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Primary CNS Lymphoma: An Institutional Study

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Abstract: ***Introduction: Primary central nervous system lymphoma (PCNSL) is a rare group of extra nodal non-Hodgkin's lymphomas. It accounts for 2.4-3% of all brain tumours. Aim & Objectives: To study the clinicopathological & immunohistochemistry profile of patients with PCNSL presented between the years 2010 to 2019 in a tertiary care centre. Materials and Methods: This was a retrospective study. Clinical data were obtained from the hospital clinical case records. All the histopathologically proven cases of PCNSL involving the cerebral parenchyma were considered. All cases were studied in H &E then subjected to immunohistochemistry for LCA, CD20, CD3, GFAP and MIB1.Possibility of secondary involvement by a systemic lymphoma was excluded in every case. Statistical analysis was done by chi square test. Results: There were a total of 41 cases with median age of presentation being 52 years and with a male to female ratio1.15:1. Headache was the most common presenting complaint. All patients were immunocompetent. Frontal lobe was the most common site of involvement. Diffuse large B cell lymphoma (DLBCL) was the histological pattern in all cases. Conclusion: All the patients were immunocompetent, association of PCNSL cases with HIV or acquired immunodeficiency syndrome was not found in our study. DLBCL constituted the majority of PCNSLs.***

Keywords: Primary central nervous system lymphoma, diffuse large B-cell lymphoma, immunophenotyping

1. Introduction

Primary central nervous system lymphoma (PCNSL) are rare form of extranodal Non-Hodgkin's lymphoma presenting in the brain, leptomeninges, eye or spinal cord, without evidence of lymphoma in other parts of body sites. It accounts for 2.4-3% of all brain tumours. In western world, the incidence of PCNSL is 3-4% of all non-Hodgkin's lymphoma (NHLs), [1] whereas in India, the incidence has been reported to range from 0.95 to 1.4%. [2] Although PCNSL has a strong association with acquired immunodeficiency syndrome (AIDS), and human immunodeficiency virus (HIV) infection carries a 3600-fold increase risk of developing the disease compared to general population, [3] recent epidemiologic data suggest a decrease in the incidence of PCNSL, particularly among young patients suffering from AIDS. Amongst immunocompetent patients, a higher incidence is seen in older patients (>60 years). [4] About 60% of all PCNSLs involve the supratentorial space, including the frontal lobe (in 15% cases), temporal lobe (in 8%), parietal lobe (in 7%) and occipital lobe (in 3%), basal ganglia and periventricular brain parenchyma (in 10%), and corpus callosum (in 5%). The posterior fossa and spinal cord are less frequently affected (in 13% and 1% of cases, respectively). [5] A single tumour is encountered in 60-70% of patients, with the remainder presenting with multiple tumours. [5] Extraneural dissemination is very rare. In cases with systemic spread, PCNSL has a propensity to home to the testis, another immunoprivileged organ. [5]

2. Material and Methods

The study was conducted from March 2010 to March 2019 over a 9 year period in the Department of Pathology SCB medical college. This was a retrospective study. Clinical data (age, sex, radiological findings, immune status and HIV serology) findings were recorded from hospital records in every case.

Inclusion criteria: Only lymphomas involving the cerebral parenchyma were included in this study. Cases of PCNSL involving the spinal cord, meninges and the orbit and intravascular large B cell lymphomas with evidence of systemic disease or secondary lymphomas were excluded.

To exclude the possibility of secondary involvement by a systemic lymphoma, details pertaining to lymphadenopathy, organomegaly, and bone marrow study were also obtained.

The neurological tumour tissue was obtained by craniotomy. The study comprised of all the cases of histologically proven PCNSL in our department. It was fixed in 10% neutral buffered formalin 18-24 hrs.It was then fixed & embedded in paraffin wax according to standard protocol. Sections cut at 3-4 microns & stained with routine H & E stain.immunohistochemistry (IHC) with leucocyte common antigen (LCA) (BioGenex Mouse Monoclonal Antibody), CD20 (BioGenex Mouse Monoclonal Antibody) as a B cell marker and CD3 (BioGenex Mouse Monoclonal Antibody)as a T cell marker, GFAP (BioGenex Mouse Monoclonal Antibody) and MIB1 were performed.

3. Results

Table 1: Age and Sex distribution

Age group (in years)	Male	Female	%
0-10	01	00	2.4
11-20	00	01	2.4
21-30	02	01	7.3
31-40	02	03	12.1
41-50	02	08	24.3
51-60	14	03	41.4
61-70	01	03	10.1
Total number of cases	22	19	

A total of 41 cases of PCNSL involving the cerebral parenchyma were identified in the study period. Twenty two cases were males (53.6%) and nineteen cases were

females (46.4%). Median age was 52 years (range 9-73 years) and male to female ratio was 1.15:1. The peak incidence was found in 5th to 6th decade. (Table no.1)

All the patients were immunocompetent. The lesion was solitary in 75% cases and multiple in 25% cases. Frontal lobe was the most common location. HIV serology findings revealed none of the case was positive.

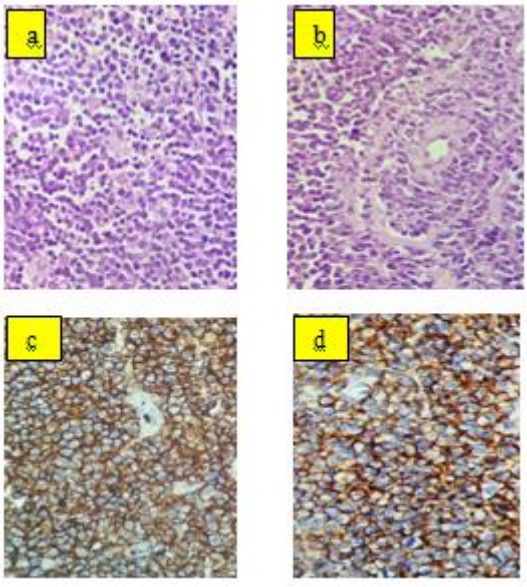
Table 2: Clinical presentation of the patients

Symptoms	Number of cases	Percentage
Increased intracranial tension (headache, nausea and vomiting	35	85.4
Focal neurologic deficit	22	53.6
Neuropsychiatric illness	10	24.3
Seizures	7	17.1
Visual impairment	1	2.4

Eighty five percent patients (35 cases) of the patients presented with symptoms of increased intracranial tension.

Histopathology and IHC findings:

All the cases showed features of NHL in which tumour cells were arranged in diffuse sheet pattern or dispersed pattern. The cells were large having a vesicular nuclei, 1-3 conspicuous nucleoli and moderate amount of pale to eosinophilic cytoplasm. Perivascular arrangement of the tumour cells was observed in the majority of cases. IHC was performed in all cases and the panel comprised of LCA, CD20, CD3, GFAP and MIB1. All the cases were positive for LCA and CD20 and hence classified as diffuse large B cell lymphoma. CD3 positivity was not elicited in any of the case.



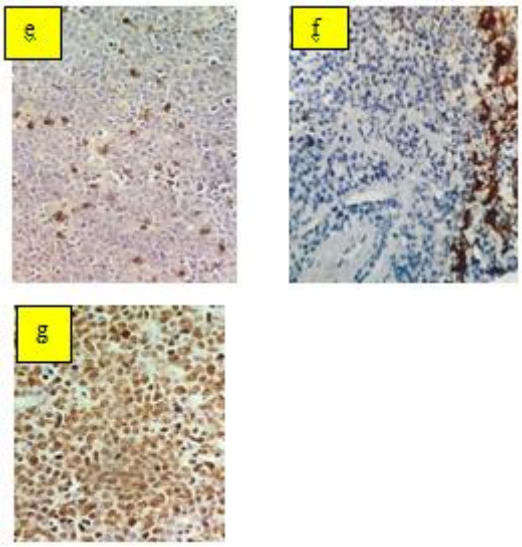


Figure 1 (a) Microphotograph showing dyscohesive tumour cells arranged in diffuse pattern (H&Ex100). (b) Micrograph showing large tumour cells having vesicular nuclei, conspicuous nucleoli and moderate amount of cytoplasm arranged in angiocentric pattern (H&Ex100). (c) Membranous LCA positivity in tumour cells x400. (d)Membranous CD20 positivity in tumour cell x400. (e) CD3 positivity in interspersed reactive lymphocytes. (f) GFAP positivity in interspersed glial tissue x400. (g)MIB1 immunostaining showing nuclear positivity in tumour cells x400.

The proliferation index (MIB1) was high (63-98%) in all cases.

4. Discussion

This study was undertaken to evaluate the clinicopathological profile of patients diagnosed as PCNSL, to determine the frequency of PCNSL among intra-cranial tumours at our institute and to compare the incidence in immunocompetent and immunocompromised people. PCNSLs are highly malignant lymphomas with a median survival of weeks to months if treatment is only symptomatic; however, with anticancer therapy 5-year survival is 31%. [6] High dose methotrexate is the most effective single active agent and a key component of all combination regimens. In the majority of patients, percutaneous fractionated whole-brain radiotherapy leads to fast and usually complete remission; however, recurrences occur early. Median survival is only 12 to 18 months. [7] With combined chemoradiotherapy, tumour control can be significantly improved with median survival times of 31 to 90 months. [8, 9]

In this study male-to-female ratio was 1.15:1 . Median age at presentation was 52 years. Bataille et al [10] analyzed 248 cases of PCNSL in immunocompetent patients and the study involved 121 males and 127 female patients (ratio 0.95:1) and the median age was 61 years (range 2-88years). Fine et al. [11] Analyzed 792 cases of PCNSL in immunocompetent patients and 315 cases of PCNSL in AIDS patients. The median age of patients with and without AIDS, was 30.8 and 55.2 years respectively. The

ratio of male-to-female ratio was 7.38 and 1.35 for the patients with and without AIDS, respectively. In our study frontal lobe as the most common location. Sarkar et al. [12] and Paul et al [13] have also reported frontal lobe as the most common location in their study. Headache was the most common complaint and B Patel et al [14] have reported the same. In this study all the cases were high grade, diffuse large B cell lymphoma which is similar to study conducted by Agarwal et al [15] they showed high grade diffuse large B cell histology in 96.2% of patients. S Pasricha et al [16] found 100 % cases were high grade diffuse large B cell lymphoma. This study also confirmed the rare occurrence of T-cell lymphoma presenting as PCNSL, which has been showed in many studies. However, a study conducted by Choi et al. [17] From Korea reveals an unusual high incidence (16.7%) of T-cell PCNSL. They also reported that T-cell PCNSL presented with certain clinical and pathological features that were distinct from B-cell PCNSL and displayed preponderance of CD8 expression. In our study all cases were immunocompetent with no HIV positive case. Sarkar et al. [13] had one HIV patient and one patient of renal allograft out of total 186 cases. Paul et al. had only one HIV patient out of 56 cases. Agarwal et al. [15] had two HIV positive patients out of 26 reported cases. In fact the frequency of PCNSL in HIV positive patients and in renal transplant recipients in India is very low. Autopsy studies conducted at Mumbai, by Lanjewar et al. [18] Did not report any case of PCNSL among 85 AIDS patients. Hence, in spite of significant number of HIV positive cases (prevalence of 2.4 million cases in 2007) in India, the incidence of PCNSL in these patients is still very low. This could be due to earlier death of AIDS patients due to opportunistic infections. Both Western and Asian literature do not support the association of Epstein-Barr virus (EBV) with PCNSL in immunocompetent individuals, and hence in our study EBV latent membrane protein (LMP) was not assessed by immunohistochemistry.

Table 3: Comparison of clinicopathological features & IHC findings of PCNSL with previous studies

Parameters evaluated	Powari et al [19] PGIMER	Paul et al [13] NIMS	Pasricha et al [16]	Present study
Study duration	15	19	13	09
Total PCNSL	40	56	66	41
Median age (years)	-	56	46	52
Male :female ratio	2:1	1.5:1	1:1	1.15:1
commonest site	Parietal	Frontal	Frontal	Frontal
Cases underwent IHC	31	56	51	41
LCA positive	100%	100%	100%	100%
CD 20 positive (B cell)	90.3%	-	100%	100%
CD 3 positive (T cell)	9.6%	-	00%	00%

5. Conclusion

The PCNSL most commonly affects the middle aged and diffuse large B cell lymphoma is the most common histological pattern. Unlike the western countries, the association of PCNSL with HIV/AIDS in India is very low in spite of substantial prevalence of HIV/AIDS cases.

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