CYPRUS JOURNAL OF MEDICAL SCIENCES

Original Article

DOI: 10.5152/cjms.2017.189

Primary Central Nervous System Lymphoma in Immunocompetent Patients: A Literature Review and the Experiment

Özben Yalçın[1], Canan Tanık[1], Yalçın Polat[2], Meltem Can[3], Fevziye Kabukçuoğlu[1]

[1]**Department of Pathology, Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Turkey**
[2]**Department of Pathology, Okan University School of Medicine, İstanbul, Turkey**
[3]**Department of Neurosurgery, Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Turkey**

BACKGROUND
Primary santral nervous system (CNS) lymphoma is a rare form of non-Hodgin's lymphoma that develops within the craniospinal axis and causes less than 5% of all primary brain tumors. It is defined as lymphoma developing in the brain, leptomeninges, spinal cord or eyes without evidence of lymphoma outside the CNS. Clinico-histopathological characteristics of eighteen patients with primary CNS lymphoma were examined and followed-up for the treatment and subsequent management in Neurosurgery, and Medical Radiation Oncology.

MATERIALS and METHODS
This study includes all cases of primary CNS lymphoma diagnosed in our Department of Pathology between 2006 and 2009. Age, sex, clinical presentation and laboratory features analysis of the cases were carried out In addition, routine hematoxylin and eosin stains (HδE) and special stains, immunohistochemistry were carried out using CD-45 CD-20, CD-19, CD-3, CD-5, CD-10, MIB-1 and Bcl-6.

RESULTS
Primary central nervous system lymphoma (PCNSL) was mostly observed in the temporal and parietal and parietal region. The mean age of the patients was 57.72, ranging from 33 to 83 years. Females outnumbered males with a ratio of 1.25: 1. The most common symptom observed, was headache which was followed by neuro communicative symptoms. Histologically, all the patients exhibited diffuse B-cell lymphoma. Two patients suffered from multiple lesions. Three of the patients died within 2 years.

CONCLUSION
There is an increase in the prevalence of primary CNS lymphomas not only in immune defiency patients, but also in the immune competent patients and therefore should be taken into account in the differential diagnosis of all tumor of the CNS.

Keywords: Primary santral nervous system lymphoma, immunocompetent, brain tumor

INTRODUCTION

An uncommon type of non-Hodgkin's lymphoma, primary central nervous system lymphoma (PCNSL), is localized in the central nervous system. Most of its lesions are supratentorial and periventricular. Deep structures such as corpus callosum and basal ganglion are mostly involved (1-3). In this study, we analyzed 18 patients with non-Hodgkin's lymphoma in order to assess their clinical features, radiological features, histology, management, and outcome.

MATERIALS and METHODS

This study includes all the cases of primary santral nervous system (CNS) lymphoma diagnosed by our Department of Pathology between 2006 and 2009. Age, sex, clinical presentation, and laboratory features analysis of the cases were conducted. Details regarding lymphadenopathy, organomegaly, and bone marrow were acquired to rule out the possibility of secondary involvement of a systemic lymphoma (Table 1). In addition, routine hematoxylin and eosin (HδE) staining (Figure 1, HδE X10; Figure 2, HδE X20) and special stainings and immunohistochemical analysis were performed using CD-20 (Figure 3, X10; Figure 4, X20) CD-45, CD-19, CD-3, CD-5, GFAP (Figure 5) and antibodies for typing these lymphomas. CD-10, MIB-1, and Bcl-6 were also used for some cases. Eighteen cases of primary CNS lymphoma were diagnosed. All cases were analyzed for imaging features and followed up for management in Neurosurgery, and Radiation and Medical Oncology.

Data from microscopical analysis were expressed as mean±standard error. The statistical analysis was performed by using Statistical Package for Social Sciences version 22 software (IBM Corp.; Armonk, NY, USA).

This study was presented at the 27th European Congress on Pathology, 5-9 September 2015, Belgrade, Serbia.

Corresponding Author: Özben Yalçın
E-mail: ozbena@yahoo.com

Received: 18.11.2016
Accepted: 02.02.2017

TABLE I. Descriptive characteristics distribution

		Min-Max	Mean±SD
AGE		33-83	57.72±14.36
		n	%
Additional diseases	No	12	66.7
	Yes	6	33.3
	Hypertension	3	16.7
	Cardiovascular disease	1	5.6
	Cardiovascular disease, Diabetes mellitus	1	5.6
	Cerebrovascular disease	1	5.6
Complication*	Headache	10	55.6
	Dizziness	3	16.7
	Amnesia	3	16.7
	Loss of consciousness	2	11.1
	Speech impairment	3	16.7
	Hemiparesis/paresis	6	33.3
	Epilepsy	1	5.6
	Central facial paralysis	2	11.1
Localization	Frontal lobe	1	5.6
	Frontal and parietal lobe	2	11.1
	Parietal lobe	3	16.7
	Periventricular	6	33.3
	Posterior fossa	1	5.6
	Supratentorial	3	16.7
	Temporal and parietal lobe	2	11.1
Stereotaxic biopsy		13	72.2
Excision		5	27.8
Radiotherapy	No	9	50.0
	Yes	6	33.3
	Ex	3	16.7
Chemotherapy	No	11	61.1
	Yes	4	22.2
	Ex	3	16.7

*Marked more than one option

Since the study was made from ready-made paraffin embedded blocks and slides in our lab archive, patient consent was not considered necessary.

Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013).

RESULTS

The study was conducted with a total of 18 cases diagnosed between 2006 and 2009. The age range of the patients was 33-83 years (average age was 57.71±14.36 years).

Six cases (33.3%) had additional diseases. Of the 6 cases, 3 had hypertension, one had cardiovascular disease, one had cerebrovascular disease, and one had cardiovascular disease and diabetes mellitus.

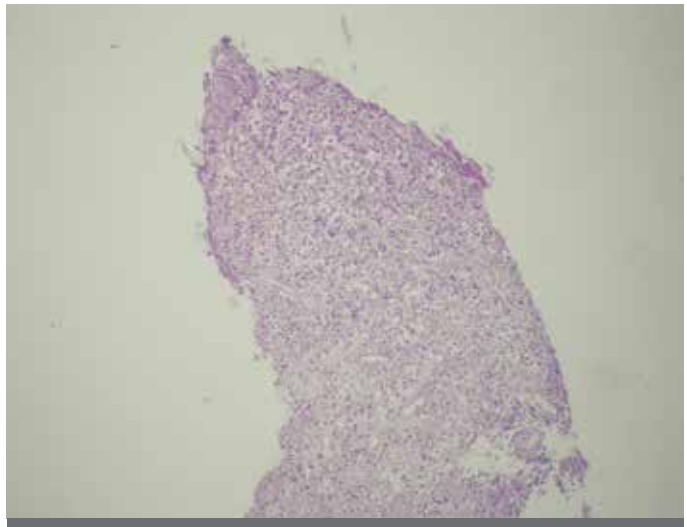

FIGURE I. H&E X10

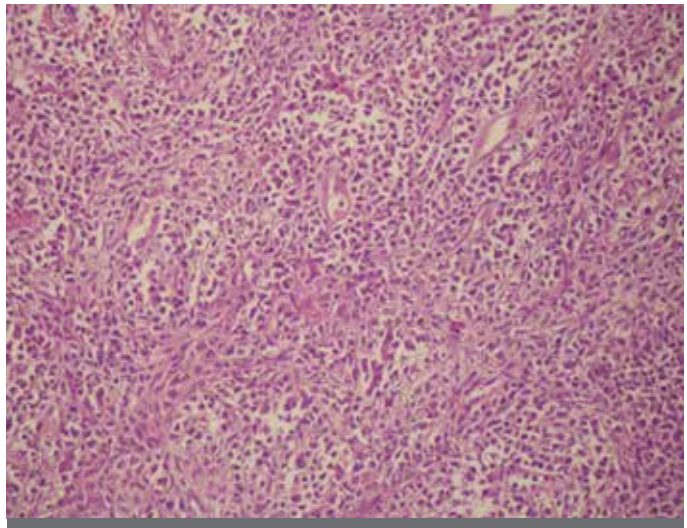

FIGURE 2. H&E X20

The analysis of the clinical symptoms indicated that 55.6% (10) suffered from headache, 16.7% (3) from dizziness, 11.1% (2) from loss of consciousness, 16.7% (3) from speech impediment, 33.3% (6) from hemiparesis/paresis, 5.6% (1) from epilepsy, and 11.1% (2) from central facial paralysis.

The analysis of localizations was conducted in all patients and 5.6% (1) frontal lobe, 11.1% (2) frontal and parietal lobe, 16.7% (3) parietal lobe, 33.3% (6) periventricular, 5.6% (1) posterior fossa, 16.7% (3) supratentorial, and 11.1% (2) temporal and parietal lobe localizations were observed.

Stereotactic biopsy was performed in 13 cases (72.2%) while excision was performed in 5 cases (27.8%). Radiotherapy was applied in 33.3% (6) of the cases, and chemotherapy was applied in 22% (4) of the cases. Death occurred in 16.7% (3) of the cases.

Microscopic features: Histopathology showed that most cases exhibited a monomorphic population of lymphoid cells with

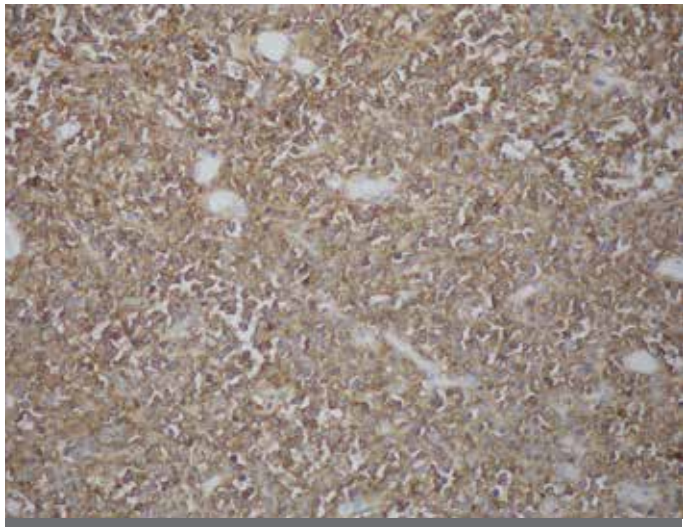

FIGURE 3. X10 (the tumor cells CD-20 positive)

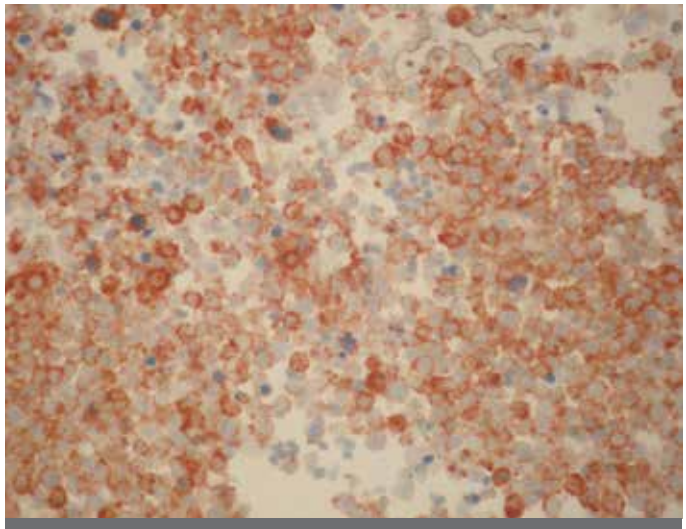

FIGURE 4. X20 (the tumor cells CD-20 positive)

areas of necrosis (Figure 1, 2). Individual cells were large with prominent nuclei.

Immunohistochemical profile: All cases were positive for CD-45, CD-19, and CD-20 (Figure 3).

Adjuvant Therapy

All patients were subjected to radio-chemotherapy after surgical decompression/stereotactic biopsy and histopathological/immunohistochemical diagnosis of lymphoma.

Follow-up was conducted jointly at the Tumor Clinic, which is managed by the Departments of Neurosurgery, Radiation Oncology, and Medical Oncology. Three patients died within 2 years. Four patients could not be followed up.

DISCUSSION

Primary central nervous system lymphoma is an uncommon tumor. The brain is an immunologically exclusive organ in the sense that it does not contain lymphatics or lymphoid tissue. Therefore, the origin of such a primary tumor is unclear. Hochberg et al. (4) argue that the clone of malignant systemic lymphocytes exhibiting distinct adhesion molecules and attaching themselves to certain proteins existing only in the CNS might be the pathogenesis.

FIGURE 5. X10 (the tumor cells GFAP negative)

The origin of PCNSL is quite unclear and therefore, it remains an obscure disease. One of the main risk factors of diseases such as PCNSL could be immunodeficiency-whether congenital or acquired. Farhangi et al. (5) report the case of a 2.5-year-old boy who suffered from autoimmune hemolytic anemia prior to PCNSL.

Studies indicate that there is a connection between Epstein Barr virus (EBV) and PCNSL in patients with HIV infection. However, no studies indicate a relationship between EBV and PCNSL in patients without HIV infection. The nature of the relationship between EBV and human lymphoma, whether it is causal or purely coincidental, remains a moot point (6). However, there has been an increase in the number of immunocompetent patients in the past few decades, and this increase has occurred independent of the developments in the field of neuroimaging or of the general aging of the population (7).

Brain biopsy remains the ideal technique for the diagnosis of PCNSL (8). High grade B-cell lymphomas comprise most of the PCNSL tumors, although a normal brain does not contain B-cells (9). The present case study is in accordance with the research conducted by Abla et al. (1) According to that study, diffuse large B-cell lymphoma (DLBCL) is the most prevalent form, while anaplastic large cell lymphoma (ALCL), lymphoblastic lymphoma, and Burkitt-like lymphoma are forms with lower prevalence. All 18 cases were B-cell lymphomas with positivity for CD-20 and CD-19.

Psychiatric symptoms together with focal neurological deficiencies are one of the several clinical indications that might be detected in PCNSL patients among other things (6). The analysis of the clinical symptoms indicated that 55.6% (10) suffered from headache, 16.7% (3) from dizziness, 11.1% (2) from loss of consciousness, 16.7% (3) from speech impediment, 33.3% (6) from hemiparesis/paresis, 5.6% (1) from epilepsy, and 11.1% (10) from central facial paralysis.

Considering the good response of CNS lymphoma to chemoradiation, PCNSLs are regarded as non-surgical tumors, and it has been reported that there is no use in undertaking resection or decompression since PCNSL exhibits a diffuse infiltration pattern and is mostly observed in deep-seated locations (2).

CONCLUSION

The distinctive features of our study were: primary CNS lymphoma was observed in immunocompetent persons; none of our patients were immunocompromised or HIV positive; and raised ICP features and focal neurological deficits were the most prevalent clinical manifestations.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013).

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - Ö.Y.; Design - Ö.Y.; Supervision - C.T.; Resource - C.T., F.K.; Materials - M.C., F.K., Ö.Y.; Data Collection and/or Processing - Ö.Y.; Analysis and/or Interpretation - M.C., Ö.Y.; Literature Search - Y.P.; Writing - Ö.Y.; Critical Reviews - Ö.Y., Y.P.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Abla O, Weitzman S, Blay JY, O'Neill BP, Abrey LE, Neuwelt E, et al. Primary CNS lymphoma in children and adolescents: a descriptive analysis from the International Primary CNS Lymphoma Collaborative Group (IPCG). Clin Cancer Res 2011; 17: 346-52. [CrossRef]
2. Hsu HI, Lai PH, Tseng HH, Hsu SS. Primary solitary lymphoma of the fourth ventricle. Int J Surg Case Rep 2015; 14: 23-5. [CrossRef]
3. Liao CH, Lin SC, Hung SC, Hsu SP, Ho DM, Shih YH. Primary large B-cell lymphoma of the fourth ventricle. J Clin Neurosci 2014; 21: 180-3. [CrossRef]
4. Hochberg FH, Baehring JM, Hochberg EP. Primary CNS lymphoma. Nat Clin Pract Neurol 2007; 3: 24-35. [CrossRef]
5. Farhangi H, Sharifi N, Ahanchian H, Izanloo A. Autoimmune Hemolytic Anemia preceding the Diagnosis of Primary Central Nervous System Lymphoma. Iran J Ped Hematol Oncol 2015; 5: 65-9.
6. Morgello S. Epstein-Barr and human immunodeficiency viruses in acquired immunodeficiency syndrome-related primary central nervous system lymphoma. Am J Pathol 1992; 141: 441-50.
7. Nakamura M, Shimada K, Ishida E, Konishi N. Histopathology, pathogenesis and molecular genetics in primary central nervous system lymphomas. Histol Histopathol 2004; 19: 211-9.
8. Eichler AF, Batchelor TT. Primary central nervous system lymphoma: presentation, diagnosis and staging. Neurosurg Focus 2006; 21: E15. [CrossRef]
9. Batchelor T, Leoffler JS. Primary CNS lymphoma. J Clin Oncol 2006; 24: 1281-8. [CrossRef]
10. Bataille B, Delwail V, Menet E, Vandermarcq P, Ingrand P, Wager M, et al. Primary intracerebral malignant lymphoma: report of 248 cases. J Neurosurg 2000; 92: 261-6. [CrossRef]