Primary malignant lymphoma of the central nervous system

Results of treatment of 11 cases and review of the literature

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Eleven patients with primary malignant lymphoma of the central nervous system (CNS) were treated at the Medical College of Wisconsin Affiliated Hospitals between 1964 and 1984. Three patients had a prior history of immunosuppressive therapy following renal transplantation. All patients had biopsy-proven disease and 10 of the 11 were treated with external radiation therapy. The doses to the primary tumor ranged from 34 to 59.4 Gray (Gy). Actuarial (life-table) survival rate was 82% at 1 year and 43% at 3 years. No recurrence was seen after 13 months.

Eighty-six reports totaling 693 cases of primary malignant lymphoma of the CNS were found in the literature. Of these, 308 cases were treated with a combination of surgery and irradiation. Overall survival at 5 years for those patients who received more than 50 Gy compared with less than 50 Gy to the primary tumor was 42.3% versus 12.8% (p < 0.05). Twenty-one patients survived longer than 5 years. Late relapse was notable, with 10 (47.6%) of 21 tumors recurring between 5 and 12.5 years after diagnosis. Based on this review, a minimum of 50 Gy radiation to the primary tumor is recommended. While no statement regarding the efficacy of craniospinal irradiation or chemotherapy can be made in view of the small numbers, the use of craniospinal irradiation and/or systemic chemotherapy should be considered for future trials.

Key Words: brain neoplasm, lymphoma, radiation therapy, microglioma

Clinical Material and Methods

Between 1964 and 1984, 11 patients were treated for primary malignant lymphoma of the CNS at the Medical College of Wisconsin. In 10 cases, specimens were obtained for histological study from primary operative procedures; cytological testing only was available in one. Patient characteristics are shown in Table 1. There were eight men and three women, with a mean age of 48 years (range 30 to 65 years). Median duration of symptoms was 4 weeks (range 1 week to 3 months). All 11 tumors were supratentorial in origin. Three patients had a history of renal transplantation, receiving immunosuppressive therapy for periods of 18 to 36 months prior to the diagnosis of an intracranial malignant lymphoma.

Two patients had prior or concurrent ocular involve-
Primary malignant CNS lymphoma

TABLE 1
Characters of 11 patients with lymphoma of the central nervous system*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yr), Sex</th>
<th>Duration of Symptoms &amp; Presentation</th>
<th>Location &amp; Size (cm) of Tumor</th>
<th>Type of Surgery</th>
<th>Radiation Dose (Gy)</th>
<th>Chemotherapy</th>
<th>Follow-Up Status &amp; Site of Recurrence†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>44, M</td>
<td>2 mos: visual dysfunction</td>
<td>vitreous, rt &amp; lt temporo-occipital, &gt; 4</td>
<td>vitrectomy</td>
<td>50.4 to primary, 50.4 to WB</td>
<td>IT-MTX</td>
<td>19 mos: NED</td>
</tr>
<tr>
<td>2</td>
<td>62, M</td>
<td>2 mos: intense smells, lt arm weakness</td>
<td>rt frontotemporal, near thalamus, &gt; 4</td>
<td>subtotal excision</td>
<td>59.4 to primary, 48.6 to WB</td>
<td>none</td>
<td>19 mos: alive with recurrence in CSF at 13 mos</td>
</tr>
<tr>
<td>3</td>
<td>43, M</td>
<td>2 mos: It weakness, seizures (?)</td>
<td>lt parietal, &gt; 4</td>
<td>gross excision</td>
<td>54 to primary, 54 to WB</td>
<td>none</td>
<td>120 mos: NED</td>
</tr>
<tr>
<td>4</td>
<td>65, M</td>
<td>2 wks: lt facial weakness, visual dysfunction</td>
<td>rt thalamus/hypothalamus, &gt; 4</td>
<td>biopsy</td>
<td>34 to primary, 34 to WB, 7.5 to spine</td>
<td>IT-MTX</td>
<td>13 mos: died of recurrence at S1–2 nerve root (CSF)</td>
</tr>
<tr>
<td>5</td>
<td>53, M</td>
<td>2 wks: lt hemiparesis, lt facial pain</td>
<td>rt frontal, &gt; 4</td>
<td>subtotal excision</td>
<td>54.3 to primary, 45.3 to WB</td>
<td>none</td>
<td>5 mos: died of recurrence at primary site</td>
</tr>
<tr>
<td>6</td>
<td>43, M</td>
<td>1 mo: frontal headaches</td>
<td>rt temporoparieto-occipital (?)</td>
<td>gross excision</td>
<td>54 to primary, 50.4 to WB</td>
<td>none</td>
<td>21 mos: NED</td>
</tr>
<tr>
<td>7</td>
<td>57, F</td>
<td>2 wks: weakness, confusion</td>
<td>lt temporoparietal, &gt; 4</td>
<td>gross excision</td>
<td>55.8 to primary, 55.8 to WB</td>
<td>none</td>
<td>70 mos: died, no documented recurrence</td>
</tr>
<tr>
<td>8</td>
<td>48, F</td>
<td>1 wk: lt arm weakness, headache</td>
<td>rt frontoparietal, &lt; 4</td>
<td>biopsy</td>
<td>55.8 to primary, 50.4 to WB</td>
<td>none</td>
<td>17 mos: died of recurrence at primary site</td>
</tr>
<tr>
<td>9</td>
<td>30, F</td>
<td>1–3 mos: photophobia, headache</td>
<td>lt frontal, &gt; 4</td>
<td>gross excision</td>
<td>none</td>
<td>none</td>
<td>2 mos: died of recurrence at primary site</td>
</tr>
<tr>
<td>10</td>
<td>50, M</td>
<td>1 mo: lt facial &amp; arm weakness, visual dysfunction</td>
<td>lt parietal, (?)</td>
<td>subtotal excision</td>
<td>50 to primary, 30 to WB</td>
<td>none</td>
<td>15 mos: died of recurrence in lt humerus</td>
</tr>
<tr>
<td>11</td>
<td>34, M</td>
<td>2 wks: headache, confusion</td>
<td>lt parietal, &gt; 4</td>
<td>biopsy</td>
<td>55.8 to primary, 50.4 to WB</td>
<td>none</td>
<td>14 mos: died of recurrence in CSF at 4 mos</td>
</tr>
</tbody>
</table>

* WB = whole brain; IT-MTX = intrathecal methotrexate; BCNU = 1,3-bis(2-chloroethyl)-1-nitrosourea; IV Ara-C = intravenous cytosine arabinoside.
† Time after diagnosis. NED = no evidence of disease; CSF = cerebrospinal fluid.

ment. Case 1 initially presented with a decrease in visual acuity; on examination vitreous involvement was found, proven cytologically to be a diffuse large-cell malignant lymphoma. A cranial computed tomography (CT) scan performed at the time of initial work-up showed a mass in the temporo-occipital regions; therefore, concurrent CNS and ocular primary sites were diagnosed. Case 5 had chronic lymphocytic leukemia and 9 years later developed bilateral vitreous seeding cytologically compatible with "reticulum-cell sarcoma." Fifteen months after local orbital irradiation and administration of cyclophosphamide, a large mass was found in the right frontonal region. Bifrontal craniotomy revealed diffuse histiocytic malignant lymphoma, histologically distinct from the prior chronic lymphocytic leukemia infiltrate in the bone marrow.

Initial evaluation for all patients included a complete blood count, routine liver function studies, chest roentgenograms, and either a CT scan or carotid artery angiography. Systemic evaluation was variable; lymphography was performed in one patient, CT of the chest and/or abdomen in four, and bone marrow aspiration or biopsy in eight. Five patients had a lumbar puncture, and cerebrospinal fluid (CSF) analysis was negative in all five. No clinical evidence of extracranial disease was appreciated in any patient.

Treatment for each patient is summarized in Table 1. The extent of surgery was gross total excision in four, subtotal excision in three, biopsy only in three, and vitrectomy in one. Case 9 did not receive postoperative irradiation, and the remaining 10 patients were treated with megavoltage therapy (4 to 25 MV photons). Whole-brain irradiation was followed by a boost to the primary tumor volume in all 10 patients. Fraction sizes were from 1.8 to 2.0 Gy/day and treatment was given 5 days/wk. Doses to the whole brain ranged from 30 to 55.8 Gy; the total dose to the primary tumor was 34 Gy in one case and between 50 and 59.4 Gy in nine patients. Two patients received limited chemotherapy as part of their primary therapy, with intrathecal methotrexate given during irradiation.

**Results**

Three patients survived without disease at 29, 30, and 129 months. One patient died at 70 months without...
documented disease recurrence. Actuarial (life-table) analysis revealed a 1-year survival rate of 81.8% and a 3-year survival rate of 43.3%. The actual 1- and 3-year disease-free survival rates were 45.4% and 36.3% (Fig. 1).

Seven patients experienced a relapse. One patient remains alive with disease 19 months after diagnosis. All recurrences were seen at 13 months or less from the time of initial diagnosis. The median time to disease recurrence was 2 months with the mean being 6.3 months. Disease recurrence was at the primary site in three patients (Cases 5, 8, and 9) 1 to 12 months after diagnosis. Of these three patients, persistence of disease at the primary site was documented in two (Cases 5 and 9) within 1 month of the completion of therapy. Subarachnoid dissemination was diagnosed by positive CSF cytology in three cases; one during initiation of postoperative irradiation (Case 4) and two as an initial manifestation of disease recurrence 13 and 4 months after diagnosis (Cases 2 and 11, respectively). Extra-axial (osseous) metastases were found 8 months after diagnosis and treatment in Case 10. This patient died 15 months after diagnosis and autopsy revealed tumor at the primary site.

Discussion

Epidemiology

First reported by Bailey in 1929 as a "perithelial small cell sarcoma," various morphological criteria have been used to categorize this tumor. The cell of origin has variously been thought to be the reticulocyte55,95 or microglia cell,72 thus giving rise to the terms "reticulum-cell sarcoma" and "microglioma." Recent interpretation at the light and electron microscopic levels suggests that the tumor is of lymphocytic origin. Newer immunochemical developments support the lymphocytic nature of this tumor. Varadachari, et al.,91 have demonstrated the B-cell nature of one lesion through the use of surface-marker analysis.

The association of primary malignant lymphoma of the CNS with immunosuppression has been recognized since the late 1960's. While this connection has been most thoroughly reviewed in those patients who have received renal transplants, it has also been noted in patients with congenital immunological deficiencies, rheumatoid arthritis, systemic lupus erythematosus, and necrotizing vasculitis. Recently, primary malignant lymphoma of the CNS has been described in patients with the acquired immune deficiency syndrome (AIDS). The male:female ratio was 1.5:1 with a mean age of 52 years (range 2 months to 90 years). The duration of symptoms prior to diagnosis varied from 3 days to 24 months, with the majority of the series reporting a median of 1 to 2 months.

For 424 of the 693 cases found in the literature, sufficient information was available to determine location (Table 2). The tumor was unifocal in 282: supratentorial in 221 and infratentorial in 61 (for a ratio of 3.6:1). The frontal lobe was the most common single primary site. Multiple lesions within a single hemisphere were described in 81 (57%) of the 142 multiple presentations, while multicentric lesions (involving more than one hemisphere or the meninges) were noted in 61. Infratentorially, the cerebellum was most frequently involved; rarely was there disease within the brain stem or extension to the upper cervical spinal cord.

Clinical Characteristics

A review of the literature revealed 86 reports totaling 693 cases of primary malignant lymphoma of the CNS from 1929 to the present. The male:female ratio was 1.5:1 with a mean age of 52 years (range 2 months to 90 years). The duration of symptoms prior to diagnosis varied from 3 days to 24 months, with the majority of the series reporting a median of 1 to 2 months.

For 424 of the 693 cases found in the literature, sufficient information was available to determine location (Table 2). The tumor was unifocal in 282: supratentorial in 221 and infratentorial in 61 (for a ratio of 3.6:1). The frontal lobe was the most common single primary site. Multiple lesions within a single hemisphere were described in 81 (57%) of the 142 multiple presentations, while multicentric lesions (involving more than one hemisphere or the meninges) were noted in 61. Infratentorially, the cerebellum was most frequently involved; rarely was there disease within the brain stem or extension to the upper cervical spinal cord.

Treatment

From this review of 693 cases, the primary treatment was specified in 406 cases (58.6%). Attempt at surgical removal was the only mode of therapy in 85 patients. Three-hundred and eight patients received external beam irradiation in conjunction with surgery and less often with chemotherapy. Chemotherapy was utilized as the primary mode of postoperative therapy in only 13 patients, including nine treated with corticosteroids alone.

Role of Surgery. Surgical biopsy or resection with postoperative irradiation has been standard therapy. Of the 85 patients treated with surgery alone, subtotal or gross total resection was performed in only 46 cases, while attempted resection was performed in 39. The median reported survival time was found to be 1 month. Long-term survival (greater than 3 years) was noted in only 1 case. There was no difference in median survival time as defined by the extent of the surgical resection. With the diffuse nature of many of these lesions and the apparent lack of benefit from sub-

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TABLE 2

<table>
<thead>
<tr>
<th>Location</th>
<th>% of Group</th>
<th>No.</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>supratentorial</td>
<td></td>
<td>221</td>
<td>52.1</td>
</tr>
<tr>
<td>frontal</td>
<td>26.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>temporal</td>
<td>15.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>parietal</td>
<td>14.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>occipital</td>
<td>4.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>deep nuclei</td>
<td>13.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pineal</td>
<td>0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>other*</td>
<td>28.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>infratentorial</td>
<td></td>
<td>61</td>
<td>14.4</td>
</tr>
<tr>
<td>cerebellum</td>
<td>80.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>brain stem</td>
<td>16.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>spinal cord</td>
<td>3.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>multiple†</td>
<td></td>
<td>142</td>
<td>33.5</td>
</tr>
</tbody>
</table>

* Not otherwise specified.
† Multiple lesions within a single hemisphere or lesions involving more than one hemisphere or involvement of the meninges.

TABLE 3

<table>
<thead>
<tr>
<th>Treatment Area &amp; Dose</th>
<th>% of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>treatment area</td>
<td></td>
</tr>
<tr>
<td>local field</td>
<td>5.2</td>
</tr>
<tr>
<td>whole brain</td>
<td>40.3</td>
</tr>
<tr>
<td>extended field</td>
<td>5.2</td>
</tr>
<tr>
<td>not specified</td>
<td>49.3</td>
</tr>
<tr>
<td>dose to primary tumor (Gy)</td>
<td></td>
</tr>
<tr>
<td>&lt; 40</td>
<td>14.0</td>
</tr>
<tr>
<td>40-&lt; 45</td>
<td>18.8</td>
</tr>
<tr>
<td>45-&lt; 50</td>
<td>14.3</td>
</tr>
<tr>
<td>50-&lt; 60</td>
<td>10.7</td>
</tr>
<tr>
<td>≥ 60</td>
<td>3.6</td>
</tr>
<tr>
<td>not specified</td>
<td>38.6</td>
</tr>
</tbody>
</table>

Role of Radiotherapy. Earlier reports have documented the importance of irradiation in increasing the median survival time of these patients. Henry, et al. reported a median survival time of 4.6 months in patients treated with surgical excision alone, while in 21 patients receiving irradiation the median survival time was 15.2 months. Clinical improvement in patients is also apparent; Berry and Simpson reported that 14 of 19 patients showed neurological improvement following irradiation. Complete resolution of lesions has been demonstrated by CT scans.

Current questions concerning radiotherapy center on the dose required for local control as well as the volume of the CNS that should be included within the irradiation fields. The volume to be irradiated has been difficult to define in view of the assumed relationship between tumor size, treatment volume, and survival time. The treatment area and total tumor dose utilized in the irradiated patients are summarized in Table 3. Megavoltage irradiation was used in the treatment of the majority of the patients. The volume irradiated included the whole brain in 124 (40.3%), local tumor irradiation in 16 (5.2%), and the entire neuraxis in 16 (5.2%). Treatment volume was not specified in 152 (49.3%). Dose to the primary tumor was relatively uniform with the great majority of the patients receiving between 40 and 45 Gy. Only 44 patients (14.0%) were reported to have received greater than 50 Gy (Table 3).

There are little data comparing whole-brain to local-field or to craniospinal irradiation. In a single report, slightly improved survival times were found when local-field irradiation (less than whole-brain) was delivered. The incidence of multicentricity and diffuse involvement as described above would nonetheless argue for a minimum of cranial irradiation. The importance of tumor size has been examined by Mendenhall, et al., who reported that two of their 12 patients had lesions of less than 3.5 cm in diameter. Both of these patients were free of disease 48 and 38 months following irradiation.

Dose-response information is difficult to obtain. Sagerman, et al., found no local control or long-term survival in patients who had received less than 3000 rads. Cox, et al., in a review of time-dose relationships for malignant lymphoreticular tumors, noted improved local control in patients with primary CNS disease given greater than 45 Gy. Berry and Simpson suggested an improved survival time in patients receiving doses greater than 50 Gy to the whole brain, with a 2-year survival in two of 10 patients compared to 0 of 8 with lower doses. Loeffler, et al., noted that their long-term survivors had received a median dose of over 50 Gy to the tumor.

To better delineate this question, we analyzed those patients who received irradiation and had adequate information concerning the dose given. We identified 198 cases, including the 10 patients from the current report. Fifty-four patients received doses of 50 Gy or higher to the primary tumor; their median survival time was 17 months. Patients with doses below 50 Gy had a median survival time of 15 months. Actuarial (life-table) survival data were calculated for these patients and are presented in Fig. 2. The overall survival rate at 5 years is 42.3% for those who had received greater than 50 Gy to the primary tumor compared with 12.8% for those receiving less than 50 Gy. This difference is statistically significant at p < 0.05. Thus, from this review, a dose-response relationship with an improved survival time associated with doses greater than 50 Gy to the primary tumor can be demonstrated. The overall survival from the present series (see Fig. 1) also closely parallels these findings.

Role of Chemotherapy. The use of chemotherapy in primary malignant lymphoma of the CNS has been reported mainly in those patients with progressive, recurrent, or disseminated disease. The earliest reports documenting response to systemic therapy related to
the use of corticosteroids. In such cases, clinical symptoms and radiographic abnormalities improved as long as corticosteroids were continued. Symptoms and signs returned in almost all patients when the medication was discontinued, although three patients survived longer than 3 years after receiving corticosteroid therapy alone.

More recently, reports have described the use of combination chemotherapy together with irradiation. Kawakami, et al., reviewed 21 cases of primary malignant lymphoma of the CNS in which 11 were treated with chemotherapy (nine of these 11 also received irradiation). Regimens included CHOP (cytoxan, adriamycin, vincristine, and prednisone), VENP or VEMP (vincristine, cytoxan, procarbazine or 6-mercaptopurine, and prednisolone), or ACNU (1-(4-amino-2-methylprifimidine-5-yl)-methyl-3-(2-chloroethyl)-3-nitrosourea). Survival time was found to be 20 and 30 months in two patients treated with surgery plus CHOP and from 5 to 38 months in nine patients receiving surgery plus irradiation plus other chemotherapy regimens (median survival 15 months). The CHOP regimen was thought to be superior, although the small number of patients limits any firm conclusion.

Loeffier, et al., reported 10 cases treated by surgery, followed in five by irradiation and in five by irradiation and chemotherapy. Regimens that penetrated the CNS included either high-dose systemic cytosine arabinoside or methotrexate in four of their five patients. A median survival time of 44 months was found in the chemotherapy group in comparison to 14 months for those who received surgery plus irradiation. To date, while these reports are encouraging, the use of chemotherapy remains investigational and its use should be defined in future clinical trials.

### Prognosis

Few long-term survivors have been reported among patients with primary malignant lymphoma of the CNS. In 1975, Littman and Wang identified five patients in the literature who were free of disease at 5 years. The current review of 693 cases found 56 (8%) who have survived for longer than 3 years. Twenty-one of the 56 are known to have survived at least 5 years. Notable in this group was the frequency of late recurrence: 10 (47.6%) of the 21 5-year survivors relapsed between 5 and 12.5 years after diagnosis. The longest survival time reported was 16.5 years in a patient initially diagnosed at 2 months of age.

#### Patterns of Failure

Improvement in therapy depends on information gathered from the failure patterns of previous patients. While the majority of the patients have recurrences at the primary site, dissemination within the neuraxis and beyond the CNS is also seen. Neuraxis recurrence may represent undetected CSF or spinal cord involvement at diagnosis. Few series report neuraxis staging (CSF cytology and myelography) before or after surgery. The results from some of the larger series are presented in Table 4. Overall, nine (10%) of 90 patients were reported to have a positive CSF finding at diagnosis.

![Graph showing survival times in 188 cases collected from the literature and 10 cases in the present series in which irradiation dosage is available. Solid line indicates those patients receiving a dosage of 50 Gy or above; broken line represents those receiving a dosage of less than 50 Gy. The difference was statistically significant (p < 0.05).](image)

**Table 4**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Cases</th>
<th>CSF Study at Diagnosis</th>
<th>Disease at Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No. Examined</td>
<td>No. Positive</td>
</tr>
<tr>
<td>Sagerman, et al., 1967</td>
<td>24</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Schaumburg, et al., 1972</td>
<td>25</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>Henry, et al., 1974</td>
<td>83</td>
<td>41</td>
<td>0</td>
</tr>
<tr>
<td>Littman &amp; Wang, 1975</td>
<td>19</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Rampen, et al., 1980</td>
<td>12</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Berry &amp; Simpson, 1981</td>
<td>21</td>
<td>NA</td>
<td>1</td>
</tr>
<tr>
<td>Gonzalez &amp; Schuster-Uitterhoeve, 1983</td>
<td>15</td>
<td>NA</td>
<td>3</td>
</tr>
<tr>
<td>Mendenhall, et al., 1983</td>
<td>12</td>
<td>NA</td>
<td>0</td>
</tr>
<tr>
<td>Sagerman, et al., 1983</td>
<td>12</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Alleganza, et al., 1984</td>
<td>12</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Helle, et al., 1984</td>
<td>22</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Loeffler, et al., 1985</td>
<td>10</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>total cases</td>
<td>267</td>
<td>92</td>
<td>9</td>
</tr>
</tbody>
</table>

* CSF = cerebrospinal fluid; NA = not available.
† Autopsy findings.
The frequency of CSF seeding as the first manifestation of disease progression has been noted in 4% to 25%. Table 4 summarizes 267 cases from the literature. Of these, disease recurrence was found in 15 (6.5%), with positive CSF cytology or overt spinal cord disease. Our own series substantiates this pattern of failure with neuraxis dissemination in three of 11 patients. The use of craniospinal irradiation has been advocated by some authors because of this risk, although no comparative data proving its efficacy are available. If higher doses of local irradiation do achieve an increase in local control and survival time, it is possible that the frequency of recurrence within the neuraxis will also increase. The role of craniospinal irradiation deserves study in future clinical trials.

Extraneural manifestations of disease are uncommon and often preceded by recurrence within the CNS. Sixteen patients demonstrated overt signs of distant disease clinically and six patients were noted to have distant disease at autopsy (Table 4). Areas of extraneural involvement were lymph nodes, testicles, kidneys, and lungs. One patient with an isolated failure in the mediastinum was subsequently salvaged with chemotherapy.

Conclusions

The overall outlook for patients with primary malignant CNS lymphoma is disappointing, with only a few long-term survivors noted in this review. The improved long-term survival demonstrated in this review with doses greater than 50 Gy would suggest that a minimum dose of 50 Gy to the primary tumor is required for local control and increased survival times. This is currently under investigation by the Radiation Therapy Oncology Group (unpublished data).

The sporadic use of chemotherapy in this review does not allow any firm conclusions regarding its value. Chemotherapy may theoretically augment irradiation and/or eradicate micrometastases within the neuraxis or beyond the CNS. With the majority of the patients having recurrences at the primary site, the effects of higher doses of radiation to the primary tumor, altered fractionation, and a combination of irradiation and chemotherapy need to be studied.

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