<td>cerebellum-pons</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>done</td>
<td>≥ 40 mos</td>
</tr>
<tr>
<td>18</td>
<td>McCue et al. (1993)</td>
<td>59, F</td>
<td>brain stem</td>
<td>cerebellum-pons</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>done</td>
<td>2 mos</td>
</tr>
<tr>
<td>19</td>
<td>Kanavos et al. (1993)</td>
<td>42, F</td>
<td>headache, anorexia</td>
<td>rt frontoparietal</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>not mentioned</td>
<td>≥ 24 mos</td>
</tr>
<tr>
<td>20</td>
<td>Matano et al. (1994)</td>
<td>89, F</td>
<td>amnesia, incontinence, hemiparesis</td>
<td>rt frontoparietal</td>
<td>biopsy</td>
<td>done</td>
<td>not done</td>
<td>done</td>
<td>≥ 36 mos</td>
</tr>
<tr>
<td>21</td>
<td>Fujimoto et al. (1996)</td>
<td>64, M</td>
<td>headache</td>
<td>cerebellum-pons</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>done</td>
<td>5 mos</td>
</tr>
<tr>
<td>22</td>
<td>Kleopa et al. (1996)</td>
<td>67, M</td>
<td>confusion, convulsion</td>
<td>cerebellum-pons</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>done</td>
<td>≥ 27 mos</td>
</tr>
<tr>
<td>23</td>
<td>Villegas et al. (1997)</td>
<td>43, M</td>
<td>gait disturbance, diplopia</td>
<td>cerebellum</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>done</td>
<td>≥ 30 mos</td>
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<tr>
<td>24</td>
<td>Present case</td>
<td>46, M</td>
<td>headache, confusion, convulsion, hemiparesis</td>
<td>rt parietal</td>
<td>biopsy</td>
<td>done</td>
<td>done</td>
<td>done</td>
<td>≥ 24 mos</td>
</tr>
</tbody>
</table>
relation of 2.2:1, while the male to female ratio observed in the whole population of primary CNS lymphomas is in general is 1.6:1 to 2:1.19,21,28

Primary lymphomas in the CNS generally carry a poor prognosis.15,37 Untreated patients with a primary lymphoma in the CNS survive for an average of 1.5 months.9 Recent management protocols combining chemotherapy and radiotherapy have achieved an increase in the median survival to 24 months in western countries,9,35 although Kubo et al.28 reported that the median survival of patients with primary CNS lymphomas non-associated with AIDS was 43 months. They also showed that the 1-, 2-, and 5-year survival rates were 53%, 38%, and 30% from the survival curve of all 36 cases. On the other hand, the Committee of Brain Tumor Registry of Japan (1981–1990) demonstrated that the 1-, 2-, and 5-year survival rates were 61.9%, 40%, and 20.7%.8

T-cell lymphomas may have a better prognosis than those of B-cell origin.34,39 In our review of 29 cases with primary parenchymatous CNS lymphoma, the clinical estimation was given in 23 of the 29 patients. Eighteen of them (78.3%) were alive 1 year after diagnosis and 10 (43.5%) were alive at 2 years. It may be emphasized that histological diagnosis is of enormous importance for treatment of primary CNS lymphomas. It is, however, not yet adequately known whether we should choose aggressive surgery or biopsy regarding survival rate from our review. The deep-seated or eloquent nature of primary CNS lymphomas may carry a high postoperative risk. Thus, surgery should probably be restricted to diagnostic biopsy.

In conclusion, primary parenchymatous CNS lymphoma non-associated with AIDS is a very rare disease. The patient was treated with radiotherapy and systemic chemotherapy, and he has survived without relapse for more than 24 months. This combination of radiation therapy and systemic therapy may be effective for patients with primary T-cell non-Hodgkin’s lymphoma in the CNS, because the prognosis of CNS lymphoma is usually not good.16,32,37

References

18) Hardwidge C, Diengdoh JV, Husband D, Nash JR: Primary cerebral lymphoma—a clinicopathological


Neurol Med Chir (Tokyo) 39, June, 1999


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