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Original Research Article

Immuno histochemical profile of primary central nervous system lymphoma (PCNSL): A case series

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ABSTRACT

Introduction: The extra nodal Non Hodgkin Lymphoma manifests in central nervous system as Primary Central Nervous System Lymphoma (PCNSL) and is often co-existent with HIV AIDS and other immunocompromised states. However, it has been gradually rising among the immunocompetent individuals. As a highly infiltrative neoplasm, histopathological diagnosis is definitive. This study was done to explore the Immuno Histochemical Profile in PCNSL.

Materials and Methods: This study was done as a case series by reviewing the specimens of 16 patients with PCNSL who underwent treatment in the tertiary care centre for three years between 2010 and 2013. After viewing H & E sections, slides were coated with chrome alum, and then treated by HRP (Horse radish peroxidase) polymer technique.

Results: The mean age of the participants was 58.2 years. In three participants, the HIV status was not known and the rest of the participants were HIV negative. Immunohistochemically the cells were positive for LCA & CD 20, hence favouring the diagnosis of Non Hodgkins lymphoma B cell type.

Conclusion: Our study clearly elucidates the alarming trend in the incidence of PCNSL among immunocompetent individuals. Moreover, the role of Ki-67 labelling and the definitive diagnosis by immunohistochemical staining have been well established.

1. Introduction

Primary central nervous system lymphoma (PCNSL) is a form of extra-nodal Non-Hodgkin Lymphoma (NHL), confined to the central nervous system (CNS) in absence of systemic disease. It constitutes 3% of all the brain tumors and 2-3% of all NHLs.[1] The incidence of PCNSL has markedly increa sed world-wide, from 0.8–1.5% to 6.6% of primary intracranial neoplasms, and most of them are diffuse large B cell Type. It has been well documented that PCNSL is an AIDS defining illness associated with low CD4 counts. Congenital immunodeficiency states and Post Transplant Lymphoproliferative Disroder (PTLD) with CNS manifestations are other common etiologies. In the same lines, the prognosis of PCNSL is also poor. However, the median survival among non-AIDS patients is far higher (18.9 months) compared to the those with AIDS (2.6 months).[2]

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]

The key histological feature of PCNSL is angiotropism or angiocentricity, which is characterized by the accumulation of lymphoma cells around small and medium blood vessels. However, PCNSL manifests as a single mass with vasogenic edema and mass effect. The histochemical diagnosis of PCNSL was done by Hans et al in 2004 using the combined immunohistochemical staining panel of CD10, Bcl-6, and MUM1 to categorize into two prognostic categories namely germinal center subtype and the non

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germinal center subtype.[5] However, there are few studies to evaluate the proliferative activity using the Ki-67 antibody. Therefore, this study was carried out as a case series to explore the immunohistochemical features of PCNSL.

2. Objective

To review the clinico-pathological and immune-histochemical features of primary central nervous system lymphomas (PCNSL).

3. Materials and Methods

Study Design: Case series

Study area: This study was carried out in the histopathology department of our tertiary care centre, Chennai.

Study population: The study was done among patients diagnosed with primary central nervous system lymphomas (PCNL) visiting the outpatient department of our tertiary care centre.

Study period: The study was carried out for three years between 2010 and 2013.

Sample size and sampling: All the patients who were diagnosed with PCNL during the study period were included in the study. A total of 16 surgical specimens of PCNL were reviewed.

3.1. Data collection tools

Cases for Immuno Histo Chemistry were selected after viewing the H &E sections. Slides were coated with chrome alum, and subjected to Antigen Retrieval using the Microwave technique with Citrate buffer solution. Slides were then treated by HRP (Horse radish peroxidase) polymer technique.

3.2. HRP polymer technique

The coated slides were taken through the following steps

1. Treatment with peroxidase block – for incubation of endogenous peroxidase in the tissue for 20 minutes, washed in PBS buffer for 5 mts.
2. Applications of power block O- to block non specific antigen – antibody reactions for 20 minutes. The excess power block was blot dried.
3. Applications of Primary antibody – Murine antibodies for 60 minutes. Washed in PBS buffer for 5 minutes.
4. Application of super enhancer for 30 minutes which increased the sensitivity of antigen -antibody reaction thereby enhancing the final reaction product.
5. Application of SS label – Secondary antibody from goat with the tagged horse radish peroxidase enzyme for 30 minutes. Washed in TRIS buffer.
6. Application of DAB (Diaminobenzidine) Chromogen for 5 minutes – which was cleared by the enzyme to give the colored product at antigen sites. Washed in distilled water for 5 minutes.

The slides were then counter stained with hematoxylin .Slides were air dried and mounted with DPX (Dibutylphalate Xylene)

The following markers were done: CD45, CD3, CD20, and GFAP were done on most cases. Other markers like CD99, Cytokeratin, S-100, Synaptophysin and Chromogranin were done in cases when needed.

Operational Definition The preliminary diagnosis of PCNL was made with MRI. MRI in most of the participants showed isointense to hyperintense images on T2, fluid inversion recovery or diffusion weighted images MRI images, densely enhancing on post-contrast images.

Ethical Approval Approval from institutional ethics committee was obtained prior to the commencement of data collection. Each participant was explained in detail about the study and informed consent was obtained prior to the data collection.

4. Results

A total of 16 surgical specimens of Primary Central Nervous System Lymphomas (PCNSL) studied. The mean age of the participants was 58.2 years. About 12(75%) were males. The most common clinical features were symptoms of raised intra-cranial tension, mental status changes, focal neurological deficits, seizures and ocular symptoms. Except in three patients in whom HIV status was not done the remaining all were HIV Negative. The age-wise distribution of the study participants is shown in Figure 1.

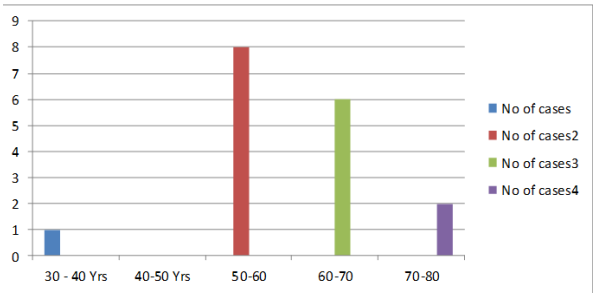

Fig. 1: Age wise distribution of the study participants

Histopathology showed sheets of medium to large sized lymphoid cells. Their nuclei had clumped chromatin and prominent nucleoli. Numerous mitoses including atypical forms were present. The angio -centric pattern was also observed. Immunohistochemically the cells were positive for LCA & CD 20, hence favoring the diagnosis of Non Hodgkins lymphoma B cell type. The site of PCNL is shown inFigure 2. In a majority (50%) of the participants, the PCNL was located in cerebral hemisphere, while in 38% of the participants, it was located in corpus callosum.

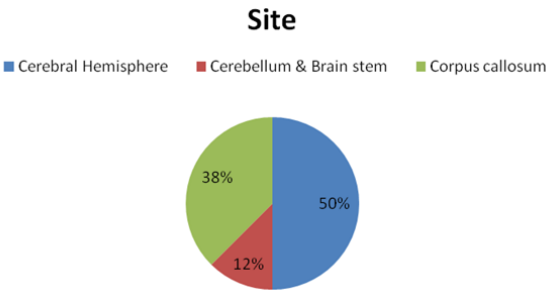

Fig. 2: Site of the PCNL

The immunohistochemical sections are given from Figures 3, 4, 5, 6, 7, 8, 9, 10 and 11.

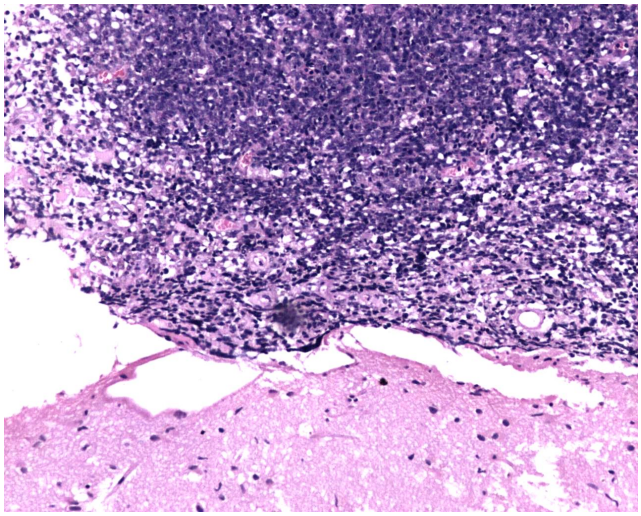

Fig. 3: Glial tissue with adjacent lesion composed of sheets of small round blue cells

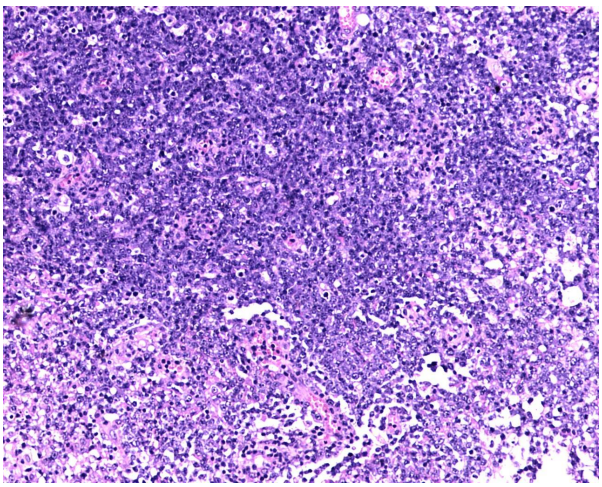

Fig. 4: Monographic small round cells

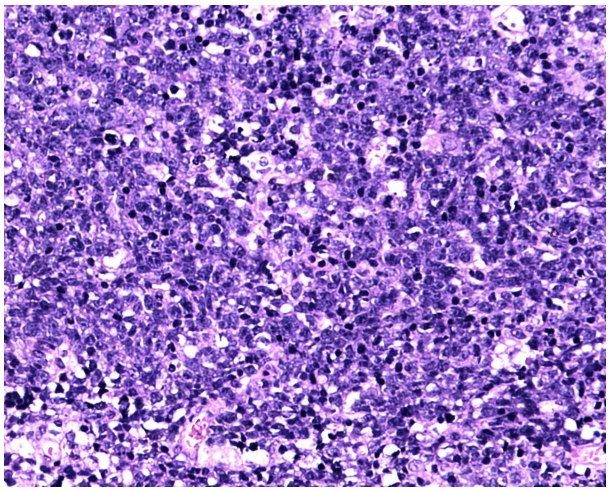

Fig. 5: Monographic small round blue cells

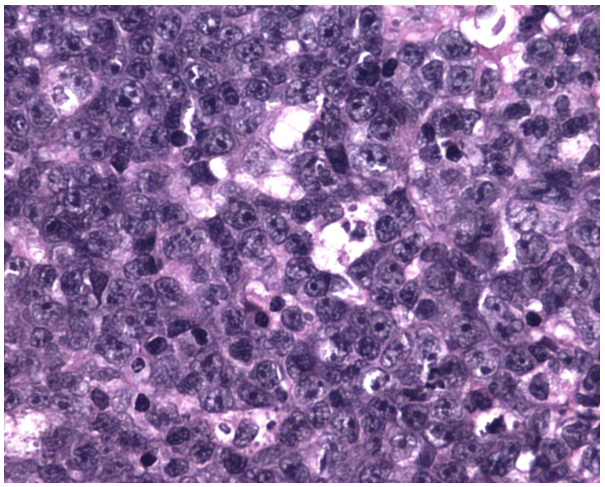

Fig. 6: Monographic cells showing coarse chromatin with prominent nucleoli

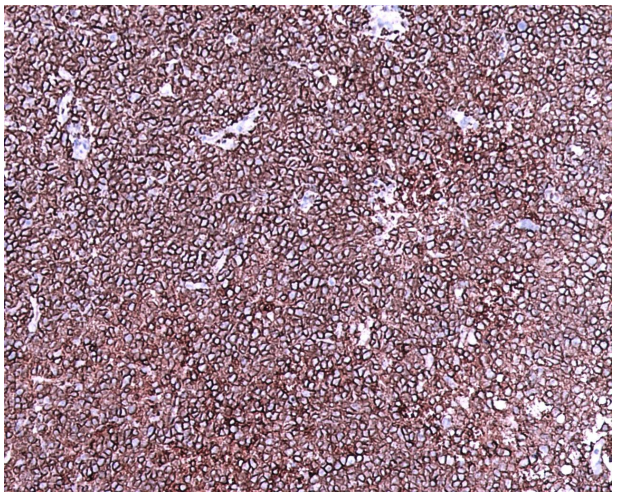

Fig. 7: CD-20 positivity

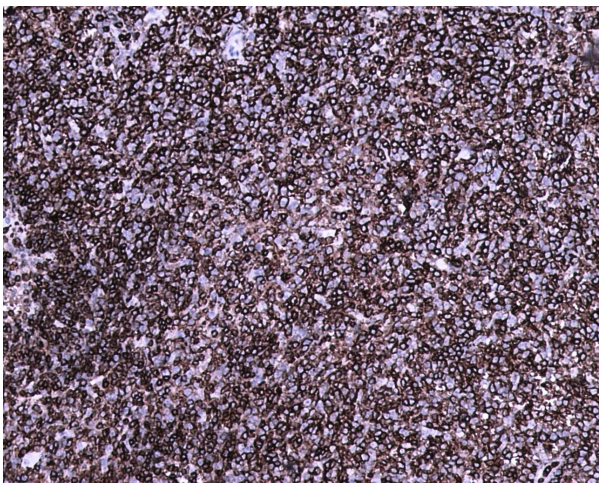

Fig. 8: CD 45 positivity

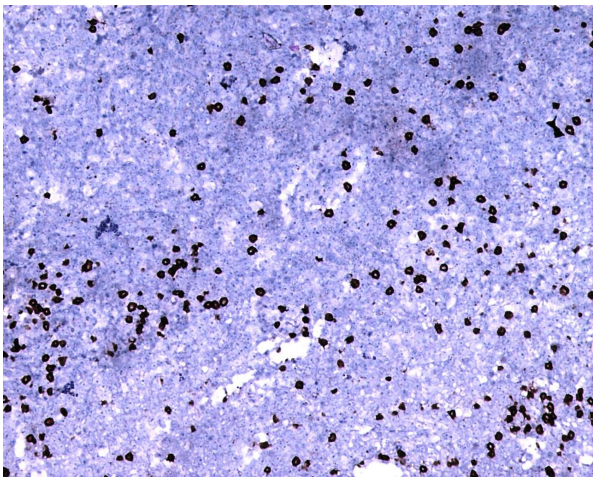

Fig. 9: CD3 focal positivity

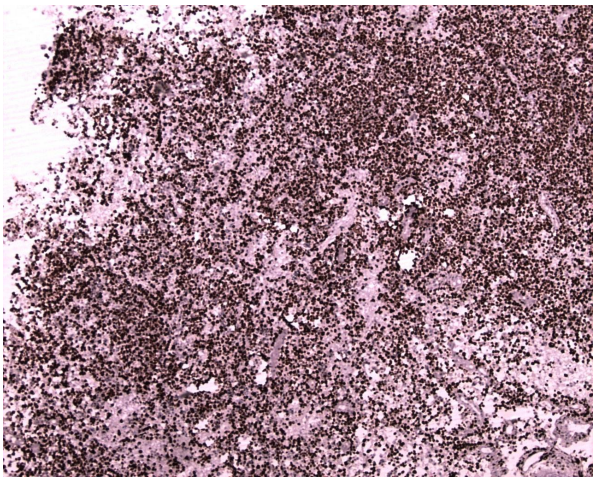

Fig. 10: High Ki labeling index

Fig. 11: Retic 2

5. Discussion

Primary CNS lymphomas constitute about 2.2% of all brain tumours. 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.[6]

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%).[7] A study done by Batallie B et al showed that 66% of the lesions were solitary and 87% of them were supratentorial.[8] In our study, MRI typically showed lesions which were hyperintense on T2 weighed images. The incidence of PCNSL is high in AIDS patients. However in our study none of the patients were associated with AIDS. All the cases seen were Diffuse Large B cell Lymphomas. The ki — 67 labelling index was more than 60%.

In a study done be Aki et al, the cells showed perivascular accumulation, and all the cases were positive for CD-10 and Bcl-6 immunostaining, similar to our study.[9] Similarly, Ambroise el al also showed periventricular location in 62.5% of the cases.[6] In a study done by Shagufta T Mufti et al, all the patients showed diffuse and strong positivity for CD 45 and CD 20. Moreover, 93.3% of the patients were immunocompetent .[10]

6. Conclusion

Our study clearly elucidates the alarming trend in the incidence of PCNSL among immunocompetent individuals. Moreover, the role of Ki-67 labelling and the definitive diagnosis by immunohistochemical staining have been well established. Our study emphasizes on the need for immuohistochemical staining as a confirmatory tool for not only the diagnosis of PCNSL but also a prognostic marker.

7. Conflict of interest

None.

8. Source of Funding

None.

9. Ethical approval

Obtained.

Conceptualization: PDE, Data curation: SfB, Formal analysis: GAV, Funding acquisition: PDE, Investigation: GAV, Methodology: PDE, Project administration PDE on: GAV, Resources: SB, Software: PDE, Supervision: GAV, Validation: PDE, Visualization: GAV, Writing original, draft: SB, Writing Reviewing and editing: GAV.

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