

Original Article

Cerebral Lymphoma: Clinical and Radiological Findings in 90 Cases

Alireza Zali MD*, Sohrab Shahzadi MD*, Alireza Mohammad-Mohammadi MD*,
Karim Taherzadeh MD*, Khosro Parsa MD*

Background: Cerebral lymphoma is a rare non-Hodgkin's lymphoma, which involves the brain primarily or after systemic involvement. Because of its infiltrating nature and its sensitivity to radio- and chemotherapy, surgical removal has a limited role in its treatment and only a stereotactic biopsy is necessary for confirming the diagnosis.

Methods: The data from all cases in whom the cerebral lymphomas were pathologically confirmed and were admitted to the Neurosurgery Department of Shohada Hospital for stereotactic biopsy during a 15-year period were analyzed retrospectively.

Results: The male to female ratio was 1.3:1 and the mean age was 51.7 years. Sixty-seven percent of the patients had multiple lesions and the remainder had solitary lesions. The most common site of involvement in patients with multiple lesions was diencephalon and in patients with solitary lesions was frontal lobe. The mean duration from symptom presentation to stereotactic biopsy was three months. Systemic lymphoma was detected in nine patients and three patients had a history of immunosuppressive drug consumption. The most common presenting symptom was headache in 42% and the most common sign was paresis in 59% of the patients.

In 53 patients, follow-up was performed by phone call. Of these, seven cases had died without treatment in an average of 40 days after diagnosis, 28 patients died despite adjuvant treatment in an average of 8.5 months, and 18 cases were alive by the time of last follow-up with average of 17 months. Overall survival of the treated group was 12 months.

Conclusion: There was no mortality related to stereotactic biopsies in these patients.

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Keywords: Cerebral lymphoma • non-Hodgkin's lymphoma • stereotactic biopsy

Introduction

Primary central nervous system (CNS) lymphoma is a type of non-Hodgkin's lymphoma. Unlike other primary brain tumors it is chemo- and radiosensitive. Despite this characteristic, it is not a curable tumor and has a poor prognosis.¹ Its incidence, which increases with age has risen among both immunocompetent and immunocompromised patients during past three decades.^{2,3} In immunocompetent patients, the disease commonly presents in the sixth decade of

life while in immunocompromised patients, it presents in the fourth decade.⁴⁻⁶ It has a male predominance of 1.5:1, which is greater in immunocompromised patients.⁷ Most of the disease are from B-cell origin and systemic involvement is found in only 10% of the patients.^{8,9}

Because of its infiltrating nature, surgical removal makes no significant change in the survival of patients and surgery plays a limited role in the treatment strategies. Only a stereotactic biopsy for confirming the diagnosis is all of the surgical procedures needed in many cases.^{7, 10} Treatment options are radiotherapy and chemotherapy, which in combination can increase the survival of patients, especially in cases without systemic involvement.^{10, 11}

In this study, 90 cases of cerebral lymphomas, which underwent stereotactic biopsy in Shohada Hospital during a 15-year period, were analyzed

Authors' affiliation: *Department of Neurosurgery, Shohada Hospital, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.

Corresponding author and reprints: Alireza Zali MD, Department of Neurosurgery, Shohada Hospital, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.
Fax: +98-212-240-0052,
E-mail: dr_a_zali@yahoo.com.

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according to their demographic data, clinical and radiological features, and their survival.

Materials and Methods

In this study, the data from all cases in whom the cerebral lymphomas were pathologically confirmed and were admitted to the Neurosurgery Department of Shohada Hospital for stereotactic biopsy during a 15-year period (1988 – 2003) were analyzed retrospectively. Follow-up by phone calls was performed to determine survival.

Variables that were analyzed consisted of demographic data such as age and gender, symptoms and signs on admission (such as headache, vomiting,...), radiological findings considering multiplicity (solitary vs. multiple), location (supra- and infratentorial featuring different anatomic regions of the brain), the enhancing pattern (homogeneous, heterogeneous, or ring enhancement), history of systemic lymphoma and immunosuppressive state, adjuvant treatment after diagnosis, and finally survival of patients with and without adjuvant treatment. Statistical analysis was performed using Student's *t*-test.

Results

Demographic data

Among 90 cases of cerebral lymphoma, there were 51 male and 39 female patients with male to female (M:F) ratio of 1.3:1. The mean age of the patients was 51.7 years (range: 8 – 77 years). The tumor was most prevalent in the sixth decade of life followed by the fifth and fourth decades. Features are shown in Figure 1.

The most common presenting symptoms were headache (42%), mental status changes (26%), seizure (13%), and aphasia (9%).

The most common neurological signs on admission were paresis in 59% (45 cases of hemiparesis, five cases of hemiplegia, and three cases of paraparesis) and cranial nerve dysfunction in 8% of the patients.

The mean duration of symptoms before confirmation of diagnosis was three months.

Radiological findings

Twenty-nine (33%) patients had solitary and 61 cases (67%) had multiple lesions. All of the lesions enhanced with contrast injection: ring enhancement in 12 cases (13%), homogeneous enhancement in 57 cases (63%), and heterogeneous enhancement in 21 cases (24%). More details according to solitary and multiple lesions are shown in Table 1.

Considering location, there were 86 cases with supratentorial and 19 with infratentorial involvement (there were some cases of both supra- and infratentorial involvement). In the 29 cases of solitary lesion, there were 26 cases (90%) of supratentorial and three cases (10%) of infratentorial involvement. In multiple lesions there were 45 cases (73%) of multiple supratentorial involvement, one case (2%) of multiple infratentorial involvement, and 15 cases (25%) of multiple supra- and infratentorial involvement. Periventricular lesions were found in 67 cases (74%). More details are shown in Table 1.

Overall, the most common location was hemispheric involvement (35%). In multiple lesions, the most common location was diencephalon (65%) and in solitary lesions, it was the frontal lobe (31%).

All of the three immunocompromised cases had solitary lesion. Homogeneous enhancement was found in one and ring enhancement in the two others. Distribution of lesions according to their location and multiplicity is shown in Figure 2.

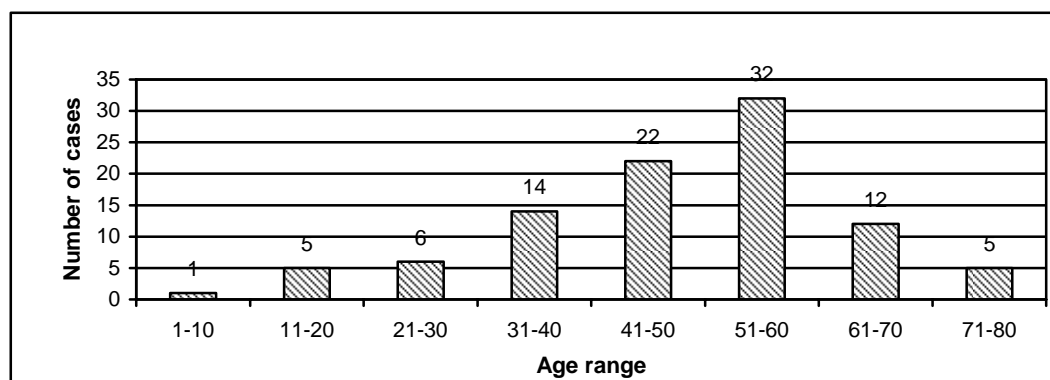


Figure 1. Age distribution of the patients.

Table 1. Distribution of different kinds of enhancement and locations considering solitary and multiple groups.

	Solitary	Multiple	Total
Total	29	61	90
Ring enhancement	9(31%)	3(5%)	12(13%)
Homogeneous enhancement	13(45%)	44(72%)	57(63%)
Heterogeneous enhancement	7(24%)	14(23%)	21(23%)
Supratentorial	26(90%)	45(74%)	71(79%)
Infratentorial	3(10%)	1(2%)	4(4%)
Supra- and infratentorial	0(0%)	15(24%)	15(17%)
Periventricular lesions	13(45%)	53(87%)	67(74%)

Medical histories

Nine cases (10%) had a history of systemic lymphoma with secondary involvement of the brain. Three cases had the history of immunosuppressive drug consumption (one patient after renal transplantation and two patients after chemotherapeutic treatment of breast cancer and leukemia). There were no patients with AIDS in this study.

Eight cases underwent ventriculoperitoneal shunt surgery because of hydrocephalus before stereotactic biopsy.

Follow-up

Follow-up by phone call was performed in only 53 cases; the other 37 cases were not reachable.

Seven cases received no adjuvant treatment and died in an average of 40 days after stereotactic biopsy (range: 1 – 3 months). Forty-six cases received adjuvant radio- and chemotherapy. Of these, 28 cases died despite adjuvant treatment in an average of 8.5 months after the biopsy (range: 1 – 36 months) and 18 patients survived by the time of the last follow-up with an average of 17 months (range: 6 – 66 months). Overall, median survival for the treated group was 12 months after biopsy.

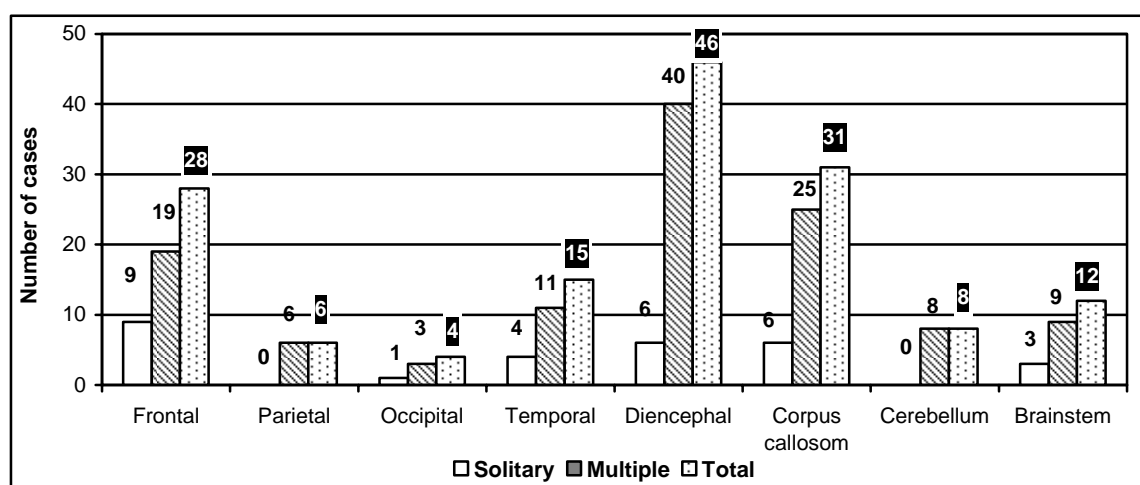
In 53 cases who had follow-up, two-month survival was 83%, six-month survival was 68%, and one-year survival was 40%. The results for those who received adjuvant treatment and the untreated patients are shown in Figure 3.

Discussion

The demographic data of the patients in our study shows a M/F ratio of 1.3:1, mean age of 51 years, and maximum prevalence of the disease in the sixth decade of life. These findings correlate well with some other studies. Murray et al and Corn et al reported a M/F ratio of 1.5:1 and maximum prevalence in the sixth decade of life.^{7,12}

The most common presenting symptoms and signs in our study were headache (42%) and paresis (59%). Hochberg and Miller, and Helle et al reported similar results.^{5,13}

Regarding the radiological studies, we had 33% solitary versus 67% multiple lesions, mostly in supratentorial region. The most common site of involvement in multiple lesions was diencephalon (65%) and in solitary lesions, it was the frontal lobe (31%). Periventricular location was more frequent in multiple versus solitary lesions (87%

**Figure 2.** Location of lesions according to the multiple or solitary type.

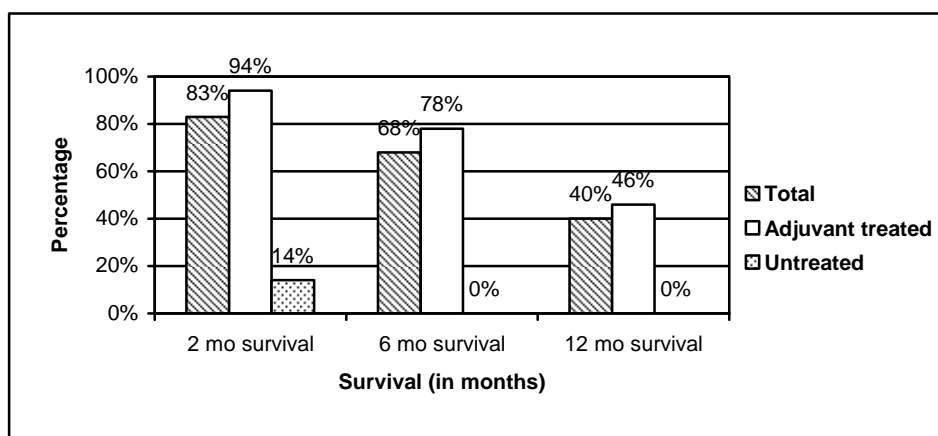


Figure 3. Comparison of the survival in patients who received adjuvant treatment with untreated patients.

vs. 45%, $P < 0.001$). Kuker et al reported that in immunocompetent patients the most common form of involvement was solitary lesions (65%) and most of them were hemispheric and the basal ganglia was the second frequent location.¹⁴ Lanfermann et al reported that 62% of cerebral lymphomas were multiple and the most common location was frontal lobe in both immunocompetent and immunocompromised patients, and periventricular location was found in 83% of cases. Besides, he reported that in different pathologic subtypes of cerebral lymphoma, special locations were more prevalent.¹⁵ In our study, multiple lesions were about two folds more frequent than solitary ones. This correlates well with Lanfermann et al's report, but the major difference is in the location of lesions.

Diencephalon was the most common site of multiple lesions in our study. This may be related to pathologic subtype of tumors, which was not evaluated in our study or due to our study design that only includes stereotactic cases. In an immunocompetent patient, a homogeneously enhanced solitary intra-axial lesion of a non-eloquent area is not necessarily referred for a stereotactic biopsy and the patient may undergo open biopsy. So the number of multiple lesions especially in eloquent areas such as diencephalon was more frequent in our study.

The most frequent enhancing pattern was homogeneous enhancement in both multiple and solitary lesions (63% of all cases), which correlates with other studies such as those reported by Jack et al and Lee et al.^{16, 17} Homogeneous enhancement was more frequent in multiple versus solitary lesions (72% vs. 45%, $P < 0.01$) and ring enhancement was more frequent in solitary versus multiple lesions (31% vs. 5%, $P < 0.001$).

Heterogeneous enhancement had similar frequency in both groups.

History of systemic lymphoma was detected in 10% of our cases. Johnson et al and Liang et al reported similar incidences.^{9, 18}

There were three immunocompromised patients in our study. All of them had the history of immunosuppressive drug consumption.

The median survival for patients who had received adjuvant treatment including radio- and chemotherapy was 12 months compared with 40 days for those who had not received such treatment ($P < 0.001$). In other studies, the median survival after radio- and chemotherapy is reported as 8.5 – 42 months, which correlates with our study.^{19, 20}

Cerebral lymphoma is a rare brain tumor that is slightly more prevalent in females and in the sixth decade of life.^{7, 12} Its most common presenting symptom and sign are headache and paresis. Multiple lesions are more prevalent in periventricular region. Although homogeneous enhancement is the most common type of enhancement in both solitary and multiple lesions, ring enhancement is more frequent in solitary lesions. Finally, survival of patients despite adjuvant treatment is about one year.

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