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Primary Central Nervous System Lymphoma: A Clinicopathological and Cytomorpholgical Study from a Tertiary Care Centre

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Abstract:

Aim: To analyze the clinicopathological and immunohistochemical features of primary central nervous system lymphoma (PCNSL) cases occurring in Indian patients and also study the utility of the crush smear preparation in intraoperative diagnosis.

Material & Methods: 40 cases of PCNSL diagnosed in the Department of Histopathology, were included in this study. Haematoxylin and Eosin (H and E) stained slides and immunohistochemistry slides (which included a minimum of Leucocyte common antigen (LCA), CD20 and CD79aof all these cases were retrieved.

Results: The mean age of the patients was 51.4 years and the median was 50 years (range 30-72 years). The male: female ratio in our study is 1:1. Of the 40 cases, one was a known case of sarcoidosis (in remission). The only T-cell lymphoma case in our series had a prior history of treatment for ulcerative colitis (in remission).

Conclusion: Our study shows that PCNSL is seen predominantly in immunocompetent patients in India. The age of presentation is relatively young. Our study also stresses the utility of crush smear preparation in establishing an intraoperative diagnosis.

Keywords: Primary central nervous system lymphoma - brain tumor - immunohistochemistry - intraoperative diagnosis

Introduction:

Primary central nervous system lymphomas (PCNSLs) are a rare form of extranodal non-Hodgkin's lymphoma that typically remain confined primarily to the central nervous system and involve the brain, leptomeninges, spinal cord and eye. [1] Historically, the first reported PCNSL was by Bailey in 1929, [2] when he used the term 'perithelial sarcoma'. Other terms that have been used are perivascular sarcoma, adventitial sarcoma, malignant reticuloendotheliosis, reticulum cell sarcoma, and microglioma. It was much later that PCNSLs were recognized as neoplasia distinct from glial tumors by immuno phenotyping and the lymphoid nature of the lesion was established.

PCNSL is a highly infiltrative neoplasm, and most radiographic imaging pictures are an underestimate of the extent and the burden of the disease. Though PCNSL manifestation is mostly confined to the CNS, dissemination into the intraocular components is quite possible in less than 5% of the cases.[3]While complete surgical resection is remote, chemotherapy and radiation are the only options. [4]

However PCNSL rates have decreased among young adults compared to the elderlybecause of effective therapies for AIDS [5]. At present, primary CNS lymphomas constitutes about 2.2% of all brain tumors in the USA [6]. Studies from Asia and India have revealed certain differences in PCNSL features compared to the West [7-8]. CNS cancers are increasing in India and to understand the etiology of these cancers, in depth, analytic epidemiological studies should be planned in the near future [9]

In the present study we analyze the clinicopathological features of 40 cases of PCNSL and also assess the utility of the crush smear preparation in the intra-operative diagnosis of PCNSL.

Material & Methods:

40 cases of PCNSL diagnosed in the Department of Histopathology, Sawai Man Singh Medical College, Jaipur were included in this study. Haematoxylin and Eosin (H and E) stained slides and immunohistochemistry slides (which included a minimum of Leucocyte common antigen (LCA), CD20, CD79a, CD3, CD43 and Ki-67) of all these cases were retrieved. Immunophenotyping was performed on formalin-fixed paraffin–embedded tissue using the streptavidin biotin conjugate immunoperoxidase method.Intraoperative crush smear preparation was available in 37/40 cases.

The histopathology of each case was reviewed with the H and E slides. The immunohistochemical features and diagnosis of all these cases were also ascertained. The intraoperative diagnosis was recorded and the cytological features of PCNSL in crush smears were studied. The immune status, clinical and radiological details of these cases were obtained from case records. Computed Tomography (CT) scans and Magnetic Resonance Imaging (MRI) were the imaging modalities. Contrast study with CT or MRI was done in 23 cases. MR

spectroscopy was also used in 7 cases. Bone marrow examination was done in24 cases. Biopsy material was obtained by stereotactic biopsy in 30 cases and by surgical excision in 2 cases.

Serological details were not available for five cases. Only Indian patients were included in this study. Patients with systemic NHL and those who showed evidence of extracranial involvement at the time of diagnosis were excluded. Skull-base lymphomas were also excluded in our study. The ethics committee of our Hospital approved this study.

Results:

The mean age of the patients was 51.4 years and the median was 50 years (range 30-72 years). The male: female ratio in our study is 1:1 [Table 1]. Of the 40 cases, one was a known case of sarcoidosis (in remission). The only T-cell lymphoma case in our series had a prior history of treatment for ulcerative colitis (in remission).

Histopathological features: Histopathology showed sheets of medium to large sized lymphoid cells (Figure 1). Their nuclei showed clumped chromatin and prominent nucleoli. Numerous mitoses including atypical forms were evident in almost all the cases. The angio-centric pattern was observed in 46% cases. Necrosis and reactive gliosis were observed in 16% and 38% cases respectively. The cytological features of the tumor cells were better appreciated in crush smears.

The cytological features in crush –smear preparation: The majority of the smears showed moderate to marked cellularity (Figure 2). At higher magnification, the tumor cells showed ill-defined scant cytoplasm, round nuclei with coarse chromatin and 1-3 prominent nucleoli. In almost all the cases, some of the tumor cells showed nuclear indentation and convoluted nuclear borders. Lymphoglandular bodies and apoptotic bodies possessing condensed chromatin were seen in almost all the smears. Mitoses were easily identified (at least 1/10 HPF) in majority of the cases.

Table 1. Characteristics of 32 PCNSL Patients at Diagnosis

		No.	%
Sex	Male	25	62.5
	Female	15	37.5
Age (in Years)	>65	4	10
	45-65	30	75
	<45	6	15
Localization	Monofocal	33	82.5
	Multifocal	7	17.5
Nature of involvement	Unilateral	28	70
	Bilateral	12	30
Site of involvement	Supratentorial	36	90
	Supra- and Infratentorial	4	10

Figure 1. Histopathological Picture of a PCNSL (H&E× 400)

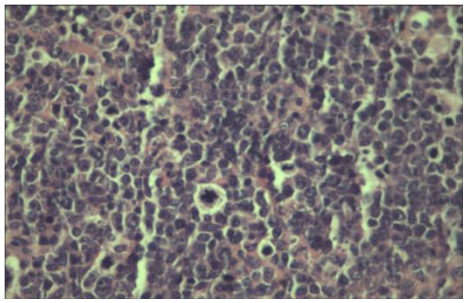
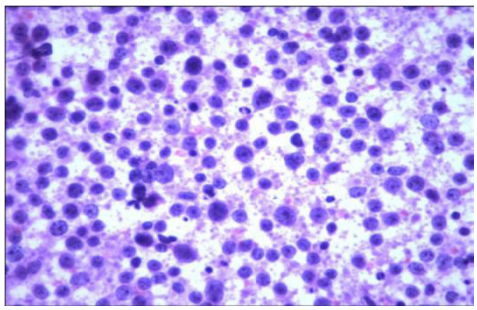


Figure 2. Smear Illustrating Monolayered Discohesive Sheets of Lymphoma Cells with Scant Cytoplasm and Round Nuclei with Prominent Nucleoli (Rapid H&E×400)



Discussion:

Primary CNS lymphomas constitute about 2.2% of all brain tumors. The incidence of PCNSL has markedly increased world-wide: from 0.8–1.5% up to 6.6% of primary intracranial neoplasms, mainly as a consequence of the AIDS epidemic .Our study shows that PCNSL are also seen predominantly in immunocompetent individuals and hence the possibility of PCNSL should be kept in mind when dealing with a intracranial neoplasm in an immunocompetent individual. Study done by Ambroise MM et al also revealed the incidence of PCNSL among immunocompetent individuals. [7]

The most common age group encountered in our study was 6th decade which is in concordance with the common age group of PCNSL quoted in the literature. Most of our patients presented with lesions in the cerebral hemispheres (50%). Corpus callosum lesions were seen in 40% of the cases which is much higher than quoted by Dolocek TA (5%).[10]A study done by Batallie B et al showed that 66% of the lesions were solitary and 87% of them were supratentorial.[11]

In a previous study of non –AIDS associated PCNSL, 5% of patients had received immunosuppressive medications for medical conditions like ulcerative colitis, renal transplantation, rheumatoid arthritis and Wegener granulomatosis [12].

The clinical presentation of immunocompetent PCNSL patients includes focal deficits, neuropsychiatric symptoms, headache, nausea, vomiting suggestive of raised intracranial

pressure, seizures and ocular symptom. Patients with AIDS related PCNSL are more likely to present with mental status changes or seizures [13].

Of the 40 PCNSLs, 39 were diffuse large cell lymphomas and one was reported as lymphoblastic. Virtually all PCNSLs show a diffuse growth pattern. A follicular growth pattern has not been described in intraparenchymal lesions. There have been occasional case reports of follicular lymphomas of the dura. [14-15] These lesions have a less aggressive behavior and survive longer than the usual intraparenchymal PCNSLs.

Steroids are generally withheld till the diagnostic procedure in suspected cases of PCNSL. Previous reports have shown that apart from their therapeutic anti-edematous effects, they can cause rapid lympho depletion .They can also produce reactive gliosis with a variable infiltration of B- or T lymphocytes and macrophages, thus obscuring the diagnosis in some cases [16-18]. However a recent study at the Mayo clinic showed that corticosteroid administration before biopsy did not significantly affect the histopathological diagnosis of PCNSL cases [19].

Conclusion:

Our study shows that PCNSL is seen predominantly in immunocompetent patients in India .The age of presentation is relatively young. Our study also stresses the utility of crush smear preparation in establishing an intraoperative diagnosis.

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